Abstracts from the XIth World DOHaD Congress

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Acknowledgement of Country

This Congress was held on the traditional lands of the Wurundjeri people of the Kulin nation. We pay our respects to Wurundjeri elders; past, present and emerging and thank them for allowing us to have our gathering on these lands.

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Welcome from Congress Chair

Dear Colleagues,

It is a great pleasure to welcome you to Melbourne for the 11th World Congress on the Developmental Origins of Health and Disease (DOHaD) 2019.

The title for the Congress is *Investing in a healthy future for all – Research, Education and Policy*. The Congress will feature the latest findings of the biomedical underpinnings of DOHaD phenomena, new insights into educating populations about DOHaD, and latest findings from intervention studies around the world.

In developing the Congress scientific program, we were tasked by the International DOHaD Society to introduce new ideas and topics and feature new speakers at the Melbourne Congress. You will see that the Congress focuses strongly on DOHaD and Indigenous populations, environmental pollutants and DOHaD, maternal stress and impacts on child mental health, the role of the microbiome in DOHaD, the long-term consequences of pre-term birth and design and delivery of complex interventions. At the same time the Congress continues to feature many of the keystone topics of our discipline.

The 2019 Melbourne Congress features many firsts. These include the first ever Public Engagement Event at a DOHaD Congress, a Trainee Awards Session featuring six of the best Trainee Abstracts, and an extensive Trainee/ECR Program. The Program also features three Satellite Meetings, nine Plenary presentations, nine Workshops, 36 Symposia and more than 750 posters. Most sessions will be co-chaired by a senior delegate and a trainee/ECR. More than 900 delegates from more than 50 countries will attend.

I would like to thank all members of the various committees that worked so hard to organise this meeting. And thanks also to members of DOHaD Council, DOHaD ANZ Council, our sponsors and Corporate Communique (Professional Conference Organiser), without whose assistance this meeting would not have been possible.

We trust that you enjoy DOHaD 2019, catch up with friends and collaborators, form new collaborations, and enjoy your time in our remarkable multicultural city and country.

On behalf of the Local Organising Committee,

Prof John Bertram

Chair, DOHaD World Congress 2019

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Message from President DOHaD Australia and New Zealand

FORWARD BY THE ANZ DOHaD PRESIDENT

As the President of DOHaD ANZ, it is incredibly exciting to be hosting the 2019 DOHaD World Congress. It has been 12 years since Australasia first hosted the DOHaD World Congress in Perth in 2007, chaired by Professor John Newnham, so a return 'Down Under' was definitely overdue!

DOHaD ANZ was established in 2014, led by Professor Susan Prescott, who was also the founding President. Since then, five annual DOHaD ANZ meetings have been held to date, in Perth, Melbourne, Adelaide, Canberra and Sydney, with del-egate numbers ranging from approximately 110 to 200.

A lot has happened in the world of DOHaD since 2007. While the challenges of 12 years ago, including the burden of obesity and chronic disease, long-term consequences of being born small and the intergenerational cycles of poor health, are still well and truly with us, new challenges have emerged. Environmental toxins and pollutants (including air pollution), the impacts of climate change, increasing recognition of intergenerational cycles of adversity and the double-burden of overnutrition and malnutrition faced by both developed and developing countries world-wide, to name just a few – and the organising committee of the 2019 Congress has worked hard to ensure that these areas are well represented in the program.

Significant traction has been gained in raising awareness of the importance of 'the first 1000 days' among international health agencies over the past 12 years. In addition, there is growing recognition of the need to educate our children and adolescents, and to empower them to affect change in their communities. Sharing the work that has already been done in this area and emphasising the critical role of education in breaking intergenerational cycles of poor physical and mental health, will be a key feature of the 2019 Congress.

As Lucilla Poston also indicates, the DOHaD World Congress is more than a scientific meeting – it is an opportunity for researchers, educators, policy makers and health professionals from across the globe to come together with the shared purpose of working towards improving the health of future generations.

On behalf of the ANZ DOHaD Society, we look forward to welcoming delegates from around the world, near and far, to the beautiful city of Melbourne, to share in 4 days of wonderful science, robust and meaningful discussions, together with the opportunity to network with others with a shared purpose, over some great Aussie food and beverages!

With very best wishes,

Bev Muhlhausler

President, ANZ DOHaD Society

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Message from the President DOHaD International

The abstracts in this special issue of *J DOHaD* reflect an enormous breadth and depth of research, much of it wonderfully new, exciting and ground breaking. Many congratulations to all who have contributed, not forgetting the many back home who have not been able to make it to the Congress, but who have helped in so many ways towards the team effort.

Melbourne DOHaD 2019 brings together a unique community of researchers, from disparate countries and settings, with different skills and backgrounds, but united in the belief that the burden of global disease, from hypertension to cancer, can be diminished by focussing on early life health. Working as a community we are producing the compelling evidence base that is gradually changing the way the world thinks; we no longer have to explain what we mean by the 'life course' of health and disease. Just two words, but how important they have become!

We should think therefore of this meeting as a Summit, from which we as ambassadors disperse and disseminate what is important and new in the field, influencing those who make those critically important decisions in public health and medicine.

DOHaD has come a long way since the 1990's when it was known as the DOHaD 'hypothesis'! Never has it been more applicable as we face so many global challenges including obesity, pollution, climate change and the ever-present poverty and conflict. The DOHaD Society and membership has a key role to play in each of these. It is an especially exciting time for those young investigators entering the field.

The Society provides this exciting opportunity to learn, communicate and collaborate. We as a Society want to support its membership in every way we can; please let us know how we can best do this for you.

Lucilla Poston

President, DOHaD Society.

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Organising Committees

Congress Chair
Prof John Bertram, Monash University, Australia

Local Organising Committee
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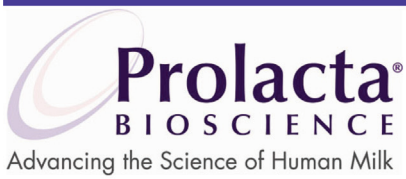

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AWARDS

David Barker Medal

The David Barker Medal is the DOHaD Society's highest honour, awarded every two years to a scientist who has made an outstanding contribution to the scientific development and broader leadership of the DOHaD field.

Recipient of the 2019 award: Prof Kent Thornburg, Oregon Health Science University, USA

Professor Kent L. Thornburg, PhD, is the M. Lowell Edwards Chair of Cardiovascular Research, Professor of Medicine, in the Knight Cardiovascular Institute at Oregon Health & Science University. He holds joint professorships in the Departments of Physiology & Pharmacology, Biomedical Engineering and Obstetrics & Gynecology. He directs the Center for Developmental Health in the Knight Cardiovascular Institute and the OHSU Bob and Charlee Moore Institute for Nutrition & Wellness. He has expertise in cardiac and pulmonary physiology, placentology, and developmental programming. He studies the physiological adaptations to pregnancy and the roles of maternal diet and body composition in regulating placental and fetal growth and lifelong health. He collaborates with scientists in England, New Zealand, Switzerland, Finland, Australia and India. He oversees clinical studies on pregnancy in rural Oregon and Alaska.

Professor Thornburg trained in developmental physiology, placentology and heart development in zoology at Oregon State University for the Master of Science and Doctor of Philosophy degrees. He studied cardiovascular physiology at OHSU as an NIH Fellow. He then completed studies at Washington University and the University of Oregon in electron microscopy and physics.

Professor Thornburg is an elected fellow of the American Physiological Society and has served as Editor of the international journal, *Placenta*, as consulting editor for *Pediatric Research*; he currently sits on the editorial board of the *American Journal of Physiology*. He serves regularly on advisory panels at the National Institutes of Health, the American Heart Association and the Children's Heart Foundation and serves on the scientific advisory board of the Preeclampsia Foundation. He has been regularly involved as director of T32 research training for the Knight Cardiovascular Institute and has held grants from four institutes at NIH. He recently co-chaired the task force to determine the 10-year vision of the developmental origins of health and disease for the National Institute of Child Health and Human Development.

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Nick Hales Award

This award, in memory of the late Professor Nick Hales, and also given every two years, is for a young and emerging investigator who is a DOHaD member and has made an outstanding scientific contribution to the DOHaD field.

Recipient of the 2019 award: Associate Professor Gabriela Conti, University College London, United Kingdom

Associate Professor Gabriela Conti holds a PhD in Economics from the University of Essex and is an Associate Professor in Economics in the Department of Economics and in the Department of Social Science at University College London; co-Investigator of the National Child Development Study (1958 British Birth Cohort); and Research Fellow at the Institute for Fiscal Studies and at IZA Bonn.

Prof Conti's research areas of interest are health economics, the economics of human development, and biology and economics. Her research draws on both the biomedical and the social sciences with the aim of understanding the developmental origins of health inequalities, the role of child development as input in the production of lifecycle health and the behavioral and biological pathways through which early life shocks and policies affect well-being throughout the lifecourse. Prof Conti has published on this topic in *Science*, *PNAS*, *Pediatrics*, the *Economic Journal*, the *Journal of Econometrics* and *Lancet*. Her research has been supported among others by the *NIH, H2020, Nuffield Foundation, Health Foundation, British Academy* and been mentioned among others in the *New York Times, Financial Times, The Times, The Guardian, The Wall Street Journal*, and discussed in the British Parliament. Prof Conti is PI of a 5-year *ERC Consolidator Award* from the European Research Council (SH1 Economics Panel) for her project "The Developmental Origins of Health: Biology, Shocks, Investments, and Policies".

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President's Trainee Awards

Dr Elie Antoun PhD

Elie Antoun is a research fellow based in the academic unit of Human Development and Health at the University of Southampton.

Elie graduated from the University of Southampton with an MBiolSci (Honours) in Biomedical Sciences and in 2018 received his PhD in Human Development and Health from the University of Southampton under the supervision of Professors Karen Lillycrop and Keith Godfrey.

Elie is involved in a variety of projects with the aim of understanding the molecular and epigenetics processes that contribute to disease over the lifecourse. His work currently focuses on understanding the molecular and epigenetic basis of sarcopenia and investigating therapeutics to treat sarcopenia, as well as understanding the effect of maternal GDM exposure on the infant in later life, and what role epigenetic processes play in these processes.

He has extensive experience in cellular and molecular biology as well as bioinformatics experience.

Ms Marcena Lepaz Rivera

Macarena graduated as a Medical Technologist, internationally certified by the ASCP and MSc in clinical biochemistry from the University of Chile. She is currently a PhD student in Medical Sciences at the Pontificia Universidad Católica de Chile (PUC), which has awarded her a PhD scholarship due to her academic merits. She has developed and academic career as a lecturer in clinical biochemistry and developed important methods in teaching innovation.

Her current research interest is to elucidate the molecular mechanisms by which maternal metabolic conditions can increase their offspring's risk of developing chronic diseases, particularly obesity and allergy. She is currently studying, the effects of pre-gestational obesity on the offspring's innate immune cell response and whether maternal DHA supplementation during pregnancy can reverse the inflammatory markers in freshly isolated cord monocytes, the DNA methylation hallmarks of this intervention and the in vitro effects of DHA in these cells.

Dr Maria C. Magnus

Maria C. Magnus was born in Lillehammer, Norway, and she studied nursing at Lovisenberg University in Oslo before moving to New Orleans to acquire a Master of Public Health from Tulane University.

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After finishing her masters in 2010, she moved back to Norway to study for a PhD at the University of Oslo. She is now an early career researcher at the Centre for Fertility and Health at the Norwegian Institute of Public Health. Her research focuses on the long-term health consequences of infertility and use of assisted reproductive technologies for both the parents and the offspring. Other active areas of research include risk factors for early pregnancy loss, genetic determinants of infertility and the relationship between female reproductive health and risk of cardiovascular disease.

Ms Siobhan Tu'akoi

Siobhan Tu'akoi is a final year PhD student from the Liggins Institute, University of Auckland in New Zealand.

Her current research explores the relevance of the DOHaD concept for the Cook Islands, a small Pacific Island where non-communicable disease rates are high but early-life influences on later health have not yet been researched. In partnership with the Cook Islands Ministries of Health and Education, Siobhan's doctoral research explores the relationship between early-life factors and later metabolic health in adolescence over three years.

She has also worked in partnership with local leaders, health professionals and the wider community to create a culturally-contextualised resource focused on early-life nutrition that aims to educate and empower Cook Island families towards healthier futures. She hopes to contribute to improving health outcomes for all Pacific Islanders and future generations to come.

Dr Rongbin Xu

Dr Rongbin Xu obtained his Masters of Medicine then Bachelor of Medicine and Bachelor of Economics from the School of Public Health, Peking University, China.

His research focuses on adolescent health, specifically childhood myopia and obesity, the health impacts of puberty development, and socioeconomic determinants of adolescent health.

Dr Xu has contributed to one original article on JAMA Paediatrics as the co-first author, and three original articles on The Lancet Diabetes & Endocrinology, Traffic injury prevention, Public health nutrition as a co-author.

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Pre-Meeting Workshops - Sunday October 19

Bringing Scientists and Stakeholders Together: Knowledge Translation Strategies, and Skills to Build Engagement
Organisers: Prof Mary Barker, Dr Wendy Lawrence, Prof Jacquie Bay, A/Prof Jeff Craig & Prof Karen Campbell
Speaker List:
- Dr Deborah M Sloboda, McMaster University, Canada
- Prof Mark Hanson, University of Southampton, United Kingdom
- Dr Kathryn Woods-Townsend, University of Southampton, United Kingdom
- Dr Wendy Lawrence, University of Southampton, United Kingdom
- A/Prof Jeff Craig, MCRI, Australia
- A/Prof Jacqui Bay, Auckland University, New Zealand

Gestational Metabolic Disorders: Impact of Maternal Interventions on Off-Spring Cardiometabolic Health
Organisers: Prof Catherine Williamson, A/Prof Bas va Rijn, Prof Rebecca Painter
Speaker List:
- Dr Wing Tam, Hong Kong
- Prof Jane Harding, University of Auckland, NZ
- Prof Louise Maple-Brown, Menzies School of Health Research, Australia
- Prof Lucilla Poston, Kings College London, UK
- Prof Tessa Roseboom, Univeristy of Amsterdam, Netherlands
- Prof Eline van der Beek, University of Groningen/Danone Nutricia Research, Netherlands
- Prof Sue Ozanne, University Cambridge, UK
- Prof Karen Lillycrop, University of Southampton, UK
- Dr Felino Cagampang, University of Southampton, UK
- Prof Matt Gillman, Harvard T.H. Chan School of Public Health, USA
- Dr Janet Rowan, University of Auckland, NZ
- Prof Catherine Williamson, Kings College London, UK
- A/Prof Bas van Rijn, Utrecht University, Netherlands

Harmonising and Combining Cohorts in DOHaD Research
Organiser: Prof Rae-Chi Huang
Speaker List:
- Prof Vincent Jaddoe, Erasmus MC, Netherlands
- Prof Keith Godfrey, University of Southampton, UK
- Prof Mark Hanson, University of Southampton, UK
- Prof Melissa Wake, Murdoch Children's Research Institute, Australia
- A/Prof Rae-Chi Huang, University of Western Australia and Telethon Kids Institute, Australia
- Dr Angela Pinot de Moira, University of Copenhagen, Denmark
- Prof Karen Lillycrop, University of Southampton, UK
- Dr Romy Gaillard, Erasmus MC, Netherlands
- Dr Sylvain Sebert, University of Oulu, NFBC and Dyna Health, Finland
- Dr Will Siero, Murdoch Children's Research Institute and University of Melbourne, Australia

Complex Interventions and Study Designs: Moving DOHaD Forward
Organisers: Prof Shane Norris, Dr Kalyanaraman Kuymaran
Speaker List:
- Dr Nigel Rollins, WHO, Switzerland
- Dr Stephen Lye, Lunenfeld-Tanenbaum Research Institute, Canada
- Prof Shane Norris, University of the Witwatersrand, South Africa
- Prof Linda Richter, University of the Witwatersrand, South Africa
- Dr Matthew Gilman, NIH, USA
- Prof Lucilla Poston, Kings College London, UK

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- Prof Caroline Fall, University of Southampton, UK
- Prof Mary Barker, University of Southampton, UK
- Prof Chittaranjan Yajnik, KEM Hospital Research Centre, India
- Prof Tessa Roseboom, Univeristy of Amsterdam, Netherlands
- Dr Kalyanaraman Kumaran, University of Southampton, UK
- Prof William Fraser, Université de Sherbrooke, Canada
- Prof Stephen Matthews, University of Toronto, Canada

Advanced Imaging Techniques: DOHaD Applications
Organisers: Prof Sendhil Velan, Prof Janna Morrison, Dr Navin Michael, Dr Suresh Sadananthan, Prof Kate Denton, Prof Mary Wlodek.
Speaker List:
- Prof Janna Morrison, University of Adelaide, Australia
- A/Prof Justin Dean, University of Auckland, NZ
- Prof Sendhil Velan, Singapore Institute for Clinical Sciences, Singapore
- Dr Alison Care, University of Adelaide, Australia
- Dr Navin Michael, Singapore Institute for Clinical Sciences, Singapore
- Dr Suresh Sadananthan, Singapore Institute for Clinical Sciences, Singapore
- Prof Stuart Hooper, Monash University, Australia
- Dr Eric Schrauben, The Hospital for Sick Kids, Canada

Novel Methods for Understanding Mechanistic Pathways in DOHaD
Organiser: Prof Tamsen Rochat, Prof Kate Tilling
Speaker List:
- Prof Kate Tilling, University of Bristol, UK
- Prof Tamsen Rochat, Human Sciences Research Council, South Africa
- Dr Brian Houle, Australian National University, Australia
- Dr Nicole Warrington, University of Queensland, Australia
- Dr Darren Dahly, University College Cork, Ireland

Emerging Research on Later-Life Interventions to Remediate and Redirect Unhealthy Life-course Trajectories Induced by Early Life Adversities
Organiser: Dr Teresa Seeman
Speaker List:
- Dr. Maya Rosen, Harvard University, USA
- Dr. Gabriella Conti, University College London, UK
- Dr. Dan Belsky, Columbia University, USA
- Prof. Karen Lillycrop, University of Southampton, UK
- Dr. Chelsea Stillman, University Pittsburgh, USA
- Prof. Keith Godfrey, University of Southampton, UK
- Dr. Teresa Seeman, University of California, USA

Plenary Session 1 Social Determinants of Health/Planetary Health and DOHaD

Mon, October 21

Importance of DOHaD for Indigenous Australia
A/ Prof Gurmeet Singh (Menzies School of Health Research, Australia)

The Chemical Environment and Health. Prof Charles Tyler (University of Exeter, United Kingdom)

Plenary Session 2 DOHaD – Education and Behavioural Change

Mon, October 21

Intervening through Education: the Pacific Islands Experience. Dr Jacquie Bay (University of Auckland NZ)
Behavioural change interventions. Prof Mary Barker (University of Southampton, United Kingdom)

Plenary Session 3 Immune and Metabolic Programming

Tues, October 22

The Human Microbiome Origins for Health and Disease. Prof Charles Mackay (Monash Biomedicine Discovery Institute, Australia)
Inflammation in Developmental Programming: Lessons from Cardiovascular Disease. Prof Neils Riksen (Radboud University Medical Centre, The Netherlands)
Diet and Lifestyle Intervention Dr Hui-xia Yang (Peking University First Hospital, China)

Plenary Session 4 Fundamental Mechanisms of Developmental Biology Central to DOHaD Outcomes

Wed, October 23

Australian Marsupials as Models of Development. Prof Marilyn Renfree (University of Melbourne, Australia)
Epigenetic Paradigms in DOHaD. Prof John Greally (Albert Einstein College of Medicine, USA)

Symposia

Early Prevention of Childhood Obesity and Diabetes
Mon, October 21
10:40 AM - 12:20 PM
Session Chair
Ling-Wei Chen, HRB Centre for Diet and Health Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin, Ireland

INVITED SPEAKER PRESENTATION:
Early Prevention of Childhood Obesity: Should We Target Diet, Activity, or Sleep?
Rachael Taylor, University of Otago
INVITED SPEAKER PRESENTATION:
What Are the Economic-Related Consequences of Early Childhood Obesity?
Victoria Brown, Deakin Health Economics, Institute for Health Transformation, Deakin University
Exploring the Association Between Birth Weight and Risk of Abdominal Obesity in Children and Adolescents
Zhaogeng Yang, Peking University; Bo Wen; Xijie Wang, Institute of Child and Adolescent Health, School of Public Health, Peking University Health Science Center; Yanhui Dong, Institute of Child and Adolescent Health, School of Public Health, Peking University; Di Gao; Yanhui Li; Zhiyong Zou, Peking University; BIN Dong; Jun Ma, Institute of Child and Adolescent Health, School of Public Health, Peking University
Baseline Profile of an Australia-Wide Pregnancy Cohort Study of Children at Risk of Type 1 Diabetes: The ENDIA Study
Lynne Giles, The University of Adelaide; Aveni Haynes, Telethon Kids Institute; Megan Penno; Kelly McGorm, School of Medicine, Robinson Research Insittute, The University of Adelaide; Simon Barry, School of Medicine, Robinson Research Institute; Peter Colman, Department of Diabetes and Endocrinology; Maria Craig, School of Women's and Children's Health; Elizabeth Davis, Telethon Kids Institute; Mark Harris, Mater Health Service; Len Harrison, Walter and Eliza Hall Institute for Medical Research; Grant Morahan, Harry Perkins Institute for Medical Research, The University of Western Australia; Claire Morbey, Hunter Diabetes Centre; William Rawlinson; Richard Sinnott, Department of Computing and Information Systems, University of Melbourne; Georgia Soldatas, Monash Centre for Health Research and Implementation; Rebecca Thomson, School of Medicine, Robinson Research Institute, The University of Adelaide; Peter Vuillermin; John Wentworth, Walter and Eliza Hall Institute for Medical Research and Royal Melbourne Hospital; Jenny Couper, School of Medicine, Robinson Research Institute, The University of Adelaide and Women's and Children's Hospital
The Effect of Metformin Intervention on the Programming of Adiposity in Offspring of Obese Pregnancy
Josca Schoonejans, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Heather Blackmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Antonia Hufnagel, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Thomas Ashmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Denise Fernandez-Twinn, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Susan Ozanne, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit
Maternal Obesity in Pregnancy and Determinants of Cardiovascular Risk in Neonates
Paul Taylor, King's College London; Tamarind Russell-Webster, King's College London; Faith Miller, King's College London; Matias Costa Vieira, King's College London; Claire Singh, Guys & St Thomas NHS Foundation Trust; Annette Briley, King's College London; Paul Seed, King's College London; Dharmintra Pasupathy, King's College London; Lucilla Poston, King's College London
Maternal Overweight/Obesity Is Associated with Markedly Greater Odds of Obesity in the Offspring at 20 Years of Age in Thailand
Kittipan Rerkasem, Faculty of Medicine and Research Institute for Health Sciences, Chiang Mai University; Kanokwan Kulprachakarn, Research Institute for Health Sciences, Chiang Mai University; José G B Derraik, Liggins Institute - University of Auckland
Association between Parental Body Mass Index and Brown Adipose Tissue in Asian Preschool Children: The GUSTO study
Tint Mya Thway, National University of Singapore; Suresh Anand Sadananthan, Singapore Institute for Clinical Sciences, A*STAR Research Entities; Navin Michael, Singapore Institute for Clinical Sciences; Khin Thuzar Hlaing; Jonathan Huang, Singapore Institute for Clinical Sciences; Keith Godfrey, Southampton Biomedical Research Centre; Lynette Pei Chi Shek; Fabian Yap;

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Kok Hian Tan; Sendhil Velan; Peter David Gluckman; Yap Seng Chong, National University of Singapore; Melvin Khee-Shing Leow, Duke-NUS Medical School; Kuan Jin Lee; Yung Seng Lee, National University of Singapore; Zhang Cuilin; Marielle Valerie Fortier; Johan Gunnar Eriksson

BMI Trajectories from Birth to 4–5 Years in a Norwegian Multi-Ethnic Population; Associations with Maternal Gestational Diabetes, Pre-pregnant Obesity and Gestational Weight Gain

Ingun Toftemo, Institute of Health and Society, University of Oslo; Line Sletner, Dept. of Pediatric and Adolescents Mediscine, Akershus University Hospital; Anne Karen Jenum, Department of General Practice, Institute of Health and Society, University of Oslo

Development of a Risk Model for Pediatric Prediction of Adult Type 2 Diabetes Mellitus: The Cardiovascular Risk in Young Finns Study

Marie-Jeanne Buscot, Menzies Institute For Medical Research, University of Tasmania

Cross-Generational Trends of the Links Between Early Life Risk Factors and Adult Cardiovascular Diseases: The Uppsala Birth Cohort, Sweden

Muhammad Zakir Hossin, Karolinska Institute; Ilona Koupil, Stockholm University

Impacts of Maternal Stress and Mental Health

Mon, October 21
10:40 AM - 12:20 PM

Presentations

INVITED SPEAKER PRESENTATION:

Exposure to Early Life Pain: Cause, Effects and Consequences

Isabelle Dutriez-Casteloot, Department of Biology at Faculty of Sciences and Technologies of University of Lille in France.

INVITED SPEAKER PRESENTATION:

Maternal Separation and Alcohol. Reversal of Its Effects Through Environmental Enrichment

Gabriela Acosta, Institute of Pharmacological Research (ININFA), National Scientific and Technologic Research Council (CONICET), University of Buenos Aires (UBA)

Preconception and Gestational Social Isolation Modifies Inflammatory and Stress Marker Profiles In Rats

Nayara Lopes, University of Alberta; Camille Wiley, University of alberta; Vaishvi Patel, University of alberta; J. Keiko Mccreary, University of Lethbrigde; Xin Fang, University of alberta; Erin Falkenberg, University of Lethbrigde; Gerlinde Metz, University of Lethbridge; David Olson, University of Alberta

AP Maternal Mental Health Influences Perinatal Programing of Socio-Emotional Development via Gene X Environment Interactions

Varsha Gupta, Singapore Institute for Clinical Sciences; Li Chen, Singapore Institute for Clinical Sciences; Irina Pokhvisneva; Anqi Qiu; Helen Chen; Yap Seng Chong, National University of Singapore; Peter David Gluckman; Kieran O'Donnell, McGill University; Birit FP Broekman; Michael J Meaney; Neerja Karnani, Singapore Institute for Clinical Sciences, A*STAR

Maternal and Paternal Mental Disorder From Adolescence and Subsequent Offspring Birth Outcomes: A 20 Year Intergenerational Cohort Study

Elizabeth Spry; Claire Wilson, Section of Women's Mental Health, King's College London; Carolyn Coffey; Lex Doyle, University of Melbourne; Anthony Hannan, Florey Institute of Neuroscience and Mental Health, University of Melbourne; Lindsey Hines, University of Bristol; Louise Howard, Section of Women's Mental Health, King's College London; Margarita Moreno-Betancur; Craig Olsson, Murdoch Children's Research Institute; Mary Wlodek, The University of Melbourne; George Patton, Murdoch Children's Research Institute

Compensating for a Difficult Start – Maternal Psychosocial Stress, Breast Milk Composition and Infant Development

Anna Ziomkiewicz, Hirszfeld Institute of Immunology and Experimental Therapy PAS; Szymon Wichary, Institute of Psychology Leiden University; Magdalena Piosek, Institute of Psychology University of Wroclaw; Anna Apanasewicz, Hirszfeld Institute of Immunology and Experimental Therapy PAS, Department of Anthropology; Magdalena Babiszewska, Hirszfeld Institute of Immunology and Experimental Therapy PAS; Marek Szoltysik, Wroclaw University of Environmental and Life Sciences Faculty of Biotechnology and Food Science

Hypertensive Disorders of Pregnancy and Autistic Traits in Offspring: The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study

Keiko Murakami, Tohoku Medical Megabank Organization, Tohoku University; Fumiya Yokozeki, Tohoku University School of Medicine; Taku Obara, Tohoku University Tohoku Medical Megabank Organization; Mami Ishikuro, Tohoku University Tohoku Medical Megabank Organization; Masato Nagai, Tohoku Medical Megabank Organization, Tohoku University; Hiroko Matsubara, Tohoku Medical Megabank Organization, Tohoku University; Aoi Noda, Tohoku Medical Megabank Organization, Tohoku University; Satoshi Mizuno, Tohoku Medical Megabank Organization, Tohoku University; Junichi Sugawara, Tohoku Medical Megabank Organization, Tohoku University; Soichi Ogishima, Tohoku Medical Megabank Organization, Tohoku University;

Masahiro Kikuya; Hirohito Metoki, Tohoku Medical Megabank Organization, Tohoku University; Shinichi Kuriyama, Tohoku Medical Megabank Organization, Tohoku University

Dramatic Impairment in the Chronically Hypoxic Fetus to Second Stressors Such As Acute Hypotension and Acute Hypoxia

Beth Allison, The Ritchie Centre; Kirsty L. Brain, The University of Cambridge; Youguo Niu, University of Cambridge; Nozomi Itani, King's College London; Katie Skeffington, University of Bristol; Thomas Ashmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Kimberley Botting, University of Cambridge; Emilio Herrera; Dino Giussani, University of Cambridge

Maternal Vomiting During Early Pregnancy and Cardiovascular Risk Factors at School-Age

Sunayna Bahadoer, The Generation R Study Group, Erasmus Medical Center

Severity of Nausea and Vomiting in Pregnancy and Early Childhood Neurobehavioural Outcomes

Wei Xin Ong, NUS Yong Loo Lin School of Medicine; Elisha Chia; Nicholas L Syn; Desiree Y Phua; Shirong Cai; Lynette Pei Chi Shek; Yap Seng Chong, National University of Singapore; Lourdes Mary Daniel; Birit FP Broekman; Keith Godfrey, Southampton Biomedical Research Centre; Michael J Meaney; Shiao-Yng Chan, National University of Singapore; Evelyn Law, National University of Singapore

Intergenerational Epigenetic Inheritance

Mon, October 21
10:40 AM - 12:20 PM

Session Chairs

Chair

Stephen Lye, Lunenfeld-Tanenbaum Research Institute, Canada

Co-Chair

Boris Novakovic, Murdoch Children's Research Institute, Australia

Presentations

INVITED SPEAKER PRESENTATION: Epigenetic Inheritance in Multiple Model Organisms

Douglas Ruden, Wayne State University

INVITED SPEAKER PRESENTATION: Four Generations of Maternal Stress: Ancestral Trauma as a Determinant of Disease Risk and Stress Resilience

Gerlinde Metz, University of Lethbridge

Detecting Epigenetic Mechanisms that Putatively Mediate the Influence of Early Life Exposures on Disease Susceptibility

Tom Richardson, MRC Integrative Epidemiology Unit

Novel Read-Level Analysis Identifies Cell-Type Specific DNA Methylation Signals in Bulk Whole-Genome Bisulfite Sequencing (WGBS) Data

Anthony Scott, Baylor College of Medicine; Cristian Coarfa, Baylor College of Medicine; Rob Waterland, Baylor College of Medicine

Epigenetic Alteration of Rho Guanine Nucleotide Exchange Factor 11 (ARHGEF11) in Cord Blood Samples in Macrosomia Exposed to Intrauterine Hyperglycaemia

Rina Su, Beijing Medical University

A Genomic Atlas of Systemic Interindividual Epigenetic Variation in Humans

Chathura Gunasekara, Baylor College of Medicine; Anthony Scott, Baylor College of Medicine; Eleonora Laritsky, Baylor College of Medicine; Harry MacKay, Baylor College of Medicine; Maria Baker, Baylor College of Medicine; Jack Duryea, Baylor College of Medicine; Noah Kessler; Garrett Hellenthal, UCL Genetics Institute, Department of Genetics, Evolution and Environment, University College London; Matt Silver, MRC Gambia at the London School of Hygiene and Tropical Medicine; Sophie E. Moore, Kings' College London; Andrew M Prentice, MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine; Yumei Li, Baylor College of Medicine; Rui Chen, Baylor College of Medicine; Cristian Coarfa, Baylor College of Medicine; Rob Waterland, Baylor College of Medicine

Assessing Causal Links Between Ancestral Exposure and Offspring Adiposity in Three Generations via Epigenetic Inheritance Mechanisms in the MULTIEPIGEN Study

Noora Kartiosuo, University of Turku; Olli Raitakari, University of Turku; Jaakko Nevalainen, Tampere University; Kari Auranen, University of Turku

Inter-generational Associations of Height, Weight and BMI in Three-Generation Families: The TMM BirThree Cohort Study

Takuma Usuzaki, Tohoku University; Mami Ishikuro, Tohoku University Tohoku Medical Megabank Organization; Taku Obara, Tohoku University Tohoku Medical Megabank Organization; Aoi Noda, Tohoku Medical Megabank Organization, Tohoku University; Keiko Murakami, Tohoku Medical Megabank Organization, Tohoku University; Masato Nagai, Tohoku Medical Megabank Organization, Tohoku University; Masahiro Kikuya; Hirohito Metoki, Tohoku Medical Megabank Organization, Tohoku University; Shinichi Kuriyama, Tohoku Medical Megabank Organization, Tohoku University; Hiroko Matsubara, Tohoku Medical Megabank Organization, Tohoku University

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Neonatal and Neurodevelopmental Outcomes in Preterm Infants According to Maternal Body Mass Index: A Prospective Cohort Study
Geraldine Gascoin, Angers University Hospital; Marie Moreau, Angers University Hospital; Mathilde Remy, Angers University Hospital; Simon Nusinovici, Nantes University Hospital; Guillaume Legendre, Angers University Hospital; Regis Coutant, Angers University Hospital; Patrick Van Bogaert, Angers University Hospital
DNA Methylation At NEGR1 Gene Locus Is Associated With Neurodevelopmental Outcomes And Childhood Obesity
Edith Breton, Université de Sherbrooke; Valérie Gagné-Ouellet, Université de Sherbrooke; Kathrine Thibeault, Université de Sherbrooke; Ryan J Van Lieshout, McMaster University; Patrice Perron, Université de Sherbrooke; Marie-France Hivert, Harvard Medical School; Luigi Bouchard, Université de Sherbrooke
Maternal Gestational Diabetes and Newborn DNA Methylation: Findings From the Pregnancy and Childhood Epigenetics Consortium
Caitlin Howe, University of Southern California; Marie-France Hivert, Harvard Medical School; Carrie V. Breton, University of Southern California

Long-Term Implications of Perinatal Alcohol Exposure
Mon, October 21
10:40 AM - 12:20 PM
Session Chairs
Co-Chair Lisa Akison, The University of Queensland, Australia
Presentations
INVITED SPEAKER PRESENTATION: Prenatal Alcohol Exposure: Programming, Stress, Immune Function, and Vulnerability Over the Lifespan
Joanne Weinberg, University of British, Columbia
INVITED SPEAKER PRESENTATION: Cardiovascular, Renal and Metabolic Outcomes Following Maternal Alcohol Exposure
Karen Moritz, The University of Queensland
Maternal Periconceptional Alcohol Consumption is Associated with Increased Child Blood Pressure
Suresh Anand Sadananthan, Singapore Institute for Clinical Sciences, A*STAR Research Entities; Wen Lun Yuan; Navin Michael, Singapore Institute for Clinical Sciences; Wei Wei Pang, National University of Singapore; Lynette Pei Chi Shek; Fabian Yap; Kok Hian Tan; Keith Godfrey, Southampton Biomedical Research Centre; Peter David Gluckman; Yap Seng Chong, National University of Singapore; Johan Gunnar Eriksson; Yung Seng Lee, National University of Singapore; Shiao-Yng Chan, National University of Singapore; Karen Moritz, The University of Queensland; Sendhil Velan; Mary Wlodek, The University of Melbourne
Periconceptional Alcohol Exposure Programs Altered Behaviour, HPA Activity And Regulation And Pituitary Abnormalities In Rat Offspring
Danielle Burgess, The University of Queensland, Faculty of Medicine, School of Biomedical Sciences; Diana Lucia, The University of Queensland, Faculty of Medicine, School of Biomedical Sciences; Helle Bielefeldt-Ohmann; James Cuffe, The University of Queensland; Karen Moritz, The University of Queensland
The Association of Alcohol PRS on Mental Health Phenotypes: A PheWAS in the Avon Longitudinal Study of Parents and Children (ALSPAC)
Kayleigh Easey, University of Bristol
Maternal and Paternal Smoking, Alcohol and Caffeine use During Pregnancy and ADHD Symptoms in Offspring from Childhood to Adolescence
Elis Haan, University of Bristol
Alcohol Consumption and Trajectories of Depressive Symptoms in Perinatal Period Over 11-Year Period: Findings from the Avon Longitudinal Study of Parents and Children (ALSPAC)
Abdul Wajid, University of Calgary
Adverse Postnatal Environment Differentially Affects Emotional Regulation and Immune System Function in Rats Prenatally Exposed to Alcohol Compared to Controls
Charlis Raineki, University of British Columbia
Physical Health Impacts of Fetal Alcohol Spectrum Disorder: Preliminary Results From a Caregiver Survey
Natasha Reid, Child Health Research Centre,University of Queensland; Karen Moritz, The University of Queensland
Supporting Practice Change for the Provision of Recommended Care for Alcohol Consumption during Pregnancy: Development and Evaluation of an Evidence-based Clinician Training Program
Julia Dray, Hunter New England Population Health; Emma Doherty, Hunter New England Population Health; Belinda Tully, Hunter New England Population Health; Brendon Williams, Maternity and Gynaecology, John Hunter Hospital,; Sophie Curtin, Maternity and Gynaecology, Tamworth Hospital; Milly Licata, Hunter New England Population Health; Christophe Lecathelinais, Hunter New England Population Health; Sarah Ward, Foundation for Alcohol Research and Education;

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Elizabeth Elliott, Faculty of Medicine and Health and Discipline of Child and Adolescent Health, University of Sydney; John Wiggers, Hunter New England Population Health; Melanie Kingsland, Hunter New England Population Health

Chronic Low-Dose Alcohol Exposure During Pregnancy Leads to Reduced Blood Pressure and Blunted Pressor Responsiveness to Stress in Female but not Male Offspring

Sarah Walton, Monash University; Melissa Tjongue; Marianne Tare; Edmund Kwok, Monash University; Megan Probyn; Helena Parkington; John Frederick Bertram, Monash University; Karen Moritz, The University of Queensland; Katherine Denton

Novel Environmental Impacts in DOHaD

Mon, October 21

10:40 AM - 12:20 PM

Session Chairs

Co-Chair Thea Golden, University of Pennsylvania United States

Presentations

INVITED SPEAKER PRESENTATION: Wildlife Behaviour, Ecology and Evolution in a Changed and Changing World

Bob Wong, Monash University, Victoria

INVITED SPEAKER PRESENTATION: Exposure to Airborne Nanoparticles During Pregnancy: Lessons From Rabbit Models

Pascale Chavatte-Palmer, INRA, University Paris-Saclay, France

Fetal and Placental Consequences Following Ancestral Paternal Exposure to Arctic Pollutants and Folic Acid Supplementation

Phanie L. Charest, Université Laval; Maryse Lessard, Université Laval; Pauline M. Herst, Université Laval; Pauline Navarro, Université Laval; Amanda MacFarlane, Health Canada; Sarah Kimmins, McGill; Jacquetta Trasler, McGill University Health Centre; Mathieu David Dalvai, Laval University; Marie-Odile Benoit-Biancamano, Université de Montréal; Janice L. Bailey, Université Laval

Influence of Maternal Dietary Inflammatory Potential and Quality on Offspring Birth Outcomes: A Pooled Analysis of 7 European Cohorts in the ALPHABET Consortium

Ling-Wei Chen, HRB Centre for Diet and Health Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin; Adrien Aubert, Centre for Research in Epidemiology and Statistics (CRESS), Inserm; Nitin Shivappa, Arnold School of Public Health, University of South Carolina; Jonathan Bernard, Inserm Centre for Research in Epidemiology and Statistics (CRESS); Rosalie Mensink-Bout, Department of Pediatrics, Erasmus MC, University Medical Center Rotterdam; Aisling A Geraghty, UCD Perinatal Research Centre, School of Medicine, University College Dublin; John Mehegan, HRB Centre for Diet and Health Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin; Matthew Suderman, MRC Integrative Epidemiology Unit, University of Bristol; Kinga Polanska, Nofer Institute of Occupational Medicine; Caroline L Relton, MRC Integrative Epidemiology Unit, University of Bristol; Nicholas C Harvey, MRC Lifecourse Epidemiology Unit (University of Southampton) Southampton General Hospital Southampton; Cyrus Cooper, MRC Lifecourse Epidemiology Unit (University of Southampton) Southampton General Hospital Southampton; Liesbeth Duijts, Erasmus MC, University Medical Center Rotterdam; Barbara Heude, Centre for Research in Epidemiology and Statistics (CRESS), Inserm; James R Hebert, Arnold School of Public Health, University of South Carolina; Fionnuala M McAuliffe, UCD Perinatal Research Centre, School of Medicine, University College Dublin; Cecily C Kelleher, HRB Centre for Diet and Health Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin; Catherine M Phillips, HRB Centre for Diet and Health Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin

Placental Multidrug Resistance Transporter Expression and Offspring Behaviour After Prenatal Administration of the Viral Mimetic poly(I:C) in the Mouse

Victoria R. S. Monteiro, Universidade Federal do Rio de Janeiro; Hannaily Ribeiro Gomes; Mila W Reginatto; Klaus N Fontes; Cherley B V Andrade; Flavia F Bloise; Guinever E Imperio; Daiane A Spiess; William S Rangel; Stephen Matthews, University of Toronto; Enrrico Bloise; Pedro Moreno Pimentel-Coelho; Tania M Ortiga-Carvalho, Universidade Federal do Rio de Janeiro

Maternal Folate in Pregnancy and Offspring Bone Health: The Vitamin D in Pregnancy Study

Mia Percival, Deakin University; Julie Pasco, Deakin University; Sarah Hosking, Deakin University; Lana Williams, Deakin University; Kara Holloway-Kew, Deakin University; Natalie Hyde, Deakin University

Vitamin B12 Deficiency Leads To Dysregulation of Fatty Acid Metabolism in Human Adipocytes and Maternal Subcutaneous and Omental Adipose Tissue

Jinous Samavat, University of Warwick; Antonysunil Adaikalakoteswari, Nottingham Trent University; Joseph Boachie, University of Warwick; Ponnusamy Saravanan, University of Warwick

Maternal Dietary LA:ALA Ratio and Total Fat Intake During Pregnancy Has Implications on Offspring Growth, Hepatic Gene Expression and Omega-3 Fatty Acid Elongation Efficiency

Sally Draycott, University of Nottingham/University of Adelaide; Bev Muhlhausler, CSIRO/The University of Adelaide; Matthew Elmes, University of Nottingham; Simon Langley-Evans, University of Nottingham

Combined Impact of Maternal and Infant Infection and Antibiotic Use in Pregnancy and Infancy in Relation to Childhood Obesity: A Longitudinal Birth-Cohort Study With Long-Term Follow-Up

De-Kun K. Li, Division of Research, Kaiser Permanente; Hong Y. Chen, Division of Research, Kaiser Permanente; Andrew K. Hirst, Division of Research, Kaiser Permanente; Jeannette R. Ferber, Division of Research, Kaiser Permanente; Roxana X. Odouli, Division of Research, Kaiser Permanente

Prenatal Cooking May Increase Hyperactive Behaviors at around 3 Years of Age: Findings from Shenzhen Longhua Child Cohort Study

Xin-Yu Fang, Department of Biostatistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou, China

Maternal Smoking During Pregnancy and Offspring Intellectual Disability: Causal Analysis in an Inter-Generational Danish Cohort of Over 1 Million Individuals

Paul Madley-Dowd, Bristol Medical School; Dheeraj Rai, Bristol Medical School; Amy Kalkbrenner, University of Wisconsin-Milwaukee; Stan Zammit, Bristol Medical School; Jon Heron, Bristol Medical School; Hein Heuvelman, Bristol Medical School; Diana Schendel, Aarhus University

Twin and IVF studies for DOHaD

Mon, October 21
10:40 AM - 12:20 PM

Session Chairs

Chair Michael Boyne, University of the West Indies Jamaica
Co-Chair Maria Magnus, Norwegian Institute of Public Health Norway

Presentations

INVITED SPEAKER PRESENTATION: What Can Be Learnt About Epigenetics and Causation From Studies of Twins and Families?

John Hopper, University of Melbourne

INVITED SPEAKER PRESENTATION: Metabolic Biomarkers of Monochorionic Twins Complicated With Selective Intrauterine Growth Restriction

Chao Chao Tong, Shanghai Jiao Tong University

The Impact Of The Artificial Periconception Environment On Preimplantation Embryonic Morphokinetic Parameters

Linette van Duijn, Erasmus University Medical Centre; Esther Baart, Erasmus Medical Center; Eva van Marion, Erasmus Medical Center; Eric Steegers, Department of Obstetrics and Gynaecology, Erasmus Medical Centre, University Medical Centre; Joop Laven, Erasmus Medical Center; Melek Rousian, Erasmus Medical Center; Regine Steegers-Theunissen, Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Centre, University Medical Centre

Epigenetics of Neurodevelopmental Disorders Using Monozygotic Twins

Namitha Mohandas, MCRI, Victoria; Jeffrey Craig, Deakin University; Yuk Jing Loke, Murdoch Childrens Research Institute, Royal Children's Hospital; Kylie Crompton; Lata Vadlamudi

Lower levels of Type-2-Diabetes Markers in Children Following Longer Duration of Breastfeeding: A Longitudinal Twin Study

Heide Temples, Clemson University; Richard /. Saffery, MCRI; Yuk Jing Loke, Murdoch Childrens Research Institute, Royal Children's Hospital; William Bridges, Clemson University; Jeffrey Craig, Deakin University

Infertility Treatment as a "Natural Experiment" for the study of Congenital Heart Defects.

Michael Davies, Robinson Research Institute, The University of Adelaide

Forty Years of IVF, 8 Million babies and Counting – But Is It Safe? Effect of In Vitro Fertilization (IVF) and Prolonged Embryo Culture on Mouse Development and Postnatal Health

Anan Aljahdali, University of Southampton; Ili Khalif; Bhav Sheth, University of Southampton; Miguel Velazquez, Newcastle University; Katrine Wallen, University of Southampton; Clive Osmond, MRC Lifecourse Epidemiology Unit, University of Southampton; Neil Smyth, University of Southampton; Tom Fleming, University of Southampton

AP Young Children Born After In Vitro Fertilization Grow Faster and Are Taller and Leaner Than Naturally-Conceived Children

José G B Derraik, Liggins Institute - University of Auckland; John Gibbins, Liggins Institute - University of Auckland; Anna-Karin Wikström, Uppsala University; Linda Lindström, Uppsala University; Maria Lundgren, Uppsala University; Wayne Cutfield, Liggins Institute University of Auckland; Fredrik Ahlsson, Uppsala University

AP Shorter Gestational Age Explains a Large Proportion of the Poorer Educational Attainment of Twins Compared With Singletons: A Population-Based Data Linkage Study

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Justin Zeltzer, Children's Hospital at Westmead Clinical School; Antonia Shand; Patrick Kelly, The University of Sydney; John Hopper, University of Melbourne; Natasha Nassar, Children's Hospital at Westmead Clinical School; Katrina Scurrah, The University of Melbourne

Sex Differences in Perinatal Mortality and Morbidity in Twins: A Population Case-Control Study in Scotland

Sarah Murray, The University of Edinburgh; David Stoye, University of Edinburgh

Preimplantation Glucocorticoid Exposure: Reprogramming our Future Generations?

Sophie Petropoulos, Université de Montréal

DOHaD & Society

Mon, October 21

2:00 PM - 3:45 PM

Session Chairs

Chair TBA

Co-Chair Siobhan Tu'akoi, Liggins Institute, University of Auckland New Zealand

Presentations

INVITED SPEAKER PRESENTATION: Gender, Social Responsibility and DOHaD

Megan Warin, School of Social Sciences, Robinson Research Institute, University of Adelaide

INVITED SPEAKER PRESENTATION: Social Determinants to DOHaD Health in Low and High Income Countries

Jane Fisher, Monash University, Victoria

INVITED SPEAKER PRESENTATION: The Politics of a Permeable Womb: Misconceptions and Other Histories from the Past

Maurizio Meloni, Alfred Deakin Institute for Citizenship and Globalisation (ADI), Deakin University

Economic Development and the Nutritional Status of Chinese School-Aged Children and Adolescents: An Analysis of Five Successive National Surveys From 1995 to 2014

Yanhui Dong, Institute of Child and Adolescent Health, School of Public Health, Peking University; Yi Song, Institute of Child and Adolescent Health, School of Public Health, Peking University; Jun Ma, Institute of Child and Adolescent Health, School of Public Health, Peking University

Association of a Novel Green Space Indictor with Birthweight

Dwan Vilcins, University of Qld; Peter Baker, School of Public Health; Peter Scarth, School of Earth and Environmental Sciences; Paul Jagals; Luke Knibbs, School of Public Health; Peter Sly, University of Qld

Relationship Between Birth Season and Biomarkers of Fetal Programming in a Contemporary Population

Ilona Nenko, Institute of Public Health, Jagiellonian University Medical College; Karolina Miłkowska, Jagiellonian University Medical College; Magdalena Klimek, Jagiellonian University; Andrzej Galbarczyk, Jagiellonian University Medical College; Grazyna Jasienska, Jagiellonian University Medical College

Early Life Origins of Respiratory Disease

Mon, October 21

2:00 PM - 3:45 PM

Session Chairs

Chair **Arvind Sehgal**, Monash University, Australia

Co-Chair **Erin McGillick**, Hudson Institute of Medical Research, Australia

Presentations

INVITED SPEAKER PRESENTATION: Generation R Birth Cohort – Early Growth and Other Early Life Risk Factors vs Childhood Respiratory and Atopic Outcomes

Liesbeth Duijts, Erasmus MC, University Medical Center Rotterdam

INVITED SPEAKER PRESENTATION: Early Life Risk Factors vs Childhood Respiratory and Atopic Outcomes

Shyamali Dharmage, University of Melbourne, Australia

INVITED SPEAKER PRESENTATION: Micro RNA and Transgenerational Risk of Chronic Lung Disease

Susanne Krauss-Etschmann, Research Center Borstel, Borstel Leibniz-Zentrum für Medizin und Biowissenschaften

Maternal Pregestational Obesity Increases T Lymphocyte Subtypes in Newborns

Viviana Arroyo, Universidad de Chile; Maria Rosa Bono, Universidad de Chile; Paola Casanello, Pontificia Universidad Católica de Chile

MitoQ Antioxidant Treatment in Hypoxic Pregnancy Promotes Pulmonary Surfactant Maturation in Fetal Sheep

Mitchell Lock, University of South Australia; Kimberley Botting, University of Cambridge; Youguo Niu, University of Cambridge; Sage Ford, University of Cambridge; Sandra Orgeig, University of South Australia; Mike Murphy, University of Cambridge; Dino Giussani, University of Cambridge; Janna Morrison, University of South Australia

Early Life Undernutrition Reprograms CD4+ T-Cell Glycolysis and Epigenetics to Facilitate Asthma

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Xi Chen, International Peace Maternity & Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Environmental Chemicals, Pollution and DOHaD
Mon, October 21
2:00 PM - 3:45 PM
Session Chairs
Chair **Keith Godfrey**, Southampton Biomedical Research Centre, United Kingdom
Co-Chair **Amita Bansal**, University of Pennsylvania, United States
Presentations
INVITED SPEAKER PRESENTATION: Why Clean Air Matters During Pregnancy: Influence on Birth Outcomes and Mechanistic Links
Frank Kelly, King's College London
INVITED SPEAKER PRESENTATION: DOHAD Perspectives on Contaminants and Metabolic Disease
Audrei Pavanello, College São Paulo
INVITED SPEAKER PRESENTATION: Air Pollution Exposure During Pregnancy and Child Brain Development
Monica Guxens, Barcelona Institute for Global Health
Indoor Urban Environment and Conventional Risk Factors for Paediatric Tuberculosis Among 1–12 Years Old Children in a Megacity in Pakistan: A Matched Case Control Study
Ambreen Sahito, Isra University, Hyderabad
Periconceptional Folic Acid Supplementation Reduces the Impact of Maternal Particulate Matter Exposure on the Risk of Preterm Birth: A National Birth Cohort Study in China
Qin Li, Department of Maternal and Child Health, School of Public Health, Peking University; Yuan-Yuan Wang
Trimethylamine N-Oxide (TMAO) and Metabolic Syndrome Scores and Cardiovascular Preclinical Phenotypes in Australian Children and Their Mid-Life Adult Parents
Stephanie Andraos, The Univeristy of Auckland; Justin O-Sullivan, Liggins Institute, Auckland; Melissa Wake, Murdoch Children's Research Institute; David Burgner, Murdoch Childrens Research Institute; Richard Saffery, MCRI; Beatrix Jones

Lactation as a Window for DOHaD
Mon, October 21
2:00 PM - 3:45 PM
Session Chairs
Co-Chair **Wei Wei Pang**, National University of Singapore, Singapore
Presentations
INVITED SPEAKER PRESENTATION: The Evolution of Species-Specific Milk Composition
Katie Hinde, Arizona State University
INVITED SPEAKER PRESENTATION: Influence of Maternal Diet on Infant Metabolism As Mediated by Lactation
Bev Muhlhausler, CSIRO/The University of Adelaide
INVITED SPEAKER PRESENTATION: Impact of Pregnancy Complications on Infant Outcomes
Mary Wlodek, The University of Melbourne
Development of Visceral and Subcutaneous-Abdominal Adipose Tissue in Breastfed Infants During First 12 Months of Lactation – Effect of Human Milk Components and Maternal Factors
Zoya Gridneva, The University of Western Australia; Alethea Rea, The University of Western Australia; Ching Tat Lai, The University of Western Australia; Wan Jun Tie, The University of Western Australia; Sambavi Kugananthan, The University of Western Australia; Kevin Murray, The University of Western Australia; Peter Edwin Hartmann, The University of Western Australia; Donna Geddes, The University of Western Australia
Nutrient and Hormone Composition of Milk Is Altered in Post-Bariatric Rodent Dams
Bernadette Grayson, University of Mississippi Medical Center; Bradley Welch, UMMC; Evangeline Deer, University of Mississippi Medical Center
Association of Chemerin in Blood and Breast milk with Gene Methylation in Gestational Diabetes
Sadia Fatima, Aga Khan University; Unab I. Khan; Erum Khalik; Safina Abdul Razzak, Aga Khan University Hospital; Ibrar Ahmed

Preterm Birth and Adverse Pregnancy Outcomes
Mon, October 21
2:00 PM - 3:45 PM
Session Chairs
Chair **David Olson**, University of Alberta, Canada
Co-Chair **Sky Feuer**, University of California, United States
Presentations
INVITED SPEAKER PRESENTATION: Preterm Birth and the Risk of Adult Disease

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Frank Bloomfield, Liggins Institute, University of Auckland
INVITED SPEAKER PRESENTATION: Prediction of Preterm Birth Using Mid-Pregnany Clinical and Molecular Factors
Laura Jelliffe-Pawlowski, University of California, USA
INVITED SPEAKER PRESENTATION: Establish Pregnancy Cohort and Biorepository to Advance Understanding the Biology of Preterm Birth in Low-Income Setting
Anisur Rahman, International Centre for Diarrhoeal Disease Research, Bangladesh
Cardiovascular Risk Factors In Those Born Preterm – Systematic Review And Meta-Analysis
Prabha Andraweera, The University of Adelaide; Bradley Condon, The University of Adelaide; Gemma Collett, The University of Adelaide; Stefania Gentilcore, The University of Adelaide; Zohra Lassi, Adelaide Medical School and The Robinson Research Institute
Structural Remodelling of Cardiac Ventricles in Lambs Born Very Preterm
Bianca Le, Monash University
Increased Rates of Mental and Developmental Disorders in Term and Preterm-Born Children Exposed to Maternal Antenatal Glucocorticoids: A Nationwide Register Study
Katri Räikkönen, University of Helsinki; Mika Gissler, National Institute for Health and Welfare; Eero Kajantie, National Institute for Health and Welfare

Programming of Central Nervous System Development
Mon, October 21
2:00 PM - 3:45 PM
Session Chairs
Co-Chair **Rishikesh Behere**, Diabetes unit, KEM Hospital Research Center, India
Presentations
INVITED SPEAKER PRESENTATION: Effects of Stress and Nutrition on Fetal Brain Development
Matthias Schwab, Jena University Hospital
INVITED SPEAKER PRESENTATION: Genetic, Epigenetic and Epidemiological Approaches to Identify Adverse Mental Health and Neurodevelopment Outcomes
Kieran O'Donnell, McGill University
INVITED SPEAKER PRESENTATION: Early Life Hypoxia and MS
Mary Tolcos, RMIT University
Does Mismatch Between Retinal Vascular Endowment and Eye Size Suggest That Ocular Disease Can Be Programmed by an Inappropriate Predictive Adaptive Response?
Hafi Khan, Deakin University; Alex Gentle, Deakin University; Lisa Hanna; Andrew KC Lam, Hong Kong Polytechnic University; Chi Ho To, Hong Kong Polytechnic University; James Andrew Armitage, Deakin University
Associations of Retinal Microvasculature With Hearing Status Emerge and Strengthen From Childhood to Mid-Life: Cross-Generational Population-Based Study
Jing Wang, Murdoch Children's Research Institute, The University of Melbourne; Mengjiao Liu, Murdoch Children's Research Institute; Valerie Sung, Murdoch Children's Research Institute, The University of Melbourne; Kate Lycett, Deakin University; Anneke Grobler, Murdoch Children's Research Institute; David Burgner, Murdoch Childrens Research Institute; Melissa Wake, Murdoch Children's Research Institute
Inflammation and Saturated Fatty Acid Impair Hypothalamic Neuroprogenitor Cells Mitochondrial Function
Mina Desai, Los Angeles Biomedical Research Institute

Cross-Cohort and Novel Large Data Resources
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Co-Chair **Jesus Serrano-Lomelin**, University of Alberta, Canada
Presentations
INVITED SPEAKER PRESENTATION: Data Deus: Enabling Deeper Insights into Human Variation and Origins of Disease
Neerja Karnani, Singapore Institute for Clinical Sciences, A*STAR
INVITED SPEAKER PRESENTATION: Biomarkers From Danish Nationwide Neonatal Blood Sampling: Later Disease and Death
Berit Lilienthal Heitmann, Bispebjerg og Frederiksberg Hospital
INVITED SPEAKER PRESENTATION: CopLab: Measured Biomarkers From Copenhagen Pregnant Women and Offspring 2000–2015
Janet Janbek, Danish Dementia Research Centre, Department of Neurology, The Neuroscience Centre, Rigshospitalet and The Research Unit for General Practice, Section of General Practice, Institute of Public Health, University Copenhagen

INVITED SPEAKER PRESENTATION: The Development, Causes, and Consequences of Childhood Obesity: Exploring Heterogeneity Using Multiple Birth Cohorts
Will Johnson, Loughborough University

DOHaD and Indigenous Health
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Co-Chair **Siobhan Tu'akoi**, Liggins Institute, University of Auckland, New Zealand
Presentations
INVITED SPEAKER PRESENTATION: Traditional Birth Practices and Implications for DOHaD
Leona Star, First Nations Health and Social Secretariat of Manitoba
INVITED SPEAKER PRESENTATION: CVD in Aboriginal and Torres Strait Islander Peoples
Alex Brown, South Australian Health and Medical Research Institute
INVITED SPEAKER PRESENTATION: Supporting the Health of Young People in the Cook Islands
Neti Tamarua Herman, Tupapa, Rarotonga
INVITED SPEAKER PRESENTATION: Canadian First Nations Approach to DOHAD
Richard Oster, Department of Agricultural, Food & Nutritional Science, University of Alberta

DOHaD in Countries Experiencing Double Burden of Malnutrition
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Chair **Paulo Mathias**, Department of Biotechnology, Genetics and Cellular Biology, Brazil
Co-Chair **Krishnaveni Ghattu**, Epidemiology Research Unit, Holdsworth Memorial Hospital, India
Presentations
INVITED SPEAKER PRESENTATION: DOHaD Relevance in Addressing Double Burden of Malnutrition in Pakistan
Nuruddin Mohammed, Aga Khan University (AKU),Karachi, Pakistan
INVITED SPEAKER PRESENTATION: Double Burden and DOHaD Impacts in West Africa
Augustin Nawidimbasba Zeba, Institut de Recherche en Sciences de la Santé, Direction Régionale de l'Ouest, Burkina Faso
INVITED SPEAKER PRESENTATION: Double Burden of Malnutrition in Latin-American
Antonio Marcus Paes, Federal University of Maranhão

Epigenetics in DOHaD
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Chair **John Greally**, Albert Einstein College of Medicine, United States, United States
Co-Chair **Line Hjort**, Region Hovedstaden, Denmark
Presentations
INVITED SPEAKER PRESENTATION: Epigenetics and DOHAD-New Insights
Karen A. Lillycrop, University of Southampton
INVITED SPEAKER PRESENTATION: Novel DOHAD Insights into Epigenetic Inheritance
Jeffrey Craig, Deakin University
INVITED SPEAKER PRESENTATION: Nutrition, Conception and the Offspring Epigenome
Matt Silver, MRC Gambia at the London School of Hygiene and Tropical Medicine
INVITED SPEAKER PRESENTATION: Conceptual and Ethical Issues Provoked by the Rise of Epigenetics and Fetal Origins Research
Sarah Richardson, Harvard University
INVITED SPEAKER PRESENTATION: Placental Epigenetic Biomarkers of Risk of Autism Spectrum Disorders
Janine Lasalle, UC Davis

Maternal Obesity, Breastfeeding and Infant Outcomes
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Chair **Leon Mitoulas**, Medela, Australia
Co-Chair **Shikha Pundir**, University of Auckland, New Zealand

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Presentations
INVITED SPEAKER PRESENTATION: Understanding the Development of the Human Lactating Breast at a Single Cell Level
Alecia-Jane Twigger, Helmholtz Zentrum Muenchen
INVITED SPEAKER PRESENTATION: Modification of Infant Growth and Body Composition by Patterns of Breastfeeding
Donna Geddes, The University of Western Australia
INVITED SPEAKER PRESENTATION: Impact of Maternal Overweight and Obesity on the Milk Microbiome and Infant Health
Seppo Salminen, Functional Foods Forum, Faculty of Medicine, University of Turku
INVITED SPEAKER PRESENTATION: Modification of the Infant Microbiome and Growth Trajectories by Breastfeeding in the STRONG Kids 2 Cohort.
Sharon Donovan, University of Illinois, Urbana-Champaign
INVITED SPEAKER PRESENTATION: Infant Feeding, Weight Gain and Body Composition in the CHILD Cohort: Separating Breast Milk From Breastfeeding and Formula From Food
Meghan B. Azad, University of Manitoba

Taking DOHaD to the People
Tue, October 22
10:30 AM - 12:10 PM
Session Chairs
Chair **Caroline Fall**, MRC Lifecourse Epidemiology Unit, University of Southampton, United Kingdom
Presentations
INVITED SPEAKER PRESENTATION: You Are (Not Really) What Your Mother Ate: Conducting DOHaD Research While Avoiding Maternal Blame
Gemma Sharp, University of Bristol
INVITED SPEAKER PRESENTATION: Fresh Eyes On The Matter: DOHaD In Public
Lucy Green, University of Southampton
INVITED SPEAKER PRESENTATION: The Early Microbiome
Wayne Cutfield, Liggins Institute University of Auckland
INVITED SPEAKER PRESENTATION: "The Gut Bugs Trial": Making DOHaD and Microbiome Restoration Palatable to the Community.
Justin O-Sullivan, Liggins Institute, Auckland
INVITED SPEAKER PRESENTATION: The WRISK Project: Communicating Risk in Pregnancy – Respecting Evidence, Understanding Women's Needs
Clare Murphy, British Pregnancy Advisory Service

Developmental Origins of Cardiorenal Disease
Tue, October 22
2:00 PM - 3:45 PM
Session Chairs
Chair **Dino Giussani**, University of Cambridge, United Kingdom
Co-Chair **Sarah Walton**, Monash University, Australia
Presentations
INVITED SPEAKER PRESENTATION: Complications During Pregnancy and Fetal Development: Implications for Future CVD
Barbara Alexander, University of Mississippi Medical Center
INVITED SPEAKER PRESENTATION: Functional and Epigenetic Programming of Cardiovascular Disease
Bernardo J. Krause, Pontificia Universidad Católica de Chile
INVITED SPEAKER PRESENTATION: Birth Weight or Adiposity: Which Is Important for Cardiovascular & Hemodynamic Health?
Michael Skilton, The University of Sydney
The Relationship Between Maternal Adiposity and Offspring Kidney Development in Utero and Kidney Function in Infants: The Gomeroi Gaaynggal Study
Kirsty Pringle, The University of Newcastle; Yu Qi Lee, University of Newcastle, Australia; Kym Rae, Gomeroi gaaynggal Centre, University of Newcastle; Christopher Oldmeadow, University of Newcastle, Australia; Eugenie Lumbers, University of Newcastle, Australia; Clare Collins, University of Newcastle, Australia; Vanessa Johnson, University of Newcastle, Australia; Tracy Schumacher, University of Newcastle; Lyniece Keogh, University of Newcastle, Australia; Kathryn Sutherland, University of Newcastle, Australia; Adrienne Gordon, The University of Sydney

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Poor Fetoplacental Blood Flow is linked to Lower Kidney Volumes and Increased risk of Prehypertension in Children at 6y
Navin Michael, Singapore Institute for Clinical Sciences; Suresh Anand Sadananthan, Singapore Institute for Clinical Sciences, A*STAR Research Entities; Wen Lun Yuan; Keith Godfrey, Southampton Biomedical Research Centre; Peter David Gluckman; Kok Hian Tan; Johan Gunnar Eriksson; Yap Seng Chong, National University of Singapore; Yung Seng Lee, National University of Singapore; Shiao-Yng Chan, National University of Singapore; Fabian Yap; Lynette Pei Chi Shek; Marielle Fortier; Karen Moritz, The University of Queensland; Sendhil Velan; Mary Wlodek, The University of Melbourne
Preconception Lifestyle Intervention in Obese Women Improves Echocardiographic Indices of Cardiovascular Function in Their Offspring: Follow Up of a Randomised Controlled Trial
Tamara den Harink, Amsterdam UMC

Early Interventions and Child Outcomes
Tue, October 22
2:00 PM - 3:45 PM
Session Chairs
Co-Chair **Kimberley Botting**, University of Cambridge, United Kingdom
Presentations
INVITED SPEAKER PRESENTATION: Linking the Nurturing Care Framework to DOHaD
Stephen Lye, Lunenfeld-Tanenbaum Research Institute
INVITED SPEAKER PRESENTATION: The Nurturing Care Framework: Science and Implementation
Linda Richter, University of the Witwatersrand
INVITED SPEAKER PRESENTATION: Treating Perinatal Depression and Mother-Infant Difficulties – Impact on Child Development.
Jeannette Milgrom, Melbourne School of Psychological Sciences, University of Melbourne and Parent-Infant Research Institute, Austin Health; Charlene Holt, Parent-Infant Research Institute; Alan Gemmill, Parent-Infant Research Institute; Jennifer Ericksen, Parent-Infant Research Institute
Early LifeLab: Capitalising on UK Government Policy Initiatives to Support an Educational Intervention for Primary Schools
Hannah Davey, LifeLab, University of Southampton; Mary Barker, University of Southampton, United Kingdom; Janice Griffiths, Education School, University of Southampton; Marcus Grace, School of Education, University of Southampton; Keith Godfrey, Southampton Biomedical Research Centre; Mark A. Hanson, University of Southampton; Hazel Inskip; Kathryn S. Woods-Townsend, University of Southampton; Andri Christodoulou, Southampton Education School; Gareth Giles, Public Policy, University of Southampton
A Health Promotion Intervention Targeting Women With Prior Gestational Diabetes Mellitus and Their Families: Results From the Intervention Development Phase. The Face It Study
Helle Terkildsen Maindal, Aarhus University

Early Life Origins of Food Allergy
Tue, October 22
2:00 PM - 3:45 PM
Presentations
INVITED SPEAKER PRESENTATION: Early Life Immune Origins of Food Allergy
Melanie Neeland, Murdoch Children's Research Institute
INVITED SPEAKER PRESENTATION: Role for Early Exposure to Respiratory Allergen in Food Allergy Risk
Valerie Verhasselt, University of Western Australia
Maternal Dietary Fibre Intake During Pregnancy Is Associated With Infant Allergic Disease.
Rachelle Pretorius, University of Western Australia; Susan Prescott, The University of Western Australia; Debra Palmer, The University of Western Australia
Breastfeeding and Food Allergy in Infants - Findings from the Maternal and Infant Cohort Study (MICOS) Malaysia
Fui Chee Woon, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; Yit Siew Chin, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; Ismail Intan Hakimah; Yoke Mun Chan, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; Amir Hamzah AL; Wan Ying Gan, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; geeta Appannah, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; Marijka batterham
Late Preterm Birth Protects Against Allergies in Adulthood
Pieta Näsänen-Gilmore, National Institute for Health and Welfare; Marika Sipola, University of Oulu; Marjaana Tikanmäki, National Institute for Health and Welfare; Hanna-Maria Matinolli, National Institute for Helath and welfare; Johan Eriksson, National Institute for Health and Welfare; Marja Vääräsmäki, University of Oulu; Marjo-Riitta Jarvelin, Department of

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Epidemiology and Biostatistics, Imperial College London; Petteri Hovi, National Institute for Health and Welfare; Eero Kajantie, National Institute for Health and Welfare

Paternal Exposures and Offspring Health

Tue, October 22
2:00 PM - 3:45 PM

Session Chairs

Chair **Rebecca Simmons**, Perelman School of Medicine, University of Pennsylvania, United States
Co-Chair **Yuk Jing (Jane) Loke**, Murdoch Children's Research Institute, Royal Children's Hospital, Australia

Presentations

INVITED SPEAKER PRESENTATION: Novel Insights into the Paternal Role in DOHaD
Sarah Robertson, The University of Adelaide

INVITED SPEAKER PRESENTATION: POHaD: Paternal Origins of Health and Disease
Adelheid Soubry, KU Leuven

INVITED SPEAKER PRESENTATION: Father's Lasting Influence: Molecular Foundations of Intergenerational Transmission of the Paternal Environment
Janice L. Bailey, Université Laval

Prenatal Glucocorticoid Exposure Modifies Germ Cell MicroRNA Expression in Adult Male Offspring Across 3 Generations: Paternal Transmission
Hirotaka Hamada, University of Toronto; Vasilis Moisiadis, University of Toronto; Andrea Constantinof, University of Toronto; Alisa Kostaki, University of Toronto; Stephen Matthews, University of Toronto

Paternal miR-146a Regulation of Female Immune Receptivity and Fetal Viability in Mice
Hon Yeung (Dexter) Chan, Robinson Research Institute & Adelaide Medical School, University of Adelaide

The Impact of Paternal Diet and Methyl-Donor Supplementation on Fetal Growth and Placental Development
Hannah Morgan, Division of Child Health, Obstetrics & Gynaecology, University of Nottingham; Adam Watkins, Department of Child Health, Obstetrics & Gynaecology, University of Nottingham

Reproductive Health and DOHaD

Tue, October 22
2:00 PM - 3:45 PM

Presentations

INVITED SPEAKER PRESENTATION: Novel DOHaD Reproductive Research
Rebecca Robker, Robinson Research Institute, University of Adelaide

INVITED SPEAKER PRESENTATION: Fertility and Infertility: An African Perspective
Zephne van der Spuy , University of Capetown

INVITED SPEAKER PRESENTATION: Assisted Reproductive Technologies: Epigenetic Impacts and Long-Term Outcomes
Marisa Bartolomei, Perelman School of Medicine, University of Pennsylvania

Significant Differences In First Trimester Embryonic Growth Trajectories After Fresh and Frozen-thawed Embryo Transfer
Jeffrey Hoek, Erasmus Medical Center, Rotterdam; Linette van Duijn, Erasmus Medical Center; Sam Schoenmakers, Erasmus Medical Center; Esther Baart, Erasmus Medical Center; Eric Steegers, Department of Obstetrics and Gynaecology, Erasmus Medical Centre, University Medical Centre; Joop Laven, Erasmus Medical Center; Melek Rousian, Erasmus Medical Center; Regine Steegers-Theunissen, Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Centre, University Medical Centre

Oocyte Exposure to High Estradiol During Ovarian Stimulation and Risk of Adverse Perinatal Outcomes After Frozen-Thawed Embryo Transfer: A Retrospective Cohort Study
Cheng Li, International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University; Yan-Ting Wu, International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University; He-Feng Huang, International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University; Chen-Chi Duan, International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University

Prenatal Androgen Excess Affects Ovarian Function, PPARG and Chemerin Systems
Giselle Adriana Abruzzese, Laboratorio de Fisio-patología ovárica, CEFYBO, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina.; Maria Florencia Heber, Laboratorio de Fisio-patología ovárica, CEFYBO, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina.; Maria Jose Ferrer; Silvana Rocio Ferreira, Laboratorio de Fisio-patología ovárica, CEFYBO, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina.; Alicia Beatriz Motta, Laboratorio de Fisio-patología ovárica, CEFYBO, CONICET, Universidad de Buenos Aires, Buenos Aires, Argentina.

Role of Exercise in Developmental Programming

Tue, October 22

2:00 PM - 3:45 PM

Session Chairs

Co-Chair **Jessica Griffith**, The University of Melbourne, Australia

Presentations

INVITED SPEAKER PRESENTATION: Epigenetic Reprogramming of Muscle and Spermatozoa after Exercise

Romain Barrès, University of Copenhagen

INVITED SPEAKER PRESENTATION: Exercise in Pregnancy

Chen Wang, Peking University First Hospital, Beijing

INVITED SPEAKER PRESENTATION: Exercise Trials to Prevent GDM

Niamh Daly, University College, Dublin

DOHaD and Exercise: Physical Activity as a Tool in the Programming/Deprogramming Paradox

Douglas Lopes Almeida, Laboratory of Cellular Secretion Biology, Department of Biotechnology, Cell Biology and Genetics, State University of Maringá, Maringá/PR, Brazil; James Andrew Armitage, Deakin University; Kesia Palma-Rigo, Universidade Estadual de Maringá; Paulo Mathias, Department of Biotechnology, Genetics and Cellular Biology

Paternal Obesity Causes Bone Deficits Which Are Reprogrammed by Exercise Early in Life

Filippe Falcao-Tebas, The Ritchie Centre, Hudson Institute of Medical Research and Department of Obstetrics and Gynaecology, Monash University; Evelyn Marin, Department of Medicine (Austin Health), The University of Melbourne; Glenn McConell; Tania Romano

DNA Methylation in AgRP Neurons Regulates Voluntary Exercise Behaviour.

Harry MacKay, Baylor College of Medicine; Anthony Scott, Baylor College of Medicine; Jack Duryea, Baylor College of Medicine; Maria Baker, Baylor College of Medicine; Eleonora Laritsky, Baylor College of Medicine; Amanda Elson, Vanderbilt University; Theodore Garland, University of California Riverside; Marta Fiorotto, Baylor College of Medicine; Rui Chen, Baylor College of Medicine; Yumei Li, Baylor College of Medicine; Cristian Coarfa, Baylor College of Medicine; Richard Simerly, Vanderbilt University; Rob Waterland, Baylor College of Medicine

Complex Interventions Across the Lifespan

Wed, October 23

11:00 AM - 12:45 AM

Presentations

INVITED SPEAKER PRESENTATION: Evaluating Complex Diet and Lifestyle Interventions – Why Are We Not Seeing the Expected Outcomes?

Jodie Dodd, University of Adelaide

INVITED SPEAKER PRESENTATION: Evaluating DOHAD Interventions in an Integrated Paediatric Care Setting

Mitch Blair, Imperial College, London

Breaking Cycles: Simulating the Effects of Potential Interventions to Break the Ties Between Maternal Overweight and Child Adiposity via TMLE and Cross-Validated Machine Learning.

Jonathan Huang, Singapore Institute for Clinical Sciences; Evelyn Law, National University of Singapore; Tint Mya Thway, National University of Singapore; Izzuddin Bin Mohd Aris; Wen Lun Yuan; Mary Chong, Singapore Institute for Clinical Sciences; Keith Godfrey, Southampton Biomedical Research Centre; Yap Seng Chong, National University of Singapore; Johan Gunnar Eriksson; Neerja Karnani, Singapore Institute for Clinical Sciences, A*STAR; Yung Seng Lee, National University of Singapore

Effect of Maternal Preconceptional and Pregnancy Micronutrient Interventions on Children's DNA Methylation: Findings From the EMPHASIS Study

Issarapu Prachand, CSIR-Centre for Cellular and Molecular Biology (CSIR-CCMB), Hyderabad

Effects of Telephone Support or Short Message Service on Infant Feeding Practices: Findings From a 3-Arm Randomised Controlled Trial (RCT) at 6 and 12 Months

Li Ming Wen, School of Public Health, University of Sydney & Population Health, SLHD

Effects of Prenatal Lifestyle Counselling on Diet and Physical Activity in the Cluster-Randomised Controlled GeliS ("Gesund Leben in Der Schwangerschaft"/Healthy Living in Pregnancy) Trial

Julia Hoffmann, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Julia Katharina Günther, Technical University of Munich, Klinikum rechts der Isar; Julia Kunath, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Kathrin Rauh, Competence Centre for Nutrition; Lynne Stecher, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Eva Rosenfeld, Competence Centre for Nutrition; Luzia Kick, Competence Centre for Nutrition; Kristina Geyer, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Monika Spies, Else

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Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Dorothy Meyer, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich; Hans Hauner, Else Kröner-Fresenius-Centre for Nutritional Medicine, Klinikum rechts der Isar, Technical University of Munich

Hidden Hungers of Camden: A Pilot Intervention Unraveling the Double Burden of Malnutrition among Ethnic Minority Women Living in Deprivation

Charmaine Browne, University of Westminster

A Low-Intensity Intervention Increases Rates of Weight-Monitoring and Health Professionals' Confidence to Provide Weight Management Advice in Routine Maternity Care

Ruth Walker, Monash University; Arunaz Kumar, Monash University; Cate Bailey, MCHRI; Michelle Blumfield; Christie Bennett; Helen Truby, Monash University; Ryan Hodges, Monash Health

Effect of Placental Treatment with a Mitochondria-Targeted Antioxidant (nMitoQ) on Cardiac Function in Adult Offspring Exposed to Prenatal Hypoxia

Nataliia Hula, University of Alberta; Anita Quon, University of Alberta; Raven Kirschenman, University of Alberta; Christy-Lynn Cooke, University of Alberta; Thomas Phillips, University of Alberta; Patrick Case, University of Bristol; Floor Spaans, University of Alberta; Sandra Davidge, University of Alberta

Longitudinal Genome-Wide Association Study of Pediatric Bone Accrual Highlights Links Between Pediatric Bone Gain and Later-Life Fracture Risk

Diana Cousminer, Children's Hospital of Philadelphia; Shana McCormack, Childrens Hospital of Philadephia; Gregory Way, University of Pennsylvania; Alessandra Chesi, Childrens Hospital of Philadephia; Jonathan Mitchell, Childrens Hospital of Philadephia; Joseph Kindler, Childrens Hospital of Philadephia; Heidi Kalkwarf, Cincinnati Children's Hospital; Joan Lappe, Creighton University; Hakon Hakonarson, Childrens Hospital of Philadephia; Kurt Hankenson, University of Michigan; Vicente Gilsanz, Children's Hospital of Los Angeles; John Shepherd, University of Hawaii; Sharon Oberfield, Columbia University; Casey Greene, University of Pennsylvania; Benjamin Voight, University of Pennsylvania; Babette Zemel, Children's Hospital of Philadelphia; Struan Grant, Children's Hospital of Philadelphia

Early Life Origins of Mental Health and Well Being

Wed, October 23

11:00 AM - 12:45 AM

Session Chairs

Chair **Mary Barker**, University of Southampton, United Kingdom, United Kingdom

Co-Chair **Sofia Strommer**, Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, United Kingdom

Presentations

INVITED SPEAKER PRESENTATION: Continuities of Maternal and Paternal Emotional Health Problems From Preconception to Parenthood

Kimberly Thomson, University of British Columbia

INVITED SPEAKER PRESENTATION: Maternal Immune Activation and Brain Development

Deirdre Murray, Cork University Hospital

Growth Trajectories of the Prenatal Human Brain and Neurodevelopmental Outcome at 2 Years of Age

Mila Welling; Sofie Husen, Erasmus MC; Hilmar Bijma; Attie Go; Irene Groenenberg; Sten Willemsen, Erasmus Medical Center; Regine Steegers-Theunissen, Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Centre, University Medical Centre

Developmental Origins of Neurocognitive Performance in Young Adults of the Pune Maternal Nutrition Study (PMNS) Cohort

Rishikesh Behere, Diabetes unit, KEM Hospital Research Center; Veena Kamble, KEMHRC; Sarah Khan, Diabetes unit, KEMHRC; Chittaranjan Yajnik, Diabetes Unit, KEM Hospital Research Centre, Pune, India

Exploring Dynamic Complementarity Between High-Quality Nurse Home Visiting and Early Childhood Education and Care on Child Developmental Outcomes at 3 Years

Huu Nghia Joey Nguyen, Murdoch Children's Research Institute; Anna Price, Murdoch Children's Research Institute; Sharon Goldfeld, Murdoch Children's Research Institute

Anthropometry at Term Age is More Related With Developmental Quotient Score than Anthropometry at Birth in Preterm-born Children

Ahmad Suryawan, Department of Child Health, Soetomo Hospital/Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; Lisa Pangemanan, Universitas Airlangga, Surabaya, Indonesia; Nia Nurul Aziza, Universitas Airlangga, Surabaya, Indonesia; Andri Kurnia Wahyudhi, Universitas Airlangga, Surabaya, Indonesia

Can Childhood Mental Health and Social Outcomes be Predicted at Birth?

Vaughan Carr, University of New South Wales

Exposure to Socioeconomic Disadvantage From Birth to 32 Years and Mental Health Outcomes

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Meredith O'Connor, Murdoch Children's Research Institute and Australian National University; Shuaijun Guo, Murdoch Children's Research Institute; Sharon Goldfeld, Murdoch Children's Research Institute; Craig Olsson, Murdoch Children's Research Institute

Neonatal Vitamin D Levels and Cognitive Ability in Young Adulthood

Ina Olmer Specht, Bispebjerg og Frederiksberg Hospital; Janet Janbek, Danish Dementia Research Centre, Department of Neurology, The Neuroscience Centre, Rigshospitalet and The Research Unit for General Practice, Section of General Practice, Institute of Public Health, University Copenhagen; Fanney Thorsteinsdottir, Research Unit for Dietary Studies, The Parker Institute, Bispebjerg og Frederiksberg Hospital; Peder Frederiksen, Bispebjerg og Frederiksberg Hospital; Berit Lilienthal Heitmann, Bispebjerg og Frederiksberg Hospital

What 'Dose' of Physical Activity in the Toddler Years Predicts Health and Developmental Outcomes in the Preschool Years?

Jill Hnatiuk, Deakin University; Miaobing Zheng, Deakin University; Gavin Abbott; Lisa Barnett, Deakin University; Jo Salmon, Deakin University; Kylie Hesketh, Deakin University

The Role of Adrenal Morphology in High Fat Diet-Induced Anxiety in Mature Adult Mice

Noriko Ogawa, Department of Developmental Biology, Shimane University Faculty of Medicine; Aisha M Rasool, Institute of Developmental Sciences, University of Southampton Faculty of Medicine; Marion J Head, Institute of Developmental Sciences, University of Southampton Faculty of Medicine; Jessica L Teeling, 3Biological Sciences, Faculty of Environmental and Life Sciences, University of Southampton; Felino R Cagampang, Institute of Developmental Sciences, University of Southampton Faculty of Medicine; Lucy Green, University of Southampton; Kirsten Poore, Institute of Developmental Sciences, Faculty of Medicine, University of Southampton

Environment, Epigenetics and Cancer

Wed, October 23

11:00 AM - 12:45 AM

Session Chairs

Chair **Rob Waterland**, Baylor College of Medicine, United States

Co-Chair **Elie Antoun**, Faculty of Medicine, University of Southampton, United Kingdom

Presentations

INVITED SPEAKER PRESENTATION: Early Environmental Origins of Cancer

Joe Wiemels, University of Southern Carlifornia

INVITED SPEAKER PRESENTATION: Developmental Origins of Childhood Cancer: Research Gaps and Opportunities

Terence Dwyer, Murdoch Children's Research Institute

Maternal Obesity Drives Differential DNA Methylation in Neonatal Monocytes in a Sex-Specific Manner

Fabian Vega; Rocio Artigas, Pontificia Universidad Católica de Chile; Cherie Hernandez; Ricardo Uauy, Pontificia Universidad Católica de Chile; Paola Casanello, Pontificia Universidad Católica de Chile; Jose Antonio Castro-Rodriguez, Pontificia Universidad Católica de Chile; Bernardo J. Krause, Pontificia Universidad Católica de Chile

Methylation Marks Associated With Prenatal Smoke Exposure and Risk of Cancer in Adulthood

Pierre-Antoine Dugue, Monash University; JiHoon Joo; Chol-Hee Jung, Melbourne Bioinformatics; Ming Wong, Monash University; Allison Hodge, Cancer Council Victoria; Dallas English, Cancer Council Victoria; John Hopper, University of Melbourne; Roger Milne, Cancer Council Victoria; Graham Giles, Cancer Council Victoria; Melissa Southey, Monash University

Maternal High-Fructose Corn Syrup Consumption Modulates Brain-Derived Neurotrophic Factor Expression Through Epigenetic Modification in Offspring Hippocampus

Mirai Yamazaki, Fujita Health University

Comparison of Genome-Wide DNA Methylation Between Low Birth Weight and Normal Birth Weight Term Infants without Maternal Complications and Smoking

Ikuyo Hayashi, University of Hyogo; Ken Yamaguchi, Obstetrics and Gynecology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan; Narumi Nagai, aboratory of Nutritional Physiology, Graduate School of Human and Environmental Science, University of Hyogo; Naoki Sakane, Division of Preventive Medicine, Clinical Research Institute for Endocrine and Metabolic Disease, National Hospital Organization, Kyoto Medical Center

Programming Across Generation Through Mitochondria DNA Methylation

Marc André Sirard, Universite Laval

A Maternal High Fat Diet Is Associated With microRNA Expression Changes in the Prostate of Male Rat Offspring

Karen Kind, University of Adelaide; Carlos Rodriguez Lopez, University of Kentucky; Karen Chiam; Natalie Ryan; Sam Buckberry; Catriona McLean; Shalini Jindal; Simon Moretta; Miles De Blaso; Himawan Harryanto; Kathryn Gatford, The University of Adelaide; Lisa Butler; Wayne Tilley; Julie Owens; Tina Bianco-Miotto, University of Adelaide

Paternal Consumption of an Obesogenic Diet and Orange Juice During Preconception Influence Mice Female Offspring Breast Cancer Risk

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Lívia Beatriz A. Ribeiro Silva, University of São Paulo; Natalia Pinheiro-Castro; Caroline de Aquino Guerreiro, University of São Paulo; Vanessa Cardoso Pires; Walter Miguel Turato, University of São Paulo; Luis Barbisan; Neuza Mariko Aymoto Hassimotto; Franco Maria Lajolo, São Paulo University; Thomas Prates Ong, University of São Paulo

Maternal High Fat Diet-Induced Obesity Modulates Sexually Dimorphic Epigenetic Regulation and Expression of Lepr in Offspring Hippocampus During Development

Kelly Glendining, University of Otago

Early Life Factors in Relation to the Incidence and Prognosis of Cancer in Two Swedish Cohorts

Shantanu Sharma, Lund University; Peter Nilsson, Lund University

Environment, Epigenetics and Cancer

Wed, October 23
11:00 AM - 12:45 AM

Session Chairs

Chair **Rob Waterland**, Baylor College of Medicine, United States
Co-Chair **Elie Antoun**, Faculty of Medicine, University of Southampton, United Kingdom

Presentations

INVITED SPEAKER PRESENTATION: Early Environmental Origins of Cancer

Joe Wiemels, University of Southern Carlifornia

INVITED SPEAKER PRESENTATION: Developmental Origins of Childhood Cancer: Research Gaps and Opportunities

Terence Dwyer, Murdoch Children's Research Institute

Maternal Obesity Drives Differential DNA Methylation in Neonatal Monocytes in a Sex-Specific Manner

Fabian Vega; Rocio Artigas, Pontificia Universidad Católica de Chile; Cherie Hernandez; Ricardo Uauy, Pontificia Universidad Católica de Chile; Paola Casanello, Pontificia Universidad Católica de Chile; Jose Antonio Castro-Rodriguez, Pontificia Universidad Católica de Chile; Bernardo J. Krause, Pontificia Universidad Católica de Chile

Methylation Marks Associated With Prenatal Smoke Exposure and Risk of Cancer in Adulthood

Pierre-Antoine Dugue, Monash University; JiHoon Joo; Chol-Hee Jung, Melbourne Bioinformatics; Ming Wong, Monash University; Allison Hodge, Cancer Council Victoria; Dallas English, Cancer Council Victoria; John Hopper, University of Melbourne; Roger Milne, Cancer Council Victoria; Graham Giles, Cancer Council Victoria; Melissa Southey, Monash University

Maternal High-Fructose Corn Syrup Consumption Modulates Brain-Derived Neurotrophic Factor Expression Through Epigenetic Modification in Offspring Hippocampus

Mirai Yamazaki, Fujita Health University

Comparison of Genome-Wide DNA Methylation Between Low Birth Weight and Normal Birth Weight Term Infants without Maternal Complications and Smoking

Ikuyo Hayashi, University of Hyogo; Ken Yamaguchi, Obstetrics and Gynecology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan; Narumi Nagai, aboratory of Nutritional Physiology, Graduate School of Human and Environmental Science, University of Hyogo; Naoki Sakane, Division of Preventive Medicine, Clinical Research Institute for Endocrine and Metabolic Disease, National Hospital Organization, Kyoto Medical Center

Programming Across Generation Through Mitochondria DNA Methylation

Marc André Sirard, Universite Laval

A Maternal High Fat Diet Is Associated With microRNA Expression Changes in the Prostate of Male Rat Offspring

Karen Kind, University of Adelaide; Carlos Rodriguez Lopez, University of Kentucky; Karen Chiam; Natalie Ryan; Sam Buckberry; Catriona McLean; Shalini Jindal; Simon Moretta; Miles De Blaso; Himawan Harryanto; Kathryn Gatford, The University of Adelaide; Lisa Butler; Wayne Tilley; Julie Owens; Tina Bianco-Miotto, University of Adelaide

Paternal Consumption of an Obesogenic Diet and Orange Juice During Preconception Influence Mice Female Offspring Breast Cancer Risk

Lívia Beatriz A. Ribeiro Silva, University of São Paulo; Natalia Pinheiro-Castro; Caroline de Aquino Guerreiro, University of São Paulo; Vanessa Cardoso Pires; Walter Miguel Turato, University of São Paulo; Luis Barbisan; Neuza Mariko Aymoto Hassimotto; Franco Maria Lajolo, São Paulo University; Thomas Prates Ong, University of São Paulo

Maternal High Fat Diet-Induced Obesity Modulates Sexually Dimorphic Epigenetic Regulation and Expression of Lepr in Offspring Hippocampus During Development

Kelly Glendining, University of Otago

Early Life Factors in Relation to the Incidence and Prognosis of Cancer in Two Swedish Cohorts

Shantanu Sharma, Lund University; Peter Nilsson, Lund University

Microbiome and DOHaD

Wed, October 23
11:00 AM - 12:45 AM

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Session Chairs
Co-Chair **Evelyn Loo**, Singapore Institute for Clinical Sciences, A*STAR, Singapore
Presentations
INVITED SPEAKER PRESENTATION: Novel Insights into DOHaD and Microbiome
Geraint Rogers, South Australian Health and Medical Research Institute
INVITED SPEAKER PRESENTATION: Early Life Microbiome
Tommi Vatanen, Liggins Institute, University of Auckland
Beyond Caesarean Birth: Impact of Prolonged Labour on Infant Gut Microbiota
Ngoc Khanh Vu, University of Alberta
The Vaginal Microbiome As Predictor For In Vitro Fertilization With Or Without Intracytoplasmic Sperm Injection Outcome; the ReceptIVFity-study
Rivka Koedooder, Erasmus University Medical Center; Martin Singer; Sam Schoenmakers, Erasmus Medical Center; Paul Savelkoul; Servaas Morré; Jonathan de Jonge; Linda Poort; Andries Budding; Joop Laven, Erasmus Medical Center
Ethnic Diversity Among The Key Factors Influencing The Development Of Human Gut Microbiota
Jia Xu, Singapore Institute for Clinical Sciences, A*STAR; Blair Lawley; Gerard Kum Peng Wong, Singapore Institute for Clinical Sciences; Anna Otal; Jia Ying Toh, Singapore Institute for Clinical Sciences; Li Chen, Singapore Institute for Clinical Sciences; Xinyi Lin, Singapore Institute for Clinical Sciences; Wei Wei Pang, National University of Singapore; Yap Seng Chong, National University of Singapore; Peter David Gluckman; Yung Seng Lee, National University of Singapore; Mary Chong, Singapore Institute for Clinical Sciences; Gerald Tannock; Neerja Karnani, Singapore Institute for Clinical Sciences, A*STAR
The Not-So-Sterile Womb: Evidence That the Human Fetus Is Exposed to Bacteria Prior to Birth
Lisa Faye Stinson, University of Western Australia; Matthew S. Payne, University of Western Australia; Jeffrey A. Keelan, University of Western Australia
Caesarean Section and Childhood Hospitalisation With Infection: An International Study of 7.3 Million Births
Jessica Miller, Murdoch Childrens Research Institute; David Burgner, Murdoch Childrens Research Institute; Natasha Nassar, Children's Hospital at Westmead Clinical School; Justin Zeltzer, Children's Hospital at Westmead Clinical School; Rachel Wood, NHS National Services Scotland; Raph Goldacre, Nuffield Department of Population Health; Marian Knight, Nuffield Department of Population Health; Carole Morris, NHS National Services Scotland; Sian Nowell, NHS National Services Scotland; Hannah Moore, Wesfarmers Centre of Vaccines and Infectious Diseases; Parveen Fathima, Wesfarmers Centre of Vaccines and Infectious Diseases; Kim Carter, Wesfarmers Centre of Vaccines and Infectious Diseases; Nicholas de Klerk, Wesfarmers Centre of Vaccines and Infectious Diseases; Tobias Strunk, University of Western Australia; Jiong Li, Department of Clinical Epidemiology; Lars Pedersen, Department of Clinical Medicine
A Comparison of DNA Extraction Methods for Human Milk Microbiome Studies
Ali Sadiq Cheema, The University of Western Australia; Donna Geddes, The University of Western Australia; Matthew S. Payne, University of Western Australia; Ching Tat Lai, The University of Western Australia; Lisa Faye Stinson, University of Western Australia
Diversity of the Prenatal Faecal Microbiota and Offspring Behaviour: A Birth Cohort Study
Samantha Dawson, Deakin University; Martin O'Hely; Anne-Louise Ponsonby; Christos Symeonides, Murdoch Childrens Research Institute; Richard /. Saffery, MCRI; Mimi Tang, Murdoch Children's Research Institute; Peter Sly, University of Qld; Sarath Ranganathan, MCRI; Felice Jacka; Peter Vuillermin
Dynamic Profile of Gut Microbiota in Gestational Diabetes Mellitus With Monotherapy of Dietary Intervention
Shengtang Qin, Peking University First Hospital; Yu Liu; Ma jingmei; Baoli Zhu; Hui-xia Yang, Peking University Health Science Centre, China
Gut Metagenomic Analysis of Pregnant Women in the Third Trimester Reveals Gestational Diabetes Mellitus Related Microbial Regulators of Glucose Tolerance
Haitian Chen, Sun Yat-sen University

Placental Research in DOHaD
Wed, October 23
11:00 AM - 12:45 AM
Session Chairs
Chair **Hiroaki Itoh**, Hamamatsu University School of Medicine, Japan
Co-Chair **Hannah Morgan**, Division of Child Health, Obstetrics & Gynaecology, University of Nottingham, United Kingdom
Presentations
INVITED SPEAKER PRESENTATION: Environmental and Genetic Control of Placental Function and Impact on Fetal Development and Maternal Health
Amanda Sferruzzi-Perri, University of Cambridge
INVITED SPEAKER PRESENTATION: DOHaD Interventions Aimed at Placenta: Tweaking Endophenotypes

https://doi.org/10.1017/S2040174419000643 Published online by Cambridge University Press

Shiao-Yng Chan, National University of Singapore

Effect of Maternal Omega-3 Fatty Acid and Vitamin E Supplementation on Placental Angiogenic Factors in Subtypes of Preeclampsia

Vaishali Kasture, Interactive Research School for Health Affairs, Bharati Vidyapeeth, Pune, India

Placental Transfer and Effects of Sildenafil on the Human Placenta, an Ex Vivo Dual-sided Perfusion Study

Emilie Hitzerd, Erasmus MC; Michelle Broekhuizen; Katrina Mirabito Colafella, Erasmuc MC, Monash University; Birgit Koch, Erasmus MC; Daphne Merkus, Erasmus MC; Sam Schoenmakers, Erasmus Medical Center; Irwin Reiss, Erasmus MC; Jan Danser; Sinno Simons, Erasmus MC

Placental 11β-HSD2 and Cardiometabolic Health Indicators in Infancy

Zhong-Cheng Luo, Mount Sinai Hospital, University of Toronto

Nanoparticle-Encapsulated Antioxidant Delivery Improves Placental Nitrosative Stress and Morphology in a Sex-Specific Manner in a Rat Model of Fetal Hypoxia

Esha Ganguly, University of Alberta; Mais Aljunaidy, University of Alberta; Raven Kirschenman, University of Alberta; Floor Spaans, University of Alberta; Jude Morton, University of Alberta; Thomas Phillips, University of Alberta; Patrick Case, University of Bristol; Christy-Lynn Cooke, University of Alberta; Sandra Davidge, University of Alberta

Early Placental Growth and Utero-Placental Vascularization Assessment using Virtual Reality: Reference Values and Associations with Embryonic Growth

Annemarie Mulders, Erasmus Medical Centre, University Medical Centre; Igna Reijnders, Department of Obstetrics and Gynaecology, Erasmus Medical Centre, University Medical Centre; Wendy Koster, Erasmus Medical Center; Anton Koning, Erasmus MC, University Medical Center Rotterdam, the Netherlands; Sten Willemsen, Erasmus Medical Center; Melek Rousian, Erasmus Medical Center; Eric Steegers, Department of Obstetrics and Gynaecology, Erasmus Medical Centre, University Medical Centre; Regine Steegers-Theunissen, Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Centre, University Medical Centre

Down-Regulated Expression of microRNA-1227 in Placenta and Its Role in Fetal Growth Restriction Through Target Gene PRKAB2

Chen Liping, Second Affiliated Hospital of Nantong University

Placental Structure Is Affected by Maternal Obesity, Which Is Not Reversed by Metformin-Treatment

Antonia Hufnagel, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Josca Schoonejans, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Denise Fernandez-Twinn, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Heather Blackmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Thomas Ashmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Phoebe Wilsmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Susan Ozanne, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Catherine Aiken

Maternal and Birth Determinants of Endometriosis: A Nationwide Birth Cohort Study

Menghan Gao, Karolinska Institutet

Prenatal Endotoxemia Induces Selective Alteration in the Expression of ABC Transporters in the Mouse Yolk Sac

Lilian M Martinelli; Mila W Reginatto; Klaus N Fontes; Victoria R. S. Monteiro, Universidade Federal do Rio de Janeiro; Cherley B V Andrade; Annamaria R. Vago; Fernanda R.C.L. Almeida,; Patricia M Martinelli; Flavia F Bloise; Stephen Matthews, University of Toronto; Tania M Ortiga-Carvalho, Universidade Federal do RIo de Janeiro; Enrrico Bloise, UFMG

Sex Differences in Programming of Cardiometabolic Diseases

Wed, October 23

11:00 AM - 12:45 AM

Session Chairs

Chair **Kent Thornburg**, Oregon Health & Science University, United States

Co-Chair **James Cuffe**, The University of Queensland, Australia

Presentations

INVITED SPEAKER PRESENTATION: Sex-Specific Mechanisms of Cardiovascular Programming

Elena Zambrano, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

INVITED SPEAKER PRESENTATION: Sex-Specific Differences in Cardiovascular Programming in Non Human Primates

Geoff Clarke, University of Texas Health Science Center San Antonio

Fetal Crown-Rump Length Is Associated With Maternal Thyroid Function in Early Pregnancy, Particularly in Male Fetuses

Yong Zhang, International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, China

Placental Endocrine Malfunction Exacerbates Metabolic Response to Postnatal Obesogenic Challenge in Male Murine Offspring, but Not Female Offspring

Hannah Yong, Singapore Institute for Clinical Sciences; Jorge Lopez-Tello; Sercan Güloğlu; Efthimia Christoforou, University of Cambridge; Ionel Sandovici, University of Cambridge; Miguel Constancia; Amanda Sferruzzi-Perri, University of Cambridge

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Regulatory T Cell Deficiency Increases Resistance to Blood Flow in Mid- and Late Gestation, Leading to Growth Restriction in Male and Female Fetuses
Alison Care, The University of Adelaide
Fetal Sex and Associations With Cord Metabolic Markers and Fetal Adiposity in the Pregnancy and Adverse Neonatal Diabetes Outcomes in Remote Australia (PANDORA) Study
Federica Barzi, Menzies School of Health Research
Maternal Obesity During Pregnancy Alters Placental Structure in Mid and Late Gestation and Has Sex-Specific Effects on Labyrinth Zone Structure
Phoebe Wilsmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Daniela de Barros Mucci, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Laura Kusinski, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Thomas Ashmore, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Denise Fernandez-Twinn, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit; Susan Ozanne, University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit
Sex-Specific Effects of Prenatal Maternal Stress on Hair Copper Levels and its Association with Vocabulary Scores in 4-Year Old Children: The QF2011 Queensland Flood Study
Mirela Ambeskovic, University of Lethbridge; David Laplante, Douglas Mental Health University Institute; Thomas Kenney, University of Lethbridge; Guillaume Elgbeili, McGill University, Douglas Mental Health University Institute; Pierre Beaumier, Canalt Health Labs; Nagy Azat, Canalt Health Labs; Gabrielle Simcock, Mater Research Institute University of Queensland (MRI-UQ); Sue Kildea, Mater Research Institute University of Queensland (MRI-UQ); Suzanne King, McGill, Douglas Mental Health University Institute; Gerlinde Metz, University of Lethbridge
Testosterone Increases the Expression of the Placental Fatty Acid Transporter FAT / CD36 and the Transcription Factor PPARG
Macarena Ortiz, University of Chile; Daniela Álvarez, University of Chile; Cristian Flores, Universidad de Chile; Manuel Maliqueo, University of Chile
Prenatal Alcohol Exposure Programs Offspring Disease: Sex-Specific Impacts on Glucose Metabolism in a Rat Model of Moderate, Acute Exposure
Lisa K. Akison, The University of Queensland

Adolescence as a Critical Window for DOHaD

Wed, October 23
1:30 PM - 3:10 PM
Session Chairs
Chair **Jacquie Bay**, Liggins Institute, Auckland, New Zealand, New Zealand
Co-Chair **Kesia Palma-Rigo**, Universidade Estadual de Maringá, Brazil
Presentations
INVITED SPEAKER PRESENTATION: The Adolescent Foundations of the First 1000 Days
George Patton, Murdoch Children's Research Institute
INVITED SPEAKER PRESENTATION: The Importance of Adolescence in Influencing Health Trajectories: Perspective From Human Studies
Rae-Chi Huang, Telethon Kids Institute
INVITED SPEAKER PRESENTATION: Interrogating the Effect of Biological and Social Exposures During Puberty on Health and Wellbeing in Adulthood
Lauren Houghton, Columbia University in the City of New York
INVITED SPEAKER PRESENTATION: Transforming Adolescent Lives Through Nutrition (TALENT) in LMIC
Caroline Fall, MRC Lifecourse Epidemiology Unit, University of Southampton
INVITED SPEAKER PRESENTATION: Stress in Indian Adolescents: Responses, Perception and Scope for Intervention
Krishnaveni Ghattu, Epidemiology Research Unit, Holdsworth Memorial Hospital,

Breaking Intergenerational Cycles of Adversity

Wed, October 23
1:30 PM - 3:10 PM
Session Chairs
Co-Chair **Tint Mya Thway**, National University of Singapore, Singapore
Presentations
INVITED SPEAKER PRESENTATION: DOHaD Social Determinants of Health and Adversity
Danielle Beatty, University of Maryland

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INVITED SPEAKER PRESENTATION: Nutrition Surveillance in Early Life for Achieving the 2025 Global Target for Stunting
Michele Monroy-Valle, University of Saskatchewan
INVITED SPEAKER PRESENTATION: Pregnancy as a Window of Opportunity to Integrate Medical and Social Care to Battle Adversity
Marije van der Hulst, Department of Obstetrics and Gynecology, Erasmus MC, University Medical Centre Rotterdam
INVITED SPEAKER PRESENTATION: Adverse Child Health in South Asia
Ragha Lingam, University of New South Wales
INVITED SPEAKER PRESENTATION: Improving Health Services for Maternal and Newborn Care in Afghanistan
Karen Edmond, University of Western Australia

Developmental Programming in Non-Mammalian Species
Wed, October 23
1:30 PM - 3:10 PM
Presentations
INVITED SPEAKER PRESENTATION: Sex, Genes and the Environment
Jenny Graves, La Trobe University
INVITED SPEAKER PRESENTATION: Developmental Programming of Sex and Environmental Impacts in Dragons
Arthur Georges, Institute for Applied Ecology
INVITED SPEAKER PRESENTATION: Developmental Programming by Diet in Drosophila
Fumiaki Obata, University of Tokyo
INVITED SPEAKER PRESENTATION: Developmental Programming in Birds
Dino Giussani, University of Cambridge
INVITED SPEAKER PRESENTATION: Zebrafish and Cardiac Development
Kelly Smith, Institute for Molecular Bioscience, University of Queensland

Early Life Origins of Autoimmunity and Inflammation
Wed, October 23
1:30 PM - 3:10 PM
Session Chairs
Chair **Niels Riksen**, Radboud University Medical Center, Netherlands, Netherlands
Co-Chair **Sandra Okala**, King's College London, United Kingdom
Presentations
INVITED SPEAKER PRESENTATION: Early Origins of Innate Immune Responses and Inflammation
Siroon Bekkering, Radboud University Medical Centre
INVITED SPEAKER PRESENTATION: Quantifying Inflammation Across the Life Course
David Burgner, Murdoch Childrens Research Institute
INVITED SPEAKER PRESENTATION: DOHaD Perspectives of Coeliac Disease
Daniel Agardh, Lund University
INVITED SPEAKER PRESENTATION: Early Life Origins of Metabolic Disease and Inflammation – Evidence From Animal Models
Mark Vickers , Liggins Institute
INVITED SPEAKER PRESENTATION: Early Life Origins of Allergy and Asthma – Impact of Vitamin D
Catherine Hawrylowicz, King's College London

Pediatrics from a DOHaD Perspective
Wed, October 23
1:30 PM - 3:10 PM
Session Chairs
Chair **Susan Morton**, The University of Auckland, New Zealand
Co-Chair **Kozeta Miliku**, University of Manitoba, Canada
Presentations
INVITED SPEAKER PRESENTATION: A New Approach to Saving Preterm Babies
Matt Kemp, The University of Western Australia
INVITED SPEAKER PRESENTATION: Novel Paediatric Insights From DOHAD Cohorts
Keith Godfrey, Southampton Biomedical Research Centre
INVITED SPEAKER PRESENTATION: Neonatal Care and Trials to Improve Child Health
Jane Harding, The University of Auckland

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INVITED SPEAKER PRESENTATION: Early Life Determinants of Adiposity: Insights From GUSTO Study
Yung Seng Lee, National University of Singapore
INVITED SPEAKER PRESENTATION: Outcomes Into Adulthood for Infants Born Very Tiny or Very Early
Lex Doyle, University of Melbourne
The Future of Modern DOHaD Birth Cohorts
Wed, October 23
1:30 PM - 3:10 PM
Session Chairs
Chair **Rebecca Reynolds**, University of Edinburgh, United Kingdom
Co-Chair **Senthil Vasan**, Oxford Centre for Diabetes, Endocrinology and Metabolism, United States
Presentations
INVITED SPEAKER PRESENTATION: Child Eating Behaviours, Energy Intake and Impact on Body Composition in the GUSTO Cohort
Ciaran Forde, Clinical Nutrition Research Center, Singapore Institute for Clinical Sciences
INVITED SPEAKER PRESENTATION: Power of Large Birth Cohorts to Identify Key Exposures in Pregnancy That Programme Offspring Health: The Born in Guangzhou Cohort Study (BIGCS)
Xiu Qiu, Guangzhou Women and Children's Medical Center
INVITED SPEAKER PRESENTATION: Neurodevelopmental Trajectories During Infancy Are Divided Into Five Classes: Hamamatsu Birth Cohort for Mothers and Children (HBC Study)
Kenji Tsuchiya, Hamamatsu University School of Medicine, Research Center for Child Mental Development
INVITED SPEAKER PRESENTATION: HeLTI Cohort and DOHaD Implications
Cindy-Lee Dennis, University of Toronto
INVITED SPEAKER PRESENTATION: Doing Things Differently: Harnessing Population Based Data, Biospecimens and Early Life Phenotyping to Improve Child Health-Generation Victoria
Melissa Wake, Murdoch Children's Research Institute

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Late Breaking Abstracts

Wed, October 23
3:20 PM - 4:15 PM
Session Chairs
Chair **Lucilla Poston**, King's College London, United Kingdom
Co-Chair **John Bertram**, Monash University, Australia
Presentations
Exploring the Causality of the Association Between Maternal and Offspring Adiposity Using One-Sample Mendelian Randomization
Thomas Bond, Imperial College London; Rebecca Richmond, University of Bristol; Verena Zuber, Imperial College London; Ville Karhunen, Imperial College London; Alexessander Couto Alves, Imperial College London; Marc Gunter, Section of Nutrition and Metabolism, IARC, Lyon; Abbas Dehghan, Imperial College London; Ioanna Tzoulaki, Imperial College London; Sylvain Sebert, Northern Finland Birth Cohort; Alex Lewin, Department of Medical Statistics, London School of Hygiene and Tropical Medicine; Paul O'Reilly, Imperial College London; Deborah Lawlor, University of Bristol; Marjo-Riitta Jarvelin, Department of Epidemiology and Biostatistics, Imperial College London
Early-Life and Life-Course Factors Associated With Blood Pressure Among African Adolescents
Abubaker Swaib Lule, MRC/UVRI & LSHTM Uganda Research Unit; Helen Akurut, MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda; Alexander Mentzer, University of Oxford; Florence Akello, MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda; Alison Elliott, London School of Hygiene and Tropical Medicine; Liam Smeeth, London School of Hygiene and Tropical Medicine; Emily Webb, London School of Hygiene and Tropical Medicine
The Evolution and Role of Breastfeeding in an Early Old Human Ancestor As Revealed Through Chemical Element Signatures in Fossil Teeth
Justin Adams, Monash University; Renaud Joannes-Boyau, Southern Cross University; Christine Austin, Icahn School of Medicine at Mount Sinai; Manish Arora, Icahn School of Medicine at Mount Sinai; Ian Moffat, Flinders University; Andy I. R. Herries, University of Johannesburg; Matthew P. Tonge, Southern Cross University; Stefano Benazzi, University of Bologna; Alistair R. Evans, Monash University; Ottmar Kullmer, Johann Wolfgang Goethe University; Stephen Wroe, University of New England; Anthony Dosseto, University of Wollongong; Luca Fiorenza, Monash University

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Abstracts from the XI[th] World DOHaD Congress

President's Award Recipient Presentations

Effects of household environmental microbiota in early life on development of eczema in children-Results from the SPRESTO study

Loo EXL[1], Ta LDH[2], De Sessions PF[3], Lay C[2,4], Yap GC[2], Tham EH[2,6], Goh A[5], Teoh OH[5], Chan JKY[11,12], Van Bever H[2,6], Godfrey KM[13], Gluckman PD[1,7], Tan KH[9], Eriksson JG[1,10], Chong YS[1,10], Lee BW[2], Shek LP[1,2,6].

[1]Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (ASTAR), Singapore; [2]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [3]Genome Institute of Singapore, Agency for Science, Technology and Research Singapore, Singapore; [4]Danone Nutricia Research, Singapore; [5]Department of Paediatrics, KK Women's and Children's Hospital, Singapore, Singapore; [6]Khoo Teck Puat-National University Children's Medical Institute, National University Hospital, National University Health System, Singapore, Singapore; [7]Liggins Institute, University of Auckland, Auckland, New Zealand; [8]Department of Endocrinology, KK Women's and Children's Hospital, Singapore, Singapore; [9]Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore, Singapore; [10]Department of Obstetrics & Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; [11]Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore, Singapore; [12] Duke-NUS Medical School, Singapore, Singapore; [13]MRC Lifecourse Epidemiology Unit & NIHR Southampton BRC, Southampton, UK
Presenting Author Email: evelyn_loo@sics.a-star.edu.sg

Background/Aims: There is substantial variation in the prevalence of allergic diseases in different regions, suggesting that there may be location-specific factors such as environment, lifestyle and microbial exposure affecting allergic disease prevalence. However, there is limited knowledge on the extent of influence of environmental microbial exposure on the development of allergic diseases. Clues from few studies suggested that exposure to a diverse microbial environment during pregnancy and early postnatal life is key in determining allergy predisposition. Hence, we aimed to determine the association between household environmental microbiota and development of eczema in infants in the first 6 months of life.
Methods: In the SPRESTO (Singapore PREconception Study of long Term maternal and child Outcomes) cohort, we collected dust from the homes of all the subjects at preconception, at 34 weeks of pregnancy and when the child was 3 months old. At 6 months, the child was assessed for eczema by clinicians. In a preliminary analysis, 15 participants with and without eczema were selected. Their bed dust samples were analysed by 16S RNA sequencing. Differences in bacterial abundance between groups over time were analysed using linear mixed models. Species diversity was determined using Shannon/Simpson's alpha diversity indices.
Results: The most abundant bacterial groups detected in household dust were *Corynebacteriaceae* (25.3%), *Propionibacteriaceae* (13.4%) and *Staphylococcaceae* (12.1%). There was an increase in species diversity between the preconception timepoint and the pregnancy timepoint in both the eczema and control groups, but no significant difference in species diversity of bed dust samples between the eczema and control participants. Overall, in household dust the relative abundance of *Propionibacteriaceae* was significantly higher in control as compared to the eczema participants at all timepoints ($p<0.05$), while *Corynebacteriaceae* was higher in control group at the preconception and pregnancy timepoints.
Conclusions: We observed differences in the abundance of the major bacteria groups in household dust from the houses of eczema and control participants that might influence the development of allergic diseases. Further research will be carried out to determine the mechanism of how environmental microbiota affects allergy predisposition.

Maternal obesity induces changes in the expression of inflammatory genes in their offspring´s monocytes and gestational DHA supplementation differentially regulates PCG1α expression

Lépez M[1], Riquelme B[2], Hernández C[2], Carrasco K[2], Garmendia ML[3], Casanello P[2,4]

[1]PhD program in Medical Sciences, Pontificia Universidad Católica de Chile (PUC), Santiago, Chile; [2]Department of Obstetrics, Pontificia Universidad Católica de Chile, Santiago, Chile; [3]INTA, University of Chile, Santiago, Chile; [4]Department of Neonatology, Pontificia Universidad Católica de Chile, Santiago, Chile
Presenting Author Email: mplepez@uc.cl

Background/Aims: The offspring of women with pregestational obesity (PO) have an impaired immune function in their postnatal life. DHA supplementation during pregnancy decreases systemic inflammation in PO. The aim of this study was to determine the effect of PO and DHA supplementation during pregnancy on the expression of genes that regulate the inflammatory response in their offspring´s monocytes at birth.

Method: Women with PO (BMI ≥30 kg/m^2) were supplemented with DHA (200 or 800 mg/day in a double-blind RCT: #12 n=20 or #13 n=13) from <15 w gestation to delivery. PO and normal weight women (NW, control group n=11) who delivered in both UC Clinical Hospital and Sotero del Rio, Santiago, Chile, who accepted to participate, signed an informed consent. Neonatal monocytes were isolated from cord blood at birth and the expression of anti-inflammatory (PPARγ, PCG1α and IL10) and pro-inflammatory (MCP1, IL8, IL6 and TNFα) genes and soluble cytokines levels was evaluated by RT-qPCR and Luminex®, respectively. Fatty acids were quantified in cord blood.
Results: The offspring of PO had higher ponderal index compared to NW (p<0.03). In neonatal monocytes of PO there was an induction of PCG1α (2-fold), IL10 (~5-fold) and MCP1 (~4-fold) compared to NW (p <0.03), with differences in PCG1α expression between PO#12 *vs.* PO#13 (p<0.0008). No differences were found in the expression of PPARγ, IL8, IL6 and TNFα nor soluble cytokine levels among the three groups.
Conclusions: Maternal PO, induces the expression of important anti-inflammatory (PCG1α and IL10) and pro-inflammatory (MCP1) genes in their offspring´s monocytes, with a significant effect of maternal supplementation with DHA in the gene expression of the master regulator of energy metabolism PCG1α. DHA plasma levels during fetal development could positively affect the setting of cell metabolism in neonatal immune cells in the offspring of women with pregestational obesity.
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Growth in children conceived by assisted reproductive technologies: the Norwegian Mother and Child Cohort Study

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Background/Aims: Studies indicate that children conceived by assisted reproductive technologies (ART) have altered growth patterns. The role of parental subfertility and freezing of embryos in the growth among these children remain unclear. The aim of this study was to describe growth patterns among children conceived by ART, and to evaluate the role of both parental subfertility and frozen versus fresh embryo transfer.
Method: This study included singletons participating in the Norwegian Mother and Child Cohort Study (n=81,492) who had at least two weight and length measurements. We first compared children conceived after frozen (n=155) and fresh (n=777) embryo transfer with in vitro fertilization (IVF), and children conceived by frozen (n=84) and fresh (n=574) embryo transfer with intracytoplasmic sperm injection (ICSI), to all spontaneously conceived children. Subsequently, we compared these groups of children conceived by ART to spontaneously conceived children of parents who had tried to conceive for more than 12 months (n=5,281). We examined differences in growth between the groups by adding interaction terms with linear spline terms reflecting growth periods using mixed effects linear regression, adjusting for maternal age, parity, smoking, and education, in addition to parental body-mas index, parental height, offspring sex and gestational age. The mean number of anthropometric measurements available was 8 (minimum 2, maximum 12) between birth and 7.5 years of age.
Results: Children conceived after fresh embryo transfer IVF (adjusted β -120 grams; 95% CI: -220, -30) or ICSI (adjusted β -90 grams; 95% CI: -200, 21) had smaller birthweight compared to children born spontaneously, and experienced some catch-up growth between 3 months and 7 years of age. Compared to spontaneously conceived offspring, fresh embryo IVF offspring experienced on average an 8 grams/week (95% CI: 2.3, 14) greater weight increase, and a 0.19 mm/week (95% CI: 0.09, 0.29) greater increase in length, between 3 and 8 months of age. Children conceived by frozen embryo transfer IVF had birthweights similar to spontaneously conceived offspring (adjusted β 7 grams; 95% CI: -203, 204), and also experienced a greater weight gain (adjusted β 1.2 grams/week between 16 months and 7 years; 95% CI: 0.2, 2.3). We observed an attenuation of the difference in size at birth and childhood growth when ART children were compared to spontaneously conceived children of subfertile parents.
Conclusion: Our findings indicate an altered growth in ART children, which varies according to the procedure and whether the embryo transfer is fresh or frozen and might be partly explained by factors related to parental subfertility.

Taking DOHaD to the people of the Cook Islands

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Background/Aims: Pacific Island nations, such as the Cook Islands, have some of the highest rates of non-communicable diseases (NCDs) globally. Despite advancing research and interventions in other regions of the world, there is a lack of DOHaD knowledge translation research within these communities. The Cook Islands Ministry of Health assessed the Australia/New Zealand "First 100 days: Nutrition matters for lifelong health" booklet and identified that a contextualised adaptation of this booklet was needed in the community. Thus, the aim of this study is to explore Cook Islanders' perceptions and opinions of the original nutrition booklet used in New Zealand and Australia to create a culturally contextualised version for the Cook Island setting.
Method: 10 semi-structured focus groups involving 60 participants were undertaken in Rarotonga, Cook Islands. Participants included mothers, fathers, traditional leaders, youth, doctors, nurses, public health staff, and staff from various government sectors. Questions focused on participants' opinions of the current booklet and ways it could be improved for use within the Cook Islands.
Results: All 10 focus groups identified the clear need for such a resource in the Cook Islands. The common themes included: the importance of translation into Cook Islands Maori, the need for better visual elements such as images and colour and the importance of including traditional concepts, guidelines and foods. One participant in particular captured the essence of this theme expressing that, "In addition to the language, the content must be local from beginning to the end. It has to be local".
Conclusions: There is a need for more DOHaD knowledge translation within nations exhibiting high rates of NCDs such as the Cook Islands. Communication strategies and interventions must be developed following input from the community and be contextualised to the individual setting. Once published, research will continue to evaluate the effectiveness of this booklet.

The association between menarche and myopia and its interaction with related risk behaviours among Chinese school-aged girls: a nationwide cross-sectional study

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Background/Aims: Nearly 80% of new cases of myopia arise between 9-13 years old when puberty development also progresses rapidly. However, little is known about the association between myopia and puberty. We aim to evaluate the association between myopia and menarche, the most important puberty indicator for girls, and to test whether menarche could modify the effects of myopia-related behaviors.
Method: Participants came from three consecutive national surveys conducted in 30 provinces in mainland China in 2005, 2010 and 2014. A total of 158,613 girls aged 10 to 15 years were included. Among them, 92,809 girls had experienced menarche, while 65804 girls had not. Their potential myopia related behaviors including sleep duration, physical activity, homework time and outdoor activity were measured by self-administrated questionnaire. Myopia was defined according to unaided distance visual acuity (VA) and subjective refraction method; its relationships with menarche status and behaviors were evaluated by Robust Poisson-GEE regression models adjusting for cluster effect of school.
Results: Girls who had reached menarche were at 14% (95% confidence interval: 11%-16%) higher risk of myopia than girls who had not, after adjusting for exact age, urban-rural location and four behavioral covariates. The association remained stable when stratified by age. Insufficient sleep duration (<8 hours/d), inadequate physical activity (<2h/d), long homework time (≥1h/d) and low frequency of weekend outdoor activity increased the risk of myopia (PRs>1, P<0.05). Their effects on myopia were stronger or occurred only in post-menarche girls compared to pre-menarche girls (P-values for interaction all <0.05).
Conclusions: The onset of menarche may be an important risk factor for myopia among school-aged girls and could also enhance girls' sensitivity to myopia related risk behaviors. Differentiated recommendations of outdoor activity and homework time should be made for school-aged girls according to their menarche status.

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Oral Abstracts

Trimethylamine N-oxide (TMAO) and metabolic syndrome scores and cardiovascular preclinical phenotypes in Australian children and their mid-life adult parents

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Background/Aims: TMAO is a diet and microbiome-derived metabolite that has been proposed as a biomarker of metabolic syndrome [MetS], and cardiovascular disease, but its role remains controversial. Findings in animals and humans are inconsistent. Fish, a major source of TMAO, is associated with reduced cardiovascular risk in epidemiological studies. Our aims were to investigate the associations between: (i) family, age, and sex on TMAO levels in parent-children dyads, (ii) TMAO levels and MetS scores and pre-clinical cardiovascular phenotypes in children and adults.
Methods: Plasma EDTA was obtained from 2,492 parent-children dyads from *The Longitudinal Study of Australian Children* [LSAC] cohort. TMAO was quantified using ultra high-pressure liquid chromatography coupled with tandem mass spectrometry. MetS scores were calculated using HDL cholesterol levels, triglycerides, glucose, and systolic blood pressure. Cardiovascular phenotypes included measures of carotid intima-media thickness and distensibility, pulse wave velocity, blood pressure, and microvascular structure. Mixed models, adjusted for covariates, were developed to characterise the influence of family, age and sex on plasma TMAO and cardiovascular phenotypes. Multivariate fractional polynomial models analysed associations of TMAO with MetS.
Results: TMAO levels were highly correlated between dyads from the same family. Levels were markedly higher in adults (3.39±2.22 μM) compared to children (2.20±2.26 μM) ($P<0.001$), and in male children (2.36±2.26 μM) compared to females (2.06 ±2.25 μM) ($P=0.003$), but were similar between male and female adults. There was no evidence of association between TMAO levels and MetS. Analysis of cardiovascular phenotypes is ongoing.
Conclusions: Age, family and sex are associated with TMAO levels. Our results to date challenge the previously proposed link between TMAO and MetS. We are currently developing models to test associations with cardiovascular phenotypes, which will be analysed with adjustment for confounders including dietary intake of TMAO precursors.

Prenatal androgen excess affects ovarian function, PPARG and chemerin systems

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Background/Aims: Reproductive functions are tightly related to metabolic ones. The peroxisome proliferator-activated receptors gamma (PPARG) and the adipokine chemerin are molecules that act as links between metabolic status and ovarian functions. We aimed to evaluate the effect of prenatal hyperandrogenism on these energy sensors signaling and its impact on ovarian function at adult age.
Method: Pregnant rats were hyperandrogenized with testosterone and a Control group was obtained by vehicle injection. Prenatally hyperandrogenized (PH) female offspring and Controls were characterized according to the estrous cycle by vaginal smears. We have previously reported several derangements at early ages. Here, we evaluated at adult age body weight, basal glucose and insulin levels, and HOMA-IR. We assessed hormonal profile, ovarian morphology and quantified by qPCR and western blot the levels of PPARG, its co-activator PGC1a, chemerin and its receptor, Cmklr1. We evaluated the interaction between PPARG and PGC1a by co-immunoprecipitation, and measured the mRNA levels of steroidogenic mediators (Star, 3bhsd, Cyp17a1, 17bhsd, Cyp19a1).
Results: At adult life Control rats showed 100% regular estrous cycles, 51% of the PH group showed irregular cycles (PHirr), whereas 49% were acyclic and remained in diestrus or metaestrus (PHac). Both PH phenotypes displayed ovarian cysts, high glucose and insulin levels and an increased HOMA-IR index, without overweight. PPARG mRNA and protein levels were decreased in the PH group. PGC1a levels were decreased in the PHirr animals. PPARG and PGC1a interaction was decreased in both PH phenotypes. Chemerin and Cmklr1 mRNA levels were decreased in the PH group, while chemerin protein levels remained unaltered. Both PH phenotypes showed altered hormonal profile (with low estradiol and high testosterone in the PHac phenotype) and impaired steroidogenesis, in a phenotype specific pattern.
Conclusions: Prenatal androgen excess exposure leads to fetal programming and exerts long-term effects on metabolic and ovarian functions, affecting, at adult life, ovarian metabolic sensors (PPARG and chemerin) and inducing alterations on ovarian morphology and steroidogenesis.

Cardiovascular Risk Factors In Those Born Preterm – Systematic Review And Meta-Analysis

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Background/Aims: Spontaneous preterm birth complicates approximately 5-8% of all pregnancies and is a leading cause of infant morbidity and mortality. Emerging research demonstrates that children born preterm may be at increased risk of cardiovascular disease (CVD) in adult life. We aimed to examine evidence for increased CVD risk factors among children and young adults born preterm.
Method: We performed a systematic review and meta-analysis on studies reporting cardiovascular risk factors among those

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born preterm (< 37 weeks gestation) compared to those born at term (≥ 37 weeks gestation). The following electronic databases were searched: PubMed, CINAHL, the Cochrane Library and EMBASE with an end of search date of May 01, 2018. Information was extracted on established CVD risk factors including blood pressure, lipid profile, blood glucose, fasting insulin, body mass index (BMI) and endothelial/microvascular function. The review protocol is registered in PROSPERO (CRD42018095005).
Results: Thirty nine studies provided cumulated data on 892,024 individuals. Those born preterm had 3.45 mmHg (95% CI: 2.31 to 4.58) higher systolic and 1.49 mmHg (95% CI: 0.79 to 2.19) higher diastolic blood pressure and 0.26 mmol/l (95% CI: 0.01 to 0.50) higher total cholesterol compared to those born at term.
Conclusions: Risk factors for CVD are evident during childhood and early adulthood among those born preterm. Early screening of children born preterm may identify those at risk who may benefit from interventions targeted at improving lifestyle factors to reduce the risk for CVD in adult life.

Does mismatch between retinal vascular endowment and eye size suggest that ocular disease can be programmed by an inappropriate predictive adaptive response?

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Background/Aims: Myopia (or short-sightedness) is caused by excessive eye growth. A number of pathologies accompany myopia, including retinal degeneration and glaucoma and these conditions may be associated with vascular insufficiency. The density and total length of retinal capillaries (vascular endowment) is established prior to birth but excessive eye growth resulting in myopia manifests in adolescence, leading us to hypothesise that comorbidities of myopia may have developmental origins. We aimed to determine the relationship between eye size and retinal vascular endowment.
Method: Healthy subjects (n=107) aged 18-50 with no history of ocular disease, vascular disease or myopia control were recruited from University staff and student population in Australia and Hong Kong. Refractive error, biometry, retinal morphology and vascular morphology were quantified (optical coherence tomography angiography; OCTA; Zeiss Cirrus 5000 with Angioplex). Vascular morphology of the superficial retinal capillary plexus was assessed over a 3x3mm foveal centred area. Perfusion area and vessel length density were quantified, and data analysed by regression analyses and ANOVA on the basis of refractive error and axial length.
Results: A significant inverse association was found between axial length and both vascular density measures: **perfusion area** (r^2=0.140, p<0.001) and **vessel length** (r^2=0.090, p=0.002). Perfusion area was also significantly reduced (−1.84%, p=0.012) in the longer eyes (high myopes) compared to shorter eyes. The aggregated ganglion cell layer and inner plexiform layer thickness (GCL-IPL thickness) were also reduced significantly in the highly myopic group (p<0.001). Overall retinal thickness did not change on the basis of eye size (p=0.934).
Conclusions: This study establishes the inverse association of eye size and the superficial retinal vasculature density, highlighting potential metabolic challenges presented by excessive ocular growth in adolescence. The data support the hypothesis that diseases such as glaucoma may, at least in part, be programmed due to mismatch between a developmental prediction of vascular requirement and the eventual adult phenotype.

Maternal Pregestational obesity increases T lymphocyte subtypes in newborns

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Background/Aims: Obesity is a major public health concern since it affects a high percentage of the population worldwide and is a risk factor for autoimmune diseases. T regulatory cells (Treg) are a subpopulation of T lymphocytes and are directly associated with the prevention of autoimmune diseases. To date, there is a lack of information regarding the effects of maternal obesity, on this important tolerogenic cell population, in the newborn. The aim of this work was to evaluate the effects of maternal obesity on CD4+ T cell populations in the offspring at birth.
Methods: Cord blood was obtained at birth from newborns from women with pregestational obesity (BMI ≥ 30 kg/m^2, PO, n=7) or normal weight (BMI ≥ 18,5 < 25 kg/m^2, NW, n= 11) mothers and maintained at room temperature until analysis. Ficoll gradient density separation method was used to isolate cord blood mononuclear cells (CBMCs) and the CD4+ T cell populations was characterized by Flow Cytometry. Results are expressed as cells/ml of blood (median (interquartile range)).
Results: PO newborn had more lymphocytes (PO=24,756 (15,827-61,534) vs NW=14,517 (6,879-38,635), p<0,05) and CD4+T cells (PO=14,433 (8,411-39,432) vs NW=7,460 (3,082-23,794), p<0,01) than newborns from normal weight mothers. PO newborn had higher number of T effector cells (defined as CD4+CD25-CD127+ T cells) (Ob=13,624 (7,951-37,627) vs NW=6,852 (2,916-22,359), p<0,01), however no differences in Treg subpopulation (defined as CD4+CD25+CD127- T cells) between groups was observed (PO=402 (101-1,489) vs NW=277 (36 - 549), p=0,123).
Conclusions: Newborns from women with pregestational obesity have a higher number of T lymphocytes, CD4+ and effector T cells than newborns from normal weight mothers at birth. These results demonstrate for the first time than maternal obesity alters the number of immune cells in the newborn which could be predisposed to immune alterations later in life.
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Developmental Origins of Neurocognitive Performance in Young Adults of the Pune Maternal Nutrition Study (PMNS) Cohort

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Background/Aims: Early intrauterine exposures during critical periods of growth can affect fetal brain development. Low maternal micronutrients status (B12, folate) in pregnancy and fetal growth is associated with poorer cognitive functioning in childhood. However, the long-term impact of early life exposures on cognitive functioning in adulthood has not been well studied. Pune Maternal Nutrition Study (PMNS) is one of the few birth cohorts in the world which has serially followed up the offspring into young adulthood (24 years) and allows us to examine the association of early life exposures with adult neurocognitive performance in the offspring.
Method: As part of the ongoing assessments on subjects of the PMNS birth cohort,173 adult subjects (age 22.3±0.5 years, 75 males) were administered standardized neuropsychological tests (WAIS-Wechsler's Adult intelligence scale, WMS-Wechsler's Memory Scale, AVLT-Auditory Verbal Learning Test and CTT-Color Trail Test). Raw scores obtained on the WAIS and WMS were converted to age and gender appropriate scaled scores. Associations between maternal circulating micronutrients (B12, folate, homocysteine) at 18 weeks of pregnancy; birth size (weight, length, subscapular skin fold thickness at birth) and 10 indices of neurocognitive functioning were examined.
Results: The mean composite IQ score was 83.5 ±11.1. Female subjects scored significantly lower than males on working-memory index (p=0.03). Lower maternal folate level at 18 weeks of pregnancy and lower birth weight were associated with lower working memory index (p=0.01). On adjusting for age, gender, years of education of offspring and their mothers, socio-economic status and adverse childhood experiences; only subscapular skin fold thickness was associated with working memory (p=0.007).
Conclusion: Early fetal exposures (maternal nutrition, birth weight, adiposity at birth) predict cognitive performance in young adulthood. The association of adiposity at birth with later life cognitive functions may be independent of developmental influences. These observations need to be corroborated in a larger sample.

Periconceptional Alcohol Exposure Programs Altered Behaviour, HPA Activity And Regulation And Pituitary Abnormalities In Rat Offspring

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Background/Aims: Ethanol exposure during pregnancy is known to program dysregulated hypothalamus-pituitary-adrenal axis (HPA) activity and altered behaviour in offspring. However, the long-term impact of ethanol consumption around the time of conception on offspring is unknown. This study aims to investigate the effects of periconceptional ethanol (PC:EtOH) exposure on HPA function and regulation in offspring.
Method: Female Sprague-Dawley rats were treated with PC:EtOH (12.5% v/v EtOH, liquid diet) from 4 days before conception, until embryonic day 4. Dams littered down naturally, and at 6 months of age offspring underwent HPA activity assessment using the dexamethasone suppression and corticotropin-releasing hormone stimulation test (DST/CST). At 6 and 12 months of age, basal corticosterone was measured and mRNA expression of key steroidogenic and glucocorticoid signalling genes in the adrenals, hypothalamus and hippocampus were assessed. Pituitary glands were collected for histological assessment
Results: PC:EtOH reduced basal plasma corticosterone concentrations in female offspring at 6 and 12 months of age ($p<0.05$). At 6 months corticosterone was elevated in response to the DST/CST. Key adrenal steroidogenesis genes (*Mc2r, StAr, Cyp11a1, Cyp11b2* and *11bhsd2*) and hypothalamic genes (*Nr3c1*, *Hsp90a1*, *Crh* or *Crh-r1*) were not changed by PC:EtOH at 6 and 12 months of age, in either sex. However, at 12 months of age, *Nr3c1* and *Hsp90a1* were significantly increased in the hippocampus of female offspring exposed to PC:EtOH and pathological abnormalities were observed within pituitary glands.
Conclusions: This study demonstrated that PC:EtOH reduced basal corticosterone concentrations in female offspring, but caused HPA hyperactivity in response to a challenge in both sexes. These outcomes are likely related to pituitary abnormalities and the altered expression of hippocampal regulators of HPA function. As the appropriate function of the HPA is essential for physiological homeostasis, alcohol consumption around the time of conception may have long term implications for a range of programmed disease outcomes.

Regulatory T Cell Deficiency Increases Resistance to Blood Flow in Mid- and Late Gestation, Leading to Growth Restriction in Male and Female Fetuses

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Background/Aims: Preeclampsia is an important cause of maternal and perinatal morbidity and mortality, and increases the susceptibility of the mother and offspring to cardiovascular disease later in life. In preeclampsia, a deficiency in regulatory T (Treg) cells has been observed. Treg cells prevent maternal immune rejection of the fetus, but also contribute to vascular homeostasis in non-pregnant rats. We have previously shown

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that a reduced Treg cell population affects uterine artery hemodynamics in mid-gestation. However, the effect on late gestation hemodynamics is unknown. This study aimed to determine whether a reduced Treg cell population will alter uteroplacental hemodymamics in late gestation, and whether there are any sex-specific effects on fetal development.
Methods Transgenic *Foxp3-DTR* mice have FOXP3 promoter-driven expression of the human diphtheria toxin (DT) receptor to enable selectively depletion of FOXP3+ (Treg) cells. DT was injected (37.5 ng/g) on gestational day (GD)3.5 and GD5.5 to selectively deplete FOXP3+ cells; vehicle-treated *Foxp3-DTR* mice served as controls. On 18.5, ultrasound biomicroscopy was performed to assess uterine and umbilical hemodynamics. Mice were then euthanized and fetal biometrics assessed.
Results: Following Treg depletion by DT administration, hemodynamics were perturbed on GD18.5, with the pulsatility index increased by 22% in the uterine artery and 3.5% in the umbilical artery ($P<0.05$), indicating a persistent increase in resistance to blood flow in the uteroplacental unit. Fetal weight was reduced in male and female fetuses by 15-18% following Treg depletion ($P<0.05$). Male fetuses had a greater placental weight, and the fetal:placental weight ratio was reduced in both sexes.
Conclusions: We demonstrate an essential role for Treg cells in uteroplacental vascular function and fetal growth. Given the severe implications of preeclampsia on the future health of the mother and her baby, investigation of therapeutic strategies targeting Treg cells offers a promising intervention.

Paternal miR-146a regulation of female immune receptivity and fetal viability in mice

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Background/Aims: Factors in male seminal fluid delivered at coitus exert influence on the peri-conception environment and contribute to trajectory of fetal and placental development, through effects on female immune receptivity to implantation, as well as direct effects on the pre-implantation embryo. The full identity of permissive and inhibitory signals in seminal fluid remains to be defined. We have identified miR-146a in seminal fluid as a potential regulator of female immune response. Here we investigated the contribution of paternal miR-146a to regulating female tract cytokines, embryo implantation, and pregnancy and neonatal outcomes, using mice with genetic deficiency in miR-146a.
Method: The impact of male seminal fluid miR-146a on the female uterine response to seminal fluid was examined by qPCR analysis of endometrial tissue gene expression in BALB/c females 8 hours following mating with miR-146a$^{+/+}$ or miR-146a$^{-/-}$ males, and compared with unmated estrous BALB/c controls (n=7-11/group). Pregnancy outcomes were measured on day (D) 17.5 post-coitum (pc) (n=30-33/group). Neonatal outcomes were assessed at birth and offspring weight was measured every fortnight until week 16 post-partum (n=10-17/group). Additionally, sperm parameters in miR-146a$^{+/+}$ and miR-146a$^{-/-}$ males were assessed at 6-7 months old (n=15-21/group).
Results: Sperm analysis revealed miR-146a$^{-/-}$ males produced less motile (13% reduction) and less sperm with normal morphology (10% reduction). Seminal fluid from miR-146a$^{-/-}$ males elicited a 50% decrease in endometrial induction of Cxcl2 and Il6, compared to wildtype-mated females. Despite the reduced sperm quality, miR-146a$^{-/-}$ males sired litters containing 19% more viable pups on D17.5pc, with no change in fetal weight, but 8.0% smaller placental weight, compared to litters sired by miR-146a$^{+/+}$ males. However at birth, the difference in size of litters sired by miR-146a$^{-/-}$ and miR-146a$^{+/+}$ males was no longer evident. This corresponds to a 21% loss of viable offspring in the late gestation/early neonatal period, compared with <5% loss in litters sired by miR-146a$^{+/+}$ males. Gestation length and offspring growth trajectory was not affected by paternal genotype.
Conclusions: These findings suggest that paternal miR-146a influences the female immune response to impact female 'quality control' of embryo implantation and development. We infer that absence of male miR-146a causes progression of embryos otherwise destined for later gestation loss, or neonatal demise. Further experiments are required to elucidate the immune/non-immune mechanisms by which paternal miR-146a influences female control of embryo implantation and pregnancy progression.

Influence of maternal dietary inflammatory potential and quality on offspring birth outcomes: a pooled analysis of 7 European cohorts in the ALPHABET consortium

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Background/Aims: Maternal peri-conceptional and antenatal diets influence offspring birth outcomes; however, evidence on whole-diet maternal dietary inflammatory potential and quality is scarce and conflicting.
Method: We harmonized and pooled individual participant data from up to 16,155 mother-child pairs in 7 European mother-offspring cohorts. Maternal diets were assessed pre-conceptionally (n=2 cohorts) and antenatally (n=7; subdivided into early (n=5)

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and late pregnancy (n=4)). Information on birth outcomes was abstracted from hospital records. Low birth weight (LBW) was defined as BW<2500 g and preterm birth as delivery occurring at <37 weeks' gestation. We used multivariable regression analyses to assess the associations of maternal energy-adjusted scores of Dietary Inflammatory Index (DII) and Dietary Approaches to Stop Hypertension (DASH) with offspring birth outcomes in cohort-specific analyses, with subsequent random-effects meta-analyses. Analyses were adjusted for maternal age, pre-pregnancy BMI, parity, lifestyle factors, and socioeconomic status.
Results: A higher pre-conceptional-DII score (more pro-inflammatory) was associated with a lower BW [pooled-β (95%CI) per 1SD dietary score increment: -21.1 (-38.4,-3.8) g], a shorter birth length [pooled-β: -0.12(-0.24,-0.01) cm], and a higher risk of LBW [pooled-OR: 1.22 (1.02,1.45)]. A higher late-pregnancy-DII was associated with a smaller birth head circumference [pooled-β: -0.03 (-0.06,-0.001) cm]. A higher maternal DASH score (greater dietary quality) was associated with a longer birth length [pooled-β: 0.09 (0.02,0.16) cm for pre-conceptional-DASH and 0.10 (0.04,0.17) cm for late-pregnancy-DASH]. Sex-specific maternal diet-birth outcome relationships were observed. For instance, significant associations exist between higher pre-conceptional-, pregnancy- and late-pregnancy-DII and lower BW; higher pre-conceptional-DII and shorter gestation length; higher pre-conceptional-DASH and higher BW and longer birth length in male offspring but not females.
Conclusions: Pro-inflammatory and low-quality maternal diets are associated with suboptimal offspring birth outcomes. Diets at different stages of conception and pregnancy seem to exert different influence on offspring outcomes, with offspring sex as a potential effect modifier.

Early life undernutrition reprograms CD4$^+$ T-cell glycolysis and epigenetics to facilitate asthma

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Background/Aims: Exposure to early life undernutrition is closely related to higher risks of adverse immunologic outcomes in adulthood. Although it has been suggested that asthma has its origins in early life, its underlying mechanisms remain largely unknown. We characterized the impacts of early life undernutrition on T lymphocytes, which play a pivotal role in immune diseases, and we investigated whether this contributes to susceptibility to asthma in adulthood.
Method: Pregnant mice were fed a protein restriction diet (PRD) to establish an early life undernutrition model. Naïve CD4$^+$ T cells (CD4$^+$CD62L^{hi}CD44$^-$) from offspring were used throughout the study. Type 2 T helper (Th2) differentiation was examined by FACS and ELISA under Th2-polarized conditions *in vitro* and by ovalbumin (OVA)-induced experimental asthma *in vivo*. T-cell metabolism was measured with a Seahorse XF96 Analyzer. DNA methylation levels were measured by bisulfite sequencing.
Results: PRD CD4$^+$ T cells displayed increased activation and proliferation and were prone to differentiate into Th2 cells both *in vitro* and *in vivo*, leading to susceptibility to experimental asthma. Mechanistically, early life undernutrition upregulated mTORC1-dependent glycolysis and induced conserved noncoding DNA sequence 1 (CNS1) DNA hypomethylation in Th2 cytokine locus of CD4$^+$ T cells. Glycolysis blockades undermined increased Th2 skewing and alleviated experimental asthma in PRD mice.
Conclusions: Early life undernutrition induced mTORC1-dependent glycolysis upregulation and Th2 cytokine locus hypomethylation in CD4$^+$ T cells, resulting in increased T-cell activation, proliferation and Th2 skewing and further susceptibility to experimental asthma.

Early LifeLab: Capitalising on UK Government Policy Initiatives to Support an Educational Intervention for Primary Schools

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Background/Aims: The UK Government's strategy aims to halve childhood obesity by 2030, and provides funding for schools in the Primary Physical Education and Sport Premium (PESP). Schools use this to make sustainable improvements in physical activity (PA). Early LifeLab (ELL) is an educational intervention for primary schools, supporting schools to meet the requirements of PESP funding in an innovative manner. ELL engages children in the science behind health messages, thus improving their health literacy and their health behaviours. The Childhood Obesity strategy also names parents and families as essential stakeholders; in this study we aimed to understand parental attitudes and perceived barriers to PA. The results will support creation of a targeted resource to tackle misconceptions and barriers.
Method: Working with local partners we created a vibrant and inspiring photographic exhibition of young children engaged in

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activity and active play. Photographs demonstrated the varied ways children can achieve their recommended 60 minutes/day of PA. Parents who viewed the exhibition completed a short questionnaire on their attitudes and perceived barriers to PA.
Results: To date, responses have been collected from 110 participants. (Target 500 by September 2019). 55% of respondents stated "We don't have enough time" for more PA. For 7% the child's enjoyment was a factor. 36% felt their children preferred sedentary activities, and 20% felt cost was restrictive.
Conclusions: Evidence suggests that low numbers of UK schoolchildren achieve the 60 minutes/day of PA, half of which is to be delivered in school. This research gives ELL an opportunity to design a bespoke resource for schools, placing children and their experience at the heart of conversations to tackle barriers to PA. Engaging children as agents of change, at home and in the community, will likely ensure that initiatives promote sustainable lifestyle changes that can impact future generations.

Preconception Lifestyle Intervention in Obese Women Improves Echocardiographic Indices of Cardiovascular Function in Their Offspring: Follow Up of a Randomised Controlled Trial

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Background: Studies suggest maternal obesity directly affects foetal cardiovascular development which may explain the increased health risk in the offspring. In the present study we assess the effects of a preconception lifestyle intervention in obese women on echocardiographic indices of cardiovascular function in the offspring at the age of 6 years.
Method: This study is embedded in the WOMB project (www.womb-project.nl), which is a follow up of a randomised controlled trial that included 577 obese sub/infertile women. A 6 months preconception lifestyle intervention aimed at weight loss prior to fertility care was given to the intervention group and a control group received fertility care as usual. We conducted complete transthoracic echocardiograms in the offspring at age 6-7 years. The clinician performing the echocardiograms and offline measurements was blinded to group allocation. We used EchoPAC analysis software (GE Vingmed) for offline measurements of dimension, mass and stroke volume of the cardiac chambers.
Results: We included 44 children, mean age 6.1 years (SD 0.9), 57% girls. Children of women in the intervention group (n= 17) had a thinner interventricular septum (Z-score -0.6% [SD 0.7] vs 0.2% [SD 0.4], p <0.001) a lower left ventricular mass index (53.4 g/m^2 [SD 9.1] vs 59.9 g/m^2 [SD 7.0], p= 0.01) and an increased ejection fraction (60.9% [SD 3.5] vs. 56.6% [SD 4.6], p=0.004) compared to children of controls (n=27). These are all indices of better cardiovascular health
Discussion: Preconception lifestyle intervention in obese women results in a thinner interventricular septum, a lower left ventricular mass and higher ejection fraction in the offspring at age 6, suggesting better cardiovascular development and function. This is the first experimental human evidence of the effect of improving (pre)pregnancy maternal lifestyle to enhance cardiovascular function and potentially reduce cardiovascular disease risk in the next generation.

Inflammation and saturated fatty acid impair hypothalamic neuroprogenitor cells mitochondrial function

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Background/Aims: With the increasing rates of obesity among pregnant women, fetal growth and development occurs commonly under conditions of maternal obesity and a Western, high fat (HF) diet. Infants born to obese mothers (OB) with a HF diet are at increased risk of childhood and adult overweight/obesity. We have established a murine model of maternal OB/HF that results in offspring hyperphagia and obesity. The hyperphagia results from altered hypothalamic neurogenesis that drives neuroprogenitor cells (NPCs) to preferentially differentiate to orexigenic vs anorexigenic neurons. Maternal obesity is associated with increased maternal and fetal inflammatory cytokines and saturated fatty acids as well as mitochondrial derived oxidative stress. As mitochondrial function is critical for neurogenesis, we hypothesized that proinflammatory cytokine tumor necrosis factor (TNFα) and saturated fatty acid (palmitic acid) induce mitochondrial dysfunction.
Method: Hypothalamic NPCs from control newborns were cultured in complete media and treated with DMSO (control), palmitate (200, 400 μM) or TNFα (20, 50, 100 pg/ml) for 24h. Using the Seahorse assay, we determined mitochondrial oxygen consumption rate (OCR), including basal, ATP-linked and maximal respiration.
Results: TNFα and palmitic acid both reduced basal, ATP-linked and maximal respiration (Figure). TNFα treatment showed ~50% reduction in OCR at all doses whereas palmitate induced a dose-dependent reduction in OCR (~25% at 200 μM and ~50% at 400 μM).
Conclusions: TNFα and palmitic acid impair hypothalamic NPC mitochondrial OCR, suggesting that both inflammation and saturated fatty acids induce oxidative stress. We propose that maternal obesity-mediated fetal oxidative stress contributes to programmed neurogenesis which results in offspring hyperphagia and obesity.

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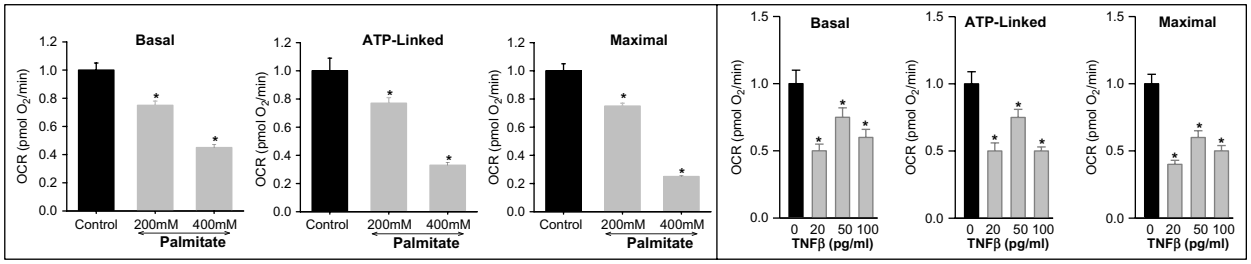

Economic development and the nutritional status of Chinese school-aged children and adolescents: an analysis of five successive national surveys from 1995 to 2014

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Background/Aims: Socioeconomic development is widely regarded as contributing to improved nutrition in children. We aimed to assess the association between socioeconomic indicators and child and adolescent nutritional status, and the difference of this association in urban and rural areas.
Method: We extracted data on 1,054,602 school students aged 7-18 years from five successive national surveys in 29 Chinese provinces from 1995 to 2014. Nutritional status (stunting, thinness, and overweight/obesity) were defined using WHO definitions. Socioeconomic indicators included gross domestic product per capita, the Engel coefficient (the proportion of household income spent on food), and urbanization. We used logistic regression models to estimate the association between socioeconomic indicators and child nutritional status; used the prevalence odds ratios (PORs) to assess the urban-rural disparity of nutritional status over time; and used generalized additive models to evaluate differences in the socioeconomic association with nutritional status between urban and rural areas.
Results: From 1995 to 2014, stunting prevalence in Chinese children and adolescents decreased from 8.1% to 2.4%, and thinness declined from 7.5% to 4.1%. Overweight/obesity increased from 5.3% to 20.5%. The urban-rural disparity in nutritional status gradually diminished, with the PORs approaching equivalence over time. Faster improvement of socioeconomic indicators was associated with changed nutritional status in children and adolescents, but with differences across urban and rural. The association between socioeconomic status and overweight/obesity was stronger in rural than in urban areas. Improvements in the Engel coefficient were accompanied by a greater reduction of stunting and thinness in rural than in urban areas.
Conclusions: Although socioeconomic development has been accompanied by continued improvements in stunting and thinness, there has been an explosive increase in overweight/obesity in Chinese children and adolescents, particularly in rural areas. There is now a pressing need for policy actions to extend beyond an emphasis on economic growth alone, to the promotion of healthy diets and physical activity.

Methylation marks associated with prenatal smoke exposure and risk of cancer in adulthood

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Background/Aims: Prenatal exposure to maternal smoking is known to be associated with DNA methylation changes in the blood of newborns [1]. It was also shown that many of these methylation marks persist to adulthood, which makes DNA methylation a potentially reliable and enduring biomarker of exposure to maternal smoking [2]. While seldom investigated, the hypothesis of an association between maternal smoking and cancer in adulthood is plausible given the known effects of maternal smoking on child health.
Method: We obtained data from 8 prospective case-control studies nested within the Melbourne Collaborative Cohort Study to assess associations between maternal-smoking-associated DNA methylation (measured at baseline) and risk of breast (N=409 cases), colorectal (N=835), gastric (N=170), kidney (N=143), lung (N=332), prostate (N=869) and urothelial cancer (N=428), and B-cell lymphoma (N=439). Conditional logistic regression was used to estimate odds ratios (OR) for associations between cancer and: 1) 568 CpG sites taken individually, using the list from [1] (Bonferroni correction $P<9x10^{-5}$); 2) a methylation score derived from these 568 CpGs, 3) a 19-CpG methylation score of maternal smoking shown to persist in adulthood [2]. Identical analyses were carried out for overall cancer risk (N=3,495 cases). All models were adjusted for confounders, including adult smoking (smoking status, pack-years, and age at starting and quitting).
Results: For the 568 CpGs individually, no association was found for either overall or individual cancer risk after adjustment for adult smoking. The two methylation scores showed similarly strong evidence of association with urothelial cancer risk (for the 19-CpG score: basic model: OR=3.6, 95% CI:1.6-7.8], P=0.0006; comprehensive smoking adjustment

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OR=2.8, 95%CI:1.2-6.2; P=0.007). No associations were observed for risk of other cancer types or cancer overall.
Conclusions: Our study suggests that there might be an association between urothelial cancer risk and a maternal-smoking methylation score based on 19 CpGs where methylation changes persist in adulthood.
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The Association Of Alcohol PRS On Mental Health Phenotypes: A PheWAS In The Avon Longitudinal Study Of Parents And Children (ALSPAC)

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Background/Aims: An emerging technique is a Phenome Wide Association Study (PheWAS), which reverses the phenotype to genotype methods used within a GWAS, instead taking a predetermined set of genetic variants, and testing which of a wide range of phenotypes these genetic variants may be associated with. We can further investigate the genetic architecture of multiple traits and disease outcomes through linking a chosen genetic variant to multiple phenotypes, in varying populations. In this study we constructed polygenic risk scores (PRS) from single nucleotide polymorphisms (SNPs) shown to be robustly related to alcohol use, to test: 1: These genetic signals within two sub populations of adolescents, and for pregnant women. 2: If there are any associations (other than with alcohol use) of these PRS with many mental health phenotypes. 3: Intrauterine effects of Maternal PRS for alcohol use for associations with offspring phenotypes.
Method: Participants were mothers and offspring from ALSPAC. Participants were genotyped and PRS were constructed based on genome-wide significant SNPs for alcohol consumption. Targeted phenotypes were selected from substance use (n = 22) and mental health/behavioural variables (n = 91) within ALSPAC. Linear and logistic regression analyses were used to investigate if PRS for alcohol use were associated with alcohol use (mothers in pregnancy; children) and health phenotypes (mothers during pregnancy; children both pre-alcohol use around ages 7-10, and post-alcohol use around ages 13-23).
Results The PRS were associated with multiple alcohol consumption phenotypes (strongest signal for alcohol amount at 18 weeks gestation: p=1.01×10-5) in pregnant mothers. There was an effect of maternal PRS for alcohol use on mother's perinatal depression (p=0.02), offspring intellect (p=0.016), and offspring ADHD (p=0.04).
Conclusions: The effects of alcohol PRS previously found in the general population are also shown during pregnancy. We found an intrauterine effect of alcohol PRS on offspring intellect and ADHD. The effects shown are not due to offspring's own alcohol use, as these effects were not found within the child's analyses.

Paternal high-fat diet causes bone deficits which are reprogrammed by exercise early in life

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Background/Aims: Paternal obesity before conception impairs offspring metabolism in skeletal muscle and pancreas; however, no study has investigated its effects on bone health. Just four weeks of exercise early in life can overcome the reduction in insulin sensitivity[1]. Thus, we investigated 1) whether paternal obesity causes bone deficits in adult rat offspring, and 2) whether early-life exercise can normalise these effects.
Methods: Male Sprague–Dawley rats consumed a high-fat diet for 10 weeks before mating with chow-fed dams. Female offspring remained sedentary or performed moderate intensity treadmill exercise (5 days week−1, 60 min day−1, 20 m min −1) from 5 to 9 weeks of age. At 25 weeks of age, the offspring's femur was dissected and stripped of all soft tissue (n=9-10 per group). Femur length was measured by a digital caliper and the bone's mineral content, density and strength assessed using quantitative computed tomography. The stress strain index of bone bending strength (SSI) was used when comparing the bending strength of a bone to a mechanical three-point bending test.
Results: There were no differences in femur length, trabecular content and density, or cortical and subcortical densities among groups (P>0.05). Paternal obesity reduced cortical and subcortical contents (8-12% less, P<0.05), periosteal and endosteal circumferences (6-9.5% less, P<0.05), and SSI (13.5-16% less, P<0.05) in adult female offspring. Early-life exercise in offspring of chow fed fathers did not affect any of the measurements (P>0.05); however, when offspring sired by obese fathers all negative outcomes were normalised (P<0.05).
Conclusions: Female rat offspring sired by obese fathers have poor bone quality in adult life which is reprogramed and normalised by exercise early in life. Using exercise early in life to improve bone quality in adulthood for individuals who were born from obese fathers may help reduce the incidence of osteopenia and osteoporosis in the future.
Reference 1. Falcão-Tebas F, Kuang J, Arceri C, Kerris JP, Andrikopoulos S, Marin EC, McConell GK. Four weeks of

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exercise early in life reprograms adult skeletal muscle insulin resistance caused by a paternal high-fat diet. The Journal of physiology. 2019 Jan;597(1):121-36.

Association of Chemerin in Blood and Breast milk with Gene Methylation in Gestational diabetes

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Background: Intrauterine environment and early-life nutrition are regulated by maternal biomarkers. Chemerin is hypothesized to play a role in the development of childhood obesity. The study compares Chemerin levels and associated genetic mutations between pregnant and lactating women who have been diagnosed with gestational diabetes (GDM) and those with normal glucose tolerance as per the IADPSG guidelines.
Method: Thirty three GDM and 33 control women were recruited from two medical centres. After informed consent, participants were followed from 12-15 weeks of gestation till 6 weeks' post-partum. Two maternal blood samples (28th week of gestation and 6 week post-partum) and two breast milk (BM) samples (within 72 hours after delivery, called colostrum, and at 6 weeks postpartum) were collected. Chemerin levels and whole genome sequencing, methyl specific PCR were performed. Baby weight was measured at birth and six weeks postpartum.
Results: Compared to controls, participants with GDM had higher serum Chemerin levels at 28th week of pregnancy (11.17 ± 0.48 versus 86.42±7.43 ng/L; p<0.001) and at 6 weeks postpartum (14.79±1.01 versus 64.60±6.17 ng/L; p<0.001). GDM cases also had higher colostrum Chemerin concentrations compared to controls (125.34±15.88ng/L versus 24.97±2.58 ng/L; p<0.001). At 6-weeks postpartum, cases continued to have elevated levels of Chemerin (177.40±22.49ng/L), whereas levels dropped in controls (20.71±2.36ng/L). Furthermore, Chemerin levels in both colostrum and serum showed a positive association with baby weight at 6 weeks postpartum (r=0.270, p=0.034 and r=0.464, p<0.001 respectively). Novel genetic mutations were seen across different functions regulating body-mass index: [FTO (6 novel); RARES (3 novel)]; appetite [POMC (4 SNPs)]; beta cell development [CDKAL1 (1153 SNPS); TCF7L2 (15 novel); INSIG2 (21 SNPs)] and insulin release [SIRT (2 novel); KCNQ1 (2 novel)]. Moreover, high levels of methylation were observed in genes such as POMC, INSIG and SIRT.
Conclusion: Environmental stresses such as GDM may cause methylation of genes that have protective affects against obesity and diabetes; and Chemerin may have a role to play in these mutations. This genetic influence may lead to the development of early childhood obesity.

Baseline profile of an Australia-wide pregnancy cohort study of children at risk of type 1 diabetes: The ENDIA study

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Background: The global incidence of type 1 diabetes (T1D) is increasing by 2-5% per year. Some 80% of children who develop clinical T1D before age 18y have detectable islet autoantibodies by 3y. This provides strong support for drivers of the autoimmune process originating in early life, including the prenatal period. The Environmental Determinants of Islet Autoimmunity (ENDIA) study is a longitudinal study of children with a first-degree relative living with T1D. ENDIA aims to investigate environmental factors and gene-environment interactions that modify risk of T1D in childhood.
Methods: Since commencement in 2013, ENDIA has recruited infants (in pregnancy or prior to age 6m) with a first-degree relative with T1D from across Australia. Data are collected in each trimester, at birth, then quarterly to 2y, with six monthly follow-up thereafter. Along with demographic, lifestyle, clinical and anthropometric measurements, samples of blood, urine, stool, saliva, breastmilk and swabs from various body sites have been collected at each study wave. Maternal and child diet have been assessed through food frequency questionnaires, diaries and 24 hour dietary recalls.
Results: As at February 2019, 1269 children (91% of target N=1400) have been recruited, with this likely to be completed mid-2019. The T1D proband relationship with study child is 61% maternal, 26% paternal, and 13% sibling. The mean age of mothers at consent was 31.7y (SD 4.7), and of fathers 33.6y (SD 5.0). To date, study children have completed a mean of 24m follow-up (range 0-71m).
Discussion: ENDIA is the world's first pregnancy-to-early childhood cohort study of children at increased genetic risk of T1D. With its comprehensive, serial data and biological sample collections, ENDIA is providing unique insights into the role of the maternal and early life environments in the development of childhood T1D.

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Nutrient and hormone composition of milk is altered in post-bariatric rodent dams

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Background/Aims: Bariatric surgery is touted to improve the various comorbidities of obesity and diabetes. Although bariatric surgery is approved for a woman of child-bearing age with an interest in subsequent pregnancy, reports of in utero growth issues during pregnancy have garnered a closer look at the impact of maternal surgical weightloss on the pre- and postpartum periods. Previously we reported that female rats undergoing vertical sleeve gastrectomy (VSG) give birth to small-for-gestational age offspring that are later predisposed to Metabolic Syndrome. We hypothesized that the catch-up growth of the VSG pups during lactation is compromised by reduced milk quality by VSG dams.
Method: Milk was obtained during postnatal day 15/16 from lactating dams that were Lean (maintained on chow), Obese and post-VSG (both maintained on high fat diet). Nutrients, adipokines and hormones were measured by gas chromatography and ELISA.
Results: Comparing the slope of growth curves, VSG pups had a significantly reduced growth trajectory in comparison to either Lean or Obese ($P < 0.001$). VSG milk had elevated glucose ($P < 0.05$) and significantly reduced triglyceride content ($P < 0.01$). Milk from Obese and VSG dams had higher levels of insulin in comparison to milk from Lean dams. VSG had the highest levels of adiponectin in milk which was significantly greater than Lean ($P < 0.001$) and Obese ($P < 0.05$). Milk from Lean dams had higher levels of immunoglobulin G than either Obese or VSG. Milk from VSG also trended towards higher levels of growth hormone than the other groups. No differences in leptin were measured in the milk.
Conclusions: There is a shift in the caloric content of VSG milk such that total calories from fat are reduced and total calories from glucose may be increased thus overall producing milk with a reduced caloric content. Further work is necessary in humans who have received VSG or other bariatric procedures to determine if similarities in milk content to what we have found are observed and whether macro- or micro-nutrient supplementation is advisable.

Development of visceral and subcutaneous-abdominal adipose tissue in breastfed infants during first 12 months of lactation – effect of human milk components and maternal factors

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Background/Aims: Abdominal visceral fat tracks from infancy to adulthood and accelerated gain is considered to be a risk factor for metabolic diseases. Studies report that subcutaneous-abdominal and visceral adiposities may be differentially regulated during infancy and that duration of exclusive breastfeeding (BF) is shown to relate positively to subcutaneous but not visceral fat. BF is implicated in development of infant body composition (BC) and is also associated with reduced risk of developing non-communicable diseases including obesity later in life. We used ultrasound imaging to assess infant abdominal visceral and subcutaneous fat to investigate relationships with concentrations and daily intakes of human milk (HM) components as well as maternal factors during first year of lactation.
Method: Abdominal subcutaneous (subcutaneous-abdominal depth, SD; subcutaneous-abdominal fat area, SFA) and visceral fat (visceral depth, VD; preperitoneal fat area) of healthy term BF infants (n=20) was assessed at 2, 5, 9 and/or 12 months postpartum using ultrasound. Maternal BC was determined with bioimpedance spectroscopy. HM components (total protein, casein, whey protein, adiponectin, leptin, lysozyme, lactoferrin, secretory IGA, total carbohydrates, lactose and HM oligosaccharides) concentrations and infant 24-h milk intake (MI) were measured and daily intakes (CDI) of HM components were calculated.
Results: Maternal weight and fat mass were negatively associated with infant SFA at 2, 5 and 12 months, at 9 months the association was positive ($p<0.05$). 24-h MI was positively associated with infant SD ($p=0.007$) and VD ($p=0.013$). CDI of total protein ($p=0.013$), total carbohydrates ($p=0.004$) and lactose ($p=0.013$) were positively associated with SFA. Lactoferrin concentration was negatively associated with infant VD at 2 and 12 months, at 5 and 9 months association was positive ($p=0.003$).
Conclusions: Daily intakes of HM components and maternal BC have a differential effect on development of infant visceral and subcutaneous abdominal fat depos during the first year of life, thus timely interventions such as maintaining healthy maternal BC and continuation of BF to 12 months of life and beyond may facilitate favourable developmental programming and reduce risk of obesity.

Maternal mental health influences perinatal programing of socio-emotional development via gene x environment interactions

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Background/Aims: The perinatal period is critical for neurodevelopment and highly sensitive to the alterations in the *in utero* and postnatal environment associated with maternal mental health. However, measures of maternal mental health explain only about 5-10% of the variance in child outcomes and derive largely from cross-sectional studies without a clear definition of effects associated with persistent maternal mental health symptoms over the perinatal period.
Method: In an Asian birth cohort, GUSTO (n=796), we used latent class analysis on Edinburgh Postnatal Depression Scale (EPDS) and State-Trait Anxiety Inventory (STAI) measures to identify trajectories of persistent maternal depression and anxiety symptoms from mid-pregnancy until 3 years post-birth. Influence of these trajectories on child's socio-emotional outcomes was studied using the Child Behavior Checklist (CBCL) at 4 years. We further interrogated the role of child genotype and its interaction with maternal mood trajectories (environment) in influencing offspring's socio-emotional development, and validated the findings in an independent cohort (MAVAN, Caucasians, n=196).
Results: A significant proportion (8.5 – 12%) of mothers showed persistent high depression and anxiety symptoms in the perinatal period. Offspring of these mothers had poorer socio-emotional outcomes ($p<0.0001$). Bayesian information criterion (BIC) analysis identified these outcomes to be primarily explained by gene x maternal mental health (GxE) interactions, than the child genotype (G) or maternal mental health (E) alone. The GxE interactions comprised of genes *ASTN2, SLC9A9*, *CTNNA2* and *HNF1B* (Bonferroni correction $\leq 2.3X10^{-6}$), implicated in attention deficit/hyperactivity disorder in previous GWAS's. These GxE interactions were also replicated in a separate and ethnically diverse birth cohort, MAVAN, reiterating that persistent perinatal depression or anxiety symptoms of mothers worsen the socio-emotional development of offspring with risk alleles.
Conclusions: These findings provide a deeper insight into gene x environment interactions in developmental psychopathology, and its benefits in bringing precision to future interventions targeting child mental health.

Prenatal Glucocorticoid Exposure Modifies Germ Cell MicroRNA Expression in Adult Male Offspring Across 3 Generations: Paternal Transmission

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Background/Aims: Prenatal synthetic glucocorticoids (sGC) are administered to women at risk of preterm labour. However, sGC treatment has been associated with poor neurodevelopmental sequelae in a number of species. Indeed, sGC exposure has been shown to impact neuroendocrine function, behaviour and brain transcriptome profiles for 3 generations following paternal transmission in guinea pigs. MicroRNA (miRNA) in the male germline are key regulatory factors that may underlie inter- and trans-generational transmission. We hypothesized that prenatal sGC exposure (F_0 pregnancy) modifies miRNA expression in adult male germline cells across 3 generations.
Method: Pregnant F_0 female guinea pigs were injected with three courses of a clinically relevant dose of betamethasone (BETA) or saline (Ctrl). Male offspring (F_1) were mated with naïve females to produce 2 further generations. Once successfully mated to produce next generation offspring, adult male offspring (F_{1-3}) were euthanized. Frozen testes from F_{1-3} males (n=6/gp) were used for germ cell isolation, and miRNA expression profiling was performed using a global miRNA microarray at The Centre for Applied Genomics. Data was processed by TAC2.0 and R. Log2-fold change(FC) >+-1.5, FDR corrected $p<0.05$ was considered significant.
Results: Maternal (F_0) treatment with BETA resulted in the differential expression of 216, 147, 232 miRNAs in germ cells derived from F_1, F_2, and F_3 compared to Ctrl, respectively. For the most part, different sets of miRNAs were affected in each generation. Overall, prenatal BETA exposure resulted in primarily down-regulation of miRNAs in F_1 male germ cells, both up- and down-regulation in F_2 and primarily up-regulation in F_3. However, a number of miRNA showed the same pattern of altered expression in germ cells from all 3 generations after sGC (mir-1279($FC_{(F1-3)}$=5.66, 5.28, 17.3), mir-2137(3.32, 3.56, 3.86), mir-638(3.12, 2.93, 3.14), mir-7008(4.59, 6.36, 3.43), mir-125b-1(-3.94, -3.66, -2.87), and mir-1305(-3.46, -3.12, -2.83)). Several of the affected miRNA have been shown to be associated with neuroendocrine function and behaviours.
Conclusions: Prenatal sGC exposure (F_0) modifies the miRNA expression in male germ cells across multiple generations (F_{1-3}). While the overall miRNA profiles are different in each generation, some changes of specific miRNA are common in F_{1-3}. These miRNA changes may be involved in the trans-generational effects of prenatal sGC on neuroendocrine function and behaviours described previously. Our findings provide new perspectives on the mechanisms of transgenerational transmission.

Placental Transfer and Effects of Sildenafil on the Human Placenta, an Ex Vivo Dual-sided Perfusion Study

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Background/Aims: Over the last years sildenafil, a phosphodiesterase-5 (PDE5) inhibitor that enhances nitric oxide (NO) mediated vasodilation, has emerged as a promising treatment for preeclampsia (PE). However, results from clinical trials are conflicting, and knowledge of the transfer over and effects of sildenafil on the human placenta itself is lacking, especially concerning the PE placenta.
Method: Placentas of uncomplicated pregnancies at term (n=6) and early onset (< 34 weeks of gestation) PE pregnancies (n=2), collected directly after caesarean section, were dually perfused for 3 hours with sildenafil (500 ug/L) to evaluate placental transfer. In isolated chorionic plate arteries of healthy (n=7) and PE (n=5) placentas that were preconstricted with the thromboxane A2 agonist U46619, the effects of sildenafil (1 µmol/L) and the non-selective PDE inhibitor vinpocetine (10 µmol/L) on NO-mediated vasodilation with sodium nitroprusside (SNP) were studied using wire-myography. Placental mRNA expression of NO synthases (eNOS and iNOS), PDE5 and PDE1 was assessed with q-PCR, and PDE5 protein expression with Western blot.
Results: After 3 hours of perfusion the mean fetal-to-maternal transfer ratio of sildenafil was 0.37±0.03 in healthy placentas vs. 0.66 and 0.47 in the 2 PE placentas. Sildenafil and vinpocetine both significantly potentiated NO-mediated vasodilation by SNP in healthy placentas (pEC50 8.0±0.2 and 7.9±0.1 vs. 7.6 ±0.1, p=0.02). In PE placentas neither PDE inhibitor affected the response. Placental mRNA levels of eNOS, iNOS and PDE5 were comparable in healthy and PE placentas, and mRNA levels of PDE1 were significantly lower in PE placentas (p=0.03). There was no significant difference in PDE5 protein expression.
Conclusions: Our study reveals that placental transfer of sildenafil is higher in early onset PE placentas compared to healthy placentas. We showed that although sildenafil improves NO-mediated vasodilation in healthy fetoplacental vasculature, it did not have these beneficial effects in PE placentas, indicating the impairment in PE is unlikely due to PDE5 upregulation. Possibly, modulating other factors of the NO pathway could prove beneficial in PE, or the NO pathway is not the appropriate target.

Significant Differences In First Trimester Embryonic Growth Trajectories After Fresh and Frozen-thawed Embryo Transfer

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Background/Aims: The 'freeze-all strategy' of resulting embryos in IVF/ICSI treatment is increasingly applied in fertility clinics worldwide, as it reduces the risk of ovarian hyperstimulation syndrome while success rates seem to be similar. However, recent studies suggest that pregnancies after frozen embryo transfer (FET) are associated with large for gestational age babies and higher birthweight. The aim of this study is to investigate whether embryonic growth trajectories in the first trimester of pregnancy are already different between pregnancies conceived *in vivo*, defined as spontaneous, and conceived after *in vitro* fertilization treatment with either fresh embryo transfer (fresh ET) or FET.
Method: A total of 567 singleton pregnancies, of which 336 were conceived spontaneously, 169 after fresh ET and 62 after FET, were selected from the prospective Rotterdam Periconception Cohort of our department. Women filled out questionnaires regarding demographic, obstetric and lifestyle characteristics at preconceptional enrolment. Serial crown-rump-length (CRL) and embryonic volume (EV) measurements were performed offline using 3D ultrasound and virtual reality techniques at 7, 9 and 11 weeks of gestation. Associations between embryonic treatment and serial embryonic size measures were assessed by linear mixed models.
Results: Embryos conceived after FET are associated with larger embryonic growth trajectories compared to spontaneous pregnancies (CRL β: 0.195 (95%CI: 0.108-0.282)) and EV β: 0.087 (95%CI: 0.042-0.132)). After adjusting for confounders (fetal sex, maternal age, body mass index, geographic origin, parity, education, smoking, alcohol and folic acid) these associations remained significant (CRL β: 0.170 (95%CI: 0.067-0.272) and EV β: 0.074 (95%CI: 0.022-0.127)). Significantly positive associations were also found when comparing the growth trajectories of FET with fresh ET pregnancies as reference (data not shown). No significant differences were found between fresh ET and spontaneously conceived pregnancies.
Conclusions: Already in the first trimester, embryonic growth trajectories are larger in embryos conceived after FET, compared to fresh ET or spontaneously conceived pregnancies indicative of epigenetic effects of the freeze-thaw procedure. Further research is needed to unravel the underlying mechanisms of these associations and the clinical implications both pre- and postnatally.

Breaking cycles: Simulating the effects of potential interventions to break the ties between maternal overweight and child adiposity via TMLE and cross-validated machine learning

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Background: Focused modelling of putative causal mechanisms for intrauterine programming of offspring cardiometabolic health can improve core DOHaD research by

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facilitating estimation of intervention benefits. We demonstrate a novel application of targeted maximum likelihood-based estimation (TMLE) to synthesize numerous, complex covariate relationships and simulate changes in population phenotype distributions when intervening on mechanistic intermediates.
Method: Using data from 562 birth cohort participants (GUSTO study; Singapore), we investigate a mechanism linking maternal pre-pregnancy BMI (ppBMI), mid-late pregnancy vitamin D, gestational weight gain (GWG), and fetal DNA methylation on child adiposity at 6 years. Each has been associated with child size in past studies. Using TMLE, we estimate the sequential effects of maternal overweight (ppBMI>27) on plasma vitamin D concentration, GWG, fetal DNA methylation, and child BMI Z-score (SD). In a subset with quantitative MRI (N=242), we investigate effects on total fat mass. We incorporate intermediate confounding by maternal depression (Beck Depression Inventory score), other plasma micronutrients (Fe, folate, B12), gestational age at birth, and duration of breastfeeding. Models were estimated via cross-validated, ensemble machine learning (*e.g.* Bayes GLM, neural net).
Results: Multivariable regressions adjusted for polygenic risk score, parental size, and sociodemographics support past associations (*e.g.* +0.08 SD/kg ppBMI; +0.17 SD/0.1 SD *ANK3* methylation). In mothers with ppBMI>27, vitamin D<75 nmol/L, GWG>11 kg (mean child Z-score =0.87), lowering average ppBMI to <27 would have resulted in lower average child BMI at 6 years by 0.86 SD (95% CI: -1.7, -0.05). A joint intervention increasing vitamin D >75 nmol/L and reducing GWG < 11 kg among overweight mothers would have lowered BMI by 0.8 SD (-1.6, 0.07). A hypothetical intervention controlling ppBMI, vitamin D, GWG, and *ANK3* methylation would result in 1.2 SD (-2.0, -0.4) lower BMI. The same intervention would have lowered total fat mass by 27% (-41%, -0.9%).
Conclusions: We demonstrate an approach to estimate potential intervention effects to break the ties between maternal ppBMI and child adiposity. Notably, intervening on intermediates may be as effective as reducing ppBMI. However, findings are contingent on formal causal inference assumptions as well as cross-validated algorithm performance, which require extensive sensitivity analyses. Preliminary bias analysis by plasmode simulation suggest TMLE may be unbiased under the observed confounding structure.

Growth trajectories of the prenatal human brain and neurodevelopmental outcome at 2 years of age

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Background/Aims: In accordance with the 'DOHaD paradigm' we hypothesize that fetal brain growth in complicated pregnancies is associated with derangements in neurodevelopment of the child later in life. The aim of this study was to evaluate associations between fetal brain growth trajectories and neurodevelopment in infants with congenital heart disease (CHD), fetal growth restriction (FGR) and preterm birth (PTB) and uncomplicated controls.
Method: We selected cases and controls from the Rotterdam periconception cohort conducted at the Erasmus MC. Serial two-dimensional and three-dimensional ultrasound (2D/3D-US) scans were performed at 22, 26 and 32 weeks gestational age. Fetal brain growth trajectories were evaluated by serial measurements of the head circumference, cerebellum, corpus callosum, Sylvian fissure, insula and parieto-occipital fissure. Different domains of neurodevelopment were evaluated using the Ages and Stages questionnaire (ASQ) and the Child Behaviour Checklist (CBCL) at two years of age. Linear mixed models and linear regression models were used to investigate associations between the growth trajectories and neurodevelopmental outcomes adjusted for potential confounders.
Results: Neurodevelopmental outcomes were obtained of 138 infants (response rate 68.3%); 12 CHD, 10 FGR, 10 PTB and 106 controls. In controls we found a negative association between the growth rate of the left insula and the ASQ score (β=-1209.87, p<0.01). In FGR a larger initial size of the right Sylvian fissure measurement was associated with a higher CBCL score (β=4.13, p<0.01). In CHD a significantly positive association was observed between the initial size of the left Sylvian fissure measurement and the CBCL score (β=3.11, p<0.01). Furthermore, a negative association was observed between the growth rate of the left Sylvian fissure and the CBCL score (β=-171.99, p<0.01).
Conclusions: This study shows that growth trajectories of several prenatal brain structures are significantly associated with neurodevelopment at two years of age. The clinical implication of these findings needs further investigation.

Increased rates of mental and developmental disorders in term and preterm-born children exposed to maternal antenatal glucocorticoids: a nationwide register study

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Background/Aims: Maternal antenatal glucocorticoids (AG) are among the most effective treatments to improve the prognosis of infants born preterm and constitute standard care for women at risk for delivery at <34 weeks. Recently, the treatment indications have been expanding to the large numbers of late preterm deliveries (34 to 36 weeks). Moreover, it is not uncommon that after the treatment pregnancy goes on to term. We studied mental and developmental disorders in

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children who were exposed to maternal AG, assessing separately those born at term and preterm.
Method: We identified all singleton children born in Finland in 2006 to 2017 from the Medical Birth Register, which also provided perinatal data; 671,430 (99.8%) had data on AG and valid ID numbers. We linked these with data from the Care Register for Health Care, which includes ICD-10 codes for all inpatient and outpatient treatments in public specialty care. We analysed data with Cox regression. We also performed within-sibpair comparisons for 242,240 term sibling pairs born at term.
Results: AG had been given to mothers of 6767/642,130 infants born at term (≥37 weeks) (1.1% of term infants, 44.5% of those exposed to AG) and of 8454/29,300 infants born preterm (43.8% of preterm, 55.5% of all exposed). Hazard ratio for any mental/developmental disorder (any ICD-10 F code) for AG-exposed among the term was 1.54 (95% CI 1.40, 1.69) and among the preterm 1.46 (1.35, 1.57), adjusting for sex, maternal age, parity, maternal mental health disorders, pregnancy and delivery conditions, gestational age, and neonatal intensive care admission. The excess was contributed to by excess rates on disorders of psychological development (F80-F83), ADHD or conduct disorders (F90-F91) and sleep disorders (F51). When we compared exposure-discordant term-born sibpairs, AG exposure was connected to increased risk of any mental/developmental disorder: 1.33 (1.13, 1.57) when adjusted for sex, maternal age, parity, maternal mental health disorders, gestational age, interpregnancy interval, and older sibling's mental/developmental disorder.
Conclusions: Over 40% of infants exposed to maternal AG are born at term. Among both term and preterm born children, exposure to maternal antenatal glucocorticoids is associated with an increased risk of developmental and mental health disorders. The association persists in sibling-comparisons, which argues for causal effects of AG. This finding calls for caution when expanding the treatment to late preterm or early term births among whom possible side effects balance with lesser neonatal risks.

Effect of Maternal Omega-3 Fatty Acid and Vitamin E Supplementation on Placental Angiogenic Factors in Subtypes of Preeclampsia

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Background/Aims: Poor maternal nutrition is known to be associated with pregnancy complications like preeclampsia. Preeclampsia is associated with abnormal placental vasculature resulting due to increased oxidative stress and disturbed angiogenesis. Long chain polyunsaturated fatty acids play a critical role in the development of the placenta. Our earlier studies have demonstrated altered levels of polyunsaturated fatty acids, increased oxidative stress, lower vitamin E levels in women with preeclampsia. The current study examines the effect of maternal omega-3 fatty acids and vitamin E supplementation on placental angiogenic factors in a rat model of preeclampsia.
Methods: Pregnant wistar rats were assigned to control and four treatment groups: early onset preeclampsia (EOP); late onset preeclampsia (LOP); early onset preeclampsia + omega-3 fatty acid supplementation +vitamin E (EOP+O+E) and late onset preeclampsia + omega-3 fatty acid supplementation +vitamin E (LOP+O+E). L-Nitroarginine methylester (L-NAME; 50 mg/kg body weight/day) was used to induce preeclampsia. Dams were dissected at d14 and d20 of gestation and placental tissues were collected. One way ANOVA was used to compare means and post-hoc Tukey was used to test the differences among the means
Results: Animals from both EOP as well as LOP groups demonstrated lower placental protein and mRNA levels of vascular endothelial growth factor ($p<0.01$). VEGFR-1 protein levels were also lower ($p<0.01$) in the EOP group. HIF-1 alpha m-RNA levels were higher only in EOP group ($p<0.05$). Maternal omega-3 fatty acids and vitamin E supplementation was beneficial in normalizing the levels of angiogenic factors only in the late onset but not in the early onset preeclampsia
Conclusion: The present study indicates that placental angiogenic factors are disturbed in both subtypes of preeclampsia. These findings suggest a differential role of maternal nutrient supplementation on angiogenesis in the two subtypes of preeclampsia.

Maternal obesity drives differential DNA methylation in neonatal monocytes in a sex-specific manner.

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Background/Aims: Maternal obesity is a risk factor for cardiometabolic and immune-related diseases in the offspring during adulthood. Monocytes from offspring born to obese women have an impaired function that could result from abnormal DNA methylation patterns associated with maternal obesity. The aim of this study was to determine changes in DNA methylation in monocytes from offspring born to obese women and to evaluate the potential effects of such epigenetic changes in immune function.
Method: Cord blood samples were obtained from neonates, matched by birthweight and gestational age, born to lean (BMI >18.5 and < 24.9, n = 12) and obese women (BMI ≥

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30, n = 15). Monocytes were isolated by adhesion. Genome-wide differentially methylated CpGs (DMC) were determined using an Infinium MethylationEPIC BeadChip (850K). Ontology and pathway analysis for DMC were performed using DAVID, and the potential effect on gene expression was validated with data from The Cancer Genome Atlas (TCGA) database.
Results: DNA methylation analysis revealed 22,313 DMC in monocytes of female offspring of obese women (FO) (adjusted $p < 0.01$ with FDR < 0.05), whereas monocytes from the male counterpart (MO) had 20,412 DMC (nominal $p < 0.01$) that lost significance after FDR correction. Functional enrichment analysis of DMC laying in promoter regions showed a hypermethylation of genes involved in immune-related processes and pathways in FO monocytes. Furthermore, TCGA data showed that many of these DMC were negatively correlated to gene expression.
Conclusions: Maternal obesity might program in a sex-specific manner the innate immune function through an altered DNA methylation pattern. These epigenetic changes occur at immune-related genes and may account for the impaired function of monocytes in female offspring.

Fetal and Placental Consequences Following Ancestral Paternal Exposure to Arctic Pollutants and Folic Acid Supplementation

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Background/Aims: Inuit people have more adverse pregnancy outcomes and shorter life expectancies. Because of their traditional diet, Inuit are highly contaminated by Persistent Organic Pollutants (POPs), known to induce negative health effects. We hypothesize that folic acid (FA) supplementation attenuates developmental disorders in fetuses and placentas associated with prenatal paternal exposure to POPs over multiple generations.
Method: We used a four-generation rat model, in which F0 founder females were divided into four treatment groups (n=8) and gavaged with corn oil or an environmentally-relevant Arctic POPs mixture before mating and until parturition. F0 diets contained either a basal level of FA (2 mg/kg), or supplemented level of FA (FAS; 6 mg/kg). Twelve F1 males/treatment were mated to untreated females to produce F2 rats and so on until F4. Histopathological examination of the fetuses and placentas were performed at gestational day 19.5. The cutoff value for significance is $p \leq 0.05$.
Results: The fetal:placental weight ratio (FW:PW) was reduced by POPs*FAS interaction in F1 and F2. In contrast, FW:PW increased due to POPs in F3 and by both POPs and FAS in F4. Placental histomorphometry reveals a reduced junctional zone area by POPs*FAS interaction in F1, whereas it was increased by both POPs and FAS in F2. No differences were present in F3 and F4. These results suggest inadequate placental efficiency and possible compensatory mechanisms. Surprisingly, FAS lineages exceeded the expected fetal malformation incidence in F1, F2 and F4 generations.
Conclusions: Prenatal paternal POPs exposure causes developmental disorders over multiple generations. FAS, however, may not represent an ideal solution to counteract the consequences of POPs. Multigenerational transmission of the paternal environment was apparent and may occur via placental disruption. Achieving our objectives will broaden current understanding of the toxicological impacts of the environment on human health and the developmental origins of disease.

Structural remodelling of cardiac ventricles in lambs born very preterm

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Background/Aims: Adults born preterm (<37 weeks' gestation) exhibit altered cardiac growth and are susceptible to impaired cardiac function. Pre-clinical sheep studies have shown that moderate preterm birth is associated with maladaptive structural remodelling of the cardiac ventricles in early postnatal life; it is likely that this would be exacerbated with decreasing gestational age at birth. The aim of this study was to examine the structure of the cardiac ventricles in 2 and 5 month old lambs born very preterm (stage of lung development equivalent to 28 weeks' gestation in humans).
Method: Lambs were delivered preterm via caesarean section at 128 days' gestation and mechanically ventilated after birth. Lambs were euthanised at 2 (n=8) or 5 (n=9) months term-equivalent age (TEA). Preterm lambs were compared to unventilated age-matched lambs that were born spontaneously at term (150 days gestation; n=9-10/age group). Cardiomyocyte number, apoptosis, cellular proliferation and interstitial collagen were analysed using immunohistochemistry, histology and stereology. Data were analysed using two-way ANOVA.
Results: Absolute and relative heart weight did not differ between preterm and term-born lambs at 2 or 5 months TEA. Cardiomyocyte number in both ventricles were not affected by preterm birth nor age. Interstitial collagen in the left ventricle increased with age (p=0.0015), and levels were exacerbated by preterm birth (p=0.0006). The percentage of interstitial collagen was greater in the right ventricle compared to the left, however levels in the right ventricle were not affected by

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preterm birth or age. Levels of cardiomyocyte proliferation and apoptosis in both ventricles were negligible in all lambs.
Conclusions: Findings from this clinically-relevant sheep study clearly demonstrate an adverse impact of very preterm birth and/or mechanical ventilation on postnatal cardiac structure and cardiomyocyte growth.

Oocyte exposure to high estradiol during ovarian stimulation and risk of adverse perinatal outcomes after frozen-thawed embryo transfer: a retrospective cohort study

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Background/Aims: Supraphysiological estradiol (E2) levels during the window of implantation and early pregnancy induced by controlled ovarian stimulation (COH) can lead to adverse pregnancy and perinatal outcomes following fresh embryo transfer. Thus, frozen-thawed embryo transfer (FET) has been used to improve perinatal outcomes compared with fresh embryo transfer. However, it is unclear whether high E2 exposure to oocytes during COH have adverse outcomes following FET, independent of the effect of elevated E2 levels during early pregnancy.
Method: This single center, retrospective cohort study included all FET cycles between 2014 and 2017. All FET cycles were categorized into three groups according to the E2 level on the day of the hCG trigger (Group I: <10,000 pmol/L; Group II: 10,000-15,000 pmol/L; Group III: >15,000 pmol/L). Pregnancy outcomes and subsequent neonatal outcomes were compared among groups using multilevel logistic regression.
Results: Among all 10,581 FET cycles, higher E2 level during controlled ovarian stimulation (COH) were associated with lower rates of chemical pregnancy (p_{trend}<0.001), clinical pregnancy (p_{trend}=0.009), ongoing pregnancy (p_{trend}<0.001) and live birth (ptrend=0.005) as well as increased rates of early miscarriage (p_{trend}=0.023). Preterm births were more common among singleton deliveries in women with higher E2 level during COH (aOR_1[adjusted odds ratio]=1.93, 95%CI [confidence interval]: 1.22-3.06; aOR_2=2.05, 95%CI: 1.33-3.16). Small for gestational age (SGA) were more common in both singletons (aOR_1=1.25, 95%CI: 0.71-2.23; aOR_2=1.92, 95%CI: 1.17-3.16) and multiples (aOR_1=1.51, 95%CI: 1.02-2.26; aOR_2=1.86, 95%CI: 1.02-3.39) among women with relatively higher E2 level. No association was found between high E2 levels during COH and the rate of macrosomia or large gestational age (LGA).
Conclusions: Increased E2 levels during COH are associated with a decreased pregnancy rate and an increased rate of early miscarriage following FET. Supraphysiological E2 exposure during COH also increases the risk of preterm birth, SGA. In women undergoing FET cycles, milder COH protocols should be used to avoid supraphysiological E2 hormone levels. be asked to resubmit. Please read the guidelines carefully. Do not change the font size or font type. The congress managers are only too happy to assist if you have any questions or queries.

MitoQ antioxidant treatment in hypoxic pregnancy promotes pulmonary surfactant maturation in fetal sheep

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Background/Aims: Chronic fetal hypoxia is commonly associated with intrauterine growth restriction (IUGR) and increased oxidative stress. IUGR babies are at increased risk of premature delivery complicated by respiratory distress syndrome. MitoQ is a mitochondria targeted antioxidant designed to improve mitochondrial function and a possible treatment for IUGR pregnancies. Here, we investigated the effect of MitoQ on fetal lung development in chronically hypoxic fetal sheep.
Method: Under general anaesthesia, sheep pregnant with a singleton male fetus were surgically instrumented with femoral catheters at 100d gestation (term, 145d). Five days later, ewes were randomly assigned to Normoxia (21% O_2; 2ml vehicle), Hypoxia (10-11% O_2), Normoxia MitoQ (1.2mg.kg-1 daily) or Hypoxia MitoQ groups. Chronic hypoxia for 1 month was induced in isobaric chambers (Brain et al. *Physiol Rep* 3(12): e12614, 2015). At 138d gestation animals were humanely killed (sodium pentobarbitone). Fetal lungs were frozen in liquid N_2 for total RNA extraction and subsequent qRT-PCR gene expression analysis. Data were analysed by Two-way ANOVA.
Results: Data presented as Mean normalised expression ± SEM. Letters represent significant changes due to treatment (a), oxygen status (b) or an interaction of these factors (c) P<0.05. PS=pulmonary surfactant, UPR=unfolded protein response TF=transcription factor NO=nitric oxide C=Vehicle Control, Q=MitoQ, N=Normoxia, H=Hypoxia.
Conclusions: We show that MitoQ promotes molecular indices of surfactant maturation in the late gestation fetal lung in normoxic and hypoxic pregnancy. The interplay between chronic hypoxia and MitoQ treatment facilitating additional effects on glucocorticoid conversion, NO signalling and UPR warrants further investigation to determine the therapeutic value of MitoQ on fetal lung development. *Support: British Heart Foundation & Australian Research Council*

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Gene	Function	Control		MitoQ		Summary
		Normoxia	Hypoxia	Normoxia	Hypoxia	
SFTP-C	PS Maturation	4.16±0.46	5.25±0.30	6.14±0.53[a]	6.03±0.72[a]	↑Q
SFTP-D	PS Maturation	0.03±0.005	0.03±0.004	0.03±0.003	0.04±0.005[c]	↑Q/H
ATF6	UPR	0.15±0.02	0.10±0.003[c]	0.13±0.02	0.13±0.01	↓C/H
TTF1	Lung develop TF	0.15±0.02	0.09±0.01[c]	0.11±0.01	0.15±0.01[c]	↓C/H;↑Q/H
ENOS	NO synthesis	0.02±0.001	0.02±0.001	0.01±0.001[a]	0.01±0.001[a]	↓Q
INOS	NO synthesis	0.05±0.004	0.04±0.001[c]	0.05±0.003	0.06±0.003[c]	↓C/H;↑Q/H

Data presented as Mean normalised expression ± SEM. Letters represent significant changes due to treatment (a), oxygen status (b) or an interaction of these factors (c) $P<0.05$. PS=pulmonary surfactant, UPR=unfolded protein response TF=transcription factor NO=nitric oxide C=Vehicle Control, Q=MitoQ, N=Normoxia, H=Hypoxia.

Preconception and Gestational Social Isolation Modifies Inflammatory and Stress Marker Profiles in Rats

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Background/Aims: Maternal stress before and during pregnancy results in adverse perinatal outcomes, such as preterm labour, leading to metabolic and cardiovascular diseases in the offspring. Social isolation (SI) as a maternal stressor is associated with altered brain development and behaviour in rodents. We hypothesize that SI before conception and during pregnancy predisposes a rat to adverse pregnancy outcomes and to an altered profile of inflammatory and stress markers.
Method: Female rats of the F0 parental and F1-F3 generations were assigned to SI or control groups. SI involved housing dams alone for two weeks before breeding and during pregnancy. This gave rise to three groups of F1-F3 dams: control, single generation SI (SG) and multigenerational SI (MG). Uterine tissues were collected at weaning of offspring. RT-qPCR for mRNA abundance analysis was performed for uterine inflammatory and stress markers such as *Il1b, Il1ra,* corticotropin-releasing hormone and receptors (*Crh, Crhr1/2*) and 11β-hydroxysteroid dehydrogenase type 2 (*Hsd11b2*). Data were analyzed by t-test (F0) and two-way ANOVA (F1-F3), $p<0.05$ with $0.05<p\leq0.1$ considered trends.
Results: SI tended to decrease gestational length of F0 pregnancies ($p=0.085$). In F0 uterus, *Hsd11b2* and *Crh* mRNA levels were significantly decreased in the SI group ($p<0.05$). No changes were detected in pro-inflammatory mediators mRNA. In F1 uteri, *Il1b* levels were significantly downregulated in the SG ($p<0.01$) and MG ($p<0.05$) groups compared to controls. *Il1ra* abundance was lower in SG ($p<0.001$) and MG ($p<0.01$). Conversely, *Hsd11b2* mRNA expression was increased in SG tissues ($p<0.05$), but not in the MG group. Analysis for the F2 and F3 generations did not show any significant results for all cytokines, *Crh* and *Hsd11b2* mRNAs.
Conclusions: SI in pregnancy differentially affects gene expression related to inflammatory/stress markers in F0 and F1 postpartum uteri, but not F2 and F3 uteri. SI has an opposite effect in F0 compared to F1 on *Hsd11b2* expression which encodes the enzyme that inactivates corticosterone, potentially altering the local corticosterone levels. Altered programming as a consequence of epigenetic changes by stress could change the offspring's ability to adapt to stress later in life.

Placental 11-HSD2 and cardiometabolic health indicators in infancy

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Background/Aims: Fetal excessive exposure to glucocorticoids may program cardiometabolic risk. Placental 11β hydroxysteroid dehydrogenase 2 (11β-HSD2) serves as a barrier to prevent fetal overexposure to maternal glucocorticoids. It has not been explored whether placental 11β-HSD2 levels are associated with cardiometabolic health in postnatal life.
Methods: In a prospective birth cohort study of 246 mother-infant pairs, we measured placental 11β-HSD2 expression, maternal (32-35 weeks of gestation) and cord plasma cortisol concentrations. The primary outcomes were homeostasis model assessment of insulin resistance (HOMA-IR) and blood pressure (BP) in infants at age 1-year. Other outcomes included fasting insulin, HOMA β-cell function, carotid intima-media thickness, weight z-score and skinfold thickness (triceps and subscapular) at age 1-y.
Results: Placental 11β-HSD2 expression was negatively correlated with HOMA-IR (r=-0.17, p=0.021) and fasting insulin (r=-0.18, p=0.017), and marginally negatively correlated to

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systolic BP (r=-0.16, p=0.057), but not correlated to HOMA-β, diastolic BP, carotid intima-media thickness and skinfold thickness (all p>0.1) in infants at age 1-y. Cord plasma cortisol was negatively correlated to skinfold thickness (r=-0.20, p=0007), but not correlated to other outcomes at age 1-y. Maternal plasma cortisol was positively correlated with maximal carotid intima-media thickness (r=0.20, p=0.03), but not correlated with other outcomes. Adjusting for maternal and infant characteristics, the associations were similar.
Conclusions: The study is the first to show that lower placental 11β-HSD2 expression is associated with higher insulin resistance in infancy. Independent cohort studies are required to confirm this novel finding.

DNA methylation in AgRP neurons regulates voluntary exercise behaviour

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Background/Aims: Adult propensity for voluntary exercise, a key determinant of metabolic health, is subject to developmental programming by the early-life environment. Agouti-Related Peptide (AgRP) neurons in the arcuate nucleus of the hypothalamus (ARH) are key mediators of energy balance. Since epigenetic mechanisms are implicated in developmental programming, we tested whether epigenetic alterations specifically in AgRP neurons affect energy balance.
Method: We generated mice lacking the *de novo* methyltransferase *Dnmt3a* specifically in AgRP neurons, subjected them to a range of metabolic and behavioural tests, and profiled DNA methylation and gene expression in ARH neurons by whole-genome bisulfite-sequencing (WGBS) and RNA-seq.
Results: Knockout mice exhibit a sedentary phenotype characterized by reduced voluntary exercise and increased adiposity. WGBS and transcriptional profiling in neuronal nuclei from the ARH in knockout vs. control mice revealed numerous differentially methylated genomic regions and reduced expression of AgRP neuron-associated genes. We used a novel method of read-level analysis to de-convolve WGBS data to localize promoter hypomethylation and increased expression of the growth factor *Bmp7* to AgRP neurons, suggesting a role for aberrant TGF-β signalling in the development of this phenotype.
Conclusions: These data demonstrate that DNA methylation in AgRP neurons is required for their normal epigenetic development and neuron-specific gene expression profiles, and that epigenetic mechanisms in the central nervous system influence individual proclivity for voluntary exercise, a phenomenon that may be involved in the developmental programming of energy balance.

A health promotion intervention targeting women with prior gestational diabetes mellitus and their families: Results from the intervention development phase. The Face it study

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Background/Aims: Gestational diabetes mellitus (GDM) is a transient condition during pregnancy associated with long-term adverse health outcomes in the woman and her offspring throughout the life course. The aim of this presentation is to demonstrate the process of developing a complex, multi-level health promotion intervention following the UK Medical Research Council's Framework and thereby address the knowledge gap of evidence-based program development.
Method: Co-production with the families was a key feature of the intervention development, which consisted of three stages: 1) evidence review and qualitative research, 2) co-production of the intervention outline, and 3) modelling and prototyping.
Results: At stage 1, literature reviews of behavioral interventions seeking to prevent diabetes in women with prior GDM showed that no specific intervention or intervention components were superior. The pooled effect on diabetes incidence was −5.02 per 100 (95% CI: −9.24; −0.80) indicating that intervention is superior to no intervention in prevention of T2DM among women with previous GDM. The qualitative research revealed that after the delivery, taking care of the baby became the women's dominant focus. Social and emotional support from partners were important to maintain motivation and healthy lifestyle. In the postpartum period, the women experienced limited initiative and support from healthcare providers to engage in a healthy lifestyle. At stage 2, digital and home-based solutions for supporting health behaviour and health literacy in the family as a unit came up from the majority of the women. The health visitor nurse was suggested as the main supportive caregiver. Finally, at stage 3 the prototype of a novel intervention was outlined. This will be presented at the DOHaD conference.
Conclusions: The Face-it health promotion intervention has been developed based on evidence and locally adapted in co-production with affected families. Its effectiveness will be evaluated in a randomized controlled trial at three sites in Denmark with an expected sample size of 460.

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Poor Fetoplacental Blood Flow is linked to Lower Kidney Volumes and Increased risk of Prehypertension in Children at 6y

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Background/Aims: Nephrogenesis in humans is complete by 34-36 weeks' gestation. Consequently, perinatal insults like reduced uteroplacental and fetoplacental blood flow can result in irreversibly reduced nephron endowment, increasing the risk of future hypertension and cardiorenal dysfunction. Our study evaluated the associations between poor fetoplacental blood flow, offspring kidney volumes and prehypertension at 6y in a mother-offspring cohort.
Method: As part of the GUSTO mother-offspring birth cohort study, we analysed singleton offspring who had umbilical artery Doppler data in the third trimester (n=1063). Resistance in umbilical artery blood flow was characterised using the systolic/diastolic (S/D) ratio. Children who had an S/D ratio above the 90th percentile were identified as having poor fetoplacental blood flow. Fetal growth velocity was calculated from fetal abdominal circumferences assessed in 2nd and 3rd trimester ultrasound scans. Kidney volumes were obtained from abdominal MRI images at age 6y using an ellipsoid approximation (n=394). Blood pressure data was available from 636 children. Prehypertension (n=102 (16%)) was defined using a paediatric threshold of 110/70 mmHg.
Results: Umbilical artery S/D ratio was associated with lower fetal growth velocity (r=-0.126, p<0.001). Children with poor fetoplacental blood flow did not differ from those with normal blood flow in weight, height or BMI at age 6y, but had smaller kidney volumes (57.4 vs 62.5 cm^3, -8.2%, p=0.019). After adjustment for ethnicity, gender & maternal factors (education, BMI & height), poor fetoplacental blood flow was linked to increased risk of prehypertension (RR=1.83 (95%CI 1.18, 2.83), p=0.007) at 6y.
Conclusions: Children who had poor fetoplacental blood flow displayed a renal volume deficit and higher risk of prehypertension at 6y. Our findings are consistent with research suggesting that nephron deficits induced by an adverse intrauterine environment are a risk factor for hypertension.

Epigenetics of neurodevelopmental disorders using monozygotic twins

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Background/Aims: Neurodevelopmental disorders such as autism spectrum disorders (ASD), cerebral palsy (CP) and epilepsy are some of the most prevalent childhood neurological disorders caused by damage to the growth and development of the brain. Early life environments predispose children to later health outcomes evidenced by the developmental origins of health and disease (DOHaD) phenomenon. Epigenetics, which refers to modifications of DNA without change in DNA sequence, is one way by which environmental exposures may contribute to development of disease. DNA methylation, arguably the most highly studied epigenetic mark, has been correlated with early life environmental exposures. These modifications most likely originate in utero, in line with the DOHaD hypothesis. The study of monozygotic (MZ) twins, in which genetics, age, sex, parental factors and shared environment are controlled for, helps in distinguishing the extent of effect of genetics and environment. Discordance for neurodevelopmental disorders has been recorded in MZ twins indicating a potential role of non-shared factors in disease risk. The aim of this research was to utilise the discordant MZ twin model to understand epigenetic changes associated with neurodevelopmental disorders.
Methods: Genome-wide DNA methylation was measured within three MZ twin cohorts discordant for a ASD, CP or epilepsy using Illumina's Infinium HumanMethylation450 and EPIC arrays. Statistical and bioinformatics pipelines were used to analyse DNA methylation data.
Results: DNA methylation analysis of CP-discordant twin pairs provides the first evidence that environmentally mediated differential methylation in genes involved in known processes such as hypoxia and inflammation, and processes such as cell adhesion, may contribute to the development of CP. An epigenome-wide analysis of epilepsy discordant MZ twin pairs revealed distinct patterns of DNA methylation within subtypes of epilepsies of unknown cause. Differentially methylated genes within epilepsy subtypes included those with a role in metabolic pathways, voltage-gated channel signaling and neurotransmitter processes.
Conclusions: This research paves the way for future larger studies, as understanding DNA methylation profiles associated with neurodevelopmental disorders, may facilitate biomarkers for earlier diagnosis. Analysing epigenetic data from disease discordant twins provides an elegant study design and has the power to explore non-shared environmental factors that further refine models of disease mechanisms and biomarkers.

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The impact of paternal diet and methyl-donor supplementation on fetal growth and placental development

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Background: The Developmental Origins of Health and Disease (DOHaD) hypothesis has a well-established focus on the significance of maternal diet for the development and health of her offspring. However, there is now evidence that poor paternal diet can also increase the likelihood of his offspring developing cardiovascular and metabolic disorders in adult life. Yet, the links between paternal diet and fetal growth, a known predictor of adult ill-health risk, remain to be defined. Therefore, the aim of this study was to ascertain the impact of sub-optimal paternal diet on fetal and placental development.
Method: Male C57/BL6 mice were fed one of five diets [NPD: normal protein (18% casein), LPD: low-protein (9% casein), MD-LPD: methyl-donor (including choline chloride, betaine, methionine, folic acid and vitamin B12) supplemented LPD, WD: western diet, or MD-WD: methyl-donor supplemented WD] for 8 weeks prior to mating. Males were then time mated to female C57/BL6 maintained on standard mouse chow prior to, and during, pregnancy. Dams were culled at embryonic day 17.5 for the collection and weighing of fetal and placental tissues.
Results: Paternal diet impacted the correlation of fetal weight to litter size, with NPD and LPD litters demonstrating a significant negative correlation; in that as litter size increases fetal weight decreases. In MD-LPD and WD litters, no correlation was observed, while in MD-WD litters a significant positive correlation was observed. Paternal WD increased fetal weight when compared to NPD litters (822mg vs 756mg; $p<0.05$). The addition of methyl-donor supplements prevented the observed fetal-overgrowth with MD-WD litters showing no differences from NPD litters (772mg vs 756mg). Placental weights did not follow the trends observed in the fetus and there were no significant differences observed between diet groups. However, the fetal:placental ratio was significantly reduced in MD-WD litters when compared to WD litters (8.5 vs 9.8; $p<0.05$).
Conclusions: This study indicates that a sub-optimal paternal diet impacts on fetal growth. Furthermore, our data suggest that supplementation with methyl-donors can negate some of these effects. Changes to fetal growth has often been attributed as a response to poor maternal diet during pregnancy. However, this study suggests that paternal nutrition also influences fetal development. Further mechanistic, reproductive, developmental and placental function studies are currently being conducted to define the biological mechanisms and pathways involved.

Late Preterm Birth Protects Against Allergies in Adulthood

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Background: Development of immunological pathways occurs during intrauterine life.
Aim: To examine whether preterm birth predicts a risk of atopy in adulthood
Methods: As a part of Ester preterm birth-cohort study, young adults born during 1985-89 in Northern Finland attended a clinical visit at mean age of 23.5 (standard deviation 1.7) years. Participants were tested for atopy for common allergens (skin-prick for birch, timothy, mugworth, dpteron, cat, dog) and provided history of atopic diseases including physician-diagnosed asthma, via a questionnaire. Mean wheal diameter (largest+perpenticular/2) ≥3mm and no reaction in negative control, was considered a positive result. 134 of the participants were those born early preterm: Gestational age (GA, weeks) ≤34, 235 late preterm: 34<37 and 331 full-term,≥37 ref. Finer GA groups used were <28, 28<32, 32<34, 34<36, 36<37, 37<39, ≥39 weeks (ref). Any atopy (positive test for any allergen) and also allergen-specific atopy status (Yes/No) were applied in logistic regression analyses, controlling for GA, age, sex (basic model). Full model also included highest parental education, maternal factors (age, prepregnancy BMI, smoking and hypertensive disorders during pregnancy, gestational diabetes, parity, birth weight z-score, caesarean section), participant factors (height, body mass index (BMI), smoking) and having a pet.
Results: 43% of all participants were tested positive for any atopy. Those born at 34<37 weeks had a lower risk of any atopy (OR: 0.63, 95% CI: 0.45/0.89) than term-born (,≥37). The association was not found among those born before GA<34 (OR: 0.94, 95% CI: 0.62/1.42). Examination of detailed GA-groups linked the lower risk of atopy to those born at GA 34<36 (OR: 0.6, 95% CI: 0.39/0.99) and especially GA 36<37 (OR: 0.54, 95% CI: 0.35/0.84). Borderline risk was also present among those born at GA 37<39 (OR0.61, 95% CI: 0.35/1.08). Adjusting for the full model did not change the results.
Conclusions: Length of gestation has a significant effect on the early development of immunity. Slight prematurity may induce tolerance (non-atopic phenotype) by exposing individuals to environmental antigens earlier. Comorbidities of early preterm birth may counterbalance this benefit.

Relationship between birth season and biomarkers of fetal programming in a contemporary population

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Background/Aims: The month of birth is related to individual's health and mortality. The external environment changes with seasons and may influence fetal development during critical windows, important for tissue differentiation and organogenesis. We investigate if people born in different seasons of a year differ in biomarkers of fetal programming (i.e. dermatoglyphics, level of fluctuating asymmetry and digit ratio - 2D:4D).
Method: The study was conducted among rural Polish population. Participants were 234 women and 32 men aged 45-93 (mean=60.5; SD=10.54). Following indicators of fetal programming were analysed: Absolute Finger Ridge Count (AFRC), the difference between mean ridge counts of both thumbs and little fingers (Md15), overall facial asymmetry, central facial asymmetry, asymmetry of 4th finger, 2D:4D for the right and left hands, difference in mean 2D:4D between left and right hands and mean 2D:4D. Months of birth were categorized into seasons: Spring (March-May), Summer (June-August), Autumn (September-November) and Winter (December-February). The analyses were performed using ANOVA models adjusted for age and sex of participants when appropriate.
Results: Overall, people born in different seasons of the year differed only in mean values of Md15 (p=0.03). There was a borderline difference between people born in a summer comparing to those born in autumn (p=0.07). People born in autumn had lower values of Md15, which may suggest that they experience better conditions in early pregnancy. All other biomarkers of fetal programming did not differ in relation to a season of birth.
Conclusions: Season of birth was not associated with most of analyzed indicators of fetal programming. To our knowledge this is the first study using comprehensive set of biomarkers to test seasonality of birth in relation to fetal programming. Season of birth is often used as information of access to resources which may influence fetal development, however our research suggests that its usefulness may be limited.

Exploring dynamic complementarity between high-quality nurse home visiting and early childhood education and care on child developmental outcomes at 3 years

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Background/Aims: To efficiently address childhood health and developmental inequities, the theory of dynamic complementarity (DC) proposes that sustained early childhood investment in high-quality programs synergistically builds developmental gains. Two well-studied interventions are nurse home visiting (NHV) and early childhood education and care (ECEC). We aim to investigate synergistic benefits of NHV (0 to 2 years), followed by ECEC (2 to 3 years) on children's developmental outcomes at 3 years.
Method: Analysis of longitudinal data (2013-2017) from the completed Australian multi-site RCT "right@home". 722 pregnant Australian women experiencing adversity were assigned NHV or usual care ages 0-2 years. 558 families consented to further follow-up. Between ages 2-3 years, carers reported self-selected ECEC. Outcomes were children's language (CELF) and parent-reported child behaviour (SDQ), physical and socio-emotional development (PedsQL 4.0) at age 3 years. Children were categorised as receiving NHV only; high-quality ECEC only; both exposures; and neither exposures (reference). For each outcome, adjusted multivariable linear regressions estimated mean differences for children with complete data. Statistical interactions between exposures examined DC.
Results: 287/558 families (51%) provided complete case data. NHV alone and NHV/ECEC were strongly associated with a respective 5.3 (95% CI: 1.8 to 8.7, p=0.005) and 5.7 (95% CI: 0.8 to 10.5 p=0.02) mean increase in socioemotional PedsQL score, and a 2.0 (95% CI: -0.1 to 4.0, p=0.06) and 4.8 (95% CI: 0.7 to 9.0, p=0.02) mean increase in physical PedsQL score compared to receiving neither exposure. There was no evidence for significant statistical interaction between NHV and ECEC for any outcome.
Conclusions: DC was not observed between NHV and ECEC in developmental outcomes at 3 years. Interestingly, NHV alone may account for observed results, which would benefit from replication with imputed full cohort data. This approach may be applied to other longitudinal studies to inform policy and programmatic designs contextualising DC throughout the life-course.

DOHaD and Exercise: Physical Activity as a Tool in the Programming/Deprogramming Paradox

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Background/Aims: Metabolism programming is a core aspect of the DOHaD concept. The literature shows that exercise affects the molecular and physiological pathways related to metabolism programming, suggesting that exercise can be a tool to stimulate good programming or reverse poor programming. Early overfeeding is a well-known animal model for studying mal-programming. To investigate the feasibility of physical exercise as a deprogramming tool, we applied a low-frequency/moderate-intensity exercise protocol for young adult obese rats programmed by early overfeeding.
Methods: Two days after Wistar rats' delivery (PN2), litters were adjusted to 9 for control (NL) or 3 pups (SL) to induce early overfeeding. After weaning (PN21), SL rats were divided

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between sedentary (SED) and exercised (EXE). At PN30 EXE rats started in a protocol with 3 sessions per week at moderate-intensity, lasting up to PN80. Feed intake of the animal was monitored throughout the experimental period, and brown adipose tissue (BAT) function was evaluated from PN87 to PN90. The rats were euthanized on PN91, white fat and BAT were extracted and weighed. The BAT was stored for further analysis.
Results: As expected, SL-SED rats presented increase in food intake and fat accumulation ($p<0.05$), and a reduction in BAT function ($p<0.0001$) compared to NL animals. Low-frequency/moderate-intensity exercise reduced food intake and fat accumulation ($p<0.05$) in SL-EXE animals and improved BAT function ($p<0.0001$), with an increase in UCP1 content in BAT ($p<0.001$), compared to SL-SED rats.
Conclusion: The protocol of moderate-intensity and low frequency exercise protocol was able to revert a series of characteristics programmed by early overfeeding in young adult rats, reducing hyperphagia, fat accumulation and improving BAT function with an increase in the content of thermogenic protein UCP1. These results reinforce the potential of exercise, even at low doses, as a tool to improve metabolism programmed in a DOHaD context.

Effect of maternal preconceptional and pregnancy micronutrient interventions on children's DNA methylation: findings from the EMPHASIS study

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Background: Maternal nutrition during pregnancy is known to influence risk of cardiovascular and metabolic disorders over an individual's life-course. Epigenetic mechanisms, notably DNA methylation, have been speculated to mediate this link, but human evidence is lacking. The EMPHASIS (**E**pigenetic **M**echanisms linking **P**re-conceptional Nutrition and **H**ealth **Ass**essed in **I**ndia and **S**ub-Saharan Africa) study combines two maternal micronutrient intervention cohorts to address this evidence gap.
Methods: The Mumbai Maternal Nutrition Project, India, is a randomized controlled trial in which women were supplemented with micronutrient-rich foods before and during pregnancy. In the Peri-conceptional Multiple Micronutrient Supplementation Trial, The Gambia, women were supplemented with multiple micronutrient tablets until pregnancy. The children born to these mothers were followed up at 5-9 years of age. Whole blood DNA methylation and genotype profiles were generated using the Illumina EPIC and GSA Arrays respectively in 698 Indian and 293 Gambian children. An Epigenome-wide Association Study was performed on individual datasets and significant loci (FDR<5%) were validated by pyrosequencing. Potential genetic influence on validated hits was assessed in a genome-wide mQTL analysis.
Results: In the Gambian cohort, six differentially methylated CpGs were identified mapping to *ESM1*, *CTNNA2* and *CDH18* (FDR<5%). The intervention reduced methylation (2.5-5.0%) at these loci. Regional analysis revealed two significant differentially methylated regions within *ESM1* and *LZTS1*. A single CpG in *TMEM106A* passed significance threshold in the Indian data; however, its effect was very small (<0.1%). The variant rs1423249 emerged as a strong mQTL for the *ESM1* CpGs, but this did not account for the effect of nutritional intervention which remained independently significant. Further analysis demonstrated enrichment of metastable epialleles and nutrition sensitive loci in the Gambian cohort.
Conclusion: The study highlights *ESM1* as a novel gene sensitive to maternal periconceptional nutrition supplementation and suggests that periconceptional nutrition has the potential to affect child's DNA methylation.

Maternal dietary fibre intake during pregnancy is associated with infant allergic disease

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Background/Aims: Maternal nutrition during pregnancy may play a profound role in infant immune development. High dietary fibre intakes contribute to gut microbial diversity and short chain fatty acid (SCFA) production. SCFA are thought to have anti-inflammatory and immunomodulatory functions. However, the influence of specific sub-types of maternal dietary fibre intakes during pregnancy on infant immune development and allergic disease outcomes remains largely unknown.
Method: In this observational study, we investigated possible associations between maternal intake of total dietary fibre, soluble fibre, insoluble fibre, resistant starch and prebiotic fibre, with allergic disease outcomes during infancy. Between 36-40 weeks gestation, pregnant women completed a semi-quantitative food frequency questionnaire reporting on their dietary fibre intakes during late pregnancy. At 12 months of age, infants attended a clinical assessment to determine symptoms and medical diagnosis history of wheeze and eczema outcomes. All infants were also skin prick tested to common foods and

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environmental allergens to determine their allergen sensitization status.
Results: A total of 639 mother-infant pairs were included in this cohort analysis. Higher maternal intakes of total dietary fibre, resistant starch and fibre from gluten rich foods were associated with increased incidence of both parent reported eczema symptoms and medically diagnosed eczema. among the dietary fibre sub-types, the strongest associations were found between high intakes of resistant starch (P=0.01) and gluten rich foods (P=0.008) with increased incidence of doctor diagnosed infant eczema. In contrast, higher maternal resistant starch dietary intakes appear protective against wheezing, especially with reduced incidence of medically treated infant wheeze (P=0.02).
Conclusions: This observational study suggests that increased consumption of maternal resistant starch intakes in late pregnancy is associated with increased risk of development of infant eczema. Randomised control trials on specific dietary fibre component intakes during pregnancy and allergic disease outcomes in early life are required.

The relationship between maternal adiposity and offspring kidney development *in utero* and kidney function in infants: the Gomeroi gaaynggal Study

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Background/Aims: Studies suggest that maternal obesity during pregnancy has a detrimental impact on offspring renal development and function. This is pertinent to Indigenous Australians as they are twice as likely as non-Indigenous Australians to develop chronic kidney disease (CKD). The aim of our study was to examine if there was an association between maternal adiposity and fetal kidney growth in late gestation (>28 weeks) and kidney function in infants, <2.5 years of age, from the Gomeroi gaaynggal study.
Method: Pre-pregnancy body mass index (BMI) was recorded at the first prenatal visit and maternal adiposity at >28 weeks gestation was measured as percent body fat and visceral fat area obtained using bioelectrical impedance analysis. Fetal kidney structure was assessed by ultrasound. Urinary albumin:creatinine and protein:creatinine were measured in infants after spot urine collection from nappies as indicators of kidney function. Multiple linear regression and multi-level mixed effects linear regression models with clustering were used to account for repeated urinary measures in infants. Sensitivity analyses were carried out to determine the covariates to be adjusted for.
Results: 147 Indigenous mother-child pairs were examined. Maternal adiposity and pre-pregnancy BMI were positively associated with estimated fetal weight (EFW) in late gestation, but not with fetal kidney size. When adjusted for smoking, maternal percentage body fat was negatively associated with combined kidney volume relative to EFW. Maternal adiposity and pre-pregnancy BMI were not associated with any alterations in infant kidney function (n=84 observations).
Conclusions: Our findings suggest that Indigenous babies born to obese mothers are experiencing glomerular hyperfiltration *in utero* possibly because nephron number is reduced relative to body weight. This may predispose them to increased risk of CKD in later life. Although no effect on renal function was observed at <2.5 years, long term follow-up of offspring is required to determine any impact in later life.

Placental multidrug resistance transporter expression and offspring behaviour after prenatal administration of the viral mimetic poly(I:C) in the mouse

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Background: The placenta features a barrier replete with the multidrug resistance ABC transporters P-glycoprotein (P-gp, encoded by *Abcb1a* and *Abcb1b* genes) and breast cancer resistance protein (BCRP, *Abcg2*). Current evidence show that gestational infection has the potential to alter placental expression and function of these transporters. As such, we used the viral mimetic polyinosinic-polycytidylic acid (poly (I:C)), a synthetic analogue of double stranded RNA, widely used to model viral infection through TLR-3 activation. We hypothesized that poly (I:C) may functionally disrupt placental ABC transporters as well as behavioral parameters in the offspring.
Aim: To evaluate the expression of selected placental ABC transporters, and behavioral changes in the offspring in a murine model of viral infection mimicked by poly (I:C).
Methods: Pregnant mice (CEUA-CCS: 036/16) were intravenously administered with poly (I:C) or PBS (control group) on gestational day (GD) 13.5. For the behavioral analysis, adult offspring from 5 pregnancies were subjected to the Rotarod performance test on 54 and 93 days of age and the T-water maze test at 96 days (n=15-22-sex separated). For placental analysis, 6 pregnant females from each group were euthanized at GD18.5. Four ABC transporters were evaluated by qPCR analysis: the *Abcb1a* and *Abcb1b* genes, *Abcg2* and *Abca1* (a lipid transporter). Student-T ($p < 0.05$) was used for statistical analysis.
Results: A decreased placental expression of *Abcb1a*, *Abcb1b* and *Abcg2* was observed following poly (I:C) administration when compared to the control group (P<0.05). No differences were observed in *Abca1* expression. The offspring exhibited an impaired performance in the Rotarod test (P<0.01) and the T-water maze task (P<0.05).

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Conclusion: Viral infection during pregnancy impairs the expression of placental multidrug resistance transporters encoding genes and has the potential to increase fetal exposure to drugs and toxins; this effect was associated with motor and cognitive deficits in the adult offspring.

Detecting epigenetic mechanisms that putatively mediate the influence of early life exposures on disease susceptibility

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Background/Aims: There is mounting evidence that prenatal and early life exposures have a profound impact on later life health and disease susceptibility. Epigenetic factors, such as DNA methylation (DNAm), have long been postulated as possible molecular mechanisms that may be responsible for these effects. In this study, we have developed an integrative approach using a technique known as Mendelian randomization (MR) to highlight changes in DNAm levels which may mediate the effect of environmental exposures on disease risk.
Method: To illustrate our approach, we identified 412 CpG sites where DNAm was associated with prenatal smoking. We then applied MR to investigate potential downstream effects of these putative changes on 643 complex traits using findings from large-scale genome-wide association studies. To strengthen evidence of mediatory mechanisms, we used multiple-trait colocalization to assess whether DNAm, nearby gene expression and complex trait variation were all influenced by the same causal genetic variant.
Results: We identified 22 associations which survived multiple testing ($P<1.89x10^{-7}$). In-depth follow-up analyses of particular note suggested that the associations between DNAm at the *ASPSCR1* and *REST/POL2RB* gene regions, both linked with reduced lung function, may be mediated by changes in gene expression. We have subsequently applied our approach to assess the association between DNAm at 181,294 CpG sites and over 700 complex traits. A web application to visualise and disseminate findings has been developed for researchers to investigate this putative causal map of associations across the human epigenome.
Conclusions: Our atlas of results should prove valuable in prioritising CpG sites which may mediate the effect of prenatal and early life risk factors on disease. In-depth evaluations of findings are necessary to robustly disentangle causality from alternative explanations such as horizontal pleiotropy.

Maternal Periconceptional Alcohol Consumption is Associated with Increased Child Blood Pressure

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Background/Aims: Experimental data indicate that maternal periconceptional alcohol intake can adversely impact fetal organ development and result in altered cardiometabolic risk in the offspring. We assessed the relationship of maternal alcohol consumption in the 1 year before pregnancy recognition with child blood pressure at age 6 years in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) mother-offspring cohort.
Method: We analysed data from 202 mother-child pairs with pre-pregnancy alcohol consumption reported at 26-28 weeks of gestation and child blood pressure measured at age 6 years. Total alcohol consumption (g/day) in the 12 months prior to pregnancy recognition was categorized as above 75th percentile (1.9 g/day, equivalent to 20% of the limit of alcohol consumption (10 g/day for women according to Singapore guidelines)), below 75th percentile, and none. The association between alcohol consumption (ln transformed) and child blood pressure was determined using multiple linear regression after adjustment for ethnicity, maternal education, age, household income, smoking exposure, and child's height.
Results: Among the 202 women reported to having consumed alcohol in the year before pregnancy recognition, a tripling of alcohol consumption (which is still well below the recommended limit) increased offspring systolic blood pressure at age 6 years by 1.3 mmHg (p=0.002). The children of mothers with alcohol consumption >75th percentile had significantly elevated systolic blood pressure compared with children of mothers with alcohol consumption <75th percentile (104.7 ± 8.6 mmHg vs. 100.1 ± 8.0 mmHg, p=0.002), and those of women who did not consume alcohol (104.7 ± 8.6 mmHg vs. 100.6 ± 8.2 mmHg, p=0.001). Alcohol consumption <75th percentile did not influence systolic blood pressure.
Conclusions: Our findings suggest that maternal alcohol consumption prior to pregnancy recognition could have adverse consequences on child blood pressure. Elevated childhood blood pressure has been linked to increased risk of adult hypertension and cardiovascular disease. Increased public awareness regarding the potential detrimental effects of alcohol consumption prior to pregnancy recognition at well below recommended levels would benefit offspring cardiovascular health.

Indoor urban environment and conventional risk factors for paediatric tuberculosis among 1-12 years old children in a megacity in Pakistan: a matched case control study

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Background/Aims: TB among children is less well-defined and its risk factors are less well-studied. Indoor environment may play a significant role particularly for childhood TB.Objectives: To determine the association of indoor urban environment and conventional risk factors for pulmonary TB among children aged 1 to 12 years.
Method: age matched case control study was conducted in two hospitals (a large tertiary and a secondary level) of megacity Karachi, Pakistan. The study recruited pulmonary TB cases (n=143), diagnosed by trained physicians using Pakistan Paediatric Association Scoring Chart for Diagnosis of Tuberculosis (PPASCT), and two age matched (±1 year) controls for each respective case (n=286) during June 2015-May 2016. The conditional logistic regression was conducted to determine the risk of pulmonary TB due to exposure to second hand smoke (SHS) and other conventional risk factors.
Results: Female child (mOR: 1.8), children belonging to minor communities in the city (mOR: 2.3 - 4.5), household TB contact (mOR: 7.5), use of open kitchen for cooking (mOR: 2.7), though insignificant but exposure to second hand smoke among under-5 year old children (mOR; 1.4), and time spent inside home (mOR: 1.1 per hour) increased the risk for TB.
Conclusions: This study strengthens the evidence that indoor air environment including time spent indoors, SHS (though insignificant), and low socioeconomic condition and being female and belonging to minor communities increase the risk for childhood TB. Concerted efforts are needed to improve indoor air environment in urban areas for healthier future generations.

Can breastfeeding reduce the adverse effect of maternal adiposity on offspring adiposity from early childhood to adolescence? Findings from the Longitudinal Study of Australian Children

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Background/Aims: Maternal adiposity increases the risk of obesity and metabolic disease in the next generation. We aimed to examine: 1) the extent to which maternal overweight/obesity and breastfeeding interact on an additive scale in relation with offspring adiposity, and 2) if breastfeeding ≥6 months has an additional beneficial effect beyond breastfeeding <6 months.
Method: We analysed prospective data from the Longitudinal Study of Australian Children (LSAC) B-cohort. Weighted generalized estimating equations were used to examine effects of maternal overweight/obesity and any breastfeeding (exclusive or non-exclusive) on offspring BMI, fat mass index (FMI) and fat-free mass index (FFMI) assessed at up to six time point between ages 2 and 13 years (N = 2,267). Analyses were adjusted for maternal age and sociodemographic characteristics, paternal BMI, and offspring age and sex. A product term was included in the models to examine interactions between maternal overweight/obesity and breastfeeding.
Results: Maternal overweight/obesity (45.2%) was associated with higher offspring BMI, FMI and FFMI, whereas breastfeeding initiation (94.8% of normal weight women and 89.9% of overweight/obese women) was associated with lower BMI and FMI. The combined effects of maternal overweight/obesity and never breastfeeding on offspring FMI [1.27 kg/m^2 (95% CI: 0.64, 1.89)] was significantly larger than the sum of the individual effects of maternal overweight/obesity [0.41 kg/m^2 (0.29, 0.53)] and never breastfeeding [-0.02 kg/m^2 (-0.47, 0.44)] (p-interaction=0.03). A similar pattern of results was found for BMI (P-interaction=0.12), but not for FFMI (p-interaction=0.23). Effects did not differ by breastfeeding duration (p>0.05).
Conclusions: Findings from this population-based study suggest that offspring of overweight/obese women who did not initiate breastfeeding were at the highest risk of adverse adiposity trajectories. Further studies are needed to examine potential maternal and perinatal risk factors that may explain these findings.

The Vaginal Microbiome As Predictor For In Vitro Fertilization With Or Without Intracytoplasmic Sperm Injection Outcome; the ReceptIVFity-study

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Background/Aims: Live birth rates for an IVF or IVF-ICSI treatment vary between 25% and 35% per cycle and it is difficult to predict who will or will not get pregnant after embryo

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transfer (ET). It has been suggested that the composition of the vaginal microbiota prior to treatment could predict pregnancy outcome. Analysis and interpretation of the vaginal microbiome prior to treatment might, therefore, offer an opportunity to improve the success rate of IVF or IVF-ICSI. We investigated if the presence or absence of certain vaginal bacteria is associated with pregnant rate after an IVF/IVF-ICSI treatment?
Method: In a prospective study, 303 women undergoing IVF/IVF-ICSI treatment were included. Women provided a vaginal swab before the start of treatment, after which the vaginal microbial composition was determined using the IS-pro technique. The predictive accuracy of the resulting microbiome profiles for IVF/IVF-ICSI outcome of fresh ET was evaluated by a prediction model based on bacterial parameters.
Results: The vaginal microbiota of 192 women who underwent a fresh ET could be analysed. Women with a low percentage of *Lactobacillus* in their vaginal sample were less likely to have a successful embryo implantation. Importantly, the prediction model identified a subgroup of women (17.7%, n=34) with a low chance becoming pregnant following fresh ET. With a sensitivity of 26% and specificity 97%, our model has a negative predictive accuracy of 94%. Additionally, the degree of dominance of *L. crispatus* was an important factor in predicting pregnancy chance since women with a profile of <60% *L. crispatus* became pregnant in >50%.
Conclusions: Our results indicate that vaginal microbiome profiling using the IS-pro technique enables stratification of the chance of becoming pregnant prior to the start of an IVF or IVF-ICSI treatment. Knowledge of their vaginal microbiota may enable couples to make a more balanced decision regarding timing and continuation of their IVF or IVF-ICSI treatment cycles.

The effect of metformin intervention on the programming of adiposity in offspring of obese pregnancy

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Background/Aims: Metformin is the first-line pharmacological treatment for gestational diabetes mellitus in several countries. However, long-term studies investigating the effects of intrauterine metformin exposure on offspring health are lacking. This study investigated adiposity outcomes in offspring exposed to maternal metformin treatment in an established mouse diet-induced obesity model.
Method: Dams were fed a control diet (7% sugars, 3% fat) or high-fat diet (10% sugars, 20% fat) supplemented with sweetened condensed milk (55% sugars, 8% fat). Upon reaching 12g fat mass, obese dams were either directly mated or treated orally with a clinically relevant dose of metformin from one-week pre-mating until E19. Dams were kept on their respective diets throughout pregnancy and lactation. Offspring were weaned at 3 weeks of age onto a control diet fed *ad libitum*. Body weight, food intake and body composition (TD-NMR) of male and female offspring was measured weekly until 12 weeks of age.
Results: Dams fed the high-fat high simple sugar diet were heavier and fatter at mating and in late pregnancy ($p<0.0001$). Metformin-treated dams were fatter than control dams but had decreased fat mass ($p<0.0001$) compared to untreated obese dams despite no difference in caloric intake. Offspring of obese and metformin-treated dams were smaller on postnatal day (PD) 2 ($p<0.01$) but both groups displayed catch-up growth by PD7 ($p<0.001$). At 12 weeks of age metformin-exposed offspring were significantly fatter than offspring of control ($p<0.001$) and obese dams ($p<0.01$) despite no difference in body weight or caloric intake.
Conclusions: Metformin treatment during obese pregnancy lowers maternal adiposity. However, offspring adiposity was increased in both male and female exposed offspring. This study highlights the need to consider both short and long-term effects of metformin treatment during pregnancy on both mother and child. Further studies are therefore required to define the broad metabolic effects across the life-course.

Novel read-level analysis identifies cell-type specific DNA methylation signals in bulk whole-genome bisulfite sequencing (WGBS) data

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Background/Aims: Epigenetic mechanisms mediate developmental programming and CpG methylation, being the most stable epigenetic mark, is of particular interest. However, associating DNA methylation with disease is complicated by the cell-type-specificity of epigenetic regulation and further compounded by standard methylation quantification methods of averaging methylation at each CpG loci. To better understand and account for cell-type heterogeneity, we developed a method to deconvolute cell-type specific DNA methylation.
Methods: Leveraging the fact that each WGBS read originates from a single molecule of DNA – from a single cell – we developed software to identify methylation patterns arising from differing cell types in a given sample. Focusing on all 100 bp genomic bins with at least 2 CpG sites, we identify clusters of reads with matching patterns.
Results: For blood and nervous-system cells, we find a 10-fold increase in the number of cell-type specific patterns when comparing different cell types (suggesting clusters are not just sampling error). Gene ontology analyses show that cell-type specific patterns occur near genes associated with the reference cell type. The methylation clusters also empower prediction of gene

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expression differences, with higher accuracy than using promoter methylation levels alone. Additionally, *in silico* mixing demonstrate that methylation clusters are sufficient to estimate the cell-type composition ($r^2 = 0.98$).
Conclusions: Compared to current approaches, our read-level approach yields additional information from WGBS data. Our method requires no specialized sample collection protocols or sequencing methods and is compatible with all available WGBS datasets. Deconvoluting cell-type specific signals from WGBS data will accelerate investigations into the role of DNA methylation in the developmental origins of disease.

Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort – the ABC study

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Background/Aims: Both extremes of nutritional status are related to increased morbidity and medical costs in the communities involved. Nutritional status tends to track from childhood to adulthood. Little is known about tracking of overweight/obesity and underweight and the associations between socioeconomic factors and nutritional status within indigenous populations. We explored tracking of body mass index (BMI) and waist-to-height ratio (WHtR) as well as associations between BMI and socioeconomic factors and remoteness in an Australian Aboriginal birth cohort.
Methods: This prospective study utilized data from 315 Aboriginal individuals from the Northern Territory who were assessed at birth, in childhood, adolescence and early adulthood. Anthropometric measures were taken at all follow-ups and tracking of BMI and WHtR was analysed using logistic regression. The relationship between BMI and areal socioeconomic disadvantage, remoteness, birth weight and maternal BMI was assessed for all follow-ups.
Results: Both underweight and overweight/obesity are common in this cohort. Both extremes of nutritional status as defined by BMI as well as low and high WHtR track from childhood to adulthood. Underweight was significantly more common and overweight less common in areas of higher social disadvantage, remote and non-urban areas. Birth weight and maternal BMI were associated with later weight status. There were significant sex differences for prevalences and tracking of WHtR with female participants significantly more often presenting with a high WHtR after childhood.
Conclusions: Socioeconomic factors, remoteness and gender must be addressed when assessing nutrition-related issues in the Aboriginal communities due to the variation in nutritional status and its behaviour over time within the Aboriginal population.

Lower levels of Type-2-Diabetes Markers in Children Following Longer Duration of Breastfeeding: A Longitudinal Twin Study

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Background/Aims: This study assessed the relationship between markers of type-2-diabetes (insulin, homeostasis model assessment insulin resistance [HOMA2-IR] levels and glucose) and duration of breastfeeding in a cohort of Australian twins.
Methods: Insulin and glucose levels were analysed from blood specimens of the 6-7-year-old children enrolled in the Peri/postnatal Epigenetics Twins Study (n=94 individuals) to investigate the relationship between duration of breastfeeding and type-2-diabetic markers. HOMA2-IR levels were calculated to estimate the degree of insulin resistance. Participants were included if parents answered the question: "How old were your babies when you stopped breastfeeding?" at the 18-month-old visit.
Results: Infants breastfed for more than 4 months had significantly lower mean insulin levels (3.28 mIU/L; 95% CI, 0.58-3.16, p=0.005) and significantly lower mean homeostasis model assessment insulin resistance levels (0.41; 95% CI, 0.07-0.40, p=0.005) than infants breastfed for less than 4 months. There was no evidence of any significant association between the mean glucose levels (4.40 mmol/L; 95% CI, -0.06-0.36, p=0.17) and duration of breastfeeding.
Conclusions: Longer duration of breastfeeding was associated with lower levels of markers predictive of type-2-diabetes. Breastfeeding for less than 4 months was associated with an increase in insulin and HOMA2-IR markers for type-2-diabetes. The relationship between a shorter duration of breastfeeding and increased type-2-diabetic markers indicates that the development of type-2-diabetes may be influenced by human milk in early life.

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The Impact Of The Artificial Periconception Environment On Preimplantation Embryonic Morphokinetic Parameters

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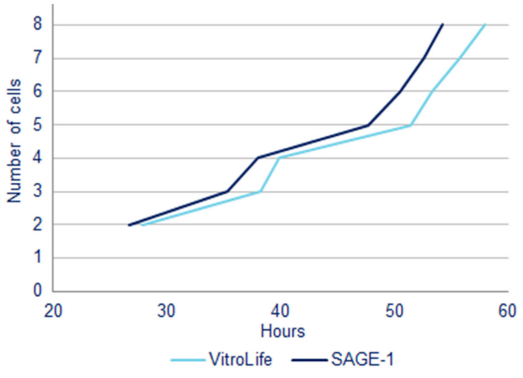
Background/Aims: Previous research has demonstrated several influences of the periconception environment on health later in life. During IVF/ICSI treatment, culture medium can be considered as the artificial environment of the preimplantation embryo. The introduction of time-lapse imaging offers the possibility to closely observe preimplantation embryonic development. The aim of this study is to investigate the influence of two widely used culture media on pre-implantation embryonic development, defined by morphokinetic parameters.
Method: Data were obtained between 2012-2017 of 545 women undergoing IVF-ICSI treatment at the Erasmus MC. In this period Vitrolife (sequential, n=255) and SAGE-1 (single-step, n=290) culture media were used subsequently. Morphokinetic parameters were observed with the EmbryoScope™ time-lapse incubator. Treatment- and patient characteristics were retrieved from medical records. Crude and adjusted associations between type of culture media and morphokinetic parameters were investigated in fresh and frozen embryos using linear mixed models.
Results: Embryos cultured in SAGE-1 medium show faster development over all developmental stages (from fading of pronuclei to 8-cell stage) compared to Vitrolife (Figure 1). For example, embryos cultured in SAGE-1 reach the 2-cell stage 2.08 (95% CI 1.57, 2.60) and 8-cell stage 3.61 (95%CI 1.78, 5.44) hours faster, respectively. After adjustment for female age, fertilisation method, type of ovarian stimulation, lowered oxygen culture and overall embryonic improvement over time, embryos cultured in SAGE-1 reach the 2-cell stage 3.07 (95%CI 1.18, 5.62) and 8-cell stage 9.89 (95%CI 2.80, 16.99) hours faster.
Conclusions: The current study shows a clear association between the type of commercially available culture medium and human pre-implantation embryo development. Several other studies implicate a relation between morphokinetic parameters and embryonic metabolism. This finding underlines the need for transparency of culture medium composition.



Further prospectively and longitudinally collected data is needed to unravel the role culture medium in human post-implantation and subsequent foetal and neonatal development.

Association of a Novel Green Space Indictor with Birthweight

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Background/Aims: There has been interest in the role of residential greenness for protecting foetal growth and development. This study makes use of a novel ground cover dataset, to explore the association of greenness, dry vegetation and bare ground with birthweight in a large population.
Method: Birth records were acquired for 512,736 live, singleton births in Queensland, Australia between 2007 and 2015. We used a novel fractional ground cover dataset, to estimate the proportion of maternal locality covered with green vegetation, dry vegetation, and bare earth. Linear regression models were developed to test the association of these measures with birthweight (grams).
Results: In univariate analysis, small increases in birthweight (0.23grams) per greenness percentile ($p < 0.001$), and highest vs lowest greenness quintiles (12grams, p 0.004), were found, but these became non-significant in the adjusted model. Dry cover increased birthweight by 0.41grams per percentile ($p < 0.01$) in the adjusted model. Each increasing quintile of dry cover lead to an increase in birthweight, with the highest quintile gaining 28grams birthweight (p 0.005). In contrast, for each percent increase in bare ground, birthweight decreased by 0.46grams ($p < 0.001$) in adjusted model. For greenness, stratification showed different effects across remoteness categories. In the adjusted model, babies in major cities gained 0.25grams birthweight for each percentile increase of greenness ($p < 0.001$), and very remote areas, where babies gained 1.22grams per percent increase (p 0.009) in greenness. All other regions were non-significant.
Conclusions: Higher greenness lead to higher birthweight in urban and very remote areas in our study, whilst dry cover offered small gains across all settings. In contrast, bare ground was associated with reductions in birthweight. While statistically significant, the changes in birthweight in our study are unlikely to be of biological importance.

Beyond Caesarean Birth: Impact of Prolonged Labour on Infant Gut Microbiota

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Background/Aims: Caesarean section delivery is a well-known factor for microbial gut dysbiosis up until mid-infancy. However, little is known about the impact of other birth events such as prolonged labour or rupture of membranes on infant gut microbiota. This study investigates the direct and indirect effects of birth mode, prolonged labour and other perinatal exposures on infant gut microbiota.
Method: In a subsample of 999 infants born at or near-term in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort, stool samples were collected at 3-4 months of age and microbial taxa profiled with 16S rRNA sequencing. Generalized structural equation model was employed to examine directional relationships between birth mode and prolonged stage 2 labour, and microbial diversity (Shannon index) and taxon abundance, taking into account primigravida status, pre-pregnancy obesity, prolonged rupture of membranes, intrapartum antibiotics prophylaxis, gestational age, exclusivity of breastfeeding and infant age at stool collection.
Results: Four early life factors were associated with reduced total gut microbiota diversity in infants: vaginal birth (β=-0.10, p=0.043), prolonged stage 2 labour (β=-0.11, p=0.01), early term birth (β=-0.07, p=0.056) and exclusive breastfeeding (β=-0.34, p<0.001). Prolonged stage 2 labour mediated the association between reduced microbial diversity and birth mode, prolonged stage 1 labour and rupture of membranes. A first pregnancy was associated with reduced colonization of *Bifidobacterium* (OR = 0.70, p<0.001) in the infant gut via 2 pathways: lower likelihood of exclusive breastfeeding and prolonged stage 2 labour.
Conclusions: Aside from the physiologic effects of exclusive breastfeeding, prolonged labour and early term birth have the capacity to reduce microbial diversity in the infant gut. Maternal primigravida status is a risk factor for childhood allergic disease. By reducing *Bifidobacterium* abundance in the infant gut, this study suggests that prolonged labour, which is more common in first pregnancies, could be a pathway to allergic disease.

Associations of Retinal Microvasculature with Hearing Status Emerge and Strengthen from Childhood to Mid-life: Cross-generational Population-based Study

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Background/Aims: The retinal and cochlear microvasculatures share similar anatomical and physical properties, but have not been thoroughly investigated together. We aimed to determine if adverse retinal parameters (narrower arterioles, wider venules) are associated with (1) mean hearing acuity and (2) hearing loss in mid-childhood and mid-life.
Method: Population-based cross-sectional study (Child Health CheckPoint) nested within the Longitudinal Study of Australian Children, with cross-generational retinal microvasculature and audiometry data (1281 children, 1255 adults). We calculated high Fletcher index (hFI, mean threshold of 1, 2, 4 kHz) and defined bilateral hearing loss as hFI >15 dB HL. Linear/logistic regression quantified associations of retinal microvascular calibre with hearing threshold/loss.
Results: Mean (SD) hFI was 7.9 dB HL (5.8) for children and 13.0 (6.8) for adults; 8.5% and 26.1% respectively had hearing loss. In adults, each SD (18.6 μm) increase in retinal venular calibre was associated with higher (worse) hearing threshold in lower frequencies (e.g. 2 kHz: β 0.63 dB HL, 95% CI 0.10 to 1.17) and hFI (β 0.52 dB HL, 95% CI 0.07 to 0.96). Similar associations were seen for children's hearing threshold at 1 kHz (β 0.47 dB HL, 95% CI 0.03 to 0.92). Each SD (18.6 μm) increase in venular calibre also predicted adult hearing loss (OR 1.20, 95% CI 1.03 to 1.40) with similar but attenuated patterns in children. Narrower arteriolar calibre was associated with adult hearing loss (OR per SD (14.0 μm) increase 0.86, 95% CI 0.73 to 1.00), but not with adult or child mean threshold; see Table.
Conclusions: Adverse retinal microvascular parameters show substantial associations with hearing loss by mid-life, which begin to emerge in childhood. This supports a life-course microvascular contribution/pathology in the pathogenesis of hearing loss. Replication and mechanistic studies could inform causal inference and prevention efforts beginning in childhood.

Periconceptional Folic Acid Supplementation Reduces the Impact of Maternal Particulate Matter Exposure on the Risk of Preterm Birth: A National Birth Cohort Study in China

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Background/Aims: There is no data about whether periconceptional folic acid supplementation could reduce the risk of preterm birth associated with maternal exposure to airborne particulate matter.
Method: We analysed the data of a national birth cohort (including information on periconceptional folic acid supplementation) of 1,240,978 singleton pregnancies during 2013-2014, with daily particulate matter concentrations for diameters of ≤10 μm (PM_{10}), 2.5 μm ($PM_{2.5}$) and 1 μm (PM_1). The air pollution concentrations were estimated by a machine learning method using satellite remote sensing, land use information, and meteorological data. We used a Cox proportion regression model with time varying exposure to examine the interactions between folic acid supplementation and PM concentration of each diameter, after controlling for individual characteristics and meteorological variables.
Results: 38.1% (473,015) of the pregnant women used periconceptional folic acid supplements regularly, and they had an 18% [HR: 0.82 (95%CI: 0.80, 0.83)] lower risk of preterm birth than those who did not use. Pregnant women who were exposed to the higher PM concentrations (the 4th quartile) exhibited a higher risk of preterm birth than those exposed to the lower PM level (the 1st quartile). Due to periconceptional folic acid supplementation, the risk of preterm birth was alleviated significantly from 12% [HR: 1.12 (95%CI: 1.11, 1.13)] to 9% [HR: 1.09 (95%CI: 1.08, 1.10)] for each 10 μg/m^3 increment in PM_1 or $PM_{2.5}$; and from 4% [HR: 1.04 (95%CI: 1.03, 1.04)] to 3% [HR: 1.03 (95%CI: 1.02, 1.03)] for PM_{10}.
Conclusions: In this Chinese national birth cohort, we found that periconceptional folic acid supplementation reduced the risk of preterm birth associated with maternal PM exposure. Our data support the health benefits of regular peri-conceptual folic acid supplementation, especially among women exposed to high levels of air pollution.

Effects of Telephone Support or Short Message Service on infant Feeding Practices: Findings From a 3-Arm Randomised Controlled Trial (RCT) at 6 and 12 Months

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Background/Aims: Promoting healthy infant feeding practices such as breastfeeding, timing of introduction of solids and cup usage have been recommended as important strategies to prevent obesity in the early years. This study aimed to determine the effectiveness of nurse-led telephone support or short message service (SMS) in promoting healthy infant feeding practices.
Method: We conducted a 3-arm RCT with 1155 women recruited in the third trimester of pregnancy across New South Wales (NSW) Australia, 2017-18. Once recruited, women were randomly assigned into one of the two intervention groups or the control. The intervention groups consisted of either nurse-led telephone support or text messages, together with 6 intervention booklets (containing healthy feeding practice information) being mailed at specific times from the third trimester until 12 months post birth. The control group received four booklets about home or car safety by mail as a retention strategy.
Results: 947 (82%) and 920 (80%) mothers completed surveys at 6 and 12 months respectively. Telephone support led to higher odds of appropriate timing of introducing solids [odds ratio (OR) 1.71 (95% CI 1.23-2.39)] and cup usage [OR 1.58 (95% CI 1.14-2.20)] at 6 months, and lower odds of having a bottle going to bed (OR 0.54, 95% CI 0.39-0.75) at 12 months than the control. SMS also led to higher odds of appropriate timing of introducing solids (OR 1.42, 95% CI 1.03-1.96) and lower odds of having a bottle going to bed (OR 0.57, 95% CI 0.42-0.79) than the control. No significant differences were found in breastfeeding duration between the telephone support, SMS and control groups.
Conclusions: Both the nurse-led telephone support and SMS interventions are effective in promoting appropriate timing of introduction of solids and encouraging cup usage. They have less effect on promoting breastfeeding, which requires further investigation.

Maternal and paternal mental disorder from adolescence and subsequent offspring birth outcomes: A 20-year intergenerational cohort study

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Background/Aims: Prematurity and fetal growth restriction (FGR) are increasingly prevalent globally and are associated with lifelong impacts on health and development. While there is some evidence for a relationship with maternal mental disorder during pregnancy, the relationships of prematurity and FGR with preconception and paternal mental health are poorly understood. Thus, the aim was to investigate whether maternal and paternal mental disorders in adolescence, young adulthood and during pregnancy were associated with offspring prematurity and being born small for gestational age.
Method: In 398 mothers with 609 children and 267 fathers with 421 children in the Victorian Intergenerational Health Cohort Study, diagnostic and screening measures of anxiety and depression during pregnancy and preconception were associated with gestational age and size for gestational age in linear and logistic regressions. Multiple imputation was used for missing data and generalised estimating equations to account for within family clustering.
Results: Preconception mental disorders present in both adolescence and young adulthood in fathers were associated with an increased risk of prematurity after adjustment for ethnicity, education, BMI and adolescent substance misuse (adjusted RR 5.5, 95% CI 1.7,18.2). On linear analyses, this translated to an earlier gestational age of almost one week. In mothers, symptoms of mental disorder at 32 weeks' gestation (but not preconception) were associated with an increased risk of prematurity (adjusted RR 3.5, 95% CI 1.1,11.9). There were no associations with being born small for gestational age.
Conclusions: Both paternal and maternal disorders are associated with earlier gestational age at delivery, but the mechanisms may differ given the different time course of the associations. Greater understanding of the mechanisms involved has the potential to lead to new strategies to prevent prematurity and reduce the intergenerational impact of mental disorder.

Breastfeeding and Food Allergy in Infants - Findings from the Maternal and Infant Cohort Study (MICOS) Malaysia

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Background/Aims: The association between breastfeeding and the development of childhood food allergy remains controversial. This study aimed to determine the contribution of exclusive and partial breastfeeding towards food allergy in infants at 1 year of age.
Method: A birth cohort of 339 infants from the Maternal and Infant Cohort Study (MICOS) in Malaysia was followed prospectively for one year. Information on breastfeeding duration, allergic symptoms, and potential confounders were obtained through face-to-face interviews with the mothers at 3, 6, and 12 months of age. Blood samples of the infants were collected at 12 months old to determine total serum immunoglobulin E (IgE) levels and specific IgE antibodies against 19 food allergens. Multivariate logistic regression was used to determine the association between exclusive and partial breastfeeding with the development of food allergy and IgE sensitization, adjusting for potential confounders.
Results: More than half of the infants were exclusively breastfed for 6 months (57.6%), followed by infants with partial breastfeeding (24.8%) and formula-fed (17.4%). The prevalence of food allergy increased from 2.9% in 3 months old to 8.2% and 18.2% in 6 and 12 months, respectively. Meanwhile, the prevalence of any food IgE-sensitization was 23.0%. After adjusting for confounding variables, no association was found between duration of exclusive and partial breastfeeding with food allergy and IgE sensitization in infants at 1 year of age.
Conclusions: This cohort study found no evidence for a protective effect of breastfeeding against food allergy and sensitization at 1 year of age.

Ethnic Diversity Among The Key Factors Influencing The Development Of Human Gut Microbiota

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Background: Gut microbiota plays a significant role in human health and disease, but the factors affecting its acquisition and dynamics in early life have not been ascertained comprehensively in a multi-ethnic study.
Methods: In an Asian multi-ethnic longitudinal study of 106 infants, we studied the influence of 7 factors (ethnicity, mode of delivery, infant feeding type, gestational age, birthweight,

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gender and maternal education) on the development of gut microbiota in first 2 years of life. Gut microbiota was profiled at 3, 6, 12 and 24 months of age by sequencing the V4 region of 16S rRNA gene.
Results: Mode of delivery, infant feeding type and ethnicity were identified as the major factors influencing the acquisition and temporal dynamics of gut microbiota in first 2 years. Effects of delivery mode on the microbiota lasted until 6M, with infants delivered by caesarean section showing higher diversity and delayed colonization of *Bacteroides* and *Bifidobacterium* than those delivered vaginally. Breastmilk feeding was associated with higher abundance of *Bacteroides*, while mixed feeding (breastmilk and formula milk) enriched *Bifidobacterium*. Ethnic diversity had a profound impact on the acquisition and longitudinal development of the infant gut microbiota. Its influences were apparent as early as 3M post-birth and remained significant even after adjusting for delivery mode and feeding type. Ethnic differences stayed significant until 12M. Microbiota of Indian infants was characterized by higher abundances of *Bifidobacteria* and *Lactobacillus*, while Chinese infants had higher abundances of *Bacteroides* and *Akkermansia*.
Conclusion: These findings provide deeper insight into the specific and temporal influences of factors influencing the development of human gut microbiota. It also advocates the consideration of ethnic diversity in future pediatric gut microbiome studies for identification of heritable taxa and precision in probiotic interventions.

Maternal high-fructose corn syrup consumption modulates brain-derived neurotrophic factor expression through epigenetic modification in offspring hippocampus

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Background/Aims: Consumption of excess high fructose corn syrup (HFCS-55) that is most commonly used in sugar-sweetened beverages, has been identified as a factor contributing to cognitive dysfunction. While excess consumption of HFCS-55 has been associated with the development of hippocampal dysfunction in adults, it is unknown to what maternal HFCS-55 consumption affect offspring hippocampus. The aim of this study is to determine the impact of exposure to maternal HFCS-55 consumption on hippocampal gene expression in offspring.
Method: After confirmation of gestation, female rats were divided into two groups: one group receiving distilled water, and one group receiving 20% (w/v) HFCS-55 water during gestation and lactation. Male offspring born to female rats that received distilled water were assigned to the control-offspring (C-offspring), whereas those born to female rats that received HFCS-55 water were assigned to the HFCS-offspring (H-offspring). After weaning, offspring were housed two per cage, and all rats received distilled water. All rats received standard chow during the entire period. Hippocampus tissue of offspring was dissected at postnatal day 28. Real-time PCR performed for quantitative assessment of mRNA expression. Bisulfite-pyrosequencing method was used for measurement for the proportion of methylated CpG sites in the hippocampus.
Results: The real-time PCR analysis exhibited that the gene expression of brain-derived neurotrophic factor (BDNF), which is critical for the differentiation and survival of neural cells was significantly lower in H-offspring (C-offspring: 1 ± 0.11; H-offspring: 0.84 ± 0.13; $p < 0.05$). The result obtained by bisulfite-pyrosequencing method indicated that maternal HFCS-55 consumption led to significantly increased methylation at the CREB binding site in BDNF promoter region (C-offspring: $5.2 \pm 1.2\%$; H-offspring: $8.8 \pm 4.1\%$; $p < 0.05$).
Conclusions: The finding of the present study indicate that maternal HFCS-55 consumption may modify BDNF DNA methylation, thereby suppressing gene expression in the hippocampus of offspring.

Exploring the Association Between Birth Weight and Risk of Abdominal Obesity in Children and Adolescents

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Background/Aims: Obesity tends to cluster in families, the aim of this study was to investigate the association between parental health status and the risk of offspring overweight/obesity in childhood.
Method: We conducted an analysis of 29,317 participants aged 6-17 (9,585 boys and 19,732 girls) from a national cross-sectional study. Information on parental health status factors (including non-smoking, light to moderate alcohol use, healthy BMI, regular moderate to vigorous physical activity, absence of hypertension, absence of diabetes mellitus, and healthy diet) was obtained from self-reported questionnaires, children's body mass index (BMI) were calculated and overweight/obesity were defined using the age and sex-specific cut-offs recommended by International Obesity Task Force (IOTF). Multivariable log-binominal regression models with generalized estimating equations were used to assess the association between parents' health status and offspring overweight/obesity.
Results: The prevalence of overweight and obesity were 23.2% and 7.1%, respectively, in offspring. The risk of offspring overweight/obesity was significantly decreased with the increasing

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number of parental health status factors. In paternal subset, with each additional paternal health status factor was associated with a 20% lower risk (PR: 0.80; 95%CI:0.76,0.84) in offspring's overweight. Corresponding rate for mothers was 8% (PR:0.92; 95%CI: 0.89,0.96). Compared those with health status factors ≤ 3, fathers with all seven health factors had a 75% lower risk of overweight/obesity in offspring (PR:0.25; 95%CI: 0.09,0.52), compared with a 26% lower risk in maternal subset (PR:0.74; 95% CI: 0.55,1.04). Similar patterns were found in different offspring sex and rural/urban groups.
Conclusions: Our findings indicated that parents', especially fathers', adherence to ideal health status is associated with a substantially lower risk of childhood overweight/obesity in their offsprings. Public health messaging and intervention designed to prevent overweight and obesity in children could obtain greater achievement if their parents were involved.

Placental endocrine malfunction exacerbates metabolic response to postnatal obesogenic challenge in male murine offspring, but not female offspring

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Background/Aims: The endocrine placenta is critical for the programming of lifelong metabolic health. Another important health determinant is the postnatal environment. Our earlier study in mice demonstrated that placental endocrine malfunction, induced by placental endocrine zone deletion of the paternally expressed imprinted *Igf2* gene, caused insulin resistance in adult male and female offspring on a standard chow diet (Placenta 2018; 69:e60-61). The current study aimed to examine if a compromised intrauterine environment, due to placental endocrine malfunction, increases susceptibility of the offspring to poor metabolic health in response to an obesogenic diet postnatally.
Method: Floxed-*Igf2* males were mated with *TpbpaCre* females to generate litters with placental endocrine malfunction. Following weaning at 3 weeks of age, offspring were fed an obesogenic diet of 45% fat and 20% sucrose solution. At 12 weeks of age, offspring underwent glucose and insulin tolerance tests and were killed a week later to determine blood lipids and whole-body composition by DEXA. Gonadal fat stores were collected for histological analyses. Offspring supported by unmanipulated placentas (reversed parental cross) served as controls. Significance was set at $p<0.05$.
Results: Adult males that were exposed to placental endocrine malfunction *in utero* had similar glucose tolerance, but were more insulin resistant than controls on an obesogenic diet postnatally (ITT AUC-malfunction:492.9±59.7 versus controls:177.0±48.8, t-test). Moreover, these males had greater circulating cholesterol (+37%, t-test), whole-body adiposity (+70%, t-test) and adipocyte size (+100%, t-test) in response to an obesogenic diet when compared to controls. In contrast, females exposed to placental endocrine malfunction had a similar metabolic phenotype to controls on an obesogenic diet.
Conclusions: Male offspring exposed to placental endocrine malfunction *in utero* displayed greater metabolic changes with an obesogenic dietary challenge, whereas no changes were observed in female offspring compared with their respective controls. Therefore, placental endocrine malfunction programs males, but not females, to be more sensitive to dietary-induced metabolic dysfunction postnatally.

Epigenetic Alteration of Rho Guanine Nucleotide Exchange Factor 11 (ARHGEF11) in Cord Blood Samples in Macrosomia Exposed to Intrauterine Hyperglycaemia

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Background/Aims: Macrosomia at birth is associated with maternal hyperglycaemia and lead to subsequent susceptibility to obesity, abnormal glucose metabolism, hypertension and dyslipidaemia in offspring. Epigenetic reprogramming has been reported to be involved in the development of human diseases caused by suboptimal environmental or nutritional factors. The study was aiming to explore epigenetic mechanism influences on macrosomic infants exposed to intrauterine hyperglycemia.
Method: 239 singleton term pregnant women in Peking University First Hospital were recruited in this study. Participants were divided into two groups based on OGTT: Group normal glucose tolerant (NGT, n=132) and Group GDM (n=107). After delivery, participants were further divided into four subgroups based on neonatal birth weight: normal birth weight (NBW) was defined as 2500g ≤ birth weight < 4000g. We performed a genome-wide analysis of DNA methylation in cord blood from macrosomic infants born to women with gestational diabetes or infants with normal birth weight born to normal glucose-tolerant women in order to identify genes related to foetal growth or early adipose tissue development. The candidate genes were then validated using SEQUENOM MassARRAY after bisulfite conversion.
Results: To analyse the epigenetic patterns in umbilical cord blood in GDM, we collected umbilical cord blood from normal glucose-tolerant women (mean pre-gestational BMI of 19.8 and mean neonatal birth weight of 3166 g) and women with GDM (mean pre-gestational BMI of 24.4 and mean neonatal birth weight of 4366 g). Differentially methylated genes in the GDM group were identified using the Infinium HumanMethylation450 BeadChip array. A total of 1251 genes were differentially methylated

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compared to the controls ($p < 0.01$). The methylation microarray data showed that two specific CpG sites (cg12604331, cg08480098) in the gene body of ARHGEF11 were significantly hypomethylated in the cord blood in macrosomic infants. Altered DNA methylation levels of ARHGEF11 were negatively correlated with glucose levels and neonatal birth weight.
Conclusions: Exposure to adverse intrauterine environments can alter foetal development, such as by affecting the nutritional status of the foetus. Such exposure can also result in significant epigenetic modifications, including DNA methylation, which could serve as a potential marker for nutrition and metabolic conditions at the neonatal stage or even in the adult.

Fetal crown-rump length is associated with maternal thyroid function in early pregnancy, particularly in male fetuses

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Background/Aims: Early pregnancy fetal growth is a relevant determinant of pregnancy outcome and child health during later life. During the first trimester, fetal growth depends on the transfer of maternal thyroid hormone and optimal thyroid hormone availability is ensured via stimulation of the maternal thyroid by human chorionic gonadotropin (hCG). The potent stimulatory effects of hCG on gestational thyroid function and its clinical relevance with early fetal growth remain unknown and need to be examined.
Method: This study comprised 46,186 mothers for whom early pregnancy TSH, FT4, T3, TPOAbs and hCG were available, as well as ultrasound crown-rump-length (CRL) measurements were available. Data were also available on potential confounders including maternal age, parity, anthropometrics and fetal gender.
Results: When absolute concentrations were analyzed, there was a negative association of TSH with CRL and a positive association of FT4 with CRL, with an effect estimate of roughly 0.1 SD across the full ranges. However, when taking into account the thyroidal stimulation by hCG we found that an impaired thyroidal response to hCG stimulation was associated with an up to 1.5 SD lower CRL (a high hCG with a high TSH) and an up to 0.8 SD lower CRL (a high hCG with a low FT4). Even within the normal range of TSH and FT4, an impaired thyroidal response to hCG stimulation was associated with an up to 0.8 SD lower CRL.
Conclusions: A low maternal thyroid function during the first trimester is associated with a modestly lower CRL. However, an impaired thyroidal response to hCG stimulation is associated with a considerably lower CRL for which effect estimates are in the range of, or even superseding those of well-known risk factors of fetal growth restriction. These data can help to better identify pregnancies at high-risk of fetal growth restriction and adverse pregnancy or child outcomes.

Prenatal alcohol exposure programs offspring disease: Sex-specific impacts on glucose metabolism in a rat model of moderate, acute exposure

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Background/Aims: Alcohol consumption is highly prevalent amongst women of reproductive age. Given that approximately 50% of pregnancies are unplanned, prenatal alcohol exposure (PAE) has the potential to affect fetal development and program chronic disease in offspring. Our aim was to investigate the impact of an acute exposure of alcohol, during the 1st trimester equivalent period, on offspring glucose metabolism in adolescence and at 6 months of age.
Method: Pregnant Sprague-Dawley dams were treated with 1 g/kg BW EtOH in saline (PAE, n=9) or an equivalent volume of saline only (Control, n=8) via gavage on embryonic days 13.5 and 14.5. This resulted in a peak blood alcohol concentration (BAC) of 0.06% at 1 h post-gavage. Fasting blood glucose and plasma insulin levels were measured at postnatal day 30 (PN30). A glucose tolerance test (GTT) and insulin tolerance test (ITT) were performed in separate cohorts of offspring at 6 months of age. Only 1 male and 1 female from each litter were used in each experiment.
Results: There was no evidence for altered circulating glucose or insulin levels due to PAE in the PN30 cohort. At 6 months, there were also no effects of PAE on fasting blood glucose. However, fasting plasma insulin levels were significantly elevated in males, as was 1st phase insulin secretion during the GTT. Indices for insulin resistance (HOMA-IR) and insulin sensitivity (QUICKI) were higher and lower respectively in PAE versus control offspring, particularly in males. Blood glucose concentration was reduced less in the PAE male offspring in response to a bolus of insulin during the ITT, resulting in a lower inverted area under the glucose curve (AUGC).
Conclusions: Our data suggests that offspring metabolic health can be programmed as a result of a relatively modest PAE during a critical period of development. Exposure occurred within the 1st trimester equivalent period (~10-12 weeks) when some women, particularly those with an unplanned pregnancy, may not yet be aware they are pregnant. The pre-diabetic, insulin resistant phenotype in male offspring of PAE dams occurred despite a relatively low BAC and without the '2nd Hit' of a high fat diet, often used to

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'unmask' disease. Therefore, this study highlights the importance of abstaining from alcohol consumption during pregnancy or when planning a pregnancy.

Forty Years of IVF, 8 Million babies and Counting – But Is It Safe? Effect of *In Vitro* Fertilization (IVF) and Prolonged Embryo Culture on Mouse Development and Postnatal Health

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Background/Aims: By 2100, in vitro fertilization (IVF) might account for 3.5% of the global population, approximately some 400 million people. It has already produced about 8 million babies. However, reports link IVF with adverse short and long-term health outcomes. Using a mouse model, we investigated the effect of IVF and duration of culture on blastocyst development and the postnatal health of offspring.
Method: Experimental groups (8-13 litters each): NM (natural mating, non-superovulated); IV-ET-2Cell (2-cell embryos derived *in vivo* from superovulated mothers (SOM) and immediately transferred (ET) to recipients; IV-ET-BL (blastocysts derived *in vivo* from SOM and immediate ET); IVF-ET-2cell (2-cell embryos generated by IVF from SOM, short culture and ET); IVF-ET-BL (blastocysts generated by IVF from SOM, long culture and ET).
Results: IVF blastocysts after prolonged culture developed slower and comprised reduced trophectoderm and ICM cell numbers compared with in vivo generated blastocysts. IV-ET-2Cell, IV-ET-BL, IVF-ET-2Cell and IVF-ET-BL groups compared with NM controls, showed increased body weight, increased Systolic blood pressure SBP, impaired GTT and abnormal organ:body weight ratios in both genders ($P<0.05$), independent of litter size. SBP and Angiotensin Converting Enzyme (ACE) for IVF-ET-BL males was increased compared to IV-ET-BL males. SBP for IVF-ET-BL males was increased compared to IVF-ET-2Cell males. However, glucose concentration 2 hours after glucose injection and AUC in male IVF-ET-BL was reduced compared with IVF-ET-2Cell males. Serum insulin for IVF-ET-BL males was significantly reduced compared with IVF-ET-2Cell, but serum glucose and G:I ratio did not show any significant differences. No differences were evident between the four treatments groups for females.
Conclusions: We conclude that reproductive treatments affect the development and potential of preimplantation embryos, influencing postnatal development and physiology compared with undisturbed reproduction. In particular, prolonged embryo culture, with normalised SO, IVF and ET, may adversely affect male offspring cardiovascular but improve the metabolic profile compared with short culture. *Liver analysis, including lipid deposition and the correlation with our metabolism data are underway.*

Dramatic impairment in the chronically hypoxic fetus to second stressors such as acute hypotension and acute hypoxia

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Background/Aims: Although sub-optimal pregnancy is thought to developmentally program the fetus with an increased vulnerability to secondary stressors, there is little evidence to support this. This gap in knowledge is due to the difficulty of obtaining cardiovascular recordings in severely hypoxic fetuses. We combined the use of isobaric chambers to simulate significant chronic fetal hypoxia and designed a wireless data acquisition system to simultaneously record continuous fetal cardiovascular data in an ovine model. Here, we investigated the fetal *in vivo* cardiovascular defence to either acute hypoxia or acute hypotension in chronically hypoxic or normoxic fetal sheep.
Method: At 80% gestation, a 30 min episode of acute hypoxia (fetal PaO_2 Δ-10±1mmHg from baseline) was induced in chronically instrumented fetal sheep before and after 10 days of either chronic fetal hypoxia (n=6) or chronic fetal normoxia (n=6). On the last day of the 10-day exposure to chronic hypoxia or chronic normoxia, fetuses also underwent a 30-min period of acute hypotension (sodium nitroprusside i.v.). Cardiovascular data were recorded throughout.
Results: ACUTE HYPOXIA: Normoxic fetuses showed traditional brain sparing circulatory responses to acute hypoxia. In contrast there was no brain sparing response to acute hypoxia in chronically hypoxic fetuses. ACUTE HYPOTENSION: Control fetuses showed traditional baroreflex responses to hypotension. In contrast, cardiac and vasomotor baroreflexes were severely abnormal in chronically hypoxic fetuses (Table 1).
Conclusions: We provide novel evidence to support that the chronically hypoxic fetus is indeed at much greater risk of demise during a superimposed challenge.

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		Chronically Normoxic (n=6)	Chronically Hypoxic (n=6)
ACUTE HYPOXIA	Max Brain Sparing Index Ratio of Carotid:Femoral blood flow	11.6 ± 4.5	1.5 ± 0.1*
	Bradycardia: Max Δ HR (bpm)	4.9 ± 1.2	0.4 ± 0.1*
ACUTE HYPOTENSION	Max Δ FVR (mmHg.(mL.min^{-1})$^{-1}$	1.3 ± 0.2	0.8 ± 0.3*
	Max Δ HR (bpm)	58.3 ± 7.8	9.7 ± 2.9*

Sex-Specific Effects of Prenatal Maternal Stress on Hair Copper Levels and its Association with Vocabulary Scores in 4-Year Old Children: The QF2011 Queensland Flood Study

Mirela Ambeskovic, David P. Laplante, Thomas Kenney, Guillaume Elgbeili, Pierre Beaumier, Nagy Azat, Gabrielle Simcock, Sue Kildea, Suzanne King, Gerlinde A.S. Metz

Introduction: The fetal brain is sensitive to the gestational environment and vulnerable to homeostatic interferences by stress. Most mental and physical outcomes are influenced by stress and are, therefore, associated with dysregulated cellular homeostasis. Here we investigated if elemental hair analysis provides a diagnostic biomarker of prenatal maternal stress (PNMS) exposure and can be used to understand associations between microelements and phenotypes in children.
Methods: Hair samples were collected from 4-year-old children (n = 40) exposed to varying levels of disaster-related PNMS (2011 Queensland Flood, Australia). Elemental hair analysis by inductively coupled plasma mass spectrometry was used to examine effects of objective (threat, loss, scope, change) and subjective (intrusive thoughts, avoidance, hyperarousal) PNMS on 33 microelements for which an associated phenotype was assessed.
Results: Our data show significant linear or curvilinear associations between PNMS and 10 microelements in boys, and 8 microelements in girls. Following multiple comparisons corrections, the curvilinear U-shaped association observed between objective PNMS and copper levels in boys remained highly significant. Mediation analyses revealed that at objective PNMS moderate levels ranging between 4 and 12, higher levels of copper were associated with lower vocabulary scores. Interestingly, this association was not observed in girls.
Conclusion: Here we show sex-specific, dose-response, linear or curvilinear, relationships between PNMS and hair copper levels and their association with vocabulary scores in boys. Our results suggest that PNMS may influence sex-specific regulatory metabolic pathways with long-term effects on phenotypes. Thus, hair microelements may serve as diagnostic biomarkers of behavioural outcomes in children exposed to gestational stress.

Maternal vomiting during early pregnancy and cardiovascular risk factors at school-age. The Generation R Study

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Background/Aims: Evidence suggests that low birth weight and fetal exposure to extreme maternal undernutrition is associated with cardiovascular disease in adulthood. Hyperemesis gravidarum, a clinical entity characterized by severe nausea and excess vomiting leading to a suboptimal maternal nutritional status during early pregnancy, is associated with an increased risk of adverse pregnancy outcomes. Not much is known about long-term offspring consequences of maternal hyperemesis gravidarum and related measures during pregnancy. We examined the associations of maternal daily vomiting during early pregnancy, as a measure related to hyperemesis gravidarum, with childhood cardiovascular risk factors.
Method: In a population-based prospective cohort study from early pregnancy onwards among 4,769 mothers and their children in Rotterdam, the Netherlands, we measured childhood body mass index, total fat mass percentage, android/gynoid fat mass ratio, preperitoneal fat mass area, blood pressure, lipids and insulin levels. We used multiple regression analyses to assess the associations of maternal vomiting during early pregnancy with childhood cardiovascular outcomes.
Results: As compared to children from mothers without daily vomiting during early pregnancy, those from mothers with daily vomiting during early pregnancy had a higher childhood total body fat mass (difference: 0.12 Standard Deviation Score (SDS) (95% Confidence Interval (CI):0.03 to 0.20), android/gynoid fat mass ratio (difference 0.13 SDS (95% CI: 0.04 to 0.23)) and preperitoneal fat mass area (difference 0.10 SDS (95% CI: 0 to 0.20)). These associations were not explained by birth characteristics but partly explained by higher infant growth. Maternal daily vomiting during early pregnancy was not associated with childhood blood pressure, lipids and insulin levels.
Conclusions: Maternal daily vomiting during early pregnancy is associated with higher childhood total body fat mass and abdominal fat mass levels, but not with other cardiovascular risk factors. Further studies are needed to replicate these

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findings, to explore the underlying mechanisms and to assess the long-term consequences.

DNA Methylation At NEGR1 Gene Locus Is Associated With Neurodevelopmental Outcomes And Childhood Obesity

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Background/Aims: Maternal pregravid obesity and hyperglycemia are associated with both neurodevelopmental dysregulation and metabolic complications later in childhood. The *NEGR1* gene is involved in brain development and its expression is dysregulated in both hypothalamic and adipose tissues in obesity. Gene expression is regulated by epigenetic mechanisms which are sensitive to the fetal metabolic environment. *NEGR1* is therefore a strong candidate gene for obesity, neurodevelopment and fetal epigenetic (DNA methylation (DNAm)) programming. Our hypothesis is that placental DNAm changes at the *NEGR1* locus contribute to the association between maternal metabolic problems in pregnancy, neurodevelopment and adiposity markers in offspring.
Method: This study was conducted on mother-child dyads (n=276) from Gen3G, a prospective birth cohort. BMI z-score (BMI-z) and the Strengths and Difficulties Questionnaire (SDQ) total score were assessed at 3 years of age (40.4 ±3.0 months). DNAm levels at 30 CpGs at *NEGR1* locus were quantified using the MethylationEPIC Array (Illumina), in fetal-side placental biopsies.
Results: DNAm at four CpGs within the *NEGR1* locus predicted childhood BMI-z (cg26153364: β=-0.16; p=0.008, cg23166710: β=0.12; p=0.04) and SDQ total score (cg04932878: β=0.20; p=0.001, cg16525738: β=-0.14; p=0.01, cg23166710: β=-0.13; p=0.03). Glucose levels at 2h post-oral glucose tolerance test (β=0,20; $p=4.4x10^{-4}$), maternal age (β=-0.13; p=0.02) and gestational weight gain (β=-0.12; p=0.05) were associated with SDQ, whereas maternal weight at second trimester of pregnancy was associated with BMI-z (β=0.16; p=0.009), although none of the maternal factors were associated with DNAm. Together, maternal and childhood characteristics with *NEGR1* DNAm levels explained 14.6% ($p=1.8x10^{-7}$) of SDQ and 7.3% ($p=3.2x10^{-4}$) of BMI-z variance at 3 years old.
Conclusions: This longitudinal study suggests that placental *NEGR1* DNAm is associated with childhood neurodevelopment and adiposity at 3 years of age.

Hidden Hungers of Camden: A Pilot Intervention unravelling the double burden of Malnutrition among Ethnic Minority Women living in Deprivation

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Women are generally more at risk for nutritional deficiencies and poor health due to gender bias and systematic discrimination; placing them at a lower worth in society than men. Using a mixed methods approach (quantitative and qualitative)-this study explores the phenomenon of demographics and socioeconomic status and its impact on nutrients intake on ethnic minority women. This study addresses research gaps that include lack of data of nutritional status for these ethnic minority women groups living in the UK and subsequently limited tailored nutrition interventions targeting them. Women were recruited by non-probability sampling approached in person within community centers(February-March 2018). Inclusion/Exclusion criteria included; gender (female) aged 25-65 years, living in deprived wards of Camden, unemployed, or employed (low-income earning annual household income between £5,200-£10,399), and those who face challenges such as; lone parenting or language barriers. Collected data of recruited participants [N=42] showed that: At baseline; 23% were classified as obesity class I [BMI 30.0-34.9 kg/m2] and 40% pre-obese [BMI 35.0-39.9 kg/m2]. 21% had an average WC > 80cm while 55% had WC > 88cm. 67% of women were unemployed and 23% reported Level 3 education qualifications. Qualitative data collected in the form of focus group discussions and case-studies revealed that based on traditional cooking women were consuming nutrient-deficient meals each day. Being overweight was perceived as "healthy weight" within cohort group which may contribute towards unhealthy eating behaviors. Based on 24hrs recall average mean nutrient intake were lower range of the normal value of recommended UK reference values for nutrients particularly for; calcium, folic acid (vitamin B9), iron, magnesium, potassium, and vitamin D. Therefore, women living in deprived wards of Camden are experiencing the double burden of malnutrition, as study reveals micronutrient deficiency along with obesity weight classification among study population. This pilot was referred to with the slogan "Women Nutrition Programme" (WNP), between 16th April- to - 25th May 2018. WNP objectives include; increase micronutrients intake through weekly nutrition education and healthy cooking sessions tailored towards ethnic subgroups of the cohort, teaching women to make their own cultural acceptable foods without compromising palatability and flavor. The WNP also included weekly Zumba sessions, interactive workshops, free access to community gym, and women empowerment sessions. Quantitative data analysis was completed using IBM SPSS software (version 24). Descriptive statistics and multivariate analysis of variance (MANVO) were main test administered to compare sample means; computed at 95% confidence level p > 0.05. 24-hour dietary recalls were administered as main nutritional assessment tool to acquire an estimate of cohort group micronutrients intake pre- and post-intervention as well as evaluate programme effectiveness. Recalls were coded using Nutritics [nutritional analysis software]. Validated health and eating habits

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questionnaires, valuable tools providing nutritional profile of cohort, identifying dietary habits and food choices. Statistical analysis revealed that there are inter-correlations between low-income and low education qualification and overweight/obesity. However, evidence from this study reveals a positive correlation between increased nutritional knowledge/understanding and micronutrients consumption throughout the tailored WNP programme.

In conclusion, participants that completed WNP (N=23) showed a significant increase in nutrients intake for instance, potassium mean intake increased by 9.9% [2073.43mg (pre) and 2279.43mg (post)]. Developing culturally tailored nutrition interventions which include skills based healthy cooking courses and nutrition education could increase nutrients status of women suffering from hidden hungers. A natural progression of this work is to assess intervention over a longer period of time using dietary biomarkers to accurately assess micronutrient intake. The issue of racial differences in body fat distribution should also be considered for BMI and WC cut-off points for identifying risk in minority ethnic groups.

Development of a Risk Model for Pediatric Prediction of Adult Type 2 Diabetes Mellitus: The Cardiovascular Risk in Young Finns Study

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Background: Type 2 diabetes mellitus (T2DM) is the leading cause of premature mortality globally but current strategies to reduce the disease burden remain largely unsuccessful. Predicting risk early in life is crucial to enable targeted prevention in those at high risk. Most T2DM prediction models focus on adult risk factors to predict later T2DM, but few have explored the importance of childhood risk factors. We aimed to identify childhood factors associated with T2DM risk in adulthood, and to construct and validate prediction models using these determinants.

Methods: In 2774 participants from the Cardiovascular Risk in Young Finns Study followed from childhood to adulthood, we considered 13 childhood factors (child's: BMI z-score, sex, diastolic blood pressure, HDL-C, insulin, total cholesterol, triglycerides and glucose; and maternal :BMI, age, smoking status, T2DM status and education level at baseline) in their prediction of adult T2DM. From saturated models, automated stepwise and penalized logistic regression was used to estimate a set of candidate prediction models, compared using Likelihood Ratio testing and correlated DeLong tests. The classification ability of candidate models was assessed at empirically determined optimal probability cut-offs, with out-of-sample model performance and predictive accuracy estimated using repeated data split, repeated K-fold, and leave-one-out cross validation.

Results: The prevalence of adult T2DM was 4.4%. Model AUCs ranged from 0.715-0.735, indicating fair discrimination of the considered childhood variables. The most important childhood predictors of adult T2DM were child BMI z-score and age, and maternal BMI and smoking. Including childhood insulin improved model sensitivity (68.6% vs. 62.9%) but slightly reduced specificity (72.1% vs. 76.9%) compared to models that included childhood blood lipids. Although glucose was strongly associated with T2DM in all models, including it did not improve model AUC, and generally resulted in more imbalanced discrimination performance (usually reduced sensitivity). Internal validation suggested satisfactory out-of-sample predictive abilities of all candidate models.

Conclusions: The model including childhood BMI z-score, age, insulin levels, maternal BMI and smoking status achieved the highest sensitivity at detecting adult T2DM both in the derivation and validation sets. This simple 5-predictor model could help identify children at higher risk of developing adult T2DM.

Maternal mood and infant sleep in the first year of life

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Background/Aims: Depression and anxiety are common during pregnancy and often co-exist. Maternal depression reportedly increases the risk of sleep problems in the offspring, but less is

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known about general maternal mental health effects on offspring sleep. Our study aims to investigate General affective factor (G factor) score, an integrated measure of maternal anxiety and depression, and its association with infant sleep in the first year of life.
Method: We studied N=1010 mother-child dyads from the Singapore birth cohort study (GUSTO). General affective factor (G factor) scores were derived at 26-28 weeks gestation and 3 months postpartum using bifactor modelling, based on data collected using the Edinburgh Postnatal Depression Scale (EPDS), Beck Depression Inventory (BDI-II) and State-Trait Anxiety Inventory (STAI)(1). Infant sleep patterns were parent-reported using the Brief Infant Sleep Questionnaire (BISQ) at 3, 6, 9 and 12 months of age. Longitudinal sleep data were modelled using repeated measures mixed multivariable linear regression, with adjustment for sex of child, ethnicity, breastfeeding at 3 months, and maternal age and education.
Results: Duration of wake after sleep onset (WASO) at 3 months of age was positively associated with antenatal G factor scores during pregnancy [β=42.7 (95% CI 13.8 to 71.6) mins] and 3 months postpartum [β=55.4 (95% CI 23.8 to 86.9) mins]. WASO throughout the first year was positively associated with antenatal [β=28.3 (95% CI 12.3 to 44.4) mins] and 3-month postpartum [β=25.8 (95% CI 6.6 to 44.9) mins] G factor scores. Postpartum G factor score at 3 months was also associated with increased number of awakenings [β=0.4 (95% CI 0.1 to 0.8)] in 3-month-old infants. In fact, increased frequency of awakenings was observed throughout the first year with higher antenatal [β=0.3 (95% CI 0.1 to 0.5)] and 3-month postpartum [β=0.5 (95% CI 0.2 to 0.8)] G factor scores. No other significant associations were observed with day, night or total sleep duration.
Conclusions: Maternal mental health during pregnancy and early postpartum are linked to the offspring's WASO and awakenings during infancy.
Reference 1. Phua DY, Kee M, Koh DXP, Rifkin-Graboi A, Daniels M, Chen H, et al. Positive maternal mental health during pregnancy associated with specific forms of adaptive development in early childhood: Evidence from a longitudinal study. Development and psychopathology. 2017;29(5):1573-87.
Phua DY, Kee M, Koh DXP, Rifkin-Graboi A, Daniels M, Chen H, et al. Positive maternal mental health during pregnancy associated with specific forms of adaptive development in early childhood: Evidence from a longitudinal study. Development and psychopathology. 2017;29(5):1573-87.

Can Childhood Mental Health and Social Outcomes be Predicted at Birth?

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Background: Effects of adverse childhood experiences associated with socio-economic disadvantage, perinatal events, and parental mental illness or criminality on child development have been widely documented. Knowledge of risk factors known at birth that can predict various child health and social outcomes could be useful to identify families for early targeted interventions to avert poor mental health and social outcomes.
Method: We used linked administrative data for more than 70,000 children and parents drawn from the NSW Child Development Study to examine associations between exposures known at birth and 6 health and social outcomes from age 5 to 13 years; namely: early childhood developmental vulnerability; educational underachievement in middle childhood; childhood mental illness; child protection reports, and; police contact as victim of crime or 'person of interest'. Logistic regression analyses were conducted for males and females separately using the General Linear Model. For models with a satisfactory Receiver Operating Characteristic (AUC>0.60), classifications functions were calculated for increasing numbers of risk factors to determine the number associated with optimal predictive utility.
Results: Models using 8-13 risk factors were associated with an AUC of between 0.63 and 0.84 for 5 of 6 outcomes (mental illness AUC=0.58-0.60). Leading risk factors for all outcomes were: young maternal age at birth, smoking during pregnancy, >2 previous pregnancies, low birth weight, prematurity, maternal and paternal mental illness, maternal and paternal criminal court charges, paternal imprisonment, and low socio-economic status. The presence of four or more risk factors at birth occurred in <10% of the population and was associated with a <10% false positive rate (specificity 93-98%) in predicting the 5 childhood outcomes.
Conclusions: Families at high risk for adverse child outcomes can be identified at the time of a child's birth to inform targeted intervention strategies for delivery from the perinatal period onwards, in order to help avert these outcomes.

A comparison of DNA extraction methods for human milk microbiome studies

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Background/Aims: Human Milk (HM) from healthy mothers contains a diverse microbial community. An essential step to characterize this microbial community is the efficient extraction of genomic DNA. This study aimed to evaluate methods for the extraction and purification of DNA from HM.
Method: HM DNA was extracted using the following kits: i) Qiagen MagAttract Microbial DNA Isolation Kit (MM), ii) Norgen Milk Bacterial DNA Isolation Kit (NM), iii) Qiagen MagAttract Microbiome DNA/RNA Isolation Kit (QM) and iv) TRIzol LS Reagent (LS). The 16S rRNA gene was amplified

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using universal bacterial primers 27F and 1492R, flanked by PacBio unitags on the 5' ends to allow barcoding of samples using an asymmetric fusion primer approach. Samples were sequenced using Pacific Biosciences single molecule real-time (SMRT) circular consensus sequencing (CCS) on the Sequel System. CCS reads were analysed using the Greenfield Hybrid Analysis Pipeline v2.1.

Results: Both kits QM and LS extracted very low amounts of DNA (<0.01 ng/μL to <0.12 ng/μL); therefore, sequencing was not performed. Kit NM produced higher DNA yield (mean=0.68 ng/μL) than kit MM (mean=0.55 ng/μL). DNA from kits MM and NM produced a similar number of CCS reads; at species level the greatest number of these were associated with *Staphylococcus epidermidis*, *Streptococcus pseudopneumoniae* and *Streptococcus vestibularis*. However, DNA from kit MM produced reads associated with *Corynebacterium singulare* in six samples; in contrast, similar reads were only identified in one sample from kit NM. In comparison, DNA from kit NM produced reads associated with *Rhodanobacter glycinis*, which was absent from all samples extracted by kit MM. In DNA extraction controls, reads associated with only *Variovorax paradoxus* were detected using kit MM. However, kit NM had a large number of reads associated with *Rhodanobacter glycinis*, *Romboutsia timonensis*, *Curvibacter gracilis*, and *Acidovorax temperans*, amongst others.

Conclusions: Our data suggest that kit MM is the best choice amongst those kits tested here for the extraction of microbial DNA from HM. Although kit NM did extract DNA associated with species not identified using kit MM, reads mapping to these species were also present in the extraction control in large numbers, suggesting they are present as contaminants.

Gut Metagenomic Analysis of Pregnant Women in the Third Trimester Reveals Gestational Diabetes Mellitus Related Microbial Regulators of Glucose Tolerance

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Background/Aims: Host physiological and microbial community changes during pregnancy alter the metabolic environment of the womb to promote a successful birth. In some women, increased insulin sensitivity and hypoglycemia accompany these adaptations and significantly increase the risk of birth complications such as macrosomia and neonatal hypoglycemia even at sub-diabetic levels. The specific role of the microbial community in these interactions remains to be explored.

Method: During the third trimester, the stool samples were collected from 23 women with gestational diabetes mellitus and 26 healthy women in the initial stage. Similarly, the stool samples were collected from another cohort of 37 GDM women and 133 healthy women in the replication stage. The samples were analyzed by Metagenomic sequencing, qualitative and quantitative analysis microbiome features, clinical variable associated loci and Real-time PCR.

Results: Metagenomic shotgun sequencing revealed no significant differences in community richness or beta-diversity associated with GDM state. Investigation of glucose response by the oral glucose tolerance test identified a statistically significant association between Bacteroides dorei and the 1-h OGTT response across the whole cohort. Employing a simple correlation strategy, we identified regions of the B. dorei genome where normalized sequence coverage correlated with OGTT response. This method identified multiple proteins involved in carbohydrate metabolism offering clues for the microbial mechanisms that impair glucose tolerance. An unseen cohort of 150 patients confirmed the association between the glucose tolerance loci of B. dorei and the 1-h OGTT response by Q-PCR validation.

Conclusions: A spectrum of risk for certain complications follows glucose tolerance levels. The designation of control or GDM did not appear to effect community level differences in the microbiome; however, specific species such as B. dorei associate with glucose response and may closely track risks associated with adverse outcomes and post-pregnancy health offering potential treatment and diagnostic pathways for the future.

Young children born after *in vitro* fertilization grow faster and are taller and leaner than naturally-conceived children

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Background/Aims: Assisted reproduction technologies (ART) are being increasingly adopted, resulting in the birth of an estimated 5+ million children worldwide. However, there are still limited data on the long-term effects of ART on offspring health. We examined the associations between ART and growth throughout early childhood.

Methods: Participants were 29,000+ pairs of women and their children born in Uppsala (Sweden), who were followed until 5 years of age. Height, weight, and body mass index (BMI) standard deviation scores (SDS) were derived. Children were classified as: naturally conceived (NC; n=26,775; 91.8%), conceived after IVF (IVF; n=2.010; 6.9%), and conceived after ovarian stimulation only (OS; n=381; 1.3%). Multivariable models were

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run accounting for important confounders, and only adjusted results are reported.
Results: After adjustment for confounders, children in the 3 groups were similar at birth. However, IVF children grew more than NC children from 18 months to 5 years, with a change in height that was 0.06 SDS greater (p=0.003). Thus, IVF children were 0.07 SDS taller at age 4 years (p<0.001) and 0.05 SDS taller at age 5 years (p=0.013). IVF children were also leaner than NC children at 3 years (adjusted BMI difference -0.05 SDS; p=0.011) and 5 years (-0.05 SDS; p=0.026). OS children were no different from either group.
Conclusions: Children conceived after IVF had a greater change in height in early childhood and were taller and leaner than naturally conceived children. These observations from Sweden corroborate our previous observations from children in New Zealand.

Infertility Treatment as a "Natural Experiment" for the study of Congenital Heart Defects.

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Background/Aims: Congenital Heart (CH) defects are a leading cause of death in the first year of life, and occur in around 8 per 1,000 births, but in 16 per 1,000 after infertility treatment. The aetiology is largely unknown. The aim here was to identify variation in specific CH defect types by mode of infertility treatment, together with a range of contributing patient factors.
Method The South Australian Birth Cohort is a census of all registrations of all births (n=302,811) and terminations of pregnancy for Jan 1986-Dec 2002, linked to all cycles of assisted reproductive technology (A.R.T.), and to all congenital anomalies notified to the 5th birthday (ICD-9 British Paediatric Association codes). Logistic regression was used to investigate associations between maternal factors, treatment modality, and the presence of CH defects.
Results: Maternal age, nulliparity, and a history of miscarriage, pre-existing diabetes, gestational diabetes and hypertension, twins and higher order multiples, female baby sex each increased the risk of CH defects.
Compared to the fertile population, and after adjustment: a) Cardiac Septal Closure anomalies (BPA 74500-74599) did not vary by A.R.T. treatment but were increased after infertility consultations conducted outside an A.R.T. clinic. b) A two-fold increase in Other Congenital Heart anomalies (BPA 74600-74699) for ovulation induction, IVF fresh, intra-uterine insemination, and 'natural' conceptions to A.R.T. patients.c) A two-fold increase in Other Congenital Circulatory System anomalies (BPA 74700-74799) was observed for fresh IVF, IUI, and conceptions after infertility consultation outside an A.R.T. clinic; a four-fold increase for ICSI frozen.
Conclusions: CH defects were related to established maternal factors, mode of fertilization, gamete source, cryopreservation, and non-A.R.T. infertility care – which most likely involves ovulation induction medication. Cryopreservation may interact with mode of fertilisation to increase risk. Further epidemiological and basic research is therefore required urgently.

Diversity of the prenatal faecal microbiota and offspring behaviour: a birth cohort study

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Background/Aims: In mouse studies, maternal gut microbiota have been shown to influence offspring neurobehavioural outcomes [1,2]. The relevance of these findings to humans is unknown. As such, we investigated the relationship between the composition of maternal gut microbiota in pregnancy and offspring behaviour at age two.
Method: We investigated a subgroup of participants from the Barwon Infant Study birth cohort (n=153 pregnant women, and 154 children, with 1 set of twins). Pregnant women provided a faecal sample at 36 weeks gestation, and parents completed the Child Behavior Checklist for their child at age two. Multiple regression models were used to investigate associations between the alpha diversity (Shannon index, linear regression) and beta diversity (Bray-Curtis dissimilarity, PERMANOVA) of maternal faecal microbiota and internalising and externalising behaviour problem (T-scores) in children. Models were adjusted for sample processing variables, household income, maternal age, country of birth, smoking, western dietary pattern, perceived stress and depression scores.
Results: There was evidence of an association between higher alpha diversity in pregnancy and lower T-scores for internalising (−2.56 T-score units per unit increase in Shannon diversity, 95%CI (−4.85, −0.27), p=0.03) but not externalising behaviours (−1.00 (−3.52, 1.52) p=0.44) in offspring. Likewise, there was evidence that beta diversity was related to internalising (1.22% of variance explained, p=0.01), but not externalising (0.62%, p=0.48) in offspring.
Conclusions: Alpha diversity and differences in beta diversity of the gut microbiota in pregnancy are related to emotional and behaviour problems in the offspring, independent of other factors.
References: [1] Kim S. et al. Maternal gut bacteria promote neurodevelopmental abnormalities in mouse offspring. Nature. 2017 Sep 28;549(7673):528–32. [2] Buffington SA. et al Microbial Reconstitution Reverses Maternal Diet-Induced Social and Synaptic Deficits in Offspring. Cell. 2016 Jun 16;165(7):1762–75.

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Background/Aims: A multi-strategy clinical practice change initiative was developed to increase antenatal care provision addressing alcohol consumption during pregnancy. Clinician training was identified as key implementation strategy. Significant challenges have been reported in ensuring adequate clinician participation in training for clinical practice improvement. This study assessed the effectiveness of a comprehensive program designed to maximise clinician receipt of evidence-based training.
Methods: The training consisted of an interactive online module (45 mins) and a series of five interactive and didactic face-to-face group and one-on-one sessions delivered by a Clinical Midwife Educator or expert. Based on evidence from systematic reviews, the strategy aimed for each clinician to attend training: of at least 1 hour in total length 'exposure' and was a mix of modes and interactive formats. Regression analysis was performed to examine differences in training attendance, exposure and modes by clinician profession (midwifery; Health Support Workers (HSW); medical).
Results: 98% of antenatal clinicians (n=184) received training, 40% received 1-2 hours, (33% <1 hour; 26% >2 hours; average 88 mins/clinician). There was no significant difference in proportion of midwifery (41%), HSW (45%), and medical (39%) receiving 1-2 hours training (p=0.94). Overall proportion of staff receiving online training (midwifery: 49%; HSW: 36%; medical 4%; p<0.001) and the proportion of staff receiving all training modes (midwifery: 20%; HSW: 27%; medical 0%; p<0.001) varied. There were significant differences in proportion of clinicians who attended training sessions: face-to-face didactic session (midwifery: 71%; HSW: 91%; medical 41%; p<0.001) and completion of online module (midwifery: 29%; HSW: 36%; medical: 4%; p<.001).
Conclusion: The comprehensive approach to maximise clinician receipt of training was effective in achieving substantial reach. Attendance was highest at didactic face-to-face training whilst completion of online training was lowest. Variability of receipt of training suggests tailoring of training to particular types of clinicians may be warranted.

Maternal dietary LA:ALA ratio and total fat intake during pregnancy has implications on offspring growth, hepatic gene expression and omega-3 fatty acid elongation efficiency

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Background: The pro-inflammatory and pro-adipogenic/lipogenic properties of omega-6 fatty acids has led to suggestions that *in utero* exposure to the increasing ratio of linoleic acid (LA, omega-6) to alpha-linolenic acid (ALA, omega-3) in the Western diet could be contributing to the current epidemic of childhood obesity.
Objective: To determine the effects of maternal consumption of an omega-6 linoleic acid (LA):omega-3 alpha-linolenic acid (ALA) ratio similar to that of modern Western diets (9:1), in comparison to a lower ratio (1:1.5), on circulating fatty acid proportions, offspring growth and expression of key lipogenic genes in the liver. The study also determined whether any differences between ratios were exacerbated by an increase in total dietary fat content (18% vs 36% fat w/w).
Method: Female Wistar rats (n = 6-9 per dietary group) were assigned to their experimental diets four weeks prior to mating and throughout pregnancy. At 3 weeks of age all offspring were weaned onto standard laboratory chow with LA and ALA as the only omega-6 and omega-3 source respectively. Offspring were weighed weekly and euthanized by CO_2 asphyxiation for collection of blood and tissue samples at 4 weeks post-partum.
Results: Maternal consumption of a high fat diet, irrespective of dietary LA:ALA ratio, caused a significant reduction in offspring body weight (Male: P<0.001, 107.4 ± 4.6g vs 85.5 ± 3.4g; Female: P<0.001, 95.9 ± 3.5g vs 78.9 ± 3.7g) as well as reduced liver weight (%BW). Hepatic expression of *Srebf1* was also reduced in these groups (P<0.01) and, unexpectedly, appeared to have no influence on hepatic *Fasn* expression. Interestingly exposure to a low LA:ALA diet significantly increased the proportion of circulating omega-3 fatty acids but only at the 18% fat level (P<0.05).
Conclusions: We have shown that exposure to a high fat diet *in utero* and during lactation has consequences on offspring growth and hepatic gene expression. Further to this, exposure to a high omega-3 diet *in utero* and during lactation appears to increase offspring capacity to produce long-chain omega-3 polyunsaturated fatty acids when maternal total fat intake was low. Whilst these observations extend beyond direct dietary

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exposure, further investigation is required to identify the long-term health consequences.

Nanoparticle-Encapsulated Antioxidant Delivery Improves Placental Nitrosative Stress and Morphology in a Sex-Specific Manner in a Rat Model of Fetal Hypoxia

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Background/Aims: Pregnancy complications leading to chronic fetal hypoxia have been linked to the development of adult cardiovascular disease. Prenatal hypoxia has been shown to increase placental oxidative stress in a sex-specific manner. nMitoQ, an antioxidant encapsulated into nanoparticles, can be used against placental oxidative stress without transplacental passage and off-target fetal effects. We hypothesized that nMitoQ reduces placental nitrosative stress (peroxynitrite/nitric oxide (NO)) and improves angiogenesis (Vascular Endothelial Growth Factor (VEGF-A) expression) and morphology.
Methods: Pregnant rats were exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from gestational day (GD) 15-21. On GD15, rats were intravenously injected with saline or nMitoQ (100 µl of 125 µM). On GD21, placentae (labyrinth zones) from males and females were collected for detection of peroxynitrite (nitrotyrosine staining), NO (DAF-FM staining), VEGF-A mRNA expression (qPCR) and morphology (CD31 endothelial cell staining to assess the area of fetal capillaries).
Results: Only in hypoxic female placentae, nitrotyrosine levels ($p<0.05$) and NO levels ($p<0.01$) increased; and nMitoQ treatment reduced only the nitrotyrosine levels (0.018±0.001 a.u. vs. 0.015 ±0.001 a.u.; $p<0.05$). Prenatal hypoxia decreased placental VEGF-A expression (male and female: $p<0.05$) and area of CD31 staining (male and female: $p<0.05$) in both males and females, while only in hypoxic female placentae nMitoQ treatment increased VEGF-A expression (0.74±0.10 vs. 1.59±0.09; $p<0.01$) and area of CD31 staining (8.45±1.21 a.u. vs. 17.99±1.35 a.u.; $p<0.05$).
Conclusions: nMitoQ reduced placental nitrosative stress and increased VEGF-A with evidence for enhanced number of fetal capillaries, only in the female hypoxic offspring. This suggests that nMitoQ treatment appears effective as placental treatment in fetal hypoxia in a sex-specific manner.

Maternal and Birth Determinants of Endometriosis: A Nationwide Birth Cohort Study

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Background: Endometriosis is a chronic and common gynaecological condition among women of reproductive-age. Previous studies have identified several adult risk factors for endometriosis. Less is known about whether the disease has a life course aetiology. We examined the associations of maternal and birth characteristics with risk of endometriosis during early to mid-reproductive period.
Method: This total population-based female cohort study included 628,312 singleton women born in Sweden between 1973 and 1987. We followed them for first diagnosed endometriosis in the national inpatient and outpatient registers from 15 years of age until December 31, 2012. Perinatal characteristics were obtained from national registers. Cox proportional hazards regression models with adjustment for multiple perinatal confounding factors were used to investigate the rate of endometriosis. Within-family analyses were further conducted to account to residual maternal-level confounding.
Results: In total, 8,262 women were diagnosed with endometriosis at the end of follow-up. The mean (standard deviation) age at first diagnosed endometriosis was 27.4 (5.0) years. After adjustment for measured maternal characteristics and shared maternal-level confounders, increased rate of endometriosis remained associated with lower maternal education, mother's history of endometriosis, maternal smoking during pregnancy [adjusted hazard ratio (aHR), 1.25; 95% confidence interval (CI), 1.12-1.39], lower birth weight (aHR, 1.16; 95% CI, 1.10-1.21, per 1kg decrease), and small-for-gestational age (aHR, 1.19; 95% CI, 1.11-1.27). We estimated a quarter of the total association between maternal smoking during pregnancy and endometriosis was mediated through birth weight-for-gestational age.
Conclusions: Several perinatal factors, especially maternal smoking and slow foetal growth rate were associated with an increased risk of endometriosis during early to mid-reproductive period, suggesting the importance of developmental origins of disease for the aetiology of endometriosis.

Neonatal and neurodevelopmental outcomes in preterm infants according to maternal body mass index: a prospective cohort study

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Background/Aims: Maternal obesity is associated with an increase of maternal, foetal and neonatal morbidity and

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mortality. The aim of our study was to evaluate in preterm infants the relationships between maternal pre-pregnancy body mass index (1), neonatal outcome, (2) and neurodevelopmental outcome at 2 years of corrected age.

Method: We conducted a single-center cohort study. Infants born between 24+0 and 33+6 weeks of gestation between January 2009 and December 2013, hospitalized in the neonatal intensive care unit of Angers University Hospital, and with available data regarding maternal pre-pregnancy body mass index were eligible. Three groups were defined according to maternal body mass index: normal (n=418), overweight (n=136) and obese (n=89). The primary outcome was neurodevelopment at 2 years of corrected age. The secondary outcome was composite criteria of neonatal complications. We included in the multivariable analysis the following variables: mother's age, smoking during pregnancy, magnesium sulfate and steroid treatment during pregnancy, twin status, gender, socioeconomic status and social security benefits for those with low incomes.

Results: The study population was composed of 643 preterm infants. Among them, 520 were assessed at 2 years. There was no difference in the proportion of infants with non-optimal neurodevelopmental outcome between the three groups (16.6% for obese, 13.5% for overweight, 16.9% for normal body mass index mothers; p=0.73). According to multivariable analysis, being born from an overweight or obese mother was not associated with an increased risk of non-optimal neuro-development at 2 years (adjusted OR = 0.81 [0.39-1.68] for obese, adjusted OR = 0.8 [0.42-1.5] for overweight mothers). There was no difference in the proportion of preterm infants with non-optimal composite criteria of neonatal complications between the three groups. In the multivariable analysis, being born from an overweight or obese mother was not associated with an increased risk of non-optimal neonatal outcome (adjusted OR = 0.88 [0.51-1.51] for obese, adjusted OR = 0.98 [0.63-1.54] for overweight mothers).

Conclusions: In this large prospective cohort of preterm infants born before 34 weeks of gestation, we found no relationship between maternal body mass index and neurodevelopmental outcomes at 2 years of corrected age and no relationship between maternal body mass index and neonatal outcomes.

Maternal high fat diet-induced obesity modulates sexually dimorphic epigenetic regulation and expression of *Lepr* in offspring hippocampus during development

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Background/Aims: Maternal obesity during pregnancy is associated with a greater risk for metabolic disorders in offspring, and also increases offspring susceptibility for neurodevelopmental disorders. Disrupted epigenetic regulation of gene expression has been proposed as a potential mediator of maternal obesity-induced developmental programming of disease in offspring. The neuroendocrine signals Leptin and Insulin are each intrinsically linked to metabolic processes, and brain development, we therefore aimed to investigate whether maternal high fat diet (mHFD)-induced obesity alters gene expression of receptors for leptin and insulin in the brain of offspring. We also aimed to determine if maternal obesity-induced transcriptional changes in the offspring brain were associated with altered histone modifications at the gene promoter.

Method: Using a C57BL/6 mouse model of high fat diet-induced maternal obesity, we performed real time qPCR to examine mRNA expression of insulin receptors (*Insr-A*, *Insr-B*), and Leptin receptor (*Lepr*) in prefrontal cortex, hippocampus, amygdala, and hypothalamus of gestational day (GD) 17.5 offspring from control or obese dams. Next, we performed chromatin immunoprecipitation (ChIP) - qPCR to assess whether gene expression changes were associated with altered histone binding at the proximal gene promoter region. Data were analysed by 2-way ANOVA.

Results: We found a significant main effect of sex, and a significant interaction effect of offspring sex and maternal diet on *Lepr* expression in the offspring hippocampus, with female offspring from control dams expressing 2-fold higher *Lepr* than male offspring from control or obese-dams ($p<0.05$), and female offspring from obese dams expressing a 4-fold increase in hippocampal *Lepr* over male control or obese-dam offspring ($p<0.05$). ChIP-qPCR analysis revealed significantly decreased binding of the repressive histone mark H3K9me3 at the *Lepr* promoter in hippocampus of female offspring from obese dams ($p<0.05$).

Conclusions: Together, this data indicates that maternal obesity induces sexually dimorphic changes to gene transcription in the developing hippocampus of offspring which may be underpinned by epigenetic mechanisms, contributing to current knowledge of how early life nutrition can impact the epigenome.

Longitudinal genome-wide association study of pediatric bone accrual highlights links between pediatric bone gain and later-life fracture risk

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Background/Aims: Our prior work with the postmenopausal bone loss-associated *COLIA1* locus suggests that genetic factors operating in adulthood also impact childhood bone gain. Although many loci are established for adult areal bone mineral density (aBMD), less is known about genetic determinants of bone accrual. We therefore performed genome-wide association studies (GWAS) to identify loci for longitudinally modeled pediatric aBMD and bone mineral content (BMC), and then assessed the impact of these loci on later-life fracture risk in the UK Biobank.
Method: Leveraging the 'Bone Mineral Density in Childhood Study' (BMDCS), a mixed-ethnicity cohort of healthy children and adolescents from five US clinical sites with up to seven annual DXA scans, we modeled longitudinal bone gain in 1,362 subjects using 'SuperImposition by Translation and Rotation' (SITAR). 36 parallel GWAS were performed on SITAR parameters *a-size*, *b-timing*, and *c-velocity* using a linear mixed model in GEMMA for aBMD and BMC at the distal 1/3 radius, lumbar spine, femoral neck, total hip, total body less head, and skull. Resulting signals were then queried against published later-life fracture genetic data and an online PheWAS resource, PheWEB.
Results: We observed 27 genome-wide significant signals, plus an additional 13 suggestive signals supported by more than one phenotype. Only five of these forty signals were known, with just one previously reported in children. Additionally, four signals were suggestively associated with adult heel BMD. Fifteen are near genes involved in Mendelian disorders of bone density and/or had functional annotations for osteoblast or osteoclast regulation. Finally, five showed suggestive association with later-life fracture risk (P=0.05-9x10^{-5}).
Conclusions: By longitudinally modeling bone gain we substantially increased the number of loci associated with aspects of pediatric bone accrual. Furthermore, some of these novel variants impact later-life fracture risk, highlighting the importance of optimizing childhood bone gain in preventing osteoporosis and fracture.

A genomic atlas of systemic interindividual epigenetic variation in humans

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Background/Aims: Methylation of cytosines in CpG dinucleotides (DNA methylation) is an epigenetic mechanism with essential roles in mammalian development. Since DNA methylation is established during development and stably governs gene expression potential throughout life, it is a prime candidate mechanism in DOHaD. Elaborating causal pathways in DOHaD (linking early exposures, induced epigenetic changes, and consequent disease) is complicated, however, by the inherent cell-type specificity of most epigenetic marks. We therefore set out to identify human genomic regions exhibiting non tissue-specific, i.e. systemic, interindividual variation (SIV) in DNA methylation. Like genetic variation, SIV is a potential determinant of phenotype and can be assessed in any easily biopsiable DNA sample.
Method: We designed an unbiased screen for human genomic regions exhibiting SIV. We performed deep whole-genome bisulfite-sequencing (WGBS) on genomic DNA from tissues representing all three germ layers – endoderm (thyroid), mesoderm (heart), and ectoderm (brain) – from each of 10 donors from the NIH Genotype-Tissue Expression (GTEx) project. We developed a computational algorithm to identify genomic regions at which interindividual variation in DNA methylation is consistent across the three tissues. After evaluating the characteristics of these regions using publicly available datasets, a web-based application was developed to share this resource with the research community.
Results: We identified 9,926 correlated regions of systemic interindividual variation (CoRSIVs). Although comprising just 0.1% of the human genome, we show that CoRSIVs are intercorrelated over long genomic distances, associated with transposable elements and subtelomeric regions, conserved across diverse human ethnic groups, sensitive to periconceptional environment, and associated with genes implicated in various human disorders and phenotypes.
Conclusions: We have uncovered, characterized, and charted a previously unexplored molecular level of human individuality. Our atlas of human CoRSIVs provides a valuable and timely resource for population-based investigations into epigenetic mechanisms in DOHaD.

Maternal and paternal smoking, alcohol and caffeine use during pregnancy and ADHD symptoms in offspring from childhood to adolescence

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Background/Aims: Several studies have indicated that maternal substance use during pregnancy may be associated with offspring ADHD via intrauterine effects. We investigated

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associations between maternal alcohol, tobacco and caffeine use during pregnancy with symptoms of ADHD during childhood and adolescence using paternal substance use as a negative control.
Method: We used data from the Avon Longitudinal Study of Parents and Children, a longitudinal pregnancy cohort. ADHD symptoms were measured using the Development And Well-Being Assessment (DAWBA) at ages 7, 10, 13 and 15 years. Maternal and paternal smoking, alcohol and caffeine use were measured at 18 weeks of gestation.
Results: After adjusting for covariates (child's gender and ethnicity, parity, parental age, education, SES, financial difficulties, smoking, alcohol and caffeine use) and partner substance use, we observed a dose-response relationship between maternal smoking heaviness and ADHD hyperactivity symptoms (Age 7: 1-9 cigarettes $OR_{1\text{-}9}$ 1.02; 10-19 cigarettes $OR_{10\text{-}19}$ 1.07; >20 cigarettes $OR_{>20}$ 1.66), (Age 10: $OR_{1\text{-}9}$ 1.05; $OR_{10\text{-}19}$ 1.02; $OR_{>20}$ 2.28), (Age 13: $OR_{1\text{-}9}$ 0.84; $OR_{10\text{-}19}$ 1.05; $OR_{>20}$ 1.56). We found no clear evidence of a dose-response relationship between paternal smoking and ADHD symptoms and either between maternal or paternal alcohol consumption and ADHD symptoms in offspring. Caffeine consumption in mothers had a slightly stronger association with offspring's hyperactivity symptoms at age 7 (OR 1.03, p=.01) than fathers caffeine consumption (OR 1.01, p=.15) but this association did not persist at older ages.
Conclusions: Our findings suggest that there is a stronger link between offspring ADHD symptoms and maternal antenatal smoking, than with paternal smoking. This suggests a potential intrauterine effect. Neither alcohol nor caffeine use in pregnancy appeared to be clearly associated with ADHD symptoms in offspring. We are currently undertaking Mendelian Randomization analysis to investigate whether there is a causal relationship between substance use in pregnancy and ADHD symptoms in offspring.

Comparison of Genome-Wide DNA Methylation Between Low Birth Weight and Normal Birth Weight Term Infants without Maternal Complications and Smoking

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Background/Aims: Low birth weight (LBW: < 2,500 g) is a major public health issue in Japan and has negative health consequences throughout life. DNA methylation of several genes varies in preterm infants. However, epigenetic changes in LBW term infants (T-LBWs) have received little attention. This study aimed to compare DNA methylation between T-LBWs and normal birth weight term infants (T-NBWs) without maternal complications and smoking.
Method: Genome-wide DNA methylation was compared between T-LBWs (n=4) and T-NBWs (n=5). Exclusion criteria included preterm delivery, multiple pregnancy, maternal infections, tumours, hypertensive disorders of pregnancy, hypertension, gestational diabetes mellitus, diabetes, mental disorders and smoking. A total of 673,844 CpG sites were assessed in cord blood using the Illumina Infinium Methylation EPIC BeadChip.
Results: The maternal pre-pregnancy body mass index in T-LBWs was significantly lower than that in T-NBWs (17.1 ±1.6 kg/m^2 vs. 22.2±2.9 kg/m^2, respectively). Overall, 483 hyper differentially methylated genes (DMGs) and 35 hypo DMGs were identified in T-LBWs. In biological process analysis using DAVID v6.8, 11 categories were enriched among hyper DMGs and none were enriched among hypo DMRs. These categories included "Immune system", "DNA metabolism and repair" and "Organism growth and organization". Intriguingly, genes related to apoptosis (e.g., *CASP8, CASP10* and *BH3*), cell cycle progression (e.g., *HUS1*, *APOBEC3A_B* and *APOBEC3A*), the inflammatory response (e.g., *NLRP12* and *SHARPIN*) and cell growth were involved in these biological processes.
Conclusions: These findings suggest that term LBW linked to epigenetic modulation of the immune system.

What 'dose' of physical activity in the toddler years predicts health and developmental outcomes in the preschool years?

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Background/Aims: Engagement in physical activity during early childhood is important for health. However, the optimal 'dose' (i.e., daily duration) of physical activity is not known, despite the importance of dose for health messaging and monitoring. This study examined whether a 'dose' of physical activity at 19m old was associated with adiposity, social and emotional competence, and fundamental movement skills (FMS) at 3y and 5y of age.
Method: Data were drawn from the Melbourne InFANT and InFANT Extend Programs. Children's physical activity was assessed over 7 days via ActiGraph accelerometers. Height, weight (to calculate z-BMI) and waist circumference (WC) were measured. FMS were assessed via the Test of Gross Motor Development. Children's social and emotional competence was assessed through the Pediatric Quality of Life Inventory (PedsQL; parent-reported). Models were fitted to examine linear and curvilinear relationships between light- (LPA) and moderate- to vigorous-intensity physical activity (MVPA) and the outcome variables. LOWESS plots were used to visually inspect for 'threshold' points. Spline models were

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utilised for those outcomes where a potential 'threshold' was identified.
Results: Linear and curvilinear models showed few associations between LPA, MVPA and LMVPA at 19m and the outcome variables at 3y and 5y old. However, a 'threshold' was identified for WC and PedsQL Psychosocial at 3y old, at approximately 1 hour MVPA/day. Specifically, there was evidence of an association between MVPA and WC (β=-2.95 [95%CI: -5.61, -0.30]) and MVPA and PedsQL Psychosocial (β=15.30 [95% CI: 1.62, 28.98]) at 3y old for children engaging in MVPA less than 1 hour/day, but no evidence of an association for those engaging in MVPA greater than 1 hour/day.
Conclusions: This study provides the first empirical evidence that toddlers' MVPA, up to approximately 1 hour/day, is favourably associated with some health indicators in the early preschool years; beyond this 'threshold' the benefits plateau. This finding suggests that engagement in daily MVPA should be recommended in National 24-Hour Movement Guidelines for toddlers.

Effects of prenatal lifestyle counselling on diet and physical activity in the cluster-randomised controlled GeliS ("Gesund leben in der Schwangerschaft"/Healthy living in pregnancy) trial

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Background/Aims: A healthy diet and regular physical activity are important factors for an adequate weight development during pregnancy. Over the last decades, the number of women gaining weight excessively has been increasing. Effective intervention strategies that counteract this and that are feasible in "real-life" settings are urgently needed. With lifestyle counselling within the German routine care system, the GeliS study ("Gesund leben in der Schwangerschaft"/Healthy living in pregnancy) was designed to optimise dietary and physical activity behaviour and thus to reduce excessive gestational weight gain (GWG).
Method: The GeliS study is designed as a multicentre, prospective, cluster-randomised, controlled, open intervention trial, including 2286 pregnant women. Three counselling sessions in pregnancy and one session postpartum addressed a healthy diet, regular physical activity and self-monitoring of GWG in the intervention group. The control received standard care. Behavioural data was collected with a food frequency questionnaire (DEGS-FFQ) and a pregnancy physical activity questionnaire (PPAQ).
Results: The intervention was effective in modifying several aspects of dietary and physical activity behaviour. In the intervention group, the consumption of soft drinks was lower ($p < 0.001$) and the intake of vegetables and fish higher compared to the control group (p=0.023, p=0.002). Energy intake was not influenced by lifestyle advice. Counselling had a significant impact on total physical activity ($p < 0.001$) as well as the proportion of women reaching the recommended activity level ($p < 0.001$).
Conclusions: Lifestyle advice alongside routine prenatal care could effectively modify dietary and physical activity behaviour, although these changes were not sufficient to reduce the proportion of women with excessive GWG. Potential long-term effects of this behavioural intervention on maternal and infant health remain to be evaluated and are currently assessed in a 5-year follow-up.

Cross generational trends of the links between early life risk factors and adult cardiovascular diseases: The Uppsala Birth Cohort, Sweden

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Background/Aims: The adverse social and biological experiences around the time of birth are well documented as risk factors for cardiovascular diseases (CVD) in adult life. However, it remains to be seen if the associations between early life exposures and CVDs have changed across generations. Exploring the cross-generational trends of the recognized associations is the aim of this study.
Method: The study base comprises two biological generations born in Sweden during 1915-1929 (n=10 880) and 1932-1978 (n=6763) respectively. They were followed through hospital and death records from 1960 to 2008 for the incidence of stroke and Coronary Heart Disease (CHD) – the two cardiovascular outcomes of interest. The follow up was restricted to age 30-65 to make the second generation (G2) comparable with the first generation (G1). The exposures were family social class (high, medium, low), birthweight corrected for gestational age (divided equally into 3 quartiles), and gestational weeks (pre-term, term, post-term). The hazard ratios (HR) with 95% confidence intervals (CI) for generation-specific associations were estimated using proportional Cox regression models. The change in HRs between two generations were expressed as the ratio of HRs (rHR).
Results: The study found an increased risk of CHD incidence among individuals at the bottom of the birthweight continuum in both generations (G1: HR 1.12, CI 1.03-1.22; G2: HR 1.46, CI 1.11-1.92). Similarly, low family social class was associated with an excess risk of CHD in both generations (G1: HR 1.22, CI 1.04-1.36; G2: HR 1.31, CI 1.01-1.70). As for stoke, associations were found, in G1 only, with low family social class (HR 1.18, CI 1.01-1.37) and pre-term births (HR 1.26, CI 1.09-1.45). The effect sizes, however, did not differ significantly between

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generations. An exception is the effect of family social class on stroke that showed a marginally significant attenuation (rHR 0.65, CI 0.42-1.00).
Conclusions: Our study findings broadly point to the stability of the associations between early life risk factors and two major CVD outcomes in Sweden. The persistence of the associations over time calls for more research on establishing causal mechanisms for guiding efficacious interventions.

Maternal Gestational Diabetes and Newborn DNA Methylation: Findings From the Pregnancy and Childhood Epigenetics Consortium

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Background/Aims: Maternal gestational diabetes mellitus (GDM) has been associated with adverse outcomes in the offspring, both at birth and later in life. Growing evidence suggests that the epigenome may play a role. However, most studies examining associations between maternal GDM and newborn DNA methylation have been relatively small, and findings have been inconsistent.
Method: The current study meta-analyzed the association between maternal GDM and cord blood DNA methylation. Seven cohorts (3677 mother-newborn pairs, 317 with GDM) in the Pregnancy and Childhood Epigenetics consortium participated. Cohorts measured DNA methylation using the Infinium HumanMethylation450 array and ran independent epigenome wide association studies (EWAS) according to the same analysis plan. Associations between GDM and DNA methylation were examined using robust linear regression, adjusting for potential confounders, including cord blood cell types. Fixed-effects meta-analyses were performed using METAL. Differentially methylated regions were identified by taking the intersection of results obtained using two software: comb-p and DMRcate.
Results: GDM was associated with lower %methylation levels ($P_{FDR}<0.05$) at two intergenic CpGs (cg11187204: -1.6%; 95% CI: -2.1%, -1.0%; $P=5.2x10^{-8}$ and cg10139436: -0.4%; 95% CI: -0.5%, -0.2%; $P=6.1x10^{-8}$) and two regions, one in the *OR2L13* promoter and one in the gene body of *CYP2E1*, and with higher %methylation at a third intergenic CpG (cg00812770: 0.8%; 95% CI: 0.5%, 1.1%; $P=1.7x10^{-7}$), which overlaps a long non-coding RNA (*LINC01342*).
Conclusions: GDM was associated with methylation differences in cord blood at three CpGs and two regions, including the promoter of *OR2L13*, a gene associated with autism, and the body of *CYP2E1*, which is upregulated in Type 1 and Type 2 diabetes. Future studies are needed to understand whether these associations are causal and, if so, whether they have long-term health consequences.

Placental structure is affected by maternal obesity, which is not reversed by metformin-treatment

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Background/Aims: Obesity in pregnancy is associated with higher risk of cardiometabolic diseases in the offspring. It is crucial to determine the mechanisms by which this arises and to define interventions to prevent detrimental effects. We hypothesize that the placenta as the main interface for maternofetal communication is important in mediating this developmental programming. The first aim of this study was to investigate effects of maternal obesity on placental structure using a mouse model of maternal diet-induced obesity. The second aim was to assess the ability of the drug metformin to prevent detrimental effects of maternal obesity on the placenta.
Methods: Mice were fed with chow or obesogenic diet from 10 weeks prior to mating and during pregnancy. A third obese group was supplemented with metformin one week prior to mating and throughout pregnancy. Fetuses and placentae were studied at the end of pregnancy (E19). Placentae were stained for CD31 (immunohistochemistry) and the labyrinth area quantified.
Results: Compared to fetal weights of control pregnancies (1.15 ± 0.02g), the fetal weights from obese (1.01± 0.02g) and metformin-treated pregnancies (0.95 ± 0.04g) were significantly reduced. In the placentae from obese pregnancies, there was a significant ($p < 0.01$) reduction in the labyrinthine zone (40±2% vs. 46±1%). In addition, calcification was seen in the labyrinth of obese placentae whereas none was observed in the control group. Neither the reduction of the labyrinth nor the calcification were prevented by metformin.
Conclusions: We conclude that maternal obesity has an impact on the structure of the placenta and promotes calcification potentially associated with impaired placental perfusion. This might lead to the observed fetal growth restriction. Metformin did not prevent the immediate detrimental consequences of maternal obesity on the placenta. However, its ability to prevent long-term detrimental effects of obesity during pregnancy remain to be determined.

Effect of Placental Treatment with a Mitochondria-Targeted Antioxidant (nMitoQ) on Cardiac Function in Adult Offspring Exposed to Prenatal Hypoxia

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Background/Aims: Fetal hypoxia is a major consequence of complicated pregnancies that results in cardiac dysfunction in adult offspring. Hearts from adult offspring of hypoxic pregnancies display enhanced susceptibility to ischemia/reperfusion (I/R) injury and decreased mechanical performance. We tested an early intervention strategy using nanoparticles loaded with a mitochondrial antioxidant (nMitoQ) as placental treatment (thus preventing potential off-target fetal effects) in dams exposed to prenatal hypoxia, to improve cardiac function in the adult offspring. We hypothesized that nMitoQ treatment improves cardiac performance in adult offspring from hypoxic pregnancies.
Methods: Pregnant Sprague-Dawley rats were exposed to normoxia (21% O_2) or hypoxia (11% O_2) from gestational day (GD) 15 to GD21 and intravenously injected with saline or nMitoQ (100 µL of 125 µM nMitoQ) on GD15. Male and female offspring were aged to 4 months (n=4-10) and *ex vivo* cardiac susceptibility to I/R (20 minutes of ischemia and 40 minutes of reperfusion) was assessed. Cardiac β/α myosin heavy chain (MHC) ratio (a marker of hypertrophy) was analyzed using Western blotting.
Results: At 4 months of age, prenatal hypoxia decreased male body weight (722.1±12.2 g vs 686.1±9.9 g; p=0.03) and increased the β/α-MHC ratio in male (6.0±1.0 vs 9.4±1.1; p=0.03) but not female (3.7±0.6 vs 5.0±1.0) offspring, that was not changed by nMitoQ. Prenatal hypoxia decreased cardiac recovery after I/R in both sexes. nMitoQ tended to improve cardiac recovery in the hypoxia group in females (55.8±8.0% vs 79.6 ±3.0%; p=0.06) while in males, nMitoQ increased cardiac recovery (71.3 ±8.0% vs 97.6 ±9.0%; p=0.07) in the hypoxia group (interaction: p=0.04).
Conclusions: nMitoQ treatment had no effect on body weight and cardiac hypertrophy, but improved cardiac capacity to recover from I/R in adult male and female hypoxic offspring. Our data suggest that treating the placenta can improve later life cardiac function of offspring from complicated pregnancies.

Maternal Folate in Pregnancy and Offspring Bone Health: The Vitamin D in Pregnancy Study

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Background/Aims: Folic acid may affect bone formation *in utero* and influence offspring bone mass and fracture risk. We thus aimed to determine the association between maternal folate consumption and supplementation with offspring bone health.
Method: Pregnant women were recruited from the Geelong Hospital (n=475). Women self-reported dietary intake (µg/day), using the Cancer Council Food Frequency Questionnaire and folate supplementation (yes/no) at recruitment (before 16 weeks gestation) and 28-32 weeks gestation. Mother-child pairs returned for the 11-year follow-up (n=210), of which 171 (81.4%) had complete data for the current analyses. Trained personnel measured offspring's bone mineral density (BMD), content (BMC) and area using dual-energy X-ray absorptiometry (Lunar) and obtained parental reported childhood fractures. Regression modelling was used to examine associations between dietary folate and supplementation and bone health and was adjusted for child height, weight, sex and Tanner stage.
Results: Women consumed more folate in early pregnancy vs late [282µg (230-357) vs 260µg (212-324)], and 45 (26.5%), 115 (67.7%) and 57 (34.3%) took a folate supplement before and in early and late pregnancy, respectively. There were 42 fractures (2 clavicle, 17 forearm, 6 elbow, 6 wrist, 4 finger, 1 toe, 1 nose and 5 unknown) from 36 children. There was a positive trend between dietary folate in early pregnancy and total body less head (TBLH) BMD (β=0.00006, p=0.071). Supplementation at recruitment was associated with spine BMC (β=1.40, p=0.041), spine area (β=1.02, p=0.007) and TBLH-area (β=28.0, p=0.035). No associations were found between dietary folate or supplementation with fracture risk at any other time point, nor associations with folate intake or supplementation at 28-32 weeks with any outcome.
Conclusions: Maternal folate supplementation during early gestation, but not late, was associated with aspects of offspring bone health. Folate supplementation in early pregnancy may influence bone development *in utero*, and therefore bone health in childhood.

Resveratrol Administration in Obese Rat Dams Confers Sex-Specific Cardio-Metabolic Protection in Offspring

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Background/Aims: Emerging evidence from both epidemiological and animal studies implicates maternal obesity as a major risk factor for childhood obesity and related cardio-metabolic disease in later life. Employing an established rodent model of maternal obesity, we hypothesised that resveratrol, a polyphenol with antioxidant properties, would improve offspring cardiometabolic function. The aim of the current study was to determine the effects of maternal resveratrol supplementation pre-pregnancy through to lactation on offspring cardiovascular reactivity and glucose tolerance.
Method: Female rats (n=10/group) were fed control (C) or obesogenic (O) diet ad libitum from weaning with vehicle or resveratrol (R) treatment (20mg/kg/d) from 90d of age, through mating at 120d, to the end of lactation. Offspring was weaned on to normal chow. At 6 months of age, one male and one

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female from each litter (four groups; maternal (M)C, MO, MCR and MOR) were surgically implanted with radio-telemetry blood pressure probes (HD-S10, DSI). Following a two-week recovery period, animals were subjected to a 10min restraint stress, in a humane perspex restraining cylinder during which cardiovascular parameters were recorded every minute. At 8 months, a separate cohort of offspring were subjected to glucose tolerance test (GTT): rats were given a glucose load (2g/kg intraperitoneal) and their blood glucose level was measured at -10, 10, 20, 30, 45, 60, 90 and 120min. Data were calculated as mean±SEM and analysed by Two-way ANOVA with Tukey's posthoc test.

Results: MO female offspring had a significantly enhanced pulse-pressure response to restraint stress, which was partially prevented by maternal R treatment (MC[n=4]:9.8±5; MO[n=5]: 26.7±3*; and MOR[n=4]:17.7±3, % change in Pulse Pressure [mmHg] from baseline; *p=0.04). In addition, MO females displayed a significantly impaired glucose tolerance, which was prevented by maternal R treatment (MC[n=4]:902±62; MO[n=8]:1392 ±100*; and MOR[n=9]:886±63^, Arbitrary units of area under the curve; *p=0.01 and ^p=0.001). Similar effects were not observed in male offspring.

Conclusions: Maternal supplementation with resveratrol throughout pregnancy and lactation prevented the programming of enhanced cardiovascular reactivity to restraint stress and impaired glucose tolerance in the female but not male offspring. Sex-differences in the development of autonomic regulation may underlie these divergent responses to maternal obesity in offspring.

Assessing causal links between ancestral exposure and offspring adiposity in three generations via epigenetic inheritance mechanisms in the MULTIEPIGEN study

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Background/Aims: Interest in mechanisms of epigenetic inheritance is peaking. Most data on this phenomenon in humans derive from retrospective studies or tragic natural experiments, or are limited to only two successive generations. Our aim is to establish a series of analysis steps to infer causal links from ancestral exposures (e.g. tobacco smoke) to offspring phenotypes (e.g. obesity) via epigenetic mechanisms across multiple generations.

Method: The MULTIEPIGEN study extends the Cardiovascular Risk in Young Finns Study (YFS). The YFS cohort has been followed since 1980's, and data on exposures, phenotypes and epigenome are available. The MULTIEPIGEN population includes the YFS population (G1), their parents (G0) and children (G2). Data for each generation are being collected during 2019. A series of statistical methods are developed to study inheritance of epigenetic markers and their effect on specific phenotypes. The causal pathway between grandparental exposure and offspring adiposity via epigenetic markers is first described using directed acyclic graphs. Based on these graphs, the sources of confounding or inadvertent selection are identified. Subsequently, the analysis is divided in appropriate sub-problems that can be tackled using e.g. mediation analysis, SEM, or two-step Mendelian randomisation.

Results: Statistical methods for investigating hypotheses on intergenerational epigenetic inheritance in the MULTIEPIGEN context are presented. As a first step towards identifying epigenetic mediator mechanisms, we identify epigenetic marks related to own/parental smoking and their associations with obesity in the G1 population.

Conclusions: Modelling causal pathways in multigenerational data requires appropriate statistical methods accounting for potential confounders. The MULTIEPIGEN study provides an opportunity for studying the pathways of epigenetic inheritance over generations, allowing distinguishing between direct exposure (e.g. passive smoking) and epigenetically-transmitted inheritance.

Combined impact of maternal and infant infection and antibiotic use in pregnancy and infancy in relation to childhood obesity: A longitudinal birth-cohort study with long-term follow-up

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Background: Both maternal antibiotic use during pregnancy and infant antibiotic use have been associated with childhood obesity. However, recent studies have reported that the association with antibiotic use could have been confounded by the underlying infection since both maternal and infant infections have also been associated with increased risk of childhood obesity.

Methods: To assess the combined effects of maternal and infant infections, as well as the combined effect of maternal and infant antibiotic use after controlling for underlying infections, we conducted a birth cohort study examining the associations among 182,923 mother-child dyads with up to 11 years of follow-up (2007 to 2017). We used electronic medical records (EMRs) to ascertain information on maternal and infant infection diagnoses and antibiotic use. EMRs were also used to ascertain anthropometric measurements of offspring. Childhood obesity was defined as BMI $\geq$ 95th percentile based on age- and gender-specific criteria set by the Centers for Disease Control and Prevention. Based on the status of maternal and infant infection and antibiotic use, we created eight cohorts. Mixed effects logistic regression for repeated measurements was used to make use of multiple BMI measurements per child during the follow-up period.

Results: After controlling for multiple confounders, infant infection alone without maternal infection was associated with 15% higher risk of childhood obesity (adjusted odds ratio (aOR)=1.15, 95% confidence interval (CI): 1.07-1.23), compared to the control group, dyads without either maternal or infant infection. Maternal infection alone without infant infection had 7% higher risk of obesity (aOR=1.07, 95%CI: 0.98-1.18), though not statistically significant. Combined maternal and infant infection was associated with 22% higher risk of

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obesity (aOR=1.22, 1.10-1.34), indicating an additive effect of maternal infection (15%) with infant infection (7%). In contrast, neither maternal nor infant antibiotic use alone nor the combination of both was associated with increased risk of childhood obesity once the underlying infection was controlled for: aOR=0.97 for infant antibiotic use alone, aOR=1.02 for maternal antibiotic use alone, and aOR=1.01 for both maternal and infant antibiotic use.
Conclusions: In this large longitudinal birth cohort study, we observed that it was the infection (both during pregnancy and infancy), rather than antibiotic use, that was associated with increased risk of childhood obesity. Maternal and infant infection appeared to impact the obesity risk independently. with an additive effect.

Down-regulated expression of microRNA-1227 in placenta and its role in fetal growth restriction through target gene PRKAB2

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Background/Aims: Fetal growth restriction (FGR) is a common complication of pregnancy, which adversely affects pregnant women and fetuses. In previous study, we found that there was significant difference in the expression of miR-1227 between non-diabetic macrosomia and normal placentas, suggesting the level of miR-1227 might be related to fetal abnormal growth in uterus. Subsequent bioinformatics studies showed that miR-1227 was located in intron 3 of human chromosome 19 PLEKHJ1 gene. This study aims to elucidate the role of miR-1227 in placental tissues and cells and its possible regulatory mechanism of FGR.
Method: The pregnant women with FGR (n=30) and normal pregnant women (n=30), who gave birth in the Second Affiliated Hospital of Nantong University from May 2017 to April 2018 were recruited in the study. The total RNA and total protein, extracted from placental tissue and HTR-8/SVneo cells transfected with miRNA mimic/inhibitor, were tested by quantitative real-time PCR and western blot. Cell proliferation, cell cycles and apoptosis were evaluated using a colorimetric proliferation assay and flow cytometry. The invasion and migration of cells assessment were conducted with Transwell test and monolayer Monostratal wound healing test. The putative targets and regularity pathways of miR-1227 were predicted using the TargetScan, PicTar, miRwalk and DIANA algorithms. Dual luciferase reporter assay was used to determine the relationship between miR-1227 and PRKAB2.
Results: PLEKHJ1-derived miR-1227 downregulated in FGR placentas, and thus inhibited proliferation in HTR-8/SVneo cells and positively impacted its host gene PLEKHJ1. PRKAB2 is a direct target gene of miR-1227, acting as an important mediator in miR-1227 regulated cell growth.
Conclusions: miR-1227 regulates the proliferation of trophoblast cells through targeting PRKAB2 and participates in the development of FGR, which might be a potential marker for prevention and treatment of FGR.

Maternal smoking during pregnancy and offspring intellectual disability: causal analysis in an intergenerational Danish cohort of over 1 million individuals

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Background/Aims: Maternal smoking during pregnancy may impair child cognitive development. In the limited research on the association between maternal smoking during pregnancy and offspring intellectual disability (ID), however, there is mixed evidence for a causal effect with suggestion that the association is due to residual confounding.
Method: Cohort study of all Danish births between 1995 and 2012 (n after exclusions=1,025,956), with prospectively recorded data for cohort members, parents and siblings. Cox proportional hazard models were used to assess the association between maternal smoking during pregnancy (18.5% exposed, collected during prenatal visits) and offspring ID (7,523 individuals, measured using ICD-10 diagnosis codes F70-F79). Models were adjusted for confounders including measures of socio-economic status and parental psychiatric diagnoses and were adjusted for family averaged exposure between full siblings. Adjustment for a family averaged exposure allows calculation of the within-family effect of smoking on child outcomes which is robust against confounders that are shared between siblings. In secondary analyses among smokers, we assessed the hazard ratio of the number of cigarettes smoked per day on time to diagnosis of ID.
Results: We found an increased hazard ratio (HR) for exposure to smoking in pregnancy on offspring ID after adjustment for confounders (HR=1.23, 95% CI: 1.17-1.30) which attenuated to a null effect following adjustment for family averaged exposure (HR=0.88, 95% CI: 0.74-1.05). Our secondary analyses showed a 3% increased hazard (HR=1.03, 95% CI: 1.02-1.04) for every cigarette smoked per day after adjustment for confounders, which again attenuated to the null following adjustment for family averaged number of cigarettes (HR=1.00, 95% CI: 0.98-1.03).
Conclusions: Our findings are not consistent with a causal association between maternal smoking during pregnancy and risk of offspring ID. Our results highlight that analyses that do not assess the within family effect are likely to be subject to residual confounding induced by unmeasured genetic or environmental characteristics of families in which mothers smoked that are also determinants of offspring ID.

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Caesarean section and childhood hospitalisation with infection: an international study of 7.3 million births

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Background/Aims: Caesarean section (CS) has been associated with increased risk of infections in childhood, but studies are generally small and focus on specific infections. Rates of CS vary considerably between countries. We investigated the relationship between mode of delivery and subsequent childhood infection-related hospitalisation (IRH), using total population-linked data from over 7 million births in 4 countries.

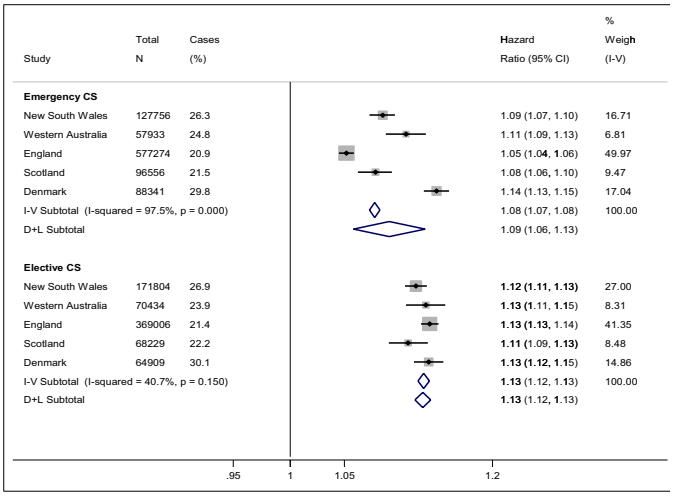
Method: Our multi-country population-based cohort study of all singleton live births from 1996-2015 used record-linked birth and hospitalisation data from Australia (NSW and WA), Denmark, Scotland and England. Mode of delivery was categorised as vaginal or CS (emergency/elective). We defined IRH (overall, and by clinical group) by pre-defined principal and additional ICD-10 discharge diagnosis codes for children aged <5 years. Cox regression models, adjusting for maternal factors, birth parameters and socio-economic status, were used to obtain hazard ratios (HR) and results pooled by meta-analysis.

Results: The study followed 7.29 million children, of whom 1.55 million (21.3%) had ≥1 IRH. Across all sites, CS rates varied from 18-29%, of which half (39-57%) were elective CS. Compared to vaginal delivery, CS was associated with increased risk for total IRH (pooled HR 1.10, 95%CI 1.09-1.10). The risk was higher following elective CS than for emergency CS (elective 1.13, 1.12-1.13; emergency 1.08, 1.07-1.08, Figure) and the risk persisted until age 2-5 years (all CS 1.10, 1.10-1.11). For specific infection groups, compared to vaginal delivery, the HR for elective CS was 1.21 (1.20-1.23) for lower respiratory infection and 1.16 (1.15-1.17) for gastrointestinal infection.

Conclusions: CS is associated with increased risk of IRH in young children. Differences in early microbial exposure by mode of delivery is a likely mechanism; the effect was most marked for elective CS and for those infections where direct inoculation of the maternal microbiome may impact on the development of local immune responses. Mechanistic studies are warranted, and intervention trials should be considered.

Figure: Hazard ratios for infection-related hospitalisation following delivery by emergency or elective caesarean section, compared to vaginal delivery

Adjusted for: sex, gestational age, birth weight, smoking during pregnancy (not available for England data), maternal age at birth, parity, area level deprivation, birth year, indication for type of delivery and season of birth. I-V= inverse-variance weighted fixed effects estimate, D+L=DerSimonian and Laird random effects estimate



The effect of maternal folic acid deficienncy during early pregnancy on the carcinogen sensitivity of offspring in mice

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Background/Aims: Gestational nutrition is widely known to affect the offspring's future risk of lifestyle-related diseases. This suggests the involvement of offspring gene regulation via epigenetic modulation during disease development. We thus investigated how maternal folic acid (FA) intake during early pregnancy influences the sensitivity to tumor formation in the offspring, as FA is an essential nutrient for the modulation of DNA methylation.

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Method: Dams were maintained on an FA-depleted [FA(-)] or normal [2 mg FA/kg; FA(+)] diet from 2–3 days before mating to 7 days post-conception. Their offspring were challenged with chemical tumorigenesis, using 7,12-dimethylbenz[a]anthracene and phorbol 12-myristate 13-acetate for the skin and 4-nitroquinoline N-oxide for the tongue, for 16 weeks.
Results: Tumorigenesis was more progressive in the offspring of the FA(-) dams than FA(+) dams with respect to both squamous tissues. Notably, in the skin of the FA(-) offspring, the expression and activity of cylindromatosis were decreased because of the altered DNA methylation status in its promoter region, which contributed to increased tumorigenesis coupled with inflammation.
Conclusions: Maternal FA deficiency during early gestation accelerates abnormal differentiation and tumor development in the offspring after maturation. Our study clarified that adequate maternal FA intake plays a critical role in preventing tumor progression in the squamous tissues of the offspring and identified an additional beneficial effect of adequate FA intake during pregnancy on the future health of the offspring.

Early Placental Growth and Utero-Placental Vascularization Assessment using Virtual Reality: Reference Values and Associations with Embryonic Growth

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Background/Aims: Early pregnancy failure or placenta-related pregnancy complications can be caused by derangements in the process of placentation starting in early pregnancy. Furthermore, associations between first-trimester placental growth, uteroplacental vascularization and embryonic growth remain unclear. The aim of this study was to determine first-trimester reference values for longitudinal placental growth and utero-placental vascularization measured by three-dimensional (3D) ultrasound (US) and Virtual Reality (VR). Furthermore, we assessed the associations between these placental parameters and first-trimester embryonic growth.
Method: Pregnant women were included in the ongoing Rotterdam periconception cohort. 3D US examinations, including Power doppler (PD) techniques, at 7, 9 and 11 weeks gestational age (GA) were performed to obtain volumes encompassing the whole gestational sac including the placenta. Placental volumes (PV) were measured using the VOCAL™ algorithm. VR software was used to perform semi-automated volume and length measurements calculating the placental vascular volume (PVV), embryonic vascular volume (EVV), crown-rump length (CRL) and embryonic volume (EV). Also, PVV/PV and EVV/EV ratios were calculated. Analyses were performed using SPSS software (version 21.0; SPSS Inc., Chicago, IL, USA) and RStudio Statistics (version 3.5.0, 2018).
Results: A total of 218 ongoing pregnancies were included for analysis. From these pregnancies, a total of 490 3D ultrasound datasets were available for evaluation, of which 342 (69.8%) and 364 (74.2%) were usable for VOCAL and VR measurements, respectively. Women had a median age of 32.1 years (interquartile range: 20.9-48.0), the majority was nulliparous (143 women; 65.6%) and 91 women (41.7%) conceived after IVF/ICSI. Median PVV and median PV increased from 7 (3.13 cm^3; 14.34 cm^3) to 11 (17.89 cm^3; 92.14 cm^3) weeks GA. The PVV/PV ratio remained relatively constant over time (0.16; 0.19). Reference values were composed for PV, PVV, EVV and the ratios PVV/PV and EVV/EV. Overall, placental measurements were positively associated with embryonic measurements, mainly at 7 weeks GA (all r-values >0.5) and 9 weeks GA (r-values between 0.18 and 0.66). Median value distributions of placental/embryonic parameters were not significantly different between nulliparous and multiparous women and between spontaneous and IVF/ICSI pregnancies,
Conclusions: First-trimester placental development is associated with embryonic growth. VR offers new possibilities for the understanding of early pregnancy physiology and pathophysiology.

Hypertensive disorders of pregnancy and autistic traits in offspring: The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study

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Background/Aims: Previous studies suggest the association between hypertensive disorders of pregnancy (HDP) and neurodevelopmental disorders including autism spectrum disorder. However, most of these were case-control studies or retrospective cohort studies from America or Europe. Two meta-analyses revealed slightly higher risk of preeclampsia for autism spectrum disorder than other types of HDP. This study aimed to prospectively examine the association between HDP and autistic traits in offspring, including subgroup analyses of HDP subtypes such as superimposed preeclampsia in Japan.
Method: A total of 23493 pregnant women were recruited between 2013 and 2017 in the Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study in Japan. At the offspring's age of 2 years, 4832 women completed Tokyo Autistic Behavior Scale, with a cut-off score of 16 to identify those with autistic traits (total score range, 0-39).

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The HDP diagnosis criteria of the Japan Society for the Study of Hypertension in Pregnancy consists of 4 subtypes; chronic hypertension, gestational hypertension, preeclampsia, and superimposed preeclampsia. Multiple logistic regression analyses were conducted adjusting for maternal age and offspring's sex.
Results: The prevalence of HDP was 10.7%; 2.7% (chronic hypertension), 4.0% (gestational hypertension), 2.7% (preeclampsia), and 1.3% (superimposed preeclampsia). The odds ratio (OR) (95% confidence interval [CI]) of HDP for autistic traits was 1.21 (0.98-1.50). The offspring of mothers with superimposed preeclampsia had significantly higher risk for autistic traits compared with those of mothers without HDP; the OR (95% CI) was 1.85 (1.08-3.19). Chronic hypertension, gestational hypertension, and preeclampsia were not significantly associated with autistic traits in offspring; the ORs (95% CIs) were 0.92 (0.59-1.42), 1.18 (0.85-1.66), and 1.31 (0.88-1.96), respectively.
Conclusions: Exposure to HDP, especially superimposed preeclampsia, may be associated with increased risk of autistic traits in offspring.

Association between Parental Body Mass Index and Brown Adipose Tissue in Asian Preschool Children: The GUSTO study

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Background: Recent studies suggest an inverse relationship between brown adipose tissue (BAT) and adiposity in adults in Western populations. This study aimed to investigate the association of parental body mass index (BMI) and child BMI with BAT in Asian children.
Methods: The study was conducted among 198 preschool children (86 Chinese, 66 Malay, 46 Indians; 89 boys and 109 girls) from a prospective mother-offspring cohort (Growing up in Singapore Towards healthy Outcomes (GUSTO)) who underwent MRI at age 4.5 years. Colour maps of fat-signal fractions (FF) were created from MRI images from the base of the neck to the inferior border of the scapula. Regions with FF 20~80% within supraclavicular and axillary fat depots (FD_{SA}) were considered BAT, and manually segmented for quantification. % BAT was calculated as 100*ratio of BAT volume within FD_{SA} and total FD_{SA} volume. Ethnicity, child's sex and age were adjusted in multivariable regression analyses to explore the association between parental and child BMI as exposures and child's %BAT as an outcome.
Results: Child BMI was inversely associated with %BAT; a 1 kg/m^2 increase in BMI was associated with 2.58% (95%CI: -3.32, -1.84) lower %BAT. Maternal BMI was not associated with child's %BAT in regression analyses even after additionally adjusting for maternal education, gestational diabetes status and weight gain during pregnancy and child's BMI. Each 1 kg/m^2 increase in paternal BMI was associated with 0.34% (0.03, 0.66) higher %BAT in the child taking account of ethnicity, child's sex, age and BMI. Ethnicity and child's sex did not modify these associations.
Conclusion: Unlike white adipose tissue, child's %BAT was not associated with maternal BMI, whereas, positively related to paternal BMI. Our findings suggest that BAT in children may be determined at least in part by paternal factors.

The Great East Japan Earthquake and perinatal outcomes: The TMM BirThree Cohort Study

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Background/Aims: Little is known about the association between the Great East Japan Earthquake occurred on March 11, 2011 and perinatal outcomes. The purpose of this study was to investigate the association between disaster exposure and perinatal outcomes among pregnant women in Miyagi Prefecture and to examine these effects by timing of disaster exposure during pregnancy.
Method: We used the data of pregnant women who had delivery during 2010-2011 among the subject who participated in the Tohoku Medical Megabank Birth and Three-Generation Cohort Study (the TMM BirThree Cohort Study), which is conducted in Japan. Women who delivered in 2010 were classified

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as "non-exposed" and women who delivered in 2011 were classified as "exposed". To examine the association between the disaster and perinatal outcomes, timing of disaster exposure, the date of birth, gestational age at delivery, birth weight of the infant, and sex of the infant were analyzed. Women were classified into three groups by the timing of disaster exposure: women who were exposed disaster in their first trimester, women in their second trimester; and women in their third trimester.
Results: A total of 916 eligible deliveries occurred during 2010 and of 1,260 during 2011. The proportion of preterm birth (gestational age at delivery <37 weeks) was not significantly different between 2010 and 2011 in all groups. The proportion of low birth weight (<2,500g) was significantly higher among women who were exposed disaster in their first trimester (10.2%) than among women who were not exposed (5.6%) (P=0.02).
Conclusions: In this cohort, the proportion of children with low birth weight was high in children born from pregnant women who experienced the disaster in their early pregnancy than from pregnant women who did not experienced it in their early pregnancy.

Exposure to socioeconomic disadvantage from birth to 32 years and mental health outcomes

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Background: The relationship between socioeconomic disadvantage and mental health is well documented, but lacks a precise understanding of how timing of this exposure impacts on mental health outcomes. This study examines associations between exposure to socioeconomic disadvantage from birth to 31-32 years of age and adult mental health outcomes, using a prospective cohort design.
Methods: Data was analyzed from the Australian Temperament Project (ATP), a representative longitudinal birth cohort in Victoria, Australia (N=2443). Socioeconomic position (education, occupation, and income) was measured at six time points from birth to 31-32 years of age. Mental health at 31-32 years was examined according to difficulties (depression, anxiety, stress, eating problems, and risky alcohol use) and positive psychosocial functioning (life satisfaction, quality of romantic relationship, and civic engagement). Logistic regression models were used to examine associations between socioeconomic disadvantage at each time point and each mental health outcome.
Results: Socioeconomically disadvantaged children had four times the odds of being socioeconomically disadvantaged in adulthood (OR=4.00 to 4.56). Socioeconomic position established in adulthood tended to have a closer association with mental health outcomes compared to early life exposure. For example, the effect on depression at 31-32 years was stronger for socioeconomic disadvantage in young adulthood than during infancy (OR=2.12; 95% CI=1.24-3.62 versus OR=1.13; 95% CI=0.70-1.83).
Conclusions: The association between socioeconomic disadvantage and mental health differs by the timing of exposure and the specific aspect of mental health examined. Results suggest that early life disadvantage impacts on young adults' own socioeconomic position, which in turn has a more direct influence on their mental health outcomes. This needs to be considered in the development of more nuanced and precise intervention approaches to reducing inequities in mental health.

The Role of Adrenal Morphology in High Fat Diet-Induced Anxiety in Mature Adult Mice

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Background/Aims: Obesity is a major risk factor for non-communicable diseases, including psychiatric disorders such as anxiety. This may be due to altered hypothalamo-pituitary adrenal function. However, we showed previously that anxiety in young adult life was not affected by a maternal or post-weaning obesogenic high fat (HF) diet. Here we examined the effect of these HF diets on anxiety in mature adult life and related it to adrenal morphology.
Method: Female C57BL/6 mice were fed either HF (HF: 45% kcal fat) or control diet (C: 7% kcal fat) 6 weeks before mating and throughout pregnancy and lactation. Male and female offspring were fed C or HF diet from weaning (CC: n=8-10; CHF: n=4-12; HFC: n=9-12; HFHF: n=7-8/sex). In 52-week offspring, anxiety markers (distance travelled in centre [DTC] and entries to centre [EC]; open field test) and basal plasma ACTH concentrations (ELISA) were measured. Adrenal glands, cortex area, nuclei density (H&E) and lipid content (Oil Red O) were measured (ImageJ). Data were analysed by mixed effects model (SPSS).
Results: In males and females, maternal HF and postweaning HF diet increased anxiety (reduced DTC: maternal P<0.05, postweaning P<0.01; reduced EC: postweaning P<0.001).

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Postweaning HF diet increased cortex area in males and females (P<0.01, P<0.001, respectively), without any change in nuclei density. In females only, postweaning HF diet increased basal ACTH concentrations (P<0.01) and adrenal lipid content (P<0.05). Maternal HF diet did not affect offspring adrenal cortex area or lipid content.

Conclusions: These finding suggest that maternal and postweaning HF diet increase the risk of anxiety, which becomes apparent with advancing age. Postweaning, but not maternal, HF diet was associated with expansion of the adrenal cortex due to hyperplasia. This could contribute to the elevated basal corticosterone we previously observed in these animals and to their anxiety. In females, the increase in adrenal cortex area following postweaning HF diet could be driven by elevated ACTH concentrations and was associated with adrenal lipid content, which may impair normal adrenal function.

Severity of Nausea and Vomiting in Pregnancy and Early Childhood Neurobehavioural Outcomes

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Background/Aim: The relationship between nausea and vomiting in pregnancy (NVP) and outcomes of the offspring has not been investigated previously in a non-clinical population. The aim of this study was to understand the early social-emotional, behavioral, and cognitive outcomes of children born after exposure to various severity of NVP in a multi-ethnic Asian cohort.

Method: The Growing Up in Singapore Towards Healthy Outcomes (GUSTO) prospective birth cohort studied 1235 mother-child dyads. Mothers responded to a structured questionnaire on first- and second-trimester NVP at 26 to 28 weeks' gestation and the responses were later confirmed with medical records (N=1172). The children had rigorous social-emotional, behavioral, and cognitive phenotyping after birth, including 1-year Infant-Toddler Social and Emotional Assessment (ITSEA), 2-year Bayley Scales of Infant and Toddler Development, 2- and 4-year Child Behavior Checklist (CBCL), and 4.5-year Kaufman Brief Intelligence Test. Multivariable regression analyses were adjusted for household income, maternal mental health trajectory, maternal lifestyle variables during pregnancy, delivery and birth parameters, and other relevant medical-related confounders. Model-adjusted mean scores and their 95% confidence intervals were obtained using post-estimation predictive margins.

Results: Cases were categorized into 1) **no** (n=296, 25.3%), 2) **mild-moderate** (n=686, 58.5%), and 3) **severe NVP** (n=190, 16.2%), of whom 67 required hospital admission. Mild NVP was defined as nausea only, moderate as nausea with intermittent vomiting, and severe as regular vomiting and difficulty retaining food. After controlling for confounders, NVP was associated with poorer emotional and behavioural functioning at all time points from age 1 to 4. Compared to children of mothers who experienced less severe NVP, children with exposure to severe NVP largely exhibited more externalizing behaviours (e.g. hyperactivity, aggression) prior to age 2 and more internalizing behaviours (e.g. anxious, depressive symptoms) after age 2. There was no convincing evidence of a direct association between NVP and cognitive outcomes of the offspring.

Conclusions: Severe NVP was highly prevalent in this Asian cohort and was associated with unfavourable neurobehavioural outcomes in the offspring. Further studies are warranted to examine the unexpectedly early presentation of affective behaviours in children born to mothers with severe NVP.

Testosterone increases the expression of the placental fatty acid transporter FAT/CD36 and the transcription factor PPARG

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Background/Aims: Maternal obesity can affect the health of the newborn by increasing fetal adiposity and the onset of metabolic disorders. It has been observed that in obese pregnant women with a male fetus show an increase in the serum testosterone concentration. In different metabolic tissues, it has been observed that testosterone modulate fatty acids (FA) transporter. However, this has not been explored in placental tissue. In addition, testosterone seems to activate the placental STAT3 pathway, an important regulator of nutrient transport in the placenta. Then, the aim of the present study was to evaluate the effect of testosterone on the expression of FA transporter and molecules related with the FA metabolism in an in vitro model of human chorionic villus explants culture.

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Method: 10 women between 18-40 years, with term pregnancies and without pathologies or complications during pregnancy were recruited. Placental explants were cultured in DMEM/F-12 (10% FBS at 37 °C with 21% O_2 and 5% CO_2) and was stimulated with different concentrations of testosterone (10^{-5}, 10^{-7} and 10^{-9} M) for 24 hours. The viability of the tissue was controlled by measurements of LDH activity and hCG concentration in the culture media. Protein expression of FAT/CD36 and phopho-STAT3 were measured by western blot and gene expression of FA transporters and molecules related to FA metabolism were measured by qPCR. Differences were evaluated by Friedman nonparametric test followed Dunns post test. A p-value $p < 0.05$ was considered as significant.
Results: The protein expression of FA transporter FAT/CD36 decreases in a dose-response manner in placental explants from male fetus ($P = 0.053$). On the contrary, in those from female fetus, testosterone induced an increase of FAT/CD36 protein expression. Besides, there was a dose-dependent increase in the expression of mRNA of PPARG in placental explants from male fetus ($P = 0.02$). The expression of phospho-STAT3 was not significantly altered for testosterone.
Conclusions: It seems that testosterone affects, differently according to fetal sex, the expression of placental transporter of FA FAT/CD36 and the transcription factor PPARG. More analysis about FA uptake and metabolism will be added to corroborate the testosterone effects on placental FA metabolism.
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Preimplantation Glucocorticoid Exposure: Reprogramming our Future Generations?

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Background/Aims: Insults during the 1st week post-fertilization may affect the developmental trajectory and long-term health outcome of the human embryo since during this window, the initial lineages of the are established. Subfertility affects 1 in 6 couples, and glucocorticoids (GCs) are used as an adjuvant during IVF to improve success; however, the impact of preimplantation GC exposure on human embryo development has not been thoroughly investigated. The aim of this study was to investigate the impact of preimplantation GC exposure.
Method: Using scRNA-seq (Smartseq2), Lightsheet microscopy and single-cell small noncoding RNA sequencing (small-seq), we profiled GC exposed (n= 11 embryos, 384 cells) and control (n=6 embryos, 144 cells) human embryos on embryonic day 7 (E7).
Results: Morphological assessment revealed no significant differences in terms of blastocyst size or the number of cells within any lineage. However, striking differences in gene expression were observed in the trophectoderm (TE; future placenta) following GC exposure. Briefly, we observed that GC exposure resulted in the precocious maturation and differentiation of the TE lineage supported by decreased pluripotency (i.e. *DDPA5*, *HAND1*, *LEFTY1/2*) and increased expression of genes associated with TE maturation (i.e. *ERRV2* and *AMOTL2*). Further, GO analysis revealed increased growth pathways, metabolic processes, insulin pathway and immune pathways following GC exposure. These results are in concert with pathways previously reported in studies examining prenatal GC exposure or maternal stress. Candidate microRNAs have been identified as a potential mechanism underlying the transcriptional changes observed.
Conclusions: These data suggest that the human preimplantation embryo may be susceptible to long-term programming of GCs; potentially giving rise to generations of children with an increased incidence of metabolic, neurodevelopmental and behavioural disorders. Data from these studies may aid with the therapeutic use of GCs during ART and highlights the need for more thorough assessment of IVF protocols and adjuvants.

Dynamic profile of gut microbiota in gestational diabetes mellitus with monotherapy of dietary intervention

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Background/Aims: Changes of gut microbiota in pregnancy women have been reported in many papers. Hormone secretion and dietary modification during pregnancy can lead to corresponding changes in the gut microbiota structure which contribute to elevated blood glucose levels. However, the microbial variations in patients with gestational diabetes mellitus (GDM), especially after a systematic dietary intervention remains unclear. Here we aimed to clarify the pattern of gut microbial communities during pregnancy in GDM patients, and its changes under standardized dietary management in these women.
Method: We conducted a prospective nested case-control study enrolling 276 women within 10 weeks of gestation and collected feces samples and clinical information in early (T1), middle (T2) and late (T3) pregnancy from all participants. A final total of 45 pregnancies were confirmed with GDM which were only suffered dietary intervention, and 45 non-GDM women were matched to the GDM pregnancy group by age and pre-pregnancy BMI. Gut microbiota profiles throughout pregnancy were explored by next-generation sequencing of the 16S rRNA gene.

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Results: Age and BMI were the biggest factors affecting the gut microbiota during pregnancy. Excluding the impact of the above two variables, changes in alpha diversity and beta diversity were observed in the GDM group during pregnancy. Before diagnosis and intervention initiated at T2, compared with non-GDM, the GDM group was characterized with more abundant *Blautia* and *Faecalibacterium*, less abundant *Odoribacter*, *Butyricimonas*, *Akkermansia* and *Christensenellaceae* at the genus level and Victivallaceae and Rhodospirillaceae at the family level. At T3, with glucose metabolism improved through dietary intervention, differences in alpha diversity and microbial relative abundance nearly vanished.
Conclusions: Diet intervention can improve the gut microbiomes of GDM women, which suggests the importance and necessity of dietary intervention on blood glucose homeostasis and gut microbial regulation in pregnant women.

Prenatal endotoxemia induces selective alteration in the expression of ABC transporters in the mouse yolk sac

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Background: Infection and inflammation alter the expression and activity of ABC efflux transporters localized at the syncytiotrophoblast barrier of the placenta. These transporters confer fetal protection against xenobiotics and environmental toxins that may be present in the maternal circulation. However, information about the effect of inflammation controlling the expression of the multidrug resistance ABC transporters, P-glycoprotein (P-gp, encoded by *Abcb1a* and *Abcb1b* genes) and breast cancer resistance protein (BCRP, *Abcg2*) in the yolk sac is limited. We investigated the expression profile of these ABC transporters in the mouse yolk sac following lipopolysaccharide (LPS, modeling bacterial infection) exposure.
Aim: To evaluate the expression of selected placental ABC transporters in the mouse yolk sac following LPS exposure in mid- and late-pregnancy.
Methods: Yolk sac samples were obtained at gestational ages (GD) 15.5 and GD18.5, after 4 or 24 hours of LPS exposure (150ug/Kg; n=6/group), from C57Bl/6 mice (CEUA-CCS: 036/16). Samples were processed to evaluate the volumetric proportion of the histological components of the yolk sac wall (endodermal epithelium, endothelial cells, connective tissue and mesothelium), the gene expression (qPCR) profile of *Abca1* (an ABC lipid transporter), *Abcb1a*, *Abcb1b* and *Abcg2* transcripts, as well as protein immunolocalization (immunohistochemistry) of Abca1 and P-gp. Statistical analysis was undertaken using the student T-test.
Results: The volumetric proportions of the histological components of the yolk sac did not change in response to LPS. LPS increased *Abcg2* expression at GD15.5, after 4h of treatment ($P<0.05$). No changes in *Abca1, Abcb1a* and *Abcb1b* were observed. P-gp and Abca1 transporters were localized in the endodermal epithelium and to a lesser extent in the mesothelium, whereas Abca1 was also localized in the endothelial of the yolk sac blood vessels.
Conclusion: Expression and localization of lipid and multidrug resistance ABC transporters in the yolk sac wall, suggest this fetal membrane acts as an important protective barrier, mediating the exchange of toxic substances and nutrients in and out of the fetal cavity. We also provide evidence that infection and inflammation may alter efflux transport expression and compromise the yolk sac transport function.

Adverse postnatal environment differentially affects emotional regulation and immune system function in rats prenatally exposed to alcohol compared to controls

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Background/Aims: Prenatal alcohol exposure (PAE) negatively alters brain development, leading to neurobehavioral dysregulation. Early-life adversity (ELA) also negatively affects brain development and individuals with PAE are more likely to experience ELA. However, how ELA contributes to the pervasive effects of PAE is poorly understood. Given the increasingly appreciated role of the immune system for brain development, here we examined whether PAE and/or ELA increases vulnerability to immune dysregulation, which may alter brain development increasing the risk for psychopathology.
Method: PAE and control litters were exposed either to limited bedding [postnatal day (PN) 8-12] to model ELA or to normal bedding. During early (PN30) or late (PN45) adolescence, male and female offspring were tested in the open field (OF), elevated plus maze (EPM), and forced swim test (FST). Following FST, we evaluated peripheral (serum) and central (amygdala) immune function (cytokines).
Results: In females, PAE alone resulted in anxiety-like behavior in the OF. This anxiogenic profile emerged at PN30 and was still seen at PN45. Conversely, in males, PAE in association with ELA increased anxiety-like behaviors in the EPM at PN30 and PN45. Exposure to ELA resulted in depressive-like behaviors in the FST at PN45 in both male and female control but not PAE animals. Analysis of immune function indicates that PAE alone affected the peripheral immune system of females. In males, peripheral immune alterations were observed following PAE and/or ELA. In the amygdala, PAE females showed increased levels of IL-6, TNF-α, IFN-γ, and IL-1β at PN30 and PN45. However, in males, ELA increased amygdala levels of IL-4, IL-5, IFN-γ, and IL-10 in control but not PAE animals at PN30. At PN45, ELA reduced amygdala levels of IL-4 and IL-5 only in control animals.

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Conclusions: Our results indicate that PAE and ELA have unique and interactive effects on emotional regulation and immune function, and these alterations in the immune system could be an underlying mechanism of the emotional dysregulation observed following PAE and/or ELA.
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Physical health impacts of fetal alcohol spectrum disorder: Preliminary results from a caregiver survey

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Background/Aims: To date there has been extensive clinical research documenting the impacts that prenatal alcohol exposure can have on the developing brain. However, comparatively limited clinical research has investigated the influence that prenatal alcohol exposure can have on other health outcomes. Preclinical research has demonstrated that prenatal alcohol exposure can result in high blood pressure, renal dysfunction and early signs of diabetes and obesity. Outcomes from an informal survey conducted in a cohort of young adults with fetal alcohol spectrum disorder (FASD) suggested they experience a myriad of diseases including early onset arthritis, and hypertension. Consequently, the aim of the current research was to investigate potential health impacts for children and young people with FASD.
Method: We conducted an online survey of caregivers who have children or young people with a formal diagnosis of FASD. Caregivers were asked to report whether their child experienced and/or had been with diagnosed a range of health conditions.
Results: To date, we have had 125 surveys completed. Children/young people ranged from 0– 25-years and 60% were male. Responses were obtained from Australia (30%); United States (31%); Canada (14%); UK (2%); New Zealand (17%) and South Africa (2%). Caregivers reported high rates of sleep problems (70%), bowel/digestive problems (36%), allergies (38%) and joint pain (35%). In addition, children/adolescents with FASD had been diagnosed with heart problems (33%); skin problems 32%; e.g. eczema, dermatitis); asthma (33%); and recurrent infections (22%).
Conclusions: The preliminary results from the caregiver survey suggest that children and young people with FASD may be at increased risk of experiencing some health conditions. Further research is needed, specifically direct assessments of health outcomes for children and young people with FASD compared to age and sex matched typically developing children and young people.

Maternal Overweight/Obesity Is Associated With Markedly Greater Odds Of Obesity In The Offspring At 20 Years Of Age In Thailand

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Background/Aims: Worldwide, there is an increasing number of women entering pregnancy with obesity. Maternal obesity is associated with increased risk of adverse pregnancy and neonatal outcomes. There is increasing evidence also showing long-term adverse effects in the offspring. We examined associations between maternal BMI early in pregnancy and offspring obesity risk and cardiometabolic health.
Methods: Participants were the offspring from the Chiang Mai low-birth-weight study (1989-1990), where pregnant women were recruited at their first antenatal visit in. From the 632 offspring followed up ~20 years later, we studied 565 individuals (53.8% females) born at term (37–41 weeks of gestation), aged ~20.6 years. Assessments included anthropometry, lipid profile, clinic blood pressure, and insulin resistance assessed using HOMA-IR. Overweight/obesity was defined as BMI ≥25 kg/m^2; obesity as ≥30 kg/m^2.
Results: Increasing maternal BMI at the first-antenatal visit was associated with increasing BMI in the offspring [β=0.43 (95% CI 0.29, 0.57); p<0.0001). Further, every 1 kg/m^2 increase in maternal BMI was associated with adjusted odds ratio (aOR) of obesity 23% greater in the offspring (95%CI 6.1, 41.9%; p=0.006). Thus, the offspring of mothers who were overweight and/or obese early in pregnancy had odds nearly 5 times greater of obesity [aOR 4.88 (95% CI 1.74, 13.75); p=0.003). There were however, no observed associations with cardiometabolic outcomes.
Conclusions: Maternal overweight/obesity early in pregnancy associated with a marked increase in the odds of obesity in the offspring. Public health measures should target women of reproductive age, encouraging healthier lifestyle choices prior to pregnancy.

Paternal consumption of an obesogenic diet and orange juice during preconception influences mice female offspring breast cancer risk

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Background/Aims: Breast cancer is the most common cancer in women worldwide. Paternal consumption of a high fat diet

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has been shown to program breast cancer risk in female offspring. Orange juice is widely consumed and is known for its content of bioactive compounds that may have a role in regulating epigenetic processes. Therefore, the aim of the present study was to evaluate the effects of paternal obesity and orange juice consumption on female offspring susceptibility to chemically-induced breast carcinogenesis.

Method: Three-week-old C57BL/6 male mice were distributed in control (C), control-orange juice (CJ), obese (O) and obese-orange juice (OJ) groups, fed either a standard chow or an obesogenic diet (45% lard-based diet supplemented with sweetened condensed milk), with water or orange juice, for 11 weeks before mating. Female offspring were weaned onto standard chow until 7 weeks of age and then were initiated with 7,12-dimethyl-benzo[a]anthracene to induce mammary tumors. This study was approved by FCF Ethical Committee. Data analyses was performed using ANOVA fallowed by LSD test.

Results: CJ female offspring presented higher multiplicity of mammary tumors (P<.05) compared to C offspring. Female offspring from O group showed higher tumor latency (P<.05), lower tumor incidence (P<.05), higher multiplicity of tumors (P<.05), lower cell proliferation (KI67) in the mammary ducts (P<.05) and lower global levels of H3K27me3 in the mammary gland (P<.05) when compared to C offspring. No differences (P>.05) were observed between O and OJ female offspring regarding these parameters.

Conclusion: Consumption of orange juice by non-obese fathers during preconception increased susceptibility of female offspring to mammary carcinogenesis. Although paternal consumption of an obesogenic diet during preconception decreased incidence and increased latency of tumors, the multiplicity of lesions increased. Regarding consumption of orange juice by obese fathers, some level of protection against the development of breast cancer in female offspring is suggested.

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Vitamin B12 Deficiency Leads to Dysregulation of Fatty Acid Metabolism in Human Adipocytes and Maternal Subcutaneous and Omental Adipose Tissue

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Background: Vitamin B12 (B12) is an essential micronutrient required for two key metabolic reactions.Longitudinal studies showed that B12 deficiency during pregnancy is associated with maternal obesityand metabolic syndrome phenotype. Although the mechanisms underpinning metabolic disorders remain poorly defined, it has become increasingly clear that dysregulation of lipids is associated with obesity and its comorbidities.Therefore, we investigated the role B12 deficiency in lipid metabolism in human adipocytes (and maternal Subcutaneous(Sc) and Omental(Om) adipose tissue(AT).

Methods: AbdSc pre-adipocytes cell line (Chub-S7) and human AbdSc primary pre-adipocyte cells were differentiated under different B12 concentrations (25pM,100pM,1nM,500nM) to assess B12 deficiency effects. Human Om, Sc ATand blood samples were also collected from 106 white pregnant women at delivery. Serum B12 as well as relevant metabolic risk factors were measured. Gene expression was performed by q-RTPCR, de novo triglycerides synthesis was quantified using radioactive tracing technique by incorporation of; ^{14}C-oleate and ß-oxidation and palmitate-induced oxygen consumption rate(OCR) was determined using seahorse XF analyser.

Results: Adipocytes cultured in low B12 condition showed significantly increased expression of genes involved in triglyceride biosynthesis (P<0.01) such as elongation of very long chain fatty acids protein 6(ELOVL6), stearoyl-CoA desaturase(SCD), glycerol-3-phosphate acyltransferases (GPAT), phosphatidate phosphatase(LPIN1), diacylglycerol O-acyltransferase 2 (DGAT2) and a significantly decreased expression of genes involved in ß-oxidation (P<0.01) such as fatty acid translocase(FAT/CD36), carnitine palmitoyl transferase I(CPT1-ß), acyl-CoA dehydrogenase long chain(ACADL), enoyl-CoA hydratase short chain 1(ECHS1) and acetyl-CoA acyltransferase 2(ACAA2). These data were also confirmed in the Sc and Om AT from pregnant women with B12 deficiency. We also observed the real-time fatty acid flux synthesis and fatty acid oxidation induced by palmitate was significantly altered in B12 deficient adipocytes.

Conclusion: Our data highlights that low B12 induces a dysregulation of fatty acid metabolism, which might lead to adipocyte dysfunction and suggest a possible role of B12 deficiency in metabolic disorders.

Shorter gestational age explains a large proportion of the poorer educational attainment of twins compared with singletons: a population-based data linkage study

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Background/Aims: Twins tend to have poorer perinatal and early life health and neurodevelopmental outcomes than singletons. Poor educational outcomes are themselves risk factors for

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disease and poorer health in later life. Whether this disadvantage is due to twin-specific factors or confounders and whether, and for how long, it persists into childhood, is unclear. We aimed to assess these issues using educational attainment as a measure of neurodevelopmental outcome.
Methods: Birth records from 1994-2012 were obtained from the NSW Perinatal Data Collection and probabilistically linked to school test results from the National Assessment Program for Literacy and Numeracy (NAPLAN). Five study outcomes were defined as children performing below the national minimum standard (NMS) in the domains of: i) reading, ii) writing, iii) spelling, iv) grammar/punctuation, and v) numeracy. Logistic and Poisson regression models were fitted using generalized estimating equations to estimate unadjusted and adjusted relative risks (RR).
Results: The cohort comprised 619,317 livebirths of which 16,780 (2.7%) were twins. Almost half of twins were preterm (47.5%) compared with 5.3% of singletons. Twins had a greater risk of performing below the NMS than singletons in all five domains (all RR > 1.19 and all p < 0.02) and 65% or more of these risk gradients was explained by the twins having on average shorter gestational age.
Conclusions: Twins are disadvantaged compared with singletons across multiple areas of educational attainment. Much of this disadvantage could be due to the reduced gestational age of twins. Effective strategies for optimising gestation of twin births where possible, and providing additional support for twins at school, might help close this gap. Similar analyses of other neurodevelopmental and health outcomes are in progress and will help clarify the extent, persistence and underlying likely causes of twins' disadvantage.

Early Life Factors in Relation to the Incidence and Prognosis of Cancer in Two Swedish Cohorts

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Background/Aim: Early life factors have been found to be associated with cancer risk. Most previous studies lack adjustments for potential confounders, and cancer post-treatment prognosis has rarely been studied. We assessed the association of birth weight (BW), birth length (BL) and gestational age (GA) with the onset and prognosis of cancer.
Methods: We examined data from Malmö Birth Data Cohort (MBDC) of 4648 elderly individuals and Malmö Offspring Study (MOS) of 1401 younger individuals (<45 years). The MBDC is derived from two Swedish nested case-cohort studies in the Malmö Preventive Project cohort (MPP), and the Malmö Diet and Cancer Study (MDCS). In total, there were 1991 and 47 incident cases of any cancer until end of 2016 within MBDC and MOS cohorts, respectively. Cancer risks and prognosis by BW, BL, and GA were estimated as hazard ratios (HR) using Cox regression model.
Results: There were 4172 men and 476 women in MBDC, and 672 men and 729 women in MOS. There was a statistically significant difference (p= 0.01) in mean BW between cases (3553 g) and controls (3514 g) from MBDC. BW and BL, used as continuous variables and adjusted for GA, were not associated with the onset (incidence) or survival (prognosis) of cancer in both cohorts. In the MBDC, a GA of 40-41 weeks was, however, associated with a lower risk of cancer compared to both shorter, HR 0.88 (0.78-1; p= 0.05) and longer GA, HR 0.85 (0.74-0.97; p=0.02).
Conclusion: In the elderly case-control cohort, cancer was associated with a higher mean birth weight as compared to matched controls. However, neither birth weight nor birth length were associated with risk of cancer or prognosis during follow-up. A gestational age of 49-41 weeks was associated with the lowest overall cancer risk.

Programming across generation through mitochondria DNA methylation

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Background/Aims: The numerous evidences documenting the intergenerational health programming are mostly associative and there is a need for a mechanistic or molecular pathway to further explain the consequences of early environment effects. Epigenetic changes including DNA methylation are perceived as candidates for the observed effects but the very small amount of DNA in oocytes is limiting the capacity of mapping the genome for such marks. Our aim was is to investigate if the mitochondrial DNA which is very abundant in oocytes (>200,000 copies) could be a mean to program the next generation metabolism from the embryo onward using the bovine as a model.
Method: Bovine oocytes and blastocysts recovered from cows subjected to ovarian stimulation (OS) or from non-stimulated abattoir ovaries (AO) followed by IVF and culture. Pools of 10 GVO or 10 blastocysts were digested with proteinase K and restriction enzyme was used (200 U of Sal1 for 4 h at 37°C) to linearize the bovine mtDNA. Samples were treated with 130 µL of Pico Methyl-Seq Library Prep kit (Zymo Research). Whole Genome Bisulfite libraries were made with10 pg to 1 ng of DNA with 10 cycles for two PCR amplification rounds and sequenced.
Results: Oocytes and early embryos, contains high number of mitochondria resulting in very high coverage (140-4000x) and very low p values. Overall Methylation level was lower in oocytes compared to blastocysts and was not restricted to CG sites but was found also at CHG and CHH sites. The OA oocytes showed 72, 106 and 1045 hypermethylated sites (P<0.05) for the CpG CHG and CHH cytosines respectively compared to the OS oocytes. The correlation between cytosines in OS oocytes and OS blastocysts was 0.81 (p<0.001). When compared to level of gene expression of 12 mitochondrial genes (ATP6-8, COI-III, CYB, ND1-2-3-4-4L-5-6) obtained by

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RNAseq an inverse correlation of -0.71 was obtained for oocytes and -0.74 for blastocysts ($p<0.01$).
Conclusions: Collectively, our findings show differences between oocytes sources but a conserved pattern of mtDNA methylation in early embryos which could indicate a programming role during gametogenesis that would be subject to epigenetic regulation according to the maternal environment.

Neonatal vitamin D levels and cognitive ability in young adulthood

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Background/Aims: Intelligence has a strong influence on life and thus identifying early modifiable risk-factors for lower cognitive ability is of public health interest. During pregnancy, vitamin D is transported from the mother to the fetus through the placenta in the form of 25-hydroxyvitamin D (25(OH)D). 25(OH)D has in some studies been associated with childhood neurodevelopment, however results are conflicting. We investigated if neonatal $25(OH)D_3$ concentrations were associated with Børge Priens IQ test score (BPP) in young adulthood.
Method: In this nested cohort study, $25(OH)D_3$ concentrations were measured in dried blood spots from 818 new-borns. We followed the children in the Danish Conscription Register, which holds information on test results from the BPP test on individuals who have been recruited for the mandatory military draft board examination since 2006. Using general linear models, we investigated the crude and adjusted relationship between quintiles of $25(OH)D_3$ concentrations and BPP IQ test results.
Results: The study population consisted of 95.8% men, with a mean age of 19.4 years. The median and range of the neonatal $25(OH)D_3$ levels were 26.2 nmol/L (0 to 104.7 nmol/L). The overall Wald test did not show an association between neonatal 25(OH)D_3 levels and BPP IQ scores ($p=0.23$), however when the first quintile was the reference (BPP IQ=97.6, 94.6-100.6), individuals within the 3rd (BPP IQ=101.0, 98.0-103.9) and 4th (BPP IQ=101.2, 99.1-104.3) quintiles had slightly higher BPP IQ scores.
Conclusions: Our results support the hypothesis that low levels of neonatal vitamin D might affect fetal brain development, however more studies are need on adults with a larger study population.

The not-so-sterile womb: Evidence that the human fetus is exposed to bacteria prior to birth

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Background/Aims: The human microbiome includes trillions of bacteria, many of which play a vital role in host physiology. Numerous studies have now detected bacterial DNA in first-pass meconium and amniotic fluid samples, suggesting that the human microbiome may commence *in-utero*. However, these data have remained contentious due to underlying contamination issues.
Method: Here, we have used a novel method for reducing contamination in microbiome workflows to determine if there is a fetal bacterial microbiome beyond the level of background contamination. We recruited 50 women undergoing elective caesarean section deliveries with no evidence of intra-uterine infection and collected first-pass meconium and amniotic fluid samples. Full-length 16S rRNA gene sequencing was performed using PacBio SMRT cell technology, to allow high resolution profiling of the fetal gut and amniotic fluid bacterial microbiomes. Levels of inflammatory cytokines were measured in amniotic fluid, and levels of immunomodulatory short chain fatty acids (SCFAs) were quantified in meconium. Propidium monoazide (PMA) was used to test the viability of bacteria detected in meconium samples.
Results: All meconium samples and most amniotic fluid samples (84%) contained bacterial DNA. Meconium contains a low diversity and low-biomass microbiome, which was remarkably variable between patients. Importantly, PMA testing confirmed that this community consisted of viable bacterial cells. The amniotic fluid microbiome was more diverse and contained mainly reads that mapped to typical skin commensals. All meconium samples contained acetate and propionate, at ratios similar to those previously reported in infants. Neonates born from mothers with Type 2 diabetes had significantly lower levels of propionate in their meconium compared to those born from mothers with normal pancreatic function ($P = 0.0048$) or from mothers with gestational diabetes ($P = 0.00328$). These differences were not associated with alterations in the fetal microbiome, suggesting that they may be driven by the maternal microbiome.
Conclusions: Our results demonstrate that viable bacterial cells and SCFAs are present *in-utero*, and have the potential to influence the developing fetus.

Insert Abstract title here: Sex Differences in Perinatal Mortality and Morbidity in Twins: A Population Case-Control Study in Scotland

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Background/Aims: Male fetuses in a singleton pregnancy have worse perinatal outcomes than females. In this study we aim to examine the role of fetal sex on perinatal morbidity and mortality in twin pregnancies. \
Method: We performed a population based matched case-control study in sex discordant twins using routinely collected data from Scottish maternity facilities. Twin pregnancies

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delivered in Scotland at 24 weeks' gestation or greater between 1st January 1980 and 31st December 2015 were included. A sex discordant file was made from the full twin database. The exclusion criteria included same sex twins, twin pregnancies complicated by fetal anomaly and babies born before 24 weeks' gestation. We used conditional logistic regression modelling to determine the association between fetal sex and the primary outcome of perinatal death. The secondary outcome was perinatal morbidity (a composite of neonatal morbidity consisting of a baby with a low apgar score (<7) at 5 minutes, or who required admission to the neonatal unit or assisted ventilation).
Results: A perinatal death case-control study of 498 twin infants was created from the Scottish twin birth population of 52,660 infants. For the combined perinatal morbidity or perinatal death outcome a study of 1698 twin infants was created. Results showed that male infants in a sex discordant twin pregnancy have increased odds of perinatal mortality compared to their female co-twins (adjusted odds ratio 1.42, 95% confidence intervals 1.10-1.83). When perinatal mortality was combined with a composite of perinatal morbidity there was also increased odds of mortality or morbidity in male infants compared to their female co-twins (adjusted OR 1.18, 95% CI 1.01-1.37).
Conclusions: Our data shows that male infants in a sex-discordant twin pregnancy are at increased risk of perinatal morbidity and mortality. We aim to go on to investigate if the difference exists in same sex twins.

Anthropometry at Term Age is More Related With Developmental Quotient Score than Anthropometry at Birth in Preterm-born Children

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Background/Aims: The most commonly anthropometry examination of preterm-born children which may be important for predicting its future developmental outcomes are at birth rather than at the time they reach term age by means of 40 weeks post menstrual age (PMA). Preterm-born infants may have a vary anthropometric characteristics at term age. The aim of this study was to determine the correlation between anthropometry at birth and at 40 weeks PMA with developmental quotient (DQ) score at different ages below 2 years in preterm-born children.
Method: A total of 50 eligible preterm-born children were studied prospectively. Anthropometry as weight (W), length (L), and head circumference (HC) were measured at birth and 40 weeks of PMA. The DQ was assessed using The Capute Scale as score of Full Scale (FS)-DQ at 4, 8, 12, and 18 months corrected age (CA). Statistical analysis using correlation test, with p <0.05 being considered significant
Results: Anthropometry at 40 weeks PMA was shown to be significantly correlated with DQ at several ages such as at 4 months (W_{40w} vs DQ_4, r=0.312; p=0.028; L_{40w} vs DQ_4, r=0.309; p=0.029; HC_{40w} vs DQ_4, r=0.364; p=0.009), at 12 months (W_{40w} vs DQ_{12}, r=0.283; p=0.047), and at 18 months (L_{40w} vs DQ_{18}, r=0.303; p=0.033). While anthropometry at birth was correlated with DQ at 18 months only (W_{birth} vs DQ_{18}, r=0.358; p=0.011 and L_{12} vs DQ_{18}, r=0.294; p=0.038).
Conclusions: Anthropometric measurements for preterm-born children should be performed not only at birth, but also at the age of term as it's related with DQ scores at every stage of the child's age consistently.

Maternal Obesity in Pregnancy and Determinants of Offspring Cardiovascular Risk in Neonates.

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Background/Aims: The prevalence of obesity among pregnant women has risen in line with the general population, with implications not just for maternal pregnancy outcome but also for the developing fetus exposed to an obesogenic environment in utero. There is now widespread concern about the long-term effects of maternal obesity on offspring health, particularly in terms of the developmental programming of cardio-metabolic disease in later life. Here we investigated the influence of maternal obesity in pregnancy on neonatal heart rate variability (HRV) within 48 hours of birth.
Method: This trial was a nested case control study performed at Guy's and St Thomas' NHS foundation trust hospitals. We recruited pregnant women who were either obese (n=45, BMI≥30kgm2) or lean (n=60, BMI 20-25 kgm2). HRV (ECG, 20 mins), routine clinic blood pressure measurements, and anthropometric measurements were made within 48 hours of birth. The primary outcome of the study was the cardiovascular function of the neonates.
Results: The mean BMI of women in the obese cohort was 35.9 and the mean BMI of women in the lean category was 22.4. HRV analysis during sleep state revealed significant increases in the minimum HR (Mean difference: -13.74, 95% CI -26.79 to 0.69; p=0.012) and mean heart rate (Mean difference -10.55, 95% CI -20.57 to -0.53; p=0.015) of the neonates born to obese mothers in comparison to those born to lean mothers. Furthermore, the obese cohort also had significantly reduced power in the high frequency (HF) band (54.89, 2.74 to 107.04; p=0.0016) and total power (637.84, 31.89 to 1243.79; p=0.039) compared to their lean counterparts. Adiposity, as measured by skinfold thickness, and blood pressure did not differ between maternal BMI groups.
Conclusions: Exposure to maternal obesity in utero significantly alters basal parameters of cardiovascular function in neonates independent of neonatal birthweight, neonatal gender, maternal education level and mode of delivery. HRV analysis was consistent with a decline in the global activity of the autonomic nervous system, reduced efferent parasympathetic

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activity and an increase in basal heart rate and which may present a risk for susceptibility to cardiovascular disease in later life.

BMI trajectories from birth to 4-5 years in a Norwegian Multi-Ethnic population; Associations with maternal gestational diabetes, prepregnant obesity and gestational weight gain

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Background/Aims: Maternal gestational diabetes (GDM) has been associated with offspring BMI in older-, but not in small children. We examined associations between maternal GDM and children's BMI trajectories from birth to 4-5 years, and the influence of prepregnant obesity and gestational weight gain (GWG).
Method: In the population-based STORK Groruddalen cohort, followed from early pregnancy and all screened for GDM, we collected child anthropometrics from seven time-points between birth and 4-5 years of age (346 ethnic Europeans, 181 South Asians, and 152 Middle East/North Africans). Using Mixed models, we studied associations between maternal factors and children's BMI (kg/m2) and changes in BMI (growth) per month. We analyzed growth intervals 0-6 months and 6 months to 4-5 years separately.
Results: Children exposed to GDM were not heavier at birth, but had slower BMI growth (B=-0.120 SD; 95%CI: -0.18- -0.04) during the first 6 months, and faster BMI growth from 6 months to 4-5 years (B=0.009 SD; 95%CI: 0.002-0.02) compared to children not exposed, until their BMI was similar at 4-5 years. Maternal prepregnant obesity was associated with higher BMI at birth, and stable higher BMI up to 4-5 years. Maternal GWG (highest tertile) was associated with higher BMI at birth and faster BMI growth from 6 months to 4-5 years (B=0.007 SD; 95%CI: 0.0002-0.01). Although there were substantial ethnic differences in BMI trajectories, relations with maternal GDM, prepregnant obesity and GWG were similar in all ethnic groups. The effects of the three maternal factors were largely independent of each other.
Conclusion: Maternal gestational diabetes, prepregnant obesity and gestational weight gain had different and independent effects on the child's BMI trajectories.

Inter-generational Associations of Height, Weight, and BMI in Three-Generation Families: The TMM BirThree Cohort Study

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Background/Aims: Height, weight, and body mass index (BMI) are determined by interaction between environment and genetics. Examining height, weight, and BMI along family line assists to understand this interaction. The aim of this study is evaluating inter-generational associations of height, weight, and BMI in three-generation families including neonates.
Method: Analyses were performed to three-generation families had joined to Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (TMM BirThree Cohort Study). Study population was composed of neonate (n=20,115, male 10,552, female 9,563), mother (n=19,937, mean age ± SD; 31.4±4.9 years), father (6,926, 33.5±5.9), maternal grand-father (1,287, 62.8±6.2), maternal grand-mother (3,148, 58.8±6.0), paternal grand-father (653, 64.2±5.9) and paternal grand-mother (1,018, 61.1±5.8). In analyses, logarithm of BMI (logBMI) was used to ensure normality. We applied multiple linear regression adjusted by age.
Results: LogBMI was significantly and positively associated between mother and male/female neonate (r^2=0.068/0.076), father and male neonate (r^2=0.050), mother and maternal grand-father/mother (r^2=0.25/0.23), and father and paternal grand-father/mother (r^2=0.28/0.20).
Conclusions: These findings indicate that inter-generational association of BMI in early life may depend on sex. Taking mother's background information such as pregnancy complications into consideration, we are willing to examine whether logBMI depends on prenatal environment or not.

Alcohol consumption and trajectories of depressive symptoms in perinatal period over 11-year period: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC)

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Background: Almost one in four women during pregnancy experience at least one mental health problem. Half of these depressed women continue with these complaints into the postpartum period impacting both the mother and her child health. Data are scarce on the relationship between alcohol consumption during pregnancy and depressive symptoms after delivery. Drawing data from a longitudinal study, we aimed to 1) identify distinct patterns of maternal depressive symptoms at ten time-points in the perinatal period; and 2) determine the predictors of trajectories of depressive symptoms.
Method: A secondary analysis was conducted using data from more than 14,000 mothers participating in the Avon Longitudinal Study of Parents and Children (ALSPAC), a UK based birth cohort. Depression was measured using the EPDS scale; the information was obtained from 18-week

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gestation until 11-year postpartum. A longitudinal growth model was estimated followed by longitudinal growth mixture modelling to identify distinct trajectories of depressive symptoms in MPlus. Finally, predictors of trajectories of depressive symptoms were determined by using multinomial logistic regression modelling in SPSS.
Results: Four distinct trajectories of maternal depression over time were identified: low (79%), high (11%), increasing (6%) and decreasing (4%). The predictors of the trajectories with increasing depression as compared to decreasing showed that women who consumed more than 3 glass of alcohol per week before pregnancy were at a higher risk of being member of increasing depression class [aOR:2.2 (1,2-3.7)]. Similarly, high depression in comparison to decreasing depression reflected that women who were physically hurt by partners were at a higher risk of being member of high depression class [aOR:1.9 (1.2-3.1)]. All analyses controlled for mother age at birth, family income and ethnicity.
Conclusions: These analyses identified four patterns of depressive symptoms. High alcohol consumption before pregnancy and being physically hurt by partner were identified as independent predictors of increasing and high depression classes respectively. Reducing alcohol consumption and maintaining good relationship with partners may reduce depressive symptoms.

A low-intensity intervention increases rates of weight-monitoring and health professionals' confidence to provide weight management advice in routine maternity care

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Background/Aims: Maternal obesity and excessive gestational weight gain increase the risk of pregnancy complications and perpetuate the cycle of obesity and chronic disease in mothers and their children. Aims were to evaluate changes in health professionals' beliefs, confidence, knowledge and practice after participating in low-intensity professional development (PD) regarding weight management in pregnancy.
Method: Low-intensity PD was provided to maternity care staff at two sites within a large hospital network in Victoria, Australia. Change in weighing practice was evaluated in an audit of patient records six months pre (September 2017 to March 2018) and three months post-PD (June to August 2018). Pre and post-PD questionnaires were collected from health professionals who participated. Pre and post data were analysed using independent t-tests and chi-square. Logistic regression explored the impact of patient covariates on weighing practice, $p < 0.05$.
Results: Between September 2017 to March 2018 (n=3033) and June to August 2018 (n=720), 3753 women received maternity care at the two hospital sites. Post-PD, there was no change in the percentage of women weighed at their first maternity care visit (pre 80.8%, post 82.1%), p=0.42. However, the frequency of weighing during pregnancy increased (pre 52.8% of encounters, post 69.5%), p<0.01. There were significant positive changes to health professionals' confidence to provide weight management advice and self-reported practice related to seeking permission to discuss weight, advising women of recommended weight gain, individualising advice and goal setting.
Conclusions: Low-intensity PD significantly increased rates of weighing at routine maternity care visits. Health professionals reacted positively to this form of PD and it was effective in increasing their confidence and enhancing aspects of practice related to patient-centred care.

Chronic low-dose alcohol exposure during pregnancy leads to reduced blood pressure and blunted pressor responsiveness to stress in female but not male offspring

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Background/Aims: Exposure to alcohol during gestation can have a profound legacy on offspring health, most notably on cognition and behaviour. The impact of alcohol exposure on the cardiovascular system of offspring has received scant attention. Previously we have shown adult rat offspring exposed to chronic, low-dose alcohol *in utero* have reduced nephron endowment, left ventricular hypertrophy and fibrosis. The aim of this study was to determine if this was associated with changes in blood pressure, vascular function and vascular stiffness, all key determinants of cardiovascular health.
Method: Female Sprague-Dawley rats were fed an *ad libitum* liquid diet ± 6% vol/vol ethanol throughout pregnancy. Male and female offspring were studied at 12 months of age. Arterial pressure was measured over 7 days via radiotelemetry. Renal lobar arteries were isolated and studied using wire and pressure myography.
Results: Mean arterial pressure in female ethanol-exposed rats was reduced by ~5-6mmHg compared to control female offspring, whereas arterial pressure was unaffected in males. Ethanol-exposed female offspring had an attenuated pressor response to restraint stress compared to control females. Ethanol exposure did not alter endothelial function, smooth muscle reactivity, neurovascular constriction or vascular stiffness in renal arteries from either sex.
Conclusions: Chronic, low-dose ethanol exposure *in utero* results in reduced blood pressure and blunted pressor

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responsiveness to stress in female but not male offspring. Changes occurred without overt signs of fetal alcohol spectrum disorder. This suggests even relatively low amounts of alcohol consumed during pregnancy elicits significant changes to the cardiovascular system.

Maternal obesity during pregnancy alters placental structure in mid and late gestation and has sex-specific effects on labyrinth zone structure

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Background/Aims: Maternal obesity during pregnancy is associated with poor obstetric and neonatal outcomes, as well as offspring cardiovascular and metabolic dysfunction in later life. The placenta is the primary interface between the mother and fetus and thus is likely to play an important role in linking maternal obesity to poor offspring outcomes. Previously, an Ingenuity Pathway Analysis of RNA-sequence data from placentae from obese and non-obese pregnant mice suggested that maternal obesity was associated with dysfunction in cellular proliferation, and organisation and vascular development. The aim of this study was to investigate whether these transcriptional alterations translated to observable differences in placental phenotype in mid and/or late gestation.
Method: Pregnant C57BL/6J mice, fed either a standard chow diet or a highly palatable obesogenic diet, were euthanised on either the thirteenth (E13) (n = 10 per group) or nineteenth (E19) (n = 9 - 10 per group) day of pregnancy, and placentae were collected for immunostaining. Cellular growth was investigated by measuring expression of the proliferation marker Ki67. The endothelial cell marker cluster of differentiation 31 (CD31) was used to identify endothelial cells of the labyrinth zone, the exchange region of the murine placenta. Organisation and vascular development was investigated by analysing both the size of the labyrinth zone, and its structure. Sections were imaged on a Zeiss AxioScan Slide Scanner and analysed using HALO analysis software (Indica Labs).
Results: Maternal diet-induced obesity did not affect the number of actively proliferating cells across the whole placenta (Three-way ANOVA, P(Maternal Diet)=0.4). The size of the labyrinth zone was reduced in male and female placentae from mothers fed an obesogenic diet (Three-way ANOVA, P(Maternal Diet)=0.0004) at both time points. Moreover, the structure of the labyrinth zone of female placentae was affected by maternal obesity, with a decrease in the proportional area of the labyrinth zone that was fetal capillaries (Two-way ANOVA, P(Maternal Diet)=0.0499).
Conclusions: Maternal obesity was found to cause changes in the organisation of the labyrinth zone from as early as E13 which were not accompanied by changes in proliferation. Although the size of the labyrinth was reduced in both male and female placentae by maternal obesity, there were also sex-specific effects on the structure of the labyrinth zone. These findings highlight the importance of including males and females in studies of developmental programming and give insight into mechanisms by which sex-specific effects of maternal diet on offspring phenotype could arise.

Prenatal Cooking May Increase Hyperactive Behaviors at around 3 Years of Age: Findings from Shenzhen Longhua Child Cohort Study

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Background/Aims: Cooking is a main sources of indoor air pollution in China. During the cooking process, a lot of harmful substances are produced, including particulates, carbon monoxide, nitrogen dioxide and so on. Considering concerns of a link between air pollutants and neurodevelopment are emerging, we examined the relationship between household cooking during gestation and child hyperactive behaviours.
Method: During 2015 to 2017, 45518 mother of children who were firstly enrolled at kindergarten in the Longhua district of Shenzhen participated in this study. Self-administered questionnaires were used for information collection which regarding demographics and cooking exposure. Hyperactive behaviours were assessed using the Conners' Parent Rating Scale-Revised (CPRS-48). Linear regression models and Logistic regression models were employed to examine the association of prenatal cooking and hyperactive behaviours.
Results: 45.3 percent of mothers reported cooking at home during the pregnancy. Cooking was related to an increase risk of off-springs hyperactivity behaviours [OR = 1.19(1.13~1.26); β = 0.021(0.016~0.026)], after controlling for potential confounders. Compared with pregnant mothers who never cooked, those cooking sometimes [OR = 1.09(1.03~1.15); β = 0.010(0.005~0.014)] or often [OR = 2.61(2.25~3.02); β = 0.137(0.121~0.153)] were likely to show a significantly higher hyperactivity risk. Different cooking fuels including coal [OR = 3.02(2.25~4.05); β = 0.159 (0.127~0.191)]and liquefied petroleum gas [OR = 2.29(1.96~2.69); β = 0.118(0.102~0.134)] or natural gas [OR = 2.20(2.02~2.40); β = 0.116(0.108~0.124)] were also more likely to exhibit hyperactivity behaviours, when compared to electricity. Furthermore, the positive association with cooking was relatively consistent across strata defined by social class, education, and other covariates.

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Conclusions: This study suggests that cooking during the gestation are associated with an increased risk of hyperactive behaviours in children at around 3 years of age.

Compensating for a difficult start - maternal psychosocial stress, breast milk composition and infant development

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Background/Aims: Maternal stress during the pregnancy and postpartum negatively affects infant health and development with the consequences ranging from growth retardation through behavioral and cognitive problems to a higher risk of metabolic diseases. Breastfeeding has the potential to alleviate these consequences however physiological mechanism behind this effect remains unknown. We explored the impact of maternal life stressors during gestation and postpartum on the composition of breast milk and infant development during the first months of life.
Method: 150 mothers together with their healthy, born on time 4-months old infants took part in the study. Information about maternal stressors during pregnancy and postpartum were collected using the Recent Life Changes Questionnaire (RLCQ). Infant measurements of body length, weight, head and chest circumference were collected at birth and at the age of 4 months. Breast milk samples were collected at the time of the second midmorning feeding to assess the composition of the fatty acids (FA) using gas chromatography. Level of maternal cortisol was also assessed from saliva samples taken at the time of milk collection.
Results: Higher RLCQ during pregnancy and postpartum were positively associated with the level of the long chain mono- and polyunsaturated fatty acids (EFA and PUFA) and negatively with the level of the middle chain fatty acids in the breast milk after adjustment for the range of confounders. Higher RLCQ was also associated with the smaller infant size at birth but these differences disappeared at the age of 4 months.
Conclusions: Our results suggest that when facing psychosocial stress mothers invest energy to produce milk with a higher level of long chain unsaturated fatty acids. This allows for faster growth and compensation for differences in the development at the beginning of infant life.
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POSTER ABSTRACTS

Vitamin B12 deficiency induces *de novo* lipogenesis in human placental trophoblasts

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Background: Vitamin B12 (B12) deficiency is associated with maternal and childhood obesity. However, the predisposition factors to obesity is programmed in-utero. Maternal low B12 has a potential epigenetic role and therefore may perpetuate an intergenerational cycle of obesity through its effects on placental function and fetal metabolism. We have shown that maternal B12 deficiency is associated with higher cord blood lipids. Therefore, we hypothesise that B12 deficiency could affect placental lipid metabolism and may alter fetal lipid levels, potentially influencing neonatal adiposity. In this study, we assessed whether low B12 in human placental trophoblasts alters *de novo* fatty acid synthesis.
Methods: Human trophoblastic choriocarcinoma cells (Bewo) was cultured using custom made B12 deficient Ham's F12 media and cultured in sufficient (500nM - Control) and low concentrations of B12 media (25pM - low B12) until confluence was achieved. RNA isolation, cDNA synthesis and gene expression assays using RT-qPCR were employed to examine the *genes* in FA synthesis in placental cells.
Results: Placental trophoblasts cultured in low B12 showed significantly increased gene expression of (1) nuclear transcription factor regulating lipid metabolism (sterol regulatory element binding protein (SREBF1)), (2) *de novo* fatty acid synthesis (ATP citrate lyase (ACLY), acetyl CoA carboxylase (ACC), fatty acid synthase (FASN) and elongation-of very-long-chain fatty acid (ELOVL6)), and (3) triglyceride biosynthesis (stearoyl CoA desaturase (SCD), glycerol-3-phosphate acyltransferase (GPAT), acylglycerol-3-phosphate acyltransferase (AGPAT), phosphatidic acid phosphatase-1 (Lipin1) and diacylglycerol acyl transferase 2 (DGAT2)) compared to control ($p<0.05$).
Conclusion: Our study provides novel evidence that B12 deficiency in human placental cells upregulates *de novo* lipogenesis. Thus, suggesting B12 deficiency potentially alters placental lipid levels which may lead to placental dysfunction and subsequent dyslipidemia in offspring. Future studies to understand the underlying mechanisms will support the development of effective interventions to optimise maternal metabolism, placental function and future health of the offspring.

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Dramatic impairment in the chronically hypoxic fetus to second stressors such as acute hypotension and acute hypoxia

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Background/Aims: Although sub-optimal pregnancy is thought to developmentally program the fetus with an increased vulnerability to secondary stressors, there is little evidence to support this. This gap in knowledge is due to the difficulty of obtaining cardiovascular recordings in severely hypoxic fetuses. We combined the use of isobaric chambers to simulate significant chronic fetal hypoxia and designed a wireless data acquisition system to simultaneously record continuous fetal cardiovascular data in an ovine model. Here, we investigated the fetal *in vivo* cardiovascular defence to either acute hypoxia or acute hypotension in chronically hypoxic or normoxic fetal sheep.
Method: At 80% gestation, a 30 min episode of acute hypoxia (fetal PaO_2 Δ-10±1mmHg from baseline) was induced in chronically instrumented fetal sheep before and after 10 days of either chronic fetal hypoxia (n=6) or chronic fetal normoxia (n=6). On the last day of the 10-day exposure to chronic hypoxia or chronic normoxia, fetuses also underwent a 30-min period of acut hypotension (sodium nitroprusside i.v.). Cardiovascular data were recorded throughout.
Results: ACUTE HYPOXIA: Normoxic fetuses showed traditional brain sparing circulatory responses to acute hypoxia. In contrast there was no brain sparing response to acute hypoxia in chronically hypoxic fetuses. ACUTE HYPOTENSION: Control fetuses showed traditional baroreflex responses to hypotension. In contrast, cardiac and vasomotor baroreflexes were severely abnormal in chronically hypoxic fetuses (Table 1).
Conclusions: We provide novel evidence to support that the chronically hypoxic fetus is indeed at much greater risk of demise during a superimposed challenge.

Effect of testosterone in the last period of gestation in mice fed with a high fat diet on keys molecules of fetal hepatic *β-oxidation*

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Background/Aims: Maternal obesity contributes with the development of metabolic diseases in the offspring through mechanism not completely elucidated. Early alterations of hepatic β-oxidation during fetal life could lead lipid accumulation in the liver being the first hit to develop non-alcoholic fatty liver disease. The current evidence indicates that exist a sexual dimorphism in the response to development programming in utero. This is probably mediated by the action of testosterone. In this regard, the aim of this study was to elucidate the effect of maternal obesity and testosterone on key molecules involved in fetal hepatic β-oxidation.
Method: Ten weeks old C57BL/6 female mice were fed with a control diet (14,9% Kcal fat) (n=7) or an obesogenic diet (45% Kcal fat) (n=6) for 4-6 weeks previous pregnancy until gestational day (GD) 17.5. Two high fat (HF) and three control mice were received daily 100 µl subcutaneous injection of 0.5 mg/kg of testosterone propionate (Test) from the GD 15.5 until 17.5. On day 17.5 animals were fasted for 4 hours, subjected for oral glucose tolerance test, and then anesthetized and euthanazied. Fetuses and placentas were removed, dried and weighed. Liver from each pup were dissected, weighed and freeze. The hepatic expression of CPT1 and PPAR-α was determined by western blot.
Results: The weight gain during pregestational period were higher in the HF group ($P < 0.0001$, t-test), there are no difference in glycaemia post glucose ingestion. The weight of liver, visceral and subcutaneous adipose tissue were also comparable between groups, whereas the weight of retroperitoneal adipose tissue was higher in the HF+test group compared to control+test group ($P < 0.05$, One way ANOVA test). On the other hand, there are no difference in fetal weight, fetal liver and placental weight between the groups. The protein expression of PPAR-α is higher in HF+test group compared with control+test and HF+vehicle group ($P<0.05$, One-way ANOVA test). The expression of CPT1 was no altered for the HF diet or testosterone treatment.

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		Chronically Normoxic (n=6)	Chronically Hypoxic (n=6)
ACUTE HYPOXIA	Max Brain Sparing Index Ratio of Carotid:Femoral blood flow	11.6 ± 4.5	1.5 ± 0.1*
	Bradycardia: Max Δ HR (bpm)	4.9 ± 1.2	0.4 ± 0.1*
ACUTE HYPOTENSION	Max Δ FVR (mmHg.(mL.min^{-1})$^{-1}$	1.3 ± 0.2	0.8 ± 0.3*
	Max Δ HR (bpm)	58.3 ± 7.8	9.7 ± 2.9*

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Conclusions: Data suggest that HF diet plus testosterone could affect the maternal fat depots an the fetal hepatic β-oxidation. It becomes necessary to increase the number of animals treated in order to appreciate greater differences in offspring.
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Ancestral Stress Accelerates Biological Aging Across Five Generations via Epigenetic Regulation

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BACKGROUND/AIMS: Biological age is indicated by the rate of physical and mental health decline. Prenatal and ancestral stresses are among the most significant risk factors for premature aging and higher disease risk. According to the match/mismatch hypothesis, multigenerational stress, however, may promote resilience to recurrent stressors and support successful aging. Here we investigated if multigenerational prenatal stress (MPS) affects age-dependent profiles of physical and mental health, stress response, and epigenetic regulation by microRNA (miRNA) expression.
METHODS: Fourth (F4) generation male and female MPS offspring was derived from a lineage whose female ancestors (F0-F3) were exposed to gestational stress (days 12-18). Endocrine and brain function was assessed across the lifespan at 6 (young), 12 (middle-aged) and 18 (aged) months of age. RESULTS: Aging increased the incidence of anxiety- and depression-like behaviours and impaired sensorimotor behaviours in a sex-specific manner. MPS accelerated the decline of mental and physiological health during aging. MPS also increased the incidence of disease such as kidney failure, inflammatory disease and tumours. Unbiased deep sequencing revealed that MPS altered miRNAs targeting synaptic plasticity and endocrine regulators, DNA methylation regulators, B and T cell-regulators. and the senescence biomarker miR-21.
CONCLUSION: These findings suggest that cumulative ancestral stress is a significant determinant of lifetime physical and mental health trajectories and a risk factor for common age-related diseases via epigenetic regulation. Disease incidence may be regulated by sex-specific pathways. miRNAs may play a role in the transmission of generational stress and represent predictive biomarkers of age-related diseases and biological aging.

Maternal fructose consumption downregulates hepatic *Igf*-1 expression via enhanced expression of miR-29a, miR-130a and miR-301 in offspring.

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Background/Aims: The effects of maternal fructose intake on offspring health remain largely unknown, despite a marked increase in the consumption of sweetened beverages. Previously, we have demonstrated that excess maternal fructose consumption can differentially program hepatic gene expression such as insulin-like growth factor-1 (Igf-1). However, the mechanism of gene expression abnormality is unknown. In this study, we aimed to clarify the mechanism of programmed hepatic *Igf-1* expression in offspring from the viewpoint of epigenetics.
Method: Female rats were assigned to receive either distilled water (control group) or 20% fructose solution (fructose group) during gestation and lactation. Two groups of male offspring were fed with a standard chow diet and distilled water from weaning (postnatal day 21) to the age of 160 days. MicroRNA (miRNA, miR)-29a, miR-130a and miR-301 expression in the offspring liver was measured by qRT-PCR. We measured transcript activation by luciferase reporter assay. Igf-1 expressions in cell line were measured by qRT-PCR when these miRNAs overexpression and downregulation were performed by miRNA mimic and miRNA inhibitor.
Results: Hepatic expression of miR -29a, miR-130a and miR-301 in fructose group offspring were 4-6 fold higher than control group. To clarify whether *Igf-1* expression is regulated by these miRNAs, luciferase reporter assay was performed. Luciferase activity was significantly reduced when cells were transfected with vector containing putative miRNAs target site (miR-29a, miR-130/301) of *Igf-1* mRNA. While, the reduction of luciferase activity was not observed with a vector containing mutated target sequence. After the transfection of miR mimic, *Igf-1* expression was significantly suppressed. Increased *Igf-1* expression level was observed in the presence of miR-301a inhibitor.
Conclusions: in this study, we indicated that hepatic *Igf-1* expression may be mediated by miR-29a, miR-130a and miR-301.

Plasma B vitamers are associated with metabolic syndrome scores in Australian children and their mid-life parents

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Background/Aims: B group vitamers are diet-derived, water-soluble, and play pivotal roles as co-enzymes in energy production. Some studies have linked a higher intake of these vitamers with increased risk of obesity, whilst others have highlighted lower levels in individuals with metabolic syndrome (MetS). In the present study, we assessed the influence of (i) a shared gene-environment setting (within families), age, and sex on B vitamer levels in 2,492 parent-children dyads; and (ii) investigated their simultaneous associations with MetS.
Methods: Plasma EDTA was obtained from the Checkpoint wave 6.5 of *The Longitudinal Study of Australian Children* [LSAC] cohort. Thiamine (B1), Riboflavin (B2), Flavin Mononucleotide [FMN] (B2), Nicotinamide (B3), Pantothenic acid (B5), and 4-Pyridoxic acid (B6) were profiled using ultra high-pressure liquid chromatography coupled with tandem mass spectrometry. MetS was calculated based on HDL cholesterol, triglycerides, glucose levels, and systolic blood pressure, with or without BMI. Mixed models were developed to examine Aim 1, and multivariate fractional polynomial analysis to examine Aim 2.
Results: Members of the same family had highly correlated B vitamers. Strong age-associated effects were seen for all vitamers except for FMN. Boys had higher B1, B5, and B6 (4.71±1.9; 183.09±1.39; 12.68±2.38 nM) than girls (4.01 ±1.79; 165.67±1.36; 11.25±2.08 nM). However, only B5 was markedly higher in fathers (212.72±1.70 nM) than mothers (190.57±1.79 nM). B1 and B2 were strongly positively associated with MetS, whereas FMN and B6 were highly negatively associated with MetS in parents. B1 was negatively and FMN positively associated with MetS in children.
Conclusions: Familial similarities in B vitamers pinpoint strong gene-environment effects exerted on these nutritional metabolites. Generation and sex contribute to the inter-individuality of plasma B vitamers, highlighting the need for nutritional policy recommendations to be stratified by age and sex. B1, B2, and B6 vitamers are associated with MetS in our cohort, specifically in adults. Characterising vitamer-MetS associations offers the potential to identify early-life biomarkers of health.

Low birth weight predicts poor physical fitness in children: regional demographic analysis in Japan

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Background/Aims: Low birth weight (LBW) is associated with lower levels of muscle performance or cardiorespiratory fitness in later life, as suggested by cohort or clinical studies. However, it remains unclear whether these associations are observed at regional levels. This study examined regional differences in the incidence of LBW and its relationship to regional distribution of physical fitness in Japanese children.
Method: We used public data on incidence of LBW by gender and prefectures from the Vital Statistics (the Ministry of Health, Labour and Welfare) in 2002 and results of eight types performance tests by gender and prefectures from the Survey of Physical Fitness and Motor Abilities (the Ministry of Education, Culture, Sports, Science and Technology) in 2013. The former is a complete survey of all children and the latter covers all children who belong to fifth grade in primary schools (10 to11 years old) in Japan. These data were connected according to the prefectures and then analyzed.
Results: Incidence of LBW was significantly associated with five types performance tests; grip strength (r=-0.25), sit-ups (r=-0.33), side step (r=-0.36), 20 meter shuttle run (r=-0.37), and standing long jump (r=-0.33), after controlling for gender and the rate of multiple births by prefectures. The associations with sit and reach, 50 meter run, and softball throw were not significant. These results suggest that the associations between LBW and lower levels of muscle performance or cardiorespiratory fitness may exist even among regional revels.
Conclusions: Children born in regions with higher incidence of LBW seem to have lower muscle performance and cardiorespiratory fitness. Interventions to improve physical fitness might be needed especially in such regions.

Postnatal Ketogenesis Protects Hepatocytes from Feeding Induced Mitochondrial Stress

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Background/Aims: Ketone body metabolism functions as an emergent energy server in the starvated condition. Recent findings illuminated beneficial roles of ketone bodies for health and disease. However, the physiological roles of ketogenesis are poorly understood. In this study, we aimed to determine the role of perinatal ketogenesis along with growth.
Method: We characterised perinatal ketogenesis by measuring the concentration of beta-hydroxybutyrate (3OHB) and expression pattern of HMG-CoA synthase 2 (Hmgcs2), rate-limiting enzymes for ketogenesis, transcript. We also newly generated Hmgcs2 KO mice and analysed their phenotypes in the perinatal period.
Results: Compared to adult mice, 3OHB concentration in neonates was significantly elevated in the free-feeding condition. Hmgcs2 expression was gradually increased concomitantly with mitochondrial growth. CRISPR/Cas9 system allowed to establish two lines of Hmgcs2 deletion mutants. Hmgcs2 homozygous mutant (Hmgcs2 KO) could not produce hmgcs2 protein and the concentration of ketone bodies were significantly low. We could not find apparent abnormalities at birth, however, ectopic fat deposition rapidly progressed in hmgcs2 KO neonates. Metabolome analysis revealed decreased energy

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production in spite of the significant accumulation of acetyl-CoA in KO liver. Section electron microscope revealed KO neonates kept many damaged mitochondria and oxygen consumption rate was significantly decreased in hmgcs2 KO hepatocytes. Western blot analysis showed enhanced acetylation of mitochondrial proteins in KO liver. We served neonates to high-fat fed dam and found short term fatty acid milk stress caused mitochondrial protein acetylation in neonate.
Conclusions: Prenatal ketogenesis did not cause lethal effect but postnatal ketogenesis protected mitochondria from feeding induced fatty acid stress.

Parental Obesity and Offspring Pubertal Development: Findings from Project Viva

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Background: Parental obesity is strongly related to offspring adiposity. However, few studies have examined whether parental obesity programs pubertal development independently of offspring adiposity.
Methods: Among 1,377 offspring from a pre-birth cohort in Boston, USA, we examined markers of pubertal [age at peak height velocity (PHV), age at menarche (girls only), early adolescent (median 12.9 years) self-reported pubertal development score] and adrenarchal timing [early adolescent pictograph Tanner pubic hair staging]. We used multivariable regression to examine associations of parental obesity [body mass index (BMI) $\geq$30kg/m^2] with offspring pubertal indices, and further applied marginal structural models (MSMs) with stabilized inverse probability weighting to estimate the controlled direct effect of parental obesity (i.e., the effect not mediated by offspring pre-pubertal BMI).
Results: Compared to no parental obesity (i.e., neither parent obese), paternal obesity was not associated with any pubertal outcomes, while maternal obesity was associated with earlier age at PHV [boys: β -0.35 years (95% CI -0.61,-0.08); girls: -0.25 years (-0.52,0.00)], higher pubertal score [boys: 0.33 units (0.15,0.51); girls: 0.18 units (0.01,0.36)] and greater odds of higher pubic hair stage [girls only: OR 1.98 (1.06,3.71)], but not with age at menarche. Biparental obesity (both parents obese vs. both non-obese) was associated with earlier age at PHV (in boys and girls), higher pubertal score (girls only), greater odds of higher pubic hair stage (girls only) and earlier menarche. Using MSMs, maternal obesity had significant controlled direct effects on age at PHV [-0.33 years (-0.66,-0.01)] and pubertal score [0.27 units (0.05,0.49)] in boys, while no direct effects were observed for any pubertal outcomes in girls.
Conclusion: Maternal obesity programs earlier pubertal development independent of pre-pubertal BMI among boys.

Biomarkers Of Resilience In Children: Resilience And Flood Impact Predict Salivary Cortisol Measures

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Background/Aims: Exposure to a natural disaster in childhood can have long-lasting consequences, impacting physical and mental health, development and learning. Although many children experience negative effects after a disaster, the majority do not, and what differentiates these groups is not well understood. The adrenal steroid, cortisol hormone plays a crucial role in the response to adverse life events, and as a daily rhythm. Disregulation of the cortisol rhythm is associated with early adverse life events and with cortisol stress reactivity in adulthood. This study naturally included a major urban flooding event in Alberta Canada during June of 2013.
Method: For cortisol measurement, 253 children, aged 1-4 years at the time of the flood, and sampling, collected six saliva samples at home using age-appropriate Salimetrics collection tubes and child sorbettes, at 1) awakening, 2) morning – 30 minutes later, and 3) night – just before bedtime, on two consecutive days. Cortisol concentration was detected by positive LC-ESI/MRM. Awakening response (morning – awakening) was also calculated. Data were analyzed in SPSS v25. Pearson correlation was used to establish association between cortisol parameters and child resilience [Devereux Student Strengths Assessment (DESSA) scale, 28 – 72], flood impact (sum of 22 items) and child-sex (binary).
Results: Mean resilience scores (±SD) were significantly higher in females compared to males (51.08±9.24) vs (48.76±8.86). Resilience scores positively correlated with cortisol at awakening, morning and the awakening response, but negatively correlated with flood impact. Moreover, child's resilience predicted cortisol levels at awakening (unadjusted coefficient the beta; 0.07; p=0.02) and morning (unadjusted coefficient the beta: 0.11; p=0.03) in a univariate model.
Conclusions: Home-collected salivary cortisol might be a useful biomarker to screen for resilience in children impacted by early life adversity.

Web-based Mental Health Intervention to Reduce Prenatal Anxiety – Findings From The Integrated Maternal Psychosocial Assessment to Care Trial (IMPACT) Study

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Background/Aims: About one in four women experience anxiety and depression during their pregnancy. Up to 70% of the women with prenatal depression or anxiety carry these symptoms into their postnatal and early childhood periods. This randomized controlled trial (RCT) was carried out to measure the effectiveness of an integrated intervention consisted on prenatal e-screening, e-referral, and e-therapy in addressing maternal anxiety symptoms.
Methods: In this RCT, women were recruited and computer-randomized into two groups, 1) control group (CG) of routine prenatal care and 2) the intervention group (IG), that received a web-based intervention consisting of e-screening, e-referral, and e-therapy (6 modules, cognitive behaviour therapy [CBT]). The State-Trait Anxiety Inventory (STAI) and resilience (CD-RISC) data were obtained at 3 time-points: Baseline (pregnancy), 12-week, and 24-week postpartum. An independent t-test was conducted to observe difference of anxiety symptoms between and CG and IG. Anxiety trajectories were generated for IG using longitudinal latent class analysis (LLCA) and predictors were identified by multinomial regression.
Results: Out of 1789 total eligible participates, 916 and 873 belonged to CG and IG, respectively, and had no significant differences in baseline sociodemographic or mental health variables. An independent t-test results revealed that mean anxiety score (+SD) was significantly lower in IG compared to CG at 24-weeks (39.58+9.07 vs (42.29+9.89). Mean resilience score was significantly higher in IG compared to CG at 24-weeks (68.56+13.37 vs 65.35+11.46). LLCA resulted in three classes of women (low, medium and clinical anxiety) and multinomial regression analysis revealed that CBT modules, and family and partner relationship predicted anxiety for "medium anxiety" class whereas family, partner relationship, and mother's age predicted anxiety for "clinical anxiety" class of the intervention group.
Conclusion: This study shows that an integrated intervention consisting on prenatal e-screening, e-referral, and e-therapy may play a role in reducing anxiety and enhancing psychological strengths.

Developmental origins of cardiometabolic health outcomes from studies of twins: A systematic review and meta-analysis.

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Background/Aims: Studies of twins can reduce confounding and provide additional evidence about the causes of disease (due to within-pair matching for measured and unmeasured factors). Though findings from twin studies are typically applicable to the general population, few studies and systematic reviews have taken full advantage of the twin design to explore the developmental origins of cardiometabolic health outcomes. Furthermore, few systematic reviews have examined multiple early-life exposures of interest and cardiometabolic outcomes. We aimed to systematically review the evidence for the developmental origins of cardiometabolic health from twin studies and generate pooled estimates for associations of various early-life exposures with later-life cardiometabolic health.
Methods: After an initial search in March 2018, 55 studies were included in the review. Quality was assessed using the Newcastle-Ottawa scale, and we conducted a meta-analysis on eligible studies.
Results: Higher birthweight was associated with lower later-life systolic blood pressure (β: -1.83 mmHg, 95%CI: -2.48, -1.18), higher BMI (β: 0.45 kg/m^2, 95%CI: 0.42, 0.47), lower cholesterol (β: -0.07 mmoL, 95%CI: -0.11, -0.04), and decreased odds of hypertension and type two diabetes (p-values for both: <0.001). However, in studies which adjusted for gestational age, these associations were not evident.
Conclusions: Overall, birthweight appears to be associated with later-life cardiometabolic health outcomes. However, few studies examined outcomes other than BMI and blood pressure, or exposures other than birthweight, and few of these appropriately adjusted for gestational age. Few studies took full advantage of the twin design, by exploring within- and between-pair associations, instead treating twins as individuals. Additional studies are needed to address these limitations. Although twin studies can be used to learn about the health of the general population, our systematic review indicated that twin studies are yet to be fully exploited to assess the developmental origins of cardiometabolic health outcomes.

He ara ki nga rautaki e ora tonu ai te reo Māori: evidence for retention and revitalisation of indigenous language in Aotearoa/New Zealand

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Background/Aims: Te reo Māori is the indigenous language of Aotearoa/New Zealand (NZ), and an official language, despite significant challenges to its survival post colonisation. Retention and revitalisation of te reo Māori is required to: strengthen identity (and therefore health); ensure that Māori succeed as Māori; and meet our obligations under te Tiriti o Waitangi and supportive legislation such as the Declarations of Human Rights and the Rights of Indigenous Peoples. Our

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government has developed a framework for investment in te reo Māori yet evidence for the development of Māori language in early childhood, and within families is lacking. The longitudinal and lifecourse supports (and challenges) to language retention and revitalisation is also unknown. This research uses novel measures of te reo Māori within the Growing Up in New Zealand (GUiNZ) study to consider: the demographic characteristics of speaking te reo Māori during early childhood; the predictors of te reo Māori language acquisition from the antenatal and infancy period; and whether cultural connectedness is associated with te reo Māori use at 4 years of age.

Method: Mothers of the GUiNZ cohort (N = 6327) reported on their two-year old children's language development in te reo Māori using adapted versions of the MacArthur Communicative Development Inventory. At age 4 years further assessment of te reo Māori proficiency was collected from the same children. A series of analyses of variance (ANOVAs) and bivariate correlations were utilised to calculate children's proficiency in te reo Māori at ages 2 and 4 years as a function of the microsystem, mesosystem and macrosystem context – including sociodemographic indicators, family and home environment, and early childcare arrangements.

Results: Derived variables for te reo Māori use and cultural connectedness were robust with in internal reliability (Cronbach's alphas > .80). At age 2 and/or at age 4 years, te reo speakers were more likely to have a Māori mother who was born in New Zealand, who spoke Māori herself, who had high levels of cultural connection, and who had obtained a secondary school educational qualification or higher. Te reo speakers were also more likely to live in deprived neighbourhoods and attend kohanga reo (language nest early childcare). Children's screen time was a negative predictor of te reo Māori.

Conclusions: GUiNZ, and novel measures of language developed within this study, provide the most detailed insights into te reo Māori language development in Aotearoa/NZ. By aligning our research questions to the current policy environment we are not only able to present robust research evidence of indigenous language use and proficiency, but also consider language acquisition drivers and impediments. These analyses have the potential to significantly transform the manner in which language policy and strategy is developed to Aotearoa/NZ, to ensure that resources are most effectively targeted, and that policy change leads to language gains.

Maternal peanut consumption and peanut introduction while breastfeeding are associated with a reduced risk of peanut sensitization at 5 years of age in the CHILD cohort

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Background/Aims: New evidence-based guidelines recommend introducing peanut during infancy to reduce the risk of peanut allergy. However, evidence is lacking on the potential impact and interaction of maternal peanut consumption and breastfeeding on the development of peanut allergy in offspring. We addressed this question in the prospective national CHILD birth cohort.

Method: Maternal peanut consumption, breastfeeding (BF) and infant peanut consumption were reported using repeated questionnaires. Peanut exposure during infancy was classified as: introduced while BF, introduced without BF, or avoided. Peanut sensitization was determined by skin prick testing at 1, 3 and 5 years of age. Analyses were adjusted for maternal atopy and study site.

Results: Among 2634 dyads, 20% introduced peanut while BF, 17% introduced peanut without BF, and 63% avoided peanut until after 12 months. Introducing peanut during infancy was strongly associated with a lower risk of peanut sensitization at 1 and 3 years regardless of BF. For example, at 3 years, 5.3% of avoiders (reference group) were sensitized compared to 1.6% (aOR 0.31; 95%CI 0.14-0.60) and 2.0% (aOR 0.37; 0.17-0.72) of those who introduced peanut with or without BF, respectively. However, by 5 years of age, the apparent protection from early peanut introduction was stronger when combined with BF, with just 0.6% sensitization in this group (aOR 0.11, 0.03-0.29) compared with 2.1% for introduction without BF (aOR 0.34; 0.15-0.66) and 6.1% among avoiders. This enhanced protection from BF at the time of peanut introduction was only observed among mothers who regularly consumed peanut ($p<0.05$ for introduction with vs. without BF in this group).

Conclusions: Our findings confirm the benefit of early peanut introduction for allergy prevention, and further suggest that BF at the time of peanut introduction provides additional benefit if the mother regularly consumes peanut. The increasing effect at 5 years highlights the importance of longitudinal studies to assess trajectories of peanut sensitization and risk of allergy. Ongoing research in the CHILD cohort will assess breast milk composition to explore possible mechanisms for these associations and evaluate confirmed peanut allergy at 8 years of age.

Gestational Diabetes Mellitus and its association with adiposity in newborns: Results from the first wave of MAASTHI, an ongoing cohort study in the public hospitals in India, 2016-2019

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Background: Infants born to mothers with Gestational Diabetes Mellitus (GDM) have an increased chance of various metabolic disorders later in life. It is important to know whether GDM mediates the association of maternal obesity and newborn adiposity after accounting for known confounders.
Methods: A prospective cohort of 1120 pregnant women and infants in public hospitals was recruited during 2016 to 2018. We assessed maternal obesity as greater than 90th percentile of skinfold thickness during 8 to 23 gestational weeks and performed a 75-g, 2-hour Oral Glucose Tolerance Test (OGTT) between 24 to 36 weeks of gestational age. Skinfold thickness was assessed using Holtain's calipers soon after birth and infant adiposity was defined as greater than 90th percentile cut-off value. The association between maternal obesity with infant adiposity and mediation role of GDM was analysed using sequential ignorability assumptions in the 'mediation package'of R statistical computing for Causal Mediation Analysis.
Results: Women with GDM had nearly two times (OR:1.96, 95% CI, 1.21-3.13) higher odds of delivering babies with adiposity compared to euglycemic mothers. In the causal path of maternal obesity and infant adiposity, GDM was found to have significant causal mediation effect (OR:1.38, 95% CI, 1.03-2.53) with mediated proportion of 0.24. We found that maternal obesity (OR: 1.41, 95% CI; 1.21- 3.13) is associated with fetal adiposity and the total effect was significant (OR= 1.95, 95% CI 1.25–7.83) after including GDM as mediator.
Conclusions: We showed that maternal obesity and GDM are independently and causally related to offspring adiposity, in low and middle-income urban Indians. Also, we show that a part of this association is mediated by GDM in women. Results suggest that obesity may have increased incidence of GDM in pregnant women. Interventions focused on obesity prevention in women and efficient management of GDM might reduce childhood obesity.

Maternal adiposity during pregnancy is associated with greater neonatal adiposity at birth

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Background/Aims: Body mass index (BMI) is often used as a proxy for adiposity due to the ease of measurement and calculation of BMI compared to adiposity. Maternal overweight and obesity during pregnancy, defined using BMI, have been associated with greater neonatal adiposity at birth, a risk factor for childhood obesity. Few studies have assessed the association between directly measured maternal adiposity during pregnancy and neonatal body composition at birth. We assessed associations of maternal adiposity in early and late pregnancy with neonatal birthweight, body fat percentage, and fat free mass at birth.
Methods: We used data collected from 2015-2017 as part of a randomized controlled trial of a lifestyle intervention in overweight and obese pregnant women in northern California. We limited our analyses to women in the control group of this study (N=137). Maternal adiposity was defined by body fat percentage measured using bioimpedance spectroscopy at 10 weeks (range: 7-13) and 32 weeks (range: 30-35) gestation and categorized into quartiles. Neonatal adiposity was estimated using a validated equation based on birthweight, length, and flank skinfold. We used linear regression to estimate associations of maternal adiposity during pregnancy with neonatal body composition at birth.
Results: Women were 33 years old (SD=4) and delivered at 38 weeks (SD=2), on average. Maternal mean body fat percentage was 35% (SD=6) at 10 weeks and 36% (SD=5) at 32 weeks gestation. Neonates weighed 3374g (SD=507) and had 13% (SD=3) body fat at birth. Women with 35-<39% body fat (Q3) at 10 weeks gestation delivered neonates with 198g greater birthweight (95% CI: 3, 393) and 1.5% greater body fat (95% CI: 0.1, 2.9) at birth compared to women with <32% body fat (Q1). Maternal body fat percentage at 10 weeks gestation was not associated with lean mass at birth (P for trend=0.2). Maternal body fat percentage at 32 weeks gestation was not associated with neonatal birthweight, body fat percentage, or fat free mass at birth (P for trend=0.39, 0.58, 0.54, respectively).
Conclusions: Our results suggest that maternal adiposity in early pregnancy, but not in late pregnancy, is associated with greater neonatal adiposity at birth. This suggests the need for preconception interventions to reduce maternal and neonatal adiposity and reduce risk of subsequent childhood obesity.

Developing Healthy Conversation Skills Training for Teachers and Education Practitioners

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Background/Aims: Childhood obesity in the UK is a major public health problem. LifeLab is an educational intervention designed to empower school pupils through science enquiry to understand the consequences of lifestyle choices for their health. Our previous research has shown sustained changes in knowledge and motivation, with less evidence of translation into behaviour change. To address this we have added Healthy Conversation Skills (HCS) training to the LifeLab professional

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development for teachers. HCS is a programme of skills to support behaviour change developed at the University of Southampton.
Method: Prior to teaching the LifeLab module, secondary teachers attend a professional development day where they are introduced to HCS, alongside an online version. The training focuses on developing five key skills: creating opportunities for healthy conversations; asking open discovery questions; listening; reflecting; and supporting goal-setting using SMARTER action-planning. The professional development programme has been designed for practising teachers, but Primary and Secondary school trainee teachers have an opportunity to be introduced to HCS through the Southampton Education School's annual Health and Wellbeing Conference.
Results: Since April 2015, 97 qualified teachers have been trained in HCS. 100% rated the quality of the training as good (5%) or very good (95%). 75% commented on the positive impact the HCS training will have, not only in their own teaching but also in raising their awareness of the potential of affecting the lives of their students.
Conclusions: We have shown the positive impact on teachers of being trained in supporting their students in making health behaviour changes. The UK government's new Personal, Social, Health and Economic education curriculum for 2020 makes the Health and Wellbeing curriculum statutory in all schools in England, which offers a timely opportunity to further develop HCS in schools in order to support positive health behaviours.

Sex-specific Effects of Maternal Bisphenol A Exposure on Immune Response in Offspring Pancreas

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Background: Ubiquitous exposure to an endocrine disruptor, Bisphenol A (BPA), is associated with metabolic abnormalities across multiple generations. We recently demonstrated that maternal BPA exposure is associated with pancreatic beta-cell dysfunction and inflammation in male, but not female, mice offspring in adulthood. In the current study, we sought to determine whether developmental BPA exposure triggers immune dysfunction early in life, which leads to impaired beta-cell function later in life.
Methods: C57BL6/J females were exposed to 10 μg/kg/day (LowerB), 10 mg/kg/day (UpperB) of BPA, or 7% corn oil (Control) diets from 2 weeks prior to mating until weaning (n=30 litters/group). Pancreata were harvested from a subset of litters at postnatal day (PD)7, PD21, 10weeks, 5months, and 10months from male and female offspring (n=5-6 litters/sex/group/age). Pancreatic sections were immunofluorescent stained for c-Jun and c-Fos (both activated by cellular stress), insulin, and DAPI to determine beta-cell stress. CD45+ cells were isolated from pancreas, and 11 different immune-cell sub-populations were enumerated via multicolor flow cytometry using LSR Fortessa and analysed by FACSDiva. To localise immune-cell populations in different pancreatic compartments, pancreatic sections were immunostained for CD3 (T-lymphocytes) and F4/80 (macrophages). The groups were compared by one-way ANOVA, followed by post-hoc Dunnett's test between each BPA group and Control; $p<0.05$ considered significant.
Results: At PD7, immune-cell population numbers did not differ between LowerB and UpperB male and female offspring pancreas compared to Controls. However, both LowerB and UpperB males, but not females, had increased c-Jun and c-Fos staining in beta-cells. This correlated with a modest increase in cytotoxic T-cells, and recruited macrophages at PD21, which progressed to an age-associated significant increase in male (10weeks<5months<10months), but not female, offspring pancreas.
Conclusion: Maternal BPA exposure increases beta-cell stress early in life in the male offspring, which triggers a progressive recruitment of immune-cells in pancreas with age.

In utero exposure to bisphenol A alters methylome and transcriptome in human amniocytes in a sex-specific manner

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Background: Human exposure to the endocrine disruptor, Bisphenol A (BPA), is ubiquitous and associated with multiple health abnormalities. As such, it is imperative to identify early life biomarkers of abnormal health associated with BPA exposure. We recently demonstrated that increased second trimester amniotic fluid (AF) BPA concentrations are associated with decreased birth weight in humans. In the current study, we sought to determine whether health outcomes including decreased birth weight and later development of diabetes and obesity following gestational BPA exposure are associated with transcriptomic and methylome changes in human amniocytes.
Methods: We used a nested-case-control design, and 1:1 matched for maternal race/ethnicity, age, offspring sex, and gestational age at amniocentesis and birth. Whole transcriptomic

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via RNA-Seq, and genome-wide methylation analysis via Enhanced Reduced Representation Bisulfite Seq (ERRBS) was conducted in amniocytes (n=6-7/sex/group) of BPA exposed (AF BPA 0.40-2.00 ng/mL; BPA-Male, BPA-Female) and unexposed (AF BPA<0.25ng/mL; Control-Male, Control-Female) offspring. For RNA-Seq, edgeR v3.12.1 was used to find differentially expressed (DE) genes with logFoldChange>1, positive counts per million, and p<0.01. For ERRBS, differentially methylated regions (DMRs) were identified using DEFIANT (DMRs: easy, fast, identification and ANnoTation) program with q<0.05 considered significant. *In silico* Hi-C analysis was conducted to uncover 3D interactions of identified DMRs with distal genes. Ingenuity Pathway Analysis was conducted to identify pathways of biological significance.
Results: BPA-Male v.s. Control-Male had more DE genes and DMRs than BPA-Female v.s. Control-Female. Integrating ERRBS and RNA-Seq data revealed minimal changes in expression of nearest genes, but Hi-C identified multiple interactions of DMRs with distal genes (Male>Female) that were DE, indicating DMRs as potential distal regulators. The distal DE genes were enriched in metabolic and pro-inflammatory pathways.
Conclusion: In unique repository of human amniocytes, we identified sex-specific novel genome-wide transcriptomic and methylome changes and potential distal regulators associated with developmental BPA exposure.

Effects of preterm birth induced with or without glucocorticoids on the ovine glucose-insulin axis

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Background: Antenatal glucocorticoids (ANG) are standard management for women at risk of preterm birth, but are reputed to impair glucose tolerance in preterm offspring. We recently reported that glucocorticoid induced preterm birth in sheep is associated with impaired glucose tolerance, and reduced beta-cell mass, but it is not clear whether this is due to ANG exposure, or preterm birth.
Methods: We compared lambs born preterm (137d gestation) following labour induced with glucocorticoids (G-Prem), or with a progesterone synthesis inhibitor (NG-Prem), with term-born lambs (Term; 148d). We assessed glucose tolerance, insulin secretion and sensitivity at 4 (4mo) and 10 months (10mo) *n*=11-14/group), and pancreatic and hepatic gene and protein expression at 4 weeks post-term (4wk; *n*=6/group) and 12 months (12mo; *n*=12-13/group).
Results: NG-Prem had higher plasma glucose concentrations than G-Prem, but not Term, at 4mo (Mean[SEM] mM: NG-Prem=4.1[0.1]; G-Prem=3.4[0.1]; Term=3.7[0.1]; p=0.003), and 10mo (NG-Prem=3.9[0.1]; G-Prem=3.5[0.1]; Term=3.7[0.1]; p=0.01). Insulin sensitivity decreased from 4mo to 10mo, in both preterm groups but not in Term (Mean[SEM] $\mu mol.mL^{-1}.kg^{-1}.min^{-1}.ng^{-1}$, 4mo *vs* 10mo: NG-Prem=18.7[2.5] *vs* 9.5[1.5], p<0.01; G-Prem: 20.4[2.3] *vs* 11.8[1.5], p<0.05); Term: 12.1[2.8] *vs* 10.4[1.5], p=0.44). Compared with Term, β-cell mass at 4wk and 12mo was reduced in both NG-Prem (~75% reduction, p<0.01) and G-Prem (~30% reduction, p<0.01), and was accompanied by an increased β-cell apoptosis: proliferation ratio at 12mo (both p<0.05). At 12mo, pancreatic *glucokinase*, *igf2* and *insulin* mRNA expression levels were reduced 42-80% in NG-Prem vs Term and 21-71% vs G-Prem. Hepatic *glut2* mRNA levels in NG-Prem were 250% of those in Term and G-Prem.
Conclusion: Induction of preterm birth without glucocorticoids more adversely affected offspring glucose-insulin axis than induction with glucocorticoids. These findings do not support an effect of ANG but do support an effect of preterm birth itself on offspring glucose-insulin axis function.

The Dunedin Dementia Risk Awareness Project: Pilot Study in Older Adults

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Background/Aims: Recommendations from the USA and UK governmental and academic agencies suggest that up to 35% of dementia cases are preventable. We canvassed dementia risk and protective factor awareness among local older adults to inform the design of a larger survey.
Method: The modified Lifestyle for Brain Health (LIBRA) scale quantifying dementia risk was introduced to a sample of 304 eligible participants. This scale was validated in an earlier study surveying General Practitioners (1).
Results: Two hundred and sixteen older adults (≥50 years), mean + SD age 65.5 + 11.4 (50-93 years) completed the survey (71% response rate). Respondents were mostly women (n=172, 80%), European (n=207, 96%) and well educated (n=100, 46%, with a tertiary qualification; including n=17, 8%, with a post-graduate qualification). Around half of participants felt they were at risk of suffering from dementia (n=101, 47%), and the majority felt this would change their lives significantly (n=205, 95%), that lifestyle changes would reduce their risk (n=197, 91%), and that they could make the necessary changes (n=189, 88%) and wished to start changes soon (n=160, 74%). Only 4 of the 14 modifiable

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risk or protective factors for dementia were adequately identified by the participants: Physical Exercise (81%), Depression (76%), Brain Exercises (75%) and Social Isolation (83%). Social isolation was the most commonly cited risk factor for dementia while physical exercise was the most commonly cited protective factor. Three clusters of brain health literacy were identified: psychosocial, medical and modifiable.
Conclusions: Older adults are not adequately knowledgeable about dementia risk and protective factors. However, they report optimism about modifying risks through lifestyle interventions.
Barak Y, Rapsey C, Fridman D, Scott K. The Dunedin Dementia Risk Awareness Project: a convenience sample of general practitioners. N Z Med J. 2018 May 4;131(1474):27-34.

Birth weight and its association with protein expression of FATP1 and FATP4 fatty acid transporters in placenta

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Background: The DOHaD concept suggests that deleterious environmental factors in early fetal life resulting in fetal metabolic programming and an increased risk of developing diseases in adult life. Birth weight is an indirect marker of an adverse intrauterine medium. Fetal growth depends of nutrients availability and transport capacity by placenta. Nutrients such as fatty acids are transported by specialized proteins called FATPs. There are no studies that evaluate these transporters in human placenta of healthy pregnant women. In this study, we aimed to evaluate relationship of birth weight with protein expression of FATP1 and FATP4 transporters in placentas of healthy women with newborns SGA, AGA and LGA (small, adequate, and large for gestational age, respectively).
Method: A cross-sectional study in placenta from healthy mothers with term newborns and idiopathic alterations of weight at birth: SGA (n=20), AGA (n=20) and LGA (n=20) was carried out. Protein expression of FATP1 and FATP4 was evaluated in placenta homogenates by means of western blot.
Results: Protein expression of FATP1 transporter was found to be diminished in placenta of newborns SGA compared to LGA group ($p < 0.01$). Protein expression of FATP4 transporter also showed to be decreased in placenta of newborns SGA compared to AGA group ($p<0.047$). Positive associations of protein expression of both FATP1 and FATP4 transporters with placenta weight ($r=0.358$, $p<0.015$ and $r=0.338$, $p<0.015$, respectively) and birth weight ($r=0.473$, $p<0.001$ and $r=0.346$, $p<0.012$, respectively) were found.
Conclusions: The results suggest a potential role of the fatty acid transporters FATP1 and FATP4 in the modulation of human placental and fetal growth. More studies are required to evaluate the activity of these transporters and to evaluate if their expression can be regulated by the intake of maternal nutrients. Supported by: Basic Science-CONACYT (CB-2013-222563) and UG (CIIC-288/2018).

Are inequalities in birth outcomes increasing or decreasing? Analysis of national birth registry data by neighbourhood deprivation

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Background/Aims: Socioeconomic inequalities in health can be observed since early life in the form of adverse birth outcomes. The aim of this study is to describe temporal trends in disparities in three key birth outcomes across different strata of neighbourhood deprivation to address whether inequalities in birth outcomes are widening or converging over time.
Method: Population based time trend ecological study with small area-level deprivation measure as exposure. Birth outcomes of 2,377,944 singleton births in the Netherlands from 2003-2017. Main outcomes were premature birth, small for gestational age (SGA) and perinatal mortality. Birth outcome rates by deprivation quintile were calculated.
Results: The prevalence of the three birth outcomes decreased over time, with an overall prevalence per 1000 births of 5.4 perinatal mortality, 58.9 premature birth, and 114.2 SGA. Inequalities in birth outcomes have steadily decreased in absolute terms but relative inequalities remained persistent. The absolute decline was largest for all the birth outcomes in the most deprived quintile. For example, premature birth rates decreased by 6.13 per 1000 births in the least deprived quintile and by 10.52 per 1000 births in the most deprived quintile. In relative terms, premature birth rate ratios comparing the most deprived quintile with the least deprived quintile hardly changed: from 1.22 (95% CI 1.21 to 1.24) in 2003 to 1.16 (95% CI 1.15 to 1.18) in 2017.
Conclusions: In absolute terms, inequalities in birth outcomes by neighbourhood deprivation in the Netherlands decreased but in relative terms, they were persistent over the study period.

Fat mass at 6 years is associated with CpG Methylation in cord blood at birth of children of the Southampton Women's Survey

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Background/Aims: Epigenetic processes are thought to be partly responsible for an increased risk of adiposity in the infant and older child. We aimed to identify CpGs in umbilical cord blood which associate with child's fat mass at 6 years.
Method: Cord blood was collected shortly after birth in children of the Southampton Women's Survey (SWS). At 6 years the fat mass of SWS children was measured using Dual-energy X-ray absorptiometry (DXA). We investigated a subset of the SWS cohort with available cord blood at birth and DXA measurements at 6 years (n=415). DNA Methylation in cord blood was measured using the Infinium Human Methylation EPIC Bead Chip array. BMIQ was used for normalisation and COMBAT was used to adjust for chip effects. Models were adjusted for child's sex, age at scan, batch effects and 7 estimated cord blood cell components.
Results: After QC, 740682 CpGs were available for analysis. Six CpGs were significantly associated with total fat mass at 6 years (Benjamini-Hochberg p<0.1) These CpGs were located within Protein Tyrosine Phosphatase, Non-Receptor Type 14 (PTPN14), La Ribonucleoprotein Domain Family Member 1B (LARP1B), Latrophilin-3 (LPHN3), TBK1 Binding Protein 1 (TBKBP1) and Islet Cell Autoantigen 1 (ICA1) genes and the C19orf53 region. The CpG in the PTPN14 gene remained significantly associated with total fat mass at 6 yrs (Benjamini-Hochberg p<0.1) when the model was further adjusted for maternal smoking.
Conclusions: These results suggest that DNA methylation signatures in cord blood could be used as a predictive biomarker for fat mass in later childhood. Some of the CpGs associated with fat mass are biologically plausible (PTPN14, ICA1) but these results need to be validated in a larger cohort.
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Collider bias is unlikely to influence interpretation of results when estimating intrauterine effects using mother-child pairs

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Background/Aims: Mendelian randomization (MR) may be used to estimate effects of maternal intrauterine exposures (e.g. smoking quantity) on offspring outcomes (e.g. birth weight or latr-life disease outcomes). The optimal setting is in a well-powered study of parent-offspring trios. However, genotypes are often only available in mother-child pairs, with no paternal data available. To disentangle indirect maternal effects on an offspring outcome (those acting via an intrauterine exposure) from direct offspring genetic effects on the same outcome, maternal genotype must be conditioned on offspring genotype to adjust for the maternal-offspring genotype correlation. However, offspring genotype is a collider; conditioning on it induces a correlation between maternal and paternal genotype, inducing bias in the results. If paternal genotype influences offspring outcome, MR estimates of maternal effect will be biased.
Method: We investigated the magnitude of the effect of this bias on results for differing maternal, paternal and offspring effect sizes. We simulated genotypes in 50,000 parent-offspring trios and a normally distributed offspring phenotype with differing maternal, paternal and offspring genetic effects. We then looked at the associations between maternal genotype and offspring phenotype when conditioning on offspring genotype.
Results: As expected the maternal genotype-phenotype association was partially correlated with the paternal genotype-phenotype association. The size of this correlation was relatively small compared with the true maternal genotype-phenotype association for realistic scenarios (eg. paternal smoking). The size of the bias is ~20% of the maternal effect when paternal effect is half that of the maternal effect.
Conclusions: While collider bias is present when conditioning maternal genotype on offspring genotype, the size of the bias in most cases is small and should not lead to significant differences in interpretation of results when compared with trio analyses in well-powered samples.

Policy environment around the first 1000DaysPlus of life in Ghana: analyses of policy documents and stakeholder panels.

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Background/Aim: Like most sub-Saharan African (SSA) countries, Ghana has high rates of stunting, micronutrient deficiency and underweight, with recent evidence pointing to an increase in overweight and obesity. The "Improved Nutrition Preconception, during and after Pregnancy" (INPreP3)

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research group was formed to address this double burden of malnutrition in 3 SSA countries including Ghana. One of the project objectives is to review existing nutrition policies and engage with stakeholders in health to establish barriers and the opportunities to instituting a clear 1000DaysPlus double duty healthy nutrition policy.

Method: We conducted a targeted search of in-country government documents and websites for policies relating to Maternal and Child Health/Nutrition and with emphasis on the "first 100DaysPlus" of life. In addition, we held multi-sectoral stakeholder engagements consisting of interviews and panel discussions. Policy reviews included chronology, implementing agency, details and implementation.

Preliminary results: 15 documents have been reviewed to date and 8 interviews conducted with nutrition officers, public health nurses and multinational organisations. Stakeholder engagement workshops/panels will be conducted. Policies reviewed so far focussed on adolescent girls, iron/folate supplementation, formation of mother-to-mother support groups, growth monitoring and promotion, nutrition counselling and education, media campaigns, food demonstration, empowerment of women, promotion of exclusive breastfeeding and optimal infant and young child feeding strategies. A major barrier is lack of coordination in implementation of these programmes in Ghana.

Conclusions: The review so far revealed important gaps in the policy environment for improving nutrition in the first 1000 days of life. It has also revealed lack of coordination, monitoring and evaluation of the implemented programmes. This underscores the importance of the yet to be held stakeholder panels which will serve as a conduit for continual engagement with Ghana Health Service and other sectors to prioritise nutrition in the before/during the first 1000 days of life.

Footnote

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Birth size and its relation to brain size and brain functional connectivity in young adults of the Pune maternal nutrition study (PMNS)

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Background/Aims: Early life exposures during critical periods of development can affect neurodevelopment. However, the long-term impact of these exposures on brain structure in adulthood is not well understood. While brain volumes provide information on structural growth; examining brain functional connectivity could provide insights into the specific brain processes affected by early developmental influences.

Method: As part of ongoing assessments in the PMNS, we obtained Structural MPRAGE T1 sequences and brain resting state functional connectivity time series using EPI sequence (TR=2secs) on a 3T MRI Scanner (in 50 subjects whose maternal B12 levels were in lowest quartile and 34 subjects whose maternal B12 levels were in the highest quartile). Automated surface reconstruction was performed using the open source Freesurfer software. Averaged Time series and strength of functional connectivity between cortical region of interests (ROI's) was computed using Conn toolbox in SPM12 on Matlab. Hippocampal functional connectivity scores were correlated with birth size.

Results: Total gray matter volumes were similar in both groups (low and high maternal B12) and were combined to examine for associations with birth size. Lower birth weight predicted lower total gray matter volume in young adult offspring ($p=0.03$ after controlling for age, gender, educational status, socio-economic status, adverse childhood experiences, maternal B12 level during 18 weeks of pregnancy, total intracranial volume). The associations were specifically observed for gray matter volumes in the prefrontal cortex. Lower birth weight was associated with lower strength of hippocampal functional connectivity (FDR corrected $p<0.0001$). These brain areas are known to be associated with important cognitive functions such as executive functions and verbal memory.

Conclusions: This is one of the first studies to report that birth size predicts brain size (gray matter volume) into early adulthood. Disturbed hippocampal frontal functional connectivity may underlie the mechanistic effects of early fetal life exposures on neurodevelopment.

Postnatal inflammation following intrauterine inflammation exacerbates the development of atherosclerosis in ApoE-/- mice

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Background/Aims: Atherosclerosis is a chronic inflammatory disease that has its origins in early life. Postnatal inflammation exacerbates atherosclerosis, but the possible effect of intrauterine inflammation is largely unexplored. Exposure to inflammation in utero is common, especially in infants born preterm, who have increased cardiovascular risk in adulthood. We hypothesized that exposure to inflammation before birth would accelerate the development of atherosclerosis, with the most severe atherosclerosis following exposure to both pre- and postnatal inflammation. The aim of this study was to investigate the effect of prenatal and postnatal inflammation on the development of atherosclerosis in a murine model.
Methods and Results: We established a mouse model of chorioamnionitis using ApoE-/- knockout mice. A single intra-amniotic injection of LPS caused intrauterine inflammation (i.e. histological chorioamnionitis), and increased atherosclerosis at 20 weeks postnatal age. In mice exposed to postnatal LPS, chorioamnionitis modulated subsequent responses; those exposed to both intrauterine and postnatal inflammation had the greatest size, number and severity of atherosclerotic lesions, with a concomitant decrease in collagen content and increased inflammation of the atherosclerotic plaque, compared to other groups.
Conclusions: Pre- and postnatal inflammation have additive and deleterious effects on the development of atherosclerosis in ApoE-/- mice. The findings are particularly relevant to human preterm infants, whose pregnancies are frequently complicated by chorioamnionitis and are particularly susceptible to repeated postnatal infections. Human and mechanistic studies are warranted to guide preventative strategies.

Associations of parental height, weight and BMI with offspring birthweight, early growth and adult cardiometabolic risk

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Background: Parental adiposity is associated with offspring adiposity. However, it is unclear whether it is also associated with offspring cardiometabolic risk in adult life, independent of offspring body size, and it is unclear whether any maternal and paternal effects are similar.
Methods: We studied pre-pregnancy height and weight data of 908 couples and their offspring (495 males, 413 females) data which included height and weight at birth, 3 months, and 6.5, 15, 28 and 42 years. We used conditional measures to represent offspring birth size and growth in the intervals between measurements. We used linear regression to estimate the associations between parental size and offspring size and growth, and logistic regression for associations of parental and offspring anthropometry with measures of offspring adult cardiometabolic risk (hypertension, diabetes and hypertriglyceridaemia). We adjusted for age, gender, socioeconomic status, urban/rural residence, physical activity and family history.
Results: Parental height was significantly associated with offspring height growth from birth to 28 years (except 0-3 months). Parental weight was significantly associated with offsprings birth weight, however, the effects were more strongly associated with mothers weight when mutually adjusted. Offspring conditional weight gain from 6.5 to 15 years was significantly associated only with paternal weight. Mid-parental size significantly impacted offspring birth size. No significant association between parental size and offsprings adult cardiometabolic risk was observed with and without adjustment for offspring size.
Conclusions: Parental size has positive effects on offsprings stature from birth through adulthood. Both parents contribute to their offsprings birth weight, although maternal effects predominate reinforcing predominant intra-uterine influences at birth. Paternal weight is independently associated with subsequent weight gain from childhood to adulthood suggesting inter-generational transfer of adiposity risk. The absence of associations between parental size and their offspring's cardiometabolic risk could be explained by other non-genetic mediators of adult disease risk.

Physical activity and preclinical vascular phenotypes in preschool aged children

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Background/Aims: In adults and school-aged children, physical activity is inversely associated with cardiovascular disease risk, but this relationship is less clear in children aged ≤5 years. We aimed to determine the association between objectively-assessed physical activity and preclinical vascular phenotypes in preschool-aged children.
Method: Cross-sectional assessment of a subgroup of 473 children (age 4.0±0.4y) participating in the Barwon Infant Study, an Australian birth cohort (n=1074 infants). *Exposure measures*: mean (mins/day) Actigraph accelerometer-derived overall duration and duration accumulated in bouts ≥1 minute of light-intensity (LPA), moderate- to vigorous-intensity activity (MVPA). *Outcome measures*: brachial blood pressure measured during rest in supine position (systolic, diastolic, pulse pressure), pulse wave velocity (PWV), aorta intima-media thickness (aIMT), carotid intima-media thickness (cIMT). Linear regression analyses adjusted for accelerometer wear time and

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maternal education, and stratified by sex, assessed the association between physical activity and vascular parameters. Analyses of aIMT and cIMT were adjusted for vessel size.
Results: In boys, MVPA accumulated in bouts ≥1 minute were associated with larger aIMT (B:30.7μm 95%CI:3.3, 58.2). In girls, mean overall duration (B:-21.8μm 95%CI:-40.2,-3.3) and duration of bouts ≥1 minute of LPA (B:-24.9μm 95% CI:-47.1,-2.7) were associated with smaller aIMT and overall duration and duration in bouts ≥1 minute of MVPA were associated with higher systolic blood pressure centile (B:6.4 95% CI:1.2 to 11.6 and B:10.7 95%CI:2.0 to 19.3, respectively) and pulse pressure (B:2.9 95%CI:0.1 to 5.8 and B:5.7 95%CI:1.0 to 10.4 respectively).
Conclusions: Contrary to our hypotheses, moderate to vigorous physical activity was associated with increased aIMT in boys and increased blood pressure in girls. Further studies are required to determine the longitudinal and clinical significance of these findings.

Where do Canadian women get their iron during pregnancy: Results from a prospective birth cohort study

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Background/Aims: Iron intake during pregnancy is essential to support the optimal development of the fetus. In Canada women are recommended to consume 27mg of iron a day, of which 16-20mg is recommended to come from a supplement. However there are no data on iron intakes during pregnancy in Canada and it is not known whether women are meeting these recommendations or where their sources of iron are coming from. Therefore we aimed to describe intakes of iron from both haem and non-haem dietary sources, as well as the amount contributed from supplement intakes.
Method: Women were enrolled in the Alberta Pregnancy Outcomes and Nutrition (APrON) study. In both the 2nd and 3rd trimesters a total of 1795 women completed a 24hr food recall, using the multipass method, and a Supplement Intake Questionnaire (SIQ) which assessed the name, brand, dose and frequency of all supplements taken. Dietary intake data were entered into Food Processor for nutrient calculations and iron data was linked back to food descriptions to delineate haem versus non-haem iron intakes. Data from the SIQ were linked to manufacturers information on nutrient content.
Results: In total 95% of the cohort reported taking an iron containing supplement in their 2nd and 3rd trimester. Total iron intake from food plus supplement was 41.1mg/day (SD15.3) and 44.7mg/day (SD17.8) in the 2nd and 3rd trimesters, respectively. Total iron intake from food was 15.3mg/day (SD 5.9) in the 2nd trimester and 15.5mg/day (SD 6.0) in the 3rd trimester. Of this 2.5mg/day (SD 2.6) and 2.0mg/day (SD2.1) were from haem iron sources in the 2nd and 3rd trimester respectively. A total of 78 (4%) women reported zero iron from haem sources in both trimesters, suggesting a low adherence to a vegetarian diet in this cohort.
Conclusions: Nearly all women were taking an iron containing supplement per day which provided ~26mg/day of iron, which is above the national recommendation. Furthermore women were consuming ~15mg iron/day from food sources taking their total daily iron intake to ~17mg/day over the recommendations. The implications of this on women's iron status biomarkers will be evaluated.

Dietary monounsaturated fat intake may be protective for sleep during pregnancy

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Background/Aims: Short and poor quality sleep are associated with an increase in unhealthful eating behaviours. This is marked by a decrease in dietary restraint and an increased preference for foods high in fat and refined carbohydrates. Poor quality carbohydrate and high fat intake in pregnancy has been associated with high gestational weight gain, reduced insulin sensitivity and higher foetal adiposity. Further, sleep disturbances are common in pregnancy. However, it is unknown whether there is a relationship between sleeping behaviour and dietary intake in pregnancy. This study aimed to investigate the relationships between sleeping behaviour and macronutrient intake of pregnant women.
Method: Data are from pregnant women in the Australian Longitudinal Study on Women's Health, aged 31-36 in 2009 (n=437). Latent class analysis (LCA) was used to derive sleeping behaviour patterns from self-reported sleep data. Diet was assessed using a validated 74-item food frequency questionnaire. Relationships between sleep and diet were investigated through multivariate linear models adjusted for area of residence, BMI, depression, difficulty managing on income, education level and parity.
Results: LCA identified three sleeping behaviour patterns: (LC1) average sleep (~7.8 hours) with no adverse sleep-related symptoms (n=167); (LC2) average sleep (~8.3 hours) with severe tiredness and sleep difficulties (n=193); and (LC3) short sleep (~6.6 hours) with severe tiredness and sleep difficulties (n=97). In adjusted models, LC2 was associated with a lower percentage energy (%E) from total fat (b= -0.032, p=0.039) and %E from monounsaturated fat (b= -0.050, p=0.005), but a higher %E from carbohydrate (b= 0.031, p=0.020), compared to LC1. No differences were found between LC1 and LC3.
Conclusions: Higher monounsaturated fat intake is associated with improved sleep quality during pregnancy, which may help improve health and wellbeing of mother and child. Further

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research is needed to understand the directional nature of this relationship.

Sleeping behaviour during pregnancy increases the risk of adverse birth and postpartum outcomes

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Background/Aims: Sleep disturbance is common during pregnancy and can influence the health of both mother and offspring. The aim of this study was to investigate the impact of maternal sleeping behaviour during pregnancy on antenatal, birth and postnatal outcomes including: gestational diabetes, gestational hypertension, delivery mode, birth complications, anaesthesia use, NICU/SCN admission, infant birth weight, breastfeeding, antenatal mental health and postnatal mental health, in an Australian sample.
Method: Data are from pregnant women in the Australian Longitudinal Study on Women's Health cohort, aged 31-36 in 2009 with birth outcomes reported in 2012 (n=473). Sleep, pregnancy, birth and postpartum outcomes were self-reported. Latent class analysis (LCA) derived sleeping behaviour patterns. Relationships between sleep and pregnancy, birth and postpartum outcomes were investigated through multivariate linear regression adjusted for BMI, self-rated health, difficulty managing on income, depression, trimester and area of residence.
Results: Three sleeping behaviour patterns were identified: (LC1) average sleep length (~7.8 hours) with good sleep quality (n=181); (LC2) average sleep length (~8.3 hours) with daytime tiredness, difficulty falling asleep and restless sleep (n=183); and (LC3) short sleep length (~6.6 hours) with daytime tiredness, difficulty falling asleep and restless sleep (n=109). In models adjusted for confounders, LC2 was associated with a greater likelihood of emotional distress during delivery (OR: 4.402, p<0.001), need for an emergency C-section (OR: 2.680, p=0.022), NICU admission (OR: 2.143, p=0.039), epidural use (OR: 1.859, p=0.014) and postnatal anxiety (OR: 3.915, p=0.010), compared to LC1. No relationships were found between LC3 and LC1.
Conclusions: Poorer sleep quality during pregnancy is associated with an increased risk of adverse birth and post-partum outcomes. Sleeping patterns may be modifiable and are an important consideration for screening tools and intervention studies that aim to improve the health of future generations.

The Research Advancement through Cohort Cataloguing and Harmonization initiative: A resource to leverage data usage and co-analysis

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Background/Aims: The Research Advancement through Cohort Cataloguing and Harmonization (ReACH) initiative aims to provide Canadian and international research communities with the resource to leverage and carry out leading-edge collaborative research through the optimization and use of Canadian cohorts data and biological samples. The ReACH initiative has implemented a centralized web-based catalogue documenting pregnancy and birth cohorts, complemented by tools facilitating the harmonization and integration of data across cohorts.
Method: The web-based catalogue describing the 26 pregnancy/birth cohorts which are part of the ReACH initiative was created using the software and methods developed by Maelstrom Research. In collaboration with each of the cohort investigators and data managers, information was gathered to provide study-level description of the cohorts as well as in depth description of all the variables collected at each wave of data collection. All of the variables were classified under domains of information, to facilitate identification of variables of interest and evaluation of the harmonization potential across studies.
Results: Together, the cohorts have recruited 35,070 mothers, 39,835 children, and 7,239 fathers, totaling 82,144 participants across Canada. The follow-up of participants varies in duration from 16 months to 20 years, with 19 of the cohorts still ongoing. All 26 cohorts collected information from questionnaires, 23 also collected biosamples and 21 performed physical measurements. All cohorts collected information about age, sex, anthropometric measures, and pregnancy and delivery outcomes. The majority of cohorts ($\geq$ 85%) also collected information about tobacco use, nutrition, breastfeeding, diseases of the circulatory or respiratory systems, hospitalizations, medication intake, education, income and ethnicity.
Conclusions: The ReACH web-based catalogue is increasingly used to identify studies and variables of interest to support secondary analysis of existing data. Two pilot projects studying maternal alcohol intake during pregnancy are underway, and we hope more initiatives will make use of the platform.

The Healthy Life Trajectories Initiative: A prospective harmonization of four mother and child cohorts

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Background/Aims: The Healthy Life Trajectories Initiative (HeLTI) is a collaboration between Canada, China, India,

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South Africa and WHO to develop international intervention cohorts that will implement and test approaches to prevent overweight and obesity in children – an escalating problem globally – and to improve health of pregnant women. The objective is to examine the cumulative effects of approaches starting preconception and continuing through pregnancy into childhood. To facilitate data sharing and co-analysis across the four countries, one of the objectives of HeLTI is to prospectively harmonize the information that will be collected.
Method: A harmonization working group including representatives from each cohort was set up to create the core list of variables to be collected across countries. Selection of the variables is made by consensus, over regular meetings of the working group. Once the list of core variables is defined, questionnaires allowing collection of the variables are created and, when possible, standard questionnaires or devices are adopted. The harmonization process achieved is guided by the approach developed by the ReACH (Research Advancement through Cohort Cataloguing and Harmonization) initiative.
Results: Core variables are defined for ten time points (one preconception, two during pregnancy, one at delivery and six from birth to 5 years old). Currently, the work is completed for the first three time points. The exposures and outcomes of interest selected span eleven domains of information (e.g., socio-demographic characteristics, diseases, physical measures) for a total of 578 core variables. The majority of variables created relate to the lifestyle and behaviours (n=292) and psychological measures and assessment (n=134) domains.
Conclusions: Prospectively harmonizing four mother and child cohorts with different ethnic and cultural specificities will enable comparative analysis of interventions, assessment of biological mechanisms and biological-environmental interactions. Such information should facilitate global policy development to benefit maternal and child health with a goal to reduce the burden of non-communicable diseases.

Prevalence and factors associated with alcohol use by women before, during and after pregnancy using the Canadian ReACH pregnancy cohort catalogue

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Background/Aims: Fetal Alcohol Spectrum Disorder (FASD) is a leading cause of neurodevelopmental disabilities worldwide and therefore a major public health concern. Despite intensive efforts in preventing prenatal alcohol exposure, one in ten Canadian women still consumes alcohol during pregnancy. In this study, we aim to explore the factors and characteristics of women in Canada who consume alcohol during pregnancy and to determine the profile of alcohol use before, during and after pregnancy. To achieve these aims with sufficient statistical power and data items, it is useful to combine and co-analyse data collected across multiple mother and child cohorts.
Method: Pregnancy cohorts were included in this study if they collected information on alcohol intake before, during and after pregnancy, as well as on birth weight and gestational age at delivery, and had information on at least 500 mothers. Of the 26 pregnancy cohorts with detailed information on pregnancy and infant variables in the ReACH (Research Advancement through Cohort Cataloguing and Harmonization) catalogue, five were eligible to participate in this harmonization project. Harmonization of data collected across studies is currently ongoing based on the Maelstrom guidelines for retrospective data harmonization.
Results: A total of 10,263 mothers will be included in the analysis. Information about heavy/binge drinking, frequency and quantity of alcohol consumed at multiple time points including before, during and after pregnancy is being harmonized. Potential predictors of alcohol consumption during pregnancy include consumption prior to pregnancy, maternal age, education, household income, occupation, ethnicity, smoking and parity.
Conclusions: This will be the largest study of the correlates of alcohol use before, during and after pregnancy in Canadian women with detailed information regarding the factors associated with alcohol use. The ReACH catalogue and Maelstrom harmonization process provide a unique opportunity to leverage the Canadian pregnancy cohort information regarding women's drinking during pregnancy. The results will be useful to further inform prevention strategies.

Maternal hypoxia results in low podocyte endowment in male but not female offspring

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Background/Aims: Intrauterine hypoxia is a common complication of pregnancy. Podocytes are critical components of the glomerular filtration barrier and have limited, if any, capacity for replacement after birth. Decreased podocyte number and density are associated with development of glomerulosclerosis and decreased renal function. We previously reported that maternal hypoxia is associated with decreased nephron endowment in male but not female offspring (Walton et al. Sci Reports 7:8241, 2017). Here we examined whether maternal hypoxia also resulted in low podocyte endowment in males.
Methods: From embryonic day 14.5 until birth, pregnant CD1 mice were housed in hypoxic (12% O_2) or normoxic (21% O_2)

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conditions. At postnatal day 21 (PN21) kidneys from one male and female offspring per litter (n=10-11 litters/group) were weighed and collected for measurement of podocyte number per glomerulus, glomerular volume and podocyte density.
Results: Birth weight was lower in hypoxic offspring, although bodyweight and kidney weight at PN21 were similar in normoxic and hypoxic offspring. Hypoxic male offspring had 15% fewer podocytes per glomerulus than normoxic males (normoxic male: 62.86 ± 2.26 vs hypoxic male: 53.38 ± 2.25, mean ± S.E.M., p=0.01), but no such difference was observed in female offspring. Glomerular volume and podocyte density were similar to normoxic offspring in both males and females.
Conclusion: Podocyte endowment was altered by maternal hypoxia in male but not female offspring. These results are consistent with the effect of maternal hypoxia on nephron endowment in male offspring. Histopathology observed in 12 month-old hypoxic males may be associated with the podocyte deficits observed at PN21. In conclusion, maternal hypoxia can programme podocyte endowment in a sex-specific manner, which may increase the risk of renal pathophysiology in adulthood.

Podocyte Number and the development of renal pathophysiology in a mouse model of low birth weight

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Background: Chronic kidney disease (CKD) is a major health burden, the development and progression of which is largely dependent on glomerular function. Podocytes are key components of the glomerulus and podocyte injury/loss plays a pivotal role in the development of CKD. While several feto-maternal factors have been identified in the programming of low nephron number i.e. low birthweight (LBW), their effect on podocyte number/glomerulus has not yet been explored in mice. We hypothesised that LBW offspring are born with low podocyte endowment, which will reduce their adaptive capacity when faced with a second renal insult.
Methods: C57Bl6 female mice were fed a maternal low (LPD; 8%) or normal (NPD; 20%) protein diet prior to pregnancy and until weaning (PN21), when the kidneys of one male and one female per litter were collected for analysis of nephron number, podocyte endowment, glomerular volume and podocyte density. A 'second-hit' was induced in remaining littermates using the administration of streptozotocin to induce a diabetic state.
Results: At PN21, LPD offspring had significantly lower body and kidney weights, and 30% fewer nephrons. Glomeruli in male LPD offspring were 23% smaller and had 15% fewer podocytes than male NPD offspring, a finding not observed in females. Surprisingly, at 24 weeks of age there was no difference in glomerular volume or podocyte number between LPD and NPD offspring in males or females. Following the induction of diabetes, albumin excretion was greater in LPD diabetic males than NPD diabetic males. There was no difference in albumin excretion between LPD and NPD diabetic females.
Conclusions: These findings suggest that a suboptimal fetal and neonatal environment alters the timing of podocyte differentiation in male but not female offspring. Exposure to a second hit of hyperglycaemia highlights the susceptibility of male low birth weight offspring to renal pathophysiology. Studies assessing renal pathology are ongoing.

Low birth weight, low nephron and podocyte endowment and catch-up growth contribute to adult risk of renal pathophysiology

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Background: Low birth weight is a risk factor for adult kidney disease, and is associated with reduced nephron endowment. Podocyte loss and reduced podocyte density are key early events in the pathogenesis of many forms of CKD. Whether LBW offspring have low podocyte endowment that increases their risk of renal pathophysiology is not known.
Method: Female rats were fed a normal (NPD, 20%) or low (LPD, 8%) protein diet from 3 weeks before mating until postnatal day 21 (P21) when kidneys of one male offspring per litter were taken for nephron and podocyte morphometric analysis. Remaining male littermates were fed either a normal fat (6% fat w/w) or high fat diet (HFD; 21% fat w/w) until 6 months of age.
Results: At PN21, podocyte number per glomerulus was significantly lower in LPD than NPD offspring, with the deficit greater in outer than inner cortical glomeruli. Surprisingly, podocyte number increased in outer cortical glomeruli between PN21 and 6 months of age in LPD, but remained 9% lower than in NPD offspring suggesting a permanent podocyte deficit. LPD offspring showed significant catch-up growth and had mild

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focal and segmental glomerulosclerosis (FSGS) at 6 months of age. High fat feeding induced podocyte loss and FSGS in NPD offspring and exacerbated the glomerulosclerosis observed in LPD offspring. FSGS was strongly associated with glomerular number per gram of bodyweight.
Conclusion: Our findings suggest that although a podocyte deficit is a likely contributor to the increased susceptibility to renal pathophysiology, a reduced nephron number in association with catch-up growth and postnatal weight gain also play key roles in the development of FSGS.

Environmental exposure to the widespread androgenic endocrine disruptor 17β-trenbolone alters male reproductive behaviour in fish

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Background/Aims: A leading source of endocrine-disrupting pollution in the environment is run-off of pharmaceuticals used in agriculture, including hormonal growth promotants (HGPs). Despite being banned in various regions (e.g. the EU), HGP use is still common in beef production around the world. However, relatively little is known about the potential for these contaminants to alter animal mating behaviour. This is concerning given the vulnerability of behaviour to disruption by contaminant exposure, and the dire ecological and evolutionary implications of disrupted reproductive processes in wildlife.
Method: A flow-through system was used to expose wild-caught adult male guppies (*Poecilia reticulata*) to a low environmentally realistic level (average measured concentration = 2 ng/L) of the growth-promoting androgenic steroid 17β-trenbolone (17β-TB)—a leading HGP that commonly enters surface waters via livestock effluent run-off—or a freshwater control. Subsequent to a 21-day exposure period, we compared the response of exposed and unexposed males to sequentially presented large and small stimulus (unexposed) guppy females in reproductive behaviour trials, in terms of male reproductive behaviour and sequential mating effort. Due to a positive size-fecundity relationship, larger females are generally expected to be preferred by males.
Results: While we found no evidence that the size of a previously encountered female affected the amount of courtship or coercive 'sneak' mating behaviour performed by guppy males during the second presentation, males from both exposure treatments conducted more frequent courting events towards larger females during both presentations, suggesting an absolute preference for greater female size. Further, across both presentations, 17β-TB exposure caused a shift in male mating strategy towards increased coercive copulatory behaviour, although male sequential mating effort was not impacted.
Conclusions: In combination, our findings demonstrate that exposure to a field-realistic level of a widespread androgenic agricultural pollutant alters male reproductive strategy in fish, and contribute to a growing understanding of sub-lethal impacts of pollution on complex behaviours in wildlife.

Promoting a healthy dietary intake in pregnant women with a low socioeconomic status in the Netherlands

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Background/Aims: Pregnant women do not adhere well to dietary guidelines, especially women with a low socioeconomic status (SES). Midwives might be able to improve pregnant women's dietary intake. They play a central role in maternity care and are a trusted information source, but an effective strategy for promoting a healthy dietary intake in pregnant women is lacking. To develop such a strategy, we aimed to gain insight into (1) factors influencing low SES pregnant women's dietary intake and (2) Dutch midwives' current and desired role in nutrition communication and resources they need to improve pregnant women's dietary intake.
Method: For each aim a systematic literature review was performed, followed by semi-structured interviews with 14 low SES pregnant women and 20 midwives in the Netherlands
Results: According to literature, motivation (especially the child's health), physical factors (e.g. nausea) and psychological state, as well as social and built environment, (cultural) food norms, responsibilities, self-perception of diet quality, and self-efficacy influence dietary intake of pregnant women. In the interviews, most low SES pregnant women expressed no strong motivation to eat healthier or seek nutrition-related information, while all women avoided unsafe foods and some mentioned increasing their fruit and vegetable intake during pregnancy.
As found in both literature and interviews, midwives' feel responsible for providing nutrition communication but do not consider themselves experts. Dutch midwives also pointed upon the roles of other professionals (e.g. dietitians), of society and of pregnant women themselves in improving dietary intake during pregnancy. They recognize a need for more extensive, tailored nutrition communication and suggested resources such as knowledge, time or funding for innovative organisation of maternity care (e.g. group consultations), and efficient (visual) tools to support them.
Conclusions: A range of individual and collective factors should be considered when promoting a health dietary intake

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in low SES pregnant women. Midwives could take up a more active role in providing nutrition advice (together with dietitians) if supported by additional training, time and tools.

PM2.5 reduces the pluripotency of embryonic stem cells through the PI3K/AKT signaling pathway

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Background: The fine particulate matter (PM) the environment toxicant doesn't only causes respiratory diseases in adult and children, but that exposure during pregnancy can lead to impaired embryonic development leading to poor birth outcomes and even long-term disease. Embryonic stem cell is a good in vitro cell model for studying embryonic development. Recently, several lines of investigation have revealed that PM2.5 can have an impact on embryonic development, but the exact molecular mechanism remains to be elucidated.
Method: Embryonic stem cells were treated with various concentrations of PM2.5 (5, 50, 100μg/mL) for 72h. The expression of pluripotency-related Oct4 and NANOG mRNA was quantified by qPCR. The protein expression of NANOG and OCT4 were detected by fluorescent microscopy, western blot, and flow cytometry. The role of PI3K/AKT pathway in the treatment groups was assessed by western blotting.
Results: PM2.5 reduced the ability of clonal proliferation by microscopic observation. The numbers of treated cells increased 24 h compared with the untreated group, but the cells decreased after 24 hours. The expression of NANOG and OCT4 was significantly reduced in the 50 and 100μg/mL treatment groups. The expression of ERK1/2, AKT didn't change in PM2.5 treatment groups, however, p-ERK1/2 was upregulated and p-AKT was downregulated in PM2.5 treatment groups through western blotting.
Conclusions: These findings suggested that PM2.5 treatment reduced the pluripotency of embryonic stem cells which may affect long-term development of the embryo via inhibiting of the PI3K/AKT pathway in vitro.

A maternal high fat diet is associated with microRNA expression changes in the prostate of male rat offspring

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Background/Aims: Evidence from human epidemiological studies support that an excess nutritional supply *in utero*, as indicated by a high birth weight, is associated with an increased risk and mortality of prostate cancer. A maternal high fat diet (HFD) has recently been shown to promote prostate cancer in transgenic male mouse offspring. Using a rat model, we set out to investigate if a maternal HFD alters microRNA expression in the prostate of male offspring.
Method: Female rats were fed a control (7% total fat) or HFD (23% total fat) before mating and during pregnancy. All females received a control diet after giving birth. Control male offspring (n=15) were exposed to a control diet throughout life. Maternal HFD male offspring (n=21) were exposed to a HFD *in utero* only. All offspring were sacrificed at day 100.
Results: A microRNA microarray analysis was performed on the prostates from 8 control and 8 maternal HFD offspring. Increases in rno-miR-142-3p, rno-miR-142-5p and rno-miR-34b were detected in the prostates of offspring exposed to a maternal HFD compared to controls. These microRNAs have been shown to act as tumour suppressors.
Conclusions: Ongoing studies will combine these microRNA analyses with gene expression and DNA methylation analyses to try and delineate how a maternal HFD may program future cancer risk in offspring.

Differences in Hemodynamic Response to a Cardiopulmonary Exercise Test in Pregnant and Non-pregnant Women

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Background/Aims: The maternal cardiovascular system starts to adapt already in the first weeks of pregnancy. A cardiopulmonary exercise test (CPET) is used to functionally assess the integrative exercise response of the cardiovascular, respiratory and the peripheral muscular systems. Since pregnancy alters the

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cardiovascular physiology of women, we hypothesize that the hemodynamic response during CPET is different during pregnancy.
Method: In a prospective pilot study, 17 women in their first trimester of pregnancy and 17 non-pregnant women performed a CPET until 70% of their calculated maximum heart rate on a cycle ergometer. Hemodynamic parameters were monitored with bio-impedance cardiography using Physioflow®. Using linear regression analysis, relative changes (%) in heart rate (HR), stroke volume (SV) and their product cardiac output (CO) were compared between the two groups.
Results: The pregnant women were older (34 vs. 26 years; p<0.001) and had higher body mass index (25.9 vs. 21.5 kg/m^2, p=0.022) compared to the non-pregnant women. During the CPET, there were no differences in increases of CO (β= -10.3% [-40.7 ; 20.2]; p=0.496), HR (β= -12.1% [-28.6 ; 4.5]; p=0.146) and SV (β= 3.3% [-11.1 ; 17.7]; p=0.643) between the two groups after adjustment for age. After 1 minute of rest after cycling, the decrease in CO (β= 12.4% [-0.2 ; 25.0]; p=0.053), HR (β= 12.2% [2.9 ; 21.5]; p=0.012) and SV (β= 2.0% [-8.6 ; 12.6]; p=0.705) was lower in pregnant women compared to non-pregnant women after adjustment for age.
Conclusions: The results of this pilot study suggest that the hemodynamic response during CPET in pregnant women is comparable to the response outside pregnancy. However, in pregnant women the time to recover from the same amount of exercise is significantly longer, specifically for HR. We recommend further research using CPET from the preconception period onwards, preferably in the same women, to evaluate its use in cardiovascular risk-assessment in relation to pregnancy course and outcome.

Transgenerational Effects of Grandpaternal Obesity along with Micronutrient Intervention on Metabolic Health of Female Offspring

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Background/Aims: Our previous work in rodents showed high fat diet (HFD) induced paternal obesity, reduced female offspring glucose tolerance. It has been reported that paternal obesity can initiate metabolic disturbance in subsequent generations. Here, we investigated transgenerational effects of paternal obesity on metabolic health of female F2 offspring. We designed a novel micronutrient supplement to ameliorate any transgenerational effects.
Method: Founder (F0) male Sprague Dawley rats (12 per group, 48 total) were weaned (Day21) onto control (CD) or HFD, or micronutrient supplemented versions of these (CDS; HFDS). At 19 weeks of age (woa), they were mated with CD females. 48 F1 offspring (one from each F0 pairing) were weaned onto CD, generating four F1 groups. They were mated with CD fed females at 17woa. Sibling F2 females fed CD or HFD from weaning, underwent Echo MRI and oral Glucose Tolerance Test (oGTT) after 6 and 8 weeks on diet, respectively.
Results: HFD increased adiposity by 15% (versus CD) and glucose intolerance in founders whereas, supplementation normalized adiposity and increased insulin sensitivity. Feeding HFD or HFDS to F0 had no effect on the adiposity and glucose homeostasis of male F1 offspring (Fathers to F2). No effects of F0 HFD or HFDS were observed on body weight or adiposity of F2 female offspring. However, HFD fed F2 sired by HFD-F0 had reduced glucose tolerance at 15mins during GTT. Supplementation of the grandpaternal HFD reduced glucose tolerance in F2 female (on CD or HFD). Post weaning HFD increased adiposity (28-39%) and glucose intolerance regardless of founders' diet.
Conclusions: Our results suggest grandfathers' HFD can influence glucose homeostasis of grandoffspring indicating transgenerational effect, if grandoffspring are themselves challenged by HFD. Dietary micronutrient supplementation reduced adiposity and increased insulin sensitivity in grandfathers but could impair glucose homeostasis in the female grandoffspring.

Breastfeeding duration and relationships with BMI in childhood and adolescence: findings from the Santiago Longitudinal Study

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Background/Aims: The relationship between breastfeeding (BF) duration and adiposity has been inconsistent, with some strong relationships found in high-income countries (e.g., longer BF, lower BMI) and a lack of significant relations in low- and middle-income countries. We explored the relationship of BF duration and type (exclusive or mixed) with BMI at 1, 5, 10 and 16y in a Chilean cohort followed since infancy.
Method: Infants were recruited at 6m between 1994 and 1996 from community health clinics in four low- to middle-socioeconomic neighborhoods in Santiago, Chile (n=805). For infants receiving formula/cow milk supplementation at 6m, mothers retrospectively reported date of first bottle (equivalent to the end of BF). For all other infants, mothers were asked weekly, between 6 and 12m, if they continued to BF and if infants had received bottle supplementation. Participants were weighed and measured at 1, 5, 10, and 16y and BMIz was calculated. We tested two models at each age: 1) whether type of BF at 6m (no, partial, versus exclusive) and 2) duration of exclusive BF (<1m, 1 to <3m, 3 to <6m, and >= 6m) related to BMIz. Models adjusted for child sex, maternal and paternal education, maternal age, gestational age, and birth weight.

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Results: At 6m, 35% of infants were receiving both breastmilk and formula ("partial BF", n=282) and 38% were exclusively breastfed (n=307). Compared to exclusive BF, partial BF at 6m was related to lower BMIz at 1 (B= -0.13, 95% CI -0.28 to 0.01), 5 (B= -0.27, 95% CI -0.50 to -0.04), 10 (B= -0.25, 95% CI -0.48 to -0.02), and 16 y (B= -0.20, 95% CI -0.43 to 0.02). Compared to exclusive BF for 6m or greater, exclusive BF for 3 to 6m was associated with significantly lower BMIz at all time points. No other duration category related to significantly different BMIz at any time point.
Conclusions: Our results are in partial accordance with others that have shown a protective effect of BF for later BMI. However, further study is needed to understand why partial, but not exclusive, BF at 6m might be related to lower BMIz in childhood in adolescence.

Secular trends and predictors of preterm birth in Temuco, Chile, 2009-2015

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Background/Aims: Preterm birth (PTB) is associated with increased risk of infant mortality and morbidity. Our objective was to explore secular trends and determine predictors of PTB in Temuco, a mid-sized city in the south of Chile, which has rates of PTB higher than the national average.
Method: Between 2009-2015, information on all live births from the single regional public hospital to mothers from the Temuco urban area was collected (n=15510). Gestational age was calculated based on ultrasound, and PTB was classified as gestational age <37 weeks. We estimated trends of PTB prevalence by year. Birth year, season of conception, maternal characteristics (age, marital status, gestational weight gain, smoking, preeclampsia, parity, and number of prenatal visits) and socioeconomic status variables (public versus private insurance, maternal education, and work status) were tested as potential predictors of PTB in survival analysis. Term births were considered censored events. Only variables significantly ($p<0.05$) related to PTB were retained in a final adjusted model, adjusted hazard ratios (HR) were calculated.
Results: Over the entire period, 10% (1570) of infants were classified as PTB. PTB increased ($p<0.05$) from 9% (2009-2012) to 11% (2013-2015). In the final adjusted model, PTB related to having private insurance (HR=1.43, 95% CI 1.19-1.73), employment (1.44, 95% CI 1.25-1.66), and preeclampsia (5.05, 95% CI 4.16-6.15). Mothers who had completed secondary school or higher had higher risk of PTB (HR=1.26 95% CI 1.03-1.55 and HR=1.43 95% CI 1.13-1.81, respectively) than mothers with <secondary school. Protective factors included number of prenatal visits (HR=0.70, 95% CI 0.68-0.72) and excessive gestational weight gain (HR=0.71, 95% CI 0.61-0.84). After adjusting for other variables, birth year no longer related to PTB.
Conclusions: The increase in PTB in the study period appeared largely attributed to maternal factors. Unlike other studies conducted in higher-income countries, we found that markers of better SES (greater education and having private insurance) were risk factors for PTB. Additional risk factors reported in other studies (e.g., maternal smoking and age) were not associated with increased risk of PTB after adjusting for other variables. Further study is needed to understand why predictors might be different in this context.

Vitamin B12 deficiency impairs the lipid lowering effect of metformin in the liver

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Abstract
Background: Metformin improves hyperglycaemia in patients and is the first drug of choice for type 2 diabetes (T2D) treatment. Metformin, via activation of AMPKα, can also reduce lipid levels in patients. Prolonged oral metformin therapy limits the bioavailability of vitamin B12 (B12) leading to deficiency in T2D patients. Observational studies in humans also show that low B12 is associated with higher triglycerides (TG) and low HDL. Therefore, we investigated whether B12 deficiency impairs the action of metformin on the lipid lowering effect in the liver.
Methods: Hep G2 cell line was cultured using custom made B12 deficient Eagle's Minimal Essential Medium (EMEM) and seeded in four different concentrations of B12 media such as 500nM (control), 1000pM, 100pM and 25pM (low) B12 until 100% confluence was achieved. The cells were exposed to 24hour treatment with 1mM and 2mM metformin before harvest. Gene expression assays, protein expression and mitochondrial spare respiratory capacity were characterized using real time PCR (qRT-PCR), western blotting and seahorse XF24 assays respectively.
Results: Low B12 in Hep G2 cell line decreased levels of AMPKα and its downstream target pACC, compared to control. Administration of increasing concentrations of metformin to low B12 treated hepatocytes significantly impaired the upregulation of pAMPKα and pACC. In addition, we found that downregulation of nuclear transcriptional factor sterol regulatory element binding protein (SREBF1) and the genes involved in

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hepatic *de novo* fatty acid synthesis pathway, [fatty acid synthase (FASN), acetyl coenzyme A carboxylase (ACC) and elongation-of very-long-chain fatty acid (ELOVL6)] and TG biosynthesis [glycerol-3-phosphate acyltransferase (GPAT) and diacylglycerol acyl transferase 2 (DGAT2)] were significantly impaired in low B12 cells treated with metformin. In the fatty acid oxidation (FAO) pathway, upregulation of the rate limiting enzyme carnitine palmitoyl transferase 1 alpha (CPT1α) and downstream genes carnitine acyl carnitine translocase (CACT) and Long chain Acyl –CoA dehydrogenase (ACADL) were significantly impaired in low B12 hepatocytes. Finally, spare respiratory capacity of mitochondria in low B12 hepatocytes was impaired following palmitate and metformin treatment.

Conclusion: Our study provides novel evidence that Vitamin B12 deficiency (1) lowers levels of pAMPKα and pACC, and (2) metformin administration in low B12 treated hepatocytes failed to restore the levels of pAMPKα and pACC, and the genes involved in lipid metabolism. This supports that the lipid lowering effect of metformin in vitamin B12 deficiency may be compromised. The mechanisms involving regulation via AMPK requires further studies.

Vitamin B12 deficiency induces *de novo* fatty acid synthesis and increases unsafe fatty acid levels in the liver

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Abstract

Background: Vitamin B12 (B12) deficiency is associated with metabolic disorders such as obesity, adipocyte dysfunction, dyslipidaemia, type 2 diabetes mellitus (T2DM), and excessive accumulation of lipids in the liver (non-alcoholic steatohepatitis, NASH). Although the main source of circulating of fatty acids (FAs) is through diet, the human body is capable of synthesizing several of these fatty acids endogenously via *de novo lipogenesis* in the liver. However, dysregulation leading to distortion in FA levels are associated with the development of adverse consequences in foetuses and new-borns. We therefore assessed B12 regulation of *de novo* fatty acid synthesis and the profile of various FAs in hepatocytes.

Methods: Hep G2 cell line was cultured using custom made B12 deficient Eagle's Minimal Essential Medium (EMEM) and seeded in four different concentrations of B12 media such as 500nM (control), 1000pM, 100pM and 25pM (low) B12 until 100% confluence was achieved. Oil Red O (ORO) staining, RNA isolation, cDNA synthesis, gene expression assay using RT-qPCR, radioactive flux assay, commercial TG quantification kit and gas chromatography analysis of total lipids in hepatocytes were employed to examine the effect of B12 deficiency on *de novo* FA synthesis and FA profile in hepatocytes.

Results: Hepatocytes in low B12 (25pM) had more lipid droplets that were intensely stained with ORO compared to few oil droplets and lower ORO staining in control B12 (500nM). We also observed higher total intracellular TG level under low B12, and low B12 hepatocytes further synthesized higher amount of radiolabelled TGs than control when exposed to radiolabelled fatty acid (^{14}C-Oleate). Transcription factor SREBP1 and enzymes of *de novo* fatty acid synthesis such as ATP citrate lyase (ACLY), acetyl CoA carboxylase (ACC), fatty acid synthase (FASN), elongation of very-long-chain-fatty acid (ELOVL6) and stearoyl CoA desaturase (SCD1) were upregulated under low B12. Total FAs was significantly higher in low B12 hepatocytes. Saturated fatty acids (SFA) were predominant compared to other classes of FAs such as monounsaturated fatty acid (MUFA), total polyunsaturated fatty acids (PUFA-total), trans fatty acids (TFAs) which were 1.6-fold, 2.1-fold and 99.7-fold lower than SFAs respectively, in hepatocytes. Low B12 showed higher levels of SFAs, MUFAs and TFAs but had no significant effect on PUFA-total compared to control. Among individual fatty acids, palmitic acid (C16) was most abundant (30.91%) with higher levels in low B12 hepatocytes than control. Even chain FAs such as stearic acid (C18) and Oleic acid (C18:1 n-9) and odd chain FAs such as margaric acid (C17), heneicosylic acid (C21) and tricosylic acid (C23) were also higher in low B12 than control.

Conclusion: Our study provides novel evidence that vitamin B12 deficiency upregulates hepatic *de novo* FA synthesis and increases levels of SFAs including the even-chain and odd-chain FAs. Thereby suggesting that B12 deficiency leads to dysregulation of lipids in hepatocytes which might lead to development of insulin resistance and other metabolic disorders.

Associations between socioeconomic status and immune activity during pregnancy: Implications for child development

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Background/Aims: Changes in the maternal immune environment during pregnancy have been linked to an increased risk for neurodevelopmental disorders and adverse health outcomes throughout the life-course. Using data from CANDLE (Conditions Affecting Neurocognitive Development and Learning in Early childhood), a birth cohort with broad variability in socioeconomic status (SES), we investigated whether psychosocial and environmental factors are associated with disruption of the maternal immune milieu, and explored the implications for offspring birth and child outcomes.

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Methods: We performed a comprehensive examination of the maternal immune milieu by measuring cytokines from blood samples collected during the second trimester of pregnancy (n=188). Cytokines were measured using the Meso Scale Discovery (MSD) human biomarker kit, which allows for the measurement of 40 proteins including cytokines/chemokines, and vascular and angiogenesis markers. To probe for a relationship between the environment and maternal immune activity, a composite measure of SES was generated, comprising measures of parental education, income relative to the US poverty guidelines, family structure, and health insurance status.
Results: Preliminary regression analyses identified SES as a significant predictor of 14 maternal cytokines, including IFN-γ, IL-5, IL-7, and TNF-β. Ongoing analyses are exploring whether the immune profile linked to socioeconomic disadvantage is associated with an increased risk of neurodevelopmental disorders and other adverse birth and health outcomes.
Conclusions: Taken together, through measurement of a broad panel of immune proteins, these data support and enrich our understanding of the association between SES and gestational immune activity, and the implications for offspring outcomes.
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Phenotypic covariance between maternal and offspring body mass index explained by offspring genotype: evidence from three birth cohorts

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Background/Aims: Maternal pre-pregnancy body mass index (BMI) is positively associated with offspring adiposity from birth to adulthood. However, converging evidence suggests that the association with offspring adiposity from later childhood onwards may be largely due to confounding. Genotype is an important potential confounder; we therefore aimed to investigate the extent to which this association is due to the direct effects of genotype, as captured by the offspring's imputed genetic variants genome-wide.
Method: In pooled analyses of individual participant data from three European birth cohorts we examined the associations of maternal pre-pregnancy BMI with offspring weight at birth (BW) and offspring BMI at 1, 5, 10 and 15 years of age (N up to 11 498). We used bivariate Genomic-relatedness-based Restricted Maximum Likelihood implemented in the GCTA software (bivariate GCTA-GREML) to estimate the extent to which phenotypic covariance was explained by offspring genotype. We then used maternal GCTA-GREML to test for indirect effects of maternal genotype on offspring phenotype, mediated via the offspring's pre- or postnatal environment, in the subset of individuals with maternal genotype data available (N up to 5514).
Results: Phenotypic covariance between maternal BMI and offspring phenotype was 0.15 (95% CI: 0.13, 0.17) for offspring BW, increasing to 0.29 (95% CI: 0.26, 0.31) for offspring 15 year BMI. The phenotypic covariance explained by offspring genotype was negligible for BW (-0.04 [95% CI: -0.09, 0.01]), but increased to 0.12 (95% CI: 0.04, 0.21) at 15 years, which is equivalent to 43% (95% CI: 15%, 72%) of the phenotypic covariance. Maternal GCTA-GREML results suggested that direct effects of maternal and offspring genotype play a major role in explaining this genetic covariance.
Conclusion: Maternal genotype, inherited by the offspring, may be a confounder of the association between maternal pre-pregnancy BMI and offspring adolescent BMI.

Resting-State Functional Connectivity in The Aging Brain After Prenatal Famine Exposure

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Background/Aims: Prenatal undernutrition during early gestation negatively affects the structure and function of the developing brain. Furthermore, it has been associated with premature brain aging in the Dutch Famine Birth Cohort, predominantly in men. This premature brain aging may be reflected in a rearrangement of resting-state (RS) functional brain networks, which can be a predictor for the future development of Alzheimer's disease. The aim of this study is to investigate the effect of prenatal undernutrition in early gestation and sex-specific effects on RS large-scale functional brain network connectivity at age 68 years.
Method: The study will be performed in the Dutch Famine Birth Cohort, a cohort of men and women born around the time of the Dutch famine in the Wilhelmina Gasthuis. RS functional magnetic resonance images of the brain were collected in 118 (41 exposed to prenatal undernutrition in early gestation, 77 unexposed) cohort members at the age of 68 years. RS networks will be computed using a data-driven analysis approach. In brief, spatial-spectral clustering will be used to derive ~200 evenly distributed brain regions of interest (ROIs). The CONN

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toolbox will then be used to compute whole-brain connectivity matrices for each subject between all ROI pairs. Infomax will be used to cluster ROI pairs into brain subnetworks within and between which group comparisons will be made. Secondary analysis will examine sex effects.
Results: We expect that changes related to prenatal undernutrition will be reflected in both decreased and increased functional connectivity, possibly indicating processes related to premature brain aging and compensatory activity to prevent cognitive decline. We also expect to find sex-specific differences.
Conclusions: If significant differences between the exposure groups are observed, this would confirm previously reported long-term associations between prenatal undernutrition and brain aging, with specific effects on RS network function, stressing the importance of nutrient availability during this critical period of brain development for healthy aging.

Novel three-dimensional framework for clinical information delivery in LactaMap, an online lactation care support system

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Background: Lactation is associated with significantly improved health outcomes for mothers and infants across the life-course. Despite improvements in initiation rates, little impact has been made on sustained lactation with most women (in high income countries) failing to continue to breastfeed for minimum recommended durations. Doctors report insufficient training to treat patients with lactation difficulties. LactaMap is a comprehensive online care support system designed to deliver evidence-based clinical lactation information to doctors during a medical consult (the point of care).
Method: Established methodologies for clinical practice guideline (CPG) development were used as a starting point to develop content. A common sense approach was used, then quality appraised and modified according to AGREE II methodology.
Results: A customised three-dimensional framework for translation of lactation research to doctors was developed. The first dimension involved definition of scope and creation of initial drafts of 112 clinical practice guidelines by a multidisciplinary expert group. To assist with identification of appropriate CPGs by the clinician, the additional layer of an overarching decision tree was conceptualised and CPGs organised around this accordingly. The second dimension involved creation of framework for ongoing literature review and content update after initial manuscripts were complete. Content needed to be usable at the point of care and therefore succinct. An online format was used, enabling additional supporting information and patient information documents to be linked to guidelines without compromising accessibility of core content. This necessitated development of the third and novel dimension, a process that considers consistency of all interlinked content in LactaMap.
Conclusions: The need for evidence-based lactation information precipitated the development of LactaMap, an online lactation care support system. Existing guideline development methodology was insufficient for effective clinical information delivery, resulting in development of a novel 3-D framework that has potential value in other areas of health.

Antenatal glucocorticoid therapy protects the chronically hypoxic fetus from programmed endothelial dysfunction and hypertension in adulthood

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Background/Aims: Antenatal glucocorticoid therapy (AGT) reduces respiratory distress and death in preterm infants (1). Despite benefits, AGT may programme adverse cardiovascular function in the offspring. This knowledge base is mostly derived from studies in healthy animal models, with comparatively little known in complicated pregnancy. Here, we isolated the long-term effects of AGT on cardiovascular function at adulthood in sheep which were born at term and were either normally grown or IUGR due to chronic fetal hypoxia.
Method: From 0.7 of gestation, pregnant ewes were exposed to normoxia (N) or chronic hypoxia (H, 10% maternal inspired air) followed by maternal treatment with steroids (0.8 gestation; 2x12mg dexamethasone (D) i.m. 24h apart) or saline vehicle. A week before natural delivery, all hypoxic ewes were returned to normoxia. Offspring were maintained until 9 months, then chronically instrumented under general anaesthesia to determine *in vivo* cardiovascular physiology followed by ex vivo femoral vascular function with wire myography. Data analysed by 2-way ANOVA, $P<0.05$.
Results: Offspring of hypoxic pregnancy were smaller at birth and showed hypertension with peripheral endothelial dysfunction at adulthood (Table 1). AGT in hypoxic pregnancy restored the programmed hypertension via mechanisms including increased NO bioavailability. Offspring of hypoxic pregnancy with AGT had a greater fall in femoral conductance during *in vivo* NO blockade and protection against the programmed peripheral endothelial dysfunction (Table 1).
Conclusions: Antenatal glucocorticoid therapy in human clinically relevant doses protects the chronically hypoxic IUGR fetus from programmed hypertension by increasing NO bioavailability and improving peripheral endothelial function.
Reference: 1. McKinlay, C.J., S.R. Dalziel, and J.E. Harding, Antenatal glucocorticoids: where are we after forty years? J Dev Orig Health Dis., 2015. 6(2): p. 127-42.

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	N (n=10)	H (n=10)	HD (n=10)	ND (n=7)
Birth weight (kg)	3.5 ± 0.1	3.0 ± 0.1*	2.9 ± 0.2*	4.0 ± 0.3
Adult blood pressure (mmHg)	87.8 ± 1.9	96.4 ± 1.9*	88.2 ± 1.1+	90.3 ± 2.8
FVC (Δ to LNAME (ml.min^{-1}/mmHg))	–1.2 ± 0.3	–1.2 ± 0.3	–3.0 ± 0.4+	–2.1 ± 0.3+
Vasodilatation to MCh (AUC)	366 ± 14	255 ± 14*	314 ± 20+	338 ± 19

Table 1. FVC, femoral vascular conductance; LNAME, NO inhibitor; MCh, methacholine; *, v H; +, v D

The mitochondria-targeted antioxidant MitoQ prevents programmed cardiovascular dysfunction at adulthood while maintaining fetal brain sparing

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Background/Aims: Chronic fetal hypoxia programmes cardiovascular dysfunction in adolescence via oxidative stress. In rodents and sheep, maternal vitamin C in hypoxic pregnancy is protective, however only at high concentration incompatible with human translation. Further, vitamin C suppresses the fetal brain sparing response to acute hypoxia. Combining sheep and chicken embryo model systems, we show that MitoQ provides alternative antioxidant therapy to prevent programmed hypertension in the adult offspring of hypoxic pregnancy while maintaining fetal brain sparing.
Method: Chronic hypoxia (10% O_2) was induced in pregnant sheep (last third of gestation) or in chicken embryos (whole incubation period, 21 d). Work in chicken embryos determined the direct actions of MitoQ on the fetus by wire myography, respirometry and mitochondria ratiometric mass spectrometry. Pregnant sheep closely modelled human pregnancy to determine if MitoQ protected against programmed hypertension in the adult offspring using *in vivo* physiological techniques.
Results: Treatment of the chicken embryo with MitoQ prevented chronic hypoxia-induced increases in mitochondrial ROS *in vivo* (MitoP:MitoB) and normalised cardiac mitochondrial respiration (Table 1). Treatment of hypoxic ovine pregnancy with MitoQ maintained fetal brain sparing during acute hypoxia (data not shown) while preventing hypertension in the adult offspring. Mechanisms of MitoQ-induced protection against programmed cardiovascular dysfunction in the adult included enhanced basal nitric oxide concentration and signalling and improved vascular relaxation (Table 1).
Conclusions: Maternal MitoQ treatment in complicated pregnancy preserves fetal brain sparing and protects the adult offspring from programmed cardiovascular dysfunction. We provide promising human clinical therapy to protect against developmentally programmed heart disease.
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Metabolic Profiles of Adult Survivors of Severe Acute Malnutrition

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Background: Severe acute malnutrition (SAM) is a major contributor to mortality in children under the age of 5 years. However, its long-term consequences are not well understood. The clinical phenotypes of SAM (severe wasting and oedematous malnutrition) have distinct clinical features and metabolism during the acute illness. It is unclear whether these metabolic changes persist and influence the adult cardio-metabolic phenotype. This study aimed to assess the long-term risk of childhood exposure to SAM by comparing the metabolic profiles of adult SAM survivors and a control group using targeted metabolomics.
Methods: From a retrospective cohort, 122 Jamaican adults hospitalized for childhood SAM (1963-1993) were matched with 90 community controls by age, sex and BMI. Serum metabolites (n = 130; biogenic amines [13], amino acids [22], glycerophospholipids [34], acylcarnitines [40], organic acids [16] and others [5]) were quantified using tandem mass

		N (n=10)	H (n=10)	HQ (n=7)	NQ (n=9)
Chicken embryo	MitoP : MitoB (*in vivo* ROS production)	0.08 ± 0.1	0.20 ± 0.04*	0.14 ± 0.2	0.17 ± 0.4
	Cardiac respiratory control ratio	2.4 ± 0.2	1.5 ± 0.1*	2.37 ± 0.26+	1.97 ± 0.20
Adult sheep	Mean arterial blood pressure (mmHg)	87.8 ± 1.9	96.4 ± 1.9*	86.8 ± 2.2+	88.0 ± 2.7
	FVC [Δ to LNAME (ml.min^{-1}/mmHg)]	–1.2 ± 0.3	–1.2 ± 0.3	–2.3 ± 0.2+	–2.7 ± 0.3+
	Max. vasodilatation to SNP (%)	94.6 ± 1.7	83.4 ± 4.7*	95.2 ± 1.1*+	96.0 ± 2.2+

Table 1. FVC, *in vivo* femoral vascular conductance; *vs.* H; +*vs.* Q, Two-Way ANOVA with Tukey test.

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spectrometry either coupled to liquid chromatography or directly infused. Univariate and sparse partial least square discriminant analyses were used to assess differences in metabolic profiles and identify the most discriminative metabolites adjusting for age, sex, BMI and economic status.
Results: We investigated adult survivors of severe wasting (n = 69, 27.3 ± 8.6 years, 23.4 ± 5.8 kg/m^2), oedematous malnutrition (n = 53, 29.9 ± 8.9 years, 26.4 ± 6.4 kg/m^2) and community controls (n = 90, 28.4 ± 8.9 years, 23.6 ± 4.4 kg/m^2) (mean ± SD). 71 of the 130 measured metabolites (55%) distinguished SAM survivors from the control group. Specifically, leucine, aspartic acid, glutamic acid, threonine and valine were higher in SAM survivors who also had higher BCAA, Fischer ratio, kynurenine-tryptophan (KT) ratio and urea cycle metabolites than controls (FDR-corrected p-values < 0.05). The control group had higher acylcarnitine concentrations (C5:1DC, C3:1, and C4:1) and had higher acylcarnitine to free carnitine ratio (C2:C0) (FDR-corrected p-values < 0.05), suggesting greater risk of liver fat accumulation. The profiles of survivors of severe wasting and oedematous malnutrition were similar.
Conclusions: This cohort of adult SAM survivors was metabolically distinguishable from a matched control group. Higher BCAA concentrations have been associated with higher risk of obesity and type 2 diabetes and higher KT ratios with higher risk of type 2 diabetes and coronary events. This study supports the hypothesis that childhood exposure to SAM has long term metabolic consequences.

Maternally perceived fetal movement patterns; the influence of body mass index

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Background/Aims: Maternal reports of decreased fetal movements are associated with adverse pregnancy outcome, but there are conflicting data about perception of fetal movements in women with obesity. We compared perceived fetal movements in women with obesity and with normal weight.
Method: Data from two separate pregnancy studies conducted in New Zealand were used in this analysis: The Healthy Mums and Babies study (HUMBA) which recruited women with BMI ≥30 kg/m^2, and the Multi-Centre Stillbirth Study (MCSS) from which we used data from women with ongoing pregnancy from a general obstetric population. Fetal movement data were collected using an interviewer-administered questionnaire. We compared fetal movement strength, frequency, busy times and reported strength in relation to; time-of-day, maternal position, maternal meals and fetal stimuli between HUMBA and MCSS women with obesity and MCSS women with normal weight (BMI <25kg/m^2).
Results: 233 women with obesity and 149 with normal weight were included. Mean (SD) gestation at interview was similar between groups (36.9 [2.2] weeks vs 36.6 [0.9], p=0.06). Perceived fetal movement strength, frequency and length of busy times did not differ between groups. Fetal movement strength exhibited a clear diurnal pattern, with the majority of women in both groups reporting moderate or strong fetal movements in the evening (88.7% vs 99.3%) and at night-time (92.1% vs 93.1%). Women with obesity, compared to those of normal weight were more likely to report strong fetal movements when hungry (29.1% vs 17.7%, p=0.001), and quiet fetal movements 1-hour after eating (47.4% vs 32.0%, p=0.001).
Conclusions: Fetal movement strength, frequency and length of busy times were similar in women with obesity and women with normal weight. Perception of decreased fetal movements in obese women should not be considered a benign variation attributed to maternal body size. Differences in fetal movement strength around maternal meals warrant further investigation.

Can Childhood Trauma Impact on the Health of the Next Generation?

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Background/Aims: Trauma experienced in childhood can have long term effects on health extending into the next generation causing prematurity, low birth weight and altered immune response. The aim of this study was to investigate whether bereavement (as a proxy for trauma) in childhood increases the risk of chronic inflammatory diseases in offspring, and whether this differs for women and men.
Methods: Swedish register data was used to identify a study population consisting of children born in Sweden between 2001 and 2012 (G3), their parents (G2) and grandparents (G1). Bereavement experienced by G2 between 0-15 years of age was defined as death of a parent (G1) from the Cause of death register. Inflammatory diseases in children (G3) were identified in two ways: 1) two diagnoses in the Patient register; 2) using algorithms of medication from the Prescribed drug register and/or diagnosis for each of: asthma, eczema, allergic rhinitis, autoimmune diseases. Survival analysis was used to assess associations separately for paternal and maternal bereavement. Confounders included socio-economic status (SES) of G1 (income) and birth year of G2. Mediators included SES of G2 (education) and maternal smoking during pregnancy, G3 birth weight and gestational age.
Results: Bereavement experienced by mothers was associated with an increased risk of inflammatory diseases combined,

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(adjHR 1.13 95% CI 1.07, 1.20) and asthma (adjHR 1.19 95%CI 1.12, 1.29) at 0-3 years in offspring, but not for eczema, allergic rhinitis or autoimmune diseases. Adjustment for mediators lowered associations slightly. No associations were found for bereavement experienced by mothers and inflammatory diseases over the age of 3 years, nor for bereavement experienced by fathers and inflammatory diseases at any age.
Conclusion: Early experience of trauma in women may have a transgenerational effect increasing inflammatory disease and asthma risk in the next generation. This same effect is not observed in men.

Effects Of Artificial Sweetener In The Maternal Diet On Offspring Health

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Background/Aims: Raising obesity rates and related co-morbidities including cardio-metabolic disease and infertility, pose significant health risks. Maternal obesity and unhealthy gestational diets may increase the risk of health complications for both the mother and her child. Often, 'diet' beverages high in artificial sweeteners (AS) are used as alternatives for high-sugar drinks. Despite being considered a healthier option, 'diet' beverages have been linked to metabolic dysfunction and obesity. Currently, limited information exists regarding the role maternal AS diets play in the long-term health of the offspring. This study aims to determine the effect of maternal AS exposure on the metabolic and reproductive health of both mother and offspring.
Method: Time-mated female C57/BL6J mice receive either a) a standard chow diet (Harlan 2018), b) high-fructose corn-syrup diet (HFr; standard chow diet *ad-libitum*, 20%calories from fructose), or c) AS diet (standard chow diet *ad-libitum*; supplemented with 12.5mM acesulfame-K solution) throughout pregnancy and lactation. Glucose tolerance, insulin and leptin concentrations were examined in dams. Weight and glucose concentrations were measured in the placenta, and in pups and adult offspring. Data was analysed using 1-way ANOVA.
Results: Fr and AS induced glucose intolerance in the dams, while Fr but not AS increased insulin concentrations. No mean difference in weight occurred between maternal groups. AS significantly reduced fetal weight in males, but not females. Fr and AS both induced sex specific effects on fetal glucose concentrations, with increased glucose also noted in female adult offspring of AS-fed mothers, but not males.
Conclusions: Maternal AS and Fr consumption contribute to metabolic dysfunction in the dams and offspring, indicating that a maternal diet of AS may not be a beneficial alternative to sugary foods during gestation. Sex specific fetal effects further indicate an influence on fetal health, as well as later health of the offspring.

Exclusive Breastfeeding Can Attenuate Body-Mass-Index Increase among Genetically Susceptible Children

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Background/Aims: Previous research has clearly established a link between early environment (pre-natal and post-natal), genetic, and behavioral factors on the development origin of health and diseases (DOHaD). Among the environmental factors, breastfeeding has been advocated by the World Health Organization in the prevention of overweight and obesity. This study aims to examine whether the duration and exclusivity of breastfeeding (EXBF) attenuates the risk of increased BMI among children with high genetic susceptibility, as assessed by an obesity-specific genetic risk score (GRS).
Method: A total sample of 5,266 children (2,690 boys and 2,576 girls) from the Avon Longitudinal Study of Parents and Children (ALSPAC) was used for the analysis. We calculated the GRS from 94 identified obesity-related genetic variants and applied mixed-effects models with cubic spline to test the interaction between EXBF and GRS on the child BMI growth trajectories from birth to 18 years of age.
Results: At 18 years of age, a 2.5 unit increase in the GRS was associated with a 1.98 kg/m^2 (95%CI: 1.65, 2.32; p<0.0001) and 0.75 kg/m^2 (95%CI: 0.40,1.09; p<0.0001) increase in BMI, in boys and girls respectively. A five-month duration of EXBF reduces BMI by 0.25 kg/m^2 (95%CI: -1.04, 1.53; p=0.7), 0.85 kg/m^2 (95% CI:0.27, 1.43, p=0.004) and 1.44 kg/m^2 (95% CI: 0.32, 2.57; p=0.01) at GRS values corresponding to the first quartile, median and third quartile, respectively. In girls, the respective numbers are 1.28 kg/m^2 (95%CI: 0.06, 2.51; p=0.04), 1.19 kg/m^2 (95%CI: 0.61, 1.78; p<0.0001) and 1.10 kg/m^2 (95%CI: -0.11, 2.32; p=0.08). Additionally, non-exclusive breastfeeding has much less effect on reducing BMI growth during childhood.
Conclusions: EXBF influences early life growth development and thus plays a critical role in preventing the risks of overweight and obesity even when those are exacerbated by genetic factors.

Role of Breastfeeding on Epigenetic Mechanisms Underlying Early-Life Growth Trajectories

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Background/Aims: Previous research has clearly established a link between early environment, genetic, and behavioral factors on the development origin of health and diseases. Among the environmental factors, breastfeeding has been advocated in the prevention of overweight/obesity and is recommended by WHO as the "perfect food for the newborn".
Method: We studied 953 children from the British Avon Longitudinal Study of Parents and Children (ALSPAC) cohort and conducted an epigenome-wide association study (EWAS) of birth weight and BMI at birth as well as a longitudinal analysis of child BMI up to 17 years of age in relation to DNA methylation of the EWAS hits, several candidate genes and the duration of exclusive breastfeeding (EXBF).
Results: The EWAS identified several CpG sites where methylation profile correlated significantly with either birth weight or BMI at birth. We also found several EWAS hits and CpG sites from candidate genes where methylation profile was modulated by EXBF and was associated with longitudinal BMI in children through infancy and adolescence. Many of the differential methylated genes form part of the mTOR signaling pathway. These CpG sites could be hyper- or hypo-methylated by EXBF but their interaction with EXBF resulted systematically in reduced BMI growth and stronger methylation changes the first year of life.
Conclusions: Our study demonstrates that EXBF may regulate epigenetic modifications of key genes involved in developmental programming, especially the first year of life, which in turn could impact the risks of overweight/obesity later in life. This modulation could potentially involve the mTOR pathway.

Metabolism of Tryptophan in the Healthy and Preeclamptic Human Placenta

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Background/Aims: An altered placental transfer and metabolism of tryptophan may contribute to preeclampsia (PE). We therefore aim to investigate the kynurenine pathway (KP, Figure) in PE.
Method: Healthy placentas (n=4) were dually perfused ex vivo with 8 mM tryptophan in the maternal circulation, and KP metabolites were measured in the maternal and fetal perfusate by LC/MS. Gene expression of KP enzymes was quantified by RT-qPCR in 12 healthy, 7 early onset PE (EoPE), and 4 late onset PE (LoPE) placentas.
Results: After 3 hours of perfusion, at steady state, 19% of the administered tryptophan was present in the fetal circulation, which corresponded with levels that were ≈3x lower than those maternally. Of the administered tryptophan, <1% was detected as KP metabolites. From kynurenine, 3-OH-anthranilic acid was formed mainly via anthranilic acid. Kynurenic acid and 3-OH-L-kynurenine were formed to a much smaller extent, and xanthurenic acid and serotonin were undetectable. Based on the RT-qPCR data, IDO1 was the most prominently expressed KP enzyme, lower maternally than fetally, and reduced in EoPE, but not LoPE. On the maternal side of EoPE placentas, AFMID and KAT-3 were upregulated, and KMO showed a similar trend, while HAAO was reduced. The expression of the other enzymes (Figure) was unaltered.
Conclusions: Tryptophan is transported from the maternal to the fetal side of the human placenta. The KP is altered in EoPE, but not LoPE, being more directed towards kynurenic acid and xanthurenic acid formation, whereas flux through the anthranilic acid route is reduced. To what degree this contributes to PE remains to be determined.

Mental health from pregnancy to child age 4 years in mothers experiencing adversity

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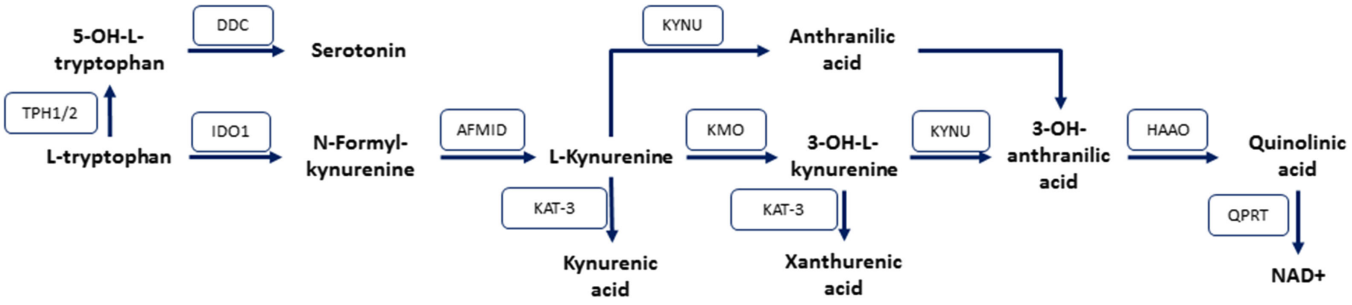

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Background/Aims: Maternal mental health is an important determinant of children's health outcomes. In families experiencing social adversity mothers are likely to have poorer mental health and fewer supports. We describe the patterns of mental health in a cohort of mothers experiencing adversity, from pregnancy across the first 4 years of their child's life.
Method: Longitudinal prospective study of 722 women experiencing adversity (≥2 of 10 risk factors) recruited during pregnancy, through the 'right@home' trial. Maternal mental health was assessed using the Depression Anxiety and Stress Scales (DASS) collected during pregnancy, and postpartum at 6 weeks, and 6 monthly until 4 years. Patterns of depressive symptoms, anxiety and stress were examined over time considering both mean scores and the proportion of women in the top 15% of symptom severity according to population normative data ('high symptom severity').
Results: The number of women providing mental health data ranged from 722 (100%) in pregnancy to 459 women (64%) at 4 years. Depressive symptoms were highest during pregnancy, at 6 weeks and at 4 years (mean scores of 3.0; 4.1; 3.0 respectively). Similar patterns were reported for anxiety (mean: 3.5; 3.6; 2.6) and stress (mean: 5.4; 8.1; 5.3). High symptom severity for depression was most prevalent at 6 weeks (27%) and 4 years (27%). Striking peaks in high symptom severity for anxiety were evident during pregnancy (42%) and at 6 weeks (35%); and similarly for stress at 6 weeks (38%).
Conclusions: Mental health problems are common during pregnancy and early childhood for mothers experiencing adversity. Although the prevalence of high symptom severity fluctuates, there is a clear pattern of poor mental health being higher in the pre- and early postpartum period and again at child age 4 years. The high overall prevalence suggest that universal services must be considered essential platforms to identify and address mental health problems. Understanding the ebbs and flows of mental health problems provides policymakers with the precision needed to craft a more equitable and responsive service system over the life of a child.

Hair cortisol in mother-child dyads: maternal parenting and stress in the context of early adversity

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Background/Aims: Long-term physiological stress is thought to be one way that early adversity can affect children's health. The extent to which this stress occurs may be determined by parental factors such as mothers' own physiological stress and parenting behaviour. Hair cortisol offers a novel method for examining long-term physiological stress in mother-child dyads experiencing adversity. We used hair cortisol to examine the associations between adversity, maternal physiological stress, parenting behaviours and children's physiological stress; and to investigate whether maternal physiological stress and parenting behaviours mediate the effects of adversity on children's stress.
Methods: Cross-sectional study of 2-year-old children whose mothers were recruited during pregnancy for their experience of adversity, within the 'right@home' trial. Confirmatory factor analysis was used to define exposures of economic adversity (e.g. unemployment, low income), psychosocial adversity (e.g. poor mental health, family violence), and positive maternal parenting (e.g. warm, responsive). Structural equation modelling examined pathways through which adversity may be associated with children's physiological stress, via maternal physiological stress and parenting.
Results: Hair cortisol data were available for 319/603 (53%) participating children. Maternal and child physiological stress (hair cortisol) were positively associated with one another (standardised estimate=0.25, $p<0.001$). Higher psychosocial adversity was associated with lower positive maternal parenting (standardised estimate=-0.34, $p<0.01$), however maternal parenting was not associated with children's physiological stress. There was no evidence that adversity was associated with children's physiological stress; as such there was no evidence of any mediating pathways.
Conclusions: These findings suggest measuring child hair cortisol at age 2 may not effectively reflect children's physiological stress response to their early environments, and that physiological stress may well be determined by endogenous genetic factors rather than exogenous environmental exposures.

Does stress mediate the association between early adversity and children's health at 3 years?

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Background/Aims: Children exposed to early socioeconomic and psychosocial adversities (including financial hardship, family violence, and parent's mental health difficulties) are at greater risk of poor health outcomes. Children's physiological stress response to adversity is one mechanism proposed to explain this pathway. We aimed to investigate associations between adversity and children's health at 3 years, and whether child stress (measured using hair cortisol) mediated these associations.
Method: Cross-sectional study of 3-year-old children whose mothers were recruited during pregnancy for their experience of adversity, within the "right@home" trial of nurse home visiting. Exposures were: total counts of 9 sociodemographic and 9 psychosocial indicators of adversity. Child hair cortisol was examined as a potential mediator. Child health outcomes were: externalising and internalising behaviour problems, physical

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and socioemotional wellbeing, and overweight/obesity. Univariable and multivariable regression and mediation analyses were conducted for each of the child health outcomes
Results: Hair cortisol data were available for 297/500 (59%) children. Sociodemographic adversity was associated with higher externalising problems in univariable regression models, and psychosocial adversity with higher externalising problems and poorer physical and socioemotional wellbeing. Multivariable regression found psychosocial (but not sociodemographic) adversity was associated with higher externalising problems (ß=0.53, p=0.002), and poorer physical wellbeing (ß=1.19, p=0.009); higher hair cortisol was associated with higher externalising problems (ß=0.76, p=0.02). There was no evidence that children's physiological stress mediated associations between adversity and health.
Conclusions: We found no evidence that children's physiological stress (measured using hair cortisol) mediated the associations between adversity and children's health. Hair cortisol may be limited as a measure of stress, or physiological stress may not be a mechanism for explaining the effects of adversity on children's health at the population level. Following children for longer periods may well start to explain these seemingly dissonant findings.

Second trimester and pre-conception folic acid supplementation are associated with birth size in an international nulliparous pregnancy cohort

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Background/Aims: Small-for-gestational-age (SGA) is associated with perinatal morbidity and mortality and there are few current preventative strategies. Data are conflicting as to whether folic acid supplementation (FAS) continued beyond the first trimester influences fetal growth. We aimed to examine the association between maternal FAS use, prior to pregnancy through to the second trimester, and birth size parameters.
Method: We utilised data from the international Screening for Pregnancy Endpoints (SCOPE) prospective cohort study undertaken in healthy nulliparous women with singleton pregnancies, with detailed data on FAS use pre-pregnancy and during the first and second trimesters. We examined the association between maternal FAS and birth size. Primary outcomes were: SGA (<10th centile) and customised birthweight centiles (CBWC). Multivariable analysis adjusted for known confounders of fetal growth and FAS use at the other time points.
Results: 5606 participants were included of whom 58% (n=3268) reported using FAS pre-conceptionally, and 70% (n=3907) at 15 ±1 weeks' gestation. Pre-conception FAS was associated with lower odds of SGA (10.0% vs 13.1%): adjusted odds ratio 0.82 (95% CI: 0.67 to 1.00). FAS use at 15 weeks was associated with higher CBWC (Beta Coefficient=2.56% (95% CI = 0.87% to 4.26%) and a 3.2% increase in birthweight z-score (p=0.003) independent of FAS prior to pregnancy. Use of FAS, at either time point, was not associated with a higher risk of large-for-gestational-age (LGA) or increased head circumference z-score.
Conclusions: FAS use pre-conception reduces the risk of SGA in healthy nulliparous women. FAS use at 15±1 weeks' was associated with a small but significant increase in CBWC and birthweight z-score, without increasing the rate of LGA or increasing head size. Continued use of FAS beyond the first trimester may have benefits for fetal growth. Ongoing follow up studies will determine whether there are any longer term implications of FAS on childhood growth.

Longitudinal Association of a Body Mass index (BMI) Genetic Risk Score with Growth and BMI Changes Across the Life Course: The Cardiovascular Risk in Young Finns Study

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Background/Aims: The relevance of 97 single nucleotide polymorphisms (SNPs) associated with adult body mass index (BMI) to predict BMI levels at different stages of the life-course is unclear. We tested whether a 97 SNPs (wGRS97) multigenetic risk score associated with average and change in BMI levels across the early life-course (from age 6 to 49 years). We also examined if the wGRS97 associated with distinct developmental trajectories of BMI.
Methods: The wGRS97 was a linear combination of published effective alleles weighted by their effect size. Associations between the wGRS97 and BMI change at different life-stages were examined using Individual Growth Curve analysis, Latent Class Growth Mixture modelling, and logistic regression.
Results: The wGRS97 associated with BMI from age 6 years with peak effect sizes observed at age 30 years (1.14 kg/m^2 and 1.09 kg/m^2 higher BMI per SD increase in wGRS97 in females and males). A higher wGRS97 associated with an increased BMI velocity in childhood and adulthood, but not with BMI change in adulthood. The association between wGRS97 and BMI became stronger with age in childhood but slowed in adolescence, especially in females. The combined

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genetic effect of these variants appears to weaken at around ~35/40 years. A one SD higher wGRS97 associated with an increased relative risk (RR) of belonging to a more adverse life-course BMI trajectory group compared with belonging to a 'normal stable' trajectory group where a normal weight-for-height-ratio was maintained from childhood to adulthood (RRs from 1.13 (95%CI:1.09-1.16) to 2.30 (95%CI:2.01-2.62) for the trajectory groups classified as 'progressively overweight' and 'persisting and worsening high obesity'.

Conclusions: Genetic susceptibility to higher adult BMI can be tracked from childhood. These data support that the prevention of obesity should begin early in life. From 24 years of age, the variants were not associated with a linear change in BMI levels within-person. The genetic effect weakened in young adulthood, highlighting the importance of environmental factors to control adult BMI levels.

Biosocial Predictors of Resilience to Adverse Childhood Experiences

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Exposure to adverse childhood experiences (ACEs) results in poorer health and social outcomes across the lifecourse. ACEs are highly prevalent, and yet some individuals do not develop stress-related dysfunctions, despite being subject to the same kind of challenges that cause long-term dysfunction in others. This 'resilience' is a well described phenomenon, yet there are considerable differences in the way resilience is defined, operationalised and measured.

In this study I use a novel approach to measure resilience, operationalised as the difference between an individuals' score on a health or behavioural measure and the score predicted by their exposure to adversity: the standardised residual scores. Taking data from a longitudinal birth cohort study, the Avon Longitudinal Study of Parents and Children (ALSPAC), with genotype data and repeated measures of stress reactivity, adversity and outcomes, I develop a resilience index across multiple domains of ACEs, beginning prenatally and continuing into adolescence. 19 ACE constructs are derived using a pragmatic approach to handle the high dimensional ALSPAC data. After creating a continuous measure of resilience across the early life course, I then assess how the resilience index varies by age and how individual, familial and community factors influence that variation. Whether the resource factors are 'protective', reducing the negative effects of adversity on functioning for children with high ACEs, or 'promotive', reducing the negative effects of adversity on functioning for all children, is discussed.

Using latent class analysis, I partition the continuous resilience index into sub-groups following homogenous developmental trajectories. Previous studies have suggested that trajectory analysis may help to refine the measurement of resilience and provide a more heritable phenotype that will improve signal in genetic association studies. Next steps to assess the SNP heritability of developmental trajectories of resilience are discussed.

Diet-induced maternal obesity impairs mitochondrial function in the hypothalamus and hippocampus of adult mice offspring

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Background: Emerging clinical and experimental studies have suggested that prenatal and early postnatal exposure to maternal obesity can have long term adverse effects on behaviour and cognitive function in the offspring. Cerebral mitochondrial dysfunction and oxidative stress are possible mechanistic links. This study determined the impact of maternal diet-induced obesity during pregnancy and lactation on cerebral mitochondrial function in adult male and female offspring.

Methods: Under the Animals (Scientific Procedures) Act 1986, female C57BL6/J mice were fed either a diet high in fat and sugar (HFHS, fat: 36% kcal, sugar: 29.5% kcal) or a standard chow diet (Control, fat: 11% kcal, sugar: 7% kcal) for 6 weeks prior to mating, during pregnancy and lactation. After birth, litter sizes were standardised to 6, and all offspring were weaned onto standard chow until the end of the study. At 14 weeks postnatal age, male (Control n=4; HFHS n=3) and female (Control n=4; HFHS n=4) offspring were euthanised, biometric data recorded and high-resolution respirometry employed to assess mitochondrial respiration in samples from the hypothalamus, hippocampus and frontal cortex. Data were analysed using a two-way ANOVA (maternal obesity and offspring sex).

Results: Crown rump length was 3% lower in HFHS offspring compared to controls (P=0.015). In the hypothalamus, Complex I (CI)-linked respiration was 11% higher in HFHS offspring (p=0.049). Further, the respiratory reserve capacity of the electron transport chain (the difference between maximal oxidative phosphorylation (OXPHOS) and FCCP-uncoupled respiration) was 6% lower in HFHS offspring (p=0.049). In the hippocampus, there was a significant interaction (p=0.032) between maternal obesity and sex for the respiratory control ratio, which reflects the coupling efficiency of ADP-stimulated respiration, with 10% lower coupling seen in HFHS male offspring compared to control male offspring (P=0.040). In addition, an overall interaction was observed for OXPHOS supported by CI & Complex II (CII)-linked substrates (P=0.040). There was no effect of maternal obesity on mitochondrial respiratory function in the cortex.

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Conclusions: Exposure to an obesogenic environment in early life can impair mitochondrial bioenergetics in different brain regions in a sex-specific manner with implications for cerebral function.

The method based on liquid chromatography tandem-mass spectrometry (LC-MS/MS) to measure endogenous ouabain is constructed

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Background/Aims: Ouabain is a cardiotonic steroid which is a specific legend of Na-K-ATPase. More and more evidence suggests that ouabain-like compound is also present in our body. Circulating Endogenous ouabain (EO) is very low and this needs a very accurate detection method. To date, methods to quantify EO has not been standardized and unified, resulting in different normal ranges of EO levels. Recently, the rapid development of tandem-mass spectrometry allows the analysis of small molecules on a very high level of metrological reliability. In this study, we attempt to develop a highly specific and reliable method for measurement of ouabain in human biological samples based on liquid chromatography tandem-mass spectrometry (LC-MS/MS), and applied to detect a series of clinical samples.
Method: After protein precipitation by methanol, the supernatant was evaporated to dryness and the resultant residue was redissolved. Chromatography was performed on a Shimadzu HPLC system coupled to an AB SCIEX 5500 MS. Ouabain in the peripheral blood plasma of pregnant women in different pregnant week (11~39 weeks of gestation) and non-pregnant women was determined. Plasma and hemocyte separated from umbilical cord blood and placenta of 11 normal pregnant women were also collected after delivery and the concentration of EO was detected using modified method.
Results: This method covered a linear range of 0.1–1000 ng/mL of concentrations in plasma for ouabain and the linear curve fitted well with r=0.995. The concentration of EO in peripheral blood plasma changed with gestational weeks. There was no significant difference between the concentration of EO in early-middle pregnancy (11~27 weeks) and that in non-pregnant women, while in late pregnancy (28~34 weeks) EO slightly increased, which significantly descended after full term (36~39 weeks). We found that EO was not only presented in the plasma but also presented in hemocyte and placenta. The concentration of EO in hemocytes was 1.734±0.972 ng/mL, which was statistically higher than that in plasma (0.408 ±0.207 ng/mL) of umbilical cord blood, and EO in placenta reached 5.013±1.487 ng/g tissue.
Conclusions: An ultra-sensitive, rapid and specific LC-MS/MS method was developed which applied direct protein precipitation for sample preparation. Our method was successfully applied to the determination of ouabain in cell lysate /biofluids/tissue homogenate.

Hepatic Murine MiR-582-5p Abundance Potentially Contributes To Liver Lipid Accumulation In Both Maternal Obesity Programming and Aging Independently

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Background/Aims: Ageing is an independent risk factor for non-alcoholic fatty liver disease (NAFLD), and recent studies indicate that *in utero* exposure to maternal obesity contributes to early onset of the disease in the offspring; however, it is unclear if the molecular mechanisms underlying the establishment of NAFLD through programming by maternal obesity and ageing are related. The aim of the current study was to identify a signature of maternally programmed hepatic miRNAs that are also sensitive to ageing and to explore their contribution to the programming of fatty liver by maternal obesity.
Method: To achieve this, we used a mouse model of maternal diet-induced obesity where the offspring exhibit augmented hepatic lipid levels and we carried out small RNA sequencing analysis of liver from male offspring of control and obese dams in young adulthood and at 12 months of age.
Results: We identified miR-582-5p as persistently upregulated by maternal diet (three-fold $P < 0.05$) and age (seven-fold $p < 0.001$). In vitro overexpression of miR-582-5p in hepatocyte and hepatocarcinoma cell lines resulted in increased intracellular triglyceride accumulation, suggesting that increased miR-582-5p levels can cause increased intracellular lipid accumulation in the liver.
Conclusions: We conclude that maternal diet-induced obesity and ageing both independently lead to an increase in hepatic miR-582-5p abundance which causes increased hepatic lipid accumulation. The precise molecular mechanisms through which this occurs remain to be defined. However these findings are consistent with the hypothesis that accelerated ageing contributes to programming mechanisms.

In placenta of women with pregestational obesity, DHA supplementation generates and imbalance in the expression of pro- and anti-inflammatory genes

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Background/Aims: Pregestational obesity (PGO) is associated with an increased long-term health risk in the offspring. In women with PGO high levels of soluble and placental proinflammatory markers have been measured. DHA supplementation during pregnancy has been proposed to revert some of these markers. Our aim was to determine if maternal DHA supplementation in women with PGO modulates the expression of pro and anti-inflammatory genes in placental fragments.
Method: This is a cross-sectional study of women with PGO participants in an ongoing double-blinded RCT(NTC02574767) randomized to receive 200 or 800 mg/day DHA during pregnancy (PGO#12 or PGO#13 indistinctively). PGO and normal weight (NW) women without DHA supplementation were included. Placentas were collected at delivery, trophoblast fragments (TF) were dissected, thoroughly washed, and kept at -80°C until analysis. NW and PGO TF were treated with DHA (24 h, 100 μM) and LPS (9 h, 1 μg/ml). The mRNA expression of pro-(IL-6, IL-8, MCP-1 and TNFα) and anti-inflammatory (IL-10) genes were evaluated by RT-qPCR. The concentration of these cytokines was detected in cord blood by Luminex®.
Results: In offspring from PGO#13, an increased expression of MCP-1 in female TF and IL-6 in male TF was observed ($p<0.05$). TNFα expression was decreased and IL-10 increased in female TF from PGO, compared to NW, and this was reverted by DHA supplementation (PGO#12 and #13). The cord cytokines were not different among groups. In vitro LPS treatment of TF increased the expression of all genes studied both in NW and PGO. The TF of PGO showed an increased response to LPS for IL-6 and decreased for IL-10 in PGO compared to NW.
Conclusions: Maternal PGO induces an imbalance in the pro and anti-inflammatory genes in female placenta which would be reverted by DHA supplementation, the later could affect the pro-inflammatory response in a dose and gender-dependent manner.

Impact of maternal pregestational obesity on the offspring early life adiposity

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Background/Aims: Pregestational obesity (PGO) increases offspring´s obesity risk. Maternal DHA intake may influence adiposity in early life. MIGHT study allocates PGO women to receive 200 or 800 mg/day of DHA and EpiFat is a nested cohort of their offspring. The aim of this study was to evaluate the effect of PGO and DHA supplementation on children adiposity.
Method: EpiFat participants were recruited at birth. Body composition (BC) was assessed between 24-72 hrs postpartum and at 4 months (4m). Fat% at birth was assessed by anthropometry and skinfolds thickness using Catalano´s formula and by anthropometry and PEAPOD at 4m. Offspring of PGO (n=154) and normal weight (NW) without DHA supplementation (n=26) were compared. BC at birth and 4m and perinatal factors were studied in 89 children of women with PGO.
Results: More obese women exceeded the gestational weight gain (GWG) IOM guidelines (45.5% vs 23.1%, p=0.05). Skinfolds and fat% at birth were higher among PGO´s offspring (13.64% vs 10.84%, p=0.001), compared to NW. Fat% at birth was related to high birth weight and maternal obesity, corrected by sex and gestational age (GA) (R^2 0.593 $p<0.001$). Among PGO, fat% at birth was related mainly to weight-to-length ratio (r:0.833 $p<0.001$) and GA (r:0.380 p:<0.001). There was no difference in BC between PGO-DHA supplementation groups neither at birth or 4m. Fat% at 4m was related to ileocrestal skinfold thickness and weight-to-length ratio at birth and exclusive breastfeeding at 4m (R^2 0.239 p:<0.001).
Conclusions: Maternal obesity associates with higher fat% in the offspring at birth, where ileocrestal skinfold thickness could be a good early indicator of adiposity at 4 months.

DHA supplementation during pregnancy in women with pregestational obesity regulates placental expression of Folate and Vitamin B12 transporters

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Background/Aims: Pregestational obesity (PGO) is a high-risk obstetric condition and has been related with higher folate and lower vitamin B12 and DHA maternal levels. It is unknown if PGO could affect cord blood folate and vitamin B12 levels by reducing their placental transporters expression and whether maternal DHA supplementation could overpass these effects.
Method: This is a cross-sectional analysis of a subset of placental of women with PGO belonging to an ongoing double-

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blinded RCT (NTC02574767), who received 200 or 800 mg/day DHA during pregnancy (#12_n=34 or #13_n=32 indistinctively). Women with PGO (BMI ≥30 kg/m^2) PGO (G-OB_n=15 and normal weight (NW_n=31) without DHA supplementation were also included. All participants signed informed consent. Placentas were collected at delivery, and fragments from the trophoblast layer were dissected, thoroughly washed, and kept at -80°C until analysis. The mRNA expression (RT-qPCR) and protein levels (Western Blot, IHQ) of FOLR1 and CD320/TCblR were determined in placentas of all four groups. Maternal and cord blood folate and vitamin B12 levels were measured by chemiluminescence.
Results: The neonatal characteristics were not different between groups. The protein levels of CD320/TCblR were higher in PGO compared to NW (p=0.0007). In the DHA-supplemented PGO groups (#12 and #13) the expression of this B12 transporter was comparable to the NW values (p>0.05). Female placentae had higher levels of CD320/ TCblR in NW and PGO. Placentas from #12 and #13 showed lower expression of FOLR1 compared to NW and PGO and male placentas show the greatest changes among groups. Data of Folate and B12 levels are under analysis.
Conclusions: Placental folates and vitamin B12 transporters are differently regulated in PGO women compared to NW and the B12 transporter shows a relevant sex dysmorphism. Maternal DHA supplementation exerts a regulatory effect on both placental transporters possibly due to local anti-inflammatory and cell signaling effects.
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DHA supplementation in women with pregestational obesity and folate/vitamin B12 unbalance regulates lipid metabolism genes in the placenta

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Background/Aims: Pregestational obesity (PGO) has been related with alterations on placental lipid metabolism and with unbalanced folate and vitamin B12 maternal levels (high F/B12 ratio). DHA supplementation in women with PGO have maternal anti-inflammatory effects. Furthermore, an interaction between maternal folate, B12 and DHA with effects on lipid metabolism in rat liver has been evidenced. However, this interaction and its effects on lipid metabolism genes has not been studied in human placenta.
Method: In a cross-sectional study of women with PGO belonging to an ongoing double-blinded RCT (NTC02574767), who received 200 or 800 mg/day DHA during pregnancy (#12_n=34 or #13_n=32 indistinctively). Women with PGO (G-OB_n=15 and normal weight (NW_n=31) without DHA supplementation were included. Placentas were collected at delivery, trophoblast fragments were dissected, thoroughly washed, and kept at -80°C until analysis. The mRNA expression of *PPARα* and *CPT-1* (β-oxidation markers), *PPARγ* (lipogenesis marker) were evaluated by RT-qPCR. *In vitro,* Folate/B12 imbalance was assayed in trophoblast fragments of NW.
Results: In G-OB-placentas, the expression of *PPARα* and *CPT-1* was higher (p<0.02) compared to NW; the differences in CPT-1 were mostly in male. A lower expression of *PPARα* in #12 and #13 (p<0.01) *and* CPT-1 in #13 (p=0.005) compared to G-OB was observed. Oppositely, *PPARγ* expression was lower (p=0.0072) in G-OB compared to NW and increased in both DHA-supplemented groups (#12 and #13 <p=0.02) compared to G-OB. In NW cultured trophoblast fragments treated with normal folate (20 nM)/low B12 (50 nM), PPARα and CPT-1 expression was reduced (p<0.02); high folate (2000 nM)/normal B12 (500 nM), CPT-1 expression was reduced (p=0.0017); high folate/low B12 the expression of *PPARγ* and CPT-1 were reduced compared to normal folate/B12.
Conclusion: Maternal obesity induces the expression β-oxidation markers, which are partly mimicked by in vitro folate/B12 imbalance in placenta. These effects are reverted by DHA supplementation during pregnancy.
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Poverty and cognitive ageing in Europe

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Background/Aims: Cognitive aging is a life-long process that may have its roots in a disadvantaged childhood socioeconomic position. We aimed to investigate whether socioeconomic position in childhood has an effect on the level of cognitive performance and the rate of cognitive decline in older adults, testing 3 conceptual frameworks – passive cognitive reserve, active cognitive reserve or risk factors path.
Method: We performed a prospective cohort study of individuals enrolled in a multi-center population-based study Survey on Health, Ageing and Retirement in Europe (SHARE). Interviews were conducted in 6 waves at approximately 2 years intervals and included examinations of cognitive performance (memory, verbal fluency, delayed recall) and measurements on

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childhood socioeconomic position (participants' household characteristics at the age of 10 years). We estimated the associations of socioeconomic position with the level of cognitive performance using linear regression and the relation to the rate of cognitive decline with mixed-effects models.
Results: This study included 20 244 participants from 16 European countries (median age at baseline 71 years, 54% women). Adverse childhood socioeconomic position was associated with a lower level of baseline cognitive performance in a dose-response fashion. This association was attenuated after adjustment for clinical and social risk factors but remained statistically significant. Childhood socioeconomic position was not related to the rate of cognitive decline.
Conclusions: Variation in childhood socioeconomic position helps to explain differences in cognitive performance between older people, but not the rate of decline from their previous level of cognition. This is in line with the hypothesis that socioeconomic situation in childhood provides a foundation for the passive cognitive reserve. Strategies to protect cognitive health should be shifted into early life and children that are raised in poverty should be provided appropriate resources to their disadvantage so they can fully develop their potential.

Variations of Physical Activity and Sedentary Behaviors in The Middle East and North Africa: A Systematic Overview, Meta-Analysis, and Evidence Gap Mapping

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ABSTRACT
Background/Aims: Insufficient physical activity (PA) and sedentary behavior are key risk factors for noncommunicable diseases. We aimed to synthesize the evidence on PA and sedentary behaviors in the Middle East and North Africa (MENA).
Methods: We conducted a systematic overview. We searched PubMed/MEDLINE for systematic reviews (SRs) published between 2008-2017. Data on PA and sedentary behavior on the 20 MENA countries were extracted from eligible SRs and included primary studies. A random-effects meta-analysis was utilized to pool PA prevalence estimates. A Meta-regression and subgroup analyses were performed to identify factors associated with higher PA prevalence.
Results: Forty-four studies reported by five SRs and involving 78,621 participants from 13 MENA countries were included. In MENA, 53.9% of adults were sufficiently active with country-level PA pooled prevalence ranging from 35.1% in Kuwait to 85.6% in Tunisia. Among youth, the prevalence was 28.1%, with country-level pooled prevalence ranging from 8.3% in Egypt to 55.1% in Kuwait. Females and youth appear less physically active than males and adults. Validated questionnaires were associated with higher PA prevalence compared with non-validated questionnaires. A wide variability and inconsistency in sedentary behavior measurement was found. The recognition of sedentary behaviors as a public health issue in the MENA region remains unclear, mainly due the absence of guidelines for its quantification and interpretation.
Conclusion: The global epidemic of insufficient PA is also prevalent in MENA countries. Since insufficient PA is a key risk factor for lifestyle-related diseases, focused interventions should be implemented to encourage youth and adults to adhere to recommended levels of PA and reduce sedentary behavior. Limited data on PA behaviors were available for MENA countries other than the Gulf Cooperation Council countries. Measuring both behavior trends using standardized tools consistent at national and international levels, is essential to allow meaningful comparisons and implement effective interventions.

Social Circumstances And Cultural Beliefs Influence Maternal Nutrition, Breastfeeding And Child Feeding Practices In South Africa

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Background/Aims: Maternal and child undernutrition remain prevalent in developing countries with 45% and 11% of child deaths linked to poor nutrition and suboptimal breastfeeding, respectively. Maternal undernutrition during pregnancy and breastfeeding has adverse effects on child growth and development as mothers' ability to fully satisfy the needs of their infants is limited. The study sought to explore the relationship between maternal nutrition, breastfeeding and infant and young child feeding (IYCF) practices in five rural communities in South Africa. The perceptions of mothers, caregivers and grandmothers regarding mothers' eating behavior, breastfeeding and IYCF practices, and the reasons for acting in a particular way were determined.
Methods: The study used mixed methodology technique. A total of 84 household surveys pairing mother/caregiver and a child aged 0-24 months were conducted to collect data on maternal dietary diversity, child feeding and breastfeeding practices. Nine focus group discussions with 94 participants were done to obtain information on perceptions about breastfeeding, IYCF practices and eating habits for lactating mothers.
Results: Exclusive breastfeeding for the first six months of life was rarely practiced. Young children were exposed to poor-quality diets lacking essential nutrients for child growth and development. Maternal dietary diversity was very low, only 14% of women consuming a good quality diet. Both mother and child diets were dominated by starchy staples, lacking essential nutrients, especially fruits and vegetables.
Conclusions: Social circumstances including lack of income, dependence on food purchasing, lack of support from fathers, unwillingness to employ indigenous knowledge as well as cultural beliefs were the drivers of mothers' decisions regarding their eating habits, breastfeeding and IYCF practices. Paternal inclusion, promotion to safeguard indigenous knowledge on IYCF practices as well as finding a balance between mothers' income, dietary diversity, cultural beliefs, breastfeeding and considering feeling and life of lactating mothers is recommended.

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The study provides comprehensive information for South African context that can promote maternal nutrition, breastfeeding and good IYCF practices as an intervention measure to fight against malnutrition and obesity in young children.

Improving efficiency of maternal nutrition and infants' growth surveillance by midwives using electronic application

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Background/Aims: Surveillance activity for maternal nutrition and infants' growth is very important for early intervention or decision making on nutritional problems of pregnant women and infants' growth. Midwives as the primary health care provider responsible in maternal and infant health data surveillance need tools to help facilitate data reporting and reduce the time needed for data collection and analysis. This study aimed to determine the efficiency of using application compared with using pen and paper in maternal nutrition and infants' growth surveillance by midwives.
Method: After training 107 midwives to use the application, each was asked to recorded at least 10 first-trimester pregnant women aged 20–35 years and follow until their infants aged three months old. Midwives still conduct the surveillance using pen and paper, also were assigned to record the time needed to fill data in each visits for both tools. The time needed since data collection ends until the data can be accessed by researchers to be used as surveillance data for making reports were also calculated for both tools.
Results: Time needed to fill surveillance data for each visit was 30.0±1.5 minutes using pen and paper and 17.1±1.2 minutes using electronic application ($p<0.001$; paired t-test). Time needed before researcher can access the data was 3 (0–7) days for the report using pen and paper while for the report using electronic application need no time since the data was automatically uploaded and can be downloaded by the researcher in the same time as it was filled ($p=0.001$; Wilcoxon test).
Conclusions: The efficiency of using the electronic application for surveillance of pregnant women nutrition and infant's growth by midwives is better than paper-based method. The electronic application can be considered to be used in improving efficiency of the national maternal and child health surveillance to support early life nutrition.

Association between maternal weight change during the year before pregnancy and infant birth weight

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Background/Aims: Weight-control interventions in pregnant women with overweight or obesity are poorly effective on fetal growth and birth outcomes. Thus, it has been suggested that interventions or prevention programs should aim at the pre-pregnancy period. We investigated the association between weight changes over the year before pregnancy and infant birth weight.
Methods: We analysed singleton pregnancies (N= 16395) from the ELFE French longitudinal birth cohort. Maternal weight changes were self-reported and classified into 3 groups: "moderate weight variation or stable weight" (SW), "weight loss > 5 kg" (WL) and "weight gain > 5 kg" (WG). Multiple linear regression models were used to investigate the association between pre-pregnancy weight changes and birth weight, adjusted for a large set of maternal characteristics. The analyses were stratified on maternal body mass index (BMI) at conception (< 25 vs ≥ 25 kg/m^2) and further adjusted for BMI within these categories. We used the MacKinnon method to test the mediating effect of gestational weight gain (GWG) on these associations.
Results: For either BMI category at conception, GWG was more than 2 kg higher, on average, for women with WL than SW before pregnancy. For women with BMI < 25 kg/m^2 at conception, birth weight was significantly higher with WL than SW before pregnancy, but this association was totally explained by a significant mediating effect of GWG. For women with BMI ≥ 25 kg/m^2, birth weight was not associated with pre-pregnancy weight. On mediation analysis for these women, the direct effect of pre-pregnancy WL that would have resulted in a smaller birth weight was cancelled out by the GWG. We found no significant association between pre-pregnancy WG and birthweight.
Conclusions: Health professionals should be aware that GWG may offset the expected effect of weight loss before conception on fetal growth for women with overweight and obesity.

High birth weight is associated with non alcoholic fatty liver disease. Results from the French Constances cohort

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Background/Aims: Both small and high birth weight are markers of adverse intrauterine conditions that have well recognized long term consequences on cardiometabolic health. The consequences on liver disease have more recently gained awareness. Our aim was to describe the associations between birthweight and non alcoholic fatty liver disease (NAFLD) in a large sample of French young adults
Method: A random sample of adults affiliated to the main French national health insurance provider were invited to participate in the Constances cohort and to take part in a health exam. From the 160,431 subjects included between 2012 and 2018, we selected 43 828 subjects <60 years for whom recorded weight at birth was available from their personal health booklet. NAFLD were defined by a non-invasive score, the Fatty Liver Index (FLI*) > 60. Obesity was defined by a body mass index > 30kg/m^2. The association with birthweight (BW) categorised in sex specific centiles was investigated with age-adjusted logistic regression separately in men and women, after additional exclusion of 1065 subjects with history of hepatitis or self-declared alcohol intake missing or respectively > 30 and 20 g/day.
Results: Mean age (sd) was 38 (1) yrs. Prevalences of obesity and NAFLD were respectively 8.5% and 12.8%. Compared to subjects with BW 25^{th}-50^{th} percentiles, OR for NAFLD for those with BW < 5^{th} were 1.01, 95% confidence interval (0.81 ;1.29) for men and 1.19 (0.95;1.48) for women. Compared to the same reference group, women with BW > 95^{th} percentile had an increased OR for NAFLD: 1.40 (1.08;1.1.81)). The corresponding OR for men were 1.17 (0.98;1.40)
Conclusions: Our results show that high birth weight is associated with an increased risk of NAFLD especially in women. The increased obesity prevalence associated with high birth weight probably explains in part its association with NAFLD. The association between birthweight and a non invasive score predicting hepatic fibrosis in subjects with NASH will be further investigated.
*Bedogni G et al; BMC Gastroenterol. 2006;6(1):33

Hyperglycemia altered DNA methylation status and impaired pancreatic differentiation of human embryonic stem cells

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Background/Aims: The prevalence of diabetes has quadrupled since 1980 to more than 400 million people worldwide. Fetal exposure to maternal diabetes was correlated with higher prevalence of impaired glucose tolerance and type II diabetes (T2D) later in life. Previous studies showed aberrant DNA methylation patterns in pancreas of T2D patients. In addition, intrauterine hyperglycemia altered DNA methylation status of the placenta related to insulin and diabetes signalling. It is hypothesized in this study that maternal hyperglycemia during early embryo development dysregulated human fetal pancreatic development through aberration of DNA methylation pattern.
Method: Human embryonic stem cell (hESC) line, VAL3, was used as an in-vitro model. To simulate hyperglycemic intrauterine environment, VAL3 was cultured under hyperglycemic condition. The genome-wide DNA methylome profiling of VAL3 cultured in different conditions was performed using reduced representation bisulfite sequencing. The DNA methylation status was further validated by gene-specific bisulfite sequencing. VAL3 at different conditions were differentiated into pancreatic progenitor cells using commercially available differentiation kit (STEMCELL Technologies).
Results: Global DNA methylome profiling showed 1,391 differentially hypermethylated and 1,284 hypomethylated CpG sites in VAL3 cultured under hyperglycemic condition. Gene ontology analysis revealed that hypermethylated genes were enriched for embryonic morphogenesis and cell fate specification; while hypomethylated genes were enriched for processes like cell adhesion and cell cycling. Among the promoter-associated genes, NKX6-2 was validated to be hypermethylated in VAL3 under hyperglycemic condition. Interestingly, the hypermethylation status of NKX6-2 maintained upon differentiation into pancreatic progenitor (PP) cells. Concordantly, PP differentiation under normal glucose level was impaired in the hyperglycemic-treated VAL3.
Conclusions: Early embryonic exposure to hyperglycemic condition led to persistent hypermethylation of pancreatic gene NKX6-2 and impairment of early pancreatic differentiation.

Childhood Psychological Violence Victimization Experiences And Its Associations With Health-Related Risk Behaviors In Adolescents

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Background/Aims: To investigate the prevalence of childhood psychological violence (CPV) victimization and to explore the associations of CPV victimization experiences with health-related risk behaviors in adolescents.
Method: A self-administered questionnaire survey was conducted anonymously in students from two colleges in Beijing and Henan provinces.

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Results: Of 1355 students surveyed, 41.6% (males 43.0%, females 40.4%) reported that they had experiences of CPV victimization, exerted by their parents or other adults in the family, before the age of 16. Logistic regression analysis indicated that, compared with respondents who reported no CPV victimization experiences, those who reported CPV victimization experiences were at significantly increased risk of some health-related risk behaviors, e.g. feeling sad or hopeless, suicidal ideation, getting drunk, and fighting during the past 12 months.
Conclusions: The association of CPV victimization experiences with adolescents' risk behaviors highlights the needs to develop programs of preventing psychological violence against children, to increase the public awareness and help parents learn parenting skills and use nonviolent child discipline.

Association of Pre-pregnancy Overweight and Obesity with Pregnancy Outcomes – Findings from the Maternal and Infant Cohort Study (MICOS) Malaysia

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Background/Aims: While about half of the Malaysians were overweight and obese, there were increased number of women with overweight and obesity problem enter their pregnancy. Hence, this Maternal and Infant Cohort Study (MICOS) aimed to determine the impact of pre-pregnancy overweight and obesity among women at third trimester of pregnancy.
Method: A total of 416 women who attended the selected maternal and child health clinics in Selangor and Kuala Lumpur, Malaysia were enrolled in this study. Information on maternal complications during pregnancy included gestational diabetes mellitus (GDM), hypertension (HPT), excessive gestational weight gain (GWG), and pregnancy outcomes included preterm birth (PTB), low birth weight (LBW), and delivery method were obtained from the health record books. The pregnant women self-reported their pre-pregnancy weight and height, and their body mass index was calculated to determine their pre-pregnancy body weight status.
Results: About two in five of the women were overweight/obese before pregnant (41.1%), 19.2% with GDM, and 2.9% had HPT during pregnancy, and 30.3% gained weight excessively. About one quarter of the infants were delivered via cesarean section (27.4%), 7.0% were pre-term, and 8.8% had low birth weight. Pre-pregnancy overweight/obesity was associated with higher risk of GDM (OR=1.666, 95%CI=1.020-2.720), HPT (OR=16.775, 95%CI=2.145-131.196), excessive GWG (OR=3.120, 95%CI=2.023-4.811), and cesarean delivery (OR=1.570, 95%CI=1.017-2.720). No significant associations were found for PTB and LBW with pre-pregnancy overweight and obesity.
Conclusions: Unhealthy maternal weight before pregnancy has been linked to multiple adverse obstetric and fetal outcomes. About two in five of the pregnant women were overweight or obese before pregnant. Maternal overweight/obesity is associated with increased risks of GDM, HPT, excessive GWG, and Cesarean delivery, which underline the importance of targeting these women for pre-conception counselling on weight management.

How Do Parental Characteristics Affect Adolescent Diet And Physical Activity In Mumbai Slums?

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Background: The Mumbai Maternal Nutrition Project (MMNP) was a randomised controlled trial of a micronutrient rich food supplementation to women preconceptionally and throughout pregnancy to improve children's cardiometabolic health and neurodevelopment. 6513 women were randomised from slums of Mumbai and 1962 women delivered live singleton newborns. Supplementation increased birthweight and reduced gestational diabetes mellitus. A subsample of these offspring are being followed-up (N=300) at 10-12y to examine the association of maternal nutritional supplementation with offspring stress responses. Parents' education and socioeconomic status influence their children's diet. Physical inactivity and increased consumption of junk foods are associated with obesity. Obesity is a predisposing factor for many non-communicable diseases. In the current study we will assess dietary patterns and physical activity (PA) among these children and examine their associations with parental attributes.
Methods: Dietary intake of adolescents (n=300) is assessed using a semi-quantitative food frequency questionnaire (FFQ). PA is measured using the International Physical Activity Questionnaire (IPAQ). In a subgroup (N=50), accelerometers (MTI Actigraph) are used to measure PA objectively over 7 days. IPAQ and Actigraph data will give self-rated and objective measures respectively of time spent in sedentary, moderate or vigorous intensity activities. Associations of parental exposures with dietary intakes and PA of adolescents will be analysed using regression analysis.
Results: Data have so far been collected from 24 children. The accelerometers are acceptable to the children, and have obtained good quality data.
Conclusion: Data collection is ongoing and will complete in June 2019. This study will guide us in planning and targeting effective strategies to promote healthy diets and PA among adolescents.

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Influence of maternal ethnicity on placental pathology of stillbirths and small babies

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Background: Maternal ethnicity has been linked to differences in pregnancy, and perinatal outcomes. In a separate abstract, we present the relationship between maternal ethnicity and neonatal outcomes of small for gestational age (SGA) babies. In this study, we studied the influence of maternal ethnicity on placental pathology of stillbirths and SGA babies.
Methods: We conducted a retrospective cohort study, comparing the placental pathology reports of stillborn and SGA babies born across a large metropolitan hospital network in 2015. Univariate analysis was used to compare macroscopic and microscopic placental characteristics between babies born to mothers from Australia or New Zealand (ANZ), or to mothers born in South Asia (SA).
Results: Three hundred and eleven SGA babies and 26 stillbirths were included. Demographic differences between ANZ and SA mothers were similar to previous reports. Data is presented below as mean (SD) or n (%).
Conclusions: Despite differences in maternal demographics, there were no significant differences seen in placenta pathology by maternal ethnicity, but there were differences in placental pathology seen between SGA babies and stillbirths. Growth restriction seems to be associated with a similar placental pathology, in these ethnically diverse populations.

Endocrine Zone Overgrowth In The Mouse Placenta Impacts The Metabolic Health Of Adult Offspring

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Background/Aims: Alterations in the endocrine and nutritional state of the mother during pregnancy are known to programme changes in the metabolic health of offspring postnatally. However, little is known about the role of the placenta, which regulates the endocrine and nutritional environment of the fetus *in utero*, in the metabolic health outcomes of offspring. This study aimed to assess the effect of genetically-induced overgrowth of the mouse placental endocrine zone (junctional zone, Jz) on offspring metabolic health with a chow and obesogenic diet postnatally.
Method: Overgrowth of the placental Jz was achieved through conditional overexpression of the growth gene, *Igf2* (Jz *Igf2*-OE). Female mice in which the DMR of the *H19-Igf2* locus is flanked by LoxP were mated with Tpbpa-Cre males to achieve Jz expansion. Litters were delivered naturally and reduced to 3 males and 3 females on postnatal day 3. Offspring were weaned at three weeks of age and fed either a chow or obesogenic diet. At 16 weeks of age one female and one male offspring received either an insulin or glucose tolerance test and adipose tissue weights recorded one week later. Findings were compared to offspring born from the reverse parental cross (no change in Jz-*Igf2*).
Results: Both female and male Jz *Igf2*-OE adult offspring had decreased adiposity on a chow diet compared to controls. Male Jz *Igf2*-OE offspring on a chow diet were less sensitive to insulin compared to control offspring, and increasingly so on an obesogenic diet. Conversely, female Jz *Igf2*-OE offspring on an obesogenic diet were more tolerant to glucose than control offspring on an obesogenic diet.
Conclusions: Altered placental endocrine function programmes changes in adult offspring metabolic health in a sex-dependent fashion. The molecular mechanisms underlying the sexually dimorphic programming of the offspring as a result of placental endocrine malfunction are currently being explored.

	SA SGA live born, n=171	SA stillbirths, n=13	ANZ SGA live born, n=140	ANZ stillbirths, n=13
Birth weight, gms	2582 (316)	1138(1417)	2497 (351)	1258 (1149)
Gestation, wks	38.7 (1.6)	26.5 (7.1)	38.3 (1.7)	27.8(6.5)
Placental weight, gms	376 (72)	220 (140)	382 (77)	239 (116)
Cord length, mm	329 (105)	251 (207)	320 (107)	301 (117)
Cord abnormalities	45 (26)	-	26 (18)	-
Significant placental pathology	138 (80)	12 (92)	113 (80)	13 (100)

Differences in microscopic placental characteristics of SGA babies and stillbirths, including chorionic plate anomalies, placental fibrin, indentations, parenchymal thrombus, villi maturation, villitis, villous infarcts and agglutination were identified. Maternal ethnicity did not contribute to placental differences observed between groups.

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Addition of Anthropometry to HbA1c Improves Screening for Dysglycaemia in Asian Women Preconception: The S-PRESTO Cohort

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Background/Aims: HbA1c is a common screening test for dysglycaemia despite poor sensitivity, but few studies have evaluated its performance vs. standard anthropometric measures in predicting dysglycaemia in women of reproductive age. We evaluated the discriminative ability of anthropometry and HbA1c in screening for dysglycaemia among Asian women preconception.
Method: In the Singapore PREconception Study of long-Term maternal and child Outcomes (S-PRESTO) cohort, Chinese, Malay, Indian women aged 18-45 years trying to conceive were recruited from the community and largest public maternity unit in Singapore. Anthropometric (weight, height, waist & hip circumferences, 4-site skinfold thicknesses), HbA1c measures, and a 75-g oral glucose tolerance test were performed. The associations of anthropometry and HbA1c with dysglycaemia (diabetes and pre-diabetes) were assessed by multiple regression and area under receiver-operating characteristic (AUROC) curve.
Results: Among 971 women, 106 (10.9%) had dysglycaemia. Adjusting for sociodemographic and medical history, dysglycaemia was most strongly associated with BMI (Odds ratio [OR]=1.62 [95% CI 1.32-1.99]), waist-to-height ratio (OR=1.74 [1.39-2.17]) and total skinfolds (OR=2.02 [1.60-2.55]); each demonstrated similar sensitivities, specificities, and AUROC, but none outperformed HbA1c (OR=4.09 [2.81-5.94]). A body shape index (ABSI) showed no association with dysglycaemia. As continuous variables, the performance of the above anthropometry trio with HbA1c to detect dysglycaemia (AUROC=0.80 [0.75-0.85]) was comparable to HbA1C alone (AUROC=0.79 [0.74-0.84]). Using clinically-defined thresholds, the anthropometry trio and HbA1c≥5.7% in combination (AUROC=0.75 [0.69-0.8]) outperformed HbA1c≥5.7% alone (AUROC=0.71 [0.65-0.76]). Without consideration of history, as in common clinical practice, the performance of BMI≥23kg/m^2 combined with HbA1c≥5.7% (AUROC=0.70 [0.64-0.75]) showed even greater improvement over HbA1c≥5.7% alone (AUROC=0.61 [0.57-0.65]).
Conclusions: Addition of anthropometry to HbA1c improves screening for dysglycaemia in Asian women preconception. Adding BMI alone to HbA1C is easily incorporated into current clinical practice but the cost-benefit of introducing non-routine measures into practice needs to be evaluated.

High Placental Inositol Content May Protect the Fetus from Pro-Adipogenic Effects of Maternal Glycaemia

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Background/Aims: Maternal glycaemia across the continuum promotes fetal adiposity. Inositol, an insulin sensitizer and key component of intracellular signalling pathways, is being tested for prevention of gestational diabetes. We identified factors associated with placental inositol content and assessed whether placental inositol could modify the fetal pro-adipogenic impact of maternal glycaemia.
Method: Maternal fasting (FPG) and 2-hour (2hPG) plasma glucose were assessed during a 75g oral glucose tolerance test around 26 weeks' gestation and placental inositol was quantified by liquid chromatography-mass spectrometry in 885 term placentae from the GUSTO mother-offspring cohort. Neonatal skinfold thicknesses (subscapular and triceps) were measured 1-3 days post-delivery. Subcutaneous and internal abdominal adipose tissue (AAT) volumes were measured in a subset of 262 neonates using MRI. Multiple linear regression analysis was performed.
Results: Higher 2hPG, lower gestational age, absence of tobacco exposure, vaginal delivery and longer timing of placental collection postpartum were associated with lower placental inositol. Placental inositol showed inverted U-shaped (quadratic) associations with birthweight (p=0.020) and sum of skinfolds (p=0.007), and there were significant interactions between placental inositol and maternal FPG in relation to birthweight and AAT. To evaluate whether placental inositol modulated the effects of maternal FPG on offspring adiposity, analyses were stratified according to inositol tertiles. FPG was positively associated with birthweight and AAT volume within the lowest [β (95% CI): birthweight 176.25g/mmol glucose (82.82, 269.69), total AAT 21.30ml/mmol glucose (13.37, 29.24)] and middle [birthweight 195.13g/mmol (96.96, 293.30), total AAT 19.98ml/mmol (10.22, 29.74)] inositol tertiles but not in the highest inositol tertile [birthweight 86.58g/mmol (-15.51, 188.67), total AAT -0.23ml/mmol (-9.45, 8.99)].
Conclusions: A high placental inositol level may protect the fetus from pro-adipogenic effects of maternal glycaemia. Studies are needed to see if inositol supplementation in pregnancy can increase placental inositol content and reduce fetal adiposity.

An Evolutionary Perspective Highlights Morning Sickness as a Proximate Mechanism for Allocating Resources to the Fetus and Placenta

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Background/Aims: An increased placental weight relative to birth weight has been associated with a higher risk of adult diseases such as diabetes and hypertension. However, universal proximate mechanisms that reduce the nutrient supply to the fetus remain elusive. This study uses an evolutionary framework from life history theory to explore severe morning sickness as a potential mechanism that allocates resources to the fetus. One life history theory model predicts that in more risky and uncertain environments, it may be adaptive for an individual to accelerate reproductive timing and produce more offspring, ultimately investing fewer resources in each. Here, severe morning sickness is presented as a proximate mechanism that may reduce investment during pregnancy.
Method: An observational study of 663 first time mothers who were recruited in antenatal classes. Maternal characteristics and life-course demographics were collected via questionnaire administered during pregnancy. Hyperemesis, other conditions of pregnancy, birth characteristics, depression and medication use were extracted from the medical records. Placental weight was recorded after delivery.
Results: Hypermesis was associated with a higher placental weight (mean diff = 39 grams, p=0.006) and placental weight to fetal weight ratio (mean diff = .011, p<0.0005), but not birth weight. In regression models, a range of factors across the lifespan predicted morning sickness and placental weight. These included higher maternal birth weight, increased childhood stress (0-15 years), younger maternal age, higher BMI, more symptoms of depression and medication use during pregnancy. Alternate factors that influence the fetal supply line including maternal smoking, low iron stores, pregnancy induced hypertension and medically assisted reproduction are briefly examined.
Conclusions: This study suggests morning sickness may be usefully considered within an evolutionary perspective as a mechanism that influences the allocation of resources to the fetus and placenta during pregnancy.

Intergenerational influences on breastfeeding rates in Perth, Western Australia

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Background/Aims: Breastfeeding is a highly evolved biological mechanism with proven positive effects on the health status of mothers and infants. But it has been rendered complex in societies with a strong influence of western medicine and heavy marketing of infant formula. While the factors affecting rates of breastfeeding vary widely, grandparents remain a source of influence across time and cultures.
Method: A qualitative study of 73 adults from 17 focus groups was conducted in Perth, Western Australia. Different family member types were present in each focus group. Transcribed data from the focus groups were coded in vivo and analysed using an interpretative phenomenological framework.
Results: grandparents' breastfeeding experiences, beliefs and attitudes influenced parents' expectation to successfully breastfeed. In cases where grandmothers failed to breast feed, mothers found it easier to justify formula feeding their infants.

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Grandparents, while agreeing that breast feeding was best for infants said as parents they were curtailed by the inability to feed in public. The lack of commercially produced infant foods was a source of anxiety for grandmothers when efforts to breastfeed failed, which often led to early introduction of solid foods. Grandparents' experience contrasts with the challenges faced by parents today as mothers are forced to return to work, and the abundance of commercial infant food means failure to initiate and sustain breastfeeding has a relatively easier solution.
Conclusions: The intergenerational influence on breastfeeding seen in this study sample underscores the importance of breastfeeding education and support for parents to ensure future generations benefit from this unique mammalian trait.

Impact of intrauterine growth restriction (IUGR) on cortical development in the neonatal and adolescent rat

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Background/Aims: IUGR is associated with impaired brain development and cognitive functioning. The neocortex - part of the brain controlling higher order processes - developsin a highly structured manner, and disturbances to the formation of the neocortex have implications in many neuropsychiatric disorders. However, whether IUGR interferes with this process is not yet known. This study aimed to determine if cortical development is impaired following IUGR.
Method: Pregnant Wistar rats underwent bilateral uterine vessel ligation (BUVL; n=11) or sham (n=9) surgery at embryonic day (E) 18 to produce IUGR or control pups. At postnatal day (P) 1, pups from BUVL surgeries were classified as IUGR if their body weight was 2 standard deviations below mean control weights. Brains were collected and weighed at either neonatal (P7, control n=4; IUGR n=6) or adolescent (P45, control n=10; IUGR n=11) timepoints. Immunostaining for Ctip2 (layer V-VI; predominantly layer V corticospinal projection neurons) and Satb2 (layer II-VI; predominantly layer II-III corticocallosal projection neurons) were assessed in motor (MOT), somatosensory (SOM) and auditory (AUD) cortices at the level of the dorsal hippocampus. Data were analysed using Prism 7.0. A two-way ANOVA with Bonferroni post-hoc testing was used, with a significance level of $p<0.05$
Results: At P7, IUGR rats weighed less than sham rats ($p=0.024$), but IUGR weights had normalised to controls at P45. Brain weight and cortical thickness was not different between IUGR and control rats at both ages. At P7 there was an increase in the density of Satb2+ve (SOM, p=0.0013; AUD, p=0.0043) and Ctip2+ve (SOM, p=0.0008; AUD, p=0.0004) cells in IUGR compared to control pups; there was no difference in the motor cortex. At P45, there was a reduction in the density of Satb2+ve cells in the IUGR cerebral cortex overall (p=0.04), but this was not specific to any region; there were no differences in Ctip2+ve cells between groups.
Conclusions: IUGR results in an increase in corticospinal and corticocallosal projection neurons in the cerebral cortex of the neonate. Although these numbers are somewhat restored (or reduced) in adolescents, this could influence connectivity and possibly lead to cortical dysfunction. Analysis of other neuronal populations and the neurobehavioural implications of these findings need to be assessed.

Preterm birth is associated with increased blood pressure in young adult women

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Background/Aims: While there is some evidence of elevated blood pressure later in life in preterm survivors, data on adult women are still lacking. Thus, we assessed the associations between preterm birth and blood pressure in young adult females.
Methods: We studied 5,973 young adult women who volunteered to military service in Sweden between 1990 and 2007. Anthropometric and clinic blood pressure data were collected during the medical examination at the time of conscription.
Results: There was a progressive decline in systolic and diastolic blood pressures, as well as in mean arterial pressure with increasing gestational age. Women born preterm had an adjusted increase in systolic blood pressure of 3.7 mmHg and mean arterial pressure of 1.9 mmHg compared with young females born at term. Rates of systolic hypertension were also considerably higher in young women born preterm (14.0% vs 8.1%, p<0.0001), as were rates of isolated systolic hypertension. The adjusted relative risk of systolic hypertension in women born preterm was 1.76 (95% CI 1.30, 2.37) that of women born at term or post-term, but there was no detectable difference in the risk of diastolic hypertension (adjusted relative risk 1.66; 95% CI 0.51, 5.41).
Conclusions: Young adult females born preterm display elevated systolic blood pressure and an increased risk of hypertension compared to peers born at term.

Increased risk of visual and hearing impairments in young adult males born preterm

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Background/Aims: We examined the association between preterm birth and visual and hearing impairments among young adult males. Further, we assessed the co-occurrence of visual and hearing impairments with low intelligence quotient and poor psychological performance.
Methods: Participants were 522,410 Swedish male conscripts (~18.2 years) examined in 1991–2007, grouped according to gestational age: very preterm (<32 weeks of gestation), moderately preterm (32–36 weeks), term (37–41 weeks), and post-term (≥42 weeks). Severe visual impairment was defined as uncorrected acuity of ≤0.1 in both eyes as per decimal notation; three-frequency hearing loss was inability to detect ≤20 dB at 0.5, 1.0, and 2.0 kHz in either ear.
Results: The adjusted relative risk (aRR) of any visual impairment in men born very preterm was 1.09 times higher than for those born at term, while the aRR of severe visual impairment was 1.25 times higher. For men born very and moderately preterm, the aRR of any hearing impairment was 1.24 and 1.08 times higher, respectively, than for those born at term, and the aRR of having three-frequency hearing loss was 1.76 and 1.14 times higher, respectively. Importantly, the aRR of sensorial deficits co-occurring with low intelligence quotient and poor psychological performance was 3.07 and 1.41 times greater for men born very preterm and moderately preterm, respectively, compared to those born at term.
Conclusions: Young males born preterm were more likely to experience vision and hearing deficits, and had a markedly increased risk of additionally having low intelligence quotient and poor psychological performance.

Maternal overweight/obesity is associated with markedly greater odds of obesity in the offspring at 20 years of age in Thailand

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Background/Aims: Worldwide, there is an increasing number of women entering pregnancy with obesity. Maternal obesity is associated with increased risk of adverse pregnancy and neonatal outcomes. There is increasing evidence also showing long-term adverse effects in the offspring. We examined associations between maternal BMI early in pregnancy and offspring obesity risk and cardiometabolic health.
Methods: Participants were the offspring from the Chiang Mai very-low-birth-weight study (1989-1990), where pregnant women were recruited at their first antenatal visit in. From the 632 offspring followed up ~20 years later, we studied 565 individuals (53.8% females) born at term (37–41 weeks of gestation), aged ~20.6 years. Assessments included anthropometry, lipid profile, clinic blood pressure, and insulin resistance assessed using HOMA-IR. Overweight/obesity was defined as BMI ≥25 kg/m^2; obesity as ≥30 kg/m^2.
Results: Increasing maternal BMI at the first-antenatal visit was associated with increasing BMI in the offspring [β=0.43 (95% CI 0.29, 0.57); p<0.0001). Further, every 1 kg/m^2 increase in maternal BMI was associated with adjusted odds ratio (aOR) of obesity 23% greater in the offspring (95%CI 6.1, 41.9%; p=0.006). Thus, the offspring of mothers who were overweight and/or obese early in pregnancy had odds nearly 5 times greater of obesity [aOR 4.88 (95% CI 1.74, 13.75); p=0.003). There were however, no observed associations with cardiometabolic outcomes.
Conclusions: Maternal overweight/obesity early in pregnancy associated with a marked increase in the odds of obesity in the offspring. Public health measures should target women of reproductive age, encouraging healthier lifestyle choices prior to pregnancy.

Potentially modifiable determinants of obesity and adiposity in children of obese mothers

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Background/aims: Children of obese mothers are at an increased risk of obesity. In this study we have investigated relationships between dietary intake, eating behaviours and body composition in a cohort of 3-year-old children born to mothers who participated in the UPBEAT study: a lifestyle intervention targeting maternal diet and physical activity in 1555 obese pregnant women.
Method: Children's dietary intake and eating behaviour was assessed using an 86-question Food Frequency Questionnaire (FFQ) and the Children's Eating Behaviour Questionnaire (CEBQ), respectively. Body composition was assessed by WHO z-scores, sum of skinfolds (SSF), waist and arm circumferences. The FFQ was reduced to 39 food groups and factor analysis was performed to define the dietary patterns. Using linear regression, we examined relationships between: (1) body composition and the dietary patterns and (2) body composition and CEBQ scores for satiety (SR), food responsiveness (FR), slowness in eating (SE) and enjoyment of food (EF).

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Results: Four-hundred and ninety children had complete FFQ and CEBQ data, average age 3.5 years ±3.3 months; Three distinct dietary patterns were defined; "healthy/prudent", "African/Caribbean" and "processed/snacking". In an adjusted linear regression model, the "processed/snacking" pattern was associated with an increased odds of childhood obesity (WHO BMI z-score >2SD); odds ratio 1.46; 1.04 to 2.03, p=0.02. The "healthy/prudent" and "African/Caribbean" patterns were associated with a lower SSF (p<0.03). Enjoyment of food was associated with an increase in arm and waist circumferences, weight-for-age (WAZ) and weight-for-height (WHZ) z-scores (p<0.05). Satiety and slowness in eating were associated with reduced arm and waist circumferences, BMI z-score, WAZ and WHZ (p<0.05).
Conclusion: In at 3-year old children born to obese women of ethnic diversity from UK inner-city settings, a "processed/snacking" diet, defined as a diet high in confectionary, crisps, processed foods, chips, cakes and biscuits was associated with a higher odds of being obese. In contrast slowness in eating was associated with protection against increased adiposity. Theses represent modifiable behaviours in high risk children which could be assimilated into public health strategies for prevention of childhood obesity.

Relationships between maternal body mass index and plasma biomarkers with childhood body mass index and adiposity at 6 years; the Children of SCOPE study

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Background/Aims: Maternal obesity has been implicated in the origins of childhood obesity through a sub-optimal environment in-utero. We examined relationships of maternal early pregnancy body mass index (BMI), overweight/obesity and plasma biomarkers with measures of childhood BMI and adiposity.
Methods: BMI z-score, sum of skinfold thicknesses (SST), body fat percentage (PBF, by bioelectrical impedance), waist, arm and hip circumferences were measured in 1,173 6-year-old children of nulliparous pregnant women in the SCOPE study, New Zealand. Relationships of maternal early pregnancy (15 weeks' gestation) BMI and 15 biomarkers with these childhood anthropometric measures were assessed by linear regression, with appropriate adjustment for confounders.
Results: Higher maternal BMI was associated with higher child BMI z-score, SST and PBF (all p<0.001). 28.1% of mothers were overweight and 10.1% obese and compared with normal weight mothers, the PBF of their children were 5.3% higher [0.16 SD (95% CI 0.04 to 0.29) p=0.01] and 7.8% higher [0.27 (0.08 to 0.47) p=0.006], respectively, with comparable values for BMI z-score, arm, waist and hip circumferences. Maternal plasma placental growth factor (PlGF) was independently associated with higher child's SST, BMI z-score, hip circumference and PBF. None of the maternal metabolic or inflammatory maternal biomarkers were associated with childhood obesity.
Conclusion: In this contemporary large prospective cohort study with in depth maternal/childhood phenotyping and a high incidence of maternal overweight/obesity, we found independent relationships of maternal BMI with childhood BMI and adiposity. Similar associations were observed with PlGF which may imply a role for placenta function in offspring adiposity development.

POHaD: Paternal Origins of Health and Disease. Impact of environmentally-relevant contaminants on the spermatogonial stem cell epigenome and transcriptome

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Background/Aims: Environmental contaminants, including persistent organic pollutants (POPs) and methyl-mercury (CH_3Hg), are ubiquitous worldwide and have been associated with pathologies, developmental anomalies and epigenetic changes following both *in utero* and adult exposures. Although maternal exposures influence offspring health, perturbation of the paternal germline is also of concern as it may impact the development of offspring and subsequent generations. Moreover, the impact of multiple pollutants simultaneously remains poorly established. Finally, a strategy to reduce the negative impact of such pollutants is desirable.
Method: To fill these research gaps, we used mouse spermatogonial stem cells (SSCs) as an *in vitro* model to test three hypotheses pertaining to paternal transmission of environmental exposures:
1-An environmentally-relevant POPs mixture ± CH_3Hg perturbs SSC proliferation.
2-POPs+CH_3Hg synergistically disrupt the SSC transcriptome and epigenome.
3-Pollutant-induced phenotypes are offset by omega-3 fatty acids (n-3).
Results: Time- and dose-dependent experiments showed that POPs reduce SSC proliferation while n-3 has no effect ($n = 3$; $P < 0.01$). CH_3Hg increases SSC proliferation until 50 nmol/L $n = 3$; $P < 0.05$) but reduces proliferation at 100 nmol/L ($n = 3$; $P < 0.01$). Surprisingly, a combination of POPs+ CH_3Hg at levels below regulatory recommendations, similar to those observed in European and Canadian

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populations, increased proliferation ($n = 3$; $p < 0.001$). These effects are prevented by n-3 ($n = 3$; $p < 0.05$). Transcriptomic analysis further demonstrated that n-3 partially restore gene expression, while chromatin immunoprecipitation revealed that H3K4me3, H3K27me3 and H2A.Z variant are modulated corresponding to gene expression.
Conclusions: Together, these results support all three hypotheses. Environmentally-relevant contaminants synergistically disrupt the epigenome and transcriptome of SSC, which could explain paternally-mediated effects on offspring development and challenge the relevance of regulatory agency guidance values. Moreover, n-3 may be a nutri-epigenetic strategy to protect or reverse SSC from these perturbations.

The ORIGINS Project: Harmonising data across multiple cohort studies

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Background/Aims: The ORIGINS Project aims to improve the health and quality of life of the next generation through a better understanding of how to optimise the early environment. As well as facilitating strategic long-term research capacity, ORIGINS is a pipeline for short-term productivity through clinical trials, early interventions, mechanistic studies, and targeted research questions. While ORIGINS is a community Project, it aims to address the rising global burden of non-communicable diseases. Collaboration nationally and internationally will enable harmonisation of multiple data collections and testing of interventions in different population groups.
Method: ORIGINS is building a world-class Research Platform: the ORIGINS biobank and databank consist of biological samples, routine data and web-based questionnaires assessing physical and mental health, diet, physical activity patterns and a range of environmental factors. The Project is recruiting 10,000 families capturing their data over 10 years; to date we have recruited almost 2,000 families, collected over 3 million data points and 80,000 aliquots of blood and other biological samples. ORIGINS is working with national and international early life cohort studies to harmonise data and biological sample collections to provide researchers with extensive metadata across multiple timepoints.
Results: Nationally, ORIGINS is collaborating with the Raine Study (WA) and GenV (Victoria) to curate and harmonise multiple data fields, using techniques such as ontology mapping. Internationally, ORIGINS has linkages with new interventional cohorts such as the Born in Bradford's Better Start (United Kingdom). Repeated observational measures and testing interventions from pregnancy through to early childhood, across multiple cohorts, provides extensive opportunities for early detection and intervention.
Conclusion: Population-based longitudinal, interventional cohort studies provide an ideal platform to conduct numerous scientifically robust studies and translational impact for future generations.

The ORIGINS Project: The development phase of a decade long pregnancy intervention cohort

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Background/Aims: There is a pressing need to understand how the modern environment is contributing to the unsustainable health burden of non-communicable diseases. The ORIGINS Project is a pregnancy intervention cohort that aims to develop a robust data bank and biobank repository of information, utilise new technologies, initiate and integrate harmonised nested trials.
Method: The ORIGINS Project commenced in January 2017; it aims to recruit 10,000 women and their partners early in pregnancy over a 5-year period, and follow their children for a further five years. The Project provides real time feedback to participants on a number of health issues and encourages interventions. Biological samples, routine data and web-based questionnaires are collected at a range of time points. We have recently completed the initial, 'development phase' of the decade long Project. During this phase we commenced, assessed and reviewed Project processes, capturing information and integrating across multiple systems along with developing strong and critical partnerships.
Results: Currently we have recruited nearly 2,000 families, which includes 600 participating fathers, have collected over 3 million data points and 90,000 aliquots of biological samples in our databank and biobank respectively. Over 1,500 babies have been born and over 350 have attended their one-year check clinical assessment, including integrated and harmonising ten nested Sub projects. Updated profile of the cohort will be presented which includes their clinical data, physical, mental, emotional, nature relatedness and real time feedback to participants including the flow on effect of community engagement.
Conclusion: ORIGINS is a novel approach to implementing a community interventional cohort with an emphasis on pregnancy and the early years. The inclusion of real time feed back with nested clinical trials, provides a novel way to develop future cohorts that will increase research capacity, productivity, collaboration and translational impact for future generations.

Influence of Birth, Childhood and Current Size on Blood Pressure in Australian Young Indigenous adults

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Background/Aims: Cardiovascular disease (CVD) is the leading cause of death in Indigenous Australians. Hypertension is the most common CVD and is a major risk factor for chronic diseases such as coronary heart disease, stroke and kidney failure. It is estimated that at least 75% of the incidence of hypertension is related directly to obesity.
Method: Prospective Aboriginal Birth Cohort (n 686), with follow-ups at mean age 11.4yrs (childhood; n 571), 17.8yrs (adolescence; n 469) & 25.4yrs (adulthood; n 459). Birth; accurate gestational age (Dubowitz; n 671) and weight used to calculate small for gestational age (SGA; <10th centile). Face-to-face follow-up including height, weight, body mass index (BMI), waist, hip, mid upper arm circumference, blood pressure, smoking status and area of residence (remote or urban).
Results: One in five (20.4%) babies were born SGA (males 68, females 69). In childhood, adolescence and young adulthood, SGA babies were smaller than non-SGA on all anthropometric markers. By young adulthood, 8 people had a past history of hypertension and a further 12 had elevated BP (systolic>140 &/or diastolic>90). In young adulthood, females had a lower BP than males (mean systolic 105 vs 118; diastolic 69 vs 74), with lower BP in remote residing. SGA was not associated with BP in childhood, adolescence or young adulthood. Current BMI was significantly associated with BP (diastolic and systolic) at each time point (childhood, adolescence and young adulthood). This association remained on adjustment for gender, remoteness and smoking status (adolescence and young adulthood).
Conclusions: Birth size has been shown to increase the risk of chronic diseases such as hypertension in adulthood. However, in this study current size had the strongest influence from childhood into young adulthood. Rates of obesity in this cohort remain lower than national rates, and lowest in those born SGA. This may, in part, explain the lack of association seen between SGA and adult BP. Rates of obesity are rising, and this is reflected in an increase in hypertension rates.

Undernutrition in lactation increases brown adipose tissue in rat-offspring, which may block obesity onset

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Background/Aims: Nutritional insults in early life is a risk to impair autonomic nervous system function. Brown adipose tissue (BAT) as a thermogenic tissue through the sympathetic nervous system controls body energy. We aimed to assess the sympathetic activity by BAT in adult rat-offspring whose dams underwent food restriction in lactation.
Methods: Control dams were fed ad libitum throughout lactation, whereas food restricted group received 50% of diet (FR50 group) until the day 14th of lactation. At 21-days-old, the rat-offspring were weaned, and then fed ad libitum until 100-days-old, where body weight and food intake were assessed each two days. At 100-days-old, the food intake during dark-cycle (from 6 PM to 11 PM and 6 PM to 6 AM) was evaluated and after that rats were euthanized and had tissues removed to body composition analyzes. The weight of BAT was quantified as a marker for sympathetic nervous activity.
Results: In relation to control rats, the area under the curve (AUC) regarding body weight gain from FR50 rat-offspring was reduced by 9%, while the AUC of food intake was increased by 10% (n=20, P<0.01). At dark-cycle, FR50 group was normophagic during the first 4h of assessment, however they were hyperphagic in overnight (+13%, n=5, P<0.01). The body composition markers in FR50 rats were reduced (mesenteric, –36%; retroperitoneal, –25%; peri-epididymal fat pad, –21%; and extensor digitorum longus, –52%; n=15, P<0.05). By other hand, when compared to control rats the BAT weight was increased by 38% in FR50 rats (n=20, P<0.001).
Conclusions: Maternal food-restriction in lactation programs a lean phenotype, even associated with a paradoxical hyperphagia, in other words "obesity resistance", which might be due to hyperfunction in BAT that implicates hyperactivity of the sympathetic nervous system.

Evaluation of anthropometry-based algorithms in predicting body composition in early infancy using air displacement plethysmography (ADP-PeaPod) as the criterion

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Background/Aims: Accurate quantification of infant body composition is essential for investigating early life nutrition and the developmental origins of obesity and related co-morbidities. Generally, body composition is estimated using anthropometry-based equations, which have been widely applied in studies. We aimed to assess the accuracy of published equations for predicting body composition in early infancy, using ADP as the criterion
Method: A total of 119 infants (55 at 6 weeks and 64 at 3 months of age) participating in the Cambridge Baby Growth Study had available data on anthropometry, including skinfold thicknesses (SFT) at 4 sites (triceps, subscapular, quadriceps and flank), and ADP derived fat mass (FM). Predicted FM was calculated from SFT and other anthropometric variables

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using 4 identified equations (Slaughter-1988, Deierlein-2012, Catalano-1995, and Aris-2013). Bland-Altman analyses were used to assess the bias and 95% limits of agreement (LoA) of predicted FM versus ADP-FM.
Results: Mean (±SD) ADP-FM was 0.96(±0.37) kg at 6 weeks and 1.39(±0.51) kg at 3 months. Across both time-points, predicted FM by Catalano-1995 showed the strongest correlation with ADP-FM (r=0.78 p<0.0001) with the lowest mean bias -0.02 kg (95% LoA: -0.42 to 0.68). Slaughter-1988 and Aris-2013 predicted FM showed weaker correlations with ADP-FM (r=0.75, p<0.0001 and r=0.76, p<0.0001 respectively) and overestimated FM with mean bias 0.42 kg (-0.15 to 0.99) and 0.13 kg (-0.42 to 0.68), respectively. Deierlein-2012 predicted FM correlated poorly with ADP-FM (r=0.66, p<0.0001) and substantially underestimated FM, mean bias -1.82 kg (-3.15 to -0.48). Findings were similar at each time-point separately.
Conclusions: The Catalano-1995 equation was the most accurate predictor of ADP derived FM; other equations performed poorly. Notably, the Catalano-1995 equation includes flank SFT, which is not widely measured in infant studies. Hence, alternative validated prediction equations would be valuable research tools.

Early detection of cardiometabolic risk in a paediatric population from a low-income setting

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Background/Aims: Cardiometabolic diseases are often treated at the point where patients present with advanced disease or complications i.e. when a cardiovascular incident had occurred. Cardiometabolic risk factors are increasingly prevalent among younger individuals i.e. children, adolescents and women. Apart from the association between lifestyle factors and the development of cardiometabolic diseases, the programming during the pre- and postnatal environments possibly contribute more to this development. The influence of socioeconomic status and poverty resulting in micronutrient deficiencies together with exposure to environmental toxins are associated with early development of cardiometabolic risk. Aim: to identify children at primary school age level (6-12 years) with the presence of cardiometabolic disease risk factors. In a previous study among 500 five-year-old children from a low-income setting, whom were exposed to alcohol and nicotine during pregnancy, we demonstrated higher carotid intima media thickness (cIMT) values, an indication of early onset atherosclerosis as well as increased blood pressure when compared to normal paediatric values. In the present study we build on these findings. Towards this goal were collected anthropometric measurements as indicators of adiposity, blood pressure measurements, lipid profiles as well as ultrasound measurements of the aorta and carotid wall thickness.
Method: Longitudinal data collection from sixty primary school children from a low-income setting.
Results: Overweight and obesity increased with age (35-43%), significant positive associations between blood pressure and indicators of adiposity. After adjusting for age, SBP significantly positively associated with BMI (r=0.61, p<0.01), waist circumference (r=0.53, p<0.01), skinfold thickness (r=0.42, p=0.05). Significant association between waist circumference and triglycerides (p=0.05). Significantly higher mean vascular wall thickness (IMT) values in males compared to females (0.65mm, SD 0.09 versus 0.58mm, SD 0.09, p=0.02)
Conclusions: Cardiometabolic risk factors are present in low-income setting primary school aged children possible due to adiposity programming during the early postnatal period. The strong positive association between waist circumference (abdominal adiposity) and blood pressure could serve as an easy tool to identify young children at risk and thus introduce preventive measures to alleviate the burden of cardiometabolic diseases on the individuals' later life but also on the health care systems later of a low-income country.

Measuring Life Expectancy in the Absence of Non-Communicable Diseases among Youth in South Africa

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Background/Aims: Youth are becoming increasingly susceptible to non-communicable diseases with their exposure to fast foods and sedentary lifestyles placing them at a higher risk of lifestyle diseases such as obesity and diabetes. The challenges youth in Sub-Sahara Africa face, namely poverty, unemployment and under-education, increases their risk of high blood pressure and coronary heart diseases associated with stress. In South Africa, evidence showing that youth suffer from overweight and obesity, hypertension and diabetes has been found. And while infectious disease and non-disease causes of death have been extensively studied among youth in South Africa, there is dearth of research on non-communicable disease mortality among youth.
Method: The data that will be used include the South African Causes of Death data. The study population are youth aged 15-24 years old. Both males and females will be included in the study. Youth from all racial groups and provinces will be represented in the study. To estimate youth mortality from the various causes of death the

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following statistical and demographic techniques will be used: (1) for the levels and trends, frequency tables and chi-square will be used; (2) life table techniques which estimate the probability of dying from non-communicable causes of death will be employed.
Results: Preliminary results show that almost 5% of all youth deaths in the country are due to non-communicable disease. Of these, suicide, related to mental health illness is high. Youth have life expectancy of 45 for females and 48 for males with theses causes of disease in the population. That is, youth can expect to live until 65 and 68 years old at present. Further analysis to estimate decrement-deleted life expectancy is still to be completed.
Conclusions: From the preliminary results above, non-communicable diseases in youth is resulting in premature and avoidable mortality. The study will be completed by the end of April 2019 and more results on the years of life that could be gained if non-communicable diseases did not occur will add to policy and programme recommendations in the country.

Offspring of women treated for gestational diabetes mellitus show normal fetal kidney volume and infant urinalysis

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Background/Aims: The prevalence of gestational diabetes mellitus (GDM) is increasing worldwide. Animal studies have indicated that hyperglycaemia during pregnancy alters kidney development in offspring. However studies examining these effects in humans are scarce. The aim of this study was to evaluate the impact of treated GDM on fetal size and conduct a preliminary assessment of infant urinary protein and electrolyte excretion.
Method: A prospective cohort study was conducted between June 2013 and August 2016 in Melbourne, Australia. Participants were recruited at a large tertiary hospital (Monash Medical Centre) and clinical data were collected from women diagnosed and treated for GDM (n=76) and women without GDM (n=82). GDM was diagnosed by routine screening at 26-28 weeks gestation. Women with GDM received additional routine antenatal care for glucose monitoring, including diet and exercise interventions. One-third of women with GDM also required insulin therapy. Participants underwent an obstetric ultrasound at 32-34 weeks gestation for fetal biometry and fetal kidney volume measurement. Quantitative urinalyses were performed in infans at 3 months of age.
Results: 21% of GDM women were diagnosed with fasting hyperglycaemia, while 91% had an elevated 2-hour glucose level Maternal age, weight and body mass index were similar in non-GDM and GDM women. Estimated fetal weight, fetal kidney dimensions and total kidney volume were similar in women with and without GDM. Birth weight and infant urinary albumin and electrolyte levels at 3 months of age were also similar. Fetal kidney size did not differ by mode of GDM treatment (i.e. diet and exercise alone, or diet and exercise with insulin therapy). There were no associations between maternal glucose levels at screening and fetal kidney volume.
Conclusions: Our findings suggest that a period of mild hyperglycaemia prior to diagnosis of GDM and treatment initiation does not alter fetal kidney volume at 32-34 weeks gestation or urinalysis in 3-month-old infants. This is an encouraging finding given the increasing number of women diagnosed with GDM.

Enhanced adipogenesis via nutrient sensor-epigenome regulation in programmed obesity

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Background/Aims: Our mouse model of maternal obesity and a high fat diet (HF) mimics the human scenario wherein the newborn pups are heavier at birth and develop obesity. Enhanced adipogenesis results, in part, from early induction of PPARγ which facilitates preadipocyte differentiation to mature adipocytes which store fat. The mechanism for increased fetal adipose PPARγ may involve SIRT1, a nutrient sensor and a histone deacetylase, which may be suppressed in response to increased nutrient energy. SIRT1 interacts with developmental histone methyltransferase (EZH2; regulates cell differentiation) which modulates Wnt10b, a known inhibitor of PPARγ. We hypothesized that in HF newborns, SIRT1-EZH2 mediated effects suppress Wnt10b promoting increased PPARγ and preadipocyte differentiation.
Method: Female mice were fed either a control (10% k/cal) or HF (45% k/cal) diet to create maternal obesity prior to mating, and diets continued throughout pregnancy and lactation. Inguinal adipose tissue was collected from one day old males. Isolated preadipocytes were cultured for 48h (time 0) and subsequently induced to differentiate. Protein was extracted at day 0, 2, 4 and 6 of induction for expression of SIRT1, EZH2, Wnt10b and PPARγ.

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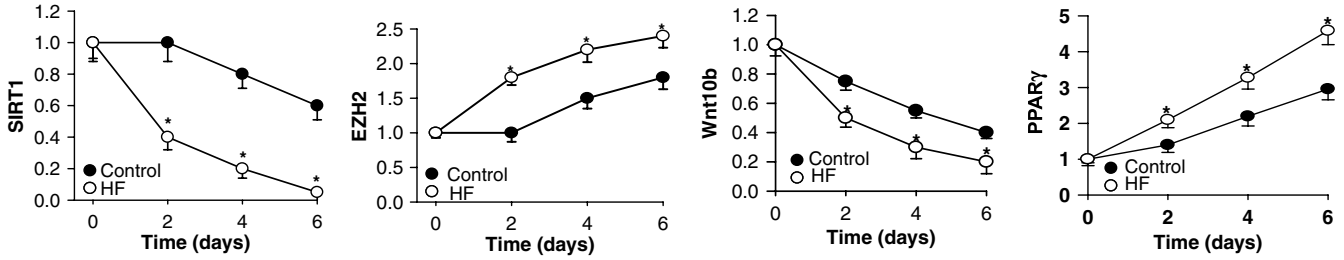

Results: In HF preadipocytes, prior to differentiation at day 0, SIRT1 and Wnt10b expression were downregulated whereas EZH2 and PPARγ were upregulated as compared to Control. With differentiation, both HF and Control cells showed progressively decreased expression of SIRT1 and Wnt10b with increased expression of EZH2 and PPARγ, though HF cells maintained decreased SIRT1 and Wnt10b and increased EZH2 and PPARγ as compared to Controls (Figure).
Conclusions: In HF newborns, decreased SIRT1 and increased EZH2 suppress Wnt10b and likely promote adipogenesis, contributing to obesity. Ex vivo culture results indicate an intrinsic programming of adipogenesis in HF offspring, independent of the body hormonal milieu.

Reactive oxidative stress (ROS) promotes hypothalamic neuroprogenitor cell (NPC) proliferation via activation of Notch pathway

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Background/Aims: Developmental programming increases the risk of offspring obesity and diabetes and impairs neurological development and function. Our established murine model of maternal obesity (OB) and high fat diet (HF) results in offspring obesity, hyperphagia and altered neuroprogenitor cell (NPCs) proliferation. OB and HF diet are associated with increased reactive oxidative stress (ROS) in mothers and newborns. ROS is known to activate Notch/Hes1 pathway which maintains NPCs in a proliferating state, potentially altering developmentally time-sensitive NPC differentiation. A potential mechanism for maternal OB/HF-mediated offspring hyperphagia may involve ROS effects on NPC. We hypothesize that increased ROS promotes continued NPC proliferation via Notch/Hes1 pathway.
Method: Hypothalamic NPCs from Control newborns were cultured in complete medium and treated with H_2O_2 (0, 2.5, 5, 10 μM) for 24h. ROS levels (fluorescence assay) and protein expression of NPC marker (nestin); activated notch (ICD) and neuroproliferative bHLH factor (Hes1) were analyzed.
Results: With increasing H_2O_2 doses and quantitative increase in ROS, NPCs expressed increased ROS, activated Notch 1 (ICD) and Hes1 (10μM H_2O_2), consistent with increased proliferation and Nestin expression (Figure).
Conclusions: ROS promotes NPC proliferation via Notch/Hes1 pathway potentially delaying the developmental period for NPC differentiation with consequent effects on neurodevelopment.

Reactive oxidative stress (ROS)-mediated reduced hypothalamic neuroprogenitor cell (NPC) differentiation via Mash1/Ngn3 pathway: Mechanism for programmed hyperphagia and obesity

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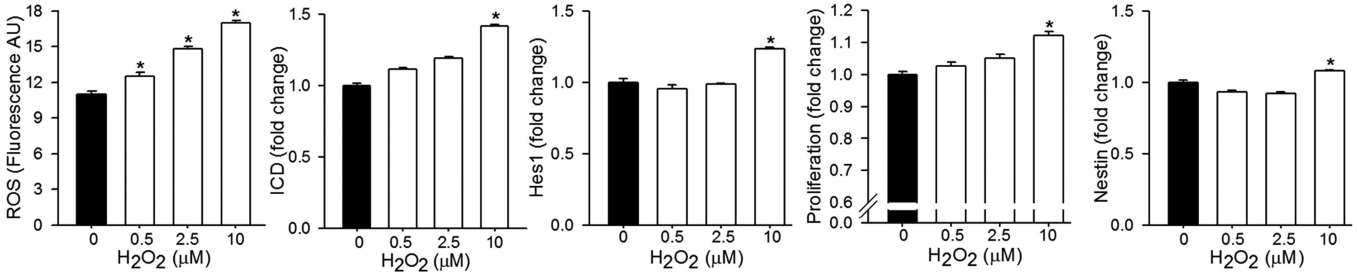
Background/Aims: An important etiology of the obesity epidemic is developmental programming effects of in utero exposures. Maternal obesity predisposes offspring to adult obesity and metabolic syndrome. Our murine model of maternal obesity (OB) and high fat diet (HF) results in offspring obesity and hyperphagia. The increased food intake is a result of increased hypothalamic orexigenic (NPY/AgRP) vs anorexigenic (POMC) neuropeptide expression and neuronal counts. As maternal OB is associated with increased levels of reactive oxidative stress (ROS) in both mothers and newborns, we



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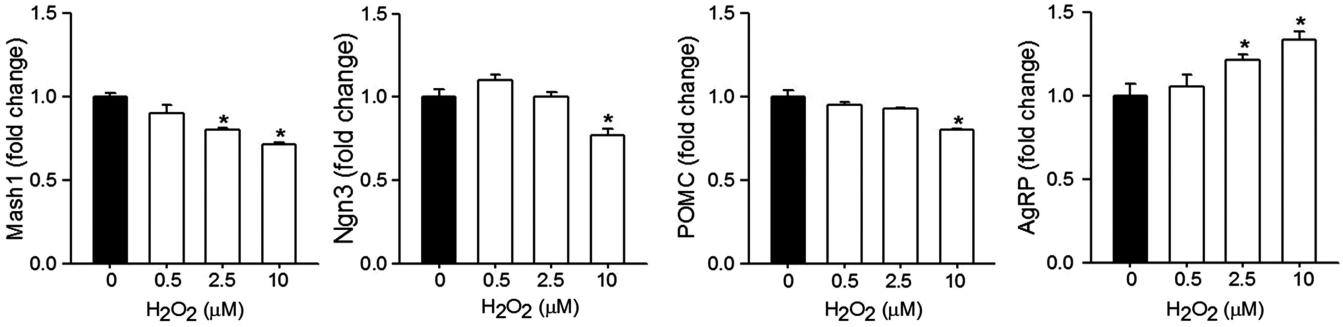

investigated the effects of ROS on neuroprogenitor (NPC) differentiation. NPC differentiation is regulated by bHLH proneurogenic transcription factors (Mash1, Ngn3). We hypothesized that elevated ROS levels suppress Mash1/Ngn3 expression, altering NPC differentiation and suppressing anorexigenic peptide expression.

Method: Hypothalamic NPCs from Control newborns were cultured in differentiation medium and treated with H_2O_2 (0, 2.5, 5, 10 μM) for 24h. ROS levels (fluorescence assay) and protein expression of proneurogenic transcription factors (Mash1, Ngn3) and neuropeptides (AgRP, POMC) were analyzed.

Results: With increasing H_2O_2 doses and quantitative increase in ROS, NPCs expressed reduced protein expression of Mash1 and Ngn3, consistent with decreased POMC and increased AgRP expression (Figure).

Conclusions: ROS-induced decreased Mash1/Ngn3 likely contributes to reduced NPC differentiation with preferential differentiation to orexigenic vs anorexigenic neurons. Thus maternal OB-mediated oxidative stress effects on NPC may be the mechanism by which maternal OB causes offspring hyperphagia.

Proinflammatory cytokine TNF*α*-mediated increased oxidative stress promotes hypothalamic neuroprogenitor cell (NPC) proliferation via upregulation of Hes[1]

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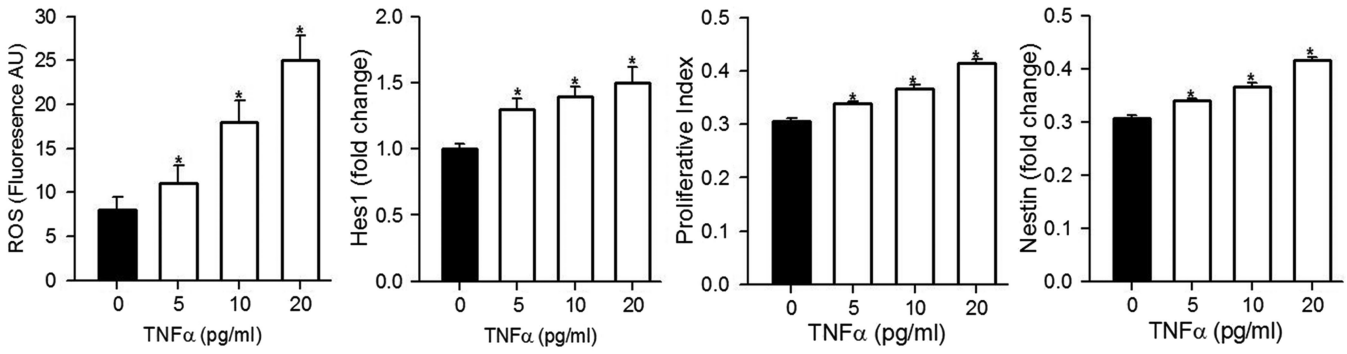
Background/Aims: A primary cause of the obesity epidemic is the developmental programming effects of the *in utero* environment. Infants born to obese mothers (OB) with a Western high fat (HF) diet are at increased risk of childhood and adult overweight/obesity. In obese pregnant women, the proinflammatory cytokine TNFα expression is increased in placenta, amniotic fluid and umbilical cord blood. We have established a murine model of maternal OB/HF that results in altered properties of hypothalamic NPC which likely contribute to the offspring hyperphagia and obesity. TNFα influences NPC proliferation via its association with the bHLH neuroproliferative transcription factor (Hes1) and/or via production of reactive oxygen species (ROS). Notably, ROS also influences Hes1 signalling. We hypothesize that TNFα promotes ROS production and NPC proliferation via Hes1.

Method: Hypothalamic NPCs from control newborns were cultured in complete medium and treated with TNFα (0, 5, 20 pg/ml) for 24h. ROS levels (fluorescence assay), NPC proliferation index (MTT assay) and protein expression of NPC marker (Nestin) and Hes1 were analyzed by Western blot.

Results: With increasing TNFα doses, NPCs exhibited increased levels of ROS and Hes1, consistent with the dose-dependent increase in proliferation and Nestin expression (Figure).

Conclusions: TNFα-mediated increased NPC ROS levels and Hes1 expression promotes NPC proliferation. Both increased hypothalamic proliferation as well as developmentally time-altered differentiation may program neurogenesis resulting in hyperphagia and obesity.



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Proinflammatory cytokine TNFα suppresses hypothalamic neuroprogenitor cell (NPC) differentiation and promotes appetite versus satiety neuropeptide

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Background/Aims: Maternal obesity (OB) with a Western high fat (HF) diet increases the risk of childhood and adult obesity, though the underlying mechanism is unclear. Our mouse model of maternal OB/HF mimics the human scenario of offspring obesity and increased food intake. Offspring hyperphagia results from altered hypothalamic neurogenesis that drives neuroprogenitor cells (NPCs) to preferentially differentiate to appetite (NPY/AgRP) vs satiety (POMC) neurons. Obesity is associated with inflammation and oxidative stress, and the proinflammatory cytokine TNFα interacts with Mash/Ngn3, critical factors regulating neurogenesis. We hypothesize that TNFα increases reactive oxygen species (ROS) which induce preferential NPC differentiation to appetite vs satiety neurons via suppression of bHLH proneurogenic transcription factors (Mash1, Ngn3).
Method: Hypothalamic NPCs from control newborns were cultured in differentiation medium and treated with TNFα (0, 5, 20 pg/ml) for 24h. Protein expression of Mash1, Ngn3, AgRP and POMC were analyzed by Western blot.
Results: With increasing TNFα doses (10 and 20 pg/ml), NPCs exhibited decreased protein expression of Mash1 and Ngn3, consistent with increased AgRP and decreased POMC (Figure).
Conclusions: TNFα-mediated suppressed proneurogenic factors promote appetite versus satiety neuropeptide expression, suggesting that this may be a putative mechanism by which maternal obesity causes offspring hyperphagia and obesity.

Sex-specific Metabolic Programming in a Mouse Model of Preeclampsia

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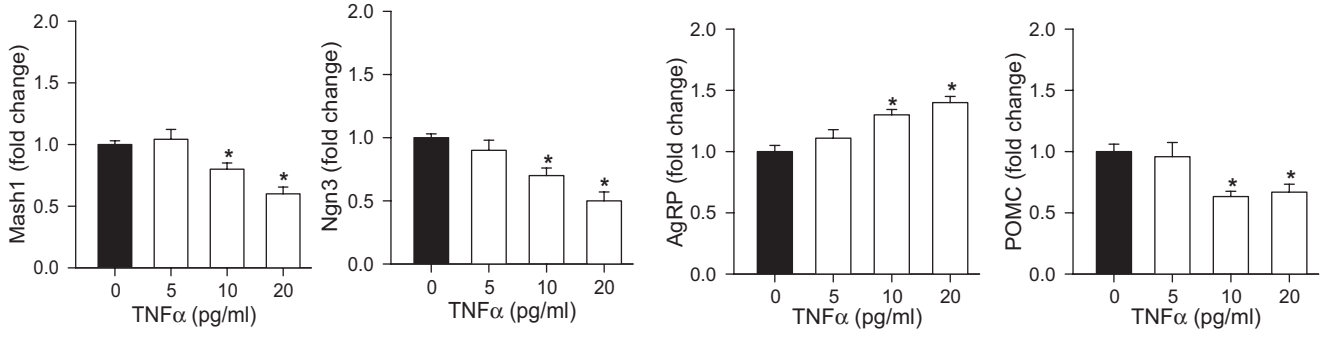
Background/Aims: Epidemiological data shows that preeclampsia (PE) increases the susceptibility for metabolic diseases later in life in the offspring. PE is a multifactorial disease, involving inflammation, anti-angiogenesis, and other factors. We recently described a novel double-hit model of preeclampsia (1). Here we aim to characterize the long-term metabolic outcome for the offspring.
Method: Pregnant C57Bl/6 mice were treated with low-dose LPS and sFlt1-adenovirus as described (1); controls received saline and empty virus. After weaning, all offspring was fed a semi-synthetic control diet (D13100302, Research Diets). At 12 weeks of age, half of the animals were changed to a Western-Style Diet (WSD); D12079B, Research Diets). All mice were followed for an additional 12 weeks. Food intake and body weight were monitored constantly. Body composition (MRI) and insulin production and sensitivity (oGTT and ITT) were measured at 12 and 24 weeks of age. Lipogenesis was assessed using ^{13}C-labelled acetate. At 24 weeks of age, blood pressure was measured and organs were collected for detailed molecular analyses. Males and females were analysed separately, resulting in 8-12 animals per group.
Results: From weaning until 12 weeks of age, body weight did not differ between PE-exposed and control offspring. Strikingly, PE-exposed females had a significantly higher amount of fat mass at week 12. After starting WSD, body weight of the PE-exposed female offspring increased drastically, and at



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23 weeks of age their fat mass was twice as heavy compared to control WSD females. Preliminary data suggests that glucose tolerance and insulin tolerance are not affected by PE exposure.
Conclusions: Intrauterine exposure to PE in combination with a Western-Style Diet leads to dramatic changes in fat metabolism of the female offspring. Gene expression, epigenetic and histological analyses of liver and fat pads are likely to give insight in the underlying mechanisms.
(1) Stojanovska V, Dijkstra DJ, Vogtmann R, Gellhaus A, Scherjon SA, Plösch T. A double-hit pre-eclampsia model results in sex-specific growth restriction patterns. Dis Model Mech. 2019 doi: 10.1242/dmm.035980.

Healthy growth patterns may modify the effect of abnormal birth weight on cardiovascular risks in children and adolescents: a retrospective cohort study in China

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Background/Aims: This study aimed to examine the association between birth weight (BW) and cardiovascular risks in children and adolescents and to further investigate whether different growth patterns could modify the abnormal BW on cardiovascular risks.
Method: This study recruited 51,685 children and adolescents aged 6 to 18 years using data from Chinese national survey conducted in 2012. BW was determined using the medical certificate of birth. Current cardiovascular indicators included obesity, abdominal obesity, hypertension, impaired fasting glucose (IFG), abnormal total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Growth patterns were divided into catch-up growth, trajectory growth, and retarded growth by using the percentiles difference of birth length and current height. We used logistic regression models and generalized additive models to estimate the association between BW and cardiovascular indicators based on different growth patterns.
Results: The prevalence of obesity, abdominal obesity, hypertension, IFG, abnormal TC, TG, HDL and LDL were 11.6%, 5.7%, 9.4%, 3.1%, 6.0%, 13.3%, 13.9%, and 5.3% in children and adolescents. High BW increased the risks of obesity, abdominal obesity, and abnormal TG, and low BW increased the risks of hypertension, IFG, and abnormal TC, but both of them presented no significant risks changes in abnormal HDL and LDL in childhood and adolescence. Catch-up growth and retarded growth decreased the risks of hypertension, IFG, and abnormal TC caused by high BW, as well as the IFG risks caused by low BW. But catch-up growth increased the risks of hypertension and abnormal TC caused by low BW.
Conclusions: Our findings suggest that different growth patterns after birth could modify cardiovascular risks caused by the BW abnormalities in the childhood and adolescents. This study with national large data provided an obvious evidence for guiding the scientific and reasonable growth and development of children and adolescents after birth.

Pathways to neurodevelopmental risk and resilience: examining neurodevelopmental trajectories of infants in the ORIGINS cohort

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Background/Aims: Every nine minutes, an Australian child is born who is at developmental risk and 22% commence school with heightened risk of neurodevelopmental and mental health problems. Without timely identification, there are missed opportunities for intervention when neuroplasticity is at its greatest. Intervening early offers the opportunity to reduce adversity for children and their families, as well as the associated costs which extend and compound during school and into adulthood.
Method: The ORIGINS community-based intervention cohort aims to collect information on 10,000 pregnant mothers, fathers and their off-springs over a 10-year period, following their offspring until 5 years of age. This composite of epidemiological, clinical and biological data is ideally placed to enable multi-level analyses on all children and investigate factors associated with developmental risks prior to diagnoses. Nested intervention studies are collecting additional biomarker and neurobehavioural data to further inform the early identification of neurodevelopmental disorders.
Results: A transdiagnostic model of study to identify infants at risk of adverse developmental outcomes and apply timely interventions at the earliest opportunity, whilst engaging with key stakeholders will be presented. Specific studies will involve the ORIGINS platform and include 1) the mapping of developmental trajectories in different developmental domains to three years of age, and 2) examining their relationships with perinatal, maternal and social risk factors; markers of maternal inflammation during pregnancy and child inflammation at 12 months; and eye tracking data collected during infancy.
Conclusions: Longitudinal studies with birth cohorts that engage families and infants before developmental delays emerge are necessary to identify pathways to neurodevelopmental risk and resilience. Earlier identification of neurodevelopmental risk during the antenatal period and early years is

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crucial in prevention efforts. This approach may lead to a paradigm shift in how we identify and respond to developmentally vulnerable children.

Expression of cholesterol packaging and transport genes in rat placenta: impact of maternal dietary LA:ALA ratio and total fat intake

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Background: We have previously shown that exposure to a low protein diet in utero altered placental expression of genes involved in cholesterol packaging (Mttp, ApoA2, ApoC2) and transport (Cubilin, Fgg, Ttr). This may contribute to altered tissue development in the fetus and provide clues for the mechanism that links maternal diet to adverse health outcomes in the offspring. With contemporary diets shifting towards excess energy consumption and greater intakes of omega-6 polyunsaturated fatty acids, it is increasingly important to understand the role of dietary fats, particularly omega-6 fats, in the developmental origins of disease.
Objective: To determine the effects of maternal consumption of an omega-6 linoleic acid (LA):omega-3 alpha-linolenic acid (ALA) ratio similar to that of modern Western diets (9:1), in comparison to a lower ratio (1:1.5), on placental expression of genes associated with cholesterol packaging and transport. The study also determined whether any differences between ratios were exacerbated by an increase in total dietary fat content (18% vs 36% fat w/w).
Method: Female Wistar rats (n = 5-6 per dietary group) were assigned to their experimental diets four weeks prior to mating and throughout pregnancy. At day 20 of gestation (term = 22 d gestation) dams and fetuses were euthanized and placentas from male fetuses were collected for gene expression analysis.
Results and Conclusions: Placental mRNA expression of Mttp, ApoA2, ApoC2, Cubilin, Fgg and Ttr was increased in dams fed on the 36% fat diets, but only at the higher dietary LA:ALA ratio (5-7 fold increase, $P<0.05$). These results suggest the omega-6: omega:3 ratio of the diet consumed during pregnancy, in addition to total fat load, affects placental cholesterol transport. These findings concur with our previous findings in low protein diets, which may suggest the existence of a common mechanism linking different dietary perturbations with programming of adverse health outcomes, involving altered cholesterol transfer to the developing fetus.

Chlamydia trachomatis infection during pregnancy and childhood asthma risk

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Background/Aims: *Chlamydia trachomatis* is a common sexually transmitted disease and related to neonatal morbidity. Long-term respiratory consequences are unknown. Our aim was to examine if *Chlamydia trachomatis* infection during pregnancy is associated with childhood asthma and related morbidity.
Methods: This study among 2,475 mothers and their offspring was embedded in the Generation R Study, a population-based prospective cohort study from fetal life onwards in Rotterdam, the Netherlands. Urine samples at enrollment were tested for *Chlamydia trachomatis* infection during pregnancy. Childhood physician-attended lower respiratory tract infections and wheezing, and current asthma were obtained by questionnaires, and lung function by spirometry at age 10 years. Generalized estimating equation, logistic or linear regression models were applied adjusting for family history of asthma, socio-economic and lifestyle factors.
Results The prevalence of *Chlamydia trachomatis* infection during pregnancy was 3.2% (78/2,475). *Chlamydia trachomatis* infection during pregnancy was not associated with lower respiratory tract infections until age 6 years, but was with an increased risk of wheezing in children until age 10 years (odds ratio (OR) (95% confidence interval (CI)) 1.50 (1.07, 2.11)). *Chlamydia trachomatis* infection during pregnancy was associated with an increased risk of asthma (OR (95% CI): 2.28 (1.01, 5.20)), and with a lower FEV_1/FVC (Z-score difference (95% CI): -0.28 (-052 to -0.04)) and FEF_{75} (Z-score difference (95% CI): -0.24 (-0.46, -0.01), respectively) in children at age 10 years. The observed associations were not explained by mode of delivery, gestational age at birth or birth weight.
Conclusions *Chlamydia trachomatis* infection during pregnancy is associated with increased risks of childhood wheezing, asthma, and impaired lung function, but not lower respiratory tract infections, and may be a target for prevention strategies focused on improving long-term respiratory health of the offspring.

Precise Read-Level Imputation of Methylation" (PReLIM) Substantially Increases Information Content of Whole-Genome Bisulfite Sequencing Data

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Background/Aims: Methylation of cytosines in cytosine-guanine (CpG) dinucleotides in genomic DNA is an epigenetic mechanism essential for mammalian development. Analyzing CpG methylation at the read-level with whole genome bisulfite sequencing (WGBS) data involves placing overlapping sequencing reads into bins, which are represented as matrices, where rows are reads and columns are CpG sites, but these matrices are sometimes incomplete since a read may not overlap every CpG in a bin. Motivated by our aim to analyze read-level CpG methylation data to uncover cell type-specific signals, we developed a novel machine learning based approach to impute missing CpG methylation data at the read level, which we call "Precise Read-Level Imputation of Methylation" (PReLIM).
Method: We analyzed published WGBS data from mouse neurons and glia, partitioned the genome into 100 base-pair long 'bins', and trained PReLIM to classify the methylation states of individual CpGs based on local bin methylation information. After training, we evaluated PReLIM's imputation performance on the methylation states of CpGs in our data. We then tested the number of differentially methylated regions (DMRs) that could be detected in our data using PReLIM's imputation capabilities.
Results: We found that PReLIM can predict latent CpG methylation states with over 90% accuracy. Additionally, we discovered that we can find 47% more DMRs in our data by using PReLIM.
Conclusions: PReLIM can accurately predict CpG methylation states, providing a tool to facilitate read-level studies and advanced analytical techniques. We also found that PReLIM can help us find more DMRs than we can without imputation, demonstrating that PReLIM can benefit many DNA methylation researchers. Obtaining substantial additional information from WGBS data sets, at no extra cost, will be a big advantage for researchers studying epigenetic mechanisms in DOHaD.

Maternal Nutritional Status and Beta Cell Function in the First Year of Life: Preliminary Findings

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Background/Aims: Poor nutritional-status in pregnancy may predispose to higher risk of diabetes among the progeny through intra-uterine modification. The present study examines the association of maternal weight class on infant pancreatic beta-cell function at birth and at 8th month.
Methods: The study recruited 150 non-obese pregnant women aged 18-35 years and without any chronic medical conditions. Nutritional status was defined as first trimester weight class i.e. underweight(UW)_BMI<18.5kg/m^2, n=75 or non-underweight(N-UW)_BMI=18.5–27.4kg/m^2, n=75. Data on 41 mother-infant pairs are available to date with complete follow up of infants from birth to 8 months. Glucose, c-peptide, insulin, beta cell function (HOMA-B) and insulin resistance (HOMA-IR) were examined from cord blood and 8 month fasting and 30 minutes blood samples from an oral glucose tolerance test (33%,w/v) examined between first trimester weight classes using ANOVA.
Results: Infants were 53.7% female and 38.53 weeks gestation at birth. At birth, UW-infants had lower weight (UW=2402.5 (±550.63)g vs. N-UW=2853.64(±453.52)g, p<0.02) and similar length but no difference at 8 months. There were no differences in glucose, c-peptide, insulin, HOMA-IR or HOMA-B at birth. At 8 months, UW-infants had higher fasting insulin (UW=6.1(±6.4)mIU/L vs. N-UW=2.53(±1.86)mIU/L,p<0.007) and c-peptide (UW=321.3(±256.57)pmol/L vs. N-UW=194.5 (±108.17) pmol/L,p<0.03) but not fasting glucose. UW-infants had greater HOMA-IR and HOMA-B than N-UW-infants, but no differences were detected in 30-minute glucose, c-peptide, and insulin.
Conclusion: Infants of underweight women have lower birth weights and higher level of fasting c-peptide and fasting insulin at 8 months of age. The findings suggest that very early onset of metabolic changes in infants may be related to maternal nutritional status. Strategic antenatal care may be important to reduce intergenerational risk of beta cell dysfunction and related impacts on diabetes risk.

Associations of Child and Adolescent Anxiety with Later Alcohol Use and Disorders: A Systematic Review and Meta-Analysis of Prospective Cohort Studies

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Background/Aims: Despite a wealth of literature, the relationship between anxiety and alcohol use remains unclear. We examined whether (a) child and adolescent anxiety is positively or negatively associated with later alcohol use and disorders and (b) study characteristics explain discrepant results.
Method: We conducted a systematic review of 51 prospective cohort studies from 11 countries. Three studies contributed to a meta-analysis. We searched PubMed, Scopus, Web of Science and PsycINFO databases, and studies were included if they met the following criteria: English language publication, human participants, anxiety exposure variable in childhood or adolescence and alcohol outcome at least six months later. Ninety-seven associations were categorised by anxiety exposure (generalised anxiety disorder, internalising disorders,

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miscellaneous anxiety, obsessive compulsive disorder, panic disorder, separation anxiety disorder, social anxiety disorder, and specific phobias) and alcohol use outcome (drinking frequency/quantity, binge drinking, and alcohol use disorders).
Results: Study sample sizes ranged from 110 to 11,157 participants. Anxiety exposure ages ranged from three to 24 years, and alcohol outcome ages ranged from 11 to 42 years. The narrative synthesis revealed some evidence for a positive association between anxiety and later alcohol use disorders. Associations of anxiety with later drinking frequency/quantity and binge drinking were inconsistent. Type and developmental period of anxiety, follow-up duration, sample size, and confounders considered, did not appear to explain the discrepant findings. The meta-analysis also showed no clear evidence of a relationship between generalised anxiety disorder and later alcohol use disorder (OR 0.94, 95% CI 0.47 to 1.87).
Conclusions: Child and adolescent anxiety, but not generalised anxiety, appears to be positively associated with later alcohol use disorders. However, associations of anxiety with later drinking frequency/quantity and binge drinking remain unclear.

The association between parental alcohol use and offspring mental health

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Background/Aims: Previous research has shown detrimental mental health outcomes for children prenatally exposed to alcohol. However, uncertainty remains as to whether these negative offspring outcomes are due to intrauterine exposure to alcohol, or environmental influences after birth, for example parental lifetime drinking. The aim of this project is to investigate the impact of maternal and partner alcohol use on offspring mental health, and how offspring mental health may be influenced by maternal polygenic risk scores for depression.
Method: Participants were adolescents from the Avon Longitudinal Study of Parents and Children (ALSPAC). Maternal and partner drinking behaviours (number of occasions binge drank; alcohol amount) were measured when offspring were 61 months old. Offspring mental health measures (depression/hyperactivity/conduct problems/total problem scores) were measured at 17 years of age.
Results: There was evidence that the number of occasions parents binge drank alcohol was associated with an increase in offspring depression, conduct problems and hyperactivity. The frequency (amount) mothers and partners consumed alcohol was associated with reduced total problems in offspring. These associations for both binge and alcohol amount were attenuated after adjustment for potential confounders and maternal polygenic risk scores (PRS) for depression. There was little evidence of a dose response relationship between parental alcohol use and offspring outcomes. Confounding structures were explored, and parents with higher incomes consumed more alcohol than those with lower incomes. Mothers and partners shared similar patterns between drinking behaviours and confounding structures.
Conclusions: The associations shown may be explained by maternal depression across the life course (as measured by PRS) and other residual confounding factors such as socioeconomic and prenatal risk factors, explaining the difference in direction of results for alcohol amount and binge drinking. The associations found are therefore likely to be due to differences in patterns of alcohol consumption between various confounders (e.g. income) and not from parental alcohol use itself.

Male Low-Birth-Weight Infants Have Larger Adipocytes than Term Appropriate-For-Gestational-Age Infants during Infantile Period

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Background/Aims: Low-birth-weight (LBW) infants have a high risk of developing insulin resistance and associated disorders later in life. We hypothesized that LBW infants might have adipose tissue maldevelopment in terms of size or number of adipocytes at an early stage of life. Therefore, this study aimed to evaluate differences in adipocyte size during the infantile period between LBW infants and term appropriate-for-gestational-age (AGA) infants.
Method: We assessed 35 male infants (9 LBW and 28 term AGA infants) aged 0.5–4.0 years who would undergo surgery for inguinal hernia, umbilical hernia, and testicular hydrocele. Anthropometric measurements and blood samples were evaluated and obtained preoperatively. Adipose tissue samples were obtained from the patients intraoperatively. Each sample was immediately fixed by osmic acid, and the adipocyte diameters were evaluated after separating the adipocytes from each other.
Results: The length standard deviation (SD) score was found to be lower in LBW infants than in term AGA infants, but the body mass index (BMI) was similar between the groups. In a simple regression analysis, the adipocyte diameters were positively associated with BMI, subscapular skinfold thickness, and triceps skinfold thickness, but negatively associated with birth weight, gestational age, and length SD score. LBW infants have significantly larger adipocyte size, compared to term AGA infants ($p < 0.05$). Significant differences were strengthened after adjusting for variables such as age and BMI and age ($p < 0.001$). However, the adipocyte diameters were not associated

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with hematologic parameters such as glucose, insulin, homeostatic model assessment index, cholesterol levels, adiponectin, and leptin.
Conclusions: The adipocyte size of LBW male infants during the infantile period is larger than that of term AGA infants. Further studies are required to clarify whether the large size of adipocytes in LBW infants during infancy might be associated with the development of insulin resistance later in life.

The Long-Term Behavioural Effects of Intrapartum Asphyxia in the Spiny Mouse, and the Protective Capacity of Maternal Creatine Supplementation

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Background/Aims: Intrapartum asphyxia and subsequent newborn hypoxic ischemic encephalopathy (HIE) are major causes of long-term neurological morbidity. Although therapeutic hypothermia is currently employed clinically to treat HIE, its application and efficacy remain limited. One proposed alternate or adjunct therapy to hypothermia is maternal antenatal creatine supplementation. Using the validated spiny mouse model of intrapartum asphyxia, this study examined the long-term behavioural effect of intrapartum asphyxia and the protective capacity of maternal creatine supplementation.
Methods: At day 20 of gestation (term 39 days), dams were randomised to receive a diet containing 5% w/w creatine monohydrate (n=21) or remain on standard rodent chow (n=40). On day 38 of gestation, the pregnant uteri were isolated and placed in a saline bath for 7.5 min, subjecting the fetuses to progressive hypoxia and hypcapnia (n=17 control-diet & n=9 creatine-fed dams). Control offspring were delivered by c-section and recovered immediately (n=23 control-diet & n=12 creatine-fed dams). Offspring then underwent behavioural tests, including open field, elevated plus maze, novel object recognition and social interaction at multiple time-points from 3-78 days postnatal age. Data were analysed by ANCOVA using SPSS, with postnatal age, sex and litter considered as covariates.
Results: Intrapartum asphyxia caused limited thiogmotaxsis, as determined by open field testing, in offspring at 3 days' postnatal age ($P_{BIRTH}<0.01$), an effect not observed in offspring born of creatine supplemented dams ($P_{DIET}<0.01$). Creatine supplementation also increased time spent in the closed arms of the EPM at 78 days ($P_{DIET}<0.05$), implying these offspring had more developed awareness of environments that normally provoke anxiety. No other differences were observed between groups. Postnatal age in open field analysis, and sex in novel object recognition assessments, were significant cofactors.
Conclusion: The spiny mouse model of intrapartum asphyxia induced subtle neurological deficits in the first 3 days' post insult. Maternal dietary creatine supplementation improved these outcomes. Neither intrapartum asphyxia nor creatine altered other behavioural parameters tested in older offspring.
Conclusions: Please include conclusions here. All text including the above title, authors and affiliations are to fit inside this box. Abstracts exceeding this box or not adhering to the guidelines will be asked to resubmit. Please read the guidelines carefully. Do not change the font size or font type. The congress managers are only too happy to assist if you have any questions or queries.

Is there difference in eating habits between students who sleep less than what is recommended and those who sleep more?

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Background/Aims: Duration of sleep at night is important for people's health and well-being, and several studies have shown an increased risk of unhealthy behaviour and weight gain with short sleep duration. Unhealthy behaviour and weight gain may, in turn, increase the risk of a variety of lifestyle diseases, such as cardiovascular disease, cancer and diabetes. A higher focus on the importance of adequate sleep can, therefore, be an important public health topic. In this cross-sectional study among 618 students at the University of Agder we wanted to investigate whether there were differences in the students' eating habits depending on whether they were sleeping according to the guidelines or not. We also explored potential differences in factors like BMI and tobacco use.
Method: An invitation to participate in a study about students eating and living habits was sent to all the students (12 000), at Agder University, Norway of which 722 students responded. Not all the students completed the comprehensive food frequency questionnaire with additional questions about sleep, thus, 618 students are included in the analysis of the students sleeping habits.
Results: Our results show that there were differences between the students who sleep less than the recommended seven hours at night and those who sleep more. We found differences especially among male students. Male students who slept less than recommended were more likely to consume coffee and energy drinks than their fellow students with longer sleep duration. A higher BMI among students with short sleep duration was also observed. In addition, a higher percentage of the sleep deprived students were using snuff (a tobacco type inserted under your lip).
Conclusions: This cross-sectional study indicates that sleep duration could be of importance for the student's health since students with less sleep have more unhealthy habits than students with appropriate amount of sleep.

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Understanding the role of amino acids restriction on cell cycle regulation in C2C12 cells

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Background/Aims: Changes in homeostatic regulation and tissue function that follow exposure to maternal undernutrition are closely associated with changes to organ structure. These changes to size and/or numbers of functional units in tissues must be driven by attenuation of cell proliferation and/or differentiation during development. This, and observations from transcriptomic studies in animals, suggest that the cell cycle is a target for nutritional programming. The aim of this study was to determine the regulation of cell cycle in response to amino acids restriction in vitro.
Method: C2C12 cells were cultured in Dulbecco's modified Eagles medium (DMEM) and 10% fetal bovine serum. After 24h, cells were treated with Hanks' Balanced Salt Solution (HBSS) media with 10% FBS, supplemented with different amino acid concentrations (10-100% of stock concentration) for a further 48h. Cell cycle arrest was monitored with propodium Iodide staining by flow cytometry. Gene expression changes in cell cycle regulatory pathway was determined by quantitative real time PCR. Cells were sorted with fluorescence activated cell sorting according to cell cycle phase and quantification of transcriptomic changes was measured by RNA-Seq analyses.
Results: Limiting concentration of amino acids in culture media decreased the rate of C2C12 cell proliferation by effecting cell cycle regulation. Cells grown in medium with 10% amino acids had significantly more cells arrested at G1 compared to cells grown at 100% amino acids (76% G1 arrest vs 67%, p<0,05). Interestingly, our bioinformatics analyses of RNA-seq data demonstrated that LAA altered the expression of majority number of genes in sterol biosynthetic process pathway in G1, S and G2-M phase of cell cycle.
Ran, Cdk4, Ccnb1 were significantly up-regulated in low amino acids (LAA) group while Taf10, Apbb1, Ppm1d, Gadd45a, Mdm2, Pmp22 and Tsg101 downregulated (p<0.001).
Conclusions: Developing understanding of mechanism that link the nutritional environment during development with later health, may help to determine potential target pathways which could be therapeutic objectives in future or biomarkers of unfavourable intrauterine events.

A methodological approach to identify the most reliable human milk collection method for compositional analysis: a systematic review

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Background/Aims: Breast milk composition varies within and between days and even across a single feed. As a result, the method of breast milk sample collection can have a significant impact on the results of compositional analyses and relationships to infant outcomes as well as complicate comparisons between studies. The aim of this systematic review is to compare the results obtained for breast milk macronutrient composition between studies utilizing different sampling methodologies and to use this as a basis to identify the most reliable sampling approach.
Method: The EMBASE, MEDLINE/PubMed, Cochrane Library, Scopus, Web of Science, and ProQuest Dissertations and Theses Global databases were searched for relevant articles. Observational studies, including cross-sectional and longitudinal cohort studies which involved lactating women at any lactation stage were included, and at least two review authors independently screened studies and undertook data extraction. Quality assessment of included articles was conducted using the Newcastle-Ottawa scale.
Results: A total of 5297 publications were identified from our search, of which 101 studies were included in this systematic review (n = 5074 breastfeeding women). A broad range of methods were utilised for breast milk collection and divided into 3 categories: collection of milk from all feeds over a 24hr period (32 studies, n= 1283 participants), collection at one time point (62 studies, n= 3453 participants) and 'other methods' (7 studies, n= 308 participants). The most frequently used method was collection of a full expression at one time point (26 studies, n = 1377 participants), followed by pooling of full expressions of all feeds across a 24hr period (16 studies, n = 616 participants) and collection of pre-and post-feed samples at one time point (12 studies, n = 612 participants).
Conclusions: This review confirms the wide range of sampling methods applied in studies assessing breast milk composition. This reinforces the need for establishing a standardised method for breast milk collection to ensure accurate analysis of milk components with respect to infant outcomes. Standardised methods will also allow comparison of results between studies and enable combining of data from different research groups to enhance replicability and knowledge in the field.

Fit mum, fat dad: what are the metabolic outcomes on adult offspring?

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Background/Aims: Paternal obesity before conception impairs glucose tolerance and insulin secretion in adult offspring. Maternal physical activity (voluntary wheel) may be able to improve metabolic outcomes in adult offspring; but there is little information about the long-term outcomes of a structured program of exercise training. Therefore, we investigated whether exercise training before and during gestation can attenuate the negative effects of a paternal obesity on insulin sensitivity and secretion in adult rat offspring.
Methods: Fathers consumed a normal or high-fat diet (42% energy as fat) before mating. Mothers exercised on a treadmill before and during gestation or remained sedentary. At 24 weeks of age, female offspring (sedentary, chow-fed diet; n=9-10 per group) were assessed for insulin and glucose tolerance (IPITT and IPGTT, respectively), insulin-stimulated glucose uptake (ISGU), protein expression and pancreatic morphology.
Results: Maternal exercise did not affect IPITT, IPGTT or basal glucose uptake *ex vivo*. In offspring sired by obese fathers, maternal exercise attenuated the lower ISGU *ex vivo*, and was associated with an increase in GLUT4 protein expression ($P<0.05$). There were no effects on the phosphorylation of TBC1D4. In terms of pancreatic function and morphology, maternal exercise reversed the lower insulin secretion *in vivo* observed in offspring of obese fathers, which may be accounted by the increase in β-cell mass.
Conclusion: Maternal exercise did not affect insulin sensitivity in skeletal muscle; however, it normalised the lower insulin secretion and β-cell mass observed in the offspring of obese fathers. We present a feasible, low-cost and translatable intervention strategy that can be applied perinatally to break the cycle of metabolic dysfunction caused by paternal obesity.

Infant Weight Gain and Adult Cardiometabolic Disease - Risk Not Greater for SGA than AGA Infants

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Background/Aims: There is controversy over the long-term cardio-metabolic consequences of catch-up growth in infants born small or appropriate for gestational age (SGA/AGA). We study the associations of faster relative weight gain from 0-6 and 6-12 months with young adult cardiometabolic disease (CMD) risk factors including blood pressure (BP), glucose control, and plasma lipids among participants from the New Delhi (India) Birth Cohort and the Cebu (Philippines) Longitudinal Health and Nutrition Study, where the prevalence of SGA was 42% (New Delhi) and 22% (Cebu).
Method: We use data from adults aged 26-32y in New Delhi (N=1013), and 21-22y in Cebu (N=1790). Outcomes included systolic and diastolic BP, elevated BP (>130 systolic or >85 diastolic); fasting glucose, insulin and HOMA-IR; and fasting total, HDL and LDL cholesterol, and triglycerides. We use conditional relative weight gain from 0-6, 6-12, 12-24 months, and 2-8, 8-15, and 15-adult years to measure rapid weight gain relative to linear growth in each interval. We examine main effects of rapid relative weight gain and interactions with SGA, (birth weight <10th percentile of the INTERGROWTH-21st Newborn Size at Birth Chart). All models adjusted for birth order, maternal education, household income and wealth at birth. Models were stratified by site and sex.
Results: Across the 10 outcomes examined, we find limited and inconsistent evidence of an elevated risk of adverse outcomes associated with rapid growth during the first 6 months in SGA or AGA infants. The only significant coefficients for SGA infants represent higher systolic BP in Cebu females and Delhi males, higher risk of elevated BP in Delhi males, higher fasting glucose and HOMA-IR in Cebu males. Only 3 from 40 possible interactions indicate stronger risk of adverse adult outcomes related to rapid relative weight gain in SGA vs AGA infants: systolic BP in Delhi males and elevated glucose and HOMA-IR in Cebu males.
Conclusions: Early infant catch-up growth in weight is not more risky for SGA than AGA infants, nor is rapid relative weight gain in early infancy strongly related to adult CMD risk in these cohorts.

Relative Impact of Pre-versus Postnatal Growth Restriction on Later Life Achievement and Health

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adverse adult health and developmental outcomes. Postnatal growth is strongly influenced by size at birth. However, the relative contribution of the pre- and postnatal periods is not well studied. We examine how child IQ and young adult school attainment, BMI, waist circumference (WC), percent body fat, systolic and diastolic blood pressure (BP) relate to combinations of pre- and postnatal growth restriction. Our analysis is based on data from >1800 participants in the Cebu (Philippines) Longitudinal Health and Nutrition Study who were followed to adulthood.
Methods. We define prenatal growth restriction as birth weight or length below the 10th percentile of the INTERGROWTH size

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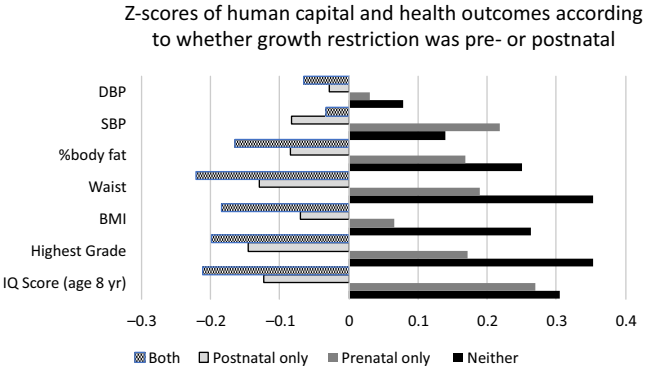
for gestational age at birth reference, and postnatal growth faltering as stunting (height-for-age Z-score<-2) at age 2 years. We define 4 groups, with adequate size for gestational age (AGA), no stunting as a referent (27.2% of sample) for comparison with SGA only 5.7%), stunting only (47.5%) or both (20.3%) ting. IQ was measured using a non-verbal test at a mean age of 8.5 yr. BP, and anthropometric data were collected at a mean age of 21.5 yr. We use linear regression models to examine how the 4 groups defined above relate to sex-specific Z-scores of the outcomes to allow for comparison of effect sizes.
Results: (figure) Coefficients on SGA alone were not significantly different than those on AGA-no stunting. Coefficients on SGA and stunting were not significantly different from those on stunting alone. However, for most outcomes, both stunting groups differed markedly from the non-stunted groups, in having lower IQ scores, less attained schooling, lower adult BMI, WC, %body fat, and BP.



Conclusions: These results suggest that postnatal recovery from SGA offers an opportunity for attainment of improved adult outcomes. However, the serious postnatal growth faltering which characterizes this sample represents serious intellectual development, and attained schooling.

Effect of iodine supplementation in pregnant women on maternal and neonatal thyroid function in a large Chinese population

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Aims: To assess the impact of iodine supplementation in early pregnancy on maternal thyroid function in late pregnancy and neonatal TSH level in mild iodine deficient area of China.
Method: A total of 10269 eligible pregnant women were recruited in early pregnancy who resided in mild iodine-deficient area of China Shanghai. According to whether taking iodine supplement during early pregnancy, the women were divided into iodine-contained group (N=1322) and non-iodine-contained group (N=8947). The main indexes of thyroid function (FT4, TSH) on pregnant women were assessed at first and third trimester, respectively. The adverse outcomes of pregnant women, including gestational diabetes mellitus (GDM), gestational hypertension, premature rupture of fetal membranes (PROM), and preterm birth were obtained. Birth weight was measured in each newborn, and the level of fetal serum TSH was examined within 72 hours of birth.
Results: The available data were 949 in iodine-contained group and 7081 in non-iodine-contained group. The results showed that the level of FT4 is higher in iodine-contained group compared with the non-iodine-contained group in third trimester. However, there is no difference for TSH level in two groups. The incidence of PROM was significantly higher in non-iodine-contained women than in iodine-contained women (19.54% vs 16.78%, p=0.02). The level of fetal TSH among slightly elevated proportion (≥75%) is significantly lower in iodine contained group compared with non-iodine contained group. A positive correlation between maternal TSH and fetal TSH was found whereas the level of maternal FT4 was not correlated with fetal TSH.
Conclusions: The iodine supplementation for early pregnant women is benefit to both pregnancy outcome and fetal thyroid function, especially for those with slightly elevated TSH. Maternal TSH in third trimester may be a predictive biomarker for fetal thyroid function.

Vascular dysfunction appears independently of metabolic disorders in offspring exposed *in utero* to maternal obesity. Impact of post-natal diet environment

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Background/Aims: Maternal obesity influences fetal development leading to metabolic and vascular disorders and consequently cardiovascular diseases during adulthood. Although current studies always linked vascular and metabolic disorders in offspring exposed *in utero* to maternal obesity, our study aims to determine 1) if maternal obesity is able to directly program fetal vascular function independently of metabolic disorders and 2) the impact of post-natal diet environment.
Method: *Sprague-Dawley* female rats were fed with a high fat diet (45%kcal from fat) during at least 8 weeks. We studied metabolic and vascular functions of 4-months old offspring 1) born to control mothers and suckled by these control mothers (CMO) or adopted by obese mothers (CAO) and 2) born to obese mothers and suckled by obese mother (OMO) or adopted by control mother (OAC). Metabolic function was evaluated by analyzing plasma glucose and lipid profiles, glucose tolerance and insulin sensitivity. Vascular function was assessed by studying vasoconstriction/vasodilation balance of resistance arteries (Mulvany myography).
Results: Although 4-months old OMO and CMO have a similar metabolic profile, we detect early vascular abnormalities with an unbalance of vasodilator pathways (i.e. increased EDHFs component in OMO males compared to CMO males while OMO females have a decreased involvement of EDHFs compared to CMO females).

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When we modify suckling diet, OAC females are smaller than other groups, OAC and CAO males have more subcutaneous fat than CMO and OMO. Moreover, OAC and CAO animals develop glucose intolerance. Concerning vascular function, CAO and OAC males have similar profiles to OMO. OAC females have a similar profile to CMO while CAO have the same profile than OMO.
Conclusions: Our study highlights an independent vascular fetal programming not related to metabolic disorders in offspring exposed *in utero* to maternal obesity. Moreover modifications of post-natal environment seems to accelerate the appearance of metabolic abnormalities without impact on vascular response compared to non-adopted animals.

Bariatric surgery improves metabolic profile of female rats and their offspring despite perinatal complications

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Background/Aims: With the increase of people suffering from morbid obesity and the failure of nutritional therapies, bariatric surgery (BS) has rapidly emerged. Currently two types of BS are used: an exclusively restrictive BS (sleeve gastrectomy) and BS combining restriction and malabsorption (gastric bypass). Considering the current knowledge about impact of maternal obesity on offspring (metabolic disorders, vascular dysfunction, liver steatosis . . .), we are interested in the consequences of these two types of BS on offspring's health.
Method: Female *Sprague Dawley* rats were submitted during 8 weeks to a high fat/high sugar (HFHS) diet. Rats were randomly assigned to one of the following 4 groups: obese, sleeve, bypass and control (classical diet). One month after surgery, female rats were mated with non-obese males to obtain offspring of control (CMO), obese (OMO), sleeve (SMO) and bypass (BMO) mothers. Metabolic, hepatic and vascular functions were studied on mothers and their offspring.
Results: Although sleeve- or bypass-operated females showed a significant decreased weight compared to obese females, no litter from bypass-operated mothers were obtained. Sleeve-operated females had a fertility rate similar to that of control mothers but associated with an increase of perinatal complications. In 3-month old offspring, analysis of metabolic function showed that SMO had a similar metabolic profile to CMO but was associated with an increased adiposity equivalent to OMO. In addition, hepatic analysis highlighted high levels of steatosis and fibrosis in SMO. Nevertheless, the 3 groups seemed to have similar vascular reactivity in conductance and resistance arteries.
Conclusions: This study is the first to be interested in the outcome of children born to BS-operated mothers. Our results suggest that maternal sleeve gastrectomy induced metabolic, hepatic and vascular profiles of 3-months old offspring similar to those observed in CMO rats. However, future endpoints at 6, 12 and 18 months will allow a better characterization of the offspring's operated-mothers.

Innate Immune Cytokine Responses And Allergic Disease In Preschool-Aged Children

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Background/Aims: Previous studies have found associations between increased innate inflammatory responses at birth and allergic disease. However, it is unclear whether this relationship persists beyond infancy. The aim of this study was to investigate the relationship between whole-blood innate cytokine responses and allergic sensitisation in preschool-aged children.
Method: We conducted a cross-sectional assessment of 285 children (aged 4-5.5 years) participating in the Barwon Infant Study (BIS) (n=1074). Whole-blood samples were stimulated with lipopolysaccharide (LPS) or peptidoglycan (PGN) and a multiplex assay was used to measure up to 27 secreted cytokines. Proportions of innate immune cells in peripheral blood samples were determined with flow cytometry (CD45+ cells sorted by size and granularity). Allergic-sensitisation status was determined by skin-prick testing (SPT) for 249/285 (87%) children. Clinical disease status was determined via questionnaire. The associations between immune parameters and allergic sensitisation were explored by regression analyses with adjusted for multiple comparisons.
Results: A total of 79/249 (32%) children demonstrated allergic sensitisation by SPT and 43/285 (15%) reported clinical allergic disease. Concentrations of cytokines IL-1RA and TNF-α were positively correlated with the proportions of innate cells in children's blood samples ($p<0.001$ and $p=0.001$). LPS-stimulation elicited generally stronger inflammatory responses than PGN-stimulation. No evidence was found for a relationship between cytokine responses to stimulation, allergic sensitisation or clinical allergic disease.
Conclusions: There was no evidence of a cross-sectional relationship between whole-blood innate cytokine responses and allergic disease in preschool-aged children in this study.

Exercising obese pregnant mice partially rescues cardio-metabolic health of male offspring

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Background/Aims: Maternal obesity during pregnancy is associated with an elevated risk of cardiovascular disease in the offspring. Our previous studies have shown that mice offspring of obese pregnancies develop pathological cardiac hypertrophy and cardiac dysfunction in early adult life. The aim of the current study was to investigate if peri-gestational exercise to the mother would improve offspring cardio-metabolic health and explore potential underlying mechanisms.
Method: Diet-induced female C57BL/6 obese mice underwent 20-minute treadmill exercise 5 days a week, 1 week prior to, and up to D17 gestation. Cardiovascular physiology was assessed by echocardiography and tail cuff plethysmography in 8-week-old male offspring; serum insulin was measured by immunoassay and cardiomyocyte cell area, re-expression of fetal genes and the expression of calcium handling and sympathetic activation proteins were also determined in cardiac tissue collected *post-mortem*.
Results: The exercise intervention prevented the development of impaired glucose tolerance and insulin resistance in the dam at E19. This occurred without changes in dam body composition. Offspring body weights and body composition were not different between groups at 8 weeks of age. Offspring of obese dams were hyperinsulinaemic, developed pathologic cardiac hypertrophy, cardiac dysfunction (characterized by reduced ejection fraction), and hypertension. Maternal exercise prevented offspring hyperinsulinaemia, cardiac hypertrophy and dysfunction, but not hypertension.
Conclusions: Our findings suggest there are at least two mechanistic pathways mediating the programming effects of maternal obesity, therefore highlighting the need for multiple approaches to combat the detrimental effects of maternal obesity on offspring health.

Molecular, morphological and functional cardiac changes in gestational protein restriction elderly offspring

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Background/Aims: The intrauterine environment is a crucial factor in the etiology of several diseases in adult life, as well as metabolic and cardiovascular diseases. This study aimed to assess the heart gene expression in gestational protein restricted elderly male rats offspring.
Method: Pregnant Wistar rats were divided into two groups according to the protein diet content offered during pregnancy: 1. NP (17% standard-protein) or 2. LP (6% low-protein). The systolic blood pressure was measured and, the mass of the heart, cardiomyocytes area, gene expression, collagen content and immunostaining of proteins was performed in 62-weeks old NP compared to LP offspring.
Results: In the current study, we showed a low birth weight followed by catch-up growth phenomena associated with high blood pressure development, increased heart collagen content and cardiomyocytes area in 62 week-old LP offspring. By genomic sequencing analysis, we verified changes in the expression of 137 genes; After gene to gene biological evaluation and relevance, the present study demonstrated significant differences in genes linked to inflammatory activity, oxidative stress, apoptosis process, autophagy and, in hypertrophy and fibrosis pathways resulting heart function disorders. Taking into account these findings, we may suppose a close link between maternal protein restriction, specific gene expression, and progressive heart failure. Therefore, we assume that the animals from LP group compared to NP offspring could present a precociously aging process that culminates with early myocardial failure and animal death, which may be verified by survival curve analysis of the LP when compared to NP offspring.
Conclusions: The present study suggests that maternal protein restriction may lead to early heart disorders in the LP offspring compared to the NP group. We may hypothesize that rapid heart dysfunction is associated with heart fibrosis, myocardial cell hypertrophy and multiple gene expression abnormalities in the LP offspring.

Trimester Specific Difference In Exosomal MicroRNA Expression

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Background/Aims: Recent studies have shown that microRNAs play important roles in fetal growth and placental regulation. Especially, microRNAs in exosomes are known to be involved in cell-to-cell communication, therefore, we can expect that exosomal microRNAs might participate in feto-maternal communications during pregnancy. We are examining expressions of exosomal microRNAs in maternal blood and their relations to fetal growth.
Method: Blood samples were collected at second and third trimester. We extracted exosomal microRNAs from maternal blood. The expression levels of microRNAs were evaluated by real-time RT-PCR. Then we analysed whether the expression levels of microRNA were associated with fetal growth.

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Results: We reproduced the association between expression levels of two microRNAs (miR-483-5p and miR-127-3p) and birth weight for gestational age (BWGA), which has been previously reported. Interestingly, the significant fetal growth-association was observed for the expression levels of miRNAs at second trimester, but not at third trimester.
Conclusions: This study suggests that importance of some miRNA levels at second trimester, which might be consistent with the idea that exosomal microRNAs from trophoblasts might facilitate normal placentation and they can be monitored in maternal blood.

Placental multi-omics data-mining in intrauterine growth restriction

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Background/Aims: Intrauterine Growth Restriction (IUGR) affects 8% of newborns and increases morbidity and mortality for the offspring even during later stages of life. Omics studies have evidenced epigenetic, gene expression and metabolic alterations in IUGR, the whole pathogenic mechanisms being not fully understood and integrated together. An in-depth strategy combining multi-omics integration could help to better understand these pathogenic processes.
Method: Methylomics and transcriptomics analyses were performed on 36 placenta samples in a case-control study. In addition to hierarchical clustering from the obtained quantitative data, machine learning algorithms were used to combine the analysis of more than 1200 genes found to be significantly modified. We used an automated text-mining approach, using the bulk textual gene annotations of the discriminant genes. The results were presented as word clouds clusters allowing a rapid visualization and summarization of the pathophysiological processes involved. Support vector machine models were then used to explore the phenotypic subgroups (prematurity, birth weight and head circumference) associated with IUGR.
Results: Gene annotation clustering highlighted the alteration of cell signaling and proliferation, cytoskeleton and intra- and extracellular structures, oxidative stress, protein turnover, muscle development, energetic and lipid metabolism with insulin resistance. Models obtained using support vector machine showed high capacity to predict the sub-phenotypes associated with IUGR.
Conclusions: Our results show that multi-omics integration using the combination of gene annotation clustering, word cloud visualization and support vector machine models are highly relevant to provide an overview of the IUGR pathogenic mechanisms.

Low fetal growth is protective for food allergy and atopic dermatitis, but not all allergic diseases – systematic review

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Background/Aims: Data from animal models and some human studies suggest that *in utero* growth restriction (IUGR) is protective against allergy. Human literature is variable and has not been system-atically reviewed to assess effects of birth weight [BW] on allergy, with lack of correction for gestational age a particular issue. We therefore designed a systematic review (1) to assess the relationship between size at birth/fetal growth, relative to gestational age, and postnatal allergic disease (eczema /atopic dermatitis [AD], hay fever/atopic rhinitis [AR], allergic asthma [AA] and food allergy [FA]).
Method: We searched 11 databases for literature describing our exposures (size at birth/fetal growth), and outcomes of interest (physician diagnosis/defined specific symptoms for AD, AR, AA or FA). We used the generalized least-squares method to estimate the linear association of BW with outcomes.
Results: Of the 15093 studies identified, 42 were eligible for inclusion in the narrative review. Only two studies reported AA. In meta-analyses, an increase of 1 kg in BW was associated with increased risks of FA ever in childhood (OR 1.4; 95% CI 1.0-2.0, P=0.001, 4 studies) and AD ever in childhood (OR 1.2; 95% CI 1.0-1.3, P=0.003, 17 studies). There was no evidence that risks of AR ever or currently in childhood, AR ever in adulthood, or current AD in childhood were altered by BW (all $P > 0.5$).
Conclusions: The positive association between BW relative to gestational age and risks of childhood FA and AD is consistent with reduced susceptibility to allergy in animal models of IUGR. Differences in outcomes between allergic diseases and age of assessment suggest low fetal growth predominantly protects against allergic diseases with early age of onset.

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Maternal Antenatal Mood and Child Development: An Exploratory Study of Early Intervention on Child Outcomes up to 5 Years

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Background: Effective treatment of maternal antenatal depression may ameliorate adverse neuro-developmental outcomes in offspring. We followed up children whose mothers had received either specialised cognitive-behavioural therapy or routine care for depression while pregnant in a randomised controlled trial (RCT).

Methodology: Of the original cohort of 54 women, renewed consent was given by 28 women for 2-year follow-up and 24 women for 5-year follow-up. Assessments included the Parenting Stress Index (PSI), Bayley Scales of Infant Development (BSID-III), Child Behaviour Checklist (CBCL), Wechsler Preschool and Primary Scales of Intelligence (WPPSI-III), Beck Depression Inventory (BDI-II) and Beck Anxiety inventory (BAI).

Results: The RCT (n=54) showed excellent adherence, acceptability and treatment efficacy. Strong reductions in anxiety were observed during pregnancy, and improvements in depression were maintained at 9 months representing a moderately large effect size. Nine-month infant outcomes showed several medium to large effects favouring the intervention in domains including problem solving, self-regulation and stress reactivity, which were independent of maternal postnatal mood.

At 2 years, intervention effects were found with lower scores on the PSI Total, Child domain and adaptability subscale (d = 1.53, 1.0, 0.91, respectively). A non-significant trend favoured the intervention group on most subscales of the CBCL and the BSID-III (most notably motor development: d = 0.53). Irrespective of treatment allocation, at 5-year follow-up, higher depression during pregnancy was associated with lower Verbal IQ and higher CBCL Anxiety/Depression and Internalizing scores. Higher anxiety during pregnancy was associated with lower IQ in all domains and with higher CBCL total problems, Anxiety/Depression, Withdrawn, Attention, Aggressive, Internalizing and Externalizing scores in children. Limitations: A small sample size and potential attrition bias.

Conclusion: There are few controlled studies of the effect of antenatal depression treatment on infant neuro-developmental outcomes. Whilst our follow-up study supports the current evidence of an association between antenatal depression and child outcomes, we found only a few statistically significant between-group differences to support our hypothesis regarding antenatal depression treatment and child cognitive and behavioural outcomes in the longer-term.

Effects of maternal diets on preterm birth and low birth weight: a systematic review

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Background: Current evidence indicates that maternal diets before and during pregnancy could influence rates of preterm birth, low birth weight (LBW), and small for gestational age (SGA), however, findings have been inconsistent. Therefore, the aim of this review was to summarize evidence concerning the effects of maternal diets before and during pregnancy on preterm birth, LBW, and SGA.

Methods: Systematic electronic database searches were carried out using PubMed, EMBASE, Scopus, and Cochrane library using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline.

Results: This systematic review included thirty-seven eligible articles comprising mostly of prospective cohort studies with five randomized controlled trials (RCT). The dietary patterns during pregnancy associated with lower risk of preterm birth were commonly characterized by high consumptions of vegetables, fruits, and whole grains. Those associated with lower risk of SGA also had similar characteristics, including high consumptions of vegetables, fruits, legumes, seafood/fish, and milk products. Results from limited number of studies suggested that there was a beneficial effect of maternal fish intake on LBW and milk intake on SGA. The evidence was mixed for the relationship between other dietary patterns during pregnancy and preterm birth and SGA. No significant association was found between dietary patterns during pregnancy and LBW. The studies assessed focused on a wide range of maternal dietary patterns, and there was large variation in the methods, time periods, extraction methods, and food items across the studies. Furthermore, little is known about the effects of pre-pregnancy diets on adverse birth outcomes.

Conclusion: Dietary pattern during pregnancy characterized by high intake of vegetables, fruits, and wholegrains may have a synergistic effect on reducing the risk of preterm birth. Dietary pattern characterized by high intake of vegetables, fruits, legumes, fish, and milk products during pregnancy may reduce the risk of having SGA infants

Pre-pregnancy diet quality and its association with offspring behavioural problems

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Objective: The aim of this study was to examine the relationship between preconception diet quality and offspring behavioural problems.
Methodology: This study was performed among 1554 mother-child dyad from Australian Longitudinal Study on Women's Health and the Mothers and their Children's Health Study. Healthy Eating Index (HEI)-2015 score was used to explore maternal diet quality before pregnancy. Child behavioural problems were assessed using Strengths and Difficulties Questionnaire. Both bivariate and multivariable logistic regression analyses were computed to examine the association between the HEI-2015 score and offspring behavioural problems. P value ≤ 0.05 at 95% CI was considered statistically significant.
Results: A total 211 cases of total behavioural disorder (13.6%) were reported among 1554 children during 12 years of follow-up period. Of which, 72.6%, 18.3%, 21.5% and 2.3% were categorized as emotional, peer, conduct, and hyperactivity problems, respectively. Better pre-pregnancy diet quality was associated with lowering risk of offspring total behavioural problems after adjustment for maternal and child characteristics, highest vs lowest tertile (AOR= 0.52, 95%CI: 0.32, 0.85) at P-value= 0.009. Pre-pregnancy diet quality was also inversely associated with risk of offspring externalizing problems (AOR= 0.64, 95% CI: 0.43, 0.94). Among the four sub-scales, hyperactivity and peer problems were significantly associated with pre-pregnancy diet quality (AOR= 0.20, 95%CI: 0.06, 0.74) and (AOR= 0.63, 95% CI: 0.42, 0.96), respectively.
Conclusion: We found that mothers who ate better diet quality before pregnancy had children with a lower risk of behavioural disorder in childhood.
Key words: Pre-pregnancy diet quality, behavioural problems, externalizing problems, hyperactivity, peer problems

The ORIGINS Project: Involving consumers in a cohort study

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Background/Aims: The ORIGINS Project is a unique pregnancy cohort with the aim of improving the health of the next generation through a better understanding of how to optimise the early environment. The Project is recruiting 10,000 families birthing at Joondalup Health Campus and capturing their data over 10 years. The biobank and databank will consist of biological samples, routine data and web-based questionnaires assessing physical and mental health, diet, physical activity patterns and a range of environmental factors. An essential part of the Project is consumer and community engagement.
Method: The Project has both a community reference group and a participant reference group. Members of the reference groups provide input and guidance on all aspects of the project and are represented in the Project governance structure.
In 2018, a monthly drop-in session at a local community centre was established. These sessions are supported by the City of Wanneroo and are an opportunity for ORIGINS families to connect with each other and ORIGINS' health professionals.
Results: Reference group members have been involved in reviewing key project documents and providing feedback on new proposed sub studies. On average, 11 families attend the monthly drop-in sessions and qualitative feedback has been positive regarding the usefulness of the sessions.
Conclusion: ORIGINS will be a significant asset for the community with potential to improve the health of the next generation. Strong community engagement and collaboration is critical to achieve this aim.

Nature Play & Grow: Promoting healthy eating, unstructured play and planetary responsibility by connecting preschool children to nature

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Background/Aims: There is good evidence that time in nature is associated with better child health, including activity, eating behaviours, sleep and all aspects of physical and mental well-being. However, there has been a significant shift from active, outdoor nature-based activities to more passive sedentary and screen-based indoor activities — with an associated rise in psychological disorders, chronic disease, and a disconnect from the natural environment. Strategies to improve lifestyle behaviours have the greatest potential in very young children. The proposed project aims to assess the feasibility, acceptability and potential efficacy of a family based healthy lifestyle intervention to promote healthy eating, physical activity, emotional well-being and connectedness to nature in preschool children.
Methods: All families participating in the ORIGINS Project, a pregnancy cohort study based in Perth WA, will be offered the opportunity to be involved in the intervention at their child's 2.5-year assessment. The proposed intervention will take the form of a group intervention based on the Play & Grow program developed and tested in Hong Kong. The intervention will consist of ten 90-minute sessions, delivered weekly. Each session will include experiential components related to healthy eating, physical activity/sedentary behaviours and nature connectedness, with the aim of providing parents with knowledge and skills to support their child's healthy lifestyle.
Results: The pilot study will provide valuable information regarding the feasibility, acceptability and potential effect of

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the intervention on key health behaviours. The intervention is expected to induce nature connectedness and result in positive changes in the key areas of nutrition, physical activity, sedentary behaviour, emotional well-being and behavioural development.
Conclusion: The findings from this pilot study will be used to inform the development of evidence-based recommendations regarding the promotion of healthy lifestyles in children through connectedness to nature. It is anticipated that this intervention will be adapted for use in a variety of early childhood settings across Australia.

Growth in childhood and age at menarche: Insights from individual trajectory modelling

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Background/Aims: The relationship between patterns of weight gain across childhood and the onset of puberty is not clearly understood, and few studies examine growth across the course of childhood. We aimed to derive growth parameters from models of weight across early, mid and late-childhood and estimate effects of the growth parameters on age at menarche.
Methods: Data from 557 children who took part in the Generation 1 cohort study and contributed serial height and weight measurements from birth to age 9.5 years were used in the present study, along with girls' menstrual history at age 12-13 years. Shape invariant random effects models were fit to log(weight+1) for all available participants' data (282 girls, 260 boys). Models with different combinations of fixed and random effects for size, tempo and velocity and up to 5 df for the spline function of time were fit. The Akaike Information Criterion (AIC) was used to identify the best-fitting model. In time-to-event models that were subsequently fit to the girls' data to estimate effects of the growth parameters on age at menarche, a censoring age of 12 years was used to define early puberty.
Results: On basis of AIC, a model with 4 df and fixed and random effects for size and tempo and a fixed effect for velocity was preferred. Some 19% of girls began menstruating before age 12 years. Size and tempo were each associated with an increased hazard of earlier menarche. A 0.1 unit gain in size was associated with a hazard ratio of 1.75 (95% CI 1.32 – 2.33), and a 0.1 unit gain in tempo was associated with a hazard ratio of 7.84 (95% CI 3.41 – 18.05).
Conclusions: Using all participants' data gave more precise estimates of growth parameters. Childhood growth should be closely monitored to identify children with unusual size or tempo. Understanding mechanisms that drive larger size and faster tempo of growth in childhood may help to elucidate the links between obesity and girls' risk of early puberty.

Novel Gasotransmitter Cardio-Protection in the Developing Heart: Comparative Roles of Hydrogen Sulphide and Carbon Monoxide

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Background: Hydrogen sulphide (H_2S) and carbon monoxide (CO) protect the heart against episodes of ischaemia/reperfusion (I/R) in adult individuals (Papapetropoulos et al. *PNAS* 106:21972, 2009; Otterbein et al. *Circ Res* **118**:1940, 2016). However, whether H_2S or CO protect the fetal heart is completely unknown, when tissue I/R injury is just as relevant in fetal life, for instance as a result of birth asphyxia in complicated labour. Using the chicken embryo model, here we show preconditioning effects of H_2S and CO, which confer significant protection against I/R to the developing heart. The molecular basis underlying fetal cardiac protection by H_2S and CO is different.
Methods: Fertilized Bovans Brown eggs were incubated under normoxia (21% O_2). On day 19 of incubation (term is 21 days), the heart was excised following cervical transection and mounted on a Langendorff preparation. Following measurement of basal cardiac function, hearts were randomly treated with a bolus of water vehicle (Control), a H_2S donor (NaHS) or a CO donor (CORM-3), with or without the non-selective K_{ATP} channel inhibitor Glibenclamide (Glib) or the mitochondrial K_{ATP} channel inhibitor 5-hydroxydecanoate (5-HD). An I/R challenge was induced 10 min after treatment by halting perfusion for 30 min, followed by 2h of reperfusion. Myocardial infarct size was determined by tetrazolium staining.
Results: Treatment with either H_2S and CO donors improved cardiac function and reduced cardiac infarct size after I/R in the chicken embryo. However, H_2S improved cardiac function earlier while CO did so later after I/R. While the cardioprotective effects of H_2S were blocked by Glib but not 5-HD, the cardioprotectve effects of CO were blocked by both Glib and 5-HD (Fig. 1).
Conclusions: We introduce new interventional gasotrasmitter therapy against I/R injury in the developing heart. While H_2S confers cardioprotection by opening of myocardial sarcolemmal K_{ATP} channels, CO does so via myocardial mitochondrial K_{ATP} channels.
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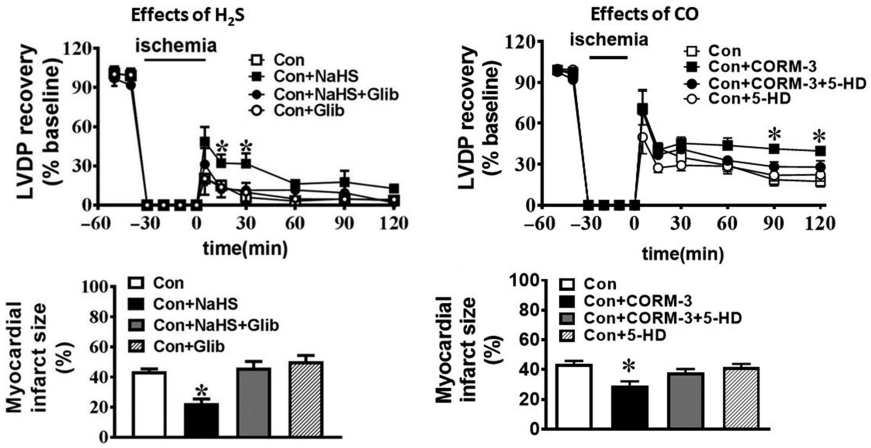

Maternal undernutrition in-utero and risk of low birth weight among young rural Indian mothers

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Background/Aims: To assess the maternal anthropometry and identify the risk of low birth weight among young rural mothers
Method: Full term mothers (n=204) registering at <13 weeks of gestation at the ANC of primary health centre in rural areas around Pune, were enrolled. Information on socio-demographic profile and anthropometric measurements at registration were recorded. Weight of baby at birth was also recorded.
Results: Majority (70.5%) of mothers were young (17-20yr) primiparous (70%), from poor income families (69.1%), engaged in farming activities (42.26%) and were educated only up to middle high school (15.2%). Mothers were thin (mean weight; 46.4 ± 6.1kg), had short stature (mean height: 153.3 ± 5.7cm) and 33.8% were undernourished with body mass index (BMI) < 18.5kg/m2. Mean birth weight was 2655± 507g and the prevalence of Low Birth Weight (LBW) was 27.5%. Maternal weight, BMI, sitting height and body fat at registration were significantly ($p<0.05$) associated with birth weight. Significant risk for LBW was observed for low (<42.3kg) weight (OR=3.6; CI:1.6- 8.1), low (<18.51kg/m2) BMI (OR=3.2; CI:1.4-7.3), low (<73 cm) sitting height (OR= 2.3;CI:1-5.1), small head circumference (<52cm) (OR= 3.3; CI: 1.6- 7.1), low (< 22.7%) body fat (OR= 4.9; CI: 2.2-11.1) at registration. Interestingly maternal sitting height and head circumference were significant even after adjusting for BMI and Body fat% indicating their independent influence on LBW.
Conclusions: Our findings highlight the role of maternal undernourishment in-utero (small head circumference; low sitting height) is a risk factor for LBW. Maternal sitting height can be used as a simplest measure for screening mothers at risk.

A Genetic Link Between Grip Strength And Neuromuscular Disorders

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Background/Aims: Genome-wide association studies have identified many risk loci associated with muscular disorders. Yet, little is known about the underlying biological mechanisms of the single nucleotide polymorphisms (SNPs) associated with neuromuscular disorders or the natural age-related decline of muscle strength. We hypothesize that the pathological development of these comorbid conditions involves shared biochemical pathways that are affected by condition-specific combinations of Expression Quantitative Trait Loci (eQTLs).
Method: SNPs (GWAS catalog; $p<5x10^{-6}$) associated with aging muscles (grip strength [GS]) were assigned to gene regulatory networks using the Contextualize Developmental SNPs in 3D (CoDeS3D) bioinformatics pipeline. CoDeS3D combines spatial (Hi-C) and functional (eQTL) data to identify eQTL-gene associations in the 3D genome. The eQTLs identified in GS were then compared to those identified in neuromuscular disorders (multiple sclerosis [MS], myasthenia gravis [MG], and amyotrophic lateral sclerosis [ALS]). Gene ontology and pathway enrichment analysis were performed.
Results: We identified 191, 106, 24 and 532 genes that spatially interact with eQTLs from GS, MG, ALS, and MS, respectively. Pathway enrichment analysis revealed overrepresentation of these genes in the immune system (HLA region) and signal transduction (*PDE11A*) pathways that are important for muscle regeneration and growth. Genes within the HLA region were regulated by eQTLs that were specific to GS, MS, and MG. By contrast, eQTLs associated with ALS do not regulate HLA

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genes. Rather, eQTLs specific to ALS and GS regulated *PDE11A*, which is involved in signal transduction.
Conclusions: Generalised age-related loss of muscle strength and neuromuscular disorders share immune system and signal transduction pathways in common. The gene regulatory networks specific to these pathways may predispose individuals to the pathological development of muscle-related comorbidities.

Low birth weight and altered growth trajectory in male offspring from older fathers

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Background/Aims: As more couples delay parenthood, there are emerging concerns for their children's health. For instance, children from older fathers present increased risk of psychiatric problems. Thus, the impact of paternal age on offspring development from conception to adulthood needs further investigation. In this study, we investigated the neonatal health and growth trajectories in offspring from older males.
Method: Naturally-aged C57BL6 male mice that were either "old" (>1-year-old), or "young" (<8 months old) were time-mated with naturally cycling, 8-10 week old females. For a subset of pregnancies, fetal development was assessed on E18.5. Another subset of pregnancies were carried to term, and neonatal and pre-pubertal development were assessed over 3 weeks. After weaning, growth trajectories of these offspring were tracked for 6 months followed by glucose and insulin tolerance test metabolic assays. Additionally, sperm analysis were conducted on the fathers 1-week after successful mating, including use in IVF, where embryo development was analyzed by time-lapse imaging.
Results: Old males presented poor sperm quality and after IVF, had decreased pre-implantation embryo development rates (N=12-12; P=0.004). After mating, older males produced ~15% fewer pregnancies. E18.5 fetuses from older males were 10% lighter (N=47-46); P<0.0001) and had smaller placentas (N=20-36; P=0.04). Litters from older males had reduced birth weight (N=12-18; P=0.01) and pup mortality was increased by 14% (P=12-8; P=0.05). For 5 days post-birth male pups presented delayed self-righting times (N=3-5; P=0.0004). Male but not female offspring of older fathers continued to have reduced weight into adulthood (N=10-20; P<0.0001), and presented disrupted glucose and insulin metabolism at 7 months old (N=10-20; P=0.003).
Conclusions: These results demonstrate that the age of the father at conception has long-term consequences on offspring phenotype and health in mice, likely as a result of compromised sperm quality impacting the earliest phases of embryo development.

Role of calcium-activated potassium channels in L-arginine/NO pathway regulated by insulin in human placenta

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Background/Aims: Insulin regulates the vascular function through the stimulation of the L-arginine/NO pathway in human endothelium. In human umbilical vein endothelial cells (HUVECs) has been determined that insulin increases the plasma membrane expression of hCAT-1 (L-arginine transporter) and induces vasodilation in umbilical and placental veins. The vascular relaxation induced by insulin in placental vessels is dependent of activity of large conductance calcium-activated potassium channels (BKCa), but the role of KCa channels in L-arginine transport or NO synthesis still is unknown.
Method: HUVECs and human placental vein endothelial cells (HPVECs) were freshly isolated from samples obtained from physiological pregnancies. Cells or tissue were incubated (30 min) in absence (control) or presence of insulin and/or tetraethylammonium (TEA), Tram-34, iberiotoxin (IBTX) or L-NAME. L-[H3]arginine uptake, membrane polarity (DiBAC(4)3 fluorescence), NO levels (DAF fluorescence), hCAT-1/BKCa expression (RT-PCR, immunofluorescence) and placenta perfusion pressure were determined.
Results: The inhibition of IKCa and BKCa increases the basal L-arginine transport through regulation of plasma membrane abundance of hCAT-1. KCa activity is necessary for NO-synthesis induced by insulin but is not relevant for L-arginine transport stimulated by hormone, meanwhile insulin increases the hCAT-1 and BKCa expression in fetoplacental endothelium. Regulation by insulin of placental perfusion pressure was reverted by TEA.
Conclusions: The activity of KCa (mainly BKCa) is relevant for basal L-arginine transport in HUVECs, but not for rapid stimulation of amino acid uptake. In NO synthesis, insulin signaling pathway involves KCa activity and higher expression of hCAT-1 and BKCa could be necessary for endothelial hyperpolarization induced by insulin.

Effects of excess and limited dietary nutrition during whole period of gestation on fetal development in Wagyu cattle.

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Background/Aims: Fetal and neonatal programming based on the concept of Developmental Origins of Health and Disease (DOHaD) would have potential to contribute not only medicine but also livestock production. In reference to Wagyu (Japanese Black cattle) which is a fatty type of beef cattle, it has not been experimentally verified that how maternal nutrition affects fetus development during the whole period of gestation. The objective of this study is to investigate the effects of excess and limited maternal nutrition during the whole gestation on muscle development and adipose tissue accumulation of fetus in Wagyu cattle
Method: Wagyu cows were allocated into high-nutrition (HN: n=5) group to meet 120% of nutrition requirements and low-nutrition (LN: n=6) group to meet 60% of it. All the experimental cattle sequentially have been artificially inseminated (AI) with male-sorted semen of an identical sire. In each group, the fetuses were taken by Caesarean section at 260±8.3 days of fetal age and killed with bleeding after anesthesia and dissected. The whole body weight, total muscle weights including 21 individual muscles weights and adipose depots at the level of half carcass of fetus were measured.
Results: Body weight of fetus, total muscle and adipose weight at the level of half carcass were significantly larger in HN group ($P<0.01$, $P<0.01$ and $P<0.01$, respectively). Their magnification in group HN compared to group LN indicated 1.39, 1.45, and 2.12 folds, respectively. Sixteen muscles of 21 muscles we investigated showed the significantly larger weight in group HN compared with group LN. Meanwhile, the weights of perirenal, subcutaneous, intermuscular and peritoneal cavity fat depots were significantly larger in group NH than in group LN ($P<0.005$, $P<0.01$, $P<0.05$, and $P< 0.05$, respectively).
Conclusions: Maternal nutrition during whole period of gestation would strongly affect parts of muscle development and almost depots of adipose tissue accumulation of fetus in Wagyu. These things might indicate that the control of maternal nutrition during the whole period of gestation has quite great potential of muscle and adipose tissue development of Wagyu fetus, which might be closely related to the future productivity of meat quantity and quality in cattle.

Preterm birth alters vascular tone and mechanics in adult offspring

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Background: Preterm birth accounts for ~8% of all births worldwide and is now recognised as a factor in the development of cardiovascular and metabolic disease risk in adolescence and adulthood. However, the precise vascular mechanisms underpinning later-life cardiovascular risk in those born preterm remains uncertain.
Aims: To examine vascular tone, myogenic responsiveness and vascular mechanics in resistance vessels of adult offspring that were born preterm.
Methods: Third order mesenteric vessels from adult male and female guinea pigs born preterm or at term were mounted on a pressure myograph. Pressure-diameter and concentration curves were constructed in the presence of L-NAME, Indomethacin (INDO), TRAM-34, and Apamin, independently and in combination with each other, to test vascular pathways. Further calculations of vascular structural and mechanical parameters, such as wall thickness, circumferential surface, luminal surface areas, stress and stiffness were also calculated.
Results: When compared to vessel mechanics of those born at term, nitric oxide-induced vasodilation in vessels of adults born preterm was significantly blunted in the presence of INDO, TRAM-34 and Apamin. Similarly, preterm birth significantly impacted structural parameters (wall thickness, circumferential surface area and luminal surface area) and vascular mechanical indices, including an increased circumferential wall stress and stiffness. Overall, no effect of sex was observed within groups.
Conclusions: Using our clinically relevant model of preterm birth we have shown that preterm birth has adverse effects on vascular structure and function that persist into adulthood. Identification of these vascular adaptations and their regulatory pathways are of major importance and will inform of potential therapeutic interventions to attenuate the increased predisposition to cardiovascular disease identified in adult survivors of preterm birth.

Consequences of maternal bariatric surgery: potential for reduced amino acid availability to the foetus

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Background/Aims: Though bariatric surgery is the most effect method of durable weight loss, it is not understood why or how it works so effectively to reduce the comorbidities of Metabolic Syndrome. Both in humans and rodents, maternal bariatric surgery prior to pregnancy results in challenges during pregnancy including increased small-for-gestational age offspring and greater risk for foetal demise. We have shown in the rodent model of vertical sleeve gastrectomy (VSG) that offspring develop greater risk for metabolic disease later in life compared to obese controls. A common gestational cause of poor growth *in utero* is maternal protein deficiency. In the current work, we

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hypothesize that the transporters within the placenta may be differentially transporting amino acids to the foetus despite previously demonstrating that protein levels in the VSG dam were not harmed by surgery and were sufficient to sustain a health pregnancy.
Method: Using gestational day 19 placenta from pregnant Lean, Obese and post-VSG dams, we performed analysis of the amino acid content of the placenta and prepared placental mRNA for quantitative PCR analysis of genes associated with amino acid transport.
Results: Aliphatic amino acids: isoleucine, leucine, proline and valine were significantly reduced in comparison to Lean dam levels ($p < 0.05$). Phenylalanine, aspartic acid and glutamic acid, arginine, histidine and methionine were also significantly reduced ($p < 0.05$). Furthermore, amino acid transporter SLC38A1 (SNAT1) and SLC38A4 (SNAT4) showed trends towards reductions in both VSG and Obese dams. On the contrary, SLC38A2 (SNAT2) and SLC7a7 (LAT1) was significantly elevated ($p < 0.05$) in VSG in comparison to Lean and Obese. This affect appeared specific to amino acids since carbohydrate transporters remained unchanged.
Conclusions: Collectively, these data suggest that despite healthy ingestion of proteins by the VSG dam, alterations in amino acid availability to the foetus may be obstructed by the placenta after bariatric surgery. This reduced level of amino acid availability may contribute to poor outcomes in bariatric pregnancy. More work is needed to determine the relevance of these findings to humans.

The Impact Of Low Maternal Vitamin D On Fetal Regional Blood Flow Resistance And Growth

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Background/Aims: Fetuses rely on maternal vitamin D, but vitamin D deficiency affects a substantial proportion of the population. In animals, low vitamin D is linked to altered musculoskeletal growth and femoral artery endothelial function. However, little is known about the relationship between maternal vitamin D status, regional fetal blood flow and growth in human pregnancies.
Method: 469 fetuses from an ongoing pregnancy trial were scanned by ultrasound between 12- and 34-weeks for head, abdomen and femur size, and at 34-weeks for blood flow to the head, legs and placenta. The relationships between maternal serum 25-hydroxyvitamin-D concentration ([25(OH)D]), fetal vascular resistance and growth were analysed using linear regression models (regression coefficient[95%CI]).
Results: Lower 14-week maternal [25(OH)D] was associated with reduced 34-week femur length (0.017[0.005-0.029]mm/nmol/L). At 34-weeks, increased femoral artery resistance was associated with reduced femur length (-0.451[-0.811- -0.091]mm/resistance), and reduced circumference of head (-0.0695[-0.151-0.0121]mm/resistance) and abdomen (-0.163[-0.264- -0.063]mm/resistance). At 34-weeks, femoral artery resistance was greatest in fetuses from women falling in the lowest quarter (14-80nmol/L) of the maternal [25(OH)D] distribution ($P < 0.01$).
Conclusions: Femoral artery Doppler ultrasound is not routinely used clinically, but its relationship with fetal size, suggests it could be a useful growth marker. If lower maternal [25(OH)D] is associated with decreased blood flow to the leg and smaller fetal size, vitamin D supplementation in pregnancy may be beneficial for fetal outcome. The efficacy of this intervention will be tested once the trial is complete.
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Hands-on Science and Debate Engagement Alters Teenage Student Perception of DOHaD and Their Health

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Background/Aims: DOHaD scientific advances have big implications for combating non-communicable diseases. But this requires coordinated multi-level action by health care professionals, policy-makers and individuals. Engaging these stakeholders in DOHaD concepts is imperative. In young students – the future medical professionals, scientists and parents - we assessed the impact of an engagement package on health perceptions and health-related science literacy.
Method: 16-17 year old UK college students (n=53, 70% female) participated in science talks and hands-on laboratory experiments at the IDS followed by a question time panel debate on major health topics. The engagement impact was assessed by online questionnaires (Wilcoxon Signed-Rank tests).
Results: Student awareness of IDS science increased (from 'poor' to 'good'-$P < 0.001$) and discussion with scientists about 'improving health in the population through science' increased (from 'never' to 1-4 times-$P < 0.001$) after the engagement. 90% felt the question time debates altered their thinking about health determinants. 45% ($P < 0.001$) felt less healthy and

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42% (P=0.075) were less optimistic about their future health after the engagement. After the engagement, students felt more able to explain the meaning of 'epigenetics' (from 'no-idea' to 'a-little-confident') and 'DOHaD' (from 'not-confident' to 'a-little-confident') (P<0.001), and 79% (P<0.001) considered diet in pregnancy to be more important in making them healthy into adult life.
Conclusions: This small study highlights the short-term effect of hands-on science and debate on young people's health perception and health-related science literacy. It reinforces the principles of Southampton's LifeLab and suggests that this sort of engagement helps raise awareness of DOHaD advances with young people.

Associations of maternal characteristics with breast anatomy and milk production during the established lactation

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Background/Aims: Animal models show a more rapid mammary gland response and more milk with subsequent lactations, as well as impairment of lactation performance by obesity, but human studies of maternal factors that may influence breast anatomy and milk production are rare.
Method: Ultrasound examination of lactating mothers (n=10; ongoing) included B mode imaging to measure number and diameters of milk ducts prior to pumping session. The amount of glandular tissue was classified as low, moderate or high. Mothers completed a 24-h milk production and breast storage capacity was calculated. Body composition was measured with bioimpedance spectroscopy.
Results: Milk production: 24-h milk production was negatively associated with maternal weight (p=0.041), BMI (p=0.007) and fat mass index (p=0.029). Breast storage capacity was negatively associated with maternal weight (p=0.027), BMI (p=0.034), fat mass (p=0.009), % fat mass (p=0.037) and fat mass index (p=0.011) and positively with mean duct diameter (p=0.037).
Glandular tissue: Amount of glandular tissue was negatively associated with maternal weight (p=0.049) and positively with both, number of the ducts (p=0.031) and sum of duct diameters (p=0.003) in the lower half of the breast.
Milk ducts: Mean duct number was positively associated with parity (p=0.015) and previous lactations duration (p=0.013). Mean duct diameter was negatively associated with maternal weight (p=0.021).
Conclusions: Preliminary results indicate multiple associations between maternal body composition, parity, amount of glandular tissue and number and size of milk ducts, providing support for animal studies. Further research may inform potential interventions, such as maintaining healthy adiposity during pregnancy and lactation as well as pre-conception to ensure the optimal lactation performance.

Maternal exercise influences the placental mitochondria in a region- and diet-specific manner, with minimal impact of maternal growth restriction

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Background/Aims: The placental mitochondria adapt to changing fetal energy demands to maintain normal fetal growth. Alterations in placental mitochondrial function have been implicated in a myriad of diseases, including intrauterine growth restriction and maternal obesity. However, little is known about the potential benefits maternal exercise has on placental mitochondrial content. Therefore, we aimed to investigate whether maternal exercise can restore placental mitochondrial content in growth restricted and obese mothers.
Method: Uteroplacental insufficiency was induced by bilateral uterine vessel ligation (Restricted) or sham (Control) surgery on embryonic day (E) 18 in Wistar-Kyoto rats. Female F1 Control and Restricted offspring were fed a Chow or High-fat (HFD) diet from weaning (35 days), then allocated to an exercise regime at 16 weeks; Sedentary, exercised on a treadmill prior to and throughout pregnancy (Exercise) or exercised only during pregnancy (PregEx). F2 placentae were excised, weighed and separated into regions (junctional zone and labyrinth) on E20; with fetal sex verified via qPCR (SRY). Citrate synthase activity was quantified along with gene expression of mitochondrial genes (*Coxiii* and *Coxiv*) and mitochondrial biogenesis markers (*Pcg-1a* and *Tfam*) using qPCR in male associated placentae.
Results: In the junctional zone, high-fat feeding in growth restricted dams increased (in PregEx) and decreased (in Sedentary) *Coxiv* mRNA abundance. Whereas in the labyrinth, high-fat feeding in growth restricted dams increased *Pcg-1a* and *Coxiii* mRNA abundance and reduced *Tfam* mRNA abundance. Exercise (HFD only) and PregEx decreased junctional zone Citrate Synthase activity and decreased the abundance of mitochondrial biogenesis markers in a diet- and region-specific manner. A novel finding was that Citrate Synthase activity was increased in the junctional zone compared to the labyrinth.
Conclusions: Overall, we have demonstrated that markers of mitochondrial content and biogenesis are reduced with maternal exercise in a region- and diet-specific manner, with minimal alterations in response to maternal growth restriction. However, the impact these alterations have on long-term F2 male offspring health remains to be elucidated.

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The Healthy living in pregnancy (GeliS) trial – a large-scaled public health approach for the prevention of excessive gestational weight gain and pregnancy complications

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Background/Aims: An alarming number of women gains weight excessively during pregnancy. As this can be accompanied by adverse health consequences for mothers and offspring, there is a clear need to develop effective intervention strategies feasible in "real-life" settings. The main aim of the GeliS study ("Gesund leben in der Schwangerschaft"/Healthy living in pregnancy) was to prevent excessive gestational weight gain (GWG) with lifestyle counselling conducted alongside routine antenatal care in Bavaria, Germany. Secondary outcomes included pregnancy and obstetric complications such as gestational diabetes (GDM) as well as neonatal health parameters
Method: The GeliS study is designed as a multicentre, prospective, cluster-randomised, controlled, open intervention trial, including 2286 pregnant women. In three structured sessions during pregnancy and one additional session postpartum, a healthy balanced diet, regular physical activity and self-monitoring of GWG were addressed in the intervention group. The control group obtained standard care. Counselling was given by specifically trained gynecologists, midwives and medical personnel.
Results: The intervention was not successful in reducing the proportion of women with excessive GWG (45.1% vs 45.7%, p=0.789). GDM and other pregnancy and obstetric complications were not significantly influenced by the counselling. Birth weight and length were slightly lower in the intervention group (3313 ± 536g vs. 3363 ± 498g, p=0.020; 51.1 ± 2.7cm vs. 51.6 ± 2.5cm, p=0.001).
Conclusions: Lifestyle advice conducted by trained healthcare providers alongside routine prenatal care was not successful in reducing GWG and pregnancy complications. Cooperation with dietary and physical activity experts may be a promising strategy for modifying the GeliS concept. Potential long-term effects of the intervention on maternal and infant health remain to be evaluated and are currently assessed in a 5-year follow-up.

Health Service Utilisation of Australian Children from Immigrant and Non-immigrant Families: A Population-based Cohort Study

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Background/Aims: Children from immigrant backgrounds have a higher risk of experiencing poor health outcomes, especially for non-communicable diseases, compared to their native-born peers. One of the likely contributors to these health inequalities is differential access to health services. The present study examines the pattern of health service utilisation in Australian children at 10-11 years by family immigration status and language background.
Methods: This study draws on data from the Longitudinal Study of Australian Children, a nationally-representative Birth (N=5107) and Kindergarten cohort (N=4983). Family immigration status (native-born/foreign-born) and language background (English speaking/non-English speaking) were collected at 0-1 years or 4-5 years for B- and K-cohort respectively. Parents reported children's use of nine health services at 10-11 years: general practitioner, paediatrician, dental service, guidance counsellor, mental health service, speech therapy, emergency ward, hospital outpatient, and hospitalisation. The distribution of health service use was examined by immigration status and language background. Logistic regression analyses were conducted to further examine associations between family immigration and child health service use.
Results: Overall, around one-third of Australian children (32-35%) came from foreign-born families. Compared with native-born and English speaking children, those from foreign-born and non-English speaking families had lower socioeconomic resources and higher health needs, but accessed fewer health services such as from a paediatrician (OR=0.47, 95% CI:0.26-0.85; OR=0.49, 95% CI: 0.26-0.91), mental health services (OR=0.35, 95% CI: 0.16-0.78; OR=0.46, 95% CI: 0.23-0.93), and emergency wards (OR=0.59, 95% CI: 0.38-0.91; OR=0.68, 95% CI: 0.47-1.00).
Conclusion: These findings suggest that children from immigrant families may face barriers in accessing health services. This is concerning because it is likely to contribute to health inequalities for these children, which can persist over the life course. Further effort is needed to ensure that the healthcare system meets the needs of all families, including those from diverse cultural and language backgrounds.

The cross-sectional investigation of iron deficiency prevalence and iron deficiency anemia prevalence in pregnant women of China's urban areas in 2016

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Abstract
Objective: To investigate the prevalence of iron deficiency and iron deficiency anemia in pregnant women in urban areas of China at this stage.
Methods: This is a national cross-sectional study. The population sampling has adopted a multi-stage stratified equal sampling. According to the classification of National Bureau of Statistics of China, a total of 24 survey points were set up in 6 regions of China, covering 21cities, and random samplings were taken to examine indicators such as serum ferritin and hemoglobin levels in pregnant women.
Results: There were 12,403 pregnant women taking part in this survey. 5,973 pregnant women were diagnosed with iron deficiency (ID), and the prevalence rate was 48.2%. 1,720 pregnant women were diagnosed with iron deficiency anemia (IDA), and the prevalence rate was 13.9%. During pregnancy, the average serum ferritin level was 20.6ng/ml (11.78 - 36.98 ng/ml), and the average hemoglobin level was 118.38 g/L (118.38±11.52 g/L); In early, mid and late pregnancy, the average serum ferritin levels were respectively 54.30 ng/ml (34.48-94.01 ng/ml), 28.60 ng/ml (16.40-50.52 ng/ml),16.70 ng/ml (10.20-27.00 ng/ml) (p<0.001), and the average hemoglobin levels were 126.78 ±10.20 g/l, 118.93±11.27 g/l, 117.06±11.32 g/l (p<0.001). The prevalence rates of IDA in early, mid and late pregnancy were respectively 2.0%, 8.4%, 17.8% (p<0.001). The prevalence rates of ID, IDA were different in different regions across the country, among which, the prevalence of ID in east and northeast China was the highest, the prevalence of IDA in northwest and east China was the highest, while the prevalence rates of ID and IDA in southwest China were both the lowest.
Conclusion: Currently, iron deficiency and iron deficiency anemia in pregnant women are still prevalent, and nutrition and health care during pregnancy should be strengthened.

Educational Attainment of Young Adults Born Preterm

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Background: Previous studies suggest that preterm birth (< 37 full gestational weeks) is associated with a higher risk of poorer educational attainment at young adulthood.
Methods: This population-based cohort study assessed attained education at 25 years of age per gestational age (GA) groups by multinomial regression. All 228,616 traceable (97.0%) children with adequate data on GA and birth weight (11,227 preterm, 4.9%) live-born in Finland 1.1.1987–30.9.1990 without major birth anomalies were followed up until 31.12.2015. Study subjects who died before 25 years of age were excluded (2395, 1.0%). Categories for education were (1) basic only or unknown /(2) secondary /(3) lower tertiary or higher. Category 2 was used as reference.
Results: 30,745 study subjects (13.6%) had achieved only basic education at 25 years of age, or their educational level was unknown. As compared with the category of secondary education, the unadjusted odds ratios (OR) and 95% confidence intervals (CI) for basic or unknown education by full weeks of GA were as follows: 23-27 weeks 1.65 (1.20-2.26), 28 to 31 weeks 1.35 (1.12-1.62), 32 to 33 weeks 1.03 (0.87-1.23), 34 to 36 weeks 1.06 (0.99-1.13), and 37 to 38 weeks 1.02 (0.98-1.05). GA group 39 to 41 was the reference. After adjustment for highest parental educational attainment the associations were attenuated in all GA categories, but remained significant among those born at 23 to 31 weeks gestation.
The unadjusted ORs and CIs for the highest education category (lower tertiary or higher) by GA were as follows: 23 to 27 weeks 0.62 (0.43-0.89), 28 to 31 weeks 0.80 (0.67-0.95), 32 to 33 weeks 1.01 (0.88-1.16), 34 to 36 weeks 0.94 (0.89-0.99), and 37 to 38 weeks 1.00 (0.97-1.03). In the adjusted model the ORs increased, but were significant only among those born at 23 to 32 weeks gestation, while the association disappeared for those born at 34 to 36 weeks gestation.
Conclusions: Young adults born preterm in 1987-1990 have lower educational attainment than their peers born at full term. This association is partly explained by parental education. Our results are in line with previous results from other Nordic countries based on births from the late 1960s to early 1980s; if anything, the association between gestational age and educational attainments of young adults within our cohort appear to be stronger than those reported in previous Nordic population-based cohort studies.

Intergenerational transmission of educational attainment and the role of gestational age: a register-linkage study of 221,351 Finns

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Background/Aims: Finland, a Nordic welfare state, is known for equal and free educational opportunities, including university studies. However, even in this setting parental education

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has a strong effect on the pathways chosen by their offspring. We examined the role of gestational age (GA) in intergenerational transmission of educational attainment using nationwide register data.

Methods: We studied all 221,351 children live-born in Finland between 1987–1990 with adequate data on GA and the key covariates (4.8% with GA<37 full wks). Data from several registers were interlinked for the cohort and their parents over a follow-up of 22 years. Children with major birth anomalies or who died or emigrated before the end of follow-up were excluded. GA was categorised into seven groups (reference: 39–41 wks). Highest parental attained education when the child was 16 and the highest education of the child at 22 years of age (degrees or current studies) were categorised into low, medium, and high. Three dichotomous outcomes were computed: child's education relative to parental education 1) lower, 2) equal, 3) higher (each: yes/no). We applied logistic regression.

Results: High level of education was attained by 16.3% of young adults whose parental education was low, whilst the shares were 35.4%/67.2% among those whose parents had medium/high level of education. GA was associated with the transmission of educational attainment with a gradient; those born extremely preterm (23–27 wks) were the most likely to attain lower education than their parents – unadjusted OR 3.58 (CI95% 2.44–5.25) if the parents had medium level education, and OR 2.94 (1.73–5.01) if the parental education level was high. Correspondingly, child born extremely preterm was the least likely to attain higher education than his/her parents, OR 0.62 (0.25–1.53) in the low and OR 0.51 (0.36–0.73) in the medium parental education group. Adjusting for sex, birth order, smoking in pregnancy, and parents' ages at the time of the child's birth had negligible effect.

Conclusions: The pattern of intergenerational transmission of educational attainment appears to be different among those born preterm. Our findings reinforce previous suggestions that special attention should be paid to support the educational pathways of the preterm.

DNA Methylation in ADIPOQ, IGF1, IGF2 and LEP are Associated with Their Respective Proteins in Cord Blood and Measures of Neonatal Anthropometry

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Background/Aims: Epigenetic changes in utero have been proposed as one of the mechanisms by which maternal obesity contributes to the risk of offspring obesity later in life. Our aim was to determine if previously reported associations with cord blood proteins adiponectin, insulin-like growth factor 1 (IGF-1), insulin-like growth factor 2 (IGF-2) and leptin with neonatal anthropometry (Patel et al, 2018) were associated with DNA methylation of ADIPOQ, IGF1, IGF2 and LEP.

Methods: We studied 518 mother-offspring pairs from the UK Pregnancies Better Eating and Activity Trial (UPBEAT) data set, all mothers were obese. Using the Infinium Human Methylation EPIC Bead Chip array we looked at 205 CpG sites in total across the four candidate genes. Linear regression models were used to determine the significance of associations between DNA methylation and either cord blood proteins or neonatal anthropometry, while adjusting for relevant covariates.

Results: Associations that reached statistical significance included: methylation at cg21917949 in IGF2 was positively associated with WHO neonate centiles, methylation at cg07583420 in the IGF2 gene was positively associated with birthweight, WHO neonatal centiles and abdominal circumference. Many more associations between methylation and anthropometry were evident using a nominal p-value of < 0.05. All four proteins were associated with methylation in at least one CpG site in their respective genes.

Conclusion: DNA methylation within candidate genes, especially IGF2, were associated with neonatal anthropometry and their respective proteins, and may have relevance to origins of childhood obesity.

Time for change: The ORIGINS Project leading a new generation of interventional birth cohorts

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Background/Aims: The ORIGINS Project is a unique community-centred pregnancy intervention cohort with the ultimate goal of improving the health of the next generation. In addition to a core observational element of the cohort, we aim to explore strategies to optimise the early environment across diverse domains. We have initiated a range of parallel nested harmonised studies aimed at early identification and/or early interventions to address a range of common health problems in children, with a particular focus on immune health, metabolic health, emotional health and neurodevelopment. This also includes strategies to improve parental physical and emotional health and family dynamics.

Method: The ORIGINS Project is a unique community-centred pregnancy intervention cohort with the ultimate goal of

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improving the health of the next generation. In addition to a core observational element of the cohort, we aim to explore strategies to optimise the early environment across diverse domains. We have initiated a range of parallel nested harmonised studies aimed at early identification and/or early interventions to address a range of common health problems in children, with a particular focus on immune health, metabolic health, emotional health and neurodevelopment. This also includes strategies to improve parental physical and emotional health and family dynamics.

Results: We have currently recruited over 2000 families and have over 10 sub-projects nested within the Project, and numerous more in the pipeline. These sub-projects include a mixture of qualitative and quantitative observational studies, intervention and mechanistic trials. The nested trials and studies examine exposures, interventions and outcomes integral to the development and prevention of non-communicable disease trajectories. Examples of specific interventions include: maternal lifestyle interventions to promote healthy gestational weight gain and combat overweight obesity trajectories; nutritional interventions to promote metabolic and immune health; trials of allergen exposure in pregnancy and lactation to reduce infant sensitisation. We are also exploring 'upstream' strategies to improve wellness behaviours including: mindfulness interventions; nature play interventions; which preliminary studies suggest improve a range of lifestyle factors that promote resilience and well-being including food choices, physical activity; mental outlook and prosocial behaviour. Qualitative feedback already suggests that the study is having benefits in both the research environment (more collaborative culture), and a stronger sense of belonging and cohesion in the local community.

Conclusions: ORIGINS is a cohort invested in making positive change—not only for children and their families, but for the wider community. It is our goal that ORIGINS will also serve as an example of how grass-roots efforts, tailored for the needs of each community, can be part of global efforts towards planetary health.

Old question revisited: Are high protein diets safe in pregnancy?

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Background : A previous randomized dietary intervention in pregnant women from the 1970s, the Harlem Trial, reported retarded fetal growth and excesses of very early preterm births and neonatal deaths among those receiving high protein supplementation. Given the nature of these findings repeating the intervention poses ethical challenges and addressing this issue in an observational setting requires large sample size. Our aim was to see if these findings could be replicated in an observational setting by combining data from two large birth cohorts.

Methods: Individual participant data on singleton pregnancies from the Danish National Birth Cohort (DNBC) (n=60,141) and the Norwegian Mother and Child Cohort Study (MoBa) (n=66,302) were merged after a thorough harmonization process. Diet was recorded in mid-pregnancy and information on birth outcomes were extracted from National Birth Registries.

Results: The prevalence of preterm delivery, low birth weight, fetal and neonatal death was 4.77%, 2.93%, 0.28% and 0.17%, respectively. Mean protein intake (standard deviation) was 89g/day (23). Overall high protein intake (>100g/day) was neither associated with low birth weight, nor fetal or neonatal death and mean birth weight was essentially unchanged at high protein intakes. A modestly increased risk of preterm delivery [OR: 1.10 (95% confidence interval: 1.01, 1.19)] was observed for high (>100g/day) compared to moderate protein intake (80-90g/day). This estimate was driven by late preterm deliveries (weeks 34 to <37) and more elevated risk was not observed at more extreme intakes.

Conclusion: High protein intake was weakly associated with preterm delivery. Contrary to the results from the Harlem Trial, no indications of deleterious effects on fetal growth or perinatal mortality were observed.

Why do levothyroxine treated subclinical hypothyroidism pregnant women with still have adverse pregnancy outcomes? laboratory characteristics analysis

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Background/Aims: To reassess the effect of levothyroxine on gestational subclinical hypothyroidism (SCH,4.0mIU/L≤TSH<10mIU/L) by analyzing pregnancy outcomes and laboratory characteristics.

Method: The medical records of pregnant women were reviewed during 2014-2017(n=14123).One hundred and sixty-five pregnant levothyroxine treated SCH women (group SCH) were screened. Controls were randomly selected by

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euthyroid (EU) women matched regarding to age, gravidities and parities with four controls in group EU (n=660). Laboratory characteristics and pregnancy outcomes were evaluated during follow-up.

Results: Group SCH had higher inadequate gestational weight gain (25.77% vs. 18.59%; p=0.041, OR=0.599,95%CI:0.402-0.892), small for gestational age offspring (4.24% vs. 0.60%; p=0.002, OR=0.069, 95%CI: 0.014-0.333) as well as premature delivery (9.09% vs. 4.39%, p=0.016; OR=2.191, 95%CI: 1.139-4.214) than group EU. After levothyroxine treatment,group SCH had significant lower high and low density lipoproteinlipoprotein level, lower fasting blood glucose and glycosylated albumin and higher serum homocysteine level before delivery (p<0.05).

Conclusions: SCH pregnant women still have adverse pregnancy effects after levothyroxine treated. We believe that besides levothyroxine, vitamin B12 and folic acid may also be needed.In addition, regular monitoring of blood lipid and homocysteine levels and intervention gestational weight gain may also improve the adverse effects of SCH on pregnancy outcome.

Status of metabolic syndrome and its geographic and economic predilections in Chinese children and adolescents: analysis from a Chinese national study

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Background/Aims: Metabolic syndrome (MetS) has become a worldwide epidemic but few studies have described its status in Chinese children. This study aims to estimate MetS status and its associations with geographic location, level of economic development, birth weight, and parental education in Chinese children and adolescents.

Method: Data was derived from 15045 participants aged 7-18 years across seven Chinese provinces. Physical measurement and blood tests were conducted to assess abdominal obesity, high blood pressure, low high-density cholesterol (HDL-C), high triglyceride and elevated fasting glucose (FG), the five

Tables:

Table 1 Prevalence of MetS according to age, sex, geographic location and economic development level(%).

Age (yr)	Overall (%)	Sex (%)		Geographic location (%)		Economic development (%)	
		Male	Female	North	South	Underdeveloped	Developed
7	0.8	0.8	0.7	1.2	0.5	0.6	0.9
8	0.7	0.5	0.8	0.5	0.8	0.6	0.7
9	1.7	1.2	2.2	2.3	1.0[b]	0.9	2.2[c]
10	2.4	2.5	2.3	3.1	1.9	1.4	3.0[c]
11	2.9	3.5	2.0	4.3	1.2[b]	0.3	5.7[c]
12	2.7	3.7	1.8[a]	3.7	2.0[b]	1.9	3.6[c]
13	3.3	4.0	2.5	4.5	1.4[b]	2.3	4.0
14	2.6	4.5	0.9[a]	4.3	1.2[b]	1.0	5.1[c]
15	2.8	4.5	1.2[a]	4.1	2.3	1.6	3.7[c]
16	3.1	4.2	2.2[a]	5.0	1.9[b]	0.7	4.2[c]
17	3.9	4.8	3.0	3.3	4.7	2.2	4.9
18	3.0	5.3	0.0	2.4	4.2	0.0	5.9
7-9	1.0	0.9	1.2	1.4	0.8[b]	0.7	1.2
10-18	2.9[*]	3.8[*]	2.0[a*]	4.0[*]	2.0[b*]	1.5[*]	3.9[c*]
Total	2.3	2.8	1.7[a]	3.1	1.5[b]	1.3	2.9[c]

Data are percentage (%). MetS, metabolic syndrome.
a p<0.05 , male vs. female, assessed by $\chi 2$ test for categorical variables.
b p<0.05 , north vs. south, assessed by $\chi 2$ test for categorical variables.
c p<0.05 , underdeveloped vs. developed, assessed by $\chi 2$ test for categorical variables,
* p<0.05 , 7-9 vs. 10-18.

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Table 2 Prevalence of individual components of MetS among 15045 Chinese children and adolescents aged 7-18 years, 2013.

MetS Component	n	Overall (n=15045)	Sex		Geographic location		Economical development	
			Male (n=7711)	Female (n=7334)	North (n=6843)	South (n=8202)	Under developed (n=5997)	Developed (n=9048)
Abdominal obesity	3282	21.8 (21.1,22.5)	21.2 (20.3,22.1)	22.5 (21.5,23.5)	24.2 (23.2,25.2)	19.8 [b] (18.9,20.7)	15.7 (14.8,16.6)	25.9 [c] (25.0,26.8)
High BP	559	3.7 (3.4,4.0)	4.6 (4.1,5.1)	2.7 [a] (2.3,3.1)	6.4 (5.8, 7.0)	1.5 [b] (1.2,1.8)	4.1 (3.6,4.6)	3.5 (3.1,3.9)
Low HDL-C	2163	14.4 (13.8,15.0)	15.8 (15.0,16.6)	12.9 [a] (12.1,13.7)	19.0 (18.1,19.9)	10.5 [b] (9.8,11.2)	15.5 (14.6,16.4)	13.6 [c] (12.9,14.3)
High TG	826	5.5 (5.1,5.9)	5.0 (4.5,5.5)	6.0 [a] (5.5,6.5)	6.1 (5.5,6.7)	5.0 [b] (4.5,5.5)	5.2 (4.6,5.8)	5.7 (5.2,6.2)
Elevated FG	454	3.0 (2.7,3.3)	4.1 (3.7,4.5)	1.8 [a] (1.5,2.1)	4.1 (3.6,4.6)	2.1 [b] (1.8,2.4)	0.7 (0.5,0.9)	4.6 [c] (4.2,5.0)

Data are percentage with 95% confidence interval.
MetS, metabolic syndrome; BP, blood pressure; HDL-C, HDL cholesterol; TG, triglyceride; FG, fasting glucose.
a $p<0.05$, male vs. female, assessed by $\chi 2$ test for categorical variables.
b $p<0.05$, north vs. south, assessed by $\chi 2$ test for categorical variables.
c $p<0.05$, underdeveloped vs. developed, assessed by $\chi 2$ test for categorical variables.

classical MetS components described by the International Diabetes Federation[1]. Logistic regression was adopted to explore possible associations between MetS and other factors.
Results: Overall, MetS prevalence was 2.3%, higher in males (2.8 vs. 1.7% in females), northern regions (3.1%), more-developed regions (2.9%) and older participants (aged 16-18 years) (all P<0.05, Table 1). Among the five MetS components, abdominal obesity and low HDL-C were most prevalent (21.8% and 14.4%, Table 2), and 35.9% of the participants had at least one component. In logistic regression, MetS itself did not correlate with birth weight or parental education. High birth weight was positively correlated with abdominal obesity (odds ratio 1.48), while negatively associated with elevated FG (odds ratio 0.49).
Conclusions: MetS itself was not common in Chinese children and adolescents, while its certain components were far more prevalent. Children from north China, more-developed areas, and at an older age were more likely to develop MetS. Strategies designed to prevent pediatric MetS in China should focus more on its prevalent components, as well as its geographic and economic-development predilections.

Vitamin B12 supplementation modifies circulating microRNAs targeting glucose and insulin metabolism

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Background/Aims: There is growing interest in the DOHaD field for the role of micronutrients in foetal programming. Vitamin B12, folate, vitamin D and other nutrients are implicated. The effect is thought to be mediated through 'epigenetic' mechanisms although only sparse human data are available. In the Pune Maternal Nutrition Study (PMNS), low maternal vitamin B12 status during pregnancy was associated with increased insulin resistance in the child at 6 years of age. It is possible that vitamin B12 deficiency exerts the effects through epigenetic regulations involving microRNAs.
Method: A vitamin B12 trial was started in the PMNS children at 17 years of age to improve their nutritional status with an objective to reduce the risk of diabetes in their future children. We have plasma samples before and 1 year after B12 supplementation in ~700 children participating in PMNS. A microRNA discovery analysis was carried out in a subset (N=10) of these children using TaqMan™ OpenArray panels at 6-, 12-, 17-years of age and after one year of vitamin B12 supplementation. Univariate analyses as well as penalized logistic multi-regression (Lasso) analyses identified microRNAs that are associated with changes in vitamin B12 supplementation and future risk of diabetes. The microRNA target pathways were identified using Ingenuity Pathway Analysis (IPA), DAVID or miRSystems.
Results: One year of B12 supplementation improved the levels of circulating microRNAs that were significantly lower at 6-, 12- or 17-years (vitamin B12 intervention baseline) of age. Nine new microRNAs were identified to be responsive to

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B12 supplementation and targeting multiple genes in pathways related to insulin signalling and glucose metabolism.
Conclusions: We found that vitamin B12 supplementation in young adolescents influenced circulating profiles of microRNAs that are associated with glucose and insulin metabolism. These findings support our previous report that vitamin B12 intervention is associated with changes in DNA methylation, which influences specific non-codingRNAs (eg. miRNA 21 expression). It will be informative to expand our findings in other intervention studies, investigate the causality of these associations and study effect on specific metabolic pathways.

Health, autonomy and caregiver frustration: exploring drivers of adolescent diet and physical activity across sub-Saharan Africa and India

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Background/Aims: There is a 'double burden of malnutrition' affecting adolescents in low-and middle-income countries (LMICs), putting them at risk of non-communicable diseases (NCDs) in adult life. The benefits of optimising adolescent nutrition are 3-fold: improved adolescent health and thus human capital development; improved adult health; and improved health in the next generation. Adolescent nutrition has been under-researched; there is a lack of understanding of the key drivers of adolescent diet and activity behaviours and how these might be improved. We therefore aimed to explore the influences on diet and physical activity behaviours among adolescents in LMICs.
Method: 51 focus group discussions (FGDs) with adolescents and their caregivers were conducted across eight TALENT sites in sub-Saharan Africa and India. FGD data was transcribed and translated before being pooled and thematically analysed. Similarities and differences were explored in relation to location, gender, age and between caregiver and adolescent accounts.
Results: The data suggest that adolescents' diets and physical activity habits may be explained by a combination of three fundamental themes. These are: diet and physical activity in relation to health, diet and physical activity as a focus of negotiations for autonomy and, diet and physical activity as a reflection of adolescents' environment and community. Adolescents were motivated to eat healthily and exercise by the desire for improved health and appearance. Despite this, they continued to engage in unhealthy behaviours, a source of conflict with caregivers. Diet and physical activity choices were used as a means to express growing autonomy, which often became a point of frustration for caregivers. Adolescents' diet and exercise habits were also heavily influenced by their environment and community including country income level, religion, culture, gender, perceived safety of outside spaces, influence of peers, and advertising.
Conclusions: Interventions to improve adolescent diet and physical activity habits in sub-Saharan Africa and India need to be complex in design and context-specific. They should effectively engage adolescents, and also address fundamental adolescent needs for autonomy and recognition.

Food consumption during the preconception period and small-for-gestational-age birth in Japanese pregnant women

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Background/Aims: Japan is the country with the highest rates of low birth weight infants in the developed countries, which is approximately 10% in 2017. The aim of this study was to examine the relationship between food consumption and small-for-gestational-age (SGA) birth.
Method: A total of 702 Japanese pregnant women were recruited in Kyoto Medical Center, Japan. Maternal diet was assessed by using a 15-items food frequency questionnaire, including rice, bread, noodle, meat, fish, any fish with a bluish back, vegetables, green and yellow vegetables, fruits, daily products, etc., and supplemental food, in the preconception, first-, and third trimester. SGA was defined as a birthweight <10th percentile for the gestational age.
Results: No significance was found of maternal age, pre-pregnancy body mass index (BMI), smoking or folic acid supplemental food for SGA birth. The adjusted odds ratio (aOR) of green and yellow vegetables consumption in the preconception period for SGA birth was 0.79 (95% confidence interval (CI): 0.78–0.96, $P = 0.010$) after adjustment of maternal age, pre-pregnancy BMI and smoking habit. However, any food consumption in first- and third trimester periods was not found significant aORs. Although gestational weight gain till third trimester periods influenced for SGA birth (aOR = 0.87, 95% CI: 0.78–0.96, $P = 0.007$).
Conclusions: The consumption of green and yellow vegetables in the preconception period was related to decrease in the risk of SGA birth. Our findings suggest that it is a priority to enhance the healthy eating: enrichment of green and yellow vegetables maybe important to avoid the SGA birth.

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Intake of Sugar-sweetened Beverages During Pregnancy And Offspring Adiposity: A Systematic Review

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Background/Aims: There is increasing evidence that nutrition during pregnancy and early childhood is critical for healthy child growth and development. However, little is known about the relationship between intake of sugar-sweetened beverages (SSB) during pregnancy and offspring adiposity and to date, the emerging literature surrounding this topic has not been systematically reviewed. We aimed to conduct a systematic review and summarize results from published articles on the association between SSB intake during pregnancy and offspring adiposity at birth and during childhood, independent of childhood SSB intake.
Method: We searched PubMed, Web of Sciences, CINAH, Embase and The Cochrane Library databases until 24th January 2019 for prospective cohort studies, controlled clinical trials and randomized clinical trials evaluating the association between SSB intake during pregnancy and offspring adiposity at birth and during childhood. Study findings were summarized narratively indicating positive, inverse or no association between SSB intake during pregnancy and offspring adiposity. We used the ROBINS-I tool to assess risk of bias of individual studies.
Results: Eight cohort studies were included. Two studies reported a positive association between SSB intake during pregnancy and offspring birth weight; two studies found no association between SSB intake during pregnancy and the risk of adiposity during infancy; three studies found no association with childhood adiposity (>1 -9 years of age), while two studies reported a positive association, indicating mixed evidence for an association between SSB intake during pregnancy and childhood adiposity. All studies had a moderate to serious risk of bias due to confounding.
Conclusions: Our systematic review provides mixed evidence for an association between SSB intake during pregnancy and offspring adiposity suggesting no evidence for an association based on previous studies. The quality of the included studies was generally low and there is therefore a great need for more studies of better quality.

Examining the effects of an eHealth intervention from 6-12 months of age on child eating behaviors and maternal feeding practices at 2 years of age.

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Background/Aims: Efficient and scalable strategies to optimize early-life nutrition could provide an important opportunity for primary prevention of childhood obesity. So far, few studies have evaluated use of web-based interventions commencing in infancy. The randomized controlled trial *Early Food for Future Health* provided parental anticipatory guidance on early protective feeding practices from child age 6 to 12 months through an eHealth intervention. Previously published outcomes at child age 12 months indicated that the intervention increased daily vegetable/fruit intake and promoted more beneficial mealtime routines. This abstract evaluates the effects of the intervention at child age 24 months.
Method: Parents with infants aged 3-5 months were recruited via Facebook and child health clinics during spring 2016. At child age 5.5 months, 715 mothers completed the web-based baseline questionnaire and were randomized to control or intervention arm. Primary study-outcomes were child eating behaviors, food intake, mealtime routines and maternal feeding practices and feeding styles. Secondary outcome was child anthropometry. Linear and logistic regression were used to estimate between-group differences for continuous and dichotomous outcomes, respectively.
Results: At child age 24 months, 295 mothers (41%) completed the questionnaire. Dietary patterns and mealtime routines at child age 24 months seemed to be reasonable consistent and in the same directions as at child age 12 months, but the between-group differences lacked precision to draw long-term conclusions. There was also no strong evidence for a group difference for child anthropometry.
Conclusions: At child age 24 months we found no evidence for effects of the eHealth intervention without further continued support. The high number of loss to follow-up limited power and validity. Future research on this field needs to consider the necessity for larger samples when planning longer-term follow-up studies.

Association between dietary diversity and food consumption patterns in Venezuelan reproductive-aged men

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Background/Aims: Male diet contribution to fecundity is relevant[1]. Reproductive-aged men in Venezuela are exposed to a severe food insecurity crisis[2], affecting both dietary quality and nutrients adequacy as possible determinants of sperm function and/or fertility. The objective of the present analysis is to investigate the associations between the dietary diversity score and foods patterns in Venezuelan reproductive-age men.
Method: This study is part of the ELANS multicentric study[3]. A sample of 1132 Venezuelan individuals, 552 men of 34.1 ± 13.4 years were studied. Sampling and study design was done following the ELANS study protocol. To describe the individual dietary diversity score (DDS), the FAO[4] tool was used with quartile classification. Values of nutrients were obtained by two 24-h recall, and processed through the NDSR software. To obtain food consumption patterns and explore associations, a canonical correlation analysis were used.
Results: The overall DDS was poor with 5.1 ± 0.9 food items, and the 50.2% were in the lowest quartiles scores. The lower DDS were significantly associated with inadequacy of key nutrients like zinc, vitamins E, C and A. The Andean and Central regions has higher diversity in 67.3% and 64.6% of the population, respectively ($p<0.05$). High educational level were associated with higher DDS ($p<0.05$). We identified 5 foods patters according to their nutritional composition: from the pattern 1 with a high quality diet to the pattern 5 with a elevate nutrients inadequacy. The level of heterogeneity in food intake patterns was also reflected in the estimates of dietary diversity across regions.
Conclusions: It was concluded that there were significant associations between DDS and food patterns in Venezuelan reproductive-age men. The lack on micronutrients intake is present and hypothetically can be a consequence of the crisis in access and availability of foods the country is facing.
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Micronutrient intake is influenced by diet's diversity in Venezuelan Childbearing age Women

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Background/Aims: Childbearing years are key for women as their health and nutrition status will impact fertility and pregnancy outcomes. Venezuelan households, have been exposed to an increasing food insecurity crisis, thus an impairment of the intake of nutrients is expected[1]. The aim of this study is to evaluate food consumption diversity score and to establish which nutrients are present according to the consumption diversity pattern.
Method: This study is part of the ELANS multicentric study. A sample of 1132 Venezuelan individuals from which 580 women were studied. Sampling and study designed was according to the ELANS study protocol. To describe the diversity score, the FAO[2] tool was used with quartile classification. Values of nutrients were obtained through the NDSR software. A canonical correlation analysis was performed to obtain the values of different nutrients present in the different food's groups.
Results: It was found that women consumed 5.2 ± 0.9 food groups according to the scale of food diversity (FD). The FD relationship/ sociodemographic conditions; showed that there was no significant association between age groups ($p = 0.545$) and socioeconomic level ($p = 0.653$). However, there was a significant association with educational level ($p = 0.020$), and geographical location ($p= 0.001$). On the other hand, the contribution of proteins and carbohydrates was increased and the contribution of iron, calcium, zinc, vitamins of the B complex, folic acid and vitamin E and D decreased, this low adequacy is related to the FD.
Conclusions: This study shows a decrease in the micronutrient intake through the diet of Venezuelan women within fertile age, essential to modulate the metabolic and epigenetic influences and avoid obtaining unfavourable pregnancy outcomes and their respective complications[3].Hypothetically, this can be related to the food insecurity crisis the country has been facing since 2014.
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Association between genetic susceptibility to obesity and childhood age at adiposity rebound

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Background/Aims: Early adiposity rebound (AR) has been associated with increased risk of overweight or obesity in adulthood. Genome-wide association studies (GWAs) have identified main genetic determinants of obesity, but little research has investigated genetic determinants of childhood age at AR (1). Our aim was to investigate the predictive role of genetic obesity susceptibility score in the kinetics of AR.
Methods: Within the Etude des Déterminants pre et post natals de la santé de l'ENfant (EDEN) mother-child cohort, weight and height were collected through clinical examinations or health booklets from birth to early adolescence. We modeled body mass index (BMI) trajectories from 2 to 12 years using mixed-effects cubic models and estimated age at AR (1). Early AR was defined as the first quintile of the distribution of age at AR. A combined obesity risk-allele score was calculated from genotypes at 27 variants identified by GWAs of adult BMI (2). In 988 children with both genetic data and estimation of age at AR, we used linear and logistic regression models to investigate the association between obesity risk-allele score and age at AR or risk of early AR, respectively. Models were adjusted for maternal age at delivery, parental education, maternal smoking during pregnancy, newborn characteristics (sex, gestational age, birth weight), and breastfeeding duration, and additionally for parental BMI.
Results: The mean (SD) age at AR was 5.5 (1.4) years. In multi-adjusted models, the obesity risk-allele score was associated with earlier age at AR (β [SE], -12[5] days per allele, p=0.021). Each additional obesity risk-allele was associated with a significant increased risk of early AR (OR [95% CI], 1.05 [1.01 - 1.12] per allele). Additional adjustment for parental BMI did not change the results.
Conclusion: Timing of AR in early childhood may contribute to the path from genetic susceptibility to obesity onset.
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Meals eaten with family in relation to dietary quality in 12-month-olds. A sub-study in the Norwegian Fit for Delivery study

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Background/Aims: Twelve-month-olds are in the transition from eating specific baby foods to sharing family meals. The nature of foods offered during this period may differ according to meal context. The aim of this study was to explore whether there are differences in diet between 12-month-olds being fed in the context of family meals and those who are not.
Method: Follow-up data from the Norwegian Fit for Delivery study were used to analyze child dietary data cross-sectionally 12 months postpartum. Linear regression models adjusted for child gender, maternal education and randomization were fit with child diet as the dependent variable (fruits, vegetables, sweetened beverages, water, cake and desserts, milk, and commercial and homemade dinners and porridge), and having main meals with family seldom (< 3 times/week) or often (≥ 4 times/week) as independent variables.
Results: Of 406 children, 74% had breakfast, 53% lunch, and 74 % dinner with their family. Children having breakfast with their family had a lower frequency of baby porridge (p<0.001) and sweetened beverages (p=0.025) and higher frequency of water (p=0.004) and desserts & cakes (p=0.037). Children having lunch with their family had a lower frequency of baby porridge (p=0.010), but higher frequency of home-made porridge (p=0.031) and water (p=0.001). Children having dinner with their family had higher intake of vegetables (p=0.038), home-made porridge (p=0.015), water (p=0.001) and milk (p=0.019), and lower intake of sweetened beverages (p=0.020) and baby porridge (p<0.001).
Conclusion: Being fed in the context of family meals was associated with a more favorable diet among 12-month-olds in the present study.

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Transfer and Effect of Endothelin Receptor Antagonists in the Human Placenta: an Ex Vivo Perfusion Study of the Isolated Cotyledon

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Background/Aims: Increasing evidence suggests a critical role for the endothelin (ET) system in the pathogenesis of preeclampsia (PE). Hence, blocking this system through endothelin receptor antagonists (ERAs) has been proposed as a potential therapy for PE. Yet, clinical studies have not been performed due to the possible teratogenic effects of ERAs. Since our knowledge regarding the placental transfer and effect of ERAs in humans is lacking, the aim of this study was to investigate the placental transfer of ERAs and their effect on ET-1 mediated vasoconstriction in the fetoplacental vasculature.
Method: Placentas of uncomplicated term pregnancies were dually perfused for 3 hours with the selective ET type A receptor blocker sitaxentan (100 ug/mL, n=5). Subsequently, placentas were exposed to ET-1 (10^{-10}-10^{-7}M) in the fetal circulation. Placentas that were perfused without ERA served as controls (n=8). ET-1 concentration-response curves for sitaxentan and the dual ET type A and B receptor blocker macitentan were also constructed in isolated chorionic plate arteries using wire-myography (n=5).
Results: After 3 hours of perfusion the mean fetal-to-maternal transfer ratio of sitaxentan was 0.32±0.05. In agreement with this observation, the E_{max} in response to fetally applied ET-1 was lower in sitaxentan-perfused placentas compared to controls (76±19 vs. 181±16 mmHg, P=0.003). Wire-myography studies revealed an equally lowered E_{max} in sitaxentan- and macitentan-exposed segments compared to control segments (2±2 and 12±4 vs. 132±15 % KCl precontraction, P<0.0001.
Conclusions: Our study is the first to show direct transfer of sitaxentan across the term human placenta. ET type A receptors exclusively mediate ET-1-induced constriction in the fetoplacental vasculature. Extending this knowledge to placentas of pregnancies complicated by PE is required to determine whether ERAs might be applied safely in PE.

Associations between first-trimester *in vivo* placental ultrasound parameters and *ex vivo* perfusion of the isolated cotyledon after delivery

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Background/Aims: Many placenta-related pregnancy complications originate already in the first trimester of pregnancy. However, early non-invasive assessment of uteroplacental development is challenging and it is unknown whether available markers actually represent placental function later in pregnancy. In this study we evaluated the correlation between *in vivo* parameters of first-trimester placental development (i.e. placental volume (PV) and placental vascular volume (PVV)) and *ex vivo* parameters of placental vascular function after delivery (i.e. fetoplacental vascular resistance (R)).
Method: A subset of uncomplicated pregnancies from the Rotterdam Periconception cohort (n=10) was included in this study. PV and PVV were measured offline using VOCAL and Virtual Reality analysis of 3D ultrasound images gathered at 7, 9 and 11 weeks gestational age (GA). Directly after delivery, the placenta was dually perfused at increasing fetal flow rates (1-6 mL/min). Pressure in the fetoplacental vascular bed was used to calculate R. The relationship between the *in vivo* and *ex vivo* parameters was assessed using Spearman's correlation coefficients (r). Correlations >0.5 were considered relevant.
Results: PV increased from a median of 20.2 cm^3 (range: 11.4-21.8) at 7 weeks GA to 92.8 cm^3 (range: 59.8-146.7) at 11 weeks GA. PVV increased from a median of 3.26 cm^3 (range: 0.28-6.17) at 7 weeks to 16.8 cm^3 (range: 10.1-32.1) at 11 weeks. Median total R decrease in relation to flow during perfusion experiments was 75% (range: 46-83). At 7 weeks GA, both PV and PVV were negatively correlated with total R decrease (R -0.90 and -0.70, respectively) and % total R decrease (R -0.60 and -0.70, respectively). At 9 weeks GA, only PVV showed a negative correlation with total R decrease (R -0.59) and % total R decrease (-0.68). At 11 weeks GA we observed no significant correlations.
Conclusions: Our study is the first to show that larger first-trimester PV and PVV are associated with less resistance decrease of the fetoplacental vasculature during *ex vivo* perfusion after delivery. A possible explanation for this negative correlation could be that smaller or less vascularized placentas have developed better adaptation to higher pressure. Our results suggest that first-trimester evaluation of placental volume and vascularization could be of value to predict placental function in later pregnancy, thereby providing opportunities for the early prevention of pregnancy-related pregnancy complications.

Signatures of fetal programming in cord blood from mothers with anaemia during early pregnancy

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Background: Anemia during early pregnancy, defined as hemoglobin (Hb) concentrations of less than 11 g/dl, is a leading health concern in developing countries like Tanzania. Anemia is caused primarily by nutritional deficiencies, infections such as malaria and inherited disorders. This can result in adverse consequences for mother and offspring. This can also result in increased risk of complex disorders in later life (DoHAD hypothesis).

Aims: We aimed to identify signatures of fetal programming as a consequence of anemia during pregnancy.

Methods: We leveraged RNA sequencing and global methylation data from 48 cord blood samples from mothers with early anemia during pregnancy and 50 mothers without. Simultaneously we also performed GWAS to assess the impact of genetic variation on gene expression.

Results: Hb levels in the mother at the time of anaemia diagnosis correlated with birth weight as well as nutritional status in the child (measured as mid-upper arm circumference). We found that expression of 123 genes and 7 alternative transcripts was altered in the cord blood of mothers with anemia during early pregnancy. This was accompanied by changes in epigenetic patterns of these genes. In total, 7134 SNPs (single nucleotide polymorphisms) from the cord blood was associated with expression of 321 genes (so called e-genes). Some of the 123 genes whose expression differed between anemic and non-anemic women in cord blood were also associated with offspring birth weight and nutritional status as well as diabetes-linked gene expression in fetal pancreas in another study. We also found multiple genes associated with maternal as well as cord insulin levels. Some of these genes were also associated with offspring birth weight and nutritional status.

Conclusion: Taken together, this study provides novel insights into fetal programming and changes in gene expression in cord blood from anemic mothers and how this potentially could impact the future health of the offspring.

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Gestational Diabetes and Obesity are associated with epigenome-wide changes in the children – cohort studies from Denmark and rural Tanzania

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Background/Aims: Offspring of women with Gestational Diabetes Mellitus (GDM) are at increased risk of developing metabolic disease, potentially mediated by epigenetic mechanisms. We aimed to identify signatures of fetal programming as a consequence of GDM and/or obesity during pregnancy in a Danish and a rural Tanzanian birth cohort.

Method: DNA methylation profiles were measured in peripheral blood of 93 GDM offspring and 95 controls from the Danish National Birth Cohort (aged 9-16 years), using the Illumina HM450K BeadChip. From a pre-conceptional pregnancy cohort study from rural Tanzania, we investigated DNA methylation profiles using the EPIC850 BeadChip, and RNA sequencing from 21 cord blood samples from mothers with GDM and 119 control women.

Results:

Danish cohort: We identified 76 differentially methylated CpGs in GDM offspring compared to controls in the DNBC (FDR $p<0.05$). Adjusting for maternal pre-pregnancy BMI reduced the number of CpG sites associated with GDM independent of maternal obesity down to 13 CpG sites. Four CpGs were validated to be associated with maternal obesity or GDM in the replication cohort ($n=905$). Interestingly, an epiallele (*VTRNA2*) was also identified to be differentially methylated in GDM offspring.

Tanzanian cohort: We found DNA methylation and expression of six genes to be differentially expressed in cord blood from GDM mothers compared to controls (FDR $p<0.05$), including the *ADCY9* gene which has previously been shown to have roles in fetal development. We also found multiple genes associated with maternal as well as cord blood insulin levels. Some of these genes were also associated with offspring birth weight and nutritional status.

Conclusions: Offspring of women with GDM during pregnancy exhibit multiple epigenetic changes in circulating blood cells. Taken together, these studies provide novel insights into

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fetal programming and changes in methylation and gene expression in cord blood and peripheral blood from GDM offspring and how this potentially could impact the future health of the offspring. For the DOHaD meeting, we will also provide recommendations for future strategies of epigenetic research in children born to women with diabetes and obesity in pregnancy.

Machine Learning Identifies the Tissue-Specific Effects of SNPs Associated with Risk of Developing Type 1 Diabetes

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Background/Aims: Disease associated variants frequently fall between genes and are often mark enhancer regions. Because enhancers loop to interact with the promoters they control, the targets of enhancers marked by disease associated variants remain largely unknown. Crucially, the 3D organization of a genome captures interactions between enhancers and their target genes. Thus, it can be used to identify the genes that are impacted by disease associated variants. Moreover, because genome organization is tissue specific, it provides us with insights into the tissue-specific regulatory impacts of genetic variants. Here we developed an integrated machine learning approach to investigate the tissue-specific contributions of genetic variants to Type 1 Diabetes (T1D).
Method: The T1D genotype data from the Wellcome Trust Case Control Consortium (WTCCC) was downloaded, cleaned and imputed (1960 T1D cases and 2933 controls, each with 5,957,907 SNPs). T1D-related SNPs from the GWAS catalog ($p<10^{-5}$) were analysed (CoDeS3D) to identify the functional targets of the SNPs. A logistic regression machine learning model that integrated information on the tissue specific impacts of T1D associated SNPs was trained on 70% of the WTCCC dataset. The remaining 30% was used as a validation dataset. The final model comprised 194 and tissue-specific eQTL effects for 107 SNPs. Model weights are log odd ratio changes of T1D risk.
Results: A risk predictor that incorporated tissue-specific spatial-regulatory disease patterns and was capable of classifying T1D patients (AUC = 0.74) was developed. The variants in the model form eQTLs with 235 genes across 47 different tissue types. Logistic regression identified the lung (model weight = 0.169), testis (0.092), thyroid (0.085), artery (0.068) and liver (0.067) as contributing the greatest model weights to T1D disease prediction. By contrast, the pancreas (0.048) and adipose tissue (0.033) contribute only modestly to the prediction model.
Conclusions: The tissue specific contributions of T1D associated SNPs to models of risk prediction suggest novel pathological pathways for the development of T1D.

Inadequate Periconceptional Maternal Vegetable Intake And Paternal smoking Are Associated With a Reduced Quality Of the Pre-implantation Embryo

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Background/Aims: Previous research demonstrated that a periconceptional healthy diet, characterized by high intakes of vegetables and fruits enhances the chance of pregnancy after IVF/ICSI treatment. The aim of this study was to investigate the associations between periconceptional parental nutrition and lifestyle behaviors and implantation potential of the embryo.
Method: Couples who underwent IVF/ICSI treatment at the Erasmus MC and filled out the screening module on the mHealth platform 'Smarter pregnancy' were included. At baseline, the adequacy of the intake of vegetables, fruits, folic acid, and the use of alcohol and cigarettes was identified by the program and translated into a risk score. A composite outcome for the combination of folic acid use, vegetable and fruit intake is the dietary risk score (DRS). A lower risk score represents more adequate behaviors. Embryos resulting from IVF/ICSI treatment were cultured in a time-lapse incubator until embryonic day 3. Time-lapse recordings were analysed to determine the exact timing of the embryonic cleavage division and morphological changes. As measure of implantation potential the morphokinetic parameters were assessed to rank embryo quality on a scale from 1 (poor) to 5 (good) based on a published algorithm. A continuation ratio model was applied to analyse associations between the maternal DRS, each nutritional separate behavior and the morphokinetic rank, with adjustment for maternal age and clustering of the embryos. For men, associations were additionally adjusted for the Corresponding female risk score.
Results: A total of 114 women and 41 partners, with a Corresponding 762 embryos of which 105 were freshly transferred and 255 were frozen, were analysed. In women, DRS was negatively associated with embryo quality (OR 0.87 (95%CI: 0.76 to 0.99)), which could mainly be attributed to inadequate vegetable intake (OR 0.79 (95%CI: 0.63 to 0.99)). The association between vegetable intake and embryo quality was only present in women who were overweight (OR 0.58 (95%CI: 0.37 to 0.91)). In men, only smoking was negatively associated with the KID-score (OR 0.69 (95%CI: 0.48 to 0.98)). DRS was also negatively associated with the KID-score (OR 0.83 (95%CI: 0.70 to 0.99)), however this effect attenuated when adjusted for maternal DRS (OR 0.89 (95% CI: 0.74 to 1.06)).
Conclusions: Inadequate periconceptional maternal vegetable intake as well as paternal smoking are significantly associated

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with a reduced implantation potential of the pre-implantation embryo based on morphokinetic parameters. These results further emphasize the importance of periconceptional nutritional advice to both women and men who undergo IVF/ICSI treatment.

Periconceptional Paternal Folate Status And The Associations With Sperm Quality, Pregnancy Outcomes And Epigenetics; a Systematic Review And Meta-analysis

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Background/Aims: Folate is amongst the most important substrates of the one carbon metabolism, which is essential for cell metabolism, DNA synthesis and epigenetics. Although, its role in reducing the risk of congenital malformations during pregnancy in women is well established, the role of the paternal folate status in reproductive medicine is scarcely investigated. The aim of this review is to investigate the evidence of the associations between periconceptional paternal folate status on semen quality, seminal epigenome, fertility and pregnancy outcomes.
Method: The following online databases were used for the search: Embase, Medline, PubMed, Web of Science, Cochrane database, PubMed and Google Scholar. The studies were scored on methodological quality using the ErasmusAGE quality score. A meta-analysis was performed on the randomised controlled trials of folic acid supplement use and semen parameters.
Results: 16 human studies and 5 animal studies were selected. 4 out of the 16 human studies showed positive associations between blood or seminal folate levels and sperm concentration, percentages of motility or normal morphology, findings that are supported by 4 out the 5 animal studies. 1 animal study found that a 20 fold folic acid supplemented diet is associated with poor sperm concentration. A meta-analysis of 4 randomized controlled trials in subfertile men showed that the sperm concentration (3.54 95%CI (-1.40 to 8.48)) and motility (percentage motile sperm) (3.06 95%CI (-1.36 to 7.48) were slightly higher and the percentage of normal morphology of sperm was slightly lower (-0.52 95%CI (-1.52 to 0.48) after 3 - 6 months of 5mg folic acid use per day compared to the control group albeit both not significantly. Moreover, 1 out of the 3 human studies and 2 out of 3 animal studies showed significant alterations in the overall methylation patterns of the sperm epigenome and 2 animal studies demonstrated a positive association between folic acid supplement use and less sperm DNA damage. 2 out of 2 animal studies showed a positive association of folate levels on the chance of pregnancy, whereas 1 human and 1 animal study showed associations between low paternal folate intake and an increased risk of congenital malformations. 2 out of 4 animal studies also reported that low paternal folate intake is associated with lower placental folate content and lower placental weight.
Conclusions: Our results underline the importance of adequate folate levels in future fathers, but also suggests possible risks associated with overdosing of folic acid supplements. These data show the importance of the periconceptional paternal folate status and further support the need to include men in preconception care.

Preconceptual Paternal Environmental Stimulation Alters Intergenerational Inheritance of Behavioural Endophenotypes and Adaptive Responses

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Background/Aims: Experimental research has recently revealed that paternal environmental conditions can influence the offspring phenotype through epigenetic mechanisms. However, it is unclear if the offspring's physiological and behavioural responses to the same paternal environmental conditions undergoes intergenerational changes. Environmental enrichment (EE) is a well-established paradigm that promotes neural plasticity. In this study, we investigated specific characteristics of EE-induced developmental plasticity in male mice and adaptive responses in their offspring.
Method: Male Swiss mice (F_0) were housed in either EE or standard housing (CT) from post-weaning to adulthood, before breeding for offspring. Their offspring (F_1) were raised in either standard housing or exposed to a short EE condition. Behavioural, physiological and molecular parameters were assessed for both F_0 and F_1 mice.
Results: F0 male mice exposed to EE had lower body weight, higher adrenal, spleen and hippocampal weights, better novelty processing and spatial learning, and higher social dominance compared to CT. Surprisingly, their male offspring (F_1) showed a maladaptive response by displaying spatial memory impairment. Additionally, they performed poorer in ethologically relevant measures such as social dominance and were less attractive to receptive females, compared to controls. Interestingly, F_1 male offspring of EE and CT F_0 males showed similar spatial memory and attractiveness to receptive females when both groups were exposed to 1 week of EE during adulthood.
Conclusions: These results provide new evidence that paternal intergenerational inheritance influences the capacity for

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environmental adaptation in the offspring and is consistent with the evolutionary mismatch hypothesis. These and other findings suggest that the intergenerational inheritance observed in the laboratory might be related to the 'missing heritability' of many complex human diseases.

Antenatal Care For Modifiable Health Risk Behaviours: Women's Receipt And Acceptability Of Guideline Recommended Care To Support A Healthy Start To Life

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Background/Aims: The assessment and management of modifiable health behaviours in pregnancy can improve birth outcomes, and maternal and child disease risk. Little is known about the conduct and acceptability of such practices in antenatal care. This study reports the proportion of pregnant women assessed and offered support to manage smoking, alcohol consumption and gestational weight gain (GWG) in line with Australian pregnancy guidelines, and women's acceptability of care.
Method: Telephone surveys with women who had recently attended public antenatal services were undertaken in one health district in Australia. Women's self-report smoking, alcohol consumption and GWG during pregnancy, and receipt and acceptability of guideline recommended care were examined. Characteristics associated with receipt of such care were analysed using multiple logistic regression.
Results: Of 465 women, 9% smoked, 17% consumed alcohol and 57% gained weight above/below GWG guidelines. 12% reported two or more behaviours. 49% of women received recommended care for smoking, 17% for alcohol, and 9% for GWG. Nine women received recommended care for all three health behaviours. Primiparous women were more likely to receive guideline care for smoking and alcohol. Women who were younger, primiparous, identified as Aboriginal, had a higher pre-pregnancy BMI or lived in regional/remote areas were more likely to receive recommended GWG care. Most Aboriginal and non-Aboriginal women agreed that recommended care for smoking (91% and 97%), alcohol (96% and 88%) and GWG (91% and 93%) should be provided as routine antenatal care.
Conclusions Most women did not receive antenatal care for health behaviors as recommended by Australian pregnancy guidelines despite high acceptability of receiving such care. There is a need for service-wide practice change to increase care to address modifiable health behaviours in pregnancy.

Prenatal alcohol exposure and early life adversity disrupt social discrimination and underlying neural circuitry in adolescent male and female rats

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Background/Aims: Social behaviour deficits are a pervasive feature of prenatal alcohol exposure (PAE), and often have widespread implications for other developmental domains. Likewise, early life adversity (ELA) can also disrupt social behaviour development. Of note, individuals with PAE experience ELA at a much higher rate than the general population; however, relatively few studies have assessed the interaction of both PAE and ELA on social behaviour development. Here, we combine two animal models to investigate the unique and/or interactive effects of PAE and ELA on social neurobehavioral function in adolescent male and female rats.
Method: PAE, pair-fed, and control litters were exposed either to limited bedding [postnatal day (P)8-12] to model ELA or to normal bedding. Offspring were evaluated on a social discrimination task beginning either in early (P30) or late (P45) adolescence. At 30 min following the second day of social discrimination testing, brains were removed and assayed for c-fos mRNA as an index of neural activation (prefrontal cortex [PFC], lateral septum, amygdala, hypothalamus).
Results: In P30 males, PAE alone and in association with ELA resulted in social discrimination deficits; however, in P45 males, only PAE with ELA showed impaired discrimination. In females, social discrimination deficits were only observed in P30 females that were exposed to PAE and ELA. Changes in neural activity (*c-fos* mRNA expression) in the amygdala, PFC, and lateral septum following PAE alone and PAE with ELA may mediate some of the social discrimination deficits observed.
Conclusions: These results suggest that PAE negatively impacts social behaviour development, which is exacerbated by ELA, presumably by altering activity of the limbic and forebrain neurocircuitry that is important for regulating social behaviour function.
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Intergenerational effects of parental early life social and health risk factors on descendants' adult socioeconomic position: The Uppsala Birth Cohort, Sweden

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Table. Gestational age (completed wks) predicting JIA or RA. Ref. group 39-41 wks.

Gestational age	Odds Ratio	(95% CI)	*P*
<37	0.73	0.560.96	0.03
37	0.99	0.781.26	0.93
38	0.96	0.821.13	0.62
≥42	1.11	0.861.42	0.42

Background/Aims: Most studies on intergenerational transmissions of inequities focus on the adult circumstances of parents and their descendants. The current study aims to extend the focus to include parents' early life social and biological characteristics and link them to children's attainment of adult socioeconomic position (SEP).
Method: The data comes from generation 1 (G1) and generation 2 (G2) of the Uppsala Multi-generational Birth Cohort, Sweden. G1 were born during 1915-1929 whereas G2, the biological descendants of G1, were born from 1932 onwards. The main outcome was adult SEP of G2 which we assessed at age 30+ by Hollingshead's Index of Social Position (HISP). HISP is an aggregate measure of education and occupation combined and has a score between 11 and 77 with a lower score indicating higher SEP. The exposures include G1's birth characteristics: family SEP, mother's marital status, birth weight corrected for gestational age, length of gestation, birth multiplicity, birth order, and mother's age at child birth. Simple linear regression models were used to examine the associations. The analysis was stratified by parents' gender to see whether the intergenerational effects differ along the paternal (n=3126) and maternal (n=3192) lines.
Results: The study found that the low family SEP of both mothers (ß: 6.62; 95% CI: 2.68, 10.57) and fathers (ß: 5.60; 95% CI: 1.55, 9.66) were associated with high HISP score (low SEP) of their children. Similarly, marital status of the mothers of both parents were associated children's adult SEP. The early life health characteristics of mothers did not show any association. On the other hand, fathers who were born preterm were more likely to have children with poorer SEP in adulthood (ß: 2.87; 95% CI: 0.50, 5.23).
Conclusions: Parents' early life social disadvantages appear to have long term implications for children's adult social position while the intergenerational transmission of biological disadvantages tend to differ by gender of parents.

Preterm birth and autoimmune arthritis - a register linkage cohort study

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Background/Aims: The immune system may play a role in several diseases that have their origins in fetal life. Preterm birth is associated with autoimmune thyroiditis. We assessed whether the cumulative incidence of juvenile idiopathic arthritis (JIA) or rheumatoid arthritis (RA) is higher among those born preterm.
Method: A total of 235,622 children were born in Finland between Jan 1987 and Sep 1990, according to the Medical birth register, which provided gestational age at birth (GA) for 98.6% of these newborns. Data were linked by using national personal identity number. The Care Register for Health Care provided ICD-10 diagnoses for specialized care for hospital stays from Jan-1, 1996, and for outpatient visits from Jan-1, 1998, both available until Dec-31, 2015. ICD coding for JIA was M08, and M05 or M06 for RA. We assessed associations by logistic regression and adjusted for sex, RA and JIA of mother or father, and their highest-ever education (4 categories).
Results: The cumulative incidences (1/100,000) of JIA and RA were 249 and 430 respectively and 616 for either of the two diagnoses. The odds for JIA or RA were 27% lower for those born preterm (see **Table**). Model that adjusted for parental JIA or RA and with parental education gave similar estimates.
Conclusions: Those born preterm develop Juvenile idiopathic arthritis and/or Rheumatoid arthritis less frequently. This result argues against an overall tendency towards higher incidence of autoimmune disease in preterm born young adults.

Dietary screening and personalized feedback on diet quality in early pregnancy

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Background/Aims: Gestational diabetes mellitus (GDM) is predominantly a lifestyle disease, with dietary habits among the most important modifiable risk factors. The aim was to evaluate whether a short dietary screening questionnaire could be used to predict gestational diabetes in a cohort of Icelandic women (n=1651) and to investigate the effect of an internet based personalized feedback on diet quality in early pregnancy as a pilot study (n=100).

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Method: The two settings were the Prenatal Diagnostic Unit at Landspitali University Hospital, Reykjavik (cohort study) and the Health Care Institution of North Iceland, Akureyri (pilot study). In the cohort study a short (40-item) food frequency screening questionnaire (FFQ) was used to assess dietary habits in gestational weeks 11-14. Stepwise backward elimination was used to identify a reduced set of factors (out of 13 predefined dietary risk factors) that best predicted GDM. Poisson log-linear regression was used to assess the association between the dietary risk score and GDM. In the pilot study, pregnant women were randomized into a group receiving internet based personalized feedback on diet quality (n=50) and a control group (n=50).
Results: In the cohort study, 16% of the women developed GDM. Identified factors that predicted GDM risk were (range 0-7): eating a non-varied diet, excessive intake of sugar/artificially sweetened beverages, sweets/ice cream/cakes/cookies and processed meat products and inadequate frequency of consumption of dairy, whole grains and vitamin-D intake. Women with a high (≥5, n=302) versus low (≤2, n=407) score had 39% higher risk of GDM (95%CI: 2 to 89%). The results from the pilot study showed that after the feedback on diet quality, soft drink consumption was significantly lower in the intervention group compared with the control group, Corresponding to approximately one litre less per week
Conclusions: The results indicate that information gathered with a short FFQ early in pregnancy might be useful in identifying women that could benefit from dietary counselling. Moreover, an internet based personalized feedback on diet quality, early in pregnancy might be a useful support in prenatal care.

Smaller body size at 6.5 years following *in vitro* fertilization is not explained by parental, gestational, and early childhood characteristics nor observed epigenetic differences

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Background: Little is known about the long term growth and cardiometabolic risk of children conceived by in vitro fertilization (IVF). Poor selection of comparison groups, accounting for underlying infertility, lack of repeat measures, and poorly characterized mechanisms limit our current understanding. Methods: In a multiethnic Asian birth cohort of 83 IVF-conceived and 1095 spontaneously-conceived children with repeated growth measures from mid-gestation to 6.5 years, we utilized several approaches to estimate effects of IVF on child anthropometry, body composition, blood pressure, fasting glucose, and fetal cord tissue DNA methylation (Illumina 450k), including inverse probability-weighted marginal structural models to account for differential treatment probability and loss to follow-up and emulating a pragmatic trial in a putatively subfertile cohort. All models accounted for parental height, weight, age, socio-demographics, and smoking; child sex and polygenic risk score for size. Results: Across all models, IVF-conceived children were shorter than spontaneously conceived children (*e.g.* 1 cm (0.5 SD) and 2.6 cm (0.5 SD) at birth and 6.5 years, respectively) and increasingly lagged in weight (1% (0.05 SD) higher at birth to 8% (0.6 SD) lower at 6.5 years). This was reflected in smaller skinfolds and lower blood pressure. No strong differences in estimated fetal weight, gestational age at delivery, or fasting glucose (at 6 years) were observed. Differences could not be explained by polygenic risk score, higher maternal glucose or blood pressures during pregnancy, breastfeeding practices, or childhood infections. After multiple testing correction, IVF status was significantly associated with DNA methylation at 3 CpGs within *NECAB3*, previously associated with maternal pre-pregnancy BMI, persistent in adolescence, and implicated in *HIF1A* expression, itself relevant to placental vascularization and fetal development. However, exploratory mediation analysis via parametric g-computation suggested differential methylation at *NECAB3* and *HIF1A* did not causal mediate the observed effects of IVF on child size. Discussion: We found children conceived by IVF were smaller than spontaneously conceived children. A novel association between IVF and fetal DNA methylation was not explained by measured parental characteristics. However, any mechanistic causal link to growth was not immediately demonstrable.

Maternal smoking during pregnancy induces persistent epigenetic changes into adolescence, independent of postnatal smoke exposure and is associated with cardiovascular risk

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Background/Aims: Several studies have shown effects of current and maternal smoking during pregnancy on DNA methylation of CpG sites in newborns and later in life. Here we hypothesized that there are long-term and persistent epigenetic effects following maternal smoking during pregnancy on adolescent offspring DNA methylation, independent of paternal and postnatal smoke exposure. Further, we explored the association between DNA methylation and cardiometabolic risk factors.
Method: DNA methylation was measured using the Illumina HumanMethylation450K BeadChip in whole blood from 995 participants attending the 17-year follow-up of the Western Australian Pregnancy Cohort (Raine) Study. Linear mixed effects models were used to identify differential methylated CpGs (DMCpGs), adjusting for parental smoking during pregnancy, and paternal, passive and adolescent smoke exposure. Additional models examined the association between DNA methylation and paternal, adolescent and passive smoking over the life-course. Offspring DMCpGs identified were analysed against cardiometabolic risk factors (blood pressure, triacylglycerols (TG), high-density lipoproteins cholesterol (HDL-C) and body mass index).
Results: We identified 23 DMCpGs (genome wide p-level: $1.06 \times 10\text{-}7$), that were associated with maternal smoking during pregnancy, including associated genes AHRR (cancer development), FTO (obesity), CNTNAP2 (developmental processes), CYP1A1 (detoxification), MYO1G (cell signalling) and FRMD4A (nicotine dependence). A sensitivity analysis showed a dose dependent relationship between maternal smoking and offspring methylation. These results changed little following adjustment for paternal, passive or offspring smoking and there were no DMCpGs identified that associated with these variables. Two CpGs (cg00253568 (FTO) and cg00213123 (CYP1A1)) out of the 23 identified were significantly associated with either TG (males and females), diastolic blood pressure (females only) or HDL-C (males only).
Conclusions: This study demonstrates a critical timing of cigarette smoke exposure over the life-course for establishing persistent changes in DNA methylation into adolescence in a dose dependent manner. There were significant associations between offspring DMCpGs and adolescent cardiovascular risk factors, namely TG, HDL-C and diastolic blood pressure. Future studies on current smoking habits and DNA methylation should consider the importance of maternal smoking during pregnancy and explore how the persistent DNA methylation effects of in utero smoke exposure increase cardiovascular risk.

Obstetric and perinatal outcomes in singleton live births resulting from the donor cycles versus autologous cycles: a retrospective study in Canada

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Background/Aims: Donor cycles (oocyte donation, sperm donation and embryo donation) have dramatically increased in order to improve infertility treatment outcomes. Limited published data exist detailing the outcomes of these gestations. Patients and clinicians would benefit from information specific to donor cycles to inform fertility treatment options, counselling, and clinical decision-making. We aimed to evaluate obstetric and perinatal outcomes in singleton live births resulting from the donor cycles compared to autologous cycles.
Method: This study used data on fertility cycles from the Canadian Assisted Reproductive Technologies Register (CARTR) Plus for the province of Ontario, Canada. Additionally, data on neonatal outcomes were obtained from the Better Outcomes Registry & Network (BORN) Ontario for live births and stillbirths that occurred from May 2013 to August 2015. The risk of adverse outcomes was accessed using univariable and multivariable logistic regression (adjusted odds ratios, aORs; and 95% confidence intervals, CI).
Results: A total of 4,221 cycles were left from 24,747 ART cycles through the data-selection process. Donor cycles had significantly higher risks for hypertensive disorders of pregnancy (HDP, aOR 1.87 95% CI 1.35 - 2.60) and cesarean section (aOR 1.39, 95% CI 1.14 -1.70 for whole subjects; aOR 1.56, 95% CI 1.22-2.01 for primipara) when compared with autologous cycles. No difference in the risk of gestational diabetes, preterm birth (PTB), moderately PTB, very PTB, extremely PTB, LBW, very LBW, SGA, LGA, Apgar score < 7 at 1 min and Apgar score < 7 at 5 mins.
Conclusions: Pregnancies from donor cycles were at higher risk of developing HDP and CS. Patients and physicians should be informed of the elevated risk of HDP and CS in these gestations and counsel accordingly.

The impact of periconceptional maternal folate status on embryonic head and brain structures

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Background/Aims: Natural folate and synthetic folic acid provide one-carbon moieties for cell multiplication and epigenetic programming. We hypothesize that growth and development of embryonic head and brain structures are influenced by maternal folate status. Therefore it is our aim to investigate whether the periconceptional maternal folate status influences the sizes of embryonic head and brain structures using three-dimensional ultrasound (3D-US).
Method: We selected the study population from the Rotterdam periconception cohort conducted at the Erasmus MC. 3D-US scans are performed at 9 and 11 weeks gestational age (GA). Embryonic head volume (HV) and head circumference (HC) are performed offline using the virtual reality technique of the BARCO ISpace. Embryonic brain structures, including mesencephalon, diencephalon and telencephalon, are performed using specialized 3D software (4D-view). For determination of red blood cell (RBC) folate, maternal venous blood samples are taken at the first visit. Linear regression models, adjusted for GA, alcohol, smoking, maternal age and mode of conception, are applied to investigate associations between RBC folate and embryonic head and brain structures. RBC folate levels are divided into quartiles (Q1-4).
Results: 166 singleton pregnancies are included for analysis. RBC folate quartiles are 466-1078 nmol/l (Q1), 1079-1342 nmol/l (Q2), 1343-1594 nmol/l (Q3) and 1595-2919 nmol/l (Q4). At 9 weeks GA, HV is smallest in Q3 and significantly largest in Q4 (β=0.246; $p<0.05$). At 11 weeks GA, HV is also smallest in Q3, but largest in Q1 (β=0.833; $p<0.01$) and Q4 (β=0.768; $p<0.01$). In addition, HC at 9 and 11 weeks GA are smallest in Q3 and at 11 weeks GA HC is largest in Q4 (β=2.764; $p=0.03$). There are no statistically significant associations between the different RBC folate quartiles and embryonic brain structures.
Conclusions: Low and high periconceptional maternal RBC folate are associated with larger embryonic head structures. The clinical implication of these findings needs further research.

Prenatal cerebellar growth trajectory as novel biomarker for body composition of the newborn

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Background/Aims: In a previous study we have shown that the periconceptional maternal body mass index (BMI) is associated with the growth trajectories of the embryonic and fetal cerebellum. Here we hypothesize that the growth trajectory of the fetal cerebellum is a determinant in the developmental origin of adiposity in the offspring. Therefore, we investigate associations between the fetal trans cerebellar diameter (TCD) and fetal thigh volume (TVol), and neonatal body composition
Method: A case control study is conducted embedded in the Rotterdam Periconception cohort at the Erasmus MC. Two- and three-dimensional ultrasound scans are performed at 22, 26 and 32 weeks gestational age (GA). Air-displacement plethysmography is used to measure neonatal body composition at 42 weeks. Cross-sectional analysis using linear regression and longitudinal analyses are performed using linear mixed models to estimate random intercept (RI) and random slope (RS) of the fetal TCD growth trajectories. Linear regression analysis of the RI and RS is used to investigate associations between TCD growth trajectories and body composition.
Results: 82 mother-child pairs are included for analysis. The cross-sectional analyses showed a positive association between TCD and fat free mass (FFM) at 22 (β=0.139; $p<0.01$), 26 (β=0.118; $p<0.01$) and 32 (β=0.076; $p<0.01$) weeks GA. Adjustment for maternal BMI, maternal age, fetal gender, parity, smoking and mode of conception shows comparable results. The longitudinal analysis shows a positive association between TCD growth trajectories and FFM (β=1.003; $p=0.02$). A positive association was shown between TCD and TVol at 26 (β=0.667; $p<0.01$) and 32 (β=1.221; $p=0.02$) weeks GA.
Conclusions: This data demonstrates that the fetal TCD is associated with TVol and neonatal FFM. Further research should elucidate whether the fetal TCD can be used as a biomarker to predict adiposity in offspring.

Prediction of periconceptional alcohol use from adolescence and young adulthood: A 20-year prospective cohort study

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Background/Aims: Periconception spans the time preceding, including and immediately following conception. This period represents a critical window of exposure for offspring growth and development. Many women drink alcohol antenatally; less is known about drinking patterns pre-pregnancy awareness, or about prior patterns of use in adolescence and young adulthood that may predict periconceptional drinking. We examined the extent to which alcohol use and disorder preconception (in adolescence and young adulthood) predicted periconception drinking.

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Method: Female participants (N=301) from the Victorian Intergenerational Health Cohort Study (VIHCS) reported on heavy binge drinking (>=11 drinks in a day) and alcohol use disorder from adolescence to young adulthood (nine waves across 14-29 years). In pregnancy (between 29-35 years) women were asked how frequently they consumed alcohol pre-pregnancy awareness.
Results: Most women reported drinking periconceptionally (77%); 18% drank frequently (3+ times a week). Frequent periconceptional drinking was common among women who reported persistent young adult heavy binge drinking (OR=7.6, 95%CI 3.1-19.0, p<0.001) or alcohol use disorder (OR=12.2, 95%CI 5.2-28.8, p<0.001). Importantly, though, 48% of frequent periconception drinkers reported no problematic preconception drinking from their mid-late 20s.
Conclusions: Alcohol use is common among women in the periconception window. Women with a history of persistent heavy binge drinking or alcohol use disorder preconception are at increased risk for periconceptional drinking. Notably, however, much frequent periconceptional drinking occurs among women with normative drinking patterns preconception. Public health initiatives for periconception alcohol use should be widely disseminated and targeted earlier in the preconception window (i.e., the mid-20s).

Maternal Vitamin D in Pregnancy and the Risk of Asthma in the Offspring: The Vitamin D in Pregnancy Study

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Background/Aims: In the Vitamin D in Pregnancy (VIP) cohort we observed an association between higher maternal vitamin D (>70nmol/L) and reduced odds of offspring asthma at age 5 in girls, but not boys. Thus, we aimed to determine whether the association persisted in offspring at age 11 years.
Method: There were 475 pregnant women recruited from the Geelong Hospital, Australia, before 16 weeks gestation (402 mother-child pairs at birth). Women provided a blood sample at recruitment (early pregnancy) and at 28-32 weeks gestation (late pregnancy). Maternal serum 25(OH)D was measured by radioimmunoassay (Immunodiagnostics Systems). At the 11 year follow-up 210 mother-child pairs were assessed. Asthma status was parentally reported using the International Study of Asthma and Allergies in Childhood Questionnaire (Has your child ever had asthma? Yes/No; and Has your child ever had wheeze or whistling in the past 12 months? Yes/No; defined as current asthma). There were 178/210 (44% of birth cohort) mother-child pairs had complete information for analyses. Univariate associations were examined using chi-square or Fisher's exact tests, and binary regression was used to examine associations adjusting for maternal age, BMI and gestational smoking.
Results: Of the 178, 45 (24%) of the offspring had parent-reported 'asthma ever'; and 25 (14%) had parent-reported 'wheeze/whistling in the last 12 months', respectively. The association between 25(OH)D and asthma ever varied by sex (25(OH)D (p for interaction=0.01). In girls, 2/22 (9%)) of offspring of mothers with high 25(OH)D in late pregnancy reported asthma vs 28/69 (41%) where maternal 25(OH)D was below 70nmol/L (p=0.008). This persisted after adjustment (aOR 0.08 95% CI 0.008,0.82, p=0.006). In boys, 6/23 (25%) of offspring with higher maternal 25(OH)D in late pregnancy reported asthma vs 17/74 (23%) with low 25(OH)D (p=0.84). Sex*25(OH)D interaction terms were unable to be explored in current asthma models due to quasi separation. In the sex-pooled sample, 2/45 (4%) of offspring of mothers with a high 25(OH)D in late pregnancy reported current asthma vs 23/133 (17%) where maternal 25(OH)D was below 70nmol/L (p=0.04). A trend remained in adjusted models (OR 0.22 95%CI 0.05, 1.00, p=0.02). There was no association detected with maternal 25(OH)D in early pregnancy with either outcome.
Conclusions: In this cohort, maternal vitamin D status in late pregnancy, but not early, is associated with an increased lifetime prevalence of asthma in girls, but not boys, aged 11 years.

Is the Association Between Maternal Vitamin D in Pregnancy and Offspring Bone Independent of Maternal Phenotype?

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Background/Aims: Some evidence suggests an association between maternal vitamin D during pregnancy and offspring bone measures. Shared genetics and environmental factors might confound this association thus we aimed to determine if the association is mediated by maternal bone quality.
Method: Pregnant women recruited from the University Hospital Geelong (2002-03) and had serum samples collected at recruitment (before 16 weeks gestation) and 28-32 weeks gestation. Vitamin D was assessed by radioimmunoassay (Immunodiagnostic Systems). Two hundred and eight mother-child pairs were re-assessed when offspring were aged approximately 11 years. Maternal and offspring bone quality was assessed for 168 pairs at the calcaneus using quantitative ultrasound (QUS, Lunar Achilles) in terms of speed of sound (SOS), broadband ultrasound attenuation (BUA) and stiffness index (SI). Linear regression was used to examine associations adjusting for offspring height, weight, Tanner stage, sex and maternal height, age, gestational smoking status, parity and education.
Results: Maternal 25(OH)D at recruitment was associated with offspring SOS (β 1.6 95% CI 0.2,3.1) and, in boys only, with SI (β

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1.0 95% CI 0.1, 1.8). These relationships remained independent of maternal QUS parameters (β 1.7 95% CI 0.3, 3.1) and (β 0.9 95% CI 0.1, 1.6), respectively. No associations were detected for BUA or with maternal 25(OH)D at 28-32 weeks.
Conclusions: These prospective data support prior evidence of a relationship between maternal 25(OH)D levels during early pregnancy and measures of bone health in offspring. Importantly, these associations were independent of maternal QUS parameters, suggesting that the relationship between gestational vitamin D status and offspring bone health is at least partly independent of maternal bone phenotype.

Maternal health literacy and child sun protective behaviours in Australian children

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Background/Aims: Emerging evidence suggests ultraviolet radiation exposure in Australian children and teens is associated with the greatest risk of development of basal cell carcinoma. We investigated associations between maternal health literacy and sun protective behaviours in their children.
Method: Data were collected from the 11yr follow-up of the Vitamin D in Pregnancy (VIP) study. Maternal health literacy was assessed using the multidimensional Health Literacy Questionnaire (HLQ), which provides scores across nine scales. Children's use of sunscreen and hats during summertime were reported by mothers as 'Always when outside', 'Sometimes' or 'Never' and avoidance of sun during summer as 'Yes' or 'No'. Categories 'Sometimes' and 'Never' were combined due to small numbers in the 'never' category. Mothers also reported how easily their child becomes sun burnt. Cluster analyses were used to identify health literacy profiles. Logistic regression analyses were used to investigate associations between maternal health literacy cluster and sun protective behaviours in children.
Results: Among 192 mother child pairs (child mean age±SD; 11.1yr±0.6), 87(45.3%) reported children 'always' used sunscreen, 60 (31.3%) reported 'always' wearing a hat and 13(6.8) reported sun avoidance. Cluster analyses determined four distinct health literacy profiles among mothers. Cluster One (n=17) had good abilities in understanding health information. Cluster Two (n=50) could find health but demonstrated poor support for health. Cluster Three (n=20) had higher support for health but struggled to access health information. Cluster Four (n=106) struggled to engage with healthcare. Holding Cluster Four as referent, Clusters Two and Three were more likely to use sunscreen (OR 2.4 [95%CI 1.2-4.7] and OR 4.9 [95%CI 1.6-14.7], respectively), Cluster Three were more likely to wear a hat (OR 4.0 [95%CI 1.4-11.2]) and Cluster One were more likely to avoid sunshine (OR 5.4 [95%CI 1.1-26.7]). Adjusting for how easily the child becomes sunburnt did not alter associations.
Conclusions: Maternal health literacy may be associated with some sun protective behaviours in children. Parental health literacy may need to be considered in targeting of sun protective messages.

Intra- and Inter- individual Differences in *CPT1A* and *SREBF1* Methylation of Maternal Leukocytes During Mid-to-Late Gestation

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Background/Aims: It is not known how pregnancy-induced weight gain or hyperlipidemia influences the methylation levels of obesity-related differentially methylated CpG sites in blood cells.
Method: We performed the prospective cohort study of pregnant women (n = 52) using the MassARRAY EpiTYPER assay, and analyzed methylation levels of *CPT1A* and *SREBF1*, which were previously verified to be robustly associated with adiposity traits. The methylation-based estimation of leukocyte proportion was also conducted using controls whose age, sex and BMI were similar to those of the pregnant women.
Results: The association of methylation levels of *CPT1A* and *SREBF1* with BMI and LDL-C was mostly reproduced as EWAS reports only at mid-gestation. Consistent with the metabolic shift from an anabolic to a catabolic state during mid-to-late gestation, those association were weakened at late gestation. However, the BMI-association with *CPT1A* intron 1 methylation was strengthened at late-gestation, which was mediated by BMI-dependent change in lymphocyte proportion.
Conclusions: By tracing the same individuals and simultaneously assessing the leukocyte composition, we have successfully shown that the blood methylation of adiposity-related differentially methylated CpGs during mid-to-late gestation followed the individual metabolic and immunological alteration.

Maternal Resveratrol Treatment Protects Against Leptin-Resistance In Male Offspring of Obese Rat Dams But Impairs Leptin Sensitivity In Offspring Of Control Dams

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Background/Aims: Life course studies increasingly implicate maternal obesity as a major risk factor for childhood obesity and related cardio-metabolic disease in later life. Developmental influences such as inflammation and oxidative stress may impact on the neuroendocrine response to metabolic stimuli and contribute to increased appetite, energy intake, and risk of obesity. Employing an established rodent model of maternal obesity, we hypothesised that resveratrol, a polyphenol with antioxidant properties, would improve offspring energy balance. The aim of the current study was to determine the effects of resveratrol supplementation pre-pregnancy through to lactation on offspring leptin sensitivity.
Method: Female rats (n=10/group) were fed control (C) or obesogenic (O) diet *ad libitum* from weaning and then supplemented with resveratrol (R, 20mg/kg/d) or vehicle from 90d of age, through mating at 120d, to the end of lactation. Offspring were weaned on to normal chow. One male and one female from each litter (four groups; maternal (M)C, MO, MCR and MOR) was subjected to a leptin challenge at 60d of age: following a 9h fast singly housed rats received a single dose of leptin (10mg/kg, intraperitoneal) and normal chow *ad libitum*. Change in body weight and food intake were measured at 12h and 24h. Mean±S.E.M analysed by two-way ANOVA with Tukey's post hoc test.
Results: Maternal obesity inhibits the leptin-mediated reduction in food intake in male offspring only which was prevented by maternal R treatment (food intake[g] following saline vs. leptin injection; MC[n=7]:31.3±1vs.23.4±2*; MO[n=6]:34.1 ±1vs. 30.4±0.7; and MOR[n=6]:33.0±2vs.27.3±2*, *p<0.01). In offspring of control dams treated with R, the leptin-mediated reduction in food intake in both sexes was absent (MCR males[n=6]:33.0±1vs.29.2±1; females [n=6]:20.9±1vs.19.1±1). Maternal R also prevented the leptin-induced reduction in body weight over 12h in female offspring of control dams. There was no difference in offspring body weight at 60d of age.
Conclusions: Maternal obesity in pregnancy programmes appetitive behaviour in juvenile offspring independently of offspring body weight. Maternal supplementation with resveratrol throughout pregnancy and lactation prevented the developmental programming of leptin resistance in the male offspring of obese rat dams but had deleterious effects in control offspring. Evidence of sex-dependent leptin resistance secondary to maternal obesity in juvenile offspring is consistent with the subsequent development of obesity in this model.

A Rapid Review of Methods to Measure the Implementation of a Life-Course Approach in Public Health Policies

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Background: A life-course approach recognizes that both past and present experiences are shaped by the wider social, economic and cultural context. The approach has increasingly become important in policy frameworks, and countries have committed to implementing the approach to improve health after the Minsk declaration in 2015. However, further evidence is required to support the development of a framework to measure the implementation of the life-course approach in public health policy.
Aim: To identify the quantitative and qualitative methods developed to measure the implementation of a life-course approach at the national level. The report identifies definitions, indicators and other examples that can be used by policymakers.
Method: A rapid review of published and grey literature was conducted on academic databases, along with general website searches and specific searches for strategy documents by government health agencies in Feb 2018. Experts were contacted for best practice examples.
Results: The review identified 22 articles globally that provided options for measuring programmes based on a life-course approach. Overall, the practical application of life-course theory was underdeveloped with implementation mainly focused on conditions such as NCDs or life-stages (e.g. pregnancy, childhood and ageing). Only two studies directly addressed the research question by reporting on ways to measure the implementation of the life-course approach. While developing measurement strategies, using a broad set of indicators and domains that are feasible to measure, aligned with existing monitoring frameworks (e.g. sustainable development goals) and reflecting multisectoral and interdisciplinary linkages are recommended.
Conclusions: This policy review suggests that a monitoring and evaluation framework collecting data longitudinally across different life stages over time should be created for Member States, and this can be done using existing survey platforms and routinely collected quantitative data.
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A systematic review and meta-analysis of school-based educational interventions to improve body mass index in adolescents

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Background/Aims: Adolescence marks a transition in behaviour and body composition that places adolescents at risk of overweight or obesity, which in turn has an adverse effect on their subsequent children. Health education in schools has been widely recommended for promoting physical activity, and healthy diet and body mass index (BMI). However, sustainable obesity prevention necessitates understanding which intervention elements are effective. We therefore reviewed the effectiveness of school-based educational interventions in improving BMI in adolescents.

Methods: In January 2017, a search of MEDLINE, PsycINFO, CINAHL, and ERIC was conducted for health education intervention studies delivered in schools for participants aged 10-19 years, published between 2006-17, including a control group and reporting BMI or BMI z-score at baseline and follow-up.**Results:** We identified 29,174 publications with 312 studies potentially meeting inclusion criteria. Twenty-five studies were included in the final review, of which 20 studies were RCTs and five used a quasi-experimental design. Most (n=18) were delivered by teachers in classroom settings, followed by researchers (n=4), school nurses (n=1), project officers (n=1) and student representatives (n=1). Additional components of the interventions included providing home-work, physical activity sessions and digital interventions. Effective interventions included features such as providing prior training for teachers on intervention delivery through workshops/seminars and involving parents through text messages, newsletters and emails. Novel techniques for intervention delivery such as games and computer-tailored advice and complex interventions that included environmental modification also led to a significant improvement in BMI. A meta-analysis for BMI z-score was conducted on data from 13 studies, using a random effects model due to the high level of heterogeneity (I^2= 65.1%). The overall pooled estimate of change in BMI Z-score in the intervention group vs. control was statistically significant [-0.10, 95% CI (-0.14, -0.05); p<0.001].

Conclusions: This systematic review demonstrates that it is possible to improve BMI and thus prevent obesity in adolescents using school-based educational interventions. Mediating factors supporting effective interventions included having a face-to-face component in class, providing training for teachers to deliver the programmes and involving parents.

Intergenerational Prevention Of Heart Failure Through Maternal Intake Of High Fibre

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Background/Aims: Dietary fibre intake protects against the development of cardiovascular disease (CVD) through the production of gut microbial metabolites. We aim to determine whether dietary fibre during pregnancy can prevent the development of heart failure through changes in the gut microbiota using the angiotensin II (Ang II) minipump model of hypertension

Method: C57BL/6 female mice were fed a diet without ('no fibre') or with high resistant starches ('high fibre') during gestation. At 6-weeks of age, male offspring had minipumps containing saline or Ang II (0.25mg/kg/day) subcutaneously implanted. Mice were followed for 4-weeks and cardiac weight, gene expression and gut microbiome composition were determined. 2-way ANOVA with adjustment for multiple comparisons was used and P<0.05 was considered significant.

Results: Mothers fed diets without or with high levels of fibre had a different gut microbiome composition (P=0.001). Pups born from high fibre mothers had distinct microbial colonisation (P=0.001), irrespective of the presence of Ang II (P=0.013). Independently of the mothers' diet, Ang II mice had higher systolic and diastolic blood pressure, but no difference in weight gain. Ang II offspring from high fibre mothers had a significant decrease in heart to body weight ratio (P=0.034). Furthermore, Ang II offspring whose mothers received a high fibre diet had lower levels of markers of fibrosis such as Col1a1 (P=0.01), Tgfb (P=0.021) and Ctgf mRNA (P=0.005) and lower levels of Nppb mRNA, a marker of cardiac remodelling and heart failure (P=0.002).

Conclusions: High fibre intake during pregnancy protected the offspring against the development of cardiac fibrosis and hypertrophy when compared to those born from mothers who consumed no fibre. The gut microbiota of the mothers was shaped by the intake of fibre during pregnancy and this had a lasting founding effect in the offsprings' microbiota.

Applying a Community Consultation Approach to Evaluate Maternal and Perinatal Health Outcomes among Métis Albertans

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Background/Aims: Métis people are one of Canada's constitutionally-recognized Indigenous peoples, yet the unique needs and experiences of Métis people are largely underrepresented

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in mainstream health literature. This knowledge gap is particularly wide for Métis-specific maternal and perinatal health outcomes. Maternal and perinatal health outcomes, the role of determinants of health, and the lived experience of pregnancy and birth in the Métis should be recognized and investigated as distinct from other Indigenous groups. We will explore the application of community consultation methods in a research project through a partnership among the Métis Nation of Alberta (MNA), and Métis and non-Métis academics, to evaluate the maternal and perinatal health status of Métis Albertans.
Method: Our research team's application of community consultation methods draws on strengths of Métis and Western ways of knowledge, and prioritizes Métis governance and self-determination in the research process, including the design, data collection, analysis, and interpretation and knowledge translation of results.
Results: This project combines a retrospective cohort study based on Alberta administrative health data and gatherings of Métis knowledge holders based on conversational methods. While epidemiological data is valuable to inform the maternal and perinatal health status of Métis Albertans, qualitative gatherings explore the "stories behind the numbers" and provide specific knowledge about the influences of colonialism, intergenerational trauma, resilience, cultural healing, and traditions on pregnancy and birthing. This approach allows for a decolonized method of data collection as themes emerge from the perspectives of Métis participants without imposing theories or structures, and ensures the information remains rooted in Métis knowledge and culture.
Conclusions: Incorporation of community consultation methods has aided our research team in designing and implementing a research protocol that prioritizes Métis ways of knowledge, while preserving self-determination, decolonization of the research process, and the unaltered "voice" of Métis participants.

A systematic literature review of the relation between iron status/anemia in pregnancy and offspring neurodevelopment

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Background/Aims: The brain is one of the fetal organs to develop earliest, and iron has been shown to play several roles for its development. However, epidemiological studies have provided inconsistent relations between gestational iron levels and offspring neurodevelopment, and systematic literature summaries have also been inconsistent. This review aims to systematically and critically review all published observational and supplementation studies that examined early life iron exposure and later life neuro-development, with specific focus on four domains: the used indicators for iron status, exposure timing, neurodevelopmental outcomes and offspring age.
Method: The review followed PRISMA guidelines. Embase, PsychInfo, Scopus and The Cochrane library were searched in February 2018. A total of 3307 articles were identified and 108 articles were assessed on full text. Studies were selected based on pre-specified eligibility criteria (PICOS tool). Results from all included studies were grouped according to the 4 domains in focus.
Results: In total 27 studies were included; 19 observational; 8 supplementation studies. There was small but fairly consistent evidence for an association with offspring behaviour, cognition and academic achievement and little evidence for associations with the offspring motor development. Iron supplementation overall did not have benefits on offspring neurodevelopment. Associations were seen/persisted beyond infancy and into adolescence, although based on few studies. Results did not depend on the timing of the exposure but depended on indicators of iron status.
Conclusions: We found some evidence that a low gestational iron level is associated with offspring neurodevelopment in particular behaviour, cognition and academic achievement. We suggest taking caution when inferring results from studies that used haemoglobin as the only iron status indicator. Using the 4 domains in focus clarified the heterogenous results derived from previous studies and led to a specific set of recommendations of what could characterize future research studies.

Associations between vitamin D status in pregnancy and offspring neurodevelopment- a systematic literature review

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Background/Aims: Vitamin D plays important roles in the developing fetal brain. Results from epidemiological studies investigating associations between gestational vitamin D levels and offspring neurodevelopment seem mixed and inconclusive, and systematic summaries of the results are inconclusive as well. We aimed to systematically review studies that examined vitamin D in pregnancy and offspring neurodevelopment, with focus on 3 domains: exposure timing during pregnancy trimesters, neurodevelopmental outcomes and offspring age.
Method: The review followed PRISMA guidelines. We searched Embase, PsychInfo, Scopus and The Cochrane Library in September 2017 and February 2018, identified 844 articles and retrieved 46 for full-text assessment. We used pre-specified eligibility criteria to select studies. Results were divided according to the 3 domains.

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Results: Fifteen studies were included, all of which were observational while no supplementation studies were identified. Vitamin D in pregnancy was associated with offspring language development and motor skills in early childhood (1 to 5 years of age). Associations also seemed to be present or persist into adolescence, whereas results did not depend on the vitamin D exposure timing during pregnancy.
Conclusions: We conclude that there is some evidence that low gestational vitamin D is associated with offspring language and motor development, especially in early childhood.

Body composition early in life in offspring from women with pregestational obesity supplemented with docosahexaenoic acid (DHA) during pregnancy

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Background/Aims: Maternal pregestational obesity (MPO) has been associated with higher body weight and fat in the offspring at birth and higher obesity risk in postnatal life. Studies in animals show that maternal DHA supplementation decreases offspring´s fat mass. This study evaluated the effect of maternal DHA supplementation MPO on the body fat in their offspring early in life.
Method: This is a longitudinal analysis of a subsample of newborns from the Epifat cohort. MPO were supplemented with DHA (200 or 800 mg/day, #12 (n=82) and #13 (n=76) blind RCT) from <15th w gestation until delivery (NTC02574767) were recruited at delivery and signed informed consent. Blood samples of the offspring of MPO at birth and 4 months were collected, erythrocytes separated and fatty acid (FA) profile determined by chromatography (%FAME). The offspring were evaluated and body fat estimated with Catalano´s equation at birth (24-72 h) and by PEAPOD at 4 months.
Results: Mothers from #12 were 2.9 years older, gained 2.3 kg less pregnancy weight and their newborns had 0,3 gestational weeks than #13 (p-value <0.05). At birth, newborns form #12 shower a lower n-6/n-3 ratio and a tendency of higher content of long-chained n-3 FA at 4 months. There were no significant differences in anthropometrics or body composition variables between #12-#13 at birth or 4 months of age. At birth, adjusted efficacy analysis showed that per each 1% of increase of DHA the %body fat decrease 0.33% (95%IC -0.75, 0.08), adjusted by gestational age, age at measure and maternal age. At 4 months, there was a decrease of 0.10% of body fat (95% IC -1.25, 1.06), adjusted by mode of feeding and age at measure; nevertheless, these associations did not reach significance.
Conclusions: At birth and 4 months, there was a tendency to high DHA associated with low body fat.

Multiple Epigenetic and Metabolic Markers Predict Glycaemic Health Longitudinally

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Background/Aims: Type 2 diabetes (T2D) is a global health burden that will benefit from personalised medicine, with omics data holding promise for it. Most studies have focussed on the improvement in T2D risk prediction using genetic markers. However, accumulating data suggests that T2D epidemic is partly related to the developmental and early life environmental conditions which are likely to alter the programming of epigenetic marks and persist across the lifespan. We aimed to identify longitudinal predictors of glycaemic traits relevant for T2D from multi-omics data, with special focus on epigenetic markers.
Method: We used data from 513 participants from the Northern Finland Birth Cohort 1966 at ages 31 (T1) and 46 (T2) years to predict fasting glucose (FG), fasting insulin (FI), glycated haemoglobin (HbA1c) and 2-hour glucose and insulin from oral glucose tolerance test (2hGlu, 2hIns) at T2 from 1,001 anthropometric, metabolic and epigenetic variables at T1 and T2. We applied six machine learning approaches: random forest (RF), boosted trees (BT) and support vector machine with four different kernels.
Results: FG and FI were best predicted, with average R^2 values of 0.38 and 0.53. RF and BT showed the most consistent performance across different predictor combinations. Multiple methylation markers at both time points were amongst the top predictors, including probes within the fatty acid and glucose metabolism regulating genes *CPT1A* and *SREBF1*. Other significant predictors were sex, branched-chain and aromatic amino acids, HDL cholesterol, glycerol, ketone bodies, blood pressure at T2 and measurements of adiposity at T1.
Conclusions: Besides metabolic markers reflecting the genetic background and recent lifestyle, we identified multiple epigenetic markers as important predictors of glycaemic health in middle age. These are likely to reflect effects across the life course, and their inclusion in the risk prediction will provide a more holistic view of the T2D risk.

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Association of Preeclampsia with Anthropometric Measures and Blood Pressure in Children

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Background: Preeclampsia (PE), a pregnancy complication, is associated with poor fetal growth and may increase cardiometabolic risk in the offspring. We have previously demonstrated a role for low omega 3 fatty acids in the development of PE. We examined differences in anthropometry and blood pressure between children born to mothers with PE and those born to normotensive control (NC) women. We also examined associations between cord omega 3 fatty acid status and offspring outcome.
Methods: We followed up a cohort of children born to well-characterized NC women (n=469) and women with PE (n=205) at Bharati Hospital, Pune, India. Anthropometry (weight, height, skinfolds) and blood pressure were measured in children at 3-7 yrs of age. Weight and height was converted to z scores by using the WHO 2007 reference. Independent t-tests were used to compare means between the two groups. Associations between offspring measures and cord plasma fatty acids were analyzed by multiple linear regression with adjustment for potential confounders.
Results: Z scores of weight [-1.39±1.02 (NC) Vs -1.20±1.25 (PE)] and height [-0.87± 0.99 (NC) Vs -0.64 ± 1.05 (PE)] were higher ($p<0.05$ for both) in children born to mothers with PE as compared to NC. Biceps, subscapular and suprailiac skinfolds were higher ($p<0.05$ for all) in these children. Systolic blood pressure was higher in children born to mothers with PE (B=1.709 mmHg, 95% CI 0.442–2.976) after adjusting for the child's gestational age, birth weight, sex and age. There was a negative association of cord plasma omega 3 fatty acids with offspring weight ($p=0.05$) after adjusting for parity, gestational age, age and sex of child, family income and mothers education.
Conclusion: *In utero* exposure to preeclampsia is associated with an increase in cardiometabolic risk factors (higher skinfolds, blood pressure) in early childhood. The role of omega fatty acids in the development of PE and its influence on health of the offspring needs further research.

Nutritional Transition Triggers the Risk of Adiposity among Undernourished Populations

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Background/Aims: In India, nutritional transition on one hand and escalating prevalence of adiposity & metabolic disorders on the other demands examination between the two. In particular, it is necessary to examine whether early life under nutrition increases risk for adiposity adversely.
Method: Rural Indian men (n=101) who had measurements for weight and height during 3+ years were followed for anthropometry and food consumption (FFQ), at age 22 (2005) and 32 years (2015). Decadal changes in food consumption were examined for its association with risk of adiposity differentially among those underweight (z-score weight <-2) or stunted (z-score height <-2) at 3+ age.
Results: Decadal changes indicate decreased consumption of protective foods viz. fruits (44.6%), GLVs (26.7%) and pulses (24.8%), but increased consumption of fried snacks (52.5%), non vegetarian foods (24.8%), marketed sweets (26.7%) and milk products (23.8%). Increase in consumption of these foods was associated with significantly ($p<0.05$) higher gains in mean indicators of adiposity. Consequently, prevalence ($p<0.05$) and risk for overweight was significantly associated with increased consumption of fried foods (OR-11.92; CI: 2.3-62.3) as well as milk products (OR-4.50; CI: 1.05-19.2) especially among those who were underweight at 3+ age. This was also true in case of stunting at age 3+ years. Additionally, increased consumption of fried snacks was also associated with higher prevalence ($p<0.05$) and risk for central obesity using WHtR (OR-6.11; CI: 1.2-31.4) or VF (OR-6.79; CI: 1.3-34.9). In contrast, the risk for adiposity was not significant among men who had normal weight or height in childhood, even if they increased the consumption of fried foods or of milk products.
Conclusions: Our observation highlights that nutritional transition triggers risk for adiposity among men experiencing childhood undernutrition and indicates dire need for nutritional and health awareness programs for rural youth for preventing risk for metabolic disorders.

Maternal Dietary Diversity and its Associated Factors with Special Focus to Food Environment in Kilteawlaelo District, Tigray Region, Northern Ethiopia, 2017/2018

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Background/Aims: Suboptimal dietary diversity during pregnancy results in pregnancy related complications, and poor fetal growth and development. Understanding the food environment and making it nutrition sensitive is emerging as a new strategy to address nutritional problems. Diet diversity among pregnant women and its associated factors especially its relation with the food environment in the developing world is not well studied. Therefore, this study is aimed to assess dietary diversity and its associated factors with special focus to food environment among pregnant women in Northern Ethiopia.
Method: Mixed cross-sectional study design was employed during a pre-harvest season. A total of 423 randomly selected pregnant women were included for the quantitative part. In the qualitative part, seven focus group discussions and seven in-depth interviews were conducted using purposive sampling. Interviewer administered structured questionnaire, open ended interview and discussion guides were used to collect the data. Women's diet diversity score was collected and categorized using the ten food groups for determination of Minimum Dietary Diversity of Women (MDDW) as per FAO/FHI 360, 2016 guidelines. Logistic regression was fitted to identify the associated factors. Inductive thematic analysis was used for the qualitative data. Finally triangulation of the qualitative and quantitative findings was done.
Results: The average diet diversity score of women was 4.65 +1.88 (4.48, 4.83). Less than half (48.2%) of pregnant women achieved MDDW (43.00, 52.70: 95% CI). Occupation, food availability, food affordability, and frequency of market days were found to be associated with diet diversity. Pregnant women reported during Focus group discussions that foods were not sufficiently available, not affordable, and the market was difficult to access.
Conclusions: The local agriculture department should work to diversify and increase agricultural production and make it nutrition sensitive. The local health office should give health education about diverse diet to the pregnant mothers.

Haemoglobin Concentration Trajectories In Rural Indian Children- PMNS study

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Background: There are few studies of the blood haemoglobin concentration trajectories during the life course and their association with parental haemoglobin concentration. PMNS has pregnancy and post-natal data to test these associations.
Methods: Pune Maternal Nutrition Study (PMNS) is a cohort established in 1993-94 in 6 rural villages of Maharashtra, India. We studied parental and child's haemoglobin concentration through the life course up to 18 years of age (gestation, 6, 12 and 18 years); maternal dietary intake and ferritin concentration during pregnancy. We aimed to study the tracking of the child's haemoglobin concentration and associations between parental and child's haemoglobin concentrations.
Outcome measure: Child's serial postnatal haemoglobin concentration (Hb) (N=551).
Results: Median (25^{th}-75^{th} percentile) maternal Hb concentration during early and late pregnancy was 11.6 (10.8, 12.4) g/dl and 11.3 (10.2, 12.1) g/dl respectively. Child's Hb concentration at 6, 12 and 18 years follow up was 11.6 (11.1, 12.1) g/dl, 12.9 (12.3, 13.5) g/dl and 13.1 (11.9, 14.2) g/dl respectively. The child's Hb concentrations at 6, 12 and 18 yrs were strongly interrelated. Univariate analysis showed significant associations between both maternal and paternal Hb and child's Hb concentrations. Adjusted multivariate regression models showed a strong association between maternal Hb concentrations and child's Hb concentration (β: 0.213; 95% CI: 0.018, 0.408) at 6 y follow-up. However, father's Hb concentration was associated more strongly with the child's haemoglobin concentration at 12y (β: 0.330; 95% CI: 0.102, 0.558) and 18y (β: 0.417; 95% CI: 0.186, 0.648) follow-up.
Conclusions: Hb concentrations of the offsprings showed strong tracking. Child's Hb concentration is associated with maternal Hb during early childhood but during adolescence paternal associations become stronger. This interesting finding needs to be further investigated for causality.

Influence of Pre-pregnancy BMI as well as Early and Late Gestational Weight Gain on Pregnancy Outcomes among Women with Gestational Diabetes Mellitus

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Background/Aims: Pre-pregnancy BMI and gestational weight gain (GWG) have been reported to be associated with pregnancy outcomes. However, their separate and joint associations with pregnancy outcomes among women with gestational diabetes mellitus (GDM) are not well understood.
Method: Women diagnosed of GDM in Peking University First Hospital from 2014 to 2016 were included. Pre-pregnancy BMI was divided into four categories (underweight, normal weight, overweight, and obese) according to Chinese BMI classification criteria. The adequacy of total, early and late GWG was defined according to Chinese BMI classification and IOM recommendations. Multivariate logistic regression analyses were used to investigate the association of interest.
Results: A total of 2,648 participants were included. Among them, 23.7%, 9.3% and 6.4% women were overweight, obese, and underweight. 30.1% and 29.1% women exhibited inadequate and excessive GWG. Compared with women of normal weight, higher pre-pregnancy BMI resulted in a higher risk of cesarean section, macrosomia, and LGA for overweight and obese group. Compared with adequate GWG, excessive

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GWG significantly increased the risk of macrosomia (P<0.001), LGA (P=0.002) and decreased the risk of SGA (P=0.005), while inadequate GWG reduced the risk of cesarean section (P=0.006), macrosomia(P=0.03) and increased the risk of preterm delivery (P=0.007). GWG before and after diagnosis of GDM have different effects on pregnancy outcomes. Excessive GWG before diagnosis may reduce the incidence of SGA (P=0.02), whereas excessive late GWG increase the risk of SGA (P=0.03). Only excessive early GWG was associated with a higher risk of macrosomia (P=0.01) and inadequate late GWG associated with a higher risk of SGA (P=0.045).
Conclusions: High pre-pregnancy BMI and excessive GWG were associated with higher risk of LGA and macrosomia among women with GDM, while lower GWG may benefit them from avoiding cesarean section and macrosomia. GWG before and after diagnosis of GDM differently affect pregnancy outcomes.

Childhood Oral Infections Associate With Risk Of Adulthood Subclinical Atherosclerosis

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Background/Aims: In adults, severe forms of chronic oral infections/inflammatory conditions, i.e. marginal and apical periodontitis, associate with increased cardiovascular disease risk. We investigated whether the early signs of these infections were associated with subclinical atherosclerosis in middle-age.
Methods: The population is The Cardiovascular Risk in Young Finns Study. Clinical oral examinations were conducted in 1980 when the children (n=755) were aged 6, 9, and 12 years. Four signs of oral infections, including bleeding on probing (BOP), periodontal probing pocket depth (PPD), caries, and dental fillings, were documented. Cardiovascular risk factors were measured at baseline and several times during the follow-up until 2007 and cumulative exposure to them was calculated. Subclinical atherosclerosis, i.e. carotid artery intima-media thickness (cIMT), was quantified in 2001 (n=468) and 2007 (n=489).
Results: Only a minority of the children had 'no signs of oral infections', who also had the lowest blood pressure values and body mass index during the whole follow-up. The cumulative exposure to risk factors correlated directly with the number of signs of oral infections both in childhood and in adulthood. If any sign of oral infection was present in childhood, the relative risk of subclinical atherosclerosis was 1.59 (95% CI 1.09-2.23). The oral infections remained as an independent predictor of subclinical atherosclerosis after adjustment for life-time risk factors, smoking, and socioeconomic status.
Conclusion: Our study with a 27-year follow-up suggests that oral infections in childhood associate with the risk of having subclinical carotid atherosclerosis in adulthood. Preventing childhood oral infections may have beneficial effects on cardiometabolic health later in life.

Lower handgrip strength in adults born preterm at very low birth weight: meta-analysis of three longitudinal cohort studies

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Background/Aims: Handgrip strength is a well established predictor of functional capacity and mortality in later life. Approximately 1 to 1.5% of newborns are born preterm at very low birth weight (VLBW; 1500 g); the first generations who have experienced modern neonatal intensive care in high-income settings are now young adults. Previous studies suggest that they undertake less physical activity and may have lower muscle mass, but there are few published data on handgrip strength.
Method: We performed an aggregated data meta-analysis based on data from three studies with 257 VLBW and 578 term controls from ESTER Preterm Birth Study in Northern Finland; 55 VLBW (36 women), 349 term controls (185 women), mean age 23.5 y, published, dynamometer Good Strength® IGS-01; Helsinki Study of Very Low Birth Weight Adults HeSVA, 166 VLBW (95 w), 172 controls (102 w), mean age 22.5 y, unpublished, Newtest®; NTNU LBW Life Study, 36 VLBW (21 w), 37 (22 w), mean age 22.6 y, unpublished, Jamar®. We analysed data with linear regression in each cohort and pooled the regression coefficients using random-effects meta-analysis.
Results: VLBW adults had lower dominant hand handgrip strength in all cohorts, and the difference was larger among men than women (p for sex interaction <0.01). Mean differences among *women* in dominant hand were 3.0 kg (95% CI 0.0, 6.1) in ESTER, 3.3 kg (1.4, 5.3) in HeSVA and 3.4 kg (0.6, 6.2) in NTNU; pooled mean difference among women was 3.3 kg (1.9, 4.7) Among *men*, they were and 12.1 kg (5.6, 21.9) in ESTER, 8.3 kg (3.7, 12.8) in HeSVA and 6.1 (-0.8, 13.0) in NTNU; pooled mean difference among men was 8.7 kg (5.2, 12.3). There was no evidence of between-cohort heterogeneity (Cochran's Q p>0.3). When we excluded the 28 VLBW and 5 controls with chronic disability, the results were similar.
Conclusions: Young adults born preterm at VLBW have substantially lower handgrip strength than their peers born at term. This may indicate increased risk for poorer functional capacity later in life. Physical activity enhancing muscular strength may be particularly beneficial for adults born preterm at VLBW.

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The effective combination of indicators considering familial information for preventing hypertension disorders of pregnancy: the TMM BirThree Cohort Study'

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Background/Aims: Environment in perinatal and neonatal periods as well as genomics are very important for understanding the origin of disease in later life. The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (the TMM BirThree Cohort Study) in Japan was started for investigating genomic and environmental factors for lifestyle diseases, allergy and developmental disorders by recruiting pregnant women and children, child's fathers and grandparents. By the year of 2017, we finished recruiting 73,499 family members, including 22,493 pregnant women (mothers), 23,113 babies, 8,823 fathers, 9,462 siblings, 8,058 grandparents and 1,550 relatives. Here, we introduce our progress focusing on follow-up period.

Method: In the follow-up period, we invite approximately 5, 10, and 16 year-old children, siblings, their parents and grandparents to our study facilities called the Community Support Centre. We ask them to take blood, urine samples and physiological assessments such as body composition, blood pressure, and so on. In the extensive research for children and siblings, we ask them to take medical check-up for atopic dermatitis by two dermatologists as well as eye examination, which enables to track their sight. Questionnaire survey by both mail and electronic ways are conducted for all family members once every 6 months or 1 year. Information from maternal and child health handbooks, medical charts, municipality's records, school health records and so on are also got from stakeholders with agreement of family members.
Results: By the end of Jan, 2019, 12,132 children and siblings, 5,070 mothers, 1,720 fathers, 3,144 grandparents, and relatives came to the Community Support Centre. Overall collecting rate of questionnaire is more than 73.0%, and over 80% of questionnaires were collected by mail. We completed to get information of antenatal care by medical records. We collected information of maternal and child health handbooks by 17,676 family members including grandparents. From municipality, we collected information of 5,438 child and sibling's health check-up records. Information of school health records and medical charts in follow-up period has also started to collect in some areas.
Conclusions: To follow-up the large size cohort, we are collecting data by several ways to complete participant's health information. The follow-up is going well so far, and we hope that findings and resources will help children to improve their health all over the world.

Maternal circulating micronutrients during pregnancy and its association with temperament and risk for common mental disorders in offspring during adulthood

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Background/Aims: Temperament is an innate and enduring characteristic. Disturbed temperamental traits predisposes one to psychopathology in later life. Maternal nutrition factors during pregnancy are associated with offspring temperament and risk for behavioural disorders in childhood (Autism, ADHD, Depression, Anxiety). However, the long-term effect of mother's micronutrient levels during pregnancy on temperamental characteristics and psychopathology in adult offspring has not been studied. Pune Maternal Nutrition Study (PMNS) is one of the few birth cohorts in the world which has serially followed up the offspring into young adulthood (24 years) and allows us to examine the association of maternal exposures on adult temperament.
Method: As part of ongoing assessments on the subjects of the PMNS birth cohort, 173 adult subjects (age 22.3 ± 0.5 years, 75 males) were administered Adult Temperament Questionnaire (ATQ), Adverse Childhood Experiences (ACE-IQ), and Brief Symptom Inventory (BSI) for psychopathology. Associations between maternal circulating micronutrients (B12, folate, homocysteine) at 18 weeks of pregnancy and four adult temperament dimensions (Negative affect, effortful control, orienting sensitivity, extraversion) and Global severity index on BSI were examined.
Results: Female subjects scored higher than males on temperament dimension of 'negative affect' ($p<0.001$). Higher maternal homocysteine levels at 18 weeks of pregnancy were significantly associated with lower scores on temperament dimension of 'effortful control' ($B = -0.19$, $p=0.02$ adjusted for age, gender, years of education of subjects, maternal education, socio-economic status, ACE-IQ). Lower scores on effortful control were significantly associated with greater global severity index on BSI ($p<0.001$). There were no associations with other temperament dimensions.
Conclusions: Higher maternal homocysteine at 18 weeks of pregnancy is a predictor for temperamental traits in offspring associated with increased risk for psychopathology in young adulthood.

Racial differences in nephron number: role of body size, kidney weight and cortical volume in adult subjects among five populations.

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Background/Aims: Developmental programming of renal structure may lead to a reduction in nephron number, which in turn may be an important determinant of adult renal function and blood pressure. To date, nephron number estimated using unbiased stereology has been studied for seven populations. Interestingly, our recent studies have shown that Aboriginal and Japanese subjects have fewer nephrons than most populations studied so far and they are at high-risk for chronic kidney disease. In this study, we examined the effects of body size, kidney weight and cortical volume on nephron number in normal adult kidneys among races.
Method: We analyzed kidneys from age and sex-matched subjects without overt kidney disease among five races; Aboriginal Australians, Japanese, Senegalese, Caucasian Americans and African Americans (n=12 in each group).
Results: Compared to Caucasian and African Americans, Aboriginal Australians and Japanese subjects had smaller body size. No statistically significant differences were observed in kidney weight or cortical volume among the races. Nephron number per kidney in Aboriginal Australians (743,296±167,572; mean±SD) and Japanese subjects (749,686 ±134,353) was significantly lower than in Senegalese (854,216±71,792), Caucasian Americans (1,002,308±240,067) and African Americans (933,664±214,550). Although this difference was still present after adjustment for height, nephron number after adjustment for BMI, BSA, kidney weight or cortical volume was similar in the five populations.
Conclusions: Our study indicates that Aboriginal and Japanese subjects with smaller body size have fewer nephrons than the other races. Further nephron loss in these subjects would likely increase the risk of CKD.

Estimated nephron number in Japanese children with Wilms tumor

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Background/Aims: It has been postulated that an inherited nephron loss would lead to the development of chronic kidney disease (CKD) in later life. Consistent with this hypothesis, recent studies have reported that low birth weight is associated with an increased risk of CKD. However, the effects of birth weight and nephron number in children on development of noncommunicable CKD in adult age have not been elucidated. We, therefore, estimated nephron number in living children with Wilms tumor.
Method: We evaluated the children with Wilms tumor at Jikei University School of Medicine Hospital who underwent an enhanced CT scan and nephrectomy. Nephron number was calculated by multiplying cortical volume of a healthy side by the glomerular density in a nephrectomy sample.
Results: Two children operated on at the age of 16 months (CASE1) and 11 months (CASE2) old for Wilms tumor were identified.
Conclusions: These results suggested the possibility of being able to estimate nephron number in living children with Wilms tumor. Further studies involving much larger numbers of subjects are required to determine the role of nephron number in children.

Effect of parental and grandparental smoking on offspring BMI in early adulthood in the STRIP cohort

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Background/Aims: Some studies have reported association between parental/grandparental smoking and offspring adiposity. Our aim is to assess associations between parental and grandparental smoking and offspring adiposity, with specific interest in sex-specific associations in maternal and paternal lines.
Method: STRIP is a cohort of Finnish children born in between 1989 and 1991 (N=1116), followed until early adulthood. We investigated the effect of grandparental and parental smoking on the study subjects' BMI measures at age 18-20y. Linear regression was applied with the subject's BMI as response and grandparental and parental smoking status and their interaction as explanatory variables. In order to study any sex-specific associations in maternal and paternal lines, a separate model for each of the four parental lines (maternal grandmother, maternal grandfather, paternal grandmother, paternal grandfather) was constructed for both sexes.

	Gestational age	Birth weight (g)	Serum Cr (mg/dl)	Nephron number (/kidney)
CASE1	40 weeks 3/7	2,318	0.17	843,590
CASE2	40 weeks 0/7	2,934	0.30	1,021,397

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Results: For overall grandparental and parental exposure, no association with offspring adiposity was found. Maternal grandmother's and mother's smoking were associated with increased BMI in girls. Especially those girls whose grandmothers and mothers had smoked had higher BMI compared to those girls whose grandmothers and/or mothers were non-smokers (mean BMI 26.3; difference and 95% CI from non-exposed 3.89 [1.58; 6.21]; only maternally exposed 3.50 [1.20; 5.80]; only grand-maternally exposed 3.83 [1.09; 6.50]). We did not find similar associations for other parental lines or sexes.
Conclusions: In our data, it appears that ancestral smoking in the maternal line may be associated with higher offspring BMI. However, associations between grandparental smoking and offspring adiposity remain inconsistent. More research with well-defined smoking exposures and larger data sets needs to be conducted.

Chapter 1 Post-Exercise Heart Rate Recovery in Adults Born Preterm

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Background/Aims: Preterm birth is associated with several cardiovascular risk factors and morbidities in later life. Impaired cardiac autonomic function, expressed as depressed vagal (parasympathetic) control, is an important and independent risk factor for cardiovascular morbidities. Attenuated heart rate recovery (HRR) after exercise, an indicator of reduced parasympathetic activity, is an independent and powerful predictor of overall mortality. We hypothesized that preterm birth across the range of gestational ages predicts impaired HRR after exercise in young adulthood.
Methods: At a mean age of 23.3 years, 103 early preterm (< 34 wk), 178 late preterm (34-36 weeks) and 264 control subjects underwent a recording of beat to beat heart rate intervals during and after a step test exercise. HRR was evaluated by calculating change in heart rate 30s and 60s after cessation of submaximal step test exercise and maximum heart rate slope during the 1st minute after. The results were adjusted for age, sex and cohort as covariates.
Results: Mean HRR 30s after exercise was 3.2 bpm (95% CI 1.1 to 5.2) lower in the early preterm group and 2.1 bpm (0.4 to 3.8) lower in the late preterm group. Mean 60s HRR was 2.5 (-0.1 to 5.1) lower in the early preterm group and 2.8 bpm (0.6 to 4.9) lower in the late preterm group. Mean maximum slope in the HRR during the 1st minute after cessation of exercise was 0.10 beats/s (0.02 to 0.17) lower in the early preterm group and 0.06 beats/s (0.00 to 0.12) lower in the late preterm group.
Conclusions: Our results suggest reduced heart rate recovery after exercise in adults born preterm, including those born late preterm. Impaired reactivation of the parasympathetic nervous system may contribute to cardiovascular risk among adults born preterm.

Evaluation of Soluble TNF-like weak inducer of apoptosis (sTWEAK) Levels to Predict Preeclampsia in Early Weeks of Pregnancy

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Introduction: Pre-eclampsia affects 5–14% of all pregnancies globally and in developing countries the prevalence is comparable as 4–18%. Previous maternal history and presence of risk factors alone are not reliable for the prediction; therefore more profound monitoring is required for prompt diagnosis and fruitful treatment strategies. Keeping this in view, detection of PE biomarkers in early pregnancy has always been an interesting field of research. Soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) is linked to endothelial dysfunction; a key factor in pre-eclamptic pathogenesis. Therefore, we aimed to compare sTWEAK levels during pregnancy to assess for its prognostic ability.
Materials and Methods: Sixty three high risk pregnant women were followed from time of booking (12 gestational week) till delivery. Serum levels of sTWEAK and platelet derived growth factor (PlGF), blood pressure, kidney and liver function tests were measured. ACOG criteria was used to classify women as PE, or PIH or normotensive at term. A negative control group of normotensive healthy pregnant women (n=17) was also recruited for comparison.
Results: The overall baseline sTWEAK level was lower (4.03 ±0.37ng/dl) in HR women who established PE which further reduced to 1.93±0.23ng/dl at term as compared to women who remained normotensive and negative control group (30.53 ±0.79ng/dl; p<0.01). Likewise PlGF levels were significantly lower (74.22±10.11pg/ml) in HR cohort that developed PE (p=0.013). At term 39.68% (n=22) HR subjects with low sTWEAK developed PIH and 34.92% (n=24) developed PE.

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Conclusion: Baseline TWEAK might serve as an independent variable for prediction of pre-eclampsia; however longitudinal studies with larger sample size are required to ascertain the causal relation.

Well-controlled gestational diabetes eliminates DNA methylation changes in cord blood cells associated with hyperglycemia and metabolic disorders in neonates

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Background/Aims: There are few studies on the epigenetic status of babies born to well-controlled (w-) gestational diabetes (GDM) mothers. Moreover, the association between epigenetic changes and neonatal plasma glucose (PG) levels in babies born to GDM mothers is unknown. The aim of this study is to investigate the effect of controlling hyperglycemia in GDM mothers on cord blood DNA methylation, and the association between cord blood DNA methylation levels and neonatal PG.
Method: We performed genome-wide DNA methylation analysis using an Illumina EPIC array. The methylation rate of 754,255 autosomal sites in cord blood samples from full-term neonates born to 165 w-GDM mothers and 61 normal glucose tolerance pregnancies (NGT) were compared. We also performed an association study between neonatal hypoglycemia and cord blood DNA methylation as well as linear regression analysis between DNA methylation in cord blood samples and continuous neonatal PG 1 hour after delivery in the w-GDM group.
Results: The comparative genome-wide DNA methylation analysis of cord blood samples from w-GDM and NGT groups revealed only two differentially methylated CpG sites (adjusted $P < 0.05$ for both), with less than 2% difference between the two groups at these sites. Considering neonatal blood glucose levels, there were no differentially methylated sites between hypo- and normoglycemia groups. In w-GDM mothers, neonatal PG 1 hour after delivery was positively correlated with cord blood methylation rates at one CpG site, an enhancer chromatin region that may be topologically associated with the gene controlling heart growth and organization.
Conclusions: The effects of GDM were negligible when maternal PG was well-controlled during pregnancy. However, the *in utero* environment that induces neonatal hypoglycemia may affect the epigenetic status of newborns.

Sexual Dimorphism in Fetal Growth Responses in a Mouse Model of IUGR

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Background/Aims: Intrauterine growth restriction (IUGR) affects 5-15% of babies, and increases their risk of perinatal death and poor health in later life. In order to test potential interventions, we have established a murine model using embryo transfer-generated pregnancies where increased litter size induces an IUGR phenotype. In this model, IUGR was evident with increasing litter size, and in large litters fetuses had smaller placentas, were thinner and evidence of brain sparing. In humans, birth weights are higher in male than female babies at every gestation [1], and adverse exposures such as maternal asthma have sex-dependent effects [2]. The aim of the current study was therefore to investigate whether increasing litter size constrains fetal growth in a sex-specific manner.
Method: CBAF1 embryos were collected at gestation day 0.5 (GD0.5) and 6, 8, 10 or 12 embryos transferred into each uterine horn of pseudopregnant CD1 mice (n=32). Fetuses and placentas were collected and weighed at GD18.5. Fetuses were genotyped for sex by PCR for *Sry*.
Results: Effects of viable litter size on fetal weight differed between sexes (interaction $P=0.002$). Weights of males ($P=0.002$), but not females ($P=0.233$), correlated negatively with litter size. Placental weight decreased with increasing litter size ($P<0.001$) and was lower in females ($P=0.020$), but effects of litter size did not differ between sexes.
Conclusions: In this model, the pattern of female growth is not affected by maternal constraint. In contrast, males are heavier when unconstrained, and their placentas are always heavier than those of females, suggesting the male fetus extracts maximal available nutrients, whereas the female maintains placental reserve capacity. This strategy is likely to place the male fetus at risk in the event of a "second hit".
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The effect of maternal uncarboxylated osteocalcin on the metabolic properties of next generation

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Background/Aims: Maternal nutrition during pregnancy has been found to have a significant impact upon the health of offspring after maturation. However, strategies for modulation of maternal energy metabolism without an adverse effect on the fetus have remained limited. It was recently shown that oral administration of uncarboxylated osteocalcin (GluOC) improves metabolic status in adult female mice, and it crosses the placenta. We thus explored the effect of daily oral GluOC administration during gestation on metabolic properties of offspring, with a particular regard to organs related to glucose and lipid metabolism of pups.
Method: Female C57BL/6 mice were fed a normal diet (ND) or high-fat, high-sucrose diet (HFS) and were given saline or GluOC by oral administration during pregnancy. The resulting offspring were in turn assigned to ND- or HFS-fed groups immediately after weaning, and their body weight, glucose metabolism, serum lipid parameters, and level of adipose tissue inflammation were subsequently assessed after maturation.
Results: Phenotypes related to glucose or lipid metabolism differed between sexes. Maternal HFS feeding during gestation had adverse effects on glucose and lipid parameters, body weight, and adipose tissue inflammation especially in female offspring fed the same diet, and these effects were attenuated by maternal oral GluOC administration.
Conclusions: Maternal oral administration of GluOC protects HFS-fed female offspring from metabolic disorders induced by maternal obesity.

Through the Voice of Children: Methods and ethics in conducting research about children and young people

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Background/Aims: The world is a subjective place, those concerned are always the best placed to describe their reality. This holds true for all age groups including children. One of the general principles of the UN Convention on the Rights of the Child is the child's rights to "express opinions and to be heard" (CRC Article 12). The DOHaD model implies that prevention interventions ought to be focused on preconception and pregnancy mental health, thus children and young people come into focus.
Method: "Voice of Children" is an educational endeavour aiming at improving knowledge on theory and practice in research with and about children and young people, developed at the Karolinska Institutet and building on a review of research acquired through Save the Children. The rights of the child and implications for research; benefits to society, to children and to research from giving children a voice in research; ethical considerations and a range of child- and youth friendly methodologies used around the world, their drawbacks and advantages, are discussed.
Results: Aside from producing better quality data, the process of children's participation in research has been shown to help heal their past. Boys and girls affected by stress, violence or any other type of discomfort may benefit especially well from participation in research. In relation to traumatic events, the process of involvement, if undertaken in a supportive and understanding environment, can help children explore past experiences and regain confidence for the future. At its best, participation can be a fundamental tool out of victimization, passivity and silence.
Conclusions: DOHaD research would benefit from methods and tools to be used with children and young people. Obtaining data from children and young people increases the possibility of presenting a picture that is freer of adult interpretations, which can inform timely and appropriate health promotion.

Fear of childbirth through the lens of culture: Perspectives from the Arabian Peninsula

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Background/Aims: Few studies have addressed women's fear of childbirth (FOC) as an intrinsic part of culture. Yemen on the Arabian Peninsula is a country of rich cultural diversity and medical pluralism, suited for such a study. Maternal and child health care in northern and southern Yemen has been strongly influenced historically by diverse childbirth traditions of the West and Eastern Europe. The aim of the study was to examine contextual and individual factors that impact women's FOC, including factors of socio-demography, place and type of childbirth care, pregnancy outcome and cultural heritage.
Method: Two hundred and twenty women with childbirth experience in urban/ rural Yemen were interviewed through a structured closed- and open-ended questionnaire. A multistage sampling process was used. Bivariate chi-square tests and multiple logistic regression analysis were performed.
Results: In multiple logistic regression analysis women who resided in the southeast Hadramout Governorate of Yemen with a previous strong matrilineal culture and distinct tradition of non-attended childbirth were close to three times less likely (95 % confidence interval (CI) 1.15 – 6.4) and Nomad women among them six times less likely (95 % CI 2.24 – 22.74) to

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experience FOC. Young women in the study population were almost twice as likely to experience FOC (95 % CI 1.08 – 2.94). Bivariate analysis showed that women who had received conflicting advise during pregnancy from Antenatal Care (ANC) staff and women in the local community and those women who had educated husbands were at excess risk of FOC.
Conclusions: FOC is deeply rooted in culture. The power of culture lies in its ability to influence the social domain of life, of which FOC is a reflection. The multiple challenges associated with women's young age in our gender segregated study population give rise to FOC. Sensitization of ANC staff to local perceptions would lessen FOC.

Periconceptional ethanol exposure alters glucocorticoid receptor (GR) isoform profile in the liver of adult offspring irrespective of fetal liver GR patterns.

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Background/Aims: Periconceptional ethanol (PC:EtOH) exposure programs metabolic dysregulation in offspring. These outcomes may be mediated by impaired glucocorticoid signalling pathways, which depends on the altered expression of various glucocorticoid receptor (GR) isoforms. This study investigated the effect of PC:EtOH exposure on GR isoform expression in the liver of adult offspring as well as within the fetal liver.
Method: Sprague-Dawley rats were given a liquid control or an isocaloric 12.5% v/v ethanol diet from E-4 to E4. Rats gave birth and livers were collected from offspring at 6 months. In a separate group of rats culled at E20 and livers were collected. Cytoplasmic and nuclear GR isoforms were analysed using western blotting. Genes shown previously to be activated by various GR isoforms were analysed by qPCR.
Results: The isoforms identified in the adult liver and fetal liver included GRα-A (94kDa), GRα-B (91kDa), GRα-C (81kDa), GRα-D1-3 (50-55kDa) as well as the splice variants GRP (74kDa) and GRA (65kDa). PC:EtOH increased protein expression of GRα-A in a sex dependent manner. Within the fetal liver, there was an increase in cytoplasmic GRα-D expression in both males and females, but these changes did not persist into adult life. Downstream genes were affected by PC:EtOH exposure and sex in both fetal and adult livers but these changes were not linked to altered GR isoform expression.
Conclusions: This study demonstrated that the long-term impact of PC:EtOH exposure on offspring may relate to altered liver expression of GRα-A in adult livers. These alterations are distinct from alterations in GR isoform patterns that occur in the fetal liver and did not affect the expression of a number of downstream genes known to be affected by glucocorticoid signalling. Further investigation is required to determine the mechanism by which PC:EtOH programs metabolic disease.

Childhood dietary trajectories predict functional cardiovascular phenotypes by age 11-12 years

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Background/Aims: We studied the extent to which lifetime dietary trajectories predict preclinical cardiovascular phenotypes and metabolic syndrome risk by age 12 years.
Method: Population-based Longitudinal Study of Australian Children, followed biennially from 2-3y, with cardiometabolic measures at the Child Health CheckPoint in 1861 children (11-12y). Exposures, 2-3y to 10-11y: repeated 24-hour dietary recall. Participants' decade-long dietary trajectories classified as: 'never healthy' (7%), 'becoming less healthy' (17%), 'moderately healthy' (21%) and 'always healthy' (56%). Outcomes, 11-12 years: Cardiovascular function (resting heart rate; blood pressure; pulse wave velocity; carotid elasticity and distensibility) and structure (carotid intima-media thickness (IMT); retinal microvasculature) and metabolic risk score. Analysis: Adjusted regression models.
Results: Less healthy dietary trajectories predicted functional but not structural vascular phenotypes or metabolic syndrome risk. Compared to 'always healthy', children in the 'never healthy' trajectory had higher resting heart rate (2.7 bpm, 95% CI 0.6, 4.8) and lower arterial elasticity (-0.032% per mmHg, 95% CI -0.057, -0.006, d 0.35) and distensibility (-1.2%, 95% CI -1.9, -0.5, d 0.38); those in the 'becoming less healthy' trajectory had higher diastolic blood pressure (1.0 mmHg, 95% CI 0.1, 1.9). Effects remained after adjusting for puberty, BMI, physical activity and cardiorespiratory fitness.
Conclusions: By age 11-12 years, poorer lifetime dietary quality predicted higher resting heart rate, now becoming established as one of the strongest precursors of all-cause mortality. The absence of associations with metabolic risk and structural phenotypes suggest an early opportunity for prevention.

Association of micronutrient deficient diets and depression and anxiety symptoms among adolescent boys and girls styding in public schools of delhi

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Background/Aims: Data on prevalence of mental health disorders indicates that 4.5% and 3% of the Indian population is suffering from depression and anxiety respectively and that the numbers are rising even among younger populations. Research suggests that a poor quality diet (lacking in micronutrients) may lead to deficiencies that are associated with depression and anxiety disorders (Jacka et al., 2012; Jacka et al., 2013). The present research was designed to study the effect of micronutrient malnutrition on the presence of depression & anxiety among adolescent boys & girls (aged 13-15 years) studying in public schools of Delhi.
Method: 546 adolescents participated in this cross-sectional study (selected from public schools in Delhi). For the assessment of depression and anxiety symptoms and dietary micronutrient deficiencies Child Behavior Checklist (CBCL; administered to the parents) and 24 hour recall and food frequency questionnaire (administered to the subjects) were used respectively.
Adolescent Micronutrient Quality Index (AMQI) was used to assess the micronutrient quality of the diets.
Results: Prevalence of depression and anxiety symptoms was 33.5% and 27.47% respectively. In *males*, higher consumption of energy was significantly associated with higher mean ***depression*** ($p = <0.001$) and ***anxiety*** scores ($p = <0.001$), whereas higher consumption of proteins was significantly associated with lower mean depression and anxiety scores. Also, lower consumption of micronutrients like iron and magnesium was significantly associated with lower depression and anxiety scores. In *females*, lower consumption of energy (<RDA) proteins, fat, iron was significantly associated with higher mean depression ($p = <0.001$) and anxiety scores ($p = <0.001$).
Conclusions: This study highlight's the association of mental health with micronutrient deficiencies among adolescents. It will also serve as a strategic tool for mental health prevention & management policies designed for adolescents. It also add to the growing body of research in the area of nutritional psychiatry.

Paternal Micronutrient Supplementation Affects Offspring Metabolic Health in a Sex Dependent Manner

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Background/Aims: Increasing evidence suggests that effects of perturbations in the father at the time of conception can be seen in the offspring. Obesity decreases sperm quality, increases sperm oxidative stress and alters epigenetic marks. Several studies have reported multiple metabolic changes in offspring of obese fathers. Here, we tested whether a micronutrient supplement would reduce oxidative stress and ameliorate the negative effects of paternal obesity on the next generation.
Methods: Male Sprague Dawley rats (3 weeks old, 12/group) were weaned on control (CD) or high fat diet (HFD) or diets containing the micronutrient supplement (CSD; HFDS), after which they were mated at 19 weeks of age with control diet fed females. Twelve F1 offspring of both sexes, each from a separate litter and from each diet group, were weaned on day 21 onto either CD or HFD, generating 8 F1 groups. After 14 weeks CD or HFD, they underwent MRI and oral glucose tolerance testing (oGTT).
Results: HFD caused increased adiposity in fathers (+15.3% versus CD), which was normalized in HFDS rats. Both male and female F1 offspring consuming HFD had higher body weight and adiposity than those on CD. There were no differences in adiposity at 17 weeks of age between the F1 groups on HFD in both sexes. During an oGTT, HFD fed male offspring from all fathers cleared glucose similarly. However, offspring from HFDS-F0 supplemented fathers released significantly less insulin to clear a similar glucose load compared to those from HFD-F0 fathers. This effect was not seen in female offspring.
Conclusions: Dietary micronutrient supplementation prevented weight gain and adiposity in fathers. Supplementing fathers modulated the effect of HFD on glucose tolerance and insulin sensitivity in their F1 male offspring. This is initial evidence that our health promoting supplement can have a positive impact on the next generation.

Assessment of neonatal growth and wellbeing following thyroid hormone-based therapy in a rodent model of intrauterine growth restriction (IUGR)

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Background: We have shown that the thyroid hormone (TH) transporter - monocarboxylate transporter-8 (MCT8) is decreased in the neonatal IUGR rat brain, perhaps contributing to impaired brain development in IUGR. We also found that the TH analogue, diiodothyropropionic acid (DITPA), which does not require MCT8 to enter cells promotes myelin recovery by P7. However the preclinical safety profile of DITPA is unknown. **Aims:** To determine if DITPA treatment in IUGR rats affects neonatal growth and wellbeing.
Method: At day 18 of pregnancy (term=22 days), rats underwent bilateral uterine vessel ligation (n=29 litters) or sham surgery (n=15 litters) to generate IUGR or control pups. DITPA (0.5mg/100g; i.p.) or saline was administered daily from P1-P13 to IUGR (DITPA, n=60; Saline, n=57) and control

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(DITPA, n=42; Saline, n=46) pups. Body weight, brain weight, body composition, thyroid function (serum free T_3 and T_4), and serum liver enzymes (alanine transaminase, ALT; alkaline phosphatase, ALP) were assessed at P14.
Results: In IUGR vs control pups, there was a significant reduction in body weight, brain weight, bone mineral content, bone mass, lean tissue mass and fat mass; DITPA did not improve or worsen these effects. In IUGR vs control pups, free T_4 and ALT were significantly decreased, and ALP was significantly increased; DITPA treatment significantly increased free T_3, ALP, and ALT (IUGR only), but reduced free T_4.
Conclusions: DITPA does not adversely impact neonatal growth or wellbeing following IUGR, despite altering free thyroxine levels and showing hepatic thyromimetic activity.

Early non-food parent-infant interactions and the development of obesity in a high-risk, diverse sample

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Background/Aims: Responsive parents who display more warmth and sensitivity toward their infants by displaying affective attunement in early infancy (1 month) and contingent responsiveness in later infancy (13 months) may nurture children's ability to regulate food consumption and increase the reward salience of social interactions. This in turn may minimize unhealthy weight gain.
Method: Our sample consisted of 143 low-income (76% receiving Temporary Assistance for Needy Families) mother-infant dyads (72% African-American) recruited at delivery. Mothers used alcohol, tobacco, cannabis, and/or cocaine in pregnancy and ranged in age from 18 to 42 years ($M = 29.53$, $SD = 6.06$). Mother-infant interactions were assessed at 1, 7 and 13 months of age (m). At 1 month, the mothers were asked to spend some time feeding their infants as they normally would at home At 7 and 13 months, mothers were asked to spend some time with their infants as they normally would at home in a room filled with toys. These interactions were coded using the Parent-Child Early Relational Assessment by two sets of coders blind to other family information. Child anthropometric measures were collected at 24, and 48-m.
Results: Higher maternal warmth during feeding, assessed at 1 m was, marginally associated with lower zBMI at 4 years of age ($\beta = -0.060$, $p = 0.051$) after controlling for potential confounders. In addition, positive maternal involvement during free play at 13-m was negatively associated with weight for length z-score at 24-m ($\beta = -0.483$, $p = 0.021$), after controlling for biological mothers' age, race, educational level and parity, and child's birthweight, sex, as well as foster care experience.
Conclusions: Nurturing and supportive home environment during infancy might protect against the development of obesity later in life.

Association of pre-pregnancy body mass index and gestational weight gain with infant birth weight

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Background/Aims: Low birth weight is a major public health concern in Japan. Sufficient nutrition before and during pregnancy can positively affect the long-term health of a child. Our study aims to examine the association of pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) with infant birth weight considering maternal dietary intake.
Methods: Totally, 250 singleton pregnancies at the Obstetrics and Gynecology hospital in Shizuoka Prefecture, Japan, between September 2015 and August 2016 were included. Dietary intake was assessed by a validated brief diet history questionnaire, and eating habits (e.g., meal-skipping, self-supplement usage, and morning sickness) were assessed during recruitment (mean: 16 weeks of gestation) and at 4 weeks after delivery. Maternal information and perinatal data such as sex, birth weight, birth height, and gestational weeks were collected from hospital records. Adjusted associations of pre-pregnancy BMI and GWG with infant birth weight were estimated by multiple linear regression analyses.
Results: Pre-pregnancy BMI and GWG were positively associated with infant birth weight in the fully adjusted model among male infants but not among female infants. There are certain sex differences among the effects of birth weight on pre-pregnancy BMI and GWG. Among available hospital record data (n=214), 121 mothers (56.7%) were prescribed iron supplementation after approximately 30 weeks' gestation. The infants of these mothers had higher birth weight than those of other mothers. This association was stronger among male infants. The mothers who showed an appropriate GWG as recommended in the Japanese governmental guidelines had a significantly higher intake of nutrients, especially vitamin K and folic acid, than those who showed a different GWG than the recommended level.
Conclusion: Our findings suggest that pre-pregnancy BMI, GWG, and iron supplementation were positively associated with birth weight among male infants.

Impairment of Growth of Children Exposed to Maternal Stress During Pregnancy Caused by Natural Disaster

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Background/Aims: Natural disasters provide excellent opportunities to examine the effects of prenatal stress on childhood outcomes because the stressors are independent of potentially confounding genetic and medical risk factors, and are relatively randomly distributed with regard to household and maternal characteristics. The aim of the study was an estimation of effect of strong prenatal maternal stress, induced by strike of tropical severe cyclone Aila in 25th May 2009 in the region of Sunderban (West Bengal, India), on growth and development of children.
Method: Anthropometric and demographic data of two groups of children; 97 boys and 88 girls consisting of Aila-affected group, and 98 boys and 96 girls consisting control group, were collected in all primary schools on the two Islands of the Sunderban area and from the rural primary schools of the adjacent district, respectively. The populations were matched in respect of the origin, culture and language. They did not differ in socio-economic background. Two-way ANOVA with generalised linear model was employed to assess the significance of differences in anthropometric parameters between the Aila and the control group of children, allowing for birthweight and socio-economic parameters.
Results: The Aila children showed lower body weight, BMI and mid-upper arm circumference, but accumulated more fat at lower part of trunk, assessed by skinfolds thickness. They had lower sitting height index, but higher relative lower leg length. Aila-affected children also showed lower body frame index.
Conclusions: The results together demonstrated that the children who were intrauterine during the cyclone showed several impairments of growth. This suggests the existence of significant and long lasting effect of prenatal stress on children's growth and development. Because of recently observed increase in intensity of extreme weather and natural phenomena, our results make contribution to understanding of their consequences within the context of human growth and development.

Contribution of miRNAs miR-21 & miR-126 to the early endothelial programming in response to fetal growth restriction

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Background/Aims: Fetal growth restriction (FGR) is associated to intrauterine chronic hypoxia and, short and long term endothelial dysfunction that would result from an altered eNOS expression mediated by epigenetic mechanisms. We previously have demonstrated the contribution of DNA methylation and histone post-translational modifications in this FGR-induced eNOS programming; however no studies have determined the role of hypoxia inducible microRNAs. (i.e. miR-21 and miR-126), as well as the potential epigenetic effects on other genes involved in the NO-dependent vasodilator pathway.
Method: Levels of miR-21 and miR-126, as well as, eNOS, DDAH1, Nrf2 y ARG2 mRNA were determined in primary cultures of umbilical artery endothelial cells (HUAEC) from FGR (n=7) and control (n=7) pregnancies by qPCR. In order to determine the effect of hypoxia controlling the explosion of these RNAs, HUAEC from control subjects were exposed to hypoxia (1% O_2, for 6 to 48 h) and the expression of the previously described miRNA and mRNA quantified. Finally, we determined the mRNA expression of miR-21 prediction targets for miRWalk database (eNOS, DDAHH1) following the transfection of HUAEC-control with 30 nM miR-21 mimic precursor.
Results: FGR HUAEC showed a decrease of miR21 levels along with higher levels of miR-126 and eNOS, but lower expression of the pro-NO genes (DDAH1, Nrf2). Control HUAEC exposed to *in vitro* hypoxia (1% O2, 6 h) showed a transient increase in pro-NO genes (eNOS, DDAH1) along with a decrease in miR-21, whilst levels of miR-126 levels were not affected by hypoxia. The overexpression of miR-21 using a miR-21 mimic in control HUAEC led to a decrease in both eNOS and DDAH1 mRNA levels to 0 and 6 hours of hypoxia.
Conclusions: Hypoxia-related miRNAs, miR-21 and miR-126, are differentially expressed in HUAEC from FGR pregnancies and their expression is associated with heterogeneous levels of pro-NO genes. The negative regulation of pro-NO enzymes by miR21 suggests that the decreased miR-21 levels in FGR contributes to an epigenetic-mediated short-term up-regulation of eNOS in the endothelium.

Living in a Single-Parent Household During the First Few Years of Life Is Associated with Earlier Pubertal Onset in Girls

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Background/Aims: Early puberty is associated with adverse health outcomes throughout adolescence and adulthood, and the average age of pubertal onset among girls has declined substantially over the past few decades. Numerous studies indicate that father absence is associated with earlier puberty, however, the majority of studies have used menarche as a proxy for pubertal onset and have not considered the role of girl's prepubertal obesity. Additionally, these studies have focused on biological father absence. We addressed these gaps and investigated whether early-life exposure to a single-parent environment is associated with earlier pubertal onset using pediatrician-assessed pubertal development stages among racially/ethnically diverse girls.

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Method: Data were drawn from a population-based prospective cohort study of 5,967 girls born at a Kaiser Permanente Northern California (KPNC) facility between 2003-06. KPNC is an integrated healthcare delivery system with diverse membership representative of the underlying source population. All data were obtained from KPNC electronic health records. Weibull regression models accommodating left, right, and interval censoring were used in all analyses, with the primary outcomes being age of transition from breast stage 1 to 2+ (BR2+) or pubic hair stage 1 to 2+ (PH2+). Models were adjusted for maternal age, education, parity and girl's race/ethnicity. We examined the role of prepubertal BMI as a mediator.
Results: Living in a single-parent household was associated with earlier onset of breast and pubic hair development compared to living with both parents (adjusted hazard ratio [HR]: 1.22; 95% confidence interval [CI]: 1.05-1.42; HR: 1.22; 95% CI: 1.04-1.43, respectively). Addition of prepubertal BMI slightly attenuated results but associations remained significant.
Conclusions: Exposure to a single-parent environment in early life may be an independent risk factor for earlier breast and pubic hair development. These findings are supported by evolutionary-developmental theories of reproductive development, which posit that early childhood experiences influence pubertal timing.

Breastfeeding Duration, Maternal Race, and Timing of Pubertal Onset in Girls

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Background/Aims: Early puberty is associated with adverse health outcomes throughout the life course. The average age of pubertal onset among girls has declined substantially over the past few decades without clear reasons. We investigated whether breastfeeding duration is associated with earlier pubertal onset in girls, and how the associations differ by race/ethnicity.
Method: Prospective cohort study of 3,331 racially/ethnically diverse girls born at a Kaiser Permanente Northern California (KPNC) facility between 2004-06. All data, including Tanner stage (established pubertal stages) assessed by pediatricians, were obtained from KPNC electronic health records. Proportional hazards model accommodating interval censoring were used in all analyses. Models were adjusted for maternal age, education, race/ethnicity, and parity. We also assessed the role of prepubertal BMI as a confounder. Lastly, we stratified the results by race/ethnicity.
Results: Not breastfeeding was associated with earlier onset of breast (thelarche) and pubic hair (pubarche) development compared to breastfeeding ≥6 months (adjusted hazard ratio [HR]: 1.25; 95% confidence interval [CI]: 1.07-1.46; HR: 1.24; 95% CI: 1.05-1.46, respectively). Inclusion of girl's prepubertal BMI slightly attenuated these associations but they remained significant in thelarche models. Breastfeeding for <6 months was also associated with increased risk of earlier pubarche compared to breastfeeding ≥6 months (HR: 1.14; 95% CI: 1.00-1.30), however this association was lost after accounting for prepubertal BMI. The association between ≥6 months vs. no breastfeeding was stronger among African American girls (HR: 1.92; 95% CI: 1.01-3.66) than other racial/ethnic groups.
Conclusions: Breastfeeding is associated with timing of pubertal onset, independent of childhood obesity, and the strength of the associations may vary by race/ethnicity.

mHealth Mindfulness Intervention for Women with Perinatal Depression: A Pilot Study Within an Integrated Health Care System

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Background/Aims: Prenatal depression is a risk factor of numerous health outcomes, including preterm birth and postnatal depression, both of which can have serious consequences for the health of the offspring. Mindfulness-based interventions have been shown to reduce depressive symptoms in pregnant women, though no previous studies have investigated whether self-paced mobile-delivered mindfulness intervention is effective. We conducted a pilot study to test the feasibility of a mobile health (mHealth)mindfulness intervention using a commercially available mindfulness mobile application for women with perinatal depression.
Methods: Single-arm trial within Kaiser Permanente Northern California (KPNC), a large integrated health delivery system. Participants were identified through KPNC's universal perinatal depression screening program. Inclusion criteria include: PHQ-9 score ≥5, English speaking, <28 weeks gestation or <6 months postpartum, and no regular mindfulness or meditation practice. Participants were asked to follow a self-guided, 6-week mindfulness meditation using a mobile app, Headspace™, for 10-20 min/day. Patient-reported outcomes were obtained before and after the intervention using validated questionnaires.
Results: To date, 23 prenatal and 18 postnatal women completed the study. Women with prenatal depression had significant improvements in depressive symptoms (PHQ8, change in score -4.0, $p<0.01$), perceived stress (-4.3, $p<0.01$) and mindfulness (+2.7, $p<0.01$) comparing before and after the intervention. Women with postnatal depression had significant improvements in depressive symptoms (-4.4, $p<0.01$), perceived stress (-6.6, $p<0.01$), sleep disturbance (-2.4, $p=0.02$), social support (+0.3, $p=0.03$) and mindfulness (+3.0, $p<0.01$). Over half of participants practiced mindfulness at least

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50% of the 6-week mindfulness program using the app (>21 days out of 6 wks.). Qualitative interviews indicate that women appreciate the convenience of the intervention and ability to engage from anywhere without driving to attend classes or arranging childcare.
Conclusions: Our study demonstrates the feasibility and acceptability of an mHealth mindfulness intervention for women with perinatal depression. Efficacy trial is warranted.

Comprehensive evaluation of one carbon metabolism in maternal and cord blood and relationship to fetal and infant growth

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Background/Aims: Maternal nutritional status is associated with fetal epigenetic changes. One carbon metabolism (OCM)-related nutrients, involving the folate and methionine cycle, play an important role in fetal epigenetic modification, We comprehensively measured OCM-related nutrients and metabolites in maternal and umbilical cord blood, and investigated the relationship between maternal and fetal OCM and infantile growth.
Method: In this prospective cohort study, we recruited 434 pregnant Japanese women. Of those, 147 participants were involved in this analysis. Serum concentrations of 18 OCM biomarkers (5-methyltetrahydrofolic acid (5-MTHF), folic acid, choline, betaine, dimethylglycine, methionine, S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), homocysteine, homocysteic acid, cystathionine, cysteine, taurine, serine, glycine, riboflavin, pyridoxine, and pyridoxamine) were measured in maternal serum obtained during the first and third trimesters, and at delivery, and in cord blood serum. Outcomes for fetal and infant size comprised weight, length (height), head circumference and chest circumference at delivery and at 1 month old, respectively.
Results: Homocysteic acid was below the limits of quantitation. Serum concentrations for of the 14 metabolites (except folic acid, homocysteine, and cysteine) in cord blood were significantly higher than those in maternal blood at delivery. Seventeen component metabolites (except taurine) showed significant positive correlations between levels in maternal serum at birth and cord blood serum. In terms of the relationship between OCM-related nutrients and metabolite concentrations in maternal blood serum and birth outcome, taurine in the first trimester correlated positively with weights at birth and at 1 month old.
Conclusions: These data have provided valuable reference values for 18 OCM biomarkers as a foundation for DOHaD research in pregnant Japanese women. Maternal OCM-related nutrients and metabolite concentrations are important predictors of values in fetal blood serum at delivery. If maternal taurine concentration in blood serum affect fetal and infant growth, maintaining optimal taurine status in the first trimester will be important.

Metabolic Adaptation in relation to Cardio-metabolic risk among Indonesian Stunted Children

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Background/Aims: Stunting among under-five children is still highly prevalent in Indonesia. Among others it is reflecting a chronic nutrient deficiency and resulting to metabolic adaptation since fetal life (intra-uterine) through infant's life (extra-uterine).
Method: This study is part of nested-cohort study aims to explore intra- and extra-uterine predispositions in relation to metabolic adaptation indicator, i.e. microRNA-148a, and its cardio-metabolic risk, i.e. waist circumference, lipid profile and fasting blood glucose expression among subjects aged 6-24 months in Bogor, West-Java, Indonesia in July 2018 to February 2018
Results: Among the 38 stunted and 46 non stunted subjects, we found that normalized ratio of microRNA-148a expression was 2.6 times higher among the stunted subjects. This finding shows that the inhibition synthesis of protein receptor of LDL-cholesterol in the liver is faster and resulting to more LDL-cholesterol circulated in the stunted (100.7±30,1 mg/dL) as compared to non-stunted subjects (94.3±23.8 mg/dL), although it is not statistically significant. As cardio-metabolic risk indicators, this study also found that blood triglyceride level was significantly higher among the stunted subjects (p=0,049), i.e. 124.9 (51-510) mg/dL versus 113,1 (48-324 mg/dL) in the non-stunted subjects.
Conclusions: Adaptation metabolic and cardio-metabolic risk among stunted children can be detected as early as 6-24 months of age. Thus, personalized nutrition is highly recommended tailored for stunted children to prevent chronic non-communicable diseases in the future life.
Keywords: cardio-metabolic risk, metabolic adaptation, stunted, Indonesia

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OBEAT – Beating Obesity: A feasibility trial

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Background/Aims: Childhood obesity is a complex disease and may be related to early exposures prior to or around birth. Thus, individuals exposed to chronic stress *in utero* may be programmed to be more susceptible to stress-related disorders like overweight and obesity later in life. This study assesses the feasibility of a stress reducing intervention among pregnant healthy women aimed to improve maternal gestational and post-partum weight and benefit offspring growth and later risk of overweight.
Method: This feasibility study will investigate stressors in pregnant women using focus group interviews. In a subsequent randomised controlled trial (RCT), 120 nullipara women with normal weight pregnancies will be included at their first midwife session. The intervention group will be introduced to a web-based stress reducing and resilience building program. An effect evaluation will analyse changes and correlations in chronic stress in mother and infant (measured by hair cortisol), maternal weight changes, perceived stress, physical activity- and dietary habits, and infant birth length and weight. Since it is a feasibility study, a parallel process evaluation will evaluate recruitment-, attrition-, and compliance- rates using web-statistics, questionnaires on frequency and satisfaction, and focus group interviews with pregnant women and midwives to investigate acceptability of the intervention.
Results: The results of the effect- and process evaluations will, depending on the results of the feasibility study, be implemented in the planning of a large RCT.
Conclusions: This project is expected to improve our understanding of the role of chronic stress during pregnancy in relation to early weight gain and childhood obesity.

Renal effects of gestation and lactation low protein intake on male offsprings

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Background/Aims: Low birthweight (LBW) is associated with a reduction in nephron number, hypertension and chronic kidney disease (CKD) in adulthood. Previously, we demonstrated that low gestational protein diet-induced 28% less nephron number associated with high arterial blood pressure beyond 8th week of age. Here, we aim to investigate the effects of the same diet throughout pregnancy and weaning.
Method: Kidneys were collected at postnatal 16 and 24 weeks from male Wistar rats exposed to a maternal low (LPW: 6%) or standard (NPW: 17%) protein diet from pregnancy to weaning end. The blood pressure was weekly measured. We performed renal stereology analysis in 16 week-old NPW relative to LPW and, in 24 week-old animals; also, we accessed the renal function, immunostaining, and western blotting.
Results: LPW offspring presented LBW, which lasted until the 24th week of life, in parallel with decreased adiposity index. In

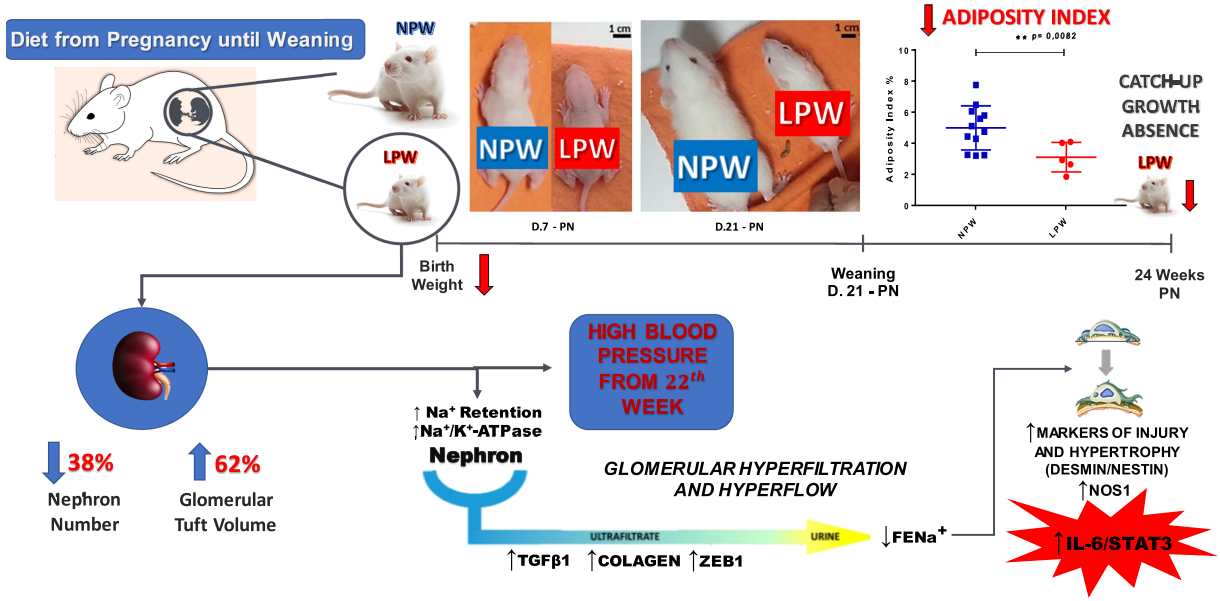

Figure – Graphical abstract of Low Protein Intake on Gestation and Lactation on Offspring Kidneys: Stereology, Hemodynamic and Metabolic Repercussions

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LPW group we found 38% reduced nephron number and 62% increased glomerular volume. Beyond a 20th week, LPW exhibited increased cardiac index and blood pressure. The elevated Na+/K+-ATPase and NOS1 in renal tissue were associated with the proximal tubule retention in LPW compared to NPW offspring. LPW animals presented renal collagen content significantly higher associated with an increased TGFβ1 and ZEB1, and the podocytes presented lesions and hypertrophy markers that may be related to renal inflammatory activity, as well as activation of the IL-6/STAT3 pathway.
Conclusions: In the current study, the LPW offspring exhibited a delayed arterial hypertension development compared to studies involving only gestational protein-restriction accompanied by an accentuated reduction of nephron number and preserved glomerular function. These findings may suggest a glomerular hyperfiltration and hyper flow phenomena with activation of the IL-6/STAT3 pathway, unprecedented in this model, indicating the protective or even attenuating effect of fetal programming when intrauterine environments and extrauterine is early matched.

Can Adult Polygenic Risk Scores for BMI Predict Childhood Obesity?

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Background/Aims: Polygenic risk scores (PRS) provide a simplified model to estimate global genetic contribution to a range of complex phenotypes. Using PRS in early life has potential to unravel early life gene-environment interactions, improve risk stratification and identify key developmental windows for targeted intervention. However, PRS are usually derived from large genome-wide association studies in adults, and studies examining the use of adult PRS for equivalent phenotypes in children are limited. Our aim was to test the predictive utility of common adult-derived PRS in childhood obesity.
Method: We generated PRS for height, weight, BMI and waist circumference based on published genome-wide association studies of large consortia (UK Biobank and GIANT) in a large population-based sample of Australian children and mid-life adults. The predictive capacity of these PRS was examined by linear regression against measured outcomes in mid-life adults and in children over the first 12 years of life.
Results: In mid-life adults, PRS predicted up to 20% of variance in height, and 10% of variance in BMI, weight and waist circumference. In children, the predictive capacity of PRS for height peaked at 6-7 years, predicting up to 18% of variance, while those for BMI, weight and waist circumference steadily increased in predictive capacity during childhood, predicting up to 8%, 6% and 4% of variance, respectively, by 11-12 years.
Conclusions: Adult-derived PRS may be useful to predict obesity-related traits emerging during mid-childhood, with a small loss in predictive accuracy. The increasing predictive capacity of PRS with age may reflect a cumulative interaction of genetic risk variants with key environmental exposures over time in the development of obesity.

Metabolic Profiles of Mental Wellbeing in Childhood and Mid-life

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Background/Aims: Lower mental wellbeing is associated with poorer physical outcomes, including increased cardiovascular disease (CVD) and reduced life expectancy. However, current research in biomarkers of mental wellbeing has focused predominantly on diagnosed mental illness in adults. We aimed to investigate associations of both positive and negative mental wellbeing with a comprehensive panel of metabolites in a population-based sample of children and mid-life adults.
Method: We examined serum Nuclear Magnetic Resonance metabolite profiles of mental wellbeing in a large sample of Australian 11-12 year old children and mid-life adults (mean age 45 years). Exposures included standard self-report scales spanning both negative and positive aspects of mental wellbeing. Linear regression (unadjusted and adjusted for age, sex, SEP and BMI) examined the cross-sectional association of wellbeing with each metabolite (n=70) in children and adults separately.
Results: For both children and adults, in general one SD unit lower in mental wellbeing was associated with 0.1 SD unit higher glycoprotein acetyls (inflammation), VLDL lipids and triglycerides (associated with cardiovascular risk), and 0.1 SD unit lower omega-3, omega-6 and polyunsaturated fatty acids (all suggested to be cardio-protective), in fully adjusted models. No significant associations were seen for LDL or IDL compositions in adults or children, nor for saturated fatty acids or amino acids in adults. Associations for most metabolites were consistent between unadjusted models and adjusting for age, sex and SEP, but were attenuated once adjusted for BMI. Metabolite profiles were consistent for adults across all wellbeing measures, whereas in children patterns of association were more pronounced for positively-framed than for negatively-framed wellbeing measures.
Conclusions: These results provide further evidence for the association between mental wellbeing and CVD in childhood, potentially partially mediated by chronic inflammation. However, small effect sizes largely attenuated by BMI suggest a complex relationship with obesity.

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The 'how to' of program scale up: Researchers reflections of establishing partnerships and systems to support the state wide scale up of the Infant Program

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Background/Aims: Obesity prevention in early life is critical, however few effective interventions have been scaled up and integrated into routine service delivery to achieve population level impact. This paper will report on key lessons learnt in the establishment of systems and partnerships to facilitate the state wide scale up of the Infant Program, a previously trialled efficacious healthy lifestyle program delivered via first time parent groups in the first 18 months of the infants' life.
Method: This is a 5 year implementation research project involving 10 practice and policy partners ensuring reach to vulnerable communities across Victoria, Australia. Researchers are using a detailed reflective journal of all interactions with practice and policy partners over the first year of the project, documenting key issues, challenges and perspectives in the establishment of systems and processes to facilitate program scale up. Thematic qualitative analysis of journal entries will be undertaken.
Results: Initial conversations suggest that equity of program access, alignment with other initiatives to avoid workforce overload and defining program 'success' locally are the primary concerns of stakeholders. Further lessons in the establishment of partnerships and systems to facilitate state wide scale up will be shared alongside recommendations for other researchers embarking on program scale up with practice and policy partners.
Conclusions: This study will provide unique insights into researchers' experiences of working with practice and policy partners to promote scale up and sustained implementation of an efficacious healthy lifestyle program in early life. This addresses an important gap in the literature regarding 'the how to' of program scale up which is critical to promoting the integration of effective interventions into routine policy and practice.

Association of SNPs in *IGF1R* and *IGBPB3* with birth anthropometry and postnatal growth

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Background/Aims: Birth weight and postnatal growth are influenced by genetic and environmental factors, and are important predictors for long term health. Growth alterations have been associated with diverse metabolic diseases. The IGF (Insulin-Like Growth Factor) system plays a key role in fetal and postnatal growth. However, few SNPs in the genes of IGF system have been associated with birth weight and postnatal growth parameters. The aim of this study was to evaluate the association of rs4966035 in the *IGF1R* gene and rs2854744 in the *IGFBP3* gene, with anthropometry at birth and early postnatal growth in the Mexican population.
Methods: We recruited 153 healthy children between 9 and 13 months old, born at term from healthy mothers. Anthropometric data was recorded. SNPs were genotyped from oral mucosal cells genomic DNA using RFLPs.
Results: All measurements were registered as z-score according to WHO tables, adjusted by age and sex. rs4966035 in *IGF1R* was found in H-W equilibrium, genotypic frequencies were GG (28.75%), AG (48.36%) and AA (22.87%). Children with 1or 2 G alleles (AG+GG) had lower birth weight (p=0.03). Accordingly, AG+GG genotypes had higher weight and length at 9-13 months, with higher weight and length gain in early postnatal life (p<0.01 for all). Differences were independent from feeding mode before 6 months (breast-fed, formula or mixed feeding). The rs2854744 variant in *IGFBP3* was not in H-W equilibrium, showing a genotypic frequency of CC (52.94%), AC (31.37%) and AA (15.68%). Birth length was lower (p=0.025), while birth weight showed a non-significant trend to be lower (p=0.056) in AA genotype compared to AC+CC. No differences in weight or length at 9-13 months were found for *IGFBP3* variant. Although % fat mass at 9-13 months was not different between genotypes of either SNP or feeding mode, formula-fed babies with rs4966035 AG+GG genotype had significantly higher fat mass at 9-13 months compared to AA genotype.
Conclusions: Our results suggest that SNPs rs4966035 in *IGF1R* and rs2854744 in *IGFBP3* are associated with fetal rather than postnatal growth in the Mexican population, potentially impacting postnatal growth through interaction with feeding mode. Further studies with larger cohorts in other populations are needed to confirm these associations. Project supported by PRODEP UGTO-PTC-443.

Interplay between Maternal and Cord Vitamin D Status and Vitamin D Receptor Polymorphism in Infant Birth Weight

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Background/Aims: Vitamin D deficiency during pregnancy may result in poor fetal growth and altered neonatal development that may persist into later life. The growth-related effect of

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vitamin D may differ between maternal and cord blood Vitamin D status and genotype. Here we determine the associations of maternal and cord Vitamin D status and genotype on infant birth weight.
Method: We measured plasma 25-hydroxyvitamin D (25OHD) concentrations in 217 maternal and umbilical cord blood by using ultra-high performance liquid chromatography (UHPLC). We determined both maternal and fetal Vitamin D Receptor (VDR) single nucleotide polymorphism (SNP)(rs2228570) by using high resolution melting (HRM). Multiple linear regression, adjusting for gestational age at birth, pre-pregnancy BMI, infant's sex, gravidity and maternal gestational weight gain, was used for statistical analysis.
Results: Mothers with deficient vitamin D (25OHD <30nmoml/L) have infants with birth weights 108.0 (SE43.8) g (p=0.014) higher compared to mothers with sufficient vitamin D (≥ 30nmol/L). This association remained significant after adjusting for cord vitamin D deficiency (p<0.05). No statistically significant association were observed between cord vitamin D status and birth weight. Cord VDR SNP (equivalent to placental VDR SNP) but not maternal VDR SNP was significantly associated with infant birth weight. Nonetheless, maternal VDR SNP modify the association between maternal vitamin D status and birth weight (p-interaction=0.036). Association of maternal vitamin D status and infant birth weight was significant among mothers with the rs2228570 'G' allele but not significant among mothers with homozygous for the 'A" allele.
Conclusions: Our findings suggest that the underlying mechanisms of vitamin D on fetal growth are likely localised in maternal compartment, mediated through placenta, rather than through cellular mechanisms within the fetus.

Depression and anxiety in adolescence and young adulthood: associations with next generation offspring behaviour problems.

Letcher, P[1], Olsson CA[1-3] and the Intergenerational Cohort Consortium

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Background/Aims: Maternal and paternal depression and anxiety have been consistently linked to offspring socio-emotional and behavioural difficulties across childhood. However, parent emotional difficulties rarely emerge for the first time during the perinatal period, and instead usually represent more extensive histories of depression/anxiety beginning before parenthood. The main aim of the present study was to examine the extent to which patterns of depression/anxiety in adolescence and young adulthood predict infant offspring behaviour problems.
Method: Data were drawn from a multi-generational cohort study that has followed Australians from infancy to young adulthood (16 waves) since 1983, and 1145 of their offspring assessed from pregnancy to 1 year of age. Generalised estimating equation (GEE) models were used to estimate associations of parents' preconception depressive and anxiety symptoms in adolescence and young adulthood with offspring behaviour problems at 1 year postpartum. Separate analyses were performed for 679 mother-infant and 466 father-infant dyads, with and without adjustment for relevant preconception confounders and concurrent symptoms of parental depression and anxiety.
Results: Elevated behaviour problems were found in infants born to women with a preconception history of depressive or anxiety symptoms across adolescence and young adulthood compared to those without heightened emotional difficulties over this period. This effect remained after adjustment for confounders and concurrent depressive/anxiety symptoms. No effect was observed for fathers, nor was there evidence of a moderating effect of offspring sex.
Conclusions: A mother's history of persistent depressive/anxiety symptoms from adolescence to young adulthood can predict behaviour problems in her infant offspring decades later. Findings support calls for greater policy and prevention focus on preconception and postnatal mental health, particularly a mother's early emotional health history prior to parenthood.

Impact of Pre- and Post-natal Exposure to Environmental Tobacco Smoke on Astigmatism in Chinese Preschool Children

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Background/Aims: We sought to investigate the association of pre- and post-natal environmental tobacco smoke (ETS) exposure with early-onset astigmatism in Chinese preschool children and to find out the relatively sensitive window of exposure for the risk.
Method: In this population-based cross-sectional study, information concerning pre- and post-natal ETS exposure, visual problems of children and parents, socio-demographics and perinatal characteristics were obtained from parent-reported questionnaires. *Cox* regression analyses were undertaken to yield adjusted prevalence ratios relating to the association

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between combinations of pre- and post-natal ETS exposure and astigmatism.
Results: Of the 29,595 children recruited in the study, 27,890 (94.2%) were included in the analysis. The estimated crude prevalence for astigmatism was 7.2%. Compared to children without exposure to ETS in any stage (including during pregnancy (S1), from born to 1 years (S2) and from 1 to 3 years (S3)), children were more likely to exhibit astigmatism only when they were exposed to ETS in S3, together with exposure in S1 (*PR* (95% CI) =1.35(1.02,1.79)) or S2 (*PR* (95% CI) =1.31(1.08,1.58)) or both S1 and S2 (*PR* (95% CI) =1.27(1.14,1.42)), after adjusting for children's gender and age, parental education level, family monthly income, parental age at childbirth, feeding pattern, birth weight and parental history of astigmatism. In addition, there was a significant dose-response relationship between the incidence of astigmatism and the amount of ETS exposure (P for trend < 0.001).
Conclusions: Among Chinese preschool children, higher amount of pre- and post-natal ETS exposure was associated with higher risk for early-onset astigmatism, and the detrimental effect was accumulating. In particular, it was likely that the early-stage influence might be reversible, given that S3 was indispensable in all of the three subgroups that showed significant effect.

Intrauterine e-vapour exposure caused metabolic and hepatic changes in mice

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Background/Aims: Approximately 15% of pregnant women vape e-cigarettes during pregnancy, exposing the developing foetus to a range of toxic compounds. Nicotine is a developmental toxin, hampering healthy brain and lung growth, promoting behavioural disorders and asthma. Furthermore, several studies have shown that the e-vapour possesses cytotoxic, inflammatory and oxidative properties, especially when heated to 300°C during vaping. However, the safety of other e-vapour components have not been established and as a result, the health impacts to the child are unknown. Therefore, the aim of this study was to understand the impacts of intrauterine e-vapour exposure, with and without nicotine, on liver and metabolic health outcomes.
Methods: E-cigarette vapour was created using a 3rd generation e-cigarette device filled with tobacco flavoured e-liquid containing either 18mg/mL or 0mg/mL of nicotine. Female Balb/c mice were exposed to e-vapour with or without nicotine for 6 weeks before mating, through gestation and lactation. Liver and plasma from 13 weeks old male offspring were examined. Data were analysed by one-way ANOVA with Fisher's LSD *post hoc* analysis.
Results: Maternal e-vapour exposure caused glucose intolerance in the offspring, independent of nicotine. Intrauterine exposure to nicotine containing e-vapour increased hepatic lipid accumulation concomitant with reduced mitochondrial antioxidant levels. Furthermore, maternal exposure to nicotine free e-vapour during pregnancy resulted in increased hepatic inflammatory and oxidative stress markers in the offspring.
Conclusion: E-vapour exposure during pregnancy represents an adverse developmental environment, leading to metabolic disorders and hepatic changes in the offspring.

Chapter 2 Early Pregnancy Risk Factors for Gestational Diabetes in Pre-pregnancy Obese Women

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Background/Aims: Obesity is a strong risk factor for gestational diabetes (GDM). However, the association between metabolic features of obese women in their early pregnancy and their subsequent risk of GDM are not clearly identified. This study aims to explore early pregnancy risk factors for GDM in obese pregnant women.
Method: This is a retrospective nested case-control study. Clinical data from 1119 Chinese obese women with pre-pregnancy BMI≥28kg/m2 who delivered at Beijing Obstetrics and Gynecology Hospital, Capital Medical University, from January 2014 to December 2016, were collected via review of medical record. Logistic regression analysis was used to assess the impact of multiple early-pregnancy metabolic features on the risk of GDM after adjustment for confounding factors. OGTT was performed at gestational week 24-28 for GDM diagnosis.
Results: Among 1119 obese women, 443 (39.59%) developed GDM. Single factor analysis identified a number of metabolic risk factors for GDM, including higher maternal age, BMI, fasting plasma glucose (FPG), TG and LDL/HDL ratio; a history of GDM and delivery of macrosomic baby; lower level of HDL; and gestational weight gain (GWG) before 15-16 weeks and 24-28 weeks of gestation. Multivariate analysis showed that age≥35, pre-pregnancy BMI≥30kg/m2, FPG≥5.1mmol/L and TG≥1.3mmol/L are independent risk factors for GDM, among which FPG had the best predictive power with an AUC of 0.70 (sensitivity 64.7%, specificity 65.7%). The number of existent

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independent risk factors also correlates positively with the risk of GDM. The risk of GDM in women with all four risk factors was 10.20-fold (95%CI: 3.94-26.40) higher compared to that in women without risk factors.
Conclusions: Advanced maternal age, high maternal BMI, and elevated early-pregnancy FPG and TG levels are independent factors for development of GDM. Interventions addressing these risk factors may help reduce the risks of GDM.

Differing risk factors for new onset GDM and recurrent GDM in multipara women: a cohort study

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Background/Aims: To assess whether recurrent gestational diabetes (GDM) and newly diagnosed GDM share similar risk factors and how a history of GDM would affect future GDM risk.
Method: A cohort of 3600 multipara women with singleton pregnancy were recruited between 2017 and 2018 in Beijing, China. Current GDM was diagnosed according to International Association of Diabetes and Pregnancy Study Group (IADPSG) Consensus Panel criteria. Prevalence of GDM and associated risk factors were analyzed between women with and without prior GDM history.
Results: Two hundred and eighty-five (7.9%) multipara women had a diagnosis of GDM during previous pregnancies. The prevalence of GDM was 54.9% (39/71) and 46.3% (99/214) if the women were diagnosed with GDM during previous pregnancies according to the National Diabetes Date Group criteria and IADPSG criteria, as compared to 15.84% (525/3315) if the women were never diagnosed with GDM before. Risk factors associated with recurrent GDM and newly diagnosed GDM are different. In women with a history of GDM, higher pre-pregnancy body mass index (PPBMI), polycystic ovary syndrome, maternal birthweight≥4000g and a history of pregnancy induced hypertension are independent risk factor for recurrent GDM. GDM history combined with these factors increased risk for GDM of up to 78%.
Conclusions: This study found that GDM occurred in approximately 50% of women with a history of GDM. Risk factors for recurrent GDM and newly diagnosed GDM largely do not overlap. Identifying additional factors for GDM recurrence can help guide clinical management for future pregnancies to prevent GDM recurrence.

Ouabain supportment during IUGR decreases the risk of rat hypertension and renal disease by rescuing kidney development through NKA/IP3R-Ca2+signaling pathway

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Background/Aims: Low birth weight due to intrauterine growth restriction (IUGR) is associated with increasing risk of hypertension and end stage renal disease in later life. This is because of IUGR endangers kidney development and results in an irreversible loss of nephrons. High apoptosis is the main reason which result in low nephrons. Ouabain is a highly specific ligand of Na,K-ATPase. In our previous work we found that ouabain could rescue kidney epithelial cells apoptosis under serium deprivation conditon. We hypothesis that ouabain can decrease the risk of rat hypertension and renal disease by rescuing kidney development through rescue cells apoptosis.
Method: 1.To mimic IUGR, pregnant rats were given a low-protein diet and treated with ouabain or vehicle throughout pregnancy. Half embryos' kidneys were collected and nephrons' number was counted. Rat offsprings were followed-up and blood pressure, renal function were measured. 2.Explanted rat embryonic kidneys were serum deprived for 24 h to mimic IUGR. Cells apoptosis were measured and nephrons number were counted.
Results: 1. Serum deprivation resulted in severe retardation of nephron formation and a robust increase in apoptosis. Ouabain decreased cells apoptosis and increased nephrons number. 2.In ouabain treated rats, the embryos' nephrons were increased compare to vehicle treated rats. We followed up the left rat offsprings for 18 months and found that in ouabain treated group, the risk of hypertension and end stage renal disease were decreased compare to vehicle treated group even under high salt diet challenge.3. By using explanted rat embryonic kidneys, we found that ouabain, by triggering a calcium–nuclear factor-κB signal, protected embryonic kidney development from IUGR.
Conclusions: We identified a novel therapeutic method to prevent adverse programming of kidney development.

Ouabain Protects Nephrogenesis Of Rats Exposed To IUGR And Partially Restores The Renal And Cardiac Function In Adulthood Following High-Salt Diet Challenge

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Background/Aims: Augmenting studies have revealed that intrauterine growth restriction (IUGR) is associated with congenital reduction of nephron number, increasing the risk of hypertension, chronic renal dysfunction and cardiovascular diseases in adulthood, especially encountering the challenge of unfavorable environmental factors. We have found that ouabain restores glomeruli reversing the unfavorable consequences of maternal malnutrition. In this study, the long-term outcomes about blood pressure, renal function and cardiac function were clarified especially under high-salt diet condition.
Method: SD rats was employed, and IUGR was induced by maternal malnutrition. Pregnant rats in ouabain group were treated with the same diet as IUGR group, and implanted with mini pump delivering low concentration of ouabain. The male offspring were fed with high-salt diet to mimic unfavorable challenge in adulthood. Birth weight, nephron number, blood pressure, morphology and function of kidney and heart were studied.
Results: We found that: 1) maternal malnutrition significantly decreased the birth weight in IUGR and ouabain groups; 2) ouabain partially restored the nephron number lessened by low protein diet; 3) blood pressure significantly increased in the IUGR offspring, especially under high salt diet challenge, while ouabain normalized the deteriorative blood pressure, even if challenged by immoderate sodium intake; 4) the renal function (including endogenous creatinine clearance and daily urinary protein excretion rate) was impaired in IUGR offspring, while improved by ouabain; 5) the morphological structure of nephron (atrophic or compensatory hypertrophic glomeruli and broken glomerular filtration barrier) were damaged, while reversed in ouabain group; 6) IUGR impaired the cardiac performance and induced myocardial hypertrophy and fibrosis, renovated by ouabain.
Conclusions: Ouabain administration during pregnancy could improve the renal endowment, normalize the blood pressure and prevent renal and cardiac dysfunction from adverse events in adulthood, suggesting that ouabain may be a new alternative to treat kidney dysplasia in IUGR.

Transient hyperthyrotropinemia of prematurity. Prevalence and associated factors. Impact of *z* weight score

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Background/Aims: The transient hyperthyrotropinemia of prematurity (HTTP) is a condition in which TSH is elevated and freeT4, (FT4) normal.
Method: The protocol was accepted by Ethical and Research Committee, 53-18A. Our inclusion criteria was an abnormal TSH and normal free T4 in two consecutive samples at two weeks of postnatal age. We used descriptive analysis. For the inferential statistics, bivariate analysis, t student, U Mann Whitney was used according the distribution. $p \leq 0.05$ was considered significant. *z* score, used paired t student or Wilcoxon. Analysed with Rcmdr 2.4-4 package.
Results: HTTP 2% of the NICU admissions, 2.9% of preterm, rate 1,5 x 1000 NB. The study form 2014 -2018, we analysed the data base from all the preterm with abnormal TSH and normal FT4, we recruited 56 patients, 5 the diagnosis was hypothyroidism and 15 second TSH measure was normal, the final population was 36 preterm, their TSH value 7.2 microUI/mL [l.6(] 5.13-16), FT4 ng/dL 1.2[0.27] (0.59-2.27). Then we compared with 105 preterm without HTTP. Significant difference in days of dopamine administration p= 0.040. Prenatal steroids were a protector factor p=0.001. The male gender had OR 3.03, CI 95% (1.26-7-75), p=0.012, for HTTP. Statistical differences in weight *z* score between not HTTP *vs* HTTP (105/36) at the hospital admission -0.62±0.81(-2.45,1.42) *vs* -1.45±0.96(-3.07,0.56), p=0.001, at discharge -1.6[1.37] (-7.04,1.10) *vs* -1.89[2.25] (-7.76, -0.08), p=0.010. The patients were follow-up until 3 years of age.
Conclusions. Deficit of the Thyroid hormones affect the neurodevelopment, in preterm the screening of thyroid dysfunction at 2 weeks of postnatal age allows the diagnosis and suitable treatment. The HTTP contributes to decrease weight rate at birth and discharge. Male gender is a risk factor for HTTP.

Low-dose aspirin reduces hypoxia-induced sFlt-1 release via the JNK/AP-1 pathway and prevents preeclampsia

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Background/Aims: Placental ischemia/hypoxia and the secretion of soluble fms-like tyrosine kinase-1 (sFlt-1) into maternal circulation are involved in the pathogenesis of preeclampsia. Low-dose aspirin (LDA) has beneficial effects in the prevention of preeclampsia; however, its effects on placental dysfunction and sFlt-1 release have not been well investigated. We aimed to investigate whether LDA has the protective effects against hypoxia-induced cell dysfunction and sFlt-1 release in trophoblast cells.
Method: JEG3 cells were exposed to hypoxia (2% O_2) with or without LDA. Cell function including cell viability, apoptosis, migration and invasion ability were assessed. Expression levels of sFlt-1, PlGF, and the activation of the c-Jun NH2-terminal kinase/activator protein-1 (JNK/AP-1) pathway were also

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determined. Binding of AP-1 components to the promoter of Flt-1 was determined by luciferase reporter assays and verified by applying chromatin immunoprecipitation (ChIP) assay. Effects of LDA were also evaluated with uncomplicated and preeclamptic placental explants.
Results: LDA protected trophoblast cells against apoptosis induced by hypoxia. LDA also ameliorated hypoxia-induced decreased cell migration and invasion ability. Moreover, LDA reduced hypoxia-induced sFlt-1 secretion via JNK/AP-1 pathway. Additionally, LDA could directly decrease the expression of the transcription factor AP-1, and thus decrease Flt-1 transcriptional activity. Finally, effects of LDA on sFlt-1 production were verified in human placental explants.
Conclusions: Our data show the protective effects of LDA against trophoblast cell dysfunction, and reveal that the LDA-mediated inhibition of sFlt-1 via the JNK/AP-1 pathway may be a potential cellular/molecular mechanism for the prevention of preeclampsia.

Risk factors for preeclampsia and its subtypes in a population-based study of China

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Background/Aims: Preeclampsia (PE) is a major cause of adverse maternal and perinatal outcomes, especially in developing countries. Research is scarce regarding the risk factors for preeclampsia and its subtypes within the same population. Therefore, we aimed to estimate the incidence and the associated clinical risk factors of PE and its subtypes in a large multicenter retrospective study of Beijing, China.
Method: A total of 15,003 pregnant women delivered from June 20th to November 30th, 2013 in Beijing were included in the analysis. Risk factors, including maternal age, pre-gestational BMI, parity, history of chronic hypertension, pre-existing diabetes, gestational diabetes mellitus, were involved as study variables. Women with PE were grouped according to clinical manifestations of the time of onset (early-onset PE or late-onset PE) and the severity (mild PE or severe PE). Logistic regressions were used to quantify the association with the above risk factors, and data show as odds risks (OR) and 95% CI. The association between the accumulated number of risk factors and the risk of PE was also performed.
Results: The overall PE rate was 2.6% and the incidence increased sharply with gestation. Early- and late-onset PE rates were 0.4% and 2.3%, respectively. Rates of severe and mild PE were 1.7% and 0.9%, respectively. The following factors were significantly associated with increased risk of PE: higher BMI [(AOR: 1.48) for overweight, and (AOR: 2.15) for obese], nulliparity (AOR: 1.73), multiple gestation (AOR: 4.58), and chronic hypertension (AOR: 34.95). Only chronic hypertension was found to be a significant risk factors for early-onset PE, whereas higher BMI (both overweight and obese), nulliparity, multiple gestation, and chronic hypertension were more strongly associated with late-onset PE. Besides, factors including obese, nulliparity, multiple gestation, and chronic hypertension were associated with both severe and mild PE. In addition, compared with patients without any identified risk factors, the more risk factors the patients exist, the higher risk for developing PE.
Conclusions: Chronic hypertension and multiple gestation were the most important factors for PE. Severe and mild PE shared common risk factors, while early- and late-onset PE differed with several risk factors. In addition, the number of risk factor is associated with the risk of PE. This information is important to guide public health efforts in PE prevention.

Infant body composition predicts childhood obesity

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Background/Aims: Early identification of infants at risk of obesity may allow early intervention to reduce later cardiometabolic risk. While low birth weight is associated with poor health in later life, early body composition (fat mass [FM] and fat-free mass [FFM]) may be a better predictor.
This study aimed to: (1) determine whether infant body composition is a better predictor of childhood obesity than birth weight, (2) determine which infant body composition factors predict childhood obesity and (3) determine what other early life factors predict childhood obesity.
Method: This was an observational follow-up study of 130 children recruited as newborns at the Royal Brisbane and Women's Hospital in 2007-2010. Body composition was measured by air displacement plethysmography using the PEA POD during infancy (at birth, 6 weeks, 3 months and 4.5 months old) and the BOD POD at 8-11 years old. Maternal risk factors (e.g. maternal body mass index [BMI]) and infant feeding information were also recorded. Backward stepwise multiple regression analysis was used to identify significant predictors of childhood obesity.
Results: There was no association between childhood percentage fat (FM/body weight) and either birth weight or birth weight z-score. Increased percentage fat at 6 weeks old was a significant predictor of increased childhood percentage fat as were higher maternal BMI and earlier exposure to formula feeding.
Conclusions: Adiposity at 6 weeks old may identify infants at risk of developing childhood obesity. This may enable timely

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intervention to prevent obesity before it develops. Interventions aimed at reducing maternal BMI prior to pregnancy and facilitating continued breastfeeding may also help reduce the risk of later obesity in children.

Engaging Disadvantaged Parents In An Early Life Prevention Intervention: The Pregnancy And Early Childhood Nutrition Trial (ECAIL)

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Background/Aims: There are great social inequalities in health, starting early in life. The French MALIN Program has been implemented in five pilot sites based on an innovative and sustainable partnership between NGOs and players from the public and private sectors, to promote healthy diet in young children from disadvantaged families. The ECAIL study, aims to test the hypothesis that it has an impact on diet and growth of children in their two first years of life.
Methods: ECAIL is an ongoing randomized controlled trial, implemented since 2017 at the Lille University Hospital (https://clinicaltrials.gov/ct2/show/NCT03003117).
Disadvantaged pregnant women are identified during their prenatal care, then recruited and followed up by dieticians at home, until the child is aged 24 months. Mothers/parents in the intervention arm (objective n=400) are offered the three components of the MALIN Program: 1) nutritional support, including breastfeeding; 2) fresh fruit and vegetable baskets made available at a reduced price from pregnancy; 3) provision of baby food and follow-on formula vouchers from 6 to 24 months. Those in the control arm (objective n=400) receive usual care. Primary and secondary outcomes include various aspects of feeding practices, diet and growth. Data are collected using face-to-face questionnaires and anthropometric measurements.
Preliminary Results (update 25/01/19): 27.8% of the women screened have been deemed eligible, of whom 31.6 % accepted to participate in the trial (n=129). The latter seem to experience a higher social vulnerability than their non-participating counterparts. So far, >98% of the expected visits, questionnaires and anthropometric measurements were implemented and 14 families were lost to follow-up.
Conclusions: The ECAIL trial implementation is so far of good quality, despite the targeted population known to be hard-to-survey. Beyond program effectiveness assessment, this study will increase knowledge on the determinants and mechanisms involved in early behavioural and growth trajectories, in at-risk populations.

Which Modifiable Perinatal Factors Mediate The Relation Between Socioeconomic Position And Child's Early Growth?

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Background/Aims: Postnatal growth in the first months of life is associated with a range of short and long-term health issues, such as childhood overweight. Whereas several studies have shown an inverse association between socioeconomic position and rapid postnatal weight growth, no study has investigated modifiable factors involved in this relation. We aimed to identify mediators of the association between socioeconomic position and early weight growth velocities.
Method: In a sample of 12,817 children from the French ELFE mother-child cohort study, we obtained weight growth velocities from the Jenss model. We investigated whether smoking during pregnancy and breastfeeding duration mediated the inverse association between maternal education and growth velocities at 3 months, using a counterfactual mediation method. Analyses were adjusted for child's sex, mother's age, height, parity and country of birth. The mediation analysis involving breastfeeding duration was further adjusted for birthweight z-score and stratified by smoking status during pregnancy. We used a bootstrap approach with 5,000 replications to obtain robust 95% confidence intervals.
Results: In children from low vs. intermediate-educated mothers, smoking during pregnancy mediated about 40% of the association with weight growth velocities at 3 months. The percentage of mediation was lower (15%) in children from high vs. intermediate-educated mothers. Breastfeeding duration mediated the association between maternal education and weight growth velocities for all categories of maternal education (i.e. low vs. intermediate or high vs. intermediate education) and whatever the smoking group, with a percentage varying from 30% to 50%.
Conclusions: Smoking during pregnancy and shorter breastfeeding duration are for a great part responsible of increased weight growth velocity in infants from less educated women compared to others. Targeting these modifiable risk factors could help to prevent the social patterning of early child growth, and thereby attenuate the socioeconomic inequalities in overweight and cardiometabolic health.

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Effect of changing lifestyle in early pregnancy on outcome of high-risk pregnant women with gestational diabetes mellitus

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Background/Aims: Gestational diabetes mellitus (GDM) is a common and special complication during pregnancy, which can cause many adverse effects on pregnant women and fetuses. Pre-pregnancy obesity/overweight and weight gain during pregnancy have been identified as independent risk factors for GDM with macrosomia. This study aims to manage the lifestyle of high-risk pregnant women with GDM in the first trimester of pregnancy (before 14 weeks gestation), and to explore its effects on pregnancy outcome of pregnant women with GDM.
Method: Total 171 pregnant women with high risk of GDM, who underwent prenatal examination and delivery in Second Affiliated Hospital of Nantong University from March 2015 to March 2016, were randomly divided into study group (n=82) and control group (n=89). The study group accepted the standardized management of diet and exercise, while the control group received routine birth examination. The incidence of pregnancy complications and pregnancy outcome were compared between these two groups.
Results: (1) The incidence of amniotic fluid hypertrophy and GDM in the study group was significantly lower than that in the control group (all $P<0.05$). (2) The rate of cesarean section and postpartum hemorrhage in the study group was significantly lower than that in the control group (all $P<0.05$). (3) The incidence of hyperbilirubinemia and macrosomia in the study group was significantly lower than that in the control group (all $P<0.05$). (4) The incidence of postpartum abnormal glucose metabolism and neonatal obesity in the study group was lower than that in the control group, but the difference was not statistically significant (all $P>0.05$).
Conclusions: Diet and exercise intervention in early pregnancy can reduce the incidence of GDM, cesarean section, postpartum hemorrhage, and fetal distress. It has positive significance in preventing adverse pregnancy outcomes such as macrosomia and neonatal hyperbilirubinemia.

Inter-Relationships between Body Mass Index, Inflammation and Retinal Microvasculature

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Background/Aims: Obesity adversely affects microvascular health from early childhood onwards and inflammation is a suggested mechanism. We aimed to examine whether the association between body mass index (BMI) and retinal microvascular parameters is mediated by inflammation and whether this relationship differs for retinal arterioles and venules in late childhood and midlife.
Method: *Design/Participants:* 1054 children (age 11-12 years, 52% female) and 1147 parents (mean age 44 years, 87% female) in the cross-sectional population-based Child Health CheckPoint study. *Exposures:* BMI (z-scores for children). *Outcomes:* Retinal arteriolar and venular calibre quantified from retinal photographs. *Mediator:* Glycoprotein acetyls (GlycA), an inflammatory marker. *Analyses:* Causal mediation analyses based on natural effects adjusting age, sex and family socioeconomic status.
Results: BMI has a small effect on retinal arteriolar calibre. Per SD unit higher BMI led to narrower arteriolar calibre in both children (-0.13 SD units, 95% CI -0.08 to -0.07) and adults (-0.16 SD, -0.21 to -0.10). Direct effects not mediated via GlycA were similar to the total effects, indicating little mediation in this case. BMI also had a small effect on wider venular calibre for children (0.03 SD, -0.04 to 0.09) and adults (0.02 SD, -0.04 to 0.07), which was mediated through GlycA for children (0.04 SD, 0.01 to 0.06) and adults (0.04 SD, -0.02 to 0.07). Direct effects not via GlycA suggest that inflammatory pathways may be counteracted by other pathways acting in the opposite direction for children (-0.01 SD (-0.08 to 0.06) and adults -0.02 SD (-0.01 to 0.05) respectively.
Conclusions: Higher BMI has small adverse effects on retinal arterioles and venules in both childhood and midlife. The effect of BMI on retinal venules was partly mediated through inflammation, even at 11-12 years of age, whereas for retinal arterioles, non-inflammatory pathways may be more important. The findings may inform pathways for intervention.

The Perturbation of Infant Gut Microbiota Caused by Caesarean Delivery Is Partially Restored by Exclusive Breastfeeding

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Background/Aims: Early establishment of infant gut microbiome is attributed to various environmental factors that may influence long-term health. The aim of this study was to determine single and combined impacts of the delivery mode, feeding pattern and postnatal antibiotic exposure on the initial establishment of infant gut microbiome.

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Method: A cross-sectional study was conducted at a single centre in China. Fecal samples were collected from 120 infants at six weeks postpartum. The 16S rRNA gene were analysed by Illumina sequencing, and clinical information was obtained from medical records and questionnaire survey.
Results: Compared with vaginally delivered infants, the gut microbial community structure of caesarean delivered infants was significantly changed(P=0.044), in parallel with the decreased relative abundance of *Bifidobacterium*(P=0.028), which was against to the normal gut microbial establishment. Regarding the vaginally delivered and exclusively breastfed (VB) infants as a reference, both within- and between-group UniFrac distance between VB and caesarean delivered and exclusively breastfed (CB) infants were significantly smaller than between VB and caesarean delivered and mixed-fed (CM) infants (P<0.001, P<0.001). LEfSe analysis showed that the relative abundances of *Enterococcus*, *Veillonella* and *Faecalibacterium* were significantly different between CB and CM infants, whereas the relative abundances of those genera in VB infants were close to CB infants and distinct from CM infants. Additionally, no significant difference of microbial composition, alpha diversity, or community structure was observed between postnatal antibiotics exposed and unexposed infants.
Conclusions: Delivery mode had a significant impact on infant gut microbial, which leaded a gut microbial perturbation in caesarean delivered infants,and this microbial perturbation was partially restored by exclusive breastfeeding in comparison with mixed feeding.

The Validation of Sterile Intrauterine Environment with Amniocentesis at Second Trimester

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Background/Aims: Recent studies based on culture-independent sequencing techniques have challenged the "sterile womb" paradigm, however, those evidences were extremely weak, given the possibility of unavoidable environmental contamination during whole experimental process. Therefore, we aimed at investigating microbiome in amniotic fluid (AF) at second trimester through amniocentesis, in parallel with negative and positive controls.
Method: This prospective study recruited four healthy pregnancies with prenatal diagnosis indication. After amniocentesis, the residual whole AFs and relevant supernatants were collected. Meanwhile, four negative controls, including sterile saline solution from operating room (n=2) and DNA buffer from laboratory (n=2), and four positive controls, including one adult stool specimen, two vaginal swabs and one artificial bacterial mixture, were selected simultaneously. The digital droplet polymerase chain reaction (PCR) and 16S rRNA Illumina sequencing were performed to detect the 16S rRNA gene copies and taxonomic composition.
Results: The 16S rRNA gene copies of AFs (372 (100-632) copies/mL) were similar to negative controls (177 (141-316) copies/mL, P=0.28), but significantly lower than that of positive controls (4935 (2979-11815) copies/mL, P<0.01). The number of sequence reads in AFs (3 (0-44)) were comparable to negative controls (5 (3-9), P=0.54), but significantly lower than that in positive controls (12840 (1150-441862), P<0.01). No operational taxonomic units (OTU) was found in AFs or negative controls. For positive controls, the OTU number and microbial composition varied depending on sample type. In artificial mixture, the composition and relative abundances were identified as expected.
Conclusions: With different negative and positive controls during whole experimental process, our study provides evidence to the "sterile womb" paradigm in healthy pregnancy at second trimester.

PPARγ Activation Does Not Affect Surfactant Maturation in the Fetal Lung

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Background/Aims: Maturation of the fetal lung is under control of a multitude of factors that prepares the fetus to survive the transition from the aqueous *in utero* environment (placental oxygenation) to pulmonary ventilation *ex utero*. To adopt this change, type II alveolar epithelial cells (AECs) produce pulmonary surfactant to help reduce the surface tension at the air-liquid interface, thus preventing alveolar collapse. Peroxisome proliferator-activated receptor γ (PPARγ) is an important factor for the activation of pulmonary lipofibroblasts to produce leptin, which binds to type II AECs and stimulates surfactant production. In this study, we examined the effect of intrafetal administration of PPARγ agonist, rosiglitazone (RGZ), on surfactant maturation in the fetal lung.
Methods: Four osmotic mini pumps containing vehicle (n=8, 15% ethanol) or RGZ (n=7, 4.28mg/fetus/day) were implanted subcutaneously into fetuses at 123-126 d gestation (term= 150

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± 3d). Fetal lung tissue was collected on gestational day 138-142 for molecular analyses. The effect of RGZ administration on surfactant production was determined using a Student's unpaired t test. $P < 0.05$ was considered statistically significant.
Results: There was no significant difference in the mRNA expression of *PPARγ*, *PPARα*, surfactant proteins (*SFTP-A, -B, -C and -D*), rate limiting enzyme in surfactant phospholipid synthesis (*PCYT1A*), phospholipid transportation (*ABCA3*) or the PPARγ target genes (*PAI-1, PGC1a, RXRa*) between the vehicle and RGZ group. There was a reduction in mRNA expression of *LPCAT* (surfactant synthesis) and *LAMP3* (marker for lamellar bodies) and an increase in *SPHK1* (PPARγ target gene) expression in RGZ group. These results indicate a decreased capacity for surfactant production, despite increased PPARγ activity in other tissues[1]. However, there was no difference in mRNA expression of the majority of genes involved in surfactant production between the RGZ and vehicle group.
Conclusion: In this study, we found RGZ administration had little effect on surfactant maturation in the fetal lung.
Reference Muhlhausler, B. S., Morrison, J. L. & McMillen, I. C. (2009). Rosiglitazone Increases the Expression of Peroxisome Proliferator-Activated Receptor-γ Target Genes in Adipose Tissue, Liver, and Skeletal Muscle in the Sheep Fetus in Late Gestation. *Endocrinology*, 150(9), pp.4287-4294.

Social determinants of health, maternal diabetes, and associations with neonatal adiposity and anthropometrics in the PANDORA study

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Background/Aims: Indigenous women experience high rates of type 2 diabetes (T2DM) in pregnancy, in the context of disadvantage and poverty. This study aims to evaluate the association of social determinants of health with neonatal anthropometric outcomes in Indigenous and Europid women with hyperglycaemia in pregnancy.
Method: Participants were women with hyperglycaemia in pregnancy (n=644), including Indigenous (n=404) and Europid (n=240) women and their offspring from PANDORA, a prospective longitudinal birth cohort, drawn from a population based registry. The associations of ethnicity, individual social determinants (education, employment, income, home tenure) and area socioeconomic measures (Socioeconomic Index for Areas - SEIFA), with neonatal birthweight z-score, percentage body fat, sum of skin folds and head circumference, were assessed with linear regression. Models were adjusted for maternal diabetes, body mass index, parity, and gestational age.
Results: Indigenous ethnicity was associated with sum of skinfolds (beta coefficient 1.95mm (95%CI 1.35,2.55) p<0.001) and birthweight z-score (0.36 (0.14,0.59) p=0.002) after adjusting for maternal age. Education (< 11 years) (1.13mm (0.31, 1.95) p=0.007), unemployment (1.07mm (0.46,1.69) p=0.001), income from welfare payments (1.00mm (0.38-1.62) p=0.001) and renting or other housing tenure (0.93mm (0.15-1.38) p=0.02) were associated with sum of skinfolds. Education was associated with birthweight z-score (0.37 (0.76-0.67) p=0.01). SEIFA decile was associated with head circumference (0.05cm (0.01, 0.09 p=0.009) and sum of skinfolds (-0.17mm (-0.26,-0.08) p<0.001). Individual social determinants were not associated with percentage body fat (p>0.05) or head circumference. Multivariate analysis showed that Indigenous ethnicity remained independently associated with sum of skinfolds, whereas individual and area social factors were not associated with the outcomes.
Conclusions: Social determinants of health, measured in our study, were not strongly associated with neonatal outcomes in this high risk cohort of women with hyperglycaemia in pregnancy.

Use of fluoxetine during pregnancy and lactation: behavioral and structural hippocampus repercussions in male rat offspring

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Background/Aims: Depression is a common mental disorder associated with the gestational period; affects the well-being of the mother and the unborn child and, have been associated with attention deficit, behavioral and psychiatric diseases in offspring. It has been recommended the treatment of depression often necessary during all pregnancy and immediate postpartum; take into account the use of drug therapy, meanly with selective serotonin reuptake inhibitors antidepressants. In the current study was analyzed the effects of fluoxetine use during pregnancy and lactation on behavior and hippocampal development in rat offspring compared with untreated control.
Method: Pregnant Wistar-HanUnib rats were divided into two groups: (1) the F group treated with fluoxetine (10 mg/kg/day) and, (2) the control group (C) receiving a saline solution. Both experimental groups with 42 days of age were submitted to behavior specific rodents tests to assay spatial learning and memory, general locomotor activity, anxiety, and willingness to explore. Also, the offspring brain and hippocampus were collected to Immunohistochemistry, and isotropic fractionate technique, respectively.
Results: The results of present study showed a state of fear-like accompanied to higher activity (by Open Field Test) and lower learning (evaluated by the Morris Water-Maze test) in the

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fluoxetine offspring; also, the study did not demonstrate significant anxiety-like behavior in F offspring, by elevated plus maze test. Additionally, immunofluorescence showed a significantly enhanced stem cells number in dentate gyros and enhanced hippocampal neuron number in fluoxetine-treated offspring compared to the control group.
Conclusions: The present study demonstrated an intimate relationship between the use of fluoxetine, a high number of stem and neurons hippocampal cells and, behavioral alterations related to retention memory (learning), fear-like and animal hyperactivity.

Predicting crying and behavioural outcomes from the microbiota of infants with colic

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Background/Aims: Infant colic is a condition of unknown cause that is associated with maternal depression and poorer behavioural outcomes in early childhood. The gut microbiota is presumed to be relevant as different microorganisms are observed in infants with colic, and probiotics have demonstrated efficacy in reducing crying time. We aimed to investigate whether the microbiota composition in infants with colic is associated with parent-reported crying time at baseline, 4-week follow-up and child behaviour at 2 years of age.
Method: Faecal samples from infants with colic (n=118) were analysed using 16S rRNA sequencing. After examining the alpha and beta diversity of the clinical samples, we performed a differential abundance analysis of the 16S data to look for taxa associated with baseline and future behavioural outcomes, while adjusting for potential confounding variables. In addition, we used a machine learning cross-validation scheme to evaluate how well baseline gut microbiota can predict future crying time.
Results: Alpha diversity of the faecal microbiota was strongly influenced by birth mode, feed type and child gender but did not significantly associate with crying or behavioural outcomes. Differential abundance analyses show several OTUs that associated with baseline crying time, persistent crying at 4-week follow-up and risk of any behavioural problems at 2 years of age. Further, by training a random forest model on the baseline sample, we show that the infant microbiota can predict 4-week crying outcomes with significantly better-than-chance accuracy.
Conclusions: Aspects of the infant faecal microbiota may be predictive of subsequent behaviour. Machine learning approaches can be used to extend evaluate predictive relationships between the microbiome and behavioural outcomes.

Neither a Dietary and Lifestyle Intervention in Pregnancy, nor Maternal Pre-Pregnancy BMI, are Associated With Differential Methylation in Newborn Cord Blood: Findings from The LIMIT RCT

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Background/Aims: Maternal obesity is associated with higher infant birthweight and adiposity, and increased risk of child obesity. Epigenetic mechanisms have been proposed as a potential causal pathway between maternal and child obesity, with several studies finding differences in DNA methylation (DNAm) in newborn cord blood associated with maternal obesity. However these findings have not been confirmed by large, robust studies; moreover it is not known whether these putative epigenetic mechanisms might be influenced by interventions in pregnancy.
Methods: We measured genome-wide methylation in 645 samples of newborn cord blood from participants in the LIMIT RCT, a randomised controlled trial of a dietary and lifestyle intervention in pregnancy for women with BMI $\geq$25.0kg/m^2. We looked for differences in DNAm between the Lifestyle Advice and Standard Care groups, as well as for evidence of effect modification by maternal BMI, and for differences in DNAm by degree of maternal overweight/obesity. We also attempted to replicate the results of other studies which had found differential methylation associated with maternal BMI and/or dietary and lifestyle interventions in pregnancy.
Results: No differential methylation was found in the cord blood of infants in the Lifestyle Advice group compared to that of infants in the Standard Care group. Similarly, there was no evidence of effect modification by maternal pre-pregnancy BMI. Moreover, in contrast to previously published findings, we also found no evidence of differential methylation by degree of maternal overweight/ obesity, and did not confirm any previous findings of differential methylation in specific loci according to maternal BMI or receipt of a dietary and lifestyle intervention in pregnancy.
Conclusions: Epigenetic mechanisms are a potential causal link between maternal and child obesity and are worth further study. However, the inability to find evidence of differences in DNAm in this large cohort, using robust analytic methods, demonstrates the need to move beyond a discovery/hypothesis-generating approach and instead emphasise the reproducibility of findings.

Young Health Champions: Hearing the Adolescent Voice for Promoting Health and Wellbeing through Peer Mentoring

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Background/Aims: Adolescence is an opportunity to change lifecourse health trajectories, for adolescents now, as future adults and also for their future children. We aimed to engage adolescents with skills to make changes to their lifestyles through small group training and peer mentoring, thereby becoming agents of change for health in their communities. LifeLab partnered with Southampton City Council to deliver the Royal Society for Public Health's Young Health Champions (YHC) qualification to train a cohort of adolescents to act as role models and champions for health in their communities.
Method: Knowing the challenges faced providing additional experiences, outside of the curriculum, this partnership enables schools to provide a health qualification for students without extra burden on teachers. The LifeLab education programme supports the curriculum of the YHC qualification. Training is carried out at LifeLab and includes activities encompassing; healthy eating, physical activity, smoking, alcohol and emotional health and wellbeing. This opportunity was offered to all schools across the South Coast of England who are participating in the LifeLab programme.
Results: In the 2018-19 academic year, 29 students are completing the qualification. All students commented that interactive activities were the most interesting and enjoyable ways of learning. Almost all (92%) of the participating students felt the training would give them skills to be Health Champions in school and felt confident to deliver health campaigns for their peers. 92% agreed/strongly agreed it gave them skills to be a YHC in school.
Conclusions: YHC empowers adolescents to take the lead on health and wellbeing. Sustainability requires buy-in from school senior leaders, and one school has already written YHC into their school improvement plan. In addition to engaging with more schools/students we plan a partnership with the local premiership football club and links with the Scout Association.

Association between inflammation and retinal vascular calibre: a meta-analysis

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Background/Aims: Non-invasive imaging of retinal vasculature allows investigation of the microvasculature. In adults, adverse retinal vascular calibre (smaller arterioles, larger venules) have been consistently associated with cardiovascular disease, but the underlying mechanisms are unclear. We aimed to investigate the relationship between inflammation and retinal vascular calibre.
Method: We identified studies in Medline, Embase and Pubmed using MESH-terms and keywords for the following topics 1) retinal microvascular calibre, 2) inflammatory markers, and 3) observational studies. Studies with general population samples and patients with disease conditions were included. We performed a narrative review of all studies with inflammatory biomarkers (ie, C-reactive protein (CRP), white blood cell count (WBC), interleukin-6 and fibrinogen). Study-specific correlation estimates of CRP and WBC were combined in meta-analyses where sufficient data were available.
Results: Of 1,920 studies identified, 23 met inclusion criteria (general population 17, patients 6). Most were cross-sectional data on mid-life adults (43 to 68 years), with three childhood studies. Of 10 studies (general population 5, patients 5), pooled results of meta-analysis showed weak evidence of an association between CRP and retinal arteriolar calibre (r =0.02, 95%CI 0.00 to 0.03) in the general population and no evidence for patient group (r =0.03, -0.13 to 0.08). The association with venular calibre was stronger, with magnitude of 0.10 ($p<0.001$) in both population groups. WBC data was only available in the adult general population. Pooled results showed evidence of an association of WBC with both arterial and venular calibre, with stronger evidence for venular calibre (r =0.20, 95%CI 0.04 to 0.36). Narrative review of other biomarkers showed consistent findings, and there were mixed results for children.
Conclusions: The association between inflammation and with retinal venular calibre may indicate that inflammation may be a mechanism linking microvasculature phenotypes and cardiovascular health. Longitudinal studies with repeated measurements will help define the mechanisms, opportunities for intervention and the clinical implications of retinal vascular phenotypes across the life course.

Body mass index throughout childhood and cardiometabolic health at 11-12 years: A population-based longitudinal study

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Background/Aims: Little is known about when and how early life body mass index (BMI) impacts childhood preclinical cardiometabolic phenotypes. We examined how (1) overweight/obesity at specific ages and (2) overall BMI growth patterns throughout childhood predict cardiometabolic phenotypes at 11-12 years.
Method: In a population-based sample of 5107 infants (the *Longitudinal Study of Australian Children*) BMI was measured every two years between ages 2-3 and 10-11 years. We identified five BMI trajectories using growth curve models. At age 11-12 years, 1811 children completed assessments for metabolic syndrome (MetS) risk scores ((a) including and (b) excluding concurrent BMI), arterial pulse wave velocity (PWV), and carotid artery intima-media thickness (IMT). Multivariable regression models estimated associations of cardiometabolic outcomes with earlier weight status and BMI trajectories, adjusted for potential confounders (e.g. age, sex, smoking exposure, and small for gestational age).
Results: Overweight/obesity from 2-3 onwards were strongly associated with higher MetS risk score *including* BMI at 11-12 years. At age 2-3 years, compared to normal weight, children with overweight had a higher MetS risk score *including* BMI by 0.29 SD units (95% 0.14 to 0.44) and with obesity by 0.61 (0.42 to 0.80). By age 10-11 years, these associations strengthened to 1.05 SD units (0.90 to 1.20) and 1.78 (1.57 to 1.99) respectively. Associations from age 6-7 years for MetS risk score *excluding* BMI remained, although attenuated by 20-40%. From 6-7 years obese (but not overweight) children had higher outcome PWV (0.64-0.73 SD units). At all ages, obese (but not overweight) children had slightly higher outcome carotid IMT (0.20-0.30 SD units). Cumulative exposure to high BMI carried the greatest cardiometabolic risk, with a gradient of risk across trajectories.
Conclusions: High BMI from as young as age 2-3 years of age is already silently associated with the development of cardiometabolic risk by 11-12 years. This highlights the need for effective action to reduce overweight/obesity early in the life course.

Maternal and Offspring Exposure to Perfluorooctane Sulfonate (PFOS) is associated with Maternal Hyperglycaemia and Adverse Neonatal and Childhood Outcomes

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Background/Aims: Perfluorooctane sulfonate (PFOS) belongs to a class of endocrine-disrupting chemicals known as perfluoroalkyl chemicals (PFCs) implicated in adiposity. Although supposedly phased out since 2002, its use remains widespread in Asia. We aim to examine the relationship between exposure to PFOS and long-term metabolic outcomes in the offspring.
Method: We measured blood PFOS and other PFCs in archived samples taken at 24-32weeks gestation from mothers in the Hong Kong centre of the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study between 2002-2004. All mothers underwent 75g OGTT and GDM was diagnosed according to the IADPSG/WHO 2013 criteria. Pregnancy outcomes, neonatal anthropometrics and childhood outcomes at 7 years were documented (Tam WH et al, Diabetes Care 2017). PFCs were measured using high performance LC-MS-MS. We completed analysis of PFCs in 1,601 maternal samples, a subset of 99 cord blood samples, and samples from 970 offspring at 7 years follow-up.
Results: There is strong correlation among PFOS and other PFCs in cord blood (ρ=0.51-0.74, $p<0.001$), as well as correlation with maternal levels (ρ=0.60, $p<0.001$). Ratio of cord blood to maternal PFOS was 0.60. Using regression analysis with adjustment for maternal age, BMI, and offspring gender, maternal PFOS showed suggestive association with maternal glucose parameters during pregnancy. Log-transformed maternal PFOS was associated with higher birthweight, lower birth length, higher ponderal index and lower neonatal sum of skin fold thickness (beta -0.337 ± 0.085, $p=7.1 \times 10^{-5}$), after adjustment for all covariates. Maternal PFOS during pregnancy was not associated with offspring glycaemic parameters or indices of beta-cell function. Log-transformed offspring PFOS levels and deciles of PFOS were associated with reduced renal function in the offspring.
Conclusions: Maternal and offspring PFOS levels were associated with adverse pregnancy outcome and offspring cardiometabolic profile. Exposure to PFOS may be an important contributing factor to the epidemic of hyperglycaemia in pregnancy and childhood metabolic disorders in Asia. (Supported by Health and Medical Research Fund (Ref. 13140761))

NIH Efforts to Advance Research Focused on Early Life Factors and Cancer Development

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Background/Aims: Most cancer research in human populations has focused on a range of exposures in the middle to later years of the lifespan. While this narrow age range yields the highest number of cancer cases, it is a phase of life in which

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cancer prevention efforts are more difficult and perhaps less effective. The emerging evidence that early life factors affect cancer development later in life call for a refocusing of efforts targeting the early life spectrum of modifiable exposures. This paradigm shift in cancer research has the potential to translate into substantial gains in cancer prevention and control.
Method: Review of NIH extramural grant portfolio, scientific initiatives, and funding opportunities relevant to research focused on early life factors and cancer development.
Results: NIH has made substantial efforts to advance research focused on early life factors and cancer development in humans and outcomes that are relevant to cancer risk, particularly breast cancer. However, much more research efforts are needed to investigate relationships with other cancer types as well.
Conclusions: Advancement of cancer research efforts focused on early life factors and the links to cancer have been slow due to methodological issues related to human study designs and research resources to account for long latency periods between exposure and cancer onset. Innovative study designs and the leveraging of existing resources can be utilized to expand research efforts on early life factors and cancer risk.

Genetic variation and intrauterine growth predict blood *LEP* methylation at birth and in infancy

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Background/Aims: Leptin is a hormone that regulates satiety and energy homeostasis throughout life. It also plays a key role in placentation and maternal–fetal exchange in pregnancy. Early life metabolic and pregnancy exposures have been reported to influence *LEP* epigenetic variation in placenta and cord blood, but previous studies have been small and have not considered the influence of underlying *LEP* genetic variation. Here, we investigated the relationship between maternal health in pregnancy, infant anthropometry, and *LEP* genetic variation with *LEP* promoter methylation at birth and at 12 months of age. We hypothesised that adverse pregnancy exposures would influence *LEP* epigenetic variation, thereby influencing early growth of offspring.
Method: *LEP* promoter methylation was measured in cord (n=877) and 12-month blood (n=761) in the Barwon Infant Study, a population-based pre-birth cohort. Cross-sectional and longitudinal regression was used to determine if maternal factors or infant anthropometry predict offspring *LEP* methylation.
Results: Pre-eclampsia was negatively associated with cord blood methylation at a single CpG site (-6.06%, p=0.01). Infant sex and genotype were associated with average methylation across the region (-2.07% in cord blood in males compared to females, p<0.001). Genotype most strongly associated with methylation at a single CpG site, also negatively associated with birth weight adjusted for age and sex (r=-0.10, p=0.003). Triceps/subscapular skinfold thickness at birth was associated with 12-month *LEP* methylation and interacted with *LEP* genotype.
Conclusions: These findings are consistent with anthropometry driving altered *LEP* epigenetic profile and expression in infancy. Further work is required to determine the long-term impact of altered *LEP* promoter methylation on offspring development and health.

Association between hyperglycaemia in pregnancy and growth trajectories of children in the Northern Territory, Australia: the PANDORA study

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Background/Aims: The incidence of type 2 diabetes (T2D) is up to 20 times higher in Aboriginal than non-Aboriginal Australian children, and also much higher in Aboriginal pregnant women, with increasing concern regarding intergenerational risk. This study explored the impact of hyperglycaemia in pregnancy on growth trajectories of offspring.
Method: The PANDORA study is a longitudinal birth cohort (1139 mother-child pairs) recruited from a hyperglycaemia in pregnancy register in the Northern Territory of Australia. Weight and height of all children were obtained from primary care health records at multiple time points from birth to 5 years of age. Mixed modelling was used to explore growth trajectories.
Results: Children born to mothers with T2D or gestational diabetes mellitus (GDM) had greater birthweight Z score (Table 1) and shorter birth length. Similar postnatal growth trajectories were seen in Aboriginal and non-Aboriginal children for weight, height and body mass index (BMI), though Aboriginal children were smaller in all measures. Compared to children of normoglycaemic mothers (Table 1), children

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	Aboriginal mothers		
	T2D	GDM	Normoglycaemia
Birthweight Z score	1.0 (0.7, 1.4)**	0.24 (0.1, 0.7)*	–0.04 (–2.4, 3.6)
Child weight at 7 months (kg)	7.7 (7.5, 7.9)**	8.2 (8.1, 8.3)*	8.5 (8.3, 8.8)
Child weight at 3 years (kg)	13.6 (13.3, 13.9)**	13.8 (13.6, 14.1)**	13.1 (12.7, 13.6)
Child BMI at 3 years (kg/m^2)	15.9 (15.3, 16.5)	15.6 (15.3, 16.0)	15.1 (14.4, 15.8)

*Data are mean (95% CI) **p value <0.01 *p value <0.05 when compared to normoglycaemia

born to Aboriginal mothers with GDM or T2D had lower weight in the first year (peak difference at 7 months), and higher weight thereafter (peak difference at 3 years). In contrast, children of Aboriginal mothers with T2D or GDM had a similar height trajectory to children of normoglycaemic mothers from the second year of life, despite smaller height from birth to 12 months.

Conclusions: Despite higher birthweights, Aboriginal children born to hyperglycaemic mothers had lower weight than children of normoglycaemic mothers until 12 months of age, but displayed higher weight thereafter. Exploration of associations between in-utero hyperglycaemia exposure and growth trajectories into later childhood, and the impact of catch up growth on metabolic risk, is required.

Growth restriction reduces islet insulin concentration but not glucose stimulated insulin secretion in rats: no effect of early life exercise

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Background/Aims: Intrauterine growth restriction (IUGR) is associated with reduced pancreatic β-cell mass, contributing to impaired glucose tolerance and diabetes. Short-term exercise training (4 weeks) early in life in rats born small restored β-cell mass in adulthood[1]. We have now repeated this study and examined whether isolated islet insulin secretion is reduced after fetal growth restriction and whether early life exercise overcomes this.

Method: Uteroplacental insufficiency was induced in Wistar-Kyoto rats by the bilateral uterine vessel ligation on day 18 of pregnancy resulted in IUGR offspring compared with sham-operated Controls. Males offspring either exercised from 5-9 weeks or were sedentary (n=7-8). At 25 weeks old, animals were killed, and pancreatic islets were isolated from the acinar tissue. In vitro insulin secretion in response to 2.8 mM glucose or 20 mM glucose and content were detected by radioimmunoassay. Insulin analysis was performed using GraphPadPrism 8.02 with one-way ANOVA applied.

Results: Insulin (ng) secretion when islets where stimulated in a higher glucose dose were statistics not different in control (0.29 ± 0.11) and restricted groups, sedentary (0.11 ± 0.07) and treadmill (0.19 ± 0.05). Insulin content (ng) was higher in control group than in the restricted groups ($p<0.05$) and early exercise had no effect on controls and IUGR offspring.

Conclusions: Growth restriction reduced isolated islet insulin concentration but did not reduce glucose-stimulated insulin secretion in adulthood. Early life exercise did not affect either insulin concentration or insulin secretion in adulthood. Taken with our initial study findings, it appears that growth restriction reduces β-cell mass and insulin concentration in islets but not ex vivo glucose stimulated insulin secretion.

Reference 1 Laker RC et al. *Am J Physiol Endocrinol Metab* 301: E931–E940, 2011.

Health and Socio-Demographic Predictors of Treatment Modality Choice for Gestational Diabetes in a Multi-Ethnic Sample: Evidence from the Born in Bradford Cohort Study

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Background/Aims: Gestational diabetes mellitus (GDM) treatment consists of lifestyle interventions, followed by pharmacotherapy if hyperglycaemia persists. Previous research has highlighted differences in maternal factors between lifestyle modifications and pharmacotherapy treatment groups. Few studies however included patients treated with metformin, in a UK clinical setting. This study aimed to identify differences in maternal characteristics by treatment courses for GDM, using a UK-based population.

Method: Maternal records from Born in Bradford cohort participants receiving treatment for GDM during their singleton pregnancies were studied (N=727). Treatment groups consisted of lifestyle modifications (diet and/or exercise), pharmacotherapy (insulin and/or metformin) and combined treatment (lifestyle modifications and pharmacotherapy). Health and socio-demographic differences between treatment groups were evaluated using Pearson's χ^2 and Fisher's tests for categorical variables and Kruskal-Wallis test for continuous variables.

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Multinomial logistic regression examined the relationships between maternal characteristics and treatment groups.
Results: 196 women were treated with lifestyle modifications, 322 with pharmacotherapy and 209 with combined treatment. Mothers receiving lifestyle modifications and combined therapy were younger than mothers receiving pharmacotherapy. 57.4% of women treated with pharmacotherapy were obese compared to 17.7% and 24.9% of women in lifestyle modifications and combined therapy groups, respectively. Higher fasting glucose levels at diagnosis increased the risk of pharmacotherapy treatment (RRR 2.1 (1.5-2.9)) and combined treatment (RRR 1.9 (1.3-2.6)) compared to lifestyle modifications. Multiparous women were more likely to be treated with combined therapy than lifestyle modifications (RRR 0.3 (0.1-0.7)).
Conclusions: Women with GDM who were older, multiparous and with a less healthy clinical profile (higher obesity rates and glucose levels) were more likely to receive pharmaceutical or combined treatments.

Treatment with cholinergic antagonist during lactation attenuates obesity in adult male rats

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Background: Obesity has become, over time, a worldwide public health problem. The DOHaD concept, through clinical and preclinical studies, suggests a strong association between environmental damages occurred in the fetal or perinatal life and the emergence of chronic diseases in adult life. The Central Nervous System is easily affected at critical stages of development, such as in lactation. Hyperinsulinemia in early life has been associated with an obese phenotype in adult life. In opposition, hypoinsulinemia in the perinatal phase is related to a lean phenotype. Cholinergic terminals activity into pancreatic beta-cell has been associated to those phenotype-early low-insulin levels. Therefore, our aim was to investigate whether the short-term treatment with a buscopan, could prevent obesity.
Methods: After birth, male Wistar rats received intraperitoneal injection of scopolamine butylbromide, 0.5 mg/Kg body weight (bw)/day during the first 12 days of lactation (Treated Group; T) or saline 0.9% (Control Group; C). At 60-days-old, the offspring from both group consumed normal fat diet (NF) or high fat diet (HF:35% of fat) by next thirty days. At 90-days-old body weight, food intake, fat tissue accumulation, glucose tolerance, insulin tissue sensitivity and fasting glucose and insulin blood levels were evaluated. The lean phenotype was observed in rats of treated group.
Results: T group presented lower body weight than C group until 60-days-old (11%, p<0,0001) associated to a lower food intake (5%, p<0,05). At 90-days-old, T-HF group showed low body weight (14%, p< 0,0001) compared to C-HF. The T-HL animals presented increased fasting glycemia and insulinemia 23% (p<0,05) and 60% (p<0,001) lower than the C-HF group, respectively. The T-HF group had greater insulin sensitivity by the HOMA index, compared to C-HF control. T groups presented lower fat tissue accretion (T-NF 30%; T-HF 14%; respectively, p< 0, 05) compared to C-NF and C-HF respectively. During intraperitoneal glucose tolerant test, the T-HF animals presented lower glucose levels than C-HL animals (p< 0,01).
Conclusions: Therefore, we conclude that treatment with a cholinergic antagonist, which allows low insulin levels during lactation protects the animals against metabolic dysfunction and obesity onset later in life; at least in part this resistance can be attributed to improvement of insulin action and secretion.

Dopaminergic System Imbalance At Adolescence Programs To Metabolic Alterations At Adulthood In Male Rats

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Background/Aims: Methylphenidate is a psychostimulant used in the treatment of Attention Deficit Hyperactivity Disorder that inhibits the reuptake of dopamine mainly in the striatal nucleus and prefrontal cortex. Adolescence, as well as pregnancy and lactation, is considered a sensitive period of development, since neural connections, including dopaminergic system, are still being formed in the brain. Therefore, stressful insults in this phase can permanently modulate the development of systems, programming metabolic diseases and behavioral changes in adult life. We evaluated the effect of Methylphenidate treatment during adolescence on biometrical parameters, glucose metabolism and anxiety of offspring adult male rats.
Method: From weaning, Wistar male rats received Methylphenidate (Ritalin) by gavage (Rit; 1 mg/kg/day) for 30 days, whereas control rats received saline (Sal; NaCl 0.9%) in the same volume. From 51 to 110 days-old both groups were untreated. At 51 and 110 days-old the metabolic and behavioural experiments were performed.
Results: During treatment, Rit reduced 12% of food intake (P<0.01), however there was no difference in body weight. At 51 days-old fat tissue stores were equal between groups

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and fasting insulinemia was decreased in 50% (P<0.05). Glucose tolerance and insulin sensitivity showed no differences between groups. Rit animals presented ansiogenic-like effect (P<0.05) as demonstrated by inhibitory avoidance in the elevated T-maze. After treatment, Rit group showed an increase of 23% in body weight (P<0.01). Fat tissue stores were increased by 20% (P<0.05) in treated animals. ivGTT showed higher glucose levels in Rit group at 15 (P<0.05), 30 (P<0.05) and 45 minutes (P<0.01) and Rit animals are insulin resistant, as demonstrated in Kitt (P<0.05). At 110 days-old there were no difference between groups in elevated T-maze test.
Conclusions: Dopaminergic imbalance at adolescence programs male rats to overweight and metabolic alterations; however, no behavioral changes at adulthood was observed.

Moderate Exercise And Fasting Does Not Present A Synergic Effect To Improve Metabolic Dysfunctions In Adult Male Rat Offspring Programmed To Obesity By Early Overnutrition

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Background/Aims: Early postnatal overfeeding leads to metabolic programming. Adult male rat offspring overfed during lactation present overweight, hyperphagia, hyperinsulinemia, high accumulation of white adipose tissue, peripheral insulin resistance and hyperactivity of the parasympathetic nervous system. Exercise and fasting are alternatives used to prevent and treat these alterations, as they increase energy expenditure and reduce caloric intake, respectively. We combined early exercise and fasting and evaluated the effect on biometrical and biochemical parameters of adult offspring rats programmed by overfeeding in early life.
Method: Male Wistar litters were adjusted to 3 pups on postnatal-day-3 (PN3). At PN21, rats were assigned into 4 groups: SL (small litter); SL-F (small litter-fasting); SL-EX (small litter-exercise); SL-FEX (small litter-fasting exercise). The exercise protocol started at PN30, with training sessions performed until PN90, 3 times per week at 55-65% of the final workload achieved in effort test. The fasting protocol also started at PN30, lasting for 8 hours of daytime before training sessions for SL-FEX group and 3 times per week for SL-F group. At PN90 metabolic and biometric data were assessed.
Results: At PN90, fasting (SL-F) promoted a reduction in AUC of body weight (8%, P<0.05), retroperitoneal fat pad (12%, P<0.05) and an improvement in glucose intolerance (-11%, P<0.05) compared to SL group. Exercised animals (SL-EX) presented decrease in AUC body weight (14%, P<0.0001), final body weight (13%, P<0.001) and fat pads store (33%, P<0.0001). SL-EX also showed improve in glucose intolerance (-10%, P<0.05), decrease in brown adipose tissue weight (31%, P<0.0001) and increase in gastrocnemius muscle weight (9%, P<0.0001). SL-FEX group showed reduction in muscle weight compared to SL-EX animals (P<0.01), while no differences were observed in other parameters between these groups.
Conclusions: Fasting does not potentiate exercise-caused metabolic improvement in adult male rat offspring programmed by overfeeding during lactation.

Maternal intake of an AGE precursor during lactation leads to offspring early in life dysfunction of glycaemic homeostasis

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Background/Aims: Increased levels of Advanced glycation end products (AGE) are related to metabolic alterations associated to diabetes, such as β-cell dysfunction and insulin resistance. Lactation is an important period for the neonatal development of organs and tissues, including pancreas. We hypothesized that maternal consumption of an AGE precursor during lactation leads neonatal offspring to glycaemic homeostasis dysfunction.
Method: Wistar pregnant rats were maintained in standard conditions until birth. All animals had free access to standard chow and water. Delivery was considered day 0, in day 1 rats litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups: Control (CO), whose mothers received saline 0,9% by gavage (1mL/kg), and Methylglyoxal (MG), treated daily by gavage with methylglyoxal (60mg/kg). Treatment starts at day 1 after birth and halt at the end of lactation. Offspring's were euthanized at 7, 14 and 21 days old for blood sample collections. Also a glucose tolerance test (GTT) was performed at day 21.
Results: MG offspring presented decreased insulin levels at 14 (p<0.01) and 21 days-old (p<0.0001), followed by increased glucose levels only at day 21 (p<0.05). No difference was observed in the AUC analysis of the GTT. However; it was observed an increased glycemia at the test time points 0' and 15'.
Conclusions: Maternal intake of an AGE precursor during lactation impairs offspring glycemic homeostasis early in life. Therefore, we suggest that this progressive deterioration of glycemic control may predispose the litters to the development of diabetes later in life.

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Maternal intake of an AGE precursor during lactation leads offspring to cardiac hypertrophy and fibrosis early in life.

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Background/Aims: Lactation is an important phase for infant development, and disturbances occurred during this period may increase the risk for cardio metabolic diseases later in life. The consumption of Advanced Glycation End products (AGE) is related to oxidative stress, inflammation and increased risk for cardiovascular disease. Methylglyoxal (MG), an important AGE precursor, may be involved in the development of diabetic cardiac myopathy. Therefore, we hypothesized that maternal intake of an AGE precursor during lactation may predispose the offspring to the development of cardiac disturbance early in life.

Method: Wistar pregnant rats were maintained in standard conditions until birth. All animals had free access to standard chow and water. Delivery was considered day 0, in day 1 rats litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups: Control (CO), whose mothers received saline 0,9% by gavage (1mL/kg), and Methylglyoxal (MG), treated daily by gavage with methylglyoxal (60mg/kg). Treatment starts at day 1 after birth and halt at the end of lactation. Offspring's were euthanized at weaning (day 21). Heart samples were collected for histological analysis.

Results: MG pups shows increased heart interstitial fibrosis ($p<0,01$), accompanied by increased cardio myocyte diameter ($p<0,05$). No difference is observed in perivascular fibrosis or heart weight.

Conclusions: Maternal intake of an AGE precursor during lactation leads neonatal offspring to cardiac remodelling, with increased tissue fibrosis and cardio myocyte hypertrophy. Therefore, we suggest that these neonatal alterations may be an important predictor, increasing the risk of cardiomyopathy later in life.

Neonatal methylglioxal exposure leads wistar rats offspring to inflammation, oxidative stress and metabolic dysfunctions at adulthood

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Background/Aims: Increased levels of Advanced Glycation End-products (AGEs) in the organism is associated with hyperglycemia, which is due to AGE-induced cell dysfunction. AGEs are formed from by-products of glucose metabolism, of which Methylglyoxal (MG) is the most reactive. During evolution, the organisms developed important system of detoxification of MG, the Glioxalases System. Inflammation and oxidative stress reduce the Glutathion Reductase (GSH) levels with impair the redox cellular system, increasing even more the endogenous levels of MG. Therefore, our aim was to study the effects of chronic administration of an AGE precursor, MG, on the metabolism and pancreatic islet function of the offspring treated with MG during the two first weeks of lactation.

Method: After birth, the offspring Wistar rats were divided into 3 groups: Control Group (CON) treated with saline injection (0.9% Kg of BW/day), Methylglyoxal 6mg Group (MG – 6mg), treated with Methylglyoxal (6mg/Kg of BW/day) and Methylglyoxal 20mg Group (MG – 20mg), treated with Methylglyoxal (20mg/Kg of BW/day) during the first 15 days of the lactation period. Each groups had 20 animals. Adult offspring rats (90-days-old) were analyzed. Was performed ivGTT following euthanasia for tissue collection. Blood and tissues samples were used for analyses of biometric and biochemistry parameters, such as lipid profile, oxidative stress and inflammation.

Results: Both MG groups show decrease in BW at 90 days-old, and in main fat pads. The liver of MG groups was lighter that CON group and shows low HDL and high LDL. The MG groups show insulin resistance in both concentration and both ages. At 90 days-old, the MG groups show increase in inflammation by Myeloperoxidase analysis and oxidative stress. All data were analyzed for ANOVA one-way with significance for $p<0,05$.

Conclusions: The neonatal treatment with Methylglyoxal in 6 and 20 mg/kg BW/day programs adult offspring rats to develop metabolic dysfunctions including significant inflammation and oxidative stress.

The impact of adolescent social well-being and mental health on future parenting behaviour

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Background/Aims: Research into parenting behaviours is increasingly considering how preconception factors can influence parenting, but very few studies have long term data to adequately assess this. Using data from the Dunedin Multidisciplinary Health and Development Study cohort, we were able to develop a comprehensive model of the relationship between childhood disadvantage, adolescents' social well-being and mental health, and their subsequent parenting behaviour.
Method: The Dunedin cohort were born in 1972/3 in New Zealand and followed up frequently during childhood, adolescence and young adulthood: assessments are ongoing. Parenting data was collected once members of the original cohort had a three year old child of their own (approximately 14 to 39 years after their age 3 assessment, depending on the age at which they became parents). Previous work on this sample has used structural equation modelling to create latent variables including a childhood measure of disadvantage, and an adolescent measure of well-being. This work uses these preconception variables as well as a measure of adolescent anxiety/depression, to predict parenting behaviour
Results: There were significant paths from childhood disadvantage to later parenting. There were also significant paths from adolescent well-being to later parenting, but not from adolescent mental health to later parenting.
Conclusions: These findings are important in that the models illustrate the importance of interventions to offset childhood disadvantage and also the potential role of adolescent well-being as a protective factor, not just among teens and the adults they become, but also among their children.

Renoprotective Effects of Brief Angiotensin-Converting Enzyme Inhibition Early in Life in Sheep Born with a Solitary Functioning Kidney

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Background/Aims: Children born with a solitary functioning kidney (SFK) develop renal injury in early adulthood. Renal hypertrophy is a characteristic compensatory response to a renal mass reduction but an inappropriate level of renal hypertrophy may increase predisposition to renal injury in SFK. It is also unknown whether pharmaceutical intervention early in life can prevent onset of renal injury. The aim of this study was to examine if treatment with angiotensin-converting enzyme inhibitor (ACEi) early in life in sheep born with a SFK altered compensatory renal hypertrophy and onset of renal injury.
Method: SFK was induced by unilateral nephrectomy in the male sheep fetus at 100 days gestation (term=150 days; n=25). Sham surgery was performed in other male fetuses (n=12). At 4 weeks of age, lambs from the SFK group were randomly assigned to undergo ACEi via administration of Enalapril (n=10; 0.5mg/kg/day, once daily, orally) until 8 weeks of age. The remaining animals received vehicle (water). At 8 weeks, renal volume and renal arterial blood flow were assessed using magnetic resonance imaging. At 8 months urine albumin levels were examined as an index of renal injury.
Results: Body weight at birth, 4 and 8 weeks of age were not different between the groups. ACEi markedly increased plasma renin activity over the 4-week treatment period. At 8 weeks of age, kidney volume relative to body weight was ~18% lower in the SFK compared with sham (P=0.001). ACEi reduced renal volume by ~15% compared with vehicle treatment in the SFK (P=0.04). Total renal blood flow was 2 fold higher in sham animals compared with SFK and ACEi had no effect on renal blood flow in SFK. Preliminary analysis (n=4/group) revealed that sheep with SFK had greater urine albumin excretion than that of sham (P=0.04). ACEi in SFK lowered urine albumin excretion by ~48%.
Conclusions: Brief and early ACEi in sheep born with a SFK reduced compensatory renal hypertrophy but did not affect renal blood flow. Preliminary evidence suggests ACEi reduced the degree of renal injury (albuminuria) in SFK.

A National Study Of Parent Knowledge, Behaviours And Barriers In Relation To Healthy Food Choices For Their Children

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Background/Aims: Poor nutrition and excessive weight gain in childhood impact on immediate and long term physical and mental health. Each day parents are tasked with making decisions about what food and drinks their children consume. This study aimed to investigate parent knowledge of and barriers to healthy food choices, and explore patterns of food consumption among children. We examined parent knowledge of Australian Dietary Guidelines for daily fruit and vegetable consumption and knowledge about food and drinks containing added sugars.

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Methods: A nationwide cross-sectional survey of 1,980 Australian parents of children aged 0-17 years was conducted online in 2017. Parents were asked a series of questions to investigate their level of knowledge of and barriers to healthy food choices. Parents also provided information on each of their children's level of consumption of fruit and vegetables and sugary foods and drinks.
Results: A sample of 1,980 parents yielded data on a total of 3,704 children. The majority of parents (57%) reported finding it difficult to know what constitutes healthy food and over half (53%) found it hard to understand nutritional labels. Two thirds found it hard to know how much added sugar was in products and only 25% knew recommendations regarding vegetable consumption for children. Only 12% of children met the recommendations for daily vegetable consumption, with the leading barrier to consumption being child food preference. A third (37%) of children consumed treat foods and one in five (21%) consumed sugary drinks most days of the week. Levels of knowledge about healthy food choices were lower among sole parents and those without tertiary education. Daily intake of fruit and vegetables was notably lower in older children as compared with infants, toddlers and preschoolers.
Conclusion: This study highlights key barriers to healthy food choices for children, including poor parent knowledge of Dietary Guidelines, low levels of parent nutritional literacy and unhealthy child food preferences. In addressing rising rates of childhood obesity, policy initiatives should include better education and support for children and their parents in making healthy food choices, including consideration of the role of clearer food labelling and marketing.

Are Australian government curriculum and health and wellbeing policies supporting implementation of obesity prevention initiatives for adolescents in high schools?

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Background/Aims: School based obesity prevention initiatives underpinned by the World Health Organisation (WHO) Health Promoting Schools (HPS) framework have been shown to have positive impacts upon adolescent health behaviours and outcomes. Yet little is known about how high schools are supported through relevant government policy to implement initiatives based upon the HPS framework to improve adolescent health and wellbeing (HWB) outcomes. This study describes the results of an analysis of the extent to which Australian government curriculum and HWB policies are supporting high schools to improve adolescent health and risk of overweight and obesity using the HPS framework.
Method: Yanow's interpretive policy analysis approach was employed to conduct a policy document analysis. Six curriculum and HWB documents from Victoria, Australia were included using theoretical and purposive sampling. Documents were analysed for references to the HPS approach using content and thematic analysis.
Results: Two main frames of interpretation were identified: (1) Policies showed commitment to HWB yet (2) references to the HPS framework were hidden to an 'untrained' or inexperienced eye. An overarching commitment to HWB was underpinned by HPS however no explicit references to HPS were identified. Two references to 'whole of school' approaches were identified across the policy set.
Conclusions: Government policies in Victoria, Australia currently provide little support or guidance for implementation of the HPS framework in high schools to prevent adolescent obesity. These results may inform future efforts to better connect the HPS framework with school-based policies.

Policymakers' perspectives and considerations on designing school based obesity prevention initiatives aimed at adolescents

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Background/Aims: Schools provide an important setting for adolescents to develop health behaviours related to nutrition and exercise. The Achievement Program was launched by the state government of Victoria, Australia in 2012 as a voluntary policy for implementation in schools to address increasing rates of overweight and obesity in children and adolescents. It was arguably the biggest investment in the state's history into obesity prevention in adolescents and was based upon the World Health Organisation (WHO) Health Promoting Schools (HPS) framework. This study aimed to explore the political considerations informing design of the Achievement Program policy for high schools and adolescents at risk of overweight and obesity.
Method: Interpretive policy analysis was undertaken using semi-structured interviews with a purposive sample of policymakers representing government and non-government agencies. Interviews explored factors influencing program design and were analysed thematically to examine interpretations of the importance and role of HPS initiatives and policies in obesity prevention in high schools.
Results: Ten in-depth interviews including 11 participants were conducted. The analysis revealed the Achievement Program was designed through (i) the establishment of strategic collaborations and good governance, involving people that made

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valuable and diverse contributions while acknowledging their (ii) positions of power, (iii) ensuring careful attention was paid to an evidence informed program design, and (iv) incorporation of real-time feedback from other settings implementing the Achievement
Conclusions: Policymakers highlighted the importance of published and local evidence to inform policy development for obesity prevention in adolescents. Policymakers believed this approach to policy development would increase policy adoption and adhesion. There is a need to explore adoption of the Achievement Program and the impacts on adolescent health outcomes.

Implementing health promoting schools to prevent obesity in secondary schools: A case study of success factors.

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Introduction: Adolescence is recognised as a key life stage for the development of healthy lifestyle behaviours to prevent overweight and obesity. School based prevention interventions based upon the World Health Organisation Health Promoting School (HPS) framework have shown improvements on health and wellbeing for school aged children, however there is little evidence related to implementation and translation to practice in secondary schools. This study sought to explore why and how secondary schools were implementing the HPS framework and factors contributing to success.
Methods: A single case study informed by Yanow's interpretive policy analysis approach was conducted in one regional Victorian secondary school. The school had implemented the *Achievement Program* as the recognised voluntary state based HPS policy. Data collection included semi-structured interviews (n=2), document retrieval (n=9) and collation, drawings and ethnographic observations (n=6). Data was analysed using framework analysis.
Results: The school had elected to implement the voluntary policy as it aligned with the school's existing health and wellbeing policy framework and importance placed on student health and wellbeing outcomes. The policy provided a flexible yet evidence based framework to guide a whole of school approach to health and wellbeing. Success was dependent upon selecting easier health priority areas to address initially, allocation of a designated team to guide policy implementation and access to a skilled health promotion worker employed in the local community health service.
Conclusion: Implementation and translation of HPS into practice can be successful in Victorian secondary schools. Further research in other secondary schools is warranted to increase transferability of these findings and explore impacts and outcomes of the HPS framework on obesity prevention.

The combination of home and clinic blood pressure and the risk of low birthweight

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Background/Aims: High blood pressure (BP) during pregnancy has been associated with higher risks of lower infant birthweight, and home BP has shown a stronger association with birthweight than clinic BP. Here, we examined the association between birthweight and the combination of home and clinic BP.
Method: The present reports are parts of the BOSHI study. The Institutional and Hospital Review Boards approved all study protocols. Home and clinic BP were measured using a semiautomatic device. The combination of home and clinic BP measurements were classified into four groups (both BP optimal, home BP optimal, clinic BP optimal, and both BP not optimal). The incidence of low birthweight was set as the outcome. Multivariate logistic regression analyses were performed after adjustment for age, height, BMI before pregnancy, smoking and drinking habits, and family history of hypertension.
Results: In total, 766 subjects were analyzed. Home BP optimal and clinic BP optimal groups showed relatively higher risks of low birthweight babies than the both BP optimal group, although these differences were not statistically significant [OR:1.5(95% CI:0.7-3.3), 2.7(95%CI:0.3-23.3), respectively]. The both BP not optimal group showed a significantly higher risk of low baby birthweight than the both BP optimal group [OR:5.6; 95%CI:2.0-15.8].
Conclusions: After adjusting for possible confounding factors, the women in the both home and clinic BP not optimal group showed a significantly higher risk of low baby birthweight than the women in the both BP optimal group. The whitecoat hypertension and masked hypertension thresholds in pregnant women might be lower than those of the general population.

Influence of the use of antidepressant, and illegal drugs during pregnancy on the neurological development of Mexican children

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Background/Aims: The presence of depression in pregnancy affects neurodevelopment. Also, it is known that psychotropic drugs used in the treatment of depression as well as illegal drugs disturb the neurodevelopment of the fetus. The use of antidepressants during the first trimester of pregnancy increases the risk of presenting functional and structural alterations in the brain of the product and interrupts the normal maturation of the serotoninergic system. The impact of these drugs on the neurological development of exposed Mexican children is unknown.
Method: A cross-sectional descriptive study was conducted in 15 children whose mother self-reported the consumption of antidepressants during pregnancy, ten who consumed illegal psychoactive substances and ten control (non-consumers). For the evaluation of depression and anxiety traits, the Edinburg perinatal depression scale and trait-state anxiety inventory was used. For the evaluation of cognitive deterioration, the Mini-Mental state examination was used. The Bayley 3 child development assessment scale was applied to all children in the first month of age.
Results: Forty percent of pregnant patients who consumed antidepressants and 50% of those who consumed illegal psychoactive substances showed features of depression. 20% of women with depression medication and 60% of those who abused illegal drugs were suspected of cognitive impairment. Pearson's correlation test identified a negative correlation between pregnant patients with features of depression, anxiety-state, and suspected cognitive decline and a delay in motor development of their children. Cognitive and motor delay was shown in 100% of children whose mothers used antidepressants and presented suspected cognitive impairment, and in 83.3% of children whose mothers used illegal drugs with suspected cognitive impairment.
Conclusions: The consumption of illegal and antidepressants drugs during pregnancy delayed the motor and cognitive development of Mexican children.
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Understandings of Japanese midwives on malnutrition in gestation period and DOHaD

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Background/Aims: Many Japanese young women are undernourished because they are eager to be skinny. Reflecting this fact, low-birth-weight babies have been increasing rapidly in Japan caused by their mother's malnutrition. Since the dietary knowledge on the requirement of pregnant women are supported mainly by midwives, this study was carried out to clarify how much midwives have the knowledge of nutrient intakes in the gestation period, and also how much Japanese midwives understand DOHaD.
Method: Four experienced midwives, who are working in the different hospitals for more than 10 years, were subjects in this study. They were interviewed and had questionnaires following Gage[1] and Oyamada[2] method. Data was analyzed by qualitative descriptive study.
Results: Though the subjects agreed that, "dietary habits of pregnant women influence the health of fetus and also the health of the adulthood", the subjects didn't understand DOHaD. Only one of the subjects has ever heard the word of DOHaD. All the subjects thought it a problem that the mothers who delivered the low-birth-weight babies increased the frequency of feeding in order to make their babies grow bigger, and it was all they understood from their experiences. It was clarified that the subjects could not support the pregnant women sufficiently on the dietary habits because they didn't have the confidence due to their lack of knowledge that the dietary habits of gestation period influenced the health of fetus and the health of the adulthood.
Conclusions: The understanding of midwives on DOHaD was very low, at the same level of the students in the division of nutrition. It was suggested in this study that midwives should be educated in nutrient intake requirements so that they could support the pregnant women more effectively in the gestation period.
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The effect of maternal high fat diet on offspring muscle regeneration

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Background/Aims: Skeletal muscle fibres are post-mitotic cells. As such, they exclusively rely on regenerative processes to restore muscle structure and function when damage has occurred through trauma or everyday tasks. Skeletal muscle quality therefore mostly relies on its development during the pre-natal period. Foetal muscle development is a highly plastic process that is influenced by the intrauterine environment. Maternal behaviour, such as diet or exercise, can alter this

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environment. Using a high fat maternal diet model, we assessed whether maternal diet hindered offspring muscle regeneration after injury, and whether post-natal diet could reverse these effects.

Method: C57Bl/6 female mice were fed a chow or high fat diet (45% of energy from fat) for 8 weeks prior to mating until the ending of the suckling period. The offspring were either maintained on their original maternal diet or switched to the other diet (chow or high fat). At 12 weeks of age, their tibialis anterior muscle was injured with a myotoxin. After 7 days of regeneration, muscle histology and markers of muscle regeneration were assessed.

Results: Adiposity levels were higher in C57Bl/6 female mice consuming a high fat diet. There was no difference in offspring weight born to lean or obese dams at weaning; however, in adulthood, offspring born to obese dams were smaller than their control counterparts regardless of post-natal diet. Markers of muscle regeneration including *Pax7*, *MyoG, Myf5 and Mrf4* were downregulated in male offspring born to an obese mother or fed a high-fat diet when compared to offspring experiencing normal growth. This was however not observed in females.

Conclusions: An obesogenic maternal diet negatively affects offspring muscle growth and markers of muscle regeneration in a sex-specific manner. These effects could not be offset by offspring diet, highlighting the importance of the pre-natal environment in muscle development and function.

Maternal *FUT2* genotype, human milk oligosaccharides and infant gut microbiota

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Background/Aims: The rs601338 single nucleotide polymorphism in the fucosyltransferase 2 (*FUT2*) gene determines secretor status and strongly influences the synthesis of human milk oligosaccharides (HMOs), which could impact the gut microbiota of breastfed infants. Most human milk studies dichotomize secretor status based on the presence of *FUT2*-dependent HMOs, rather than genetics. We examined associations between maternal *FUT2* genotypes, HMO profiles and infant microbiota.

Method: Among 487 Caucasian mothers from the CHILD cohort, rs601338 genotype was determined and the 19 most abundant HMOs were analysed in milk samples collected at 3-4 months postpartum. Infant fecal microbiota was profiled at 1 year by 16S rRNA sequencing; alpha diversity indices (Chao1 richness and Fisher diversity) were derived. Analyses were stratified on breastfeeding status at 1 year.

Results: Overall, 26% of mothers were homozygous for the *FUT2* non-secretor allele (AA), 29% were homozygous secretors (GG), and 45% were heterozygotes (AG). Infant gut microbiota richness and diversity were lowest among infants of heterozygous mothers (mean [SD] Chao1 index was 50.3 [20.7], 51.1 [19.6], and 46.3 [18.7] among infants of AA non-secretors, GG secretors, and GA heterozygotes, respectively, $p<0.05$). In stratified analyses, these associations were only observed among infants who were breastfed at the time of microbiota analysis. Moreover, concentrations of the HMO 6-sialyllactose (6'SL) were lowest in milk from heterozygous mothers, and this HMO was positively associated with infant gut microbiota richness and diversity at 1 year of age.

Conclusions: Our findings suggest that maternal *FUT2* genotype (specifically, heterozygosity at the rs601338 locus) influences the HMO profile of mothers' milk and thereby may impact the gut microbiota of breastfed infants. Further research from the CHILD cohort will examine the mediating role of specific HMOs on gut microbiota taxa, and assess the impact on infant health trajectories.

Tobacco smoke exposure during pregnancy and early childhood and child anthropometric outcomes at school age: the Hokkaido Study

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Background/Aims: Maternal smoking during pregnancy has reported to be associated with childhood overweight and obesity and also correlated with maternal postnatal smoking. We investigated the association of maternal smoking during pregnancy and postnatal period and child anthropometric outcomes at school age.

Method: 229 children in the prospective birth cohort study attended follow up anthropometric measurements at school age from Octorber 2017 to January 2019 were included in this study. Height, weight, body fat, skinfold thickness, and blood pressure were measured, and BMI and obesity index were calculated. Maternal smoking at the 1st trimester of pregnancy was self-reported. Maternal smoking status was asked when children were at 1, 2, and 4 years of age using questionnaires. We categorized children into 4 groups based on maternal smoking status; never, smoking only postnatally, smoking only during pregnancy, and smoking postnatally and during pregnancy. Linear regression models adjusted for maternal prepregnancy BMI, annual income, maternal alcohol intake during pregnancy, birth weight child sex and age at anthropometric measurement were used for the statistical analysis.

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Results: Birth weight was lower in maternal smoking during pregnancy and postnatally group compared to the other groups. Maternal smoking during pregnancy and postnatally was positively associated with obesity index (β=8.98; 95% CI:-0.43, 18.38), BMI (β=1.71; 95% CI:-0.03, 3.45), body fat (β=5.67; 95% CI:0.15, 11.19), and the sum of skinfold thickness (β=7.9; 95% CI:-1.1, 17.0) of children at school age. However, maternal smoking only postnatally was not significantly associated with children's anthropometric outcomes. Blood pressure was not associated with maternal smoking status at any period.
Conclusions: The findings from this study suggest that tobacco smoke exposure during pregnancy was related to lower birth weight and tobacco smoke exposure throughout pre and early postnatal period was associated increased child anthropometric outcomes at school age. Pregnant women and mothers at postnatal period should avoid tobacco smoking.
Background/Aims: To alert registrants to an overlooked but critical influence on global health - not only the presence or absence of bioactive species-specific milk, but also the exposure of pregnant women and neonates to inappropriate bioactive bovine products, and the possible intergenerational effects through gestation and lactation.
Abstract: Mammalian milk's bioactive powers are only now being revealed. This overview presentation outlines some of how cows milk and infant formula were used within different demographics at different times in the 20th century, and when and how infants were first exposed to which bovine products, with what amounts of protein and what fats. Inflammatory diseases such as diabetes and allergy are now being vertically communicated between generations, in bodies programmed by the epigenetic effects of gestation, birth and infant feeding. A Milk Hypothesis suggests that both pregnancy and early infant care practices, and infant and maternal diet, have created significant immune damage that was then transmitted vertically, compounding intergenerationally A Milk Hypothesis subsumes both hygiene and biodiversity hypotheses, and crucially, offers some hope for immediate harm reduction startegies.

Prevalence, awareness, treatment, control and factors associated with hypertension control among school teachers in Kerala, India

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Background/Aims: Hypertension is the most common non-communicable disease risk factor that is highly associated with cardiovascular diseases, the most common cause of death in the world. Control rates of hypertension are very low in developing countries. We investigated the prevalence, awareness, treatment, control and the factors associated with hypertension control among school teachers in Kerala, India.
Method: As part of an ongoing study on hypertension control among school teachers in Kerala, we surveyed 2216 school teachers in Thiruvananthapuram district of the state. Blood pressure, weight, height and waist circumference were measured using standard protocols. Hypertension was defined as systolic blood pressure (SBP) of at least 140 mmHg or diastolic blood pressure (DBP) of at least 90 mmHg, or self-report on current antihypertensive medication. Control of hypertension was defined as SBP<140 and DBP<90 mmHg. Information on other variables was collected using a structured interview schedule. Unadjusted odds ratios were calculated to find out the association between predictor variables and hypertension prevalence and that of hypertension control.
Results: Mean age of the study population was 44 years (SD:5.8) and 16.1% were males. The overall hypertension prevalence was 18.1% (95% CI: 16.5-19.8) [men:33.1%; women:15.3%]. Among hypertensives 62.2% were aware, 49.3% were on treatment and 34.1% achieved adequate control. Of the treated hypertensives, 69.2 % achieved adequate control. Factors associated with hypertension prevalence were older age [OR:2.91(95%CI: 2.30-3.68],self-reported diabetes [OR:2.65 (1.98-3.57)],male sex [OR:2.3(2.12-3.53)], positive family history [OR: 1.91(1.51-2.44)] and overweight [OR: 1.74 (1.35-2.25)]and that were associated with adequate control of hypertension were female sex [OR:2.27(1.38-372)],overweight [OR:2.22(1.27-3.88)], self-reported diabetes [OR:2.17(.32-3.57)] and older age [OR:1.71 (1.06-2.76)] compared to their counterparts.
Conclusions: Hypertension control rate among school teachers was higher than that of the general population in the state. Women teachers could possibly be used as role models for hypertension control for the general population in the state.

High-caloric diet preference in adult rat offspring as long-term consequence due to early malnutrition

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Background/Aims: Early nutritional imbalance may be associated with a risk of developing metabolic diseases in adult life. Here we aimed to evaluate the effect of a maternal food restriction during the first 2/3 of lactation on feed behaviour and biometrical profile of rat offspring.
Method: Female Wistar rats were fed a half of diet offered to control dams (n=8 rats for each experimental group) during the first two weeks of lactation (FR50 group). While the control dams (CONT group) were fed *ad libitum*. The rat offspring's body weight gain and food intake were quantified every 2 days. The food preference (rodent chow *versus* high-caloric diet, HCD) was assessed by 10 days. At 100-days-old rats were euthanized to remove body tissue to quantify biometrical parameters.

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Results: In relation to CONT rats the FR50 rats' body weight was reduced by 14.3% (n=17 rats, P<0.001), while the food intake throughout the experimental period was increased by 8.2% (n=3 litter, P<0.05). Regarding the food preference, even the CONT rats eat 16.3% more high fat diet, it was not statistical different, by other hand the FR50 rats eat 96.8% more high fat diet (P<0.001). In relation to CONT rats, FR50 rats presented a reduction in the retroperotoneal (-22.1%, n=17 rats) and mesenteric (-20.3%, n=15) fat pad (P<0.001) the extensor digitorum longus muscle was not different between groups.
Conclusions: Maternal food-restriction during lactation programs rat offspring to hyperphagia and high preference to calorie-enriched diet, which is a risk factor to metabolic disease development as long-term consequence.

What Factors Determine Pre-Pregnancy Maternal Nutritional Status? An Opportunity to Improve Maternal and Child Health Outcomes in Ethiopia

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Background: Pre-pregnancy period is considered as a window of opportunity to break the vicious cycle of transgenerational malnutrition. However, poor nutritional status, as expressed in low pre-pregnancy body mass index (BMI), remains pervasive in low-income countries. Moreover, little is known about factors that determine pre-pregnancy BMI. Therefore, this study is aiming to assess determinants of pre-pregnancy BMI, a key step in improving maternal and child health outcomes, in Ethiopia.
Methods: The data are collected as part of an ongoing prospective study in Kilite-Awlaelo Health and Demographic Surveillance Site, Tigray region, Ethiopia. First, weight of 17,500 women of reproductive age was measured between August and October 2017. Subsequently, 991 women who became pregnant were included at or before 20 gestational weeks (88.2% ≤ 16 weeks) between February and September 2018. Data regarding demographics, socioeconomic status, reproductive history, women empowerment, morbidity, physical activity, social support, anxiety, stress, depression, as well as nutritional status and habits (anthropometry, agricultural biodiversity, food security, dietary diversity and other dietary habits) were collected at enrolment. Most of the data were collected using pretested forms and standard anthropometric instruments while some were extracted from the surveillance site database. Weighted least squares regression was fitted to identify determinants of pre-pregnancy BMI.
Results: The mean pre-pregnancy BMI was 19.71 kg/m^2 (± 0.06). Overall, 35.9% of women were undernourished (BMI <18.5 kg/m^2) before pregnancy. Low economic empowerment, low dietary diversity, food insecurity, high stress, low social support, high partner violence, low education, rural residence, and not being certified for health extension package were associated with low pre-pregnancy BMI.
Conclusion: The prevalence of pre-pregnancy undernutrition in our study is very high. Pre-pregnancy nutritional status could be improved by advancing community awareness, empowering females, rising agricultural productivity and strengthening health extension. Additionally, it requires the coordinated efforts of concerned bodies.

Blood pressure in pregnancy and maternal and newborn anthropometry in the Croatian CRIBS cohort

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Background: The trajectory of blood pressure (BP) in pregnancy is characterized by an early decrease and a late pregnancy increase.
Aim: The aim of this study was to define trajectory of systolic (SBP) and diastolic (DBP) blood pressure in 308 pregnant participants in the CRIBS study and to analyse the association of BP with maternal pre-pregnancy BMI and newborns` anthropometry.
Methods: Pregnant women included in the CRIBS study had no history of chronic diseases. The BP of CRIBS participants was measured at least once in each trimester. Maternal pre-pregnancy weight was self-reported. Z-scores were calculated for each newborn`s birth weight, length and head circumference using the WHOAnthro software. All deliveries were term births. The analyses were performed using SPSS 10.0
Results: Less than 2% of women had pregnancy-induced hypertension (SBP >140 mmHg and/or DBP >90 mmHg). BP changed through pregnancy: mean systolic BP of 113 mmHg in the 1st and in the 2nd trimester elevated to 116 mmHg in the 3rd trimester (p<0.001). Mean diastolic BP in the 3rd trimester (69 mmHg) was also significantly higher than in the first two trimesters (66 mmHg) (p<0.01). Mean SBP and DBP of pre-pregnancy obese women (BMI>30 kg/m^2) in all three trimesters were significantly higher than in pre-pregnancy underweight, normal weight or overweight women. Positive correlations were detected between maternal SBP in the 2nd trimester and z-scored birth weight, length and head circumference (R^2=0.0205, R^2=0.0240 and R^2=0.0141, respectively) and between DBP in the 2nd trimester and z-scored weight and height (R^2=0.0175 and R^2=0.0251). No association between gestational age of newborns and maternal BP has been detected.

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Conclusion: Most of the CRIBS participants had BP within a normal range. The obesity pre-pregnancy was associated with higher BP in pregnancy and the BP in the 2nd trimester of pregnancy correlated with birth size.

Comparison of Aortic Intima Media Thickness and Diameter of Appropriate for Gestational Age Fetuses Born to Mothers with and without Gestational Diabetes Mellitus

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Background/Aims: In-utero exposure to elevated glucose has potential to adversely influence fetal vascular-health. We assessed vascular-health by comparing aortic-intima-media-thickness (aIMT) and diameter of fetuses born to mothers with and without gestational-diabetes-mellitus (GDM).
Method: In this cross-sectional study, we enrolled 49 approximate-for-gestational-age fetuses of GDM pregnancies and 71 non-GDM pregnancies. aIMT was measured at far and near vessel wall and aortic diameter was assessed with two-dimensional-echocardiographic-ultrasound.
Results: Important differences between two groups included significantly higher body-mass-index (BMI) at first antenatal-visit of GDM mothers compared to non-GDM mothers [31.33 ± 4.48 versus 27.38 ± 3.87, $p = 0.013$] and shorter gestational age (GA) at delivery [37.19 ± 0.91 versus 37.88 ± 1.29, $p = 0.003$]. GDM fetuses have significantly thicker near and far aortic wall compared to non-GDM fetuses [0.65 ± 0.16 mm versus 0.52 ± 0.17 mm, $p = 0.001$ and 0.63 ± 0.14 mm versus 0.51 ± 0.16 mm, $p = 0.001$], respectively. Similarly, aortic-diameters of GDM fetuses were thicker compared to non-GDM fetuses [5.70 ± 0.86 mm versus 5.39 ± 0.77 mm, $p = 0.059$] but results were marginally nonsignificant. Adjustment in the regression-model for booking BMI and GA at delivery retained significant differences in near-wall [β 0.250, (95% CI 0.129, 0.370), $p = 0.001$] and far-wall measurements [β 0.091, (95% CI 0.055, 0.236, $p = 0.017$]. Comparison of GDM pregnancies treated on oral-medication with those on insulin revealed no significant difference in thickness of the near-wall [0.58 ± 0.08 mm versus 0.68 ± 0.16 mm, $p = 0.254$] and of far-wall [0.52 ± 0.083 mm versus 0.65 ± 0.17 mm, $p = 0.673$] and in diameter [5.74 ± 0.97 mm versus 5.60 ± 0.97 mm, $p = 0.664$].
Conclusion: *In-utero* exposure to high maternal glucose could influence fetal vascular-health and warrants stringent maternal glucose control during pregnancy.

Does *In-Utero* Exposure to Gestational Diabetes Mellitus Influence Neurodevelopment and Socio Emotional Behaviour in Infants?

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Background/Aims: Hyperglycemia-in-pregnancy is associated with several adverse perinatal-health outcomes. However, evidence about its influence on neurodevelopment and socio-emotional-behaviour of infants is inconclusive. We aimed to examine association between *in-utero* exposure to gestational-diabetes-mellitus (GDM) and neurodevelopment and socio-emotional-behaviour in infants at one-year of age.
Method: From antenatal-records of Aga Khan University (2017-2018), we identified 100 infants born as GDM and 139 born as non-GDM babies. Using Bayley-scales-of-infant and toddler-development (BSID-III) tool, we assessed their neurodevelopment across 5 major domains: Cognition, Language-expressive-communication score, Language-receptive-communication score, Fine-motor and Gross-motor. Social-emotional behaviour was assesed using ages and stages-questionnaire. These tools were administered in a hospital set-up.
Results: Children born to GDM mothers demonstrated lower scores on cognitive-composite score [102.00 ± 12.411 versus 107.52 ± 13.888, $p = 0.002$], language-receptive-communication-scaled score [8.46 ± 2.081 versus 9.19 ± 2.038, $p = 0.008$], fine-motor-scaled score [8.94 ± 2.044 versus 9.69 ± 2.395, $p = 0.012$] and gross-motor-scaled score [8.91 ± 2.861 versus 9.94 ± 3.129, $p = 0.010$]. No difference was observed in social-emotional- behaviour between GDM and non-GDM born children (20.40 ± 9.684 versus 20.65 ± 8.843, $p = 0.838$). Linear-regression-analysis revealed independent association of GDM with cognitive-composite score [β -6.562, (CI -10.397, -2.726), $p = 0.006$], language receptive communication scaled score [β -0.844, (CI -1.416, -0.272, $p = 0.038$] and gross motor scaled score [β -0.739, (CI -1.625, 0.148), $p = 0.001$] after adjusting for gestational-age at delivery, fathers' occupation, infant's gender, weight-at-birth, birth-order, nature of housing and maternal body-mass-index during first-trimester at-booking and at-birth.
Conclusion: Infants born to GDM mothers tend to demonstrate suboptimal-performance on cognition, language and motor development at one-year of age. Targeted-interventions aimed at their comprehensive and multidimensional early-childhood-development should be initiated as early as infancy and monitored subsequently. Preconception and prevention-programs for women at-risk for GDM should also be considered.

Childhood Obesity Risk Score Development and Validation in a Large Population-level Cohort in Canada

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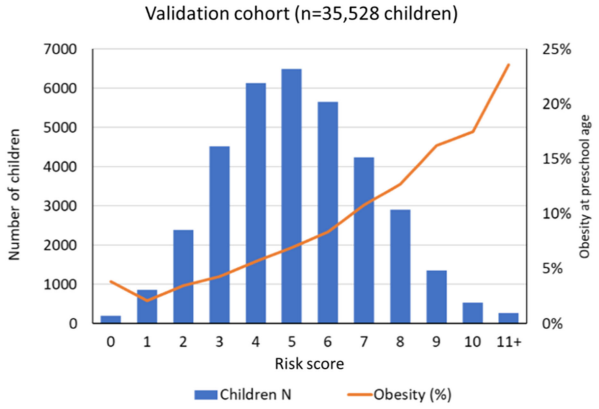
Score
General population//Chinese=0; South Asian =1
Household Income: Highest quartile=0; Third quartile=1; Lowest/second quartile=2
Maternal marital status: Not married=1;Married=0
Gestational diabetes: No=0; Yes=2
Hypertension during pregnancy: No=0; Yes=1
Delivery: Vaginal=0; Induction/C-section=1
Sex: Female=0; Male=1
Birth size: Appropriate=0; Small=0; Large=2 for gestational age
Breastfed: No=2; Yes=0
Asthma: No=0; Yes=1
Infection with no antibiotic use=1; Infection with antibiotic use=2
Total score range: 0 - 16



Background/Aims: The purpose of this study was to develop and validate a risk score to identify children (at age 2-years) who are at a higher risk of developing obesity by preschool age (4-6 years).
Method: Children born between 2008-2013 in two health zones, Calgary (n=39,361, model development cohort) and Edmonton (n=35,528, model validation cohort), in Alberta, Canada, and who were at pre-school age between 2013-2017 were included in the study. WHO criteria were used to identify children who were obese at preschool age. The adjusted odds ratios from a GEE model with multinomial logistic regression accounting for the correlation between pregnancies were used to develop a simple risk score. The model included the following maternal (ethnicity, socioeconomic status, gestational diabetes and hypertension, mode of delivery), and child (sex, birth size, preterm birth, breastfeeding, and asthma, infection and antibiotic use in first two years of life) variables.
Results: The prediction model showed moderate discriminating power (C-statistic 0.67 (development), 0.66 (validation)). The risk score (see figure) ranged from 0 – 16, with each additional unit increase in score being associated with 30% increase in the likelihood of obesity (OR (95% CI): 1.31 (1.29-1.34)).
Conclusions: The risk score can be used to identify children at 2 years of age who are at high risk of becoming obese and can be used to design and implement early intervention strategies.

Constant light exposure during pregnancy does not cause metabolic disfuntions in female offspring

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Background/Aims: The organisms have developed a rhythmicity of physiological and behavioral processes related to environmental changes, such as the light-dark cycle, determining a circadian cycle. The suprachiasmatic nucleus is a central coordinator located in the hypothalamus, in which occurs the coordination of the cycle through a feedback loop of clock genes that determine the rhythmicity of the peripheral tissues. During gestation, the rhythmicity arising from the mother is synchronized with the fetus, which is maintained after birth. Nowadays, however, due to the modern lifestyle, there have been noticed changes in the circadian cycle of pregnant women, expressing a desynchronization with the fetus. This fact may result in future cardiometabolic diseases. Therefore, our goal was to assess if the rupture of the circadian cycle during pregnancy caused metabolic dysfunctions in female offspring during adulthood.
Method: Female Wistar rats after pregnancy were separated into 2 groups: LD group (light-dark, normal cycle) and LL group (constantly exposed to light, 200 lx), both pregnancies were kept in a specific rack to study the circadian rhythms. At birth, all animals returned to the standard light-dark cycle and kept under controlled temperatures (23 ± 2 ° C). The litters were standardized: eight rats per mother. After 21 days, the animals were weaned. Weight and maternal food intake were recorded every 12 hours. The glycemic and lipid profile of milk and fat stores were also evaluated. In the female offspring, the evolution of body weight, fat stores, lipid profile and glycemic homeostasis were analyzed at 90 days of life. Data were expressed as average ± standard error of the average and analyzed by Student's t test.
Results: The rupture of the circadian cycle during gestation did not cause drastic changes in the metabolic profile of adult female offspring. The feeding behavior of the pregnant rats was altered, indicating a desynchronization of the maternal circadian cycle of the light-dark phase. LL animals in adulthood showed no change in glucose tolerance, fasting insulinemia and body fat stores. However, a small increase in weight at 90 days of life (2.74%) and decrease in total cholesterol (23.95%) was observed.

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Conclusions: We suggest a possible resistance of the mother and/or fetus to a dyssynchrony in the rupture of the circadian cycle. Thus, we conclude that the exposure to constant light during pregnancy does not promote significant metabolic changes in adult rats.

Comparing Two Approaches to Identify Adolescents at High Risk of Cardiometabolic Disorders

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Background/Aims: Although cardiovascular disease manifests in adulthood, atherosclerosis begins in childhood. Identifying risk in childhood has relied on individual risk factors or estimation of their cumulative effects defined by the metabolic syndrome that relies on cut-points and may underestimate long-term risk. This study compared the prevalence, stability and estimated cardiovascular risk in 17 and 20yr olds defined either by clustering of cardiometabolic risk factors or by the metabolic syndrome.
Method: Anthropometry, blood pressure (BP) and fasting bloods were taken at 17yr (n=1048) and 20yr (n=1120) from the West Australian Pregnancy Cohort (Raine) Study. Cluster analysis using BMI, systolic BP, triglycerides and insulin resistance defined high– and low- risk clusters. Cluster stability between 17- and 20-yrs included 806 participants with measurements at both time points. Lifetime cardiovascular risk (Q-Risk) and Framingham 30-yr risk were compared in the low-risk cluster and in the high-risk cluster with and without the metabolic syndrome.
Results: The high-risk cluster included 17.9% and 21.3% at 17- and 20yrs, respectively, whereas only 1.2% and 3.4% had the metabolic syndrome. 72% in the high-risk cluster at 17yrs remained in that cluster at 20yrs. At 20yrs, those in the high-risk cluster without the metabolic syndrome had increased BMI (7kg/m^2), waist circumference (18cm), systolic BP (7mmHg), Q-risk (17%) and Framingham risk (23%) (all P<0.001), compared with the low-risk cluster.
Conclusions: Even in the absence of the metabolic syndrome approximately one fifth of the cohort had substantially higher cardiometabolic risk. The use of absolute cardiometabolic risk scores rather than categorical metabolic syndrome cut points needs to be developed further to identify high-risk individuals in late adolescence and early adulthood.

Obstructive Sleep Apnoea and Cardiometabolic Risk Factors in Young Adults

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Background/Aims: Obstructive Sleep Apnoea (OSA) has been linked to increased risk of cardiometabolic disease and increased cardiovascular morbidity in middle-aged and older adults, but it is unknown whether such relationships also exist in young adults. This study aimed to examine the association between high risk for OSA and cardiometabolic risk factors in young adults 22yrs of age.
Method: OSA risk and cardiometabolic risk were examined in 975 participants from the Western Australian Pregnancy Cohort (Raine) Study. High risk for OSA was determined from the Berlin Questionnaire using two definitions, the first included (i) presence of snoring, (ii) daytime sleepiness and fatigue, and (iii) obesity (BMI) or hypertension. The second definition was modified to exclude BMI and hypertension. Regression analyses examined the associations between OSA risk and cardiometabolic risk factors that included adiposity, blood pressure, fasting lipids, HOMA-IR and CRP.
Results: Complete OSA risk and cardiometabolic risk factor data were available on 850 participants (413 females, 437 males). The prevalence of high risk for OSA from the Berlin Questionnaire was 14.7% and when modified to exclude obesity and hypertension was 7.9%. Those at high risk for OSA were more overweight/obese and had greater central obesity. There was a significant positive association between high risk for OSA and triglycerides, hs-CRP and a negative association with HDL-cholesterol, independent of gender and lifestyle factors. However, in the modified definition that excluded obesity and hypertension there were no associations between OSA and blood pressure or any of the cardiometabolic risk factors measured, after adjusting for BMI.
Conclusions: In young adults, high risk for OSA associates with increased cardiometabolic risk, but this relationship is most likely mediated by increased adiposity. The relationship between OSA and cardiometabolic risk is likely to be stronger with increasing age when risk factors are more marked.

Is Pregnancy a Sensitive Period? Testing Competing Explanations of the Association Between Maternal Depression and Child Behaviour and Development

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Background/Aims: There is debate regarding whether the association between maternal depressive symptoms (MDS) and child outcomes is due to timing or chronicity. In the current study, we aimed to investigate whether critical period, sensitive period or accumulation provided the best explanation for the association between MDS before, during and after pregnancy and children's behavior and development.
Method: Participants ($N = 939$) were children aged 2-12 years from the Mothers and their Children's Health study and mothers from the Australian Longitudinal Study of Women's Health. Mothers were categorized according to the timing of MDS (CESD-10). Child outcomes were maternal-rated behavior problems (SDQ) and teacher-rated social and emotional development (AEDC). We used a novel life course approach to compare the fit of a series of nested multilevel models.
Results: An accumulation model was the best fit for the association between MDS and child behavior problems (unstandardized regression coefficient (B) = 1.76, 95% CI = 1.31, 2.21), social development (B = -0.33, 95% CI = -0.56, -0.10) and emotional development (B = -0.27, 95% CI = -0.47, -0.07). Sensitive and critical period models were not supported.
Conclusions: Chronic MDS were associated with poorer child outcomes than MDS at any single time, suggesting pregnancy was not a critical or sensitive period for child behaviour and development, and that the duration of MDS is more important than when it occurs. Screening and intervention should begin pre-conception and aim to reduce the duration of symptoms, and future research should incorporate this novel life course approach.

Aortic Intima-Media Changes In Infants With Congenital Heart Disease

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Background: Aortic intima-media thickness (aIMT) measurement is an established indicator of preclinical atherosclerosis. We aimed to describe the aIMT and its determinants in newborns with congenital heart disease (CHD) undergoing cardiac surgery.
Methods: A prospective cohort study measuring aIMT preoperative, 3 months and 1 year of age in neonates with CHD undergoing cardiac surgery. The effects of rapid catch up growth, cardiac bypass and several maternal risk factors of aIMT were evaluated.
Results: Twenty four term infants with a mean gestation of 39 weeks and birth weight of 3184 gms were included. Baseline mean aIMT was 0.4mm (+0.06mm), baseline maximum aIMT 0.47mm (+0.09mm), 3 month mean aIMT 0.56mm (+0.11mm) and 3 month maximum aIMT 0.62mm (+0.11mm), 1year mean aIMT 0.52mm (+0.08mm) and 1 year maximum aIMT 0.58mm (+0.08mm). Gestation correlated inversely with baseline mean aIMT (β= -0.027, p= 0.018) and positively correlated with percentage increase in mean aIMT and maximum aIMT between baseline and 3 months (β= 17%, p=0.027 and β= 15%, p= 0.023), respectively. Maternal hypertension was significantly associated with percentage reduction in mean aIMT and maximum aIMT between baseline and 3 months (β= -56%, p=0.007 and -46%, p= 0.014). Presence of left outflow obstruction was significantly associated with increasing aIMT between baseline and 1 year (β= 34%, p=0.017 and 43%, p= 0.001), respectively. Rapid catch up growth and cardiopulmonary bypass was not associated with aIMT changes at 3 months or 1 year.
Conclusions: To our present knowledge, this is the first cohort of infants with congenital heart disease monitored for aIMT changes from birth. Gestation significantly correlated with aIMT and rate of change at 3 months. Presence of left outflow tract obstruction was significantly associated with increasing aIMT between baseline and 1 year. Rapid catch up growth and cardiopulmonary bypass were not associated with aIMT changes in the first year.

Association Between Early Lead Exposure and Externalizing Behaviours in Adolescence: A Developmental Cascade

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Background/Aims: Lead (Pb) exposure is associated with adverse developmental outcomes, and was related to externalizing behaviour symptoms among Inuit children in northern Québec. Evidence of a direct association between Pb exposure during childhood and later behaviour problems are scarce; however, as externalizing behaviours in childhood tend to persist, Pb exposure may initiate a developmental cascade that increases the risk of long-term behaviour problems. The main goals of this study are to examine direct links between childhood Pb concentrations and adolescent externalizing symptoms and substance use as well as indirect associations through childhood behaviour assessments.

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Method: The study sample is a longitudinal cohort of Inuit adolescents (*N*=212) followed since birth. Pb exposure was determined in umbilical cord, child (median age=11 years) and adolescent (median age=18 years) blood samples. Externalizing/inattentive behaviour at 11-years of age were assessed using the Teacher Report Form from the Child Behaviour Checklist and the Disruptive Behaviour Disorders Rating Scale. At the 18 year follow-up, behaviour problems were reported by using the Achenbach Youth Self-Report, the Barkley Adult ADHD-IV Rating Scale, and the Youth Conduct Disorder predictive scale from the Diagnostics Interview Schedule for Children. Adolescent substance use was also assessed through an evaluation grid. Direct and indirect associations of child blood Pb concentrations with adolescent outcomes were tested through mediation models.
Results: Child blood Pb concentrations were not directly associated with documented outcomes in adolescence but were indirectly associated through childhood externalizing behaviour assessments, with adolescent externalizing behaviours, binge drinking, and cannabis use.
Conclusions: Our results highlight the indirect but long-term impact of Pb exposure during childhood on adolescent behaviour problems and the importance of childhood externalizing behaviour in mediating this relationship. Early-life impairment may put children on a developmental trajectory, which increases the likelihood of lifelong social and behavioural problems such as binge drinking and cannabis use.

A rodent model of early postnatal growth restriction

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Background: In clinical practice, it is not uncommon for infants of normal birth weight to undergo a period of poor growth before weaning, however the short and long-term consequences of this growth pattern are poorly understood. The aim of this study was to establish a pre-clinical model of early postnatal growth restraint.
Methods: Within 24 h of birth, Wistar rat pups were cross-fostered to create litters containing either 8 pups (control group, n=9 litters) or ≥14 pups (large litter, LL, n=10 litters). Pup weight was recorded every 2 days until weaning onto standard chow (ad libitum) at 3 weeks of age. Glucose tolerance, fat mass and organ weights were assessed in 1 male and 1 female pup per litter at 3, 6 and 12 weeks of age.
Results: Pup weight was not different between groups at birth, but both male and female LL pups were ~30% lighter ($P<0.0001$) and had a ~35% lower percentage body fat ($P<0.03$) than controls by weaning. Relative brain weight at weaning was 20% higher in LL pups ($P<0.001$), and was still 13% higher in female LL pups at 6 weeks of age ($P<0.001$). Male LL pups remained 10% lighter ($P<0.01$) and 30% leaner ($P=0.01$) than control pups at 12 weeks, but the deficits in weight and fat mass were no longer present in females by 6-8 weeks. Fasting glucose concentrations were lower in male and female LL pups at weaning, but glucose tolerance was similar between groups at all time points.
Conclusions: We have successfully established a rodent model of early postnatal growth restriction, in which pups reared in large litters exhibit characteristic features of growth restriction (reduced body weight, reduced fat stores and brain sparing) at weaning. The longer-term effects of this early growth restraint appear to be sex-specific, and further studies to investigate these effects in more detail are warranted.

The impact of periconceptional maternal lifestyle on placental development and function: a systematic review

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Background/Aims: Poor maternal lifestyles can detrimentally influence placentation in the periconception period and may have an effect on placenta-related pregnancy complications with a short- and long-term impact on maternal and neonatal health. However, the extent of the impact on placentation is largely unknown. We aim to summarize the evidence of the impact of periconceptional maternal lifestyle on markers of placental development and function throughout pregnancy.
Method: A comprehensive search in online medical libraries was conducted. Keywords searched related to lifestyles, i.e., smoking, alcohol, caffeine, nutrition and body weight. Placental markers searched comprised ultrasound, blood and histological characteristics. Randomized controlled trials and observational studies published between 2000-2017 were included. Methodological quality was scored using the ErasmusAGE tool.
Results: Of 2,593 unique citations found, 82 studies were included. Maternal smoking was associated with lower first-trimester placental vascularization flow indices and adaptation of resistance later in pregnancy. Periconceptional alcohol use was associated with lower placental weight and higher placental growth factor (PlGF). Adequate nutrition, folic acid supplement intake and strong adherence to a Mediterranean diet, were all associated with lower vascular resistance in the second and third trimester. A low caloric intake resulted in a lower placental ultrasound parameters as well as weight. Higher maternal body weight was associated with a larger placenta as measured by ultrasound and weight. Higher maternal body weight was also associated with decreased PlGF levels.
Conclusions: Associations between periconceptional maternal lifestyle and placental health were demonstrated. Future research should focus more on the physiological consequences of an unhealthy lifestyle during the critical periconception

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window. This will support development and implementation of lifestyle interventions improving placental health and subsequent health outcomes.

Embryonic Body Posture: An Analysis Of Preference, Symmetry And Lateralisation

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Background/Aims: Embryonic neurobehaviour, expressed by body posture and movements, is a reflection of central nervous system development. However, little is known about normal embryonic development of posture plus movement. The aim of this study is to describe embryonic body posture preference, symmetry and lateralisation during periods of rest – the starting point of embryonic posture and movements - using state-of-the-art ultrasound and virtual reality techniques.
Method: A prospective observational study was performed in twenty-three low-risk pregnancies. Transvaginal four-dimensional (4D) ultrasound examinations of 30minutes were performed at 9 weeks gestational age (GA). Datasets were analysed longitudinally (i.e. per frame) using Virtual Reality (VR) techniques, in which embryonic body posture is studied during each resting period. Total embryonic body posture is assigned by combining positions of each joint. Inter-individual and intra-individual postures are analysed over time to determine a preference posture. (A)symmetry is scored as a difference in the position between the right versus the left extremity and lateralisation as rotated head and/or bended spine. Descriptive and statistical analysis were performed using SPSS.
Results: Sixteen embryos (N=210 frames) are analysed. In total, 27 different total embryonic body postures could be identified of which three distinct body postures account for 59% of the frames. Inter-individual and intra-individual variations in postures were seen. Symmetry is seen in the position of the shoulder (100% frontal endorotation), elbow (100% flexion), fingers (100% extension) and in all joints of the lower extremity. Asymmetry is seen in abduction/adduction of the shoulder (24%) and in the wrist (14% ulnar deviation/no deviation). Lateralisation of the head and spine is seen in 15%.
Conclusions: In this unique study embryonic body posture is evaluated. Variation in embryonic body posture (both intra-individual and inter-individual), (a)symmetry and lateralisation could already be demonstrated at 9-weeks GA. Performing future prospective follow-up studies of embryonic posture may provide insight into the development of the embryonic central nervous system and therefore possibly in embryonic health.

Placental development is associated with uterine artery vascular resistance in the first trimester of pregnancy

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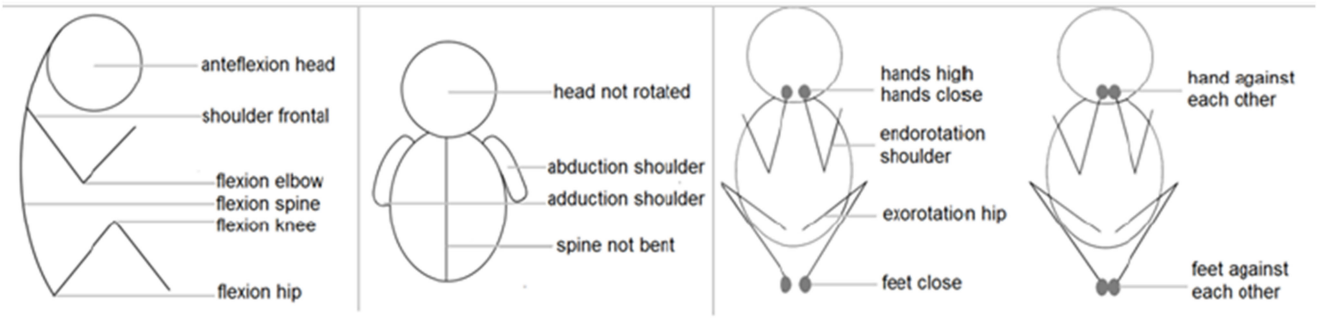
Background/Aims: Placenta-related pregnancy complications mostly originate in the first trimester of pregnancy. In this study, we investigated whether early development of the placenta and the utero-placental vasculature is associated with vascular resistance indices of the uterine arteries.
Method: In 241 pregnancies, parameters of the maternal uterine vasculature were assessed at 7, 9 and 11 weeks gestation by measurements of uterine artery Doppler pulsatility and resistance indices (PI and RI) as obtained by transvaginal ultrasound. Also, at each visit a three-dimensional (3D) power Doppler recording of the gestational sac including the placenta was made and placental vascular volume (PVV) and placental volume (PV) were measured offline using virtual reality (VR) and VOCAL analysis as representatives for placental development. Associations between PVV and PV and vascular resistance indices of the uterine arteries were studied using linear mixed models for longitudinal measurements, with stratification for parity and conception mode.
Results: After exclusion, 215 ongoing pregnancies were included. Maternal age and parity differed at baseline between spontaneously conceived (n=127) and IVF/ICSI (n=88) pregnancies. PVV was negatively associated with PI and RI (β=-0.0061, p=0.001 and β=-0.0023, p<0.001, respectively),



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PV was negatively associated with RI (β=-0.0006, p=0.016) and the PVV/PV ratio was negatively associated with PI and RI (β=-0.2003, p=0.045 and β=-0.0741, p=0.037). Associations were most evident at 9 weeks gestation. In stratified analyses, PVV and PV were significantly negatively associated with PI and RI in spontaneously conceived pregnancies, but not in IVF/ICSI pregnancies. Furthermore, PVV was significantly negatively associated with PI and RI and PV with RI in nulliparous women (n=142), but not in multiparous women (n=73).
Conclusions: First trimester PV and PVV are negatively associated with uterine artery vascular resistance indices. This suggests that early placental and utero-placental vascular development relates to placental function later in pregnancy by determination of placental blood flow. These associations are most evident in spontaneously conceived, nulliparous pregnancies.

Excess maternal fructose consumption affects estradiol synthesis in rat offspring

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Background/Aims: Recenltly, the maternal intrauterine environment has been demonstrated to affect ovarian development in the subsequent generation. Because the fructose is transferred to the fetus, excess fructose consumption may affect offspring ovarian development. As ovarian development and its function is maintained by 17β-estradiol, we therefore investigated whether excess maternal fructose intake influences offspring ovarian estradiol synthesis.
Method: Rats received a 20% fructose solution during gestation and lactation. After weaning, offspring ovaries were isolated. mRNAs for steroidogenic molecules were quantified with real-time PCR. Also, steroidogenic proteins were measured with Western blot. Circulating estradiol level were quantified by ELISA.
Results: Reduced StAR and P450(17α) protein and mRNA levels were observed in fructose offspring. Attenuated P450arom protein level was found in the absence of mRNA expression alteration. Also, fructose offspring show reduced level of circulating 17β-estradiol. Furthermore, estrogen receptor α (ERα) protein levels were also down-regulated. In accordance, the mRNA for progesterone receptor, a transcriptional target of ERα, was decreased.
Conclusions: These results suggest that maternal fructose might alter ovarian physiology in the subsequent generation

Impact of a high nutrient milk replacer feeding followed by concentrate feeding in rearing period on the liver DNA methylation in adult cattle

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Background/Aims: Intensive feeding of milk nutrients to calves has primal influence on growth and subsequent muscle characteristics, which enables highly performing beef. An alteration of liver gene expression, induced by a high protein and fat milk feeding during early stage of calf, could potentially be involved in promotion of growth of beef cattle. Here, we aimed to clarify changes in DNA methylation pattern of the liver genes in the beef cattle fed a high nutrient milk replacer and rearing concentrate.
Method: Four calves (HN) of Japanese Black (JB) steers were fed milk replacer containing 26% crude protein and 25.5% crude fat ad libitum, while the other four (CT) were fed that of 600 g/day at maximum, until 3 months of age. After 3 months, HN calves were fed concentrate until 10 months, while the CT calves were fed roughage. Thereafter, both groups were fed roughage until slaughter at 31 months. Based on methyl-CpG binding domain (MBD)-Seq method, the methylated genomic DNAs from the frozen liver samples were enriched and sequenced. The HN/CT methylation ratio of region of interest was calculated, and differentially methylated region (DMR) were compared and statistically tested between the treatments.
Results: Significant differences in carcass weight and ribeye area were observed between CT and HN groups. Statistical analysis revealed that a total of 27,685 DMRs was extracted, and DMRs showing > 2-fold change in promotor CpG islands (CGI) amounted to 673 regions. Hierarchical clustering analysis using the CGI DMRs showed that the liver samples were separated into the CT and HN groups by similarity of cluster of the genes with differentially methylated CGI. ATP5IF1 gene was extracted as one of the candidate genes of which promotor CGI was hyper methylated in liver of the HN group.
Conclusions: The results indicate that intensive feeding of milk nutrients in calf period has influence on their growth and the CGI methylation of liver genes in the maturated beef cattle.

Assessment of factors associated with adherence to Tuberculosis treatment among drug users in methadone clinics; a case study of Dar es Salaam, Tanzania

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Background: Drug users are at a higher risk of tuberculosis (TB) transmission due to poor living conditions, poor nutrition and a higher risk for HIV infection. These few risk factors are known to increase the risk of acquiring TB disease. Non adherence leads to multi-drug resistance TB (MDR-TB) which is now a public health problem worldwide. Treatment for opioid dependence is done at "methadone clinics" which offer methadone as an opioid substitution therapy in Dar es Salaam. We set out to assess adherence to TB treatment and its associated factors among drug users in Dar es Salaam.
Methods: We did a cross sectional facility based study deploying quantitative techniques where data were extracted from patient`s files and we performed interviews by structured questionnaire. Descriptive statistics were used to describe patient characteristics. To assess associations between categorical variables, chi-squared test or Fisher's exact test were used as appropriate. Bivariate and multivariate logistic regression was performed with results presented as unadjusted and adjusted Odds and their 95% confidence intervals.
Results: We recruited 239 participants during the study period where 227 (95%) were males. The mean age was 37.9 years ± 6.99 SD. The prevalence of HIV infection was found to be 14.2%, 95% CI 10.3-19.3% and significantly higher among women than male participants (i.e., 41.67%, 95% CI 18.4-69.4% vs., 12.8%, 95% CI 9-17.8%, p=0.02). The prevalence of TB among people attending methadone clinics in Dar es Salaam was found to be 9.9%, 95% CI 6.6-13.2%. Default to TB treatment was found to be 10.88% (95% CI 7.5 – 15.5%) and only males who defaulted to TB treatment. Default to TB treatment was associated with headache as withdrawal symptom where participants with headache were three times likely to default from TB treatment (i.e., with headache=17 (17.35%) vs., without headache =9 (6.38%), p=0.007). Likewise, use of more than one illicit drug was associated with default to TB treatment and missing TB drugs at health care facility was associate with defaulting to TB treatment (28% missed vs., 8.88% did not miss, p=0.004).
Conclusion: The prevalence of TB in this subgroup is significantly high than the general population. Also, default to TB treatment is associated with headache, drug abuse and missing of TB drugs at health care facilities. Public health interventions that target this vulnerable population need to take into considerations these observations so as to reduce the burden of TB in the community.

Preterm birth and risk of bone fractures during childhood and early adulthood

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Background/Aims: Children and adults born preterm have reduced bone mineral density, subnormal peak bone mass and an increased risk of osteoporosis. The role of preterm birth on bone fractures is, however, unknown. We investigated bone fracture risk during childhood and early adulthood in relation to gestational age (GA).
Method: We identified full-term and preterm births (n=12 154, 5.2%) through the Finnish Medical Birth Register in a birth cohort born 1987-1990 (n=232 525). Bone fractures were identified through the Hospital Discharge Register for inpatient (1987-2015) and outpatient (1998-2015) treatments. The association between bone fracture risk and GA was analysed with Cox regression model, censored at death, emigration or end of follow-up (31 Dec 2015).
Results: During the follow-up, bone fractures were recorded in 17.4% of the study subjects (n=40 979). Extremely preterm birth (<28 weeks) was associated with lower risk of bone fractures during childhood and early adulthood compared to those born at term (39-41 weeks) (unadjusted model HR 0.63 [95% CI 0.44 to 0.89]; p=0.008). When adjusting for sex, fetal growth (small for gestational age), severe morbidities, maternal diabetes, maternal smoking during pregnancy and maternal education, HR remained fairly unchanged (HR 0.56 [95% CI 0.37 to 0.84]; p=0.005). Adjusted HRs and confidence intervals for other GA subgroups were 0.93; 0.78-1.10 (28 to 31 weeks), 0.99; 0.86-1.15 (32 to 33 weeks) and1.00; 0.95-1.06 (34 to 36 weeks).
Conclusions: Extremely preterm birth is associated with a lower risk of bone fractures during childhood and early adulthood compared to those born at term. Risk of bone fractures among those born at 28 to 36 weeks did not differ from those born at term.

In Utero/Postnatal Nutritional Mismatch Impacts Kidney Function in Juvenile Baboons

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Background: Compelling studies show that poor nutrition during development adversely affects kidney development altering responses to later life nutritional challenges. No studies on postnatal effects of decreased perinatal nutrition exist in nonhuman primates (NHP) for translation to understanding impact on human health and disease. Animal and human studies suggest that fetal-postnatal nutritional mismatch predisposes offspring to cardiovascular diseases including high blood pressure. We hypothesized that poor fetal nutrition alters juvenile NHP renal response to a high-fat, high-carbohydrate, high-salt (HFCS) diet.
Methods: Pregnant baboons were fed *ad libitum* (Control; CTR) or 30% global calorie reduction from 0.16 gestation (G) through the end of lactation. Offspring (CTR F, CTR M, IUGR F, IUGR M, 3/group) of globally restricted mothers were IUGR at birth. At weaning all offspring were fed chow diet *ad libitum*. At ~3.5 years of age offspring received a HFCS diet plus sugar drink challenge for 7 weeks. Blood, urine, and kidney biopsies were collected at baseline and end of HFCS challenge. Kidney function clinical measures, unbiased kidney gene expression analysis, and untargeted urine metabolomics were performed.
Results: We observed sex-specific and *in utero* exposure-specific responses to the HFCS challenge in urine creatinine, urine metabolites, and renal gene expression data. Urine creatinine was elevated and mTOR signaling, and the YY1 transcription factor were inhibited in female IUGR offspring compared with controls, but not males.
Conclusions: In previous work, we showed dysregulation of mTOR signaling in IUGR 0.5G kidney. Here we show decreased renal mTOR signaling as well as increased urine creatinine and decreased YY1 transcription factor expression indicating decreased mitochondrial energetics and kidney function in IUGR female offspring fed the HFCS diet. IUGR male offspring response to the HFCS was less clear with inhibition of AMPK signaling and activation of oxidative phosphorylation suggesting a dysregulated molecular response. Our findings indicate that the impact of IUGR on the female kidney persists postnatally. Further study is needed to assess postnatal male IUGR kidney function.

Early-life environment and differences in costs of reproduction in a preindustrial human population

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Background/Aims: The measurable costs of reproduction on maternal survival vary between individuals, birth cohorts and populations. One potential factor creating such variation is differences in the early developmental conditions. The early-life environment can alter later-life health and body condition through permanent changes in body structure, physiology and metabolism, and thereby modify resource acquisition and the trade-off between reproduction and survival. However, the effect of early-life environmental conditions on the survival costs of reproduction has rarely been investigated before.
Method: We analysed individual-based life-history data collected from Finnish church records on 1899 pre-industrial women born between 1751 and 1850. We used historical records of annual spring temperature, rye yields and infant mortality in their birth parish as proxies of their early developmental conditions. We tested the effect of poor birth conditions on the survival cost of both the number of offspring born and the number of offspring raised to maturity using Cox proportional hazard models.
Results: We found considerable variation between the 100 female birth cohorts in the correlation between reproduction and longevity, as well our measures of their developmental conditions. However, spring temperature, rye yields, and infant mortality around birth did not modify the relationship between a women's reproduction and survival.
Conclusions: Our results do not provide evidence that poor early-life conditions lead to higher cost of reproduction on adulthood survival in our population. Future studies are needed to increase our understanding of the causes of variation in reproduction-survival trade-offs, and any role of the early-life developmental conditions therein.

Maternal HPAA activity early post-conception and HPAA and HPGA activity during the adolescent transition

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Background/Aims: Adolescence is a critical transition during which individuals acquire many of the social, material and energetic resources they need to succeed during adult life. The behavioural and metabolic strategies each individual adopts to navigate this transition are mediated in part by the so called stress axis, or hypothalamic-pituitary-adrenal axis (HPAA). Thus, investigating the origins of inter-individual variation in HPAA function is crucial for understanding the physiological, psychological and social changes that accompany the passage from childhood to adulthood. HPAA ontogeny is known to be sensitive to maternal HPAA activity during the second and third trimesters of pregnancy. Yet, no information is currently available about the possible effects of maternal HPAA activity during the early post-conception (EPC) period,

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a critical window of vulnerability. Here, we evaluated links between maternal HPAA activity during the first 8 weeks post-conception and their children's HPAA activity during the adolescent transition, as well as their reproductive development trajectories.
Method: Using a longitudinal, naturalistic study design we explored links between maternal EPC HPAA activity and their adolescent children's (11-16 years) HPAA activity (first morning urinary cortisol levels, salivary cortisol responses to natural and experimental stressors) and reproductive maturation (age at menarche, ovarian cycle frequency and quality, gonadal steroid profiles).
Results: Preliminary results show that variation in maternal HPAA activity at specific weeks during the EPC period are associated with children's HPAA and reproductive axis activity during the adolescent transition, including the children's ability to mount appropriate stress responses to natural and experimental challenges (all $p < 0.05$).
Conclusions: Our results provide the first analysis of the associations between maternal EPC HPAA activity, children's HPAA development and functioning, and their connection to reproductive maturation across the adolescent transition. This knowledge will further our understanding of the role early uterine environments play in developmental trajectories. This information should aid in the development of public health interventions to optimize environments for mothers to be and developing children.

Novel Biomarkers GlyFn, PAPP-A2 and inhibin-A for the Prediction of Maternal and Fetal/Neonatal Complications in Women with Suspected or Confirmed Preeclampsia

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Background/Aims: The development of preeclampsia (PE) continues to pose a significant threat to maternal and fetal well-being. Despite known risk factors and traditional laboratory changes, accurate prediction of maternal and fetal/neonatal complications remains challenging. Glycosylated fibronectin (GlyFn), a marker for endothelial dysfunction, is significantly increased during PE. In addition, women with PE display elevated circulating levels of the endocrine markers inhibin-A and pregnancy-associated plasma protein-A2 (PAPP-A2). Yet, no clinical studies have evaluated their potential for the prediction of pregnancy outcome. The aim of this study is to assess the value of novel biomarkers GlyFn, PAPP-A2 and inhibin-A for the prediction of pregnancy complications and time to delivery.
Method: In this secondary analysis of a prospective, observational cohort study, 513 women with suspected or confirmed preeclampsia admitted to the obstetric department were evaluated. Blood samples were drawn at study entry but biomarker values were determined postpartum. Logistic regression analysis was used to study the association between complications and the biomarkers and traditional predictors such as gestational age, parity, blood pressure and proteinuria. For the number of days until delivery linear regression analysis was performed.
Results: Median duration between admission and delivery was 11 days. Complications occurred in 130 mothers and 201 fetuses. To discriminate between women with and without maternal complications, PAPP-A2 showed the highest value (C-index = 0.68) on top of the traditional predictors compared with traditional predictors only (C-index=0.64), vs. C-indices of 0.65 and 0.66 for GlyFn and inhibin-A. To predict time to delivery, PAPP-A2 also showed the highest value (R^2=0.53) on top of traditional predictors versus traditional predictors alone (R^2=0.48). None of the 3 biomarkers showed additive value to predict fetal/neonatal complications.
Conclusions: This study is the first to show the role of novel biomarkers GlyFn, PAPP-A2 and inhibin-A for the prediction of adverse outcome in women with suspected or confirmed PE. PAPPA-A2 showed significant potential to predict maternal complications and time to delivery.

Chapter 3 Understanding the relationship between maternal tobacco smoking and offspring conduct disorder: are metastable epialleles present?

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Background/Aims: Metastable epialleles (MEs) are described as loci at which epigenetic regulation is established during development and maintained throughout life. Consequently, individuals can have the same genetic sequence, yet their epigenetic regulation of the underlying sequence can vary. This variation can be induced by environmental exposures. For instance, we know that maternal tobacco smoking during pregnancy can alter offspring DNA methylation. Thus, there is potential for MEs to be induced in developing human offspring in response to maternal tobacco smoking during pregnancy. Furthermore, associations between maternal smoking and offspring conduct disorder has been observed. However, currently, we do not know what links these associations. We wish to provide a molecular link between maternal smoking and later life outcomes of the offspring.

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Method: A cohort will be sub-selected from the Christchurch Health and Development Study, a longitudinal cohort of children born in Christchurch in 1977. These will consist of: those exposed *in utero* who are now non-smoking adults, those exposed *in utero* who reported as being a smoker as an adult and individuals who were not exposed to smoking *in utero* who are non-smoking adults. Bisulfite-based Amplicon Sequencing (BSAS) was used to investigate DNA methylation differences and potential MEs between the different groups.
Results: Here, we will be presenting the findings of our BSAS results which may give us insight into the biological basis of conduct disorder phenotypes later on in life, of offspring whose mothers smoked tobacco *in utero*.
Conclusions: This research implicates epigenetic mechanisms, specifically DNA methylation, in the aetiology of the observed link between maternal smoking and childhood/adolescent conduct disorder, which could provide new insights into the mechanisms involved in the detrimental outcomes associated with *in utero* tobacco smoke exposure.

Estimated fetal weight does not modify the relationship of infant weight gain with childhood adiposity and blood pressure in the Southampton Women's Survey

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Background: Rapid infant weight gain is a major risk factor for childhood obesity. This relationship may, however, depend on whether or not rapid infant weight gain is preceded by fetal growth restriction. The developmental origins of health and disease paradigm, for example, posits that non-communicable disease risk is increased in children who experienced a poor nutritional environment *in utero* (which would cause fetal growth restriction) followed by an obesogenic environment postnatally (which would cause rapid infant weight gain). Although associated with measurement error, estimated fetal weight (EFW) provides a measure of fetal growth; we examined whether EFW across gestation might modify the relationship of infant weight gain with childhood adiposity and blood pressure.
Methods: Among 788 children in the Southampton Women's Survey we related weight Z-score change between 0-2 years of age to body mass index (BMI), %body fat, trunk fat (kg), systolic blood pressure (SBP), and diastolic blood pressure (DBP) at age 6-7 years using general linear regression models. EFW (kg) at 27 weeks of gestation, EFW change (% per week) from 10-27 weeks, and EFW change (% /week) from 27 weeks to birth were separately added to the models as potential effect modifiers (i.e., by incorporating interactions with the weight Z-score change exposure). Analyses were adjusted for putative confounders. Multiple imputation was used to account for missing data.
Results: Infant weight Z-score change was positively associated with all childhood outcomes. A unit increase in infant weight Z-score change was associated with a 0.69% (95% CI 0.34 to 1.04) increase in %body fat. We found no strong, consistent evidence that these effects were modified by the EFW variables (p-values > 0.2 for all interaction terms). For example, going from the 10^{th}-90^{th} percentile of infant weight change was associated with an increase in %fat of 2.0% in those who were at the 10^{th} percentile of EFW gain between 27 weeks to birth, compared with an increase of 2.2% in those who were at the 90^{th} percentile.
Conclusions: The relationship of rapid infant weight gain with cardiometabolic disease risk factors in childhood was not modified by EFW gain in utero.

Assisted reproductive technologies induce limited epigenetic variation at birth that largely resolves by adulthood

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Background/Aims: Over 8 million individuals have been conceived by Assisted Reproductive Technologies (ART). Extensive analyses have identified evidence for a range of adverse early life outcomes including rare imprinting disorders, while limited conflicting data also supporting potential longer term adverse health outcomes. Given that the period around conception and early embryogenesis is associated with widespread epigenetic remodelling, it is plausible that the early epigenetic profile is influenced by ART with potential to alter the developmental trajectory in utero, and potentially health throughout life. However, available data are circumstantial, limited, and at times contradictory.
Method: In this study we performed the largest epigenome-wide association study (EWAS) of ART using matched birth and adult samples. Using a unique longitudinal sample of ART conceived individuals, previously shown to have no differences in health outcomes, we profiled DNA methylation in blood collected early postnatally and in adults aged 22-35 years old. DNA methylation was profiled using the Illumina EPIC array, with over 720,000 probes analysed. ART-associated differential methylation was then tested in an independent ART methylation dataset.
Results: We found compelling evidence for specific ART-induced methylation variation around birth, some of which occurred independently of embryo culturing in both cohorts. Less evidence was found to support maintenance of ART-induced differential methylation into adulthood. No evidence of differential methylation was found in imprinting associated regions and measures of global methylation relative to non-ART individuals at birth and adulthood.
Conclusions: ART-induced epigenetic variation at birth largely resolves by adulthood and there is no direct evidence that this impacts any aspect of development and health.

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Inequalities in the distribution of childhood adversity from birth to 11 years according to socioeconomic position, ethnicity and Indigenous status

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Background/Aims: Exposure to early adversity carries long term harmful consequences for health over the life course. This study aims to 1) estimate the prevalence of childhood adversity for Australian children from infancy to 10-11 years, and 2) document inequalities in the distribution of adversity according to socioeconomic position (SEP) and ethnicity and Indigenous status.
Methods: Adversity was assessed every two years from 0-1 to 10-11 years in the nationally representative birth cohort of the Longitudinal Study of Australian Children (N=5107), including legal problems; family violence; household mental illness; household substance abuse; harsh parenting; parental separation/divorce; unsafe neighborhood; family member death; and bullying (from 4-5 years). Adversities were also summed to indicate multiple adversity (2+ adverse experiences).
Results: By 10-11 years, more than half of children (52.66%, 95% CI 50.74-54.57) had been exposed to two or more adversities. When combined with low socioeconomic position, children from visible minority and Indigenous backgrounds had four and thirteen times the odds of exposure to two or more adversities than children from higher SEP Anglo backgrounds (OR 4.47, 95%CI 3.05-6.54 and OR 10.05, 95%CI 5.09-19.81, respectively). Even visible minority and Indigenous children from higher SEP backgrounds had increased odds of exposure to multiple adversity than similarly advantaged Anglo children (OR 1.86, 95%CI 1.47-2.35 and OR 2.32, 95%CI 1.27-4.21, respectively).
Conclusion: The combination of visible minority or Indigenous status with low socioeconomic position appeared to compound risk for exposure to adversity, and higher socioeconomic position did not appear to confer the same benefits to children from visible minority or Indigenous backgrounds. Childhood adversity needs to be addressed as a likely contributor to the health inequalities experienced by these groups of children in later life.

The CLOSER UK longitudinal study consortium: Opportunities and outputs from our cross-disciplinary collaboration

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Background/Aims: The CLOSER consortium of UK cohort and panel studies aims to maximise the use, value and impact of longitudinal research. The cross-disciplinary resources developed by the consortium are of particular relevance to researchers seeking a longitudinal perspective on the social and biological determinants of health.
Method: CLOSER is collating metadata from across its partner studies to develop enhanced documentation and new technological resources for facilitating research scoping exercises. CLOSER is also leading efforts to open new avenues of cross-study and cross-generational inquiry through coordinated data harmonisation and linkage projects. The learning from CLOSER's diverse areas of work is in turn used to inform the development of best practice principles and training materials.
Results: CLOSER has launched an online data discovery/search tool comprising detailed information on 80,000 variables across 8 longitudinal studies and enabling exploration of study data according to topic or life stage coverage. CLOSER's 16 cross-study harmonisation projects to date have covered many health-related domains (e.g. obesity, dietary intake, social inequality, and DNA methylation), with the outputs made available for wider research usage. The consortium has also produced new resources to help researchers link survey datasets to routinely-collected data, such as guidance on precedents set for UK health record access. CLOSER is leading work to increase the policy impact of research, including through coordinated submissions to parliamentary committees. CLOSER regularly runs capacity-building events to share learning and has created an online educational resource, the CLOSER Learning Hub, to provide open-access training on longitudinal research practice.
Conclusions: The CLOSER consortium leverages the expertise and data of its study partners to produce new resources and opportunities for researchers seeking to explore how social and biomedical characteristics evolve over the life-course and across generations. Such collaborative work offers unique opportunities for extending our knowledge of health and its diverse determinants and helps to maximise the impact and benefit of this growing understanding.

The effective combination of indicators considering familial information for preventing hypertension disorders of pregnancy: the TMM BirThree Cohort Study

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Background/Aims: Hypertension Disorders of Pregnancy (HDP) is a major risk factor for preterm delivery and stroke. The aim of this study is to investigate the effective combination of indicators considering familial information for preventing HDP.
Method: The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (the TMM BirThree Cohort Study) recruited pregnant women and children, child's father and grandparents between 2013 and 2017. A total of 22,239 pregnancies were included and we conducted multiple logistic regression analysis adjusted for the possible cofounders and estimated the performance of screening by receiver operating characteristic (ROC) curve using the data of questionnaires and medical charts of the TMM BirThree Cohort study.
Results: The total of 1,020 (4.6%) pregnancies developed HDP. In multiple logistic regression analysis, older than 35 years old (odds ratio(OR)=1.74; 95% confidence interval (CI): 1.52-2.00), higher BMI (OR=3.72; 95% CI: 2.89-4.79), multiple pregnancy (OR=2.36; 95% CI: 1.57-3.54), smoking history (OR=1.20; 95% CI: 1.05-1.38), nulliparous women (OR=2.26; 95% CI: 1.95-2.61), assisted reproductive technology use (OR=1.26; 95% CI: 1.04-1.52), previous history of HDP (OR=6.70; 95% CI: 5.22-8.61) and hypertension history of pregnancies' mother (OR=1.56; 95% CI: 1.12-2.17) were related to HDP. Areas under the curve (AUC) was 0.7237 with household income, education level, and prevalence of hypertension of pregnant women's father, sister and brother, in addition to above variables.
Conclusions: Considering not only pregnant women's own characteristics but also familial information might be useful for improving the accuracy of AUC. Genetic mutation should be considered for further analyses.

Intrauterine Mild Hypoperfusion Model Rats Have a Risk of Developing Metabolic Syndrome

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Background/Aims: Intrauterine hypoperfusion/ischemia is one of the major causes of intrauterine/fetal growth restriction, preterm birth, and low birth weight. In previous studies, we developed a rat model of preterm birth/low birth weight based on sustained mild hypoperfusion in utero. In the present study, we investigated the influence of intrauterine blood flow reduction during fetal period on postnatal physical development and health.
Methods: Only the model rats weighing less than 5.5 g (-2 SD of standard body weight) at postnatal day 0 were used in this experiment as low birth weight (LBW) rats and compared with no-surgery control rats (6.0 g or more). The rats were examined up to 40 weeks of age. In this study, we measured body weight, body fat percentage, blood pressure, and serum levels of insulin and leptin.
Results: Of the items which measured in this experiment, significant differences between the two groups were observed only in body weight change, body fat, and blood pressure. The male LBW rats remained lighter during puberty and adulthood compared with no-surgery controls. On the other hand, the average body weight of the female LBW rats became heavier than no-surgery controls during puberty and adulthood the 40 weeks observation. The percentage of body fat was also significantly higher in the female LBW group. In the blood pressure, only the pulse pressure was a significantly higher in the male model rats, and there was no difference in the female model rats.
Conclusions: Even if intrauterine hypoperfusion insult is not severe, the model rats in females have a risk of developing metabolic syndrome after growth and in males changes the circulatory dynamics of adulthood.

Season of birth predicts infant's capacity to respond to childhood vaccination: a cohort study from rural Gambia

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Background/Aims: Environmental exposures during fetal life and early infancy are known to participate in the programming of the human immune system. Here, we examined the associations between season of birth and infant antibody responses to vaccination in rural Gambia which presents a tropical climate with a rainy/hungry (June—October) season and a dry/harvest (May—November) season.
Method: This study is a secondary analysis of a randomized clinical trial; Early Nutrition and Immune Development (ISRCTN49285450). We measured the antibody response to the first dose of the diphtheria-tetanus-pertussis (DTP) vaccine, administrated to infants at 8 weeks of age, in blood samples collected from 710 infants at 12 weeks of age. The effects of birth season on mean DTP antibody titres were analysed using linear regression models with adjustment for maternal; supplement, compliance to supplement, age, haemoglobin levels, education levels, morbidity, BMI, and gestational age at delivery, and infant; birth sex, birth month, weight-for-length Z-score, haemoglobin levels, morbidity, breastfeeding, and vaccination season, and comparisons of means with t-test.
Results: There were 37.6% (267/710) infants born in the rainy season. At 12 weeks of age, infants born in the rainy season had

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42.5% (95% confidence interval (CI) 36.4—48.6) higher mean anti-diphtheria titres (0.24IU/ml, 95% CI 0.21—0.28), 13.4% (95% CI 11.1—15.6) higher mean anti-tetanus titres (0.76IU/ml, 95% CI 0.73—0.80), and 16.8% (95% CI 13.8—19.8) higher mean anti-pertussis titres (6.6EU/ml, 95% CI 6.2—6.9) compared to infants born in the dry season (all, $P<0.001$).
Conclusions: In rural Gambia, being born during the annual rainy season was associated with higher antibody responses to vaccination in early infancy indicating that seasonal fluctuations may modulate infant immune development and function. Future research should investigate the seasonal-related factors involved and the underlying molecular mechanisms.
Conclusions: Please include conclusions here. All text including the above title, authors and affiliations are to fit inside this box. Abstracts exceeding this box or not adhering to the guidelines will be asked to resubmit. Please read the guidelines carefully. Do not change the font size or font type. The congress managers are only too happy to assist if you have any questions or queries.

Effect of antenatal dietary interventions in maternal obesity on pregnancy weight-gain and birthweight: Healthy Mums and Babies (HUMBA) randomized trial

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Background/Aims: Obesity is increasing globally, especially in low socio-economic regions. Counties Manukau health region in South Auckland, New Zealand is home to a multi-ethnic population, with high socio-economic deprivation and high rates of obesity in pregnancy, especially among Māori and Pacific populations. The Healthy Mums and Babies (HUMBA) RCT investigated whether a culturally tailored dietary intervention and/or probiotic capsules in pregnant women with obesity would reduce excessive gestational weight gain (EGWG) and birthweight.
Method: Two-by-two factorial randomised controlled trial conducted in Counties Manukau, South Auckland, New Zealand. Non-diabetic, pregnant women with obesity (BMI $\geq$30 kg/m^2) and a singleton recruited between 12^0 and 17^6 weeks were randomly allocated to: tailored dietary education intervention (provided by a community health worker trained in key aspects of pregnancy nutrition plus text messaging) or to routine dietary advice; and to daily capsules containing (*Lactobacillus rhamnosus GG and Bifidobacterium lactis BB12* at 6.5 x10^9 colony forming units) or placebo. Co-primary outcomes were EGWG (>0.27kg/week) at 36 weeks (adjusted BMI) and birthweight (adjusted for gestational age, maternal BMI, infant sex, ethnicity).
Results: 230 of 455 eligible women participated (Dietary intervention N=116, Routine dietary advice N=114, Probiotics N=115, Placebo N=115). Rates of EGWG did not differ significantly between groups (Dietary vs Routine: 74% and 82%, aOR 0.67 95%CI 0.35 to 1.29, p=0.23; Probiotics vs Placebo: 82% and 73%, aOR 1.82 95%CI 0.94 to 3.54, p=0.08). Birthweight also did not differ between groups (Dietary vs Routine: 3585g and 3602g, adjusted mean difference (adj MD) -24g 95%CI -146 to 97, p=0.70; Probiotics vs Placebo: 3638g and 3550g, adj MD 106g, 95%CI -14 to 228, p=0.08). Total weight gain was less with dietary intervention compared with routine advice: (9.7 vs 11.4 kg, adj MD -1.76, 95% CI -3.55 to 0.03, p=0.05). GDM rates and other outcomes did not differ by intervention.
Conclusions: Neither a tailored dietary intervention nor probiotics reduced rates of EGWG or birthweight in this multi-ethnic population of women with obesity. Dietary intervention resulted in a modest reduction in total weight gain of 1.76 kg, which could be beneficial if sustained. No short term benefits of probiotic capsules were identified and the non-significant increase in EGWG and birthweight with probiotics raises the question of possible adverse effects with probiotic supplements.

Atopic dermatitis is associated with stunting and poor growth: results from Indonesian infants

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Background/Aims: As the leading paediatric chronic inflammatory skin disease, atopic dermatitis (AD) inflicts substantial health burdens. Although avoidance of causative food could reduce AD severity, it often leads to unnecessary food intake limitations, and ultimately nutritional deficiencies and poor growth. This early growth insufficiency is related to later adverse metabolic outcomes, as hypothesised in the Developmental Origins of Health and Diseases (DOHAD) theory. This study aimed to examine how AD status affects infancy growth in Indonesian population.
Method: From single primary healthcare in Jakarta, 395 mother-infant dyads were recruited to the Indonesian Prospective Study of Atopic Dermatitis in Infants (ISADI). All infants were term, vaginally-delivered, and with no significant pregnancy comorbidities. Weight, height, waist circumference, and skinfolds (triceps, subscapular, and suprailiac) were measured between 0-12 months. Growth measures were converted to the standard deviation scores (SDS) based on WHO growth standard, adjusted for infant sex and visit age.

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AD was diagnosed based on Hanifin and Rajka criteria by a paediatrician dermatologist.
Results: The prevalence of AD in our cohort was 15.2% (N=60) and most of them (40%) were diagnosed as early as 3 months of age. Compared to controls, infants with AD had poor gains in weight (mean±SD -0.15±0.38 vs 0.36±0.92, respectively; *p<0.0001*) and adiposity measured by skinfolds (-0.97±2.1 vs -0.32±1.86, *p=0.048*) between 9-12 months. At 12 months, infants suffering from AD were significantly shorter compared to controls (B=-1.17, *p<0.0001*), adjusted for infant and parental factors. Stunting (length ≤-2 SDS) prevalence in this cohort ranged between 16.2-26.6% across time points. Children with AD had significantly higher stunting prevalence at 12 months than controls (29.8% vs 13.1%, OR=3.84, *p=0.002*).
Conclusions: Among Indonesian infants, AD occurrence during infancy was associated with stunting and poor growth between 9-12 months. In line with previous investigations, we assume that AD may affect not only the skin but also induce systemic inflammation and intestinal mucosa damage and malassimilation, which may have long-term health implications.

Primary prevention of fat and weight gain among obesity susceptible normal weight preschool children. Results from the "Healthy Start" randomized controlled intervention

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Background/Aims: Successful treatment of obesity is well documented among children. The real public health challenge lies in understanding the primary drivers behind excessive weight gain among normal weight individuals. The objective of this primary prevention RCT was to examine if excessive weight and fat gain can be prevented among normal weight, but obesity susceptible, young children aged 2-6 years.
Method: Eligible children were identified based on information on either a high birth weight, maternal pre-pregnancy obesity, or maternal low educational level from national registries, and randomized into the intervention group, or the control group. Trained project staff took anthropometric measurements at baseline and follow-up. All overweight children were excluded from subsequent analysis (n=92), while all normal weight children were included (n=543). The intervention aimed to deliver improvement in diet and physical activity habits, optimization of sleep quantity and quality and reduction of stress in the family. Average intervention period was 1.3 years.
Results: Intention-to-treat analyses showed a higher gain in fat free mass (β = 0.37 (95% CI, 0.00;0.73, p = 0.05)), and a lower gain in %-fat mass (β = -1.81 (-3.68;0.05), p = 0.06)) in the intervention group compared to the control group. Intervention effects were generally larger in children < 4 years.
Conclusions: This primary prevention intervention, conducted among young normal weight children with a susceptibility to future obesity, suggested improved growth and body composition after 15 months intervention, especially among the youngest children.

Overview of OPERA (Optimal Pregnancy Environment Risk Assessment), a Worldwide Universities Program

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Background/Aims. OPERA is an international, interdisciplinary program of researchers, care providers, health administrators, foundations and agencies dedicated to discovering and disseminating inexpensive and accessible tools to diagnose those women at risk for adverse pregnancy and newborn outcomes as early as possible in pregnancy and to promoting effective interventions to mitigate these risks.
Methods. Meetings and workshops are organized in conjunction with interested parties internationally and regional care providers, researchers and health administrators to encourage, guide and facilitate local efforts to develop and use tools appropriate for the jurisdiction to predict risk for adverse pregnancy and newborn outcomes. OPERA meetings and workshops help local professionals learn more about the risks in their jurisdictions, the latest advances in risk assessment, and to share ideas, tools and platforms to begin predicting risk locally and the means to mitigate those risks. OPERA connects professionals in local jurisdictions with other professionals internationally to provide advice and support for each phase of a research project or trial. Its website (www.operamtg.org) is designed to describe and share the latest risk prediction tools and encourages them to be trialed in a variety of settings to determine how robust and universally applicable they may be.
Results. Preparatory workshops: World Health Organization, Geneva, 2013, 2014. International Preterm Birth – Industry Meeting: Ottawa, Canada, November 2014 (www.ptbmeeting.org). Inaugural meeting: San Francisco, March, 2015 (www.operamtg.org). OPERA China Workshop: Chongqing, November, 2016. OPERA China Update: Chongqing, September 18, 2018. OPERA Europe Meeting: Pforzheim, Germany, December 11-12, 2018. OPERA India: 18 February – 25 February, 2019. OPERA Workshop at Social determinants and the health of Indigenous peoples Satellite Meeting, Darwin, October, 2019. OPERA Preterm Birth Symposium, DOHaD Congress, Melbourne, October, 2019. OPERA Ghana Meeting, Accra, Ghana, May, 2020.

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Conclusions. The OPERA program is growing with meetings and projects in most continents.
Sponsored by the Worldwide Universities Network.

Mismatch Between Fetal And Postnatal Growth: Slow Fetal Growth Followed By Rapid Postnatal Weight Gain Is Associated With Increased Ectopic Fat In 4.5-Year-Old Children

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Background/Aims: Both poor fetal growth and a rapid postnatal weight gain have been linked to adverse cardiometabolic outcomes. Cross-sectional studies in adults and children have also linked abdominal and ectopic fat accumulation with adverse metabolic health. We investigated if a mismatch in fetal and postnatal growth can result in elevated abdominal and ectopic fat in early childhood.
Method: In 815 participants in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort, we defined fetal growth deceleration (FGD) as a decrease in ultrasound-measured abdominal circumference by at least one major centile band (0.67 standard deviation) from the 2nd to 3rd trimester, and rapid postnatal weight gain (RPWG) as increase in weight by at least one major centile band (0.67 standard deviation) from birth to 2y. At 4.5y, anthropometry was measured and a subset of 281 subjects underwent MRI and MRS to measure abdominal fat, intramyocellular lipids (IMCL), and liver fat. Associations were evaluated by multiple linear regression adjusting for confounders.
Results: Participants were classified into 4 categories, namely FGD + RPWG (12%), FGD + no RPWG (14%), no FGD + RPWG (24%), and no FGD + no RPWG (50%). RPWG alone or a combination of FGD and RPWG was associated with increased BMI and abdominal adiposity while FGD alone was not, when compared to the group without FGD and RPWG. Only a combination of FGD and RPWG was associated with increased IMCL (0.12% of water signal; 95% CI: 0.00, 0.24) and liver fat (0.20% by weight; 95% CI: 0.04, 0.36).
Conclusions: Children who experienced both FGD and RPWG had higher ectopic fat, distinctly differentiating them from those who only experienced FGD or RPWG alone. Our results suggest that a mismatch of poor fetal growth and rapid postnatal weight gain may lead to pathogenic fat accumulation and development of an unfavourable metabolic phenotype during early life.

A Qualitative Description of Parents, Perinatal Clinic staff, and Mentor Elders Experiences of an Indigenous Community-Derived Elders Mentoring Program

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Background/Aims: Responding to concerns over perinatal health risks and adverse outcomes, a community-based participatory research (CBPR) partnership was established in collaboration with a large Indigenous community in Alberta and university-based researchers. An Elders Mentoring Program was designed and implemented to provide additional support for pregnant women and their partners. Our aim was to understand the collective experiences of those involved in the Program.
Methods: We conducted a qualitative description with the principles of CBPR as an over-arching framework. A total of 14 qualitative interviews were conducted with parents utilizing the Program, perinatal clinic staff helping to facilitate the Program, and mentor Elders that engage with parents as part of the Program. Community Advisory Committee meeting notes were also used as data. All qualitative data was analyzed using content analysis.
Results: The Program helps pregnant women and their partners by fostering enhanced support networks as well as improved cultural security within the clinical environment and learning among healthcare staff. A sense of intergenerational fulfillment and enjoyment among those involved in the Program was common that was underpinned by genuine collaboration and relationships.
Conclusion: Successful implementation of a community-derived prenatal Elders Mentoring Program is possible with significant community collaboration.

Paternal aging affects to offspring's behavior and gene expression possibly through inheritance of hypomethylated DNA regions elicited in NRSF/REST binding sites

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Background/Aims: Paternal aging has deleterious effects on a risk of children's health such as low birth weight and psychiatric/neurodevelopmental disorders. Here, we establish a mouse model to analyze molecular mechanisms underlying the effects due to paternal aging on phenotypes of offspring.
Method: To examine paternal aging effect on behavioural and histological phenotypes of F1 offspring mice, F1 mice were produced from F0 young (3 month) and F0 aged (12-18 month) C57Bl/6J male mice. Body weight and ultrasonic vocalization induced by maternal separation were measured and brain structures were histologically examined at postnatal day 6 (P6). RNA-seq was performed on embryonic brain samples derived from young or aged fathers and gene set enrichment analysis (GSEA) was applied to compare with our previous data of whole genome DNA methylation in young and aged sperm.
Results: F1 offspring derived from F0 aged male showed lower body weight and impaired vocal communication at P6. Thickness of the primary motor cortex at P6 was reduced especially in the deep layer in F1 offspring derived from F0 aged male. GSEA demonstrated that late-fetal genes and autism related genes registered in the database (SFARI genes) were enriched in the embryonic brain derived from aged father. Interestingly, expression of genes with NRSF/REST binding motifs in regulatory regions were significantly up-regulated in the embryonic brain derived from F0 aged male mice. This is consistent with 16-hyper/96-hypomethylated DMRs with NRSF/REST binding motifs in the targeted DNA methylome analysis of F0 aged sperm identifying enriched.
Conclusions: Because NRSF/REST serves as a pivotal transcription factor that negatively regulates neuronal differentiation, our findings suggest a possible scenario that paternal aging may induce precocious neurogenesis in the offspring's brain through the inheritance of sperm DNA hypomethylation elicited near NRSF/REST binding sites. This scenario can explain diverse phenotypes of individual patients suffering from neurodevelopmental disorders, and paternal aging may actually be a cause for recent increase in the number of babies with low birth weight as well as unignorable rise in neurodevelopmental disorders.

Advanced maternal age and cord serum thyroid hormones in Chinese infants born via cesarean section deliveries

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Background/Aims: Thyroid hormones are essential for fetal growth and neurodevelopment. In China, rates of cesarean section (C-section), especially those on demand (without clinical indications) are high, which provides opportunity to explore cord blood thyroid hormones levels in "physiological conditions". In addition, population-based data on thyroid hormones in cord blood are sparse in China. We aimed to assess cord serum levels of free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH) in full-term Chinese newborns, and examine perinatal factors associated with thyroid hormones.
Method: This study included 922 mother-newborn pairs from a prospective birth cohort enrolled in 2012-2013, Shanghai, China. Cord serum concentrations of FT3, FT4, TSH, and TPOAb were measured by chemiluminescent immunoassays.
Results: Infants born via vaginal delivery had lower FT3 (geometric mean: 1.78 pmol/L) and higher TSH (7.59 mIU/L) than those via C-section (FT3: 1.96 pmol/L; TSH: 4.73 mIU/L). In C-section deliveries, advanced maternal age (≥30 years old) was associated with lower FT3 ($p<0.05$). Gestational age (GA) was positively associated with FT3. LGA (birth weight-for- GA >90th percentiles) was associated with elevated TSH. In vaginal deliveries, induction of labor and long duration of second stage of labor (>75th percentile) were associated with higher TSH.
Conclusions: Our study is the first to show that advanced maternal age was associated with lower FT3 in cord blood, suggesting a potential mechanism of the adverse impact of advanced maternal age on neurodevelopment in early life. We have presented the levels of thyroid hormones in a contemporary Chinese healthy term birth cohort.

Continuing questionnaire surveys on understanding of DOHaD concepts in students during undergraduate nutrition programs in Japan (2016-2018)

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Background/Aims: We have been undertaking questionnaires examining awareness and understanding of DOHaD-related terms and concepts in students during undergraduate heath professional programmes in Japan and New Zealand, and published 2015 data (JDOHaD 9: 253–259, 2018). To confirm results obtained in 2015, we continued the similar surveys in 2016-2018 in Japan. In 2018, two open-ended questions were

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added in the questionnaire to determine the level of understanding of DOHaD concepts more precisely.
Method: A standardized questionnaire (JDOHaD 9: 253–259, 2018) was completed by Year 1–4 undergraduate students studying nutrition in Japan in 2016-2018. Two open-ended questions added in 2018 are (1) "What nutritional conditions of pregnant women increase the risk of developing lifestyle-related diseases when the child reaches adults?" and (2) "What is the mechanism for this action?".
Results: Continued questionnaires performed in 2016-2018 confirmed the previous results; (1) On entry to undergraduate study, most students had no awareness of the terms and concepts of DOHaD; (2) While levels of understanding of DOHaD concepts increased across program years, overall awareness was less than optimal. The survey of each year from 2016 to 2018 showed that the level of DOHaD understanding improved between Year 1 and Year 2. However, changes in the level from Year 3 to Year 4 varied from year to year. Results from the two open-ended questions added in 2018 demonstrated that less than 20% of the students answered that both (overnutrition OR obesity) AND (undernutrition OR thinness) are associated with risk of developing lifestyle-related diseases.
Conclusions: The current study (2016-2018) confirmed that our undergraduate nutrition education program contributes to the development of understanding of DOHaD concepts. However, the final level of understanding attained by Year 4 is insufficient. Continued exploration of concepts in Years 3 to 4 is required to consolidate knowledge and promote deeper understanding of DOHaD.

High fat diet exposure during adolescence induces cardiometabolic syndrome in adulthood

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Background/Aims: Exposure to high fat diet during gestation and suckling programs metabolic syndrome in adulthood and evidence suggest that adolescence is another programming window. The present study aims to evaluate whether high fat diet exposure during adolescence induces metabolic syndrome in adulthood.
Methods: Thirty day-old Wistar rats were exposed to a high fat (HF, 35% lard w/w) diet from birth until 30 days of age then fed a normal fat diet (NF, 4.5% w/w of fat) for a further sixty days. Control animals received the NF diet throughout life. Body weight and food consumption were evaluated throughout the protocol. At 120 days of age biometric, metabolic (ivGTT, ipITT and histology of pancreas) and cardiovascular parameters were evaluated. Statistical comparisons were performed by Student´s T test.
Results: Animals showed greater body weight and food intake after exposure to HF. At 120 days of life HF diet induced increased mesenteric and retroperineal fat deposits (+55%; p<0,001), hypertriglyceridemia (+60%, p<0.001), hyperglycaemia (+56%, p<0.05) and reduced sensitivity to insulin (-33%, p<0.05) compared with control animals. Systolic blood pressure was increased in HF animals compared with control (125 mmHg ±1.8 vs. 118 ± 2.0 mmHg,, p< 0.05;), while heart rate (HF: 339 ± 10 vs. NF: 339 ± 9 bpm, p=0.49) was similar. The depressor blood pressure response to hexamethonium was greater in HF compared with NF animals (?PAS -44 ±1.4 vs. -37 ± 3.5 mmHg,, p<0.05; ?PAD -32 ±2.3 vs. -24 ± 3.0 mmHg, p< 0.05). Beta cell mass was 57% increased and islet area was 100% greater in HF compared with NF animals (p<0.001).
Conclusions: Exposure to HF during adolescence programs cardiometabolic syndrome during adulthood, characterised by insulin resistance and structural changes to beta cells as well as hyperactivity of vascular sympathetic nervous system. These data further highlight the importance of maintaining sound dietary intake during the adolescent developmental window.

Early adrenaline fall improves cardiometabolic function in adult male rats

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Background/Aims: Obesity and its comorbidities (high blood pressure, hyperglycemia and dyslipidemia) characterise the cardiometabolic syndrome, which is an important risk factor for cardiovascular death. The sympathetic nervous system has an important role in the regulation of blood pressure and glucose levels, including contribution of adrenal medulla. In this context we hypothesize that adrenodemedulation may contribute to long-term control of cardiometabolic parameters.
Method: Sixty days-old Wistar male rats were submitted to bilateral adrenodemedulation. Operated animals with 120-days-old were observed to evaluated blood pressure, fat pad deposition (retroperitoneal and mesenteric) and glucose tolerance.
Results: Early adrenodemedulation increased the body fat deposition in 51% for retroperitoneal fat pad and in 64% for mesenteric fat pad, characterizing obesity onset; however, those rats presented increased glucose tolerance, in 8.4% regarding sham-operated rats (p<0.01), and blood pressure was reduced in 12% (p<0.001).
Conclusions: The present data suggest that, although program of obesity, early blocking of adrenaline production improved cardiometabolic function when the young rats turned to adult life.

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Exposure to fructose in adolescence increases sympathetic activity and has little impact on the deleterious effects of high fat diet in adult rats

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Background/Aims: Adolescence is a critical developmental window characterized by physical, hormonal and psychological plasticity and a susceptible phase for programming of cardiometabolic syndrome. Experimental animal studies have shown that perinatal high fructose consumption induces hypertension in adulthood. Furthermore, high fat diet offered during adulthood triggers obesity and hypertension. In this context we hypothesize that exposure to fructose during adolescence may program the metabolism and potentiates the deleterious effects of the high fat diet in adulthood.
Methods: Adolescent Wistar rats (30 to 60 day-old) were exposed to fructose (Fr), (10% of fructose) in the water and also to a high fat (HF) diet in adult life (90 to 120 days-old). Control animals had access to normal commercial (NP) chow. Blood pressure and pulse interval were recorded in 120-day-old rats. Biometric parameters were evaluated during their entire lives. ANOVA two way test was used to compare groups.
Results: Fructose intake did not affect biochemical and biometric parameters of the animals, however, the HF diet induced a 25% increase in serum levels of total cholesterol and glycemia (p_{HF} <0.01), animals exposed to the HF diet presented elevation of energy consumption by 27.2% (p_{HF} <0.001) leading to a 13% (p_{HF} <0.0001) weight gain of the same animals. There was no change in blood pressure due to fructose intake, but there was a 10% increase in the systolic and diastolic blood pressures of the animals fed the HF diet (p_{HF} <0.001). Ingestion of fructose in adolescence caused a 47.4% increase in the low frequency zone of systolic blood pressure (p_{Fr} <0.01) and did not change due to the consumption of HF. It was also observed a decrease of 46% in the high frequency zone of the pulse interval of the animals ingested fructose (p_{Fr} <0.01), but the animals that ingested the HF diet increased the same parameter by 48.2% (p_{HF} <0, 01).
Conclusions: Exposure to 10% fructose during adolescence induces increased sympathetic activity in adulthood, but has little impact on the deleterious cardiometabolic effects of the high fat diet in adult animals.

Dairy Consumption and Risk of Gestational Diabetes Mellitus in China: A Prospective Cohort Study

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Background/Aims: Higher dairy consumption has been linked to lower risk of type 2 diabetes mellitus, however, its association with gestational diabetes mellitus (GDM) has received little attention. This study aimed examine the prospective association of dairy consumption with risk of GDM in a large cohort of pregnant women in western China.
Method: We analyzed dairy intakes assessed using a food frequency questionnaire at the first trimester (study baseline) in a large cohort of pregnant women enrolled between April 2017 and November 2018 in Shuangliu District of Chengdu, western China. The prospective associations between baseline dairy intakes and newly diagnosed GDM was examined using multivariable logistic regression.
Results: 215 (6.8%) developed GDM among 3163 pregnant women aged 27.0 years (standard deviation, 3.7). Only 5.1% of pregnant women met the recommended daily intakes of dairy products of 300 grams by the Chinese Nutrition Society, with the women consuming 100 gram (Interquartile range, 0, 250) of total dairy products per day. Milk and yogurt were the most frequently consumed dairy products, with 21.2% and 7.4% of women reporting daily consumption, while other dairy products including cheese, butter, and cream were consumed daily by less than 1.5%. Total dairy consumption was not statistically associated with incident GDM (odds ratio [OR] for the fourth versus first quartile of gram intakes, 1.15; 95% confidence interval [CI], 0.60, 2.20). In addition, daily consumption of major diary products did not show associations with incident GDM: OR of 1.25 (95%, 0.86, 1.80) for milk, and 1.02 (95%, 0.58, 1.77) for yogurt.
Conclusions: The intakes of dairy products were low in pregnant women in western China. Higher total dairy consumption and intake specific dairy products were not associated with incident GDM in these Chinese pregnant women. Future studies may need to be conducted in pregnant women with higher dairy intakes.

Association of breast milk feeding with later child eating behaviours

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Background/Aims: Individual differences in eating behaviours emerge early in childhood and are influenced by the early feeding environment. We examined the relationship between breastfeeding (BF) exposure and subsequent eating behaviours among children from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort.
Method: Children ($n = 970$) were grouped according to their BF exposure: high (full BF≥4 months (m) with continued BF≥6m), low (no BF or any BF<3m) and intermediate (between low and high BF categories). Eating behaviours from 15m to 6 years old (y) were captured using a combination of maternal reports (Child Eating Behaviour Questionnaire; Maternal Feeding Practices and Beliefs Questionnaire) and laboratory-based measures of meal size, eating speed, oral processing behaviours (e.g. bite size) and eating in the absence of hunger. Multiple linear regression analyses were used to examine the association between BF exposure and later eating behaviours.
Results: The majority of children had low (44.3%) or intermediate (43.5%) BF exposure, with 12.2% classed as having high BF exposure. After adjusting for maternal educational attainment, pre-pregnancy BMI, child sex and other confounders, the high BF group scored significantly lower on food fussiness at 3y when compared to the low BF group (adjusted mean differences, 95% CI: -0.38, -0.70 to -0.06); similar non-significant trends were observed at 5y and 6y (-0.19, -0.50 to 0.11 and -0.27, -0.66 to 0.11, respectively). At 3y, mothers in the high BF group also reported the least difficulty in child feeding when compared to the low BF group (-0.22, -0.43 to -0.01). There were no significant associations between BF exposure and reported satiety responsiveness or any of the laboratory measures of eating behaviour.
Conclusions: High BF exposure during infancy was associated with less food fussiness but not satiety responsiveness or measured eating behaviours in early childhood.

Understanding The Cumulative Risk Of Maternal Prenatal Bio-Psychosocial Stressors On Birthweight - A DynaHEALTH Study On Two Birth Cohorts

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Background/Aims: There are various maternal prenatal biological and psychosocial predictors of birthweight, making it difficult to quantify their cumulative relationship. We aimed by modelling to derive composite maternal prenatal bio-psychosocial (BPS) construct and explored relationship with birthweight across two European populations.
Method: We studied two birth cohorts: Northern Finland Birth Cohort 1986 (NFBC1986) born in 1985-1986, and the Generation R Study born in 2002-2006. In NFBC1986, we selected BPS variables associated with birthweight and performed factor analysis to derive latent constructs representing these variables. In Generation R, the same factors were generated weighted by loadings of NFBC1986. Factor scores were allocated into tertiles to calculate a cumulative BPS score. In all cases, we used regression analyses to explore the relationship with birthweight corrected for sex and gestational age and additionally adjusted for other factors.
Results: Factor analysis supported a four-factor structure, labelled as '*BMI*' (Body Mass Index), '*DBP*' (Diastolic Blood Pressure), '*Lifestyle*', and '*Family*'. In both cohorts, '*BMI*' was positively associated with birthweight, whereas other factors showed negative association. The psychosocial factors '*Lifestyle*' and '*Family*' had the greatest effect size, explaining 30% of the variation in birthweight. Associations of the factors with birthweight were largely driven by '*BMI*' factor. Graded decrease in birthweight was observed with increasing BPS score in both cohorts.
Conclusions: This maternal bio-psychosocial model produces factors showing consistent association with birthweight and the cumulative BPS score represents a cumulative risk of lower birthweight among those with a higher risk score in both cohorts.

Cardiovascular risk factors in offspring exposed to Gestational Diabetes Mellitus: a systematic review and meta-analysis

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Background/Aims: Gestational diabetes mellitus (GDM) is the fastest growing diabetes condition in Australia. Women exposed to GDM are at increased risk of cardiovascular disease. Emerging evidence suggests that offspring exposed to GDM *in utero* may demonstrate risk factors of cardiovascular disease. Therefore the primary aim of this systematic review and meta-analysis is to determine the cardiovascular risk factors in offspring exposed to GDM.
Method: PubMed, CINAHL, SCOPUS, and EMBASE databases were searched. Information was extracted on established CVD risk factors including blood pressure, lipids, blood glucose, fasting insulin, body mass index (BMI) and endothelial/microvascular function. Prospective and retrospective studies comparing offspring exposed to GDM *in utero* compared to

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controls (i.e. non-GDM pregnancy) were considered. We included studies which defined GDM based on the IADPSG definition, or prior definitions. The PRISMA guidelines were followed in conducting this systematic review. Methodological quality was assessed using the Newcastle – Ottawa Quality Assessment Scale. Study selection, data extraction and quality assessment were done by two independent reviewers. The data were pooled using a random-effects model. The review protocol is registered in PROSPERO (CRD42018094983)

Results: Of 59 eligible studies, 23 were included in the meta-analysis. Offspring exposed to GDM had higher systolic blood pressure (MD: 2.18 mmHg, 95% CI 1.14-3.21; seven studies, 7,264 participants), BMI (MD: 1.15 kg/m^2 (95% CI 0.46-1.83; 14 studies, 8,759 participants) and glucose (SMD 0.43, 95% CI 95% CI 0.08-0.77; 11 studies, 6,423 participants) than control participants.

Conclusions: Offspring exposed to GDM have elevated systolic blood pressure, BMI and glucose. Those exposed to GDM *in utero* may benefit from early childhood blood pressure measurements.

Adolescent Voices Matter Too: Exploring the Nutritional Views of Pacific and Māori Adolescents in a Low-income Community in Auckland

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Background/Aims: The adolescent life-phase is when significant cognitive and psychosocial behaviours are set and persist into adulthood. This life-phase in the next generation of parents offers opportunities to influence environmental exposures and nutritional choices that may affect the health of future offspring, well before conception. Experimentation and seeking autonomy are features of adolescent behaviour that can be leveraged in interventions. However, prior to interventions, it is essential to explore factors influencing adolescent health.

Pacific and Māori populations in New Zealand have high rates of noncommunicable diseases (NCD). It is known that obesity is positively associated with NCD risk factors and NCD incidence. In New Zealand, obesity rates for Pacific (65%) and Māori adults (47%) are much higher than the overall rate for the adult population (32%). Of further concern are the increasing rates of NCD risk factors among children in these populations leading to a snowball effect as these children and adolescents become adults and future parents thus perpetuate a cycle of obesity across generations.

Method: Adolescents (13 to 14 years of age) from an Auckland school in a low-income community participated in semi-structured focus groups. Eight groups with 28 adolescents (13 females, 15 males) were involved. The school demographic is representative of the community population where the majority are of Māori and Pacific descent.

Results: The adolescents discussed five key factors that influence their nutritional choices; cost, media influences, influential people, agency, and individual preference.

Conclusions: Understanding what influences adolescent nutrition choices is key to the development of effective intervention strategies. Commonly, the adolescent voice is neglected in the development of strategies. However, understanding their views and context is essential to the intervention's success.

Fecal microbiota transplantation during lactation protects against pancreatic islet disfunction in obese rats

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Background/Aims: Recently, it has been implied that the microbiota is involved in obesity onset. The first contact happens during early life but the effects of microbiota in metabolic programming at adulthood are still not understood. The aim of this work was to evaluate the transplantation of fecal microbiota during lactation to female offspring rats from lean and obese mothers.

Method: NL (normal litter) and SL (small litter) males and females (parents), from different litters, were mated, NL male vs NL female; SL male vs SL female. At birth, the litter was standardized in the 3rd day of life to NL or SL. From the 10th until the 25th day of life the offspring received gavage of a solution containing the diluted feces of the opposite dam. Four experimental groups were created: normal litter offspring saline (NLS), normal litter offspring fecal microbiota (NLM), small litter offspring saline (SLS), small litter offspring microbiota (SLM).

Results: Early life obesity caused glucose intolerance in SLS and SLM groups, fecal microbiota transplantation protected against insulin resistance. All groups had increased secretory response of insulin to glucose 5.6 and 8.3 mmol/L; however, fecal microbiota transplantation lowered secretory response to glucose 16.7 mmol/L from NLM and SLM groups. Fecal microbiota transplantation also leads to decreased cholinergic insulinotropic response. NLM animals showed increased adrenergic insulinostatic response, SLM animals showed an opposite response.

Conclusions: Fecal microbiota transplantation caused protection against pancreatic islet dysfunction caused by obesity in early life.

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Parallel Transverse Uterine Incisions, a Novel Approach for Managing Heavy Hemorrhage and Preserving the Uterus: A Retrospective Cohort Study for Patients with Placenta Previa and Accreta.

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Background/Aims: Placenta previa and accreta with prior cesarean section is an extremely serious condition that is associated with maternal morbidity and mortality from obstetric hemorrhage. We sought to evaluate the efficacy and advantages of a novel surgical technique, parallel transverse uterine incisions (PTUI), during conservative cesarean delivery in patients with placenta previa and accreta.
Method: This was a retrospective cohort study including 124 pregnant women, who had at least one prior cesarean section and were prenatally diagnosed with placenta previa and accreta between January 2014 and October 2017. Information on demographic and clinical characteristics was collected from the hospital's information system. Patients were retrospectively classified into undergoing either the PTUI surgery (Group A) or the traditional cesarean section (Group B). Main outcome measures are surgical outcomes and maternal complications during hospitalization. The results from two groups were compared and analyzed statistically.
Results: We identified 124 patients. Patients who underwent PTUI were not statistically different from patients who underwent the traditional cesarean section in terms of maternal age, parity, body mass index, number of uterine curettages, number of previous caesarean deliveries, gestational age at delivery, and so on. Neonatal outcomes were also similar between two groups. However, PTUI was associated with remarkably reduced intraoperative blood loss ($P = 0.005$), related vaginal blood loss in the first 24 hours after surgery ($P = 0.026$), and transfusion requirement of packed red cells ($P = 0.000$), compared to the traditional caesarean section. Moreover, cesarean hysterectomy (3.3% versus 21.9%; $P = 0.002$) and intensive care unit admission (1.7% versus 29.7%; $P = 0.000$) were significantly fewer among patients who underwent PTUI. Multivariable regression analyses further showed that the risk of intraoperative hemorrhage ($\beta = -2343.299$,$P = 0.000$) and cesarean hysterectomy ($OR = 0.027$,$P = 0.018$) were both significantly decreased by PTUI.
Conclusions: PTUI is a novel approach that may significantly reduce maternal complications, such as heavy bleeding, blood transfusion requirements and intensive care unit admission, while preserving the uterus for patients with placenta previa and accreta.

Associations Between Maternal Gestational Diabetes Mellitus, Body Mass Index And Breastmilk Production

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Background/Aims: Infants born to mothers with gestational diabetes mellitus (GDM) are at increased risk of overweight and obesity, hypertension, and type 2 diabetes. Human milk feeding reduces the risk of these diseases, with a dose-response effect observed. Continued breastfeeding offers a strategy to ameliorate the programming effects of GDM on the offspring. However GDM mothers have shorter breastfeeding duration. Low milk production is a commonly cited reason for early cessation of breastfeeding. High BMI is a risk factor for both GDM and early cessation of breastfeeding. It is not known whether milk production is lower in women with GDM, and whether it differs by BMI.
Method: We extracted from our database 24 h milk profile and background data for GDM mothers of singleton term infants aged 1 - 6 months. Over a 24 h period mothers used electronic scales (sensitive to ± 2 g) in their own home. to test-weigh their infants with each breastfeed, and measured any expressed milk volumes. The sum of these provided the 24 h milk production volume, with low production defined as < 600 mL/ 24 h.
Results: 24 h milk productions were available for 44 GDM mothers, with the median (range) 567 (22 – 1147) mL/24 h; lower than reference 788 mL /24 h. Low milk supply occurred in 59% (n=26). BMI categories of the sample were underweight (n=1); normal BMI (n=18); overweight (n=11) and obese (n=12), BMI data were not available for n=2. 24 h milk production volume was associated with maternal BMI (p=0.009).
Conclusions: Our data suggest GDM is associated with impaired milk production that is further impacted by a high maternal BMI. This has implications for the longer term health of infants. A prospective study will enable investigation of its aetiology and allow for consideration of extrinsic factors that influence milk production.

Influence Of Pre-natal And Early-life Animal Exposures On The Risk Of Asthma And Allergic Disease In The Danish National Birth Cohort

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Background/Aims: Evidence suggests that the human microbiome is essential for the normal development of the immune system, including protecting against immune dysregulatory diseases such as asthma and allergy. Support for the key role of the microbiome in health and disease comes from farm and pet studies, where early-life exposure to a traditional farming environment or to pets has been observed to reduce the risk of childhood asthma or allergy. However, findings from studies have been inconsistent; this could be related to differences in the timing, type and degree of animal exposures, as well as a failure to consider exposures outside the home. The aim of this study was to provide a comprehensive analysis of how pre-natal and early-life exposures to animals influence the risk of childhood allergy and asthma, taking into account type, timing and source of exposure.
Method: We used data from approximately 32,000 mother-child dyads from the Danish National Birth Cohort (DNBC), including data on mothers' pre-natal occupational and domestic animal exposures, and the child's animal exposures at 18 months of age. Wheezing phenotypes, and asthma and allergic disease were determined using data from International Study of Asthma and Allergy in Childhood questionnaires conducted at 18 months, 7 and 11 years, and linked registry data. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression with adjustment for child's sex, parental history of asthma/allergic disease, maternal smoking and socioeconomic background.
Results: Preliminary results suggest that exposure to cats during early-life but not pregnancy, may be associated with a reduced risk of asthma at 7 years (OR=0.87 (0.76-0.98); exposure to dogs, livestock and birds did not appear to influence a child's risk of asthma. Exposures to cats, dogs and livestock were associated with a reduced risk of hay fever at 7 years (ORs=0.23 – 0.85).
Conclusions: Early-life exposure to cats may offer protection against childhood asthma, whilst exposure to cats, dogs and livestock may offer protection against hay fever. Future analyses will explore the long-term influence of animal exposures on the gut microbiome in the DNBC, as a possible explanation for observed associations.

Maternal and postweaning obesity alters regulation of the hypothalamo-pituitary adrenal axis in mature adult mice

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Background/Aims: We have shown effects of both maternal and postweaning HF diet-induced obesity to increase anxiety and corticosterone output in mature adult mice, suggesting changes in the regulation of the hypothalamo-pituitary adrenal (HPA) axis. The current study investigated glucocorticoid (GR) and mineralocorticoid (MR) receptors in key brain regions of these mice, as well as FKBP51, a negative modulator of these receptors that is associated with anxiety-related disorders.
Method: Female C57BL/6 mice were fed either HF (HF: 45% kcal fat) or control diet (C: 7% kcal fat) 6 weeks before mating and throughout pregnancy and lactation. Male and female offspring were fed C or HF diet from weaning (3 weeks) (CC: n=7-8; CHF: n=4-7; HFC: n=7-9; HFHF: n=6-8/sex). In 52-week offspring brain (hippocampus [CA3] and hypothalamus [PVN]), GR, MR and FKBP51 mRNA levels were measured (RT-PCR). Data were analysed by mixed effects model (SPSS).
Results: In 52 week males, maternal HF diet reduced MR ($P<0.001$) and increased FKBP51 ($P<0.01$) in CA3. Postweaning HF diet also increased FKBP51 ($P<001$) in CA3 in males. In females, postweaning HF diet reduced MR ($P<0.01$) in CA3 but increased MR ($P<0.05$) and FKBP51 ($P<0.001$) in PVN. GR was unaffected in either sex by maternal or postweaning HF diet in PVN or CA3.
Conclusions: Changes in key factors in feedback mechanisms of the HPA axis in the mature adult brain suggest that maternal and postweaning HF diets may have long-term effects on stress responsiveness in a sex-specific manner. The increase in FKBP51 in both males and females following postweaning HF diet could be linked to the increased basal corticosterone we have previously observed in these animals, contributing to their heightened anxiety.

A rapid UPLC-MS/MS method for analysis of fat soluble vitamers in plasma and its application to population DOHaD

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Background/Aims: Fat soluble vitamers (FSV) A, D, E, K, and their metabolites are involved in key physiological functions in the human body, assisting development and growth and metabolism and cell regulation. Inadequate or excess dietary intake of FSV is a significant risk factor for lifestyle-related diseases. Unfortunately, currently available methods such as immunoassays and gas chromatography and even liquid-chromatography mass spectrometry (LC-MS) can determine only a few of the fat-soluble vitamers; are subject to non-target analyte interferences; are time consuming, and lack sensitivity.
Method: We are developing an ultra-high performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS)

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method to simultaneously quantify ~40 FSV in large population cohorts. Technical challenges to resolve include both analytical and biological complications such as bioavailability, low blood concentration of FSV, biochemical heterogeneity, and the lack of suitable stable isotope-labelled standards for chromatographic analysis.
Results: We will present an automated multiplexed prototype method using UPLC-MS/MS for the quantification of multiple FSV. The method is designed to allow separation and quantification of several parent vitamins and their metabolites without derivatisation. We will discuss the method's application and potential when applied to a large cross-generational population sample of parent-child dyads in the Child Health CheckPoint of the Longitudinal Study of Australian Children.
Conclusions: A sensitive, fast and robust method to quantify multiple FSV will greatly advance understanding of their impact and pathways to better nutritional health in large population samples.

Maternal Depression in the Perinatal Period and Infant Developmental Outcomes: Findings From the Mercy Pregnancy and Emotional Wellbeing Study

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Background/Aims: Research has identified that maternal depression during the perinatal period, here defined as the time from conception of pregnancy to the end of the first postpartum year, increases the vulnerability of children to develop difficulties in social, emotional and psychological domains. However, evidence has not clearly separated the effects of exposure to antenatal as opposed to postnatal depression, which has significant implications for the understanding of mediating variables and potential avenues for intervention. The body of literature is problematic in that there is inconsistency in defining outcomes of interest, and in appropriate measurement. In this study we review the literature investigating the association between maternal depression in the perinatal period and executive function outcomes in children, a measurable neuropsychological construct that has been associated with poorer developmental outcomes across the lifespan, and present preliminary findings from the Mercy Pregnancy and Emotional Wellbeing Study (MPEWS).
Method: A systematic review of literature reporting the association between maternal perinatal depression and child executive function outcomes found 11 relevant papers. The Mercy Pregnancy and Emotional Wellbeing Study recruited women in early pregnancy. Data from 486 women followed from early pregnancy to 12 months postpartum will be analysed. A diagnostic interview (SCID-IV) categorised depression status at recruitment, and symptoms were tracked using the Edinburgh Postnatal Depression Scale. Child developmental, emotional and behavioural outcomes were measured at 12 months postpartum using relevant items in the Brief Infant Toddler Social Emotional Assessment (BITSEA) and the Ages and Stages Questionnaire (ASQ).
Results: The systematic review found mixed executive function outcomes following exposure to maternal perinatal depression. These findings are difficult to interpret given the highly varied methodology of identified studies. The findings from this review will be explored in MPEWS data.
Conclusions: This study extends the literature examining child developmental outcomes following exposure to maternal depression by using a rigorous longitudinal design with objective and subjective measures of depression. The early findings suggest that there is an association between maternal perinatal depression and adverse child developmental, social and emotional outcomes.

Associations between abdominal adiposity, body size and objectively measured physical activity in infants from Soweto, South Africa

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Background/Aims: To determine associations between abdominal adiposity, body size, and objectively measured physical activity in infancy.
Method: Infants (n=138, aged 3-24 months) from Soweto, South Africa were recruited to this cross-sectional study. Visceral (VAT) and subcutaneous abdominal fat (SAT) were measured using ultrasound. Physical activity was objectively assessed using accelerometry and analysed at the hourly level. Multilevel linear regression analyses were run with body composition exposures adjusted for age, sex, and length; models with VAT and SAT were also adjusted for total abdominal fat. Physical activity was compared between tertiles of adjusted exposure variables using one way ANOVA.
Results: Mean (SD) age was 11.8 (7.6) months; 86% were normal weight, 7% were underweight and 7% overweight. In linear models, no body composition variable was significantly associated with physical activity. Physical activity was higher with each increasing length tertile (ANOVA $p<0.01$); with a mean(95%CI) 29(60-60)mg in the lowest tertile, 39(71-71)mg in the middle tertile, and 50(81-82)mg in the highest tertile. Infants with normal weight had higher mean(95%CI) physical activity (40(70-80)mg) than underweight (34(73-85)mg,

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p=0.01) or overweight infants (31(63-78)mg, ANOVA p<0.01). When also adjusting for total abdominal fat, infants in the lowest SAT tertile had higher physical activity than those in the middle or highest SAT tertiles (p<0.01). Infants in the middle VAT tertile had higher physical activity than those in the lowest or highest VAT tertiles (p<0.01).
Conclusions: These findings lend support for higher physical activity as a marker of healthy growth in the first two years of life. The congress managers are only too happy to assist if you have any questions or queries.

Association between human breastmilk-borne bioactives and maternal and infant phenotype:-The STEPS study

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Background/Aims: Human breast milk (BM) contains several bioactive compounds including adipokines and growth factors such as leptin, adiponectin and insulin-like-growth factor (IGF-1). *In utero* alterations of these bioactives are known to cause an adverse programming of energy balance and growth dysregulation in offspring. However, the role of BM-borne adipokines and growth factors in mediating infant metabolic response for life is relatively understudied. Maternal health status, including overweight/obesity and gestational diabetes mellitus (GDM) is a rising concern in pregnant women as can impact upon BM composition and thus may mediate transmission of risk factors to the infant. Therefore the aim of the study was to analyse the relationship between BM adipokines and growth factors with maternal BMI and metabolic status (e.g. GDM) and investigate the association with infant outcomes (birth weight and sex).
Method: Milk samples were obtained from 650 mothers, participating in the Finnish Cohort the STEPS study (Steps to the Healthy Development and Well-being of Children) when the infants were 3 months old. Leptin, adiponectin, IGF-1 were analysed via commercially sourced ELISAs that were optimised and validated for BM. Cyclic-glycine-proline (cGP), a metabolite of IGF-1, was also quantified via mass spectrometry. Maternal demographics, biological and social factors were obtained using Longitudinal Census Files.
Results: Both adiponectin and leptin displayed interactions across a range of multiple factors, including infant sex and maternal BMI for leptin (p= 0.048) and infant sex and gestational diabetes for adiponectin (p=0.009). Adiponectin was also associated with infant birthweight, with mothers of smaller babies (<2.5 kg) having higher BM adiponectin concentrations (p=0.016). IGF-1 and cGP results are currently being finalised.
Conclusions: These results demonstrate the significant role of maternal metabolic conditions in dictating the composition of BM. Further analysis is ongoing to determine the impact of BM variations on child outcomes at 2 years of age and beyond.

Non-communicable diseases (NCD's) and pregnancy outcome in LMIC

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Background: NCDs can also have significant adverse effects on maternal health and pregnancy outcomes, and can negatively impact the health of children later in life through effects experienced in utero. Strikingly, just four NCDs - cardiovascular diseases, cancer, chronic respiratory diseases and diabetes - accounted for ~82% of NCD-related mortality in 2012 with the vast majority occurring in low-middle income countries (LMICs).
Method: Medical charts were reviewed to identify pregnant women with NCD and study the pregnancy outcome. Pregnant women admitted also having an NCD were reviewed for their, basic characteristics, duration of NCD, pregnancy duration, complications and the pregnancy outcome.
Results: total of 858 women were identified during January 2015 to December 2016. Mean gestational age at first presentation was 16 weeks. Only 24.7% had a normal weight while 72.5% were overweight and obese. 71% were admitted with diagnosis of active labor while remaining were admitted either due to medical or obstetric complications. 16.5% were Hypertensive; 13.5% Diabetic; 30.5% Non-infectious respiratory disease and 39.4% Thyroid Disease. 65% women delivered by caesarean section; 1.3% had a stillborn; 9% had admission in neonatal intensive care. Women had high percentage of low birth weight baby in all groups. Odds ratio and significance will be presented for all variables.
Conclusion: presence of NCD is high risk group with perinatal risks. The in-patient population provides a unique opportunity to design strategies for intervention in pregnant women in urban setting.

Prevalence of kidney dysfunction in Indigenous infants from the Gomeroi gaaynggal cohort

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Background/Aims: Almost one in five Aboriginal and Torres Strait Islander (Indigenous) people aged > 18 years show signs of chronic kidney disease (CKD) and when adjusted for age,

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they are more than twice as likely to have indices of renal dysfunction present. Compared with non-Indigenous Australians, Indigenous children aged 10-18 years in NSW had an alarming 6:1 ratio in the prevalence of type 2 diabetes mellitus (95% CI, 3.9-9.7; p<0.001), which adversely affects kidney function.
The aim of this study was to identify the prevalence of renal dysfunction in Indigenous children < 5 years of age in the Gomeroi gaaynggal longitudinal prospective cohort of Indigenous women and their children.
Method: Urine was collected from infants (< 24 months) and children (2-5years) at study visits (at 3,6,9 months and annually thereafter). Every effort is made to encourage participants to attend every study visit. The prevalence of abnormal protein: creatinine (P:C) and albumin:creatinine (A:C) for these children was determined. An abnormal P:C is >0.5mg/mmol and >0.2mg/mmol at <24 months and 2-5 years respectively. A:C ratios vary with gender rather than age, being >3.3mg/mmol for males and >2.9mg/mmol for females (< 12 years).
Results: Eighty infants from singleton pregnancies were included. The prevalence of an elevated P:C was 4.9% (n=3/61) in infants aged 0-24 months, and 0% (n=0/30) in children aged 2-5 years. On the other hand, in children under 5 years, an elevated A:C was measured in 76% of observations from n=26 females and 62.7% of observations in 50 males.
Conclusions: It is clear from this analysis there few infants and children were identified with proteinuria. However, there was a high prevalence of infants < 5 years of age who had albuminuria. These early signs of abnormal glomerular function suggests that Indigenous children are at risk of developing CKD. This is especially the case when there is a compounding effect of the high prevalence of type 2 diabetes in childhood. Modification of diet is critical for the prevention of CKD in adult life. The GG cohort is continuing to build our understanding of the influence of maternal factors on renal dysfunction in children in this cohort. Ongoing monitoring of women and children in the cohort is embedded within a culturally supportive framework that includes community engagement, Indigenous research governance and referral for appropriate clinical follow-up when appropriate.

Prenatal Arsenic Exposure and Timing of Pubertal Development in Girls and Boys: a Follow up of the MINIMat Cohort, Bangladesh

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Background/Aims: Millions of individuals worldwide, particularly in Bangladesh, are exposed to arsenic, mainly through drinking water. Arsenic is a reproductive toxicant but there is limited knowledge whether this exposure influences pubertal development. We evaluated the associations between prenatal arsenic exposure and age at menarche and pubertal development in girls and boys in a rural area, Bangladesh.
Method: In this prospective cohort study we analysed the data from1364 children whose mothers were enrolled in the Maternal and Infant Nutrition Interventions in Matlab (MINIMat) trial from February 2002 to January 2003. Prenatal urinary arsenic concentrations in gestational week 8 and 30 had been assessed. Pubertal assessments were conducted in 2016 to 2017. Outcomes were assessed by reported age at menarche and self-assessed Tanner's stage of pubertal development in girls and boys
Results: The median age at menarche was 13.0 years. Girls of mothers exposed to the fourth quartile (222 - 977 μg/L) of urinary arsenic in comparison with the girls exposed to the first quartiles of arsenic in urine was not statistically significantly different (Hazards ratio = 0.81, confidence interval:0.64, 1.03). The odds of reaching Tanner stage 3 or more of pubic hair development was 35% lower in girls of mothers within the fourth quartile of arsenic exposure (Odds ratio = 0.55; 95% confidence interval: 0.34, 0.88). Further, the odds of reaching Tanner stage 4 or more was 51% lower in boys of mothers in the highest exposure level. We did not observe any association between arsenic exposure and breast development or genital growth in girls and boys, respectively.
Conclusions: The study suggests an association of arsenic exposure during pregnancy with pubertal development in girls and boys. The present findings along with other adverse health outcomes motivate increased efforts in mitigating arsenic contamination at the population level.

Maternal Body Mass Index in Early Pregnancy And Adverse Health Outcomes: Findings From Two Cohorts in Rural Matlab, Bangladesh

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Background/Aims: There is a lack of studies in Bangladesh that evaluated the trends of maternal nutrition and its health impact on mothers and newborn babies. The aims of the present study were to examine the trends of prenatal body mass index (BMI) and its association with pregnancy induced hypertension (PIH), caesarean section delivery (CSD), preterm birth (PB), birth weight, and small-for-gestational age (SGA).
Method: This prospective study took the advantages of two cohorts (i) the Maternal, Neonatal, and Child Health

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(MNCH) program carried out in 2008-2010, and (ii) the Preterm and Stillbirth Study, Matlab (PreSSMat) conducted in 2015-2017. In total, 3138 and 3605 women, respectively, from MNCH and PreSSMat projects were included in the analyses. Maternal BMI (weight in kg/height in meter^2) was categorized into underweight (<18.5), normal (18.5–24.9) and overweight (≥25.0) groups. PIH (systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 after 20th week of gestation), Preterm birth (delivery before 37th week of gestation), low birth weight (LBW) (birth weight <2500 gram), SGA (birth weight less than the 10th centile in reference to INTERGRWOWTH-21) were categorized as dichotomous outcomes. Results were presented in odds ratios (OR) with 95% confidence interval (CI).

Results: Between two cohort periods, underweight decreased from 17.3% to 15.4%, and overweight increased from 11.0% to 20.8%. In comparison to women in the normal weight group, odds of PIH, and CSD were 1.78 (95% CI: 1.15-2.77) and 2.39 (95% CI: 2.0-2.85), respectively in the women with overweight group. However, women with underweight the ORs for LBW, PB, and SGA were 1.50 (95% CI: 1.23-1.84), 0.95 (95% CI: 0.74-1.23), and 1.50 (95% CI: 1.26-1.80), respectively in comparison to the women with normal weight.

Conclusions: The results confirmed the existence of double burden of malnutrition in this group of rural women in Bangladesh. Pregnant women based on BMI should prioritize for appropriate counselling and preparedness to address the possible future negative health outcomes.

Maternal diet supplemented with methyl donor compounds prolongs tumour latency in neuroblastoma-prone homozygote *TH-MYCN*$^{+/+}$ transgenic mice

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Background/Aims: More than half of all childhood cancer has an embryonal origin. Embryonal childhood malignancies such as neuroblastoma, medulloblastoma and Wilms tumour often go through a well-defined pre-cancer or "rest" cell stage where residual embryonal cells in specific organs pathologically persist postnatally to later undergo malignant transformation. Rare germline predisposition syndromes activating specific driver genes associate with some embryonal cancers. However, very little is known about potential embryonal environmental mechanisms which might initiate embryonal rest cell formation and later tumorigenesis.

Methods: We examined the effects of maternal high or low methyl donor (folate and betaine) diet supplementation on tumourigenesis in neuroblastoma-prone transgenic *TH-MYCN* mice. All homozygous *TH-MYCN*$^{+/+}$ mice develop neuroblastoma by 6 weeks of age, whereas 20-30% of hemizygotes (*TH-MYCN*$^{+/-}$) develop neuroblastoma at 13 weeks. *TH-MYCN*$^{+/-}$ female breeding mice were placed on a control, methyl donor supplemented or methyl donor deficient diet two weeks prior to mating and during pregnancy and lactation. Offspring remained on the defined maternal diet throughout the experiment and were followed for tumor formation. Tumor tissues were examined for gene expression by PCR array and RT-PCR for a panel of epigenetic chromatin modifying genes and candidate tumour suppressor genes known to be frequently methylated in human neuroblastoma.

Results: Maternal and postweaning methyl donor supplementation prolonged tumour latency by 20% (7 days), while methyl donor deficient diets reduced tumour latency by 20% in *TH-MYCN*$^{+/+}$ homozygote offspring. No effects were seen in hemizygote *TH-MYCN*$^{+/-}$ mice. Among candidate genes examined, PCR Array and RT-PCR analysis demonstrated increased mRNA expression of HDAC7 and NEK6 in tumour tissues from methyl donor-deficient mice. Among the candidate tumor suppressor genes, mRNA expression of a tumour suppressor O-MGMT was significantly higher in methyl donor supplemented mice, compared to methyl donor deficient diet mice ($P < 0.05$). *In-vitro* exposure of human neuroblastoma cell lines, with doxycycline-inducible MYCN expression, to a range of methyl donor concentrations enhanced MYCN-dependent cell death.

Conclusions: These findings suggest that in homozygote *TH-MYCN* mice, maternal methyl donor supplementation is tumour-protective, while methyl donor deficient diets enhance tumorigenesis. We will further validate the candidate genes in *MYCN*-amplified neuroblastoma cells lines and perform functional studies to investigate mechanisms for the protective role of maternal methyl donor supplementation diet on the initiation and development of neuroblastoma.

Screening Tool For Early Prediction Of Risk Of Low Birth Weight In Rural Indian Women

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Background: High prevalence of low birth weight (LBW) babies can be significantly reduced if predicted early. Due to unavailability and unaffordability of modern technological tools, a quick, easy and accurate method of evaluating this risk would be of benefit to the less educated mothers in remote areas.

Aim: To develop a screening tool for early prediction of risk of low birth weight in rural Indian women.

Methods: The study population consisted of clinical normal mothers in the age group 18-40yr, with gestation age more than 37 weeks. A structured questionnaire was used to collect data at the time of registration. Anthropometric measurements and clinical findings were recorded and were followed up at every ANC check up till delivery. Simultaneous effect of components of maternal environment on birth weight was studied using Multiple Logistic Regression Analysis (MLRA). Principal

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component Analysis was attempted to identify the significantly associated variables for prediction of birth weight and their interrelationship. A simple scoring system was developed to form the screening tool.
Result: Out of 108 initial variables, 16 were found to be significantly associated with risk of LBW. These variables were grouped into socio economical, demographic, anthropometric, obstetric, diet, nutrient, and work related domains of maternal environment. The variable which showed highest risk in each group were Income, Age at registration, Parity, Previous Abortion, BMI, total Milk intake and %RDA of calorie intake. Maximum 4 Contributing components identified by principal component analysis. Final screening tool based on BMI, parity, milk intake and number of rotis (Indian bread) eaten per day was 85% sensitive.
Conclusion: The screening tool can identify risk of LBW as early as at the time of registration As the tool is based on intake of staple food, preventing the risk for LBW by simple modification in diet is possible.

Diets inducing early life high-glycemic/insulinotropic postprandial response program systolic arterial pressure.

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Background/Aims: Existing evidence associates exposure to high glycemic/insulinemic postprandial responses during adulthood with adverse metabolic profiles. We hypothesize that exposure during infancy might also have long-term health consequences.
Method: Female Göttingen Minipigs (n= 48) were randomly assigned to receive diets inducing either a low (LR) or high (HR) glycemic and insulinemic (4.5 and 2.8 fold vs. LR, respectively) postprandial response from postnatal day 21 to 3 months of age. Diets were isocaloric and isoproteic (20% protein, 7% fat, 60% cho, 3.9 MCal GE/kg) but differed in both, glycemic index and concentration of insulinotropic amino acids.
Both groups received a regular chow diet (13% protein, 2% fat, 33% cho, 3.3 MCals GE/kg) from 3 to 6 months of age and a mild obesogenic diet (13% protein, 14% fat, 33% cho, 4.4 MCals GE/kg) from 6 to 12 months of age. Eight animals per group were selected a priori for continuous heart rate, diastolic (DBP) and systolic (SBP) arterial blood pressure monitoring after overnight fasting at the end of each stage (3, 6 and 12 months).
Results: No significant differences in heart rate or DBP were detected between groups at any time point. SBP was not different between LR and HR groups at the end of the dietary intervention at 3 months (121 ± 5 vs. 115 ± 4 mmHg, respectively; P=0.38). However, a significant increase was detected at 6 months in animals fed HR diet in early life (124 ± 5 vs 108 ± 4 mmHg; P<0.05). After 6 months of a mild-obesogenic diet regime, both groups similarly worsen their SBP (LR 129 ± 3 vs HR 133 ± 3 mmHg) at 12 months of age with no significant difference among them.
Conclusions: Our data offers evidence of the potentially detrimental long-term cardiovascular effects of a chronic high glycemic/insulinotropic postprandial response during early life.

Bioinformatics pipeline for predicting drug resistant M. tuberculosis from whole genome sequencing data to identify the role Efflux pumps

Safina Razzak, Rumina Hasan, Sadia Shakoor and Zahra Hasan

Background: Tuberculosis (TB) has a very high global burden, around 10.0 million people developed TB disease in 2017 out of which 5.8 million were men, 3.2 million were women and 1.0 million were children. Pakistan ranks 5th amongst high TB-burden countries. Tackling drug resistance is critical to ending the TB epidemic, hence, there is an urgent need for internationally recognized rules for the unambiguous clinical interpretation of genetic changes that can predict phenotypic resistance to anti-TB drugs. Active efflux of drugs mediated by efflux pumps that confer drug resistance is one of the mechanisms. Whole genome sequencing (WGS) based of target genes allows identifications of single nucleotide polymorphisms (SNP) that may be associated with drug resistance.
Methods: To understand SNPs in drug efflux genes we, initially, we focused on 10 genes to pull out SNPs and INDELs (insertion/ deletions) on three MTB isolates. Further, we will run the same on 25 Efflux pumps genes in 800 MTB isolates. The data and its phenotypic drug susceptibility testing (DST) information were identified using ReSeqTB platform and extracted the SRA numbers of these isolates which were than download from ENA database. We developed customized pipeline to identify efflux gene targeted variants.
Results: In the preliminary analysis, we were able to get a total of 39 SNPs and 4 INDELS (ranging from 10 – 47bp). The SNPS were then further annotated using TBVAR that identified a deleterious mutation (G/C) on 228168 position in Rv0194 (multidrug ABC transporter) in three of the isolates that were from MDR, Pre-XDR and XDR datasets and a novel SNP on position 228069(G/A). Further, in this work we will analyse four sets of MTB phenotypes (Susceptible, multidrug resistant-MDR, Extensively drug resistant XDR, and MDR fluoroquinolone resistant – Pre-XDR) comprising of n=800 isolates from all 7 lineages
Conclusion: Through this we will establish a novel bioinformatics pipeline to analyse MTB genomes for SNPs in the genes of interest. The same can be applied to other pathogens. The future for rapid diagnosis and treatment of drug resistant TB is the combination of WGS based diagnostics with personalized medicines to treat TB.

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Whole genome sequencing of T2DM to find genetic association - Bioinformatics of Metabolomics in Diabetes Mellitus Type 2

Safina AR, Shabeen Naz Masood

Abstract

Background: Type 2 Diabetes mellitus is a multi-factorial disease caused due to gene defect as well as environmental factor. Whole Genome sequencing have played a primary role in demonstrating that genetic variation in a number of gene related to the risk of T2DM. Recently, some recently discovered genes play a key role in regulating the sensitivity to insulin. Scientists have long known that the disease often runs in families, and other genetic links. Human genetic discoveries will keep improving our knowledge about diabetes for many years to come. Varieties of prospective diabetic researches were developed to diagnose and control T2DM.

Aims: Our study aims to find T2DM pathway map of T2DM to study genetic association. We will identify genes that are involve in T2DM via KEGG pathway Database by analyzing T2DM pathways that includes Insulin signaling pathway, and WNT signaling pathway.

Methods: We do Protein-protein interaction and find out their complete target hub protein and target prediction for network hub. It provides hyperlinked information of genes, pathways, protein domains, protein structure displays, and sequence feature maps for interactive exploration of PPI data in the database.

Conclusion: The user can learn that this interaction as involved in several biological processes together, because the interacting proteins have several pathways such as insulin signaling in T2DM

The incidence of antenatal depression and anxiety across pregnancy in urban South Africa

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Background/Aims: Antenatal depression and anxiety are associated with poor compliance to antenatal care, risk of self-harm, premature delivery, decreased breastfeeding initiation and potential programming effects through mechanisms including altered placental function, epigenetic changes and stress reactivity. Some African research on antenatal depression in late pregnancy exists, but anxiety remains un-researched and almost no prospective longitudinal data exists.

Method: Women enrolled in a prospective cohort in Soweto, South Africa (2014–2016) were assessed using validated measures and cut offs (Edinburgh Postnatal Depression Scale EPDS ≥13; State Trait Anxiety Index STAI ≥12) at 2 time points in pregnancy (1st and 3rdnd trimester). Analysis was restricted to women with both measures. Incidence, persistence and co-morbidity were examined.

Results: 946 women were assessed in 1st trimester (T1); 736 (78%) in third trimester (T2); 649 (69%) had measures at both timepoints. Incidence at T1: Depression 27%; Anxiety 15% and T2: Depression 25%; Anxiety 17%. Cumulative rates were high: Depression 41%, Anxiety 28%. Patterns of depression across pregnancy included: 59% none; 10% at T1t but resolved by T2; 12% late onset at T2; persistent T1 and T2 13%. Anxiety patterns across pregnancy were: 72% none; 16% at T1 but resolved by T2; 12% late onset at T2; persistent at both 5%. Co-morbidity (34%) and reports of suicide ideation (11.6%) were high, and were stable across pregnancy.

Conclusions: Rates of both depression and anxiety are high early in pregnancy and earlier identification is critical for prevention and treatment. Research on the final trimester likely underestimates burden, leading to missed opportunities. Emerging research finds that antenatal anxiety has distinct effects on offspring mental health, more so than depression. In this first study of antenatal anxiety in South Africa, up to a third of women are affected. Research on the intergenerational effects of antenatal mental health is crucial for the DOHaD Africa chapter.

Overweight and Obesity in Infants in Cali, Colombia

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Background: Childhood overweight and obesity is a mayor public health issue in the twenty first century in the developed as well as in the developing countries. Childhood obesity can affect children´s physical health, social, emotional well-being and academic performance in school with the risk of obesity and metabolic síndrome as they reach adulthood. Several early-life factors significantly contribute to the development of overweight and obesity.

Methods: The data set for this research was extracted from several studies done in children and adolescent pregnancy during 2015-2018 in a low socioecomic and cultural community with poor living conditions in the city of Cali, Colombia. Socidemographic, anthropometric (1) and nutritional data were obtained. 250 6-months old infants were included for analysis.

Results: Famale 130 (52%). Ethnicity: mestizo 134 (62.5%), afro 66 (30.6%). Mother age: 24.2±6.1 y. Normal fullterm pregnancy 218 (88%).Normal delivery 218 (88%). C-section 30 (12%). Median birthweight 3175. At 6 months, Weight 7740 g. Length 66.9 cm. BMI 17.3. Infants with high BMI percentiles: ≥ 85th 46 (18.2%). ≥ 97th 15 (6.0%)

Conclusion: There is a clear evidence of the relationship between nutrition in early life and the development of obesity later in childhood. Physicians and maternal influences during

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gestation, breastfeeding and complementary feeding are potential targets for medical and public health interventions for the prevention of childhood obesity (2).
References: 1. Roy SM, Spivack JG, Faith MS, et al. Infant BMI or Weight-for-Length and Obesity Risk in Early Childhood. Pediatricvs 2016;137(5):e20153492. 2. Yang Z, Huffman SL. Nutrition in pregnancy and early childhood and associations with obesity in developing countries. Matern Child Nutr. 2012;9:105-119.

Quality of life in urogenital congenital malformations

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Background/Aims: Urogenital congenital malformations affect every ethnicity worldwide with both environmental and genetic mechanisms involved. Even with reconstructive surgery, these malformations may have a high impact on quality of life, such as multiple infections, increased demands on medical care, infertility, incontinence and renal failure. These factors may also cause negative psycho-social events affecting education, occupation and family building. Our research group has focused on analyzing risk-factors and psycho-social effects of bladder exstrophy in register-based studies. Bladder exstrophy affects the urinary bladder, the abdominal wall, the pelvis and genitalia.
Method: Matched cohort studies nested within the entire pool of live births in Sweden between 1952 and 2011 were conducted regarding bladder exstrophy patients. Complete nationwide health, birth and social registers were used, and cases were matched with 5 controls each. The objective was to study proxies for quality of life such as maternal risk factors, birth descriptive data, comorbidity, fertility, level of education, partnership and number of biological children.
Results: Studies demonstrated no significant maternal risk factors or birth descriptive impact. Most children born with bladder exstrophy had an isolated malformation. Comorbidity, such as inguinal hernia and non-descended testis requiring surgery were more common. Overall, educational and occupational levels were high and partnership formation was comparable to controls. Fertility and the number of biological children was, however, significantly decreased.
Conclusions: Since urogenital congenital malformations are rare, but often carried as a stigma, it is important to emphasize studies demonstrating low comorbidity and comparable outcome to controls. The awareness of no significant maternal risk factors and favorable antenatal outcome, as well as high level of education and social wellbeing, may influence priorities regarding the benefit of optimizing surgery and medical care. The clinical aspect of infertility and fewer biological children, as well as the fact that reconstructive surgery is needed must be addressed in further research.

First-borns Have A Marked Increased Risk Of Obesity At 20 Years Of Age: Findings From A Birth Cohort In Chiang Mai, Thailand

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Background/Aims: Studies have shown that birth order is associated with adverse health outcomes in the offspring. Notably, there is evidence that first-borns have an increased risk of obesity later in life. However, most studies have been carried out on Caucasians, and there is no published data from Thailand. Thus, we aimed to assess whether birth order was associated with obesity risk and cardiometabolic profile in a cohort of Thai men and women.
Methods: Participants were the offspring from the Chiang Mai low-birth-weight study, where pregnant women were recruited at their first antenatal visit in 1989-1990. A total of 632 offspring were followed up approximately 20 years later. Clinical assessments included anthropometry, lipid profile, clinic blood pressure, with insulin resistance assessed using HOMA-IR. In this study, we examined data on 565 individuals (53.8% females) who were born at term (37 to 41 weeks of gestation), at a mean age of 20.6 years.
Results: Compared to Thai men and women who were later-borns, first-borns had a height-adjusted weight 2.3 kg greater ($p=0.024$). As a result, first-borns had BMI that was 0.85 kg/m^2 greater (21.98 vs 21.13 kg/m^2; $p=0.022$), with an adjusted odds ratio of obesity that was 3.6 times that of later-borns (95% CI 1.4, 9.7; $p=0.010$). However, there were no differences in glucose homeostasis (HOMA-IR), lipid profile, or blood pressure according to birth order.
Conclusions: Our study showed that first-born men and women in Chiang Mai were heavier, had greater BMI, and marked increased odds of obesity in young adulthood.

The impact of altered IL-1 signaling on maternal high-fat diet induced developmental programming of male reproductive function

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Background/Aims: The increasing rate of global obesity poses a significant risk to health, with rising incidence of cardio-metabolic disease, infertility, and other comorbidities associated with increased fat mass. These conditions are strongly associated with persistent low-grade inflammation. Interleukin (IL)-1R1 is a key signalling mediator which bridges reproductive, metabolic and inflammatory systems. IL-1R1 knockout (IL-1R1$^{-/-}$) offers protection against metabolic dysfunction associated with high-fat diets (HFD) in young male mice. However, the role of IL-1R1 in terms of developmental programming has not been investigated. The aim of this study was to determine whether IL-1R1$^{-/-}$ has beneficial effects on developmental programming of metabolic and reproductive function in male offspring.
Method: Weight-matched female C57BL/6 and IL-1R1$^{-/-}$ mice were randomly assigned to receive either a control diet (CD;10% kcal from fat) or HFD (45% kcal from fat) 1 week prior to and throughout pregnancy and lactation (n=10/group). Offspring were weaned at day 21. Body weight and food intake was monitored weekly. Age of puberty onset and puberty weight were recorded in male offspring. Oral glucose tolerance tests (OGTT) were carried out at 12 weeks. Mice were culled at 16 weeks and testes gene expression was determined by RT-PCR. Data were analysed using 2-way ANOVA with maternal genotype and maternal diet as factors.
Results: Maternal HFD and IL-1R1$^{-/-}$ did not alter body weight or glucose tolerance in adult male offspring. Age or weight at puberty onset was not altered between groups. IL-1R1$^{-/-}$ mice displayed a reduction in the expression of genes involved in spermatogenesis (*Boll, Akap14, Brd2, Odf1*), sperm cell motility (*Ddx4, Gli3*) and androgen signalling (*Ar*) independent of maternal diet.
Conclusions: Male offspring from IL-1R1$^{-/-}$ mice exposed to HFD *in utero* are not protected from metabolic dysfunction. Furthermore, this study provides evidence that the ablation of IL-1R1 can negatively impact reproductive processes such as spermatogenesis and cell motility in the testes independently of diet. This suggests that IL-1 signalling may play an important role in maintaining normal cellular functions in the testes.

Dental Service Utilisation In Early Life: Patterns And Barriers Among Australian Children

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Background/Aims: Dental caries is a significant health problem for Australian children, with over a third affected by school entry. There is, however, little information about dental service utilisation among pre-schoolers. The aim of this study was to determine the early dental service utilisation patterns among Australian children and investigate barriers to care.
Method: Data were collected through a quantitative online Australia-wide survey conducted in January 2018, distributed to a randomly selected stratified group of adults aged 18 and older who were parents or caregivers of children under 18 years. The sample was subsequently weighted to reflect Australian population estimates. The survey questions yielded information on socio-demographic characteristics, dental service utilisation, barriers to care, and oral health related behaviours, knowledge and attitudes of parents. The data were analysed using descriptive statistics.
Results: A total 2048 parents of 3660 children completed the survey. Utilisation of professional dental care was low among young children with just 118 (27.3%) and 494 (68.5%) of 1-2 year old and 3-5 year old children respectively having professional ever had dental care, compared with over 90% of school aged children, of whom 75% had a check-up within the last 12 months. The most frequently reported reasons cited by parents/carers of preschool children who had not had professional dental care were that they were too young, their teeth were healthy or that the child would be scared. Cost was the fourth most frequently reported reason in young children. Only 459 (22.4%) of parents thought that the first dental visit should be at 1 year of age or earlier. Almost half of parents were unaware of existing government funded dental services for young children.
Conclusions: Dental service utilisation among young children is poor and barriers are multiple. Misconceptions about the importance of early dental examinations are contributing to a lack of preventive care in many young children, highlighting a need for targeted education of parents on this issue. In addition, non-dental health professionals who have frequent contact with young children, such as maternal child health nurses, paediatricians and general practitioners, have a role to play in encouraging and facilitating dental examinations in children from 12 months of age.

Paternal consumption of an obesogenic diet and orange juice during preconception programs adipose tissue inflammation and enzymatic antioxidant activity in mice female offspring

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Background/Aims: Paternal diet have been shown to influence offspring's health. Orange juice is widely consumed and is known for its content of bioactive compounds that may have a role in regulating epigenetic processes. Therefore, this study aims to evaluate the effects of paternal obesity and orange juice consumption on adipose tissue inflammation and activity of antioxidant enzymes in mice female offspring.
Method: Three-week-old C57BL/6 male mice were distributed in control (C), control-orange juice (CJ), obese (O) and obese-orange juice (OJ) groups, fed either a standard chow or an obesogenic diet (45% lard-based diet supplemented with sweetened condensed milk), with water or orange juice, for 11 weeks before mating. Female offspring were weaned onto standard chow until 7 weeks of age. Adipose tissue, plasma and liver were collected for inflammatory and enzymatic antioxidant activity analyses. This study was approved by FCF Ethical Committee. Data analyses was performed using ANOVA fallowed by Tukey test.
Results: Female offspring from C, CJ, O, OJ showed no differences (P>.05) in body weight or adiposity at 7 weeks of age. CJ female offspring presented higher SOD activity in liver (P<.05) when compared to C offspring. O female offspring had higher expression of TNF-α (P<.05) in adipose tissue, higher superoxide dismutase (SOD) activity in liver and plasma (P<.05) and lower glutathione peroxidase (GPx) activity in plasma (P<.05) when compared to C offspring. OJ female offspring showed lower expression of TNF-α in adipose tissue (P<.05) and higher GPx activity in plasma when compared to O offspring.
Conclusions: These results indicate that paternal consumption of an obesogenic diet during preconception leads to an inflammatory environment in adipose tissue that is independent of offspring adiposity. Regarding orange juice consumption by obese fathers, protection from inflammation in adipose tissue and amelioration of antioxidant status in plasma in female offspring is suggested.
Financial Support: CNPq; FAPESP/Food Research Center (Proc. 2013/07914-8).

Rising Incidence of Gestational Diabetes Mellitus: a Tale of Two Cohorts

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Background/Aims: It is well known that women who experience gestational diabetes mellitus (GDM) are at increased risk of developing Type 2 diabetes (T2DM) later. Their children tend to be heavier at birth and are more likely to be overweight or obese in childhood and later develop T2DM. With rising maternal overweight and obesity in pregnancy GDM is set to rise further. We have recruited two cohorts of nulliparous pregnant women 10 years apart (2005-2008 versus 2015-2018) and sought to determine whether the incidence of pregnancy complications has changed over time.
Method: Pregnancy outcome data for 1164 nulliparous pregnant women recruited to the **SC**reening for **P**regnancy **E**ndpoints (SCOPE) study in Adelaide in 2005-2008 were compared with those for 1313 nulliparous women recruited to the **S**creening **T**ests to predict poor **O**utcomes of **P**regnancy (STOP) Study from the same geographical area in the northern suburbs of Adelaide in 2015-2018. Data were adjusted for changing criteria for diagnosis of preeclampsia and GDM.
Results: Sadly, the percentage of women with an uncomplicated pregnancy has reduced (SCOPE 65.7% vs STOP 54.7%). The incidence of spontaneous preterm birth and small for gestational age births has not changed while that of hypertensive disorders of pregnancy has gone down (18.1% vs 15.8%). The incidence of GDM has increased 3-fold from 5% to 15.2%. Risk factors for pregnancy complications have changed over time. The percentage of women smoking at conception and at 12-15 weeks' gestation has reduced (39.1% vs 20.3% and 23.9% vs 16.5%, respectively). Maternal BMI has changed with fewer women with a BMI <20 (10.5% vs 7.2%), similar proportions of women with healthy and overweight BMI, but the percentage of obese women has increased (27.6% vs 31.1%).
Conclusions: In this socioeconomically disadvantaged population, the proportion of women with uncomplicated pregnancies is diminishing explained by the 3-fold increase in GDM. Modifiable maternal risk factors are changing. Ongoing work will identify causal factors associated with rising GDM. Increased childhood obesity and T2DM will be an inevitable consequence unless effective interventions are found.

Toll-like receptor-4 antagonist (+)-naloxone attenuates LPS-induced fetal programming of offspring adiposity in a fetal sex-specific manner in mice

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Background/Aims: Toll-like receptor 4 (TLR4) activation during infection or inflammatory insult can induce

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pro-inflammatory cytokines that adversely impact fetal development and growth, and program increasing susceptibility to metabolic disorders after birth. We utilized a mouse model to investigate the efficacy of a small molecule TLR4 antagonist (+)-naloxone, the non-opioid isomer of the opioid receptor antagonist (-)-naloxone, in protecting the offspring from altered fetal programming induced by a modest systemic inflammatory challenge.

Method: Pregnant C57B/6 mice were administered low dose (20 μg/kg) intraperitoneal lipopolysaccharide (LPS) on gestation day (GD)16.5, with or without (+)-naloxone (every 12 h from GD16.5-18.0). To investigate why male offspring may be more adversely impacted, a second cohort of females were administered LPS- and/or (+)-naloxone and killed 4 h later to collect fetal and maternal gestational tissues.

Results: In adult offspring exposed to LPS challenge in utero, male but not female offspring exhibited increased adipose tissue, reduced muscle mass and elevated plasma leptin at 20 weeks of age. (+)-naloxone attenuated the effects of in utero LPS exposure on offspring allometry and leptin. qPCR analysis showed increased expression of inflammatory cytokines *Il1a*, *Il1b*, *Il6* and *Tnf* in fetal and maternal gestational tissues from male compared to female fetuses, while (+)-naloxone exerted greater suppression of *Il1a*, *Il1b*, *Il6* and *Tnf* induced in fetal and maternal gestational tissue from female compared to male fetuses.

Conclusions: These data concur with other studies showing male fetuses are particularly susceptible to fetal inflammatory injury, and show that suppression of TLR4 signaling with (+)-naloxone can provide protection from inflammatory injury in utero, to attenuate long-term developmental effects of excessive TLR4 activation.

DNA methylation biomarkers of early life rapid weight gain and subsequent obesity: Findings from the Newcastle Thousand Families Study and the Avon Longitudinal Study of Parents and Children

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Background/Aims: There is increasing evidence that associations between early life factors and obesity in later life may be mediated through epigenetic mechanisms. We investigated if early life rapid weight gain (+0.67SD change in weight for age z-score from birth to 1 year), an intermediate risk factor for subsequent obesity, was associated with variation in DNA methylation in childhood and adulthood.

Method: Using Illumina 450K array data from the Avon Longitudinal Study of Parents and Children (ALSPAC), we conducted an epigenome-wide association study examining early life rapid weight gain (+0.67SD change in weight for age z-score) and blood methylation (in childhood and late adolescence) at individual CpG loci. RWG was associated with a 1% increase in methylation at an individual CpG loci (CG11531579) in childhood (age 7, *n*=116) in ALSPAC (Bonferroni corrected). Furthermore, the highest levels of methylation (+2%) on average were seen in those with RWG who were subsequently overweight/obese (OWOB, age 17).

The CG11531579 loci was investigated further in an older population to examine whether the associated variation in blood methylation persisted into adulthood, using the Newcastle Thousand Families study (age 50, *n*=134). Combined bisulphite modification and pyrosequencing was used to assess DNA methylation.

Results: RWG was also associated with methylation changes in an adult population, although in adults this was a decrease in methylation (-2%, age 50) for those who had RWG in infancy (age 60, *n*=91).

Conclusions: This study identified that RWG in infancy is associated with small variations in methylation. The loci was positively associated with blood methylation in childhood but negatively in adulthood, which could suggest it is an irregular, dynamic, RWG-related loci.

Associations between early life rapid weight gain, DNA methylation and subsequent overweight/obese

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Background/Aims: Early life rapid weight gain (0-12 months) has been associated with childhood adiposity, however the pathways remain unclear. DNA methylation is a hypothesised mechanism linking early life exposures and subsequent obesity. Methylation differences have been associated with adiposity, but not with RWG (+0.67SD change in weight for age z-score). Thus our aim was to investigate the associations between early life RWG, blood DNA methylation, and subsequent overweight/obese (OW/OB).

Method: Data from the Avon Longitudinal study of Parents and Children were used to estimate associations between RWG, and the outcomes (in childhood and late adolescence) including body composition (OW/OB), and methylation at individual CpG loci. Associations between RWG and OW/OB were assessed using using logistic regression. Epigenome-wide association studies were conducted with surrogate variable analysis, both with and without adjustment for cell type proportions. Variation in methylation by phenotype (RWG and/or OWOB) was evaluated (with Bonferroni correction for multiple comparisons).

Results: RWG was associated with increased odds of OW/OB (OR=3.4, p<0.001) in childhood. RWG was significantly associated with small (1% increase, 5% false discovery rate correction) changes in methylation for two distinct CpG loci in

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childhood (age 7, *n*=116). Methylation (childhood) at these loci was significantly higher in those who experienced RWG and were subsequently OW/OB (adolescence). RWG was not associated with OWOB in adolescence or changes in methylation in adolescence.
Conclusions: We identified small increases in methylation at two CpG loci associated with RWG in childhood. Furthermore, those who experienced RWG in childhood AND were subsequently OW/OB in adolescence had significantly higher methylation at these loci in childhood. Despite lack of associations between RWG and body composition or methylation in adolescence, childhood methylation could be a potential biomarker for subsequent adiposity in individuals who have undergone RWG.

Genetic influences on DNA methylation variation in the placenta

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Background: Interest in placental DNA methylation (DNAme) profiling has grown as a means to explore the mechanisms underlying the developmental origins of health and disease. Variation in DNAm results from multiple causes, with genetic variation increasingly appreciated as a major contributor. Single nucleotide polymorphisms (SNPs) that affect nearby DNAme are referred to as methylation quantitative trait loci (mQTLs). Identifying mQTLs is a powerful way to identify variants that are likely to be associated with altered gene expression and exert functional effects on the tissue of interest.
Method: We identified placental mQTLs in samples with Illumina 450K or 850K DNAme data (>450,000 and >850,000 CpGs) by two approaches: 1) A candidate SNP approach testing variants in *IL6* and *CCR5* in >300 placentas; 2) a genome wide-approach, using 37 placental samples with matched DNAme and high-density genotyping data (Illumina Omni2.5, >2.3 million SNPs).
Results: A SNP (rs1800796) near the *IL6* promoter was associated with *IL6* DNAm and expression, as well as increased birth weight and acute chorioamnionitis (both $p<0.05$). The allele frequency for rs1800796 is <5% in individuals of European Ancestry and >75% of East-Asian ancestry. A SNP (rs1799987) in the first intron of CC receptor 5 chemokine (*CCR5*), a pro-inflammatory cell surface receptor linked to HIV infection, was associated with DNAm at the *CCR5* promoter and increased birth weight ($p=0.0009$). By comparing matched 450K and high-density genotyping data, and limiting associations to SNPs with a minor allele frequency (MAF) >0.1 within 50kb of the target CpG, we found 2469 CpGs linked to 2001 unique SNPs (mQTLs) associated with 1155 distinct genes. Many of the mQTLs vary in frequency with ethnicity/ancestry. These mQTLs are located in many genes of interest and include the previously identified SNP in *IL6*. We are exploring these further for associations with perinatal outcomes.
Conclusions: Genetic variation has a substantial contribution to DNAme variation in the placenta and can vary with ethnicity/ancestry of the sample. This needs to be considered in studies testing for association between exposures and DNAme changes in the placenta. Placental mQTLs show promise for identifying genetic variants associated with pregnancy health and birth outcomes.

The relationship of early-life adversity with adulthood weight and cardiometabolic health status in the 1946 National Survey of Health and Development

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Background/Aims: Evidence linking early-life adversity with an adverse cardiometabolic profile in adulthood is equivocal. The current study investigates early-life adversity in relation to weight and cardiometabolic health status at age 60-64 years.
Methods: The study includes 1,059 individuals in the 1946 National Survey of Health and Development (NSHD). Data on adversity between ages 0-16 years were used to create a cumulative childhood psychosocial adversity score and a socioeconomic adversity score. Cardiometabolic, weight, height, and body composition data collected at ages 60-64 years were used to create four groups: metabolically healthy normal weight (MHNW), metabolically unhealthy normal weight (MUNW), metabolically healthy overweight/obese (MHO), and metabolically unhealthy overweight/obese (MUO). Associations between the two exposure scores and weight/health status were examined using multinomial logistic regression, with adjustment for sex and age at the outcome visit.
Results: 62% of normal weight individuals were metabolically healthy, whereas only 34% of overweight/obese individuals were metabolically healthy. In a mutually adjusted model including both exposure scores, a psychosocial score of ≥ 3 (compared to 0) was associated with increased risk of being metabolically unhealthy (compared to healthy) in both normal weight adults (RR 2.49; 95% CI 0.87, 7.13), and overweight/obese adults (1.87; 0.96, 3.61). However, the socioeconomic adversity score was more strongly related to metabolic health status in overweight/obese adults (1.60; 0.98, 2.60) than normal weight adults (0.95; 0.46, 1.96).
Conclusions: Independently of socioeconomic position, psychosocial adversity in childhood may be associated with a poor cardiometabolic health profile, in both normal weight and overweight/obese adults.

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The role of parenting, child executive function and lifecourse factors in the development of conduct, violent and antisocial behaviours at age 7-11 years in South Africa

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Background: Conduct disorder (CD) is on the rise and is specifically associated with adulthood anti-social, violent and criminal behaviours and non-specifically with a broad range of mental and health disorders in adulthood. Beyond hereditary components, deficits in Executive Functions (EF), which influence self-regulation and decision-making, potentially play a role.

Methods: 1536 HIV-negative children (including HIV exposed/unexposed) were assessed aged 7-11 years using the parent-reported Child Behaviour Checklist (CBCL). Five separate cognitive and neuropsychological sub-tests measured EF objectively. Structural equation modelling derived continuous latent variables representing CD, EF and parenting, examining associations with violent/antisocial behaviours. CBCL items for violent/anti-social behaviours grouped children by presence/absence of these behaviours. Proportional odds logistic regression examined associations with covariates in mother, child and parenting environment.

Results: Both CD (11.8%) and violent behaviour (20.5%) were common (violent n=174, 11.1%; violent and antisocial n=140 9.4%). Exclusive breastfeeding (≥6 months) reduced the odds of CD. Parent-child relationship and CD were strongly associated, with a significant indirect pathway between EF and CD (-0.189 p<0.003) effect size 0.389 (p<0.001). Indirect through EF (-0.081 p<0.001) explained 21% of the association. Maternal depression (aOR2.03 [1.1-3.6] 0.017; aOR3.92 [2.0-7.6] <0.001) and two parenting stress subscales (aOR2.76 [1.6-4.7] <0.001; aOR6.34 [4.1-9.9] <0.001) were associated with both behaviours, as was being male, food-insecure, HIV-affected and resident with >4 children. Antisocial behaviours were specifically associated with maternal anxiety (aOR2.63 [1.2-5.9] 0.020) while >1 smack per week reduced odds for both behaviours.

Conclusions: For the first time in LMIC we show a significant pathway involving EF. Children with CD, low EF and parents with mental health problems are particularly vulnerable. EFs are modifiable; hence interventions may be optimised with low-cost EF strategies, but must also attend to parent mental health to mitigate intergenerational and negative outcomes of CD.

Individualized Growth Trajectories for Preterm Infants – Associations with Short-Term Outcomes

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Background/Aims: Individualized postnatal growth trajectories (GTC) for preterm infants incorporate postnatal weight loss, and adjusted median intrauterine growth rate merged with WHO growth standards at term age (www.growthcalculator.org). They provide daily reference weights from birth to 42 weeks of postmenstrual age (PMA). The study aims to: 1) compare observed deviations of weight (ΔW) from the GTC trajectory between cohorts and 2) analyze relationships between ΔW and short-term outcomes.

Method: International multicohort study, including infants with a gestational age (GA) from 22 to 33 weeks with weekly or daily weight data from eight local cohorts (Austria, Germany, Sweden, Australia, Canada, USA) and the German Neonatal Network (birth weight (BW), 35 weeks PMA, discharge) during 2001 to 2017. For each infant, the GTC trajectory was calculated based on GA, BW, and sex. The difference between the GTC trajectory and 1) individual weights at various single time points (ΔW), and 2) deviations integrated over the NICU stay (ΔW-AUC) were determined. The relationship of ΔW with head circumference (HC), length (L), lean mass, fat mass, and blood pressure (BP) at discharge, adjusting for major NICU morbidities were analyzed. The relationship of ΔW-AUC with outcomes was assessed for 2-week periods from birth to discharge using a sequential multinomial logistic regression. Level of significance was p<0.05.

Results: In this study, 2,027 infants from 8 cohorts (998 <28 weeks) and 15,971 infants from the German Neonatal Network (6,558 <28 weeks) were included. At 36 weeks, preterm infants showed a significantly different ΔW for GA and cohort. For infants <28 weeks at birth, ΔW was large and cohort-specific variations significant. At discharge, HC, L, fat mass, and lean mass were significantly related. BP before

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discharge tended to be higher with high deviation from ΔW. ΔW-AUC before discharge was the strongest predictor of outcomes. Converging towards the GTC trajectory until discharge seemed to improve outcomes while diverging was related to unfavorable outcomes.
Conclusions: This is the first study to analyze growth of preterm infants by comparing them to individual GTC. The results show that outcomes were independently related to growth pattern.

Individualized Growth Trajectories for Preterm Infants – Associations with Neurodevelopment, Body Composition, and Blood Pressure

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Background/Aims: Neurodevelopment, body composition, and cardiovascular diseases relate to growth during early life. Determining an individualized growth trajectory (GTC) provides neonatologists with a reference for weight gain of preterm infants. GTC includes postnatal weight loss and median intrauterine growth rate adjusted for postnatal physiology and merges with WHO growth standards at term age (www.growthcalculator.org). The study aims to analyze the association between long-term outcomes and the deviation of weight (ΔW) from the GTC.
Design/Methods: This multicohort study includes data from 18,000 preterm infants with a gestational age (GA) from 22 to 33 weeks from eight cohorts (Austria, Germany, Sweden, Australia, Canada, USA) and the German Neonatal Network for 2001 to 2017. Their average birth weight (BW) was 1050 ± 300g and GA 27.8 ± 2.5 weeks. For each infant, the GTC trajectory based on GA, BW and sex, was calculated. The difference (ΔW) to individual weights at discharge and during NICU stay was assessed. Further, the area under the curve (AUC) of ΔW from birth to discharge divided into 2-week periods was calculated. ΔW at discharge was correlated with neurodevelopmental data from follow-up visits at 18 months, 5 and 7 years for Bayley scales, Wechsler Preschool and Primary Scale of Intelligence (WPPSI), Wechsler Abbreviated Scale of Intelligence (WASI), plus weight, length, BMI, head circumference, hipcircumference, lean mass, fat mass, and blood pressure (BP). The association of ΔW-AUC on outcomes was analyzed using a sequential multinomial logistic regression adjusted for major NICU morbidities.
Results: At 2 years, in infants <28 weeks cognitive, language and motor composite Bayley scale scores were related to ΔW (n=3152, $p<0.05$). At 5 years, the total IQ and verbal IQ WPPSI scores were significantly related to ΔW at discharge (N= 1511, $p<0.05$). At 7 years, the verbal IQ WASI assessment correlated with ΔW (N= 582, $p<0.05$). In follow up, anthropometric measurements, lean mass, and fat mass were related to ΔW. The ΔW-AUC period before discharge had the most impact on outcomes. However, its effects diminished with age. BP tended to be higher in infants with high deviation from ΔW.
Conclusion: Achieving growth at the GTC improves neurodevelopment. The GTC should be further calibrated in a prospective study to find the appropriate ΔW for optimum neurodevelopment without gaining excess fat mass.

Double–Blind RCT on Target Fortification of Breast Milk with Protein, Carbohydrate and Fat for Preterm Infants – Effect on Neurodevelopment

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Background: We recently reported a double-blind RCT on target fortification (TFO) of breast milk (BM). Using BM macronutrient analysis, fortification was individually adjusted (TFO) using a standard fortifier (SF) and 3 modular products (protein, carbohydrates (CHO), fat) to achieve ESPGHAN recommendations. This approach was found to be feasible in clinical routine and safely improved short-term growth and outcome until discharge. To investigate the impact of TFO on neurodevelopmental outcome (ND) at 18-month follow-up.
Design/Methods: Single center RCT, infants born <30 gestational weeks on BM; intervention (INTVN) group received SF+TFO, control (CTL) group only SF. For INTVN, three modulars (protein, CHO, fat) were added to SF after native BM content was measured 3x/week using a validated near-IR spectrometer (SpectraStar) to achieve intakes of 4.5, 13.2 and 6.6 g/kg/d for protein, CHO and fat, respectively. To obtain total macronutrient intake, all daily native BM samples were reanalyzed; near-IR for protein and fat; UPLCMS/MS for lactose. Weight, length, head circumference and body composition (air displacement plethysmography) was measured at 36 weeks. ND was assessed at 18 months using Bayley III scale.
Results: 103 infants received SF (n=51, CTL) or SF+TFO of BM (n=52, INTVN) per protocol. 69 infants (CTL: n=35, GA: 27.1 weeks, BW: 970g; INTVN: n=34, GA: 27.2 weeks,

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BW: 950g) had a follow-up visit and received a Bayley scale at 18.9±1.9 (CTL) and 18.5±1.3 (INTVN) months. Weight, length, and head circumference were not different between the groups. In the INVTN group, infants had higher Bayley scores for all categories. The highest differences were observed between the subgroups "CTL, low protein" and "INTVN, high protein". Statistical significance was achieved for language scores ($p<0.05$). Language score was correlated with variation of protein intake and gross-motor score related to fat-free mass index(kg/m^2).

Conclusion: TFO has a significant and clinically relevant positive effect on short-term outcome. The results on long-term ND may be explained by the combined exposure to nutrition, esp. protein and calories during short-term (NICU, TFO+SF vs. SF) and long-term (ex-NICU, high vs. low protein content of native BM). The effect of TFO is still present for long-term outcome, but attenuated, especially in the group of infants with low protein content of native BM. There might be a role for TFO following the end of routine fortification

Trajectories of fat mass accretion among preterm compared to term infants during the first 6 months of postnatal life

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Background: It is recommended that preterm infants achieve "rates of growth and composition of weight gain for a normal fetus of the same postmenstrual age". At term, however, preemies have higher %fat mass (FM) (15-22%) than newborn term infants (13-16%). It is currently unclear whether this trend increases during the following months or whether it reflects postnatal adaptation to the extrauterine environment Objective: To compare dynamics of FM accretion of preterm and term infants up to early infancy.

Design/Methods: In this prospective, observational study length, weight and body composition (air-displacement plethysmography) were measured in preterm and term infants from birth to six months corrected. Percentiles were calculated using GAMLSS; analysis was stratified by gestational age (GA) at birth (group A:<28, B:28-31, C:32-36 wks, D: term). To compare %FM change between the four groups, equations for median trajectories were developed. Missing data for the late preterm period (>32w) were extrapolated using information from Ziegler's reference fetus. Trajectories of preterm infants were then compared to term infants by shifting curves along the x-axis (Fig) for best fit.

Results: Body composition was measured in 508 infants (244 preterm; 264 term) and a total of 1071 measurements. Though groups started at different gestational ages and % FM, FM trended towards a similar average mean of 23% for all groups. Also, dynamics to reach this %FM was comparable amongst all groups (Fig). For example, at 40 weeks postmenstrual age infants born at <28wks had a FM of 21%, and at 45 weeks leveled out to 24%. Also, for other gestational ages, infants achieved a FM of 24 to 26% by 50 wks. From 50 weeks onwards, maximum %FM remained constant at approximately 24 to 26% for all infants. Median %FM trajectories for all preterm infants had their best fit with term infants when data points were shifted by 5.9, 4.6, and 1.5 wks for groups A, B, and C, respectively (Fig)

Conclusion: This study confirms that preterm infants experience increased %FM at an earlier postmenstrual age than term infants. However, dynamics of FM accretion is comparable amongst all groups of infants thought having different gestational ages at birth. It could, therefore, be hypothesized that postnatal changes in FM accretion is a physiological process induced by the transition to the extrauterine environment (thermomanagement, nutritional sources, etc.). Further research is needed to explore mechanisms underlying such postnatal adaptation.

Body Composition (Fat Mass and Fat-Free Mass) of Preterm Infants less than 32 Weeks and Neurodevelopment at 18 Months

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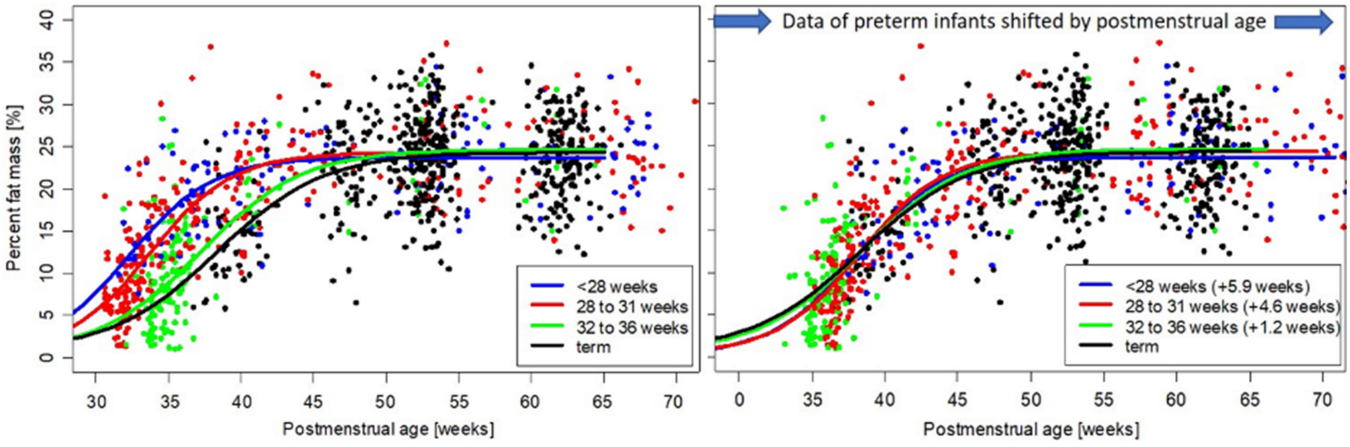

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Background: Weight measurements alone are insufficient indicators of individual body composition (i.e. fat mass and fat-free mass). Also, there is growing evidence that nutrition and resulting body composition at discharge are related to the neurodevelopment outcome. Air displacement plethysmography (PEA POD) was used to create a database of body composition measurements for preterm and term infants. To calculate percentiles for body composition measurements and to compare the body composition with the neurodevelopmental outcome at 18 months.
Design/Methods: A longitudinal observational study was conducted for infants (gestational age (GA) <32 weeks). The body composition was measured with air-displacement plethysmography using the PEAPOD during the NICU stay and also at 3, and 6 months follow-ups. Infants with respiratory support (CPAP > 6cm H O or high-flow nasal cannula > 6L/min) were excluded. Body composition indicators including % body fat (% BF), fat mass (FM), fat-free mass (FFM), fat mass/length (FMI), fat-free mass/length (FFMI) were graphed against postmenstrual age (PMA). At 18 months, the infants received a Bayley III assessment. For descriptive statistics, the infants were stratified in two gestational age groups: <28 weeks and 28 to 31 weeks. Percentiles were calculated using gamlss package in r statistics. Further, the infants were subdivided into three quantiles according to the neurodevelopment.
Results: This study includes 147 infants, 96 infants received a Bayley assessment at 18 months (Table). In total, 398 body composition measurements were performed. At 35 weeks, the younger preterm infants had higher %BF compared to those born with 28 to 31 weeks. At 50 weeks PMA, %BF leveled out in both groups at 23 to 25% and remained stable at this value until 70 weeks PMA. Preterm infants with GA <28 weeks had slightly shorter body length and lower neurodevelopmental scores. Infants with higher measurements for fat mass had higher Bayley score. For %BF, and fat mass the average curve for infants with lower language score (<33 percentile) was considerably lower (Figure). Also, fat-mass and percent free-mass were significantly correlated with language score ($p<0.05$).
Conclusion: Body composition during a NICU stay is related to neurodevelopment at 18 months. This is an important finding to support optimizing nutrition at NICU.

Gestational lipid profile associated with the lipid profile of both mothers and their children later in life

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Background/Aims: An atherogenic lipid profile is a risk factor for atherosclerosis. In early gestation, the lipid profile resembles the non-gestational atherogenic lipid profile and has been associated with a risk of pregnancy complications in both mother and child. The aim of this study is to assess whether the gestational lipid profile in early pregnancy is associated with the lipid profile of the mother and child six years after pregnancy.
Method: Mothers (n = 3912) and mother-child pairs (n = 2692) were included in this prospective, population-based study embedded in the Generation R Study. Non-fasting blood samples were obtained from mother and child in early pregnancy and six years later to determine total cholesterol, triglycerides and HDL-c levels. LDL-c, non-HDL-c and remnant cholesterol were calculated.
Results: Maternal lipids in early pregnancy were positively and independently associated with identical lipids of the mother six years afterwards. For the mother-child analyses total cholesterol, triglycerides, LDL-c and HDL-c were positively and independently associated with identical lipids of the child six years later. The associations were slightly stronger in girls compared to boys.
Conclusions: The early gestational lipid profile is positively associated with the lipid profile of both mother and child six years after pregnancy. Monitoring the gestational lipid profile might help to identify those mothers and children at risk for a postpartum atherogenic lipid profile in an early stage.

Maternal lipid profile in early pregnancy as marker for adverse perinatal outcomes

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Background/Aims: Little is known about the role of maternal lipid concentrations in this association. Possibly, an atherogenic lipid profile in early pregnancy is a risk factor for adverse perinatal outcomes.
Objective: To determine the association of maternal glucose and lipid concentrations in early pregnancy with perinatal outcomes: large for gestational age (LGA), small for gestational age (SGA), and spontaneous preterm birth (sPTB).
Method: We included 5692 women from The Generation R Study; a prospective population-based birth cohort. Maternal glucose and lipid concentrations including triglycerides, total-cholesterol, high-density lipoprotein-cholesterol (HDL-c) were measured in early pregnancy (median 13.4 weeks). Low-density lipoprotein-cholesterol (LDL-c), remnant-cholesterol and non-HDL-c were calculated. Information on birth weight and gestational age was obtained from medical files. A birth weight above the 90th percentile was defined as LGA and below the 10th percentile as SGA. Spontaneous birth before 37 weeks of gestation was defined as sPTB.
Results: Triglycerides and remnant-cholesterol were positively associated with the risk for LGA. These associations were partly

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mediated by maternal glucose concentrations in early pregnancy (10.9% and 9.0% respectively). HDL-c was negatively associated with the risk for LGA. Women with an atherogenic lipid profile (high triglycerides with either high total-cholesterol, high remnant-cholesterol or low HDL-c) were most at risk for a LGA child. We observed no associations between lipid concentrations in early pregnancy and the risk for SGA or sPTB.
Conclusions: An atherogenic lipid profile in early pregnancy is associated with a higher risk for a LGA child. This association is partly mediated by maternal glucose concentration in early pregnancy. Assessing maternal lipid profile in early pregnancy might help to identify high-risk pregnancies in an early stage.

Is maternal lipid profile in early pregnancy associated with pregnancy complications and blood pressure in pregnancy and long-term postpartum?

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Background/Aims: An atherogenic lipid profile is a risk factor for the initiation and progression of atherosclerosis. This ultimately leads to cardiovascular disease (CVD). Women with a history of hypertensive disorders of pregnancy (HDP) are at increased risk of sustained hypertension and CVD later in life. Currently it is unclear if dyslipidemia during pregnancy contributes to these risks. Therefore the aim of our study was to determine the associations between early pregnancy maternal lipid profile, HDP and blood pressure during and years after pregnancy
Method: We included 5690 women from the Generation R Study; an ongoing population-based prospective birth cohort. 218 (3.8%) women developed gestational hypertension and 139 (2.4%) preeclampsia. A maternal lipid profile consisting of total-cholesterol, triglycerides and HDL-c, LDL-c, remnant cholesterol and non-HDL-c was determined in early pregnancy (median 13.4 weeks of gestation). Systolic and diastolic blood pressure were measured in early, mid- and late pregnancy, and six and nine years after pregnancy.
Results: Triglycerides and remnant cholesterol in early pregnancy were positively associated with preeclampsia. Maternal lipid levels in early pregnancy were not associated with gestational hypertension. Total-cholesterol, LDL-c, non-HDL-c, and especially triglycerides and remnant cholesterol, were positively associated with blood pressure in pregnancy, and six and nine years after pregnancy. Triglycerides and remnant cholesterol are positively associated with sustained hypertension six years and nine years after pregnancy.
Conclusions: An atherogenic lipid profile in early pregnancy reflecting impaired triglyceride-rich lipoprotein metabolism is independently associated with preeclampsia and blood pressure throughout pregnancy, but also with sustained hypertension long-term postpartum. Lipid levels in early pregnancy may help to identify women at risk for future hypertension and perhaps also women at risk for future CVD.

Cardiovascular health and vascular age after severe preeclampsia

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Background/Aims: Severe preeclampsia increases lifetime-risk for cardiovascular disease (CVD). It remains unclear when this risk translates to subclinical atherosclerosis and whether these are related to cardiovascular health (CVH) after pregnancy. Our aims were 1) to determine CVH after severe preeclampsia, 2) to relate CVH to carotid intima-media thickness (CIMT), as a marker of subclinical atherosclerosis and 3) to relate CVH to chronological and vascular age.
Method: CVH, proposed by the American Heart Association, was assessed one year after severe preeclampsia (N=244 women). The CVH score (range 0-14) includes seven metrics (blood pressure, total-cholesterol, glucose, smoking, physical activity, diet and BMI), each weighted as poor (0), intermediate (1) or ideal (2). Vascular age was determined by CIMT (n=123). We related CVH to delta age (chronological age - vascular age).
Results: The median CVH score was 10 (90% range 7.0, 13.0). Women with low CVH (<10) had a larger CIMT than women with high CVH (≥12) (median 626.3µm vs. 567.0µm, respectively). Higher CVH was also associated with a lower vascular age (-2.0 years, 95%CI -3.3, -0.60). Women with low CVH had a larger delta age (22.5 years [90% range -3.9, 49.6) than women with high CVH (16.5 years [90% range -11.9, 43.3).
Conclusions: CVH is inversely related to subclinical atherosclerosis and to vascular age one year after severe preeclampsia. Especially low CVH is associated with a large difference between chronological age and vascular age. CVH counseling might provide the opportunity for timely cardiovascular prevention.

Sleep and the hypothalamic-pituitary-adrenal axis as modulators of metabolic energy across the adolescent transition in a group of Mayan girls - A preliminary analysis

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Background/Aims: The human adolescent transition is characterized by important energetic trade-offs imposed by physical and psychosocial developmental challenges. Two critical modulators of metabolic energy change during this transition: sleep patterns and hypothalamic-pituitary-adrenal axis (HPAA) activity. Little is known about the ways in which these two systems interact to modulate energy availability and their impact on the onset and pace of the adolescent transition. We investigate these interactions in a sample of 21 Mayan girls aged 12 to 15 years (avg = 13.5 years).
Method: Data corresponds to a cohort study taking place in rural Guatemala since 2000. Growth status was measured using BMI and waist/hip ratios. Sleep characteristics were evaluated using actigraphy data collected over 19 consecutive days in 2017. HPAA activity was monitored based on first morning urinary (FMU) cortisol quantified over the same time period. Energy availability was measured using FMU conjugates of adiponectin and C-peptide. Reproductive maturity was assessed using FMU conjugates of estrogen, progesterone, and follicle-stimulating hormone (FSH) in samples collected in 2017.
Results: As expected, BMI, waist/hip ratio and the proportion of girls reaching menarche was lower in 12 than 15 year olds (BMI: 24.0 to 31.06; W/H: 0.84 to 0.80; menarche: 40% to 100%, respectively). Sleep efficiency was similar across ages, yet sleep quality was higher in older girls (sleep fragmentation 24.24% at age 12 vs 19.99% at age 15). Cortisol and adiponectin levels were highest in 13yo (456.94 ng/ml and 7.71 ng/ml respectively) than in 15yo (251.04 ng/ml and 3.54 ng/ml, respectively). C-peptide was lowest in 13yo (31.34ng/m) than in 15yo (37.17 ng/ml).
Conclusions: Our preliminary results suggest that the lowest level of energy reserve at 13 years old coincided with a peak in HPAA activity, which suggests a shift in energy allocation at the time when most girls were reaching menarche. This study will contribute novel information regarding the modulating role that sleep and HPAA may have on metabolic trade-offs and the variation of reproductive maturation in girls.

Investing in a Healthy Future for All: Research, Education, Policy

Workplace Well-Being Through A Genomics Lens: A Key To Healthy Fetal Developmental

As the negative consequences of current global economic growth strategies escalate, there is recognition that the now dominant capitalist economic system, and the associated business model is having a negative impact on health and well-being in the workplace [1, 2]. Increased understanding of the complexity of genomic health is strongly pointing to a mismatch between employees' and workplace requirements as a causative factor. This is resulting in a range of diseases reflective of maladaptation, many of which have significant implications for healthy fetal development. Examples include genetics research demonstrating associations between workplace stress, increased levels of oxidative stress leading to increased DNA fragmentation and changes in genetically facilitated metabolic pathways leading to a range of complex life diseases. Research has linked stress to fertility issues as well as early abortion and risk of childhood cancers in offspring [3-7]. In-utero and early childhood epigenetic changes are relevant to pregnant women in the workplace. Negative impacts have been recorded in studies that demonstrate a link between chronic stress, cognitive function and mental health issues, with mouse studies confirming epigenetic causation. This has led some authors to question the nature of our moral epigenetic responsibility and, more specifically within the workplace, to ask whether workplace stress can cause transgenerational ripples of employer liability [8-14]. In addition, research is proposing a link between high levels of microRNA and a range of psychiatric conditions in offspring including anxiety and schizophrenia. Research is also exploring the interplay between the individual's functional genomic systems, the body's microbiome and the external environment. Again stress features in this discussion with the microbiome being shown to act as a regulator of stress and inflammation [15-25].
Despite these expanding fields of investigation, little of this has been discussed within the occupational health and safety literature. This paper explores the relationships between workplace stress, genomic systems and early life disease. The authors integrate their respective expertise in genomics, employment relations, psychology and epidemiology, to identify the potential implications for early life development.

Early childhood growth outcomes associated with nausea and vomiting in pregnancy (NVP) is sex-dependent in an Asian population: results from the GUSTO Study

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Background/Aims: NVP is common, with hyperemesis gravidarum (HG, the extreme form) occurring in 1-3% of pregnancies. NVP prevalence is higher among Asian women, but studies in this group are sparse and the longer-term outcomes beyond pregnancy are poorly understood. This study examined if NVP was associated with adverse pregnancy, early childhood growth and adiposity outcomes.
Method: NVP data were obtained from 1172 women with singleton pregnancies through interviewer-administered questionnaire at 26 weeks' gestation in the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) mother-offspring cohort. Pregnancy outcomes were obtained from case

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notes. Child anthropometry was assessed at birth and at 11 time-points up to age 4.5 years (4.5y) and analysed as z-scores. Abdominal adiposity was quantified by MRI in the neonate and at 4.5y. Multiple logistic regression was performed.
Results: In our cohort, 25.2% (n=296) reported no vomiting, 58.5% (n=686) mild-moderate vomiting, 10.5% (n=123) severe vomiting, and 5.8% (n=67) severe vomiting with hospitalization. Women with severe vomiting were less likely to be carrying male offspring (p=0.014). Adjusting for confounders, there were no associations of NVP with gestational diabetes, hypertensive disorders, induction of labour, or caesarean delivery. However, severe vomiting was associated with higher odds of late preterm (34-36 completed weeks) delivery (OR3.04 [95% CI 1.39,6.68]) without increased odds of NICU admission. There were no birthweight differences. Compared with no NVP, male offspring of women with severe vomiting were longer at birth (β[95%CI]: 0.38SDs [0.02,0.73]) and remained taller (0.56SDs [0.18,0.93]) and heavier (0.48SDs [0.03,0.93]) at 4.5y without differences in BMI or abdominal adiposity. Whereas female offspring of women with severe vomiting with hospitalization were lighter (-0.52SDs [-1.00, -0.03]) and had a lower BMI (-0.61SDs [-1.12, -0.09]) at 4.5y.
Conclusions: Offspring sex may influence both the prevalence of NVP and the impact of NVP on early childhood growth

Association of Trimester-Specific Gestational Weight Gain with Offspring Abdominal Adiposity in Early Infancy and at Age 4.5 years

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Background/Aims: Excessive gestational weight gain (GWG) has been linked to increased risk of childhood obesity. It remains unclear whether specific trimesters in pregnancy are more sensitive to GWG influences on the offspring's abdominal adiposity. The aim of this study was to investigate trimester-specific GWG associations with offspring's abdominal fat measured in the neonatal period and at age 4.5 years.
Method: Serial measurements of maternal weight throughout pregnancy were obtained from 1176 women in the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) mother-offspring cohort. Volumetric abdominal MRI and segmentation of subcutaneous (SAT) and visceral adipose tissues (VAT) in the offspring were obtained within 3 weeks of birth (n=331) and at age 4.5 years (n=316). Depot volumes were standardized for sex. Trimester-specific (Tri1:wk1-wk12, Tri2:wk13-wk26, Tri3:wk27-pre-delivery) conditional GWG was computed as the residual of the last available weight measured during each trimester, regressed on all previous weight measures and the corresponding gestational age. The associations of trimester-specific GWG with offspring SAT and VAT volumes were assessed using multiple linear regression with adjustment for ethnicity, maternal education, age, parity, and prepregnancy obesity.
Results: Increased 1st trimester GWG was associated with higher offspring SAT and VAT volumes in early infancy (SAT: β=0.13 (95%CI=0.01, 0.25); VAT: β=0.16 (0.04, 0.28)) and at age 4.5 years (SAT: β=0.15 (0.05, 0.25); VAT: β=0.11 (0.002, 0.22)). 2nd trimester GWG was associated to a similar degree with neonatal abdominal adiposity (SAT: β=0.14 (0.02, 0.26); VAT: β=0.17 (0.05, 0.29)), but not with adiposity at age 4.5 years. 3rd trimester GWG as not significantly associated with offspring abdominal adiposity at either ages.
Conclusions: Our findings suggest that the timing of GWG may influence childhood abdominal fat accumulation differentially, with the 1st trimester appearing particularly sensitive.

Pre-conceptional maternal metabolic status influences hepatic metabolome in male offspring

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Background/Aims: Maternal obesity is associated with fertility disorders, obstetric complications, and development of metabolic syndrome in offspring. The recommendation to overweight or obese women is to lose weight before pregnancy, but the impact of these prescriptions on the offspring health is insufficiently studied. Previous results on late-term mice fetuses have shown that maternal obesity leads to fetal growth

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restriction and to the modification of epigenetic machinery-related gene expression in fetal liver and placenta. Moreover, fetuses from the preconceptional weight loss maternal group normalize their growth, but some fetal genes stay differentially expressed (1).

Method: We analysed the metabolic phenotype of offspring born to control (CTRL), obese (OB) or weight loss after diet-induced obesity (WL) mothers. To highlight a possible conditioning effect, offspring were either fed a control (CD) or a high fat diet (HFD). Their metabolism and olfactory behavior were monitored for up to 6 months. Then, we analyzed the metabolome of three tissues involved in food intake and nutrient management (liver, olfactory bulb and hypothalamus) in male adult offspring.

Results: Multiple Factorial Analysis integration of offspring phenotypic data showed a major influence of the post-weaning diet and pointed a difference in HFD-fed males according to their maternal group (OB vs WL). This confirmed a sex-dependant metabolic conditioning by the maternal environment. The olfactory sensitivity, measured by electro-olfactogram, was reduced in WL male offspring, whatever the postnatal diet.

The metabolomics study annotated 278, 258 and 200 metabolites in the liver, olfactory bulb and hypothalamus respectively. Again, the post-weaning diet had a major effect in the three tissues but interestingly, the maternal group also influenced the hepatic metabolome of adult offspring.

Conclusions: These data, integrating metabolism, olfactory behavior and metabolome, provide new and original information on the effects of preconceptional maternal metabolic status in the offspring health conditioning upon diet challenges.

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The Association Between Maternal Macronutrient Intake During the Preconception Period and Offspring Birth Weight: Analyses in a Perined-Lifelines Linked Pregnancy Cohort

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Background/Aims. Maternal nutrition during pregnancy has been associated with offspring birth outcomes including fetal growth, birth weight, and long-term health through intra-uterine programming. However, a woman's nutritional status before pregnancy may also influence outcomes for both mother and child. Therefore, the aim of this study was to investigate the association between dietary intake in the pre-conceptional period with birth weight, by creating a Perined-Lifelines linked pregnancy cohort.

Methods. This pregnancy cohort consists of women who delivered a live born infant at term after enrolment in a large population-based cohort study (The Lifelines Cohort). Information on birth outcome was obtained through linkage to the Dutch perinatal registry (Perined). We included 1698 nulliparous women with information available on pre-conceptional dietary intake (using a food frequency questionnaire) and birth weight of the offspring. Birth weight was converted into gestational age adjusted z-scores, and macronutrient intake was adjusted for total energy intake using the nutrient residual method. Multivariable linear regression was performed, adjusting for other macronutrients (model 1) and covariates (e.g. maternal pre-conceptional BMI, parity, smoking) (model 2).

Results. Mean age was 29.5 years (SD 3.9), pre-conceptional BMI: 24.7 kg/m^2 (SD 4.2) and birth weight: 3578 grams (SD 472). In model 1, birth weight was positively associated with total protein and animal protein, fat and total carbohydrates. In model 2, a significant association (adjusted β [95% CI], P) between polysaccharides and birth weight remained (0.08 [0.01-0.15], 0.03).

Conclusion. Our results suggest that maternal macronutrient intake in the period prior to conception is associated with birth weight, with the strongest association for intake levels of polysaccharides in the diet. Further analyses will focus on the specific contribution of selective food groups to the association, and on how dietary advice could be tailored to different groups of BMI, given the strong association between maternal BMI and offspring birth weight.

Vitamin B12 deficiency induces pro-inflammatory cytokine production in human adipocytes and maternal subcutaneous and omental adipose tissue

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Background: Vitamin B12 (B12) is an essential micronutrient required for optimal hematopoietic, neurologic and other several metabolic reactions. Longitudinal studies and animal models showed that low maternal vitaminB12 deficiency is associated with the maternal obesity, development of insulin resistance and metabolic syndrome phenotype suggesting the crucial role of B12 in adipose tissue function. Although the mechanisms underpinning metabolic disorders remain poorly

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defined, the pathophysiology of obesity-induced metabolic diseases has been strongly related to white adipose tissue dysfunction through several mechanisms such as fibrosis, apoptosis and inflammation. Therefore, we investigated the role of B12 deficiency in inflammation in human adipocytes and human abdominal Subcutaneous(Sc) and Omental(Om) adipose tissue(AT).
Methods: AbdSc pre-adipocyte cell line (Chub-S7) and human AbdSc primary pre-adipocyte cells were differentiated under different B12 concentrations (25pM,100pM,1nM,500nM) to assess B12 deficiency effects. Human Om, Sc AT and blood samples were also collected from 106 white pregnant women at delivery. Serum B12 as well as relevant metabolic risk factors were measured. Gene expression was performed by q-RTPCR.
Results: Adipocytes cultured in low vitamin B12 conditions showed significantly increased gene expression of pro-inflammatory cytokines ($P<0.01$) such as interleukin-1 (IL-1) interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-18 (IL-18), transforming growth factor beta (TGF-β), tumor necrosis factor alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1/CCL2). Gene expression from both Om and Sc AT from pregnant women with B12 deficiencydemonstrated upregulated levels compared to control.
Conclusion: Our data highlights that low B12 induces higher gene expression of pro-inflammatory cytokines, which might lead to adipocyte dysfunction. This link between vitamin B12 deficiency and metabolic inflammation opens new insights into the pathogenesis of maternal obesity and the relevance of micronutrient supplementation for pregnant mothers.

Relationship between diet during pregnancy and birthweight in Japan

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Background/Aims: It has been reported that the birthweight of Japanese babies is lower than that of babies in other countries. Some studies show that this is due to low maternal weight gain during pregnancy rather than to genetic factors. Dietary intake affects weight gain during pregnancy; however, little is known about the types of foods that contribute to this problem. This study aims to identify maternal food-intake patterns that can increase birthweight in Japan.
Method: We recruited 34 healthy pregnant mothers whose babies were carried to full term (≥ 27 weeks) and delivered by Caesarean section between February 2015 and February 2016 at Jinno Ladies Clinic in Japan. Clinical data were collected after delivery from either medical records (parity and gestational age of mother, weight and sex of neonate) or via self-report (maternal age and bodyweight). Daily dietary intake was investigated using the brief self-administered diet-history questionnaire (BDHQ) that reflects the average daily dietary intake during the month before delivery. Spearman's rank correlation was used to evaluate the relationship between dietary intake and birthweight. The experimental protocol was approved by the ethics committee of the University of Shiga Prefecture.
Results: All the babies except one (2485 g) weighed more than 2500 g. There was a positive correlation between birthweight and rice intake. Although there were no other significant correlations between birthweight and individual food types consumed, rice intake was positively correlated with meat (pork and beef) and miso soup intake, and negatively correlated with bread, udon noodles (Japanese wheat noodles), ramen noodles, sashimi (raw fish), and ice cream intake. These associations may be part of the relationship that affects birthweight.
Conclusions: This analysis revealed that greater rice intake by pregnant women was associated with a higher birthweight. To increase the birthweight of Japanese babies, it is thus important for pregnant women to consume the staple foods of Japanese cuisine: rice and miso soup with meat. This study was exploratory in nature, and further studies are needed to determine the optimal diet for ensuring increased birthweights.

mHealth Interventions Targeting Pregnancy Intakes in Low and Lower-middle Income Countries: Systematic Review

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Background/Aims: Dietary intake during pregnancy plays a vital role in determining the health of both mother and baby. Maternal undernutrition affects a large proportion of women in low and lower-middle income countries (LLMIC) likely influencing high maternal, infant and child mortality in these countries. Mobile health (mHealth) interventions have been proposed as effective solutions to improve maternal and neonatal health. This paper reviews the literature to evaluate the effectiveness of mHealth interventions on improving dietary/nutrients intake of pregnant women in LLMIC.
Method: Eight electronic databases were searched from inception up to April 2018, including the MEDLINE, EMBASE, CINAHL, Cochrane, Web of Science, Scopus, Global Index Medicus and Maternity and Infant Care. Using Covidence, two reviewers assessed articles for inclusion, assessed study quality and extracted data. Only studies published in English language were included. Data were summarized narratively.
Results: In total 6778 were identified, of which four were included, with three RCTs and one pre-post experimental study. Studies were conducted in India (n=2), Indonesia (n=1) and Kenya (n=1). All articles evaluated the use of nutrient supplements; iron supplements (n=1), vitamin supplements (composition not mentioned) (n=1) or calcium supplements (n=1).

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Conclusion: This review suggests that mHealth interventions can be used to improve intake of micronutrient supplementation and nutritional status of pregnant women in LLMIC. Further studies are needed to address the limited evidence base related to mHealth nutrition interventions targeting dietary intakes of pregnant women in LLMIC.

An Attempt of Holding a Workshop of Birth Cohort Collaboration Toward Establishing Consortia in Japan

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Background/Aims: Birth cohort studies are believed to be suitable for epidemiological studies to demonstrate the DOHaD concept. These studies and their collaborations are very popular in European and Oceanian countries, whereas those are lagged behind in Japan. Recently, a new paradigm "preemptive medicine" has been proposed in Japan[1,2]. The importance of interdisciplinary studies focused on fetal and childhood periods has also been recommended as a political strategy.
Method: A workshop of birth cohort collaboration toward establishing consortia in Japan was held in Tokyo during January 29-30, 2019. Sixty-one researchers engaged in birth cohort or early intervention studies all over Japan. The workshop was composed of a symposium and a group work. In the symposium, ten speakers have reviewed health policies and collaborations among adult cohorts in Japan and pointed out remained issues among Japanese birth cohorts. In the group work, five themes, that is, infrastructure improvement, data integration, bio-samples, data health, and early intervention, were discussed by small groups.
Results: Each group proposed political strategies for collaboration of birth cohort and early intervention studies in Japan. We identified difficult problems and recommended constructive proposals.
Conclusions: This workshop organized by researchers had a significant impact on funding agencies and ministries in Japan. We just expect the realization of nation-wide large-scale interdisciplinary research projects of DOHaD and preemptive medicine and the establishment of the central research institute of these studies.
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Gestational Weight Gain and Birthweight-for-Gestational Age: TMDU Hospital Cohort Study

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Background/Aims: The problem of exceptionally high percentage of low-weight-births in Japan has been raised as a serious concern. A high frequency of underweight women in reproductive age is one of the causes, and it is also criticized that the recommended limit on weight gain during pregnancy is too strict. However, it is not yet clear whether the increase of gestational weight gain (GWG) could bring the proportional increase in birthweight-for-gestational age (BW/GA), especially in the small BW/GA group.
Method: We performed a retrospective cohort analysis of women delivering at Tokyo Medical and Dental University Hospital from 2013 through 2017. We stratified women by BW/GA centile and studied the association between GWG (and/or pre-pregnancy BMI) and BW/GA centile. We also explored the factors lowering BW/GA in the condition that GWG is optimal according to the pre-pregnancy BMI-specific guidelines.
Results: Multiple regression analysis showed that BW/GA centile was significantly associated with GWG when the centile was 50 and over ($p = 2.1 \times 10^{-3}$). When the BW/GA centile was less than 50, BW/GA centile was associated with pre-pregnancy BMI ($p = 8.4 \times 10^{-4}$) but not with GWG ($p = 0.57$). Half of the women delivered small-for-gestational age babies showed GWG of the recommended levels based on the current Japanese GWG guideline. Low maternal height and low pre-pregnancy weight was a part of factors lowering BW/GA when GWG was within the optimal range.
Conclusions: We found that linear relationship between GWG and BW/GA found in the higher BW/GA group was no longer maintained in the lower BW/GA group. It suggested that it is important to consider the effects of other factors, including maternal height and pre-pregnancy weight, when optimal GWG is sought, especially for small babies.

Sex-specific association between maternal gut microbiota and fetal growth

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Background/Aims: Maternal gut microbiota is considered as one of the important factors that affect child health. Recently, there has been significant interest in the effects of maternal gut microbiota on the fetus, specifically with reference to the concept of the developmental origins of health and disease (DOHaD). The present study examined the association between maternal gut microbiota and fetal growth.

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Method: Maternal and newborn data, and stool samples at the third trimester of pregnancy were obtained from 51 mother–newborn pairs from the participants involved in the Chiba study of Mother and Child Health (C-MACH). The gut microbiota composition of the stool was assessed using 16S rRNA sequencing and by examining the level of short-chain fatty acids (SCFAs) using gas chromatography-tandem mass spectrometry.
Results: After adjusting for covariates, a positive association was observed between maternal gut microbial diversity and newborn head circumference in males (Chao 1: adjusted $r = 0.515$, $p = 0.029$). Genus *Parabacteroides* and genus *Eggerthella* showed negative associations with newborn head circumference and weight, respectively, in males (genus *Parabacteroides*: adjusted $r = -0.598$, $p = 0.009$, genus *Eggerthella*: adjusted $r = -0.481$, $p = 0.043$). On the other hand, genus *Streptococcus* showed a negative association with newborn height in females (adjusted $r = -0.413$, $p = 0.040$). Additionally, while the univariate analyses revealed associations between hexanoate and maternal gut microbiota or newborn anthropometrics, the multivariate analysis did not.
Conclusions: These data suggest that maternal gut microbiota has sex-specific effects on fetal growth. Thus, maternal gut microbiota is an important factor that affects intrauterine growth.

Dietary intakes and diet quality of early pregnant women in comparison with non-pregnant women planning to conceive

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Background/Aims: This study examined differences in dietary intakes and diet quality between pregnant and non-pregnant women planning to conceive.
Method: Early pregnant women (10.7±0.9 gestational weeks) and women planning to become pregnant were recruited and completed 3 web-based 24-hour dietary recalls, from which energy and nutrient intakes as well as the Canadian healthy eating index (C-HEI) were calculated. According to Canada's Food Guide (2007), servings of food groups (fruits and vegetables, grain products, milk and alternatives, meat and alternatives and « other foods ») were calculated. Pregnant women (n=64) were matched for pre-pregnancy BMI (± 0.5 kg/m^2) and age (± 5 years) with 64 non-pregnant women.
Results: By design, pregnant and non-pregnant women did not differ by age (32.1±3.8 vs 31.7±3.8 years, p=0.14) and by pre-pregnancy BMI (24.2±4.4 vs 24.0±5.2 kg/m^2, p=0.60). Mean energy intakes did not differ between pregnant and non-pregnant women (2296±506 vs 2144±450 kcal/day, p=0.08), but pregnant women did report higher carbohydrates (49.7±4.8 vs 44.5±5.9 % of energy intake, p<0.0001) and dietary fibre intakes (23.9±7.2 vs 21.6±5.9 g/day, p=0.05). Fat intakes were lower in pregnant compared to non-pregnant women (34.8±4.1 vs 36.9±4.2 % of energy intake, p=0.0075). Pregnant women reported more servings of fruits and grain products, and less of their calories came from the category « other foods », resulting in a higher C-HEI score (66.2±10.4 vs 60.4±13.4 out of a total score of 100, p=0.0075).
Conclusions: Early pregnant women ate more fruits as well as grain products and had better overall diet quality when compared to non-pregnant women planning to conceive. Women planning to become pregnant may be less preoccupied by the importance of their diet's quality in the preconception period and could therefore be targeted by future sensibilization program.

Maternal caffeine consumption during pregnancy and offspring cord blood DNA methylation: a meta-analysis of epigenome-wide association studies

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Background/Aims: Current UK guidelines advise pregnant women to limit caffeine consumption to less than 200 mg per day, even though robust evidence of a causal intrauterine effect in humans is lacking. To gain clarity about the effect of intra-uterine caffeine exposure on adverse offspring outcomes, we investigated whether intrauterine exposure to caffeine is associated with genome-wide DNA methylation in human cord blood.
Method: We meta-analysed results from epigenome-wide association studies using data from the Avon Longitudinal Study of Parents and Children (ALSPAC, n = 729) and the Norwegian Mother and Child Cohort Study (MoBa, n = 1005). Methylation was assessed with the lllumina Infinium 450k array. Maternal caffeine consumption (mg/day) was derived from food frequency questionnaires at 18 or 22 weeks of pregnancy. Total caffeine and caffeine from coffee, tea and cola was studied separately.
Results: We found 10 CpG sites associated with total maternal caffeine consumption (mg/day) (range of effect estimates: 2.06e-6, 0.19e-4, FDR-adjusted p-value < 0.05), however, these associations did not survive adjustment for covariates (maternal age, BMI, smoking during pregnancy, highest education and estimated cell counts). In adjusted models, four CpG sites were associated with maternal caffeine from cola consumption only (range of effect estimates: 5.15e-5, 5.15-e; FDR-adjusted p-value < 0.05).
Conclusions: Our results indicate some evidence of association between offspring cord blood DNA methylation and maternal caffeine from cola, but limited evidence for total caffeine or caffeine from other sources. Two potential

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explanations are: 1) cola consumption during pregnancy might influence offspring methylation via an ingredient other than caffeine, or 2) the association is confounded by another factor that is not (as strongly) associated with consumption of caffeine from other sources.

Phenome-wide association study of caffeine PRS and mental health outcomes across the lifespan using the ALSPAC pregnancy cohort

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Background/Aims: Uncertainty remains whether the same genetic variants associated with caffeine consumption in the general population can be applied to proxy caffeine consumption across the life span. We applied the phenome-wide association study paradigm to (1) validate the PRS for caffeine consumption for different sources of caffeine in four time points in life (offspring: childhood, adolescence; mothers: pregnancy, adulthood) and (2) explore potential pleiotropic effects of the PRS with a variety of mental health phenotypes and substance use behaviours during these time-points.
Method: Data from the Avon Longitudinal Study of Parents and Children was used (genotype data: n children = 7977, n mothers = 7921). PRS were derived from eight genetic variants associated with coffee consumption in the general population. In addition to phenotypes for caffeine consumption, mental health, substance use, personality and sociodemographic phenotypes were included.
Results: PRS were found to be positively associated with caffeine consumed through tea (*beta* = 2.29, *CI* [0.76, 3.83], $p = 0.003$) and coffee (*beta* = 3.67, *CI* [1.20, 6.14], $p = 0.004$) at 18 weeks gestation. For cola, the PRS were neither associated with consumption at 18 weeks gestation (*beta* = -0.04, *CI* [-0.39, 0.31], $p = 0.83$) nor with consumption in mothers 97 months after pregnancy (*beta* = 0.004, *CI* [-0.002, 0.01], $p = 0.21$). PRS in offspring could neither predict caffeine consumption in children (8 years of age: *beta* = 0.55, *CI* [-0.33, 1.44], $p = 0.22$) nor adolescents (13 years of age: *beta* = 1.1, *CI* [-0.15, 2.35], $p = 0.09$). After Bonferroni adjustment for multiple testing, neither mothers' nor offspring's PRS were found to be associated with our included phenotypes.
Conclusions: Overall, our results indicate that PRS for caffeine consumption are valid instruments for assessing actual consumption of tea and coffee, but not cola, in adults and pregnant women. Further, our results suggest that the genetic variants used for caffeine consumption in adults are not related to mental health or substance use outcomes and support the application of these PRS in instrumental variable analyses of mental health outcomes.

How do women's adverse childhood experiences influence their risk of developing gestational diabetes: findings from an Australian population-based study

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Background/Aims: The influence of women's traumatic experiences in childhood on risk of developing gestational diabetes mellitus (GDM) is unclear. This study sought to examine this relationship, and identify factors that may moderate or mediate the association.
Method: This study included 6,317 women participating in the Australian Longitudinal Study on Women's Health who were followed from 1996 (age 18-23) until 2015. GDM diagnosis was self-reported and validated in a subsample. Childhood trauma was defined as exposure to any three or more of eight adverse childhood experiences that were reported, such as abuse and household dysfunction. Log-binomial regression was used to estimate relative risks (RR) and 95% confidence intervals (CI). Effect modification by preconception and antenatal mental health was tested using cross-product terms. The inverse odds ratio weighting method was used to quantify relative contributions of potential mediators to associations between childhood trauma and GDM risk.
Results: Eight percent of women developed GDM. Exposure to childhood trauma (13% of women) was associated with a 2-fold higher risk of GDM among women with preconception depressive symptoms after adjustment for country of birth and family history of diabetes (RR 1.98, 95% CI 1.58-2.37). Age at menarche, polycystic ovary syndrome, preconception diet and maternal age did not mediate this association. Preconception overweight/obesity (10%) and antenatal depression (12%) were significant mediators, but did not fully explain the relationship. Childhood trauma was not associated with GDM risk in women without preconception depressive symptoms (1.19, 0.95-1.43) (cross-product term p=0.01).
Conclusions: Our findings suggest that, in addition to primary prevention of childhood adversity, strategies to curb poor mental health trajectories among women exposed to early trauma may contribute to GDM prevention. Further studies are needed to examine additional mediating pathways that can be targeted to reduce GDM risk among women with childhood trauma who developed depression prior to pregnancy.

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The individual and combined effects of maternal BMI and diabetes in pregnancy on offspring adiposity: a life course analysis of the Longitudinal Study of Australian Children

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Background/Aims: Maternal overweight/obesity and diabetes in pregnancy (DIP) may have persistent effects on offspring adiposity. We aimed to examine the extent to which maternal overweight/obesity and DIP: 1) are independently associated with offspring adiposity from early childhood to early adolescence, and 2) interact with each other on an additive scale.
Method: We analysed prospective data from 2,436 participants in the Longitudinal Study of Australian Children (LSAC) B-cohort. Associations of maternal overweight/obesity and DIP with offspring BMI, fat mass index (FMI) and fat-free mass index (FFMI) assessed at up to six time points between ages 2 and 13 years were examined using weighted generalized estimating equations and adjusted for maternal characteristics, paternal BMI, and offspring age and sex. Product terms were added to the models to examine interactions between maternal overweight/obesity and DIP, and changes in associations with increasing offspring age.
Results: Both maternal BMI (46.5% overweight/obese) and DIP (5.5%) were associated with higher offspring BMI: 1.13 kg/m^2 (95% CI: 0.92-1.34) and 0.68 kg/m^2 (0.10-1.26), respectively. Mutual adjustment for both maternal risk factors attenuated these associations slightly to 1.11 kg/m^2 (0.90-1.32) and 0.55 kg/m^2 (-0.02-1.13), respectively. DIP interacted with maternal overweight/obesity, such that the combined effects of maternal overweight/obesity and DIP on offspring BMI [2.08 kg/m^2 (1.18-2.99)] was significantly larger than the sum of the individual effects of maternal overweight/obesity [1.05 kg/m^2 (0.84-1.27)] and DIP [-0.10 kg/m^2 (-0.62-0.43)] (p-interaction=0.04). These differences became larger with increasing offspring age (p-interaction=0.07). Similar results were found when examining the associations with offspring FMI, but not with FFMI.
Conclusions: Maternal overweight/obesity is strongly associated with childhood adiposity, and DIP may further amplify the adverse effect. Future studies should identify more effective management strategies for DIP in overweight/obese women, and determine if preconception weight loss improves offspring adiposity trajectories.

Genotype-specific effect of maternal diet rich in sucrose: the role of Zbtb16 gene

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Background/Aims: Maternal diets rich in simple carbohydrates were shown to affect the health outcomes of the offspring. A significant energy metabolism regulator, Zbtb16, participates in pathogenesis of metabolic syndrome. We tested a hypothesis that variation of *Zbtb16* gene modulates the effect of high-sucrose diet (HSD) on metabolic and transcriptomic profiles of the offspring.
Method: We utilized a minimal congenic rat strain (SHR-Zbtb16) carrying only a single gene, *Zbtb16*, from a metabolic syndrome model, the PD/Cub strain, within the spontaneously hypertensive rat (SHR) strain genomic background. 4-months-old SHR and SHR-Zbtb16 rat dams were fed either standard diet during pregnancy and lactation (control groups) or HSD (70% calories as sucrose) during the same period. We assessed the metabolic profiles of the 4 groups of dams as well as their adult offspring fed standard diet including glucose tolerance, levels of insulin, cytokines and hormones as well as concentrations of triglycerides and cholesterol in 20 lipoprotein fractions. Also, we assessed the transcriptome in liver, brown and white adipose tissue of the offspring.
Results: In both strains, the pregnancy increased levels of leptin and, exclusively in SHR-Zbtb16, the concentrations of interleukin 17. The mid-pregnancy interleukin 18 was increased and polypeptide YY was decreased in SHR compared to SHR-Zbtb16. In offspring, exposure to maternal HSD substantially increased brown fat weight in both strains (MatDIET p = 1.52E-10), decreased triglycerides in most fractions of LDL particles and impaired glucose tolerance exclusively in SHR offspring. The transcriptome assessment revealed networks of transcripts reflecting the shifts induced by maternal HSD with major nodes including *mir-126*, *Hsd11b1* in the brown adipose tissue; *Pcsk9*, *Nr0b2* in liver and *Hsd11b1*, *Slc2a4* in white adipose tissue.
Conclusions: Our results show that Zbtb16 gene substantially modulates the effect of HSD-induced programming on metabolic and transcriptomic profiles of the offspring.

Role of Nme7 interactome in metabolic programming by maternal high-sucrose diet in experimental inbred models of metabolic syndrome

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Background/Aims: We showed previously an association of nucleoside diphosphate kinase 7, non-metastatic cells 7

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(*Nme7*) with insulin resistance and dyslipidemia. We assessed the effect of Nme7 and its interactome on significant changes of hepatic transcriptome in adult male offspring of high-sucrose (HSD)-fed rat dams of two defined genetic models of metabolic syndrome, polydactylous rat (PD) and congenic BN.SHR4 rat (carrying defective allele of Cd36 of SHR origin).
Method: Rat dams were fed either HSD or standard diet (STD) for 1 week before breeding, through pregnancy, birth, till weaning of the offspring. The 5-month-old male offspring were then divided into 2 groups that were fed either HSD or STD for 2 weeks. The metabolic (incl. glucose tolerance, insulin sensitivity of adipose tissue and muscle), morphometric and transcriptomic (in liver by Affymetrix Rat Exon 1.0 ST Array) profiles were assessed in all 8 strain*maternal diet*offspring diet combinations. We used Ingenuity Pathway Analysis to assess the –omic relations.
Results: Transcriptome analysis revealed distinct pathways/clusters between matched and mismatched maternal *offspring diet combinations as well as between strains for equivalent diet settings. PD was clearly more sensitive to programming effect of HSD, showing significantly higher numbers of differentially regulated genes in offspring of HSD vs. STD-fed dams compared to BN.SHR4, corroborated by more pronounced changes of metabolic profile. We identified a substantial overlap between Nme7 interactome and the transcriptome changes elicited by programming with major hubs formed by *Hnf4, Trim27, Rel, Ofd1* and *Ywhaq* genes.
Conclusions: We show that the *Nme7* and the members of its interactome are overrepresented in sets of transcripts showing changes in expression in offspring of rat dams exposed to sucrose, suggesting a possible role of Nme7 in the underlying pathophysiological processes.

Investigation of external microbial exposures and child cognition and behaviour at 2 years of age

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Background/Aims: Epidemiological studies have identified a range of environmental factors associated with higher microbial exposure in early life and reduced risk of allergic disease. Several of these exposures impact the microbial composition of the infant gut. Despite intense interest in the influence of gut microbiome on early cognition and behaviour, the relationship between these external microbial exposures and cognition and behaviour has not been well characterised.
Method: The Barwon Infant Study is a birth cohort (n=1074) in Victoria, Australia. Comprehensive questionnaire, clinical and biological measures were collected at multiple time-points. Multiple linear regression was used to evaluate associations between 56 external microbial exposures and three outcomes; cognition (Bayley Scales of Infant and Toddler Development (BAYLEY-III) (n=667, mean (SD) age = 2.45 (0.14) years), internalising and externalising behaviour (Child Behaviour Checklist (CBCL) (n=666, mean(SD) age = 2.45 (0.14)years).
Results: Overall, there were no consistent patterns or dose response found within an outcome nor across all three outcomes, although there was some evidence for individual associations. Breastfeeding and child care were associated with higher cognitive scores (adj. mean diff. (95%CI) = 3.20 [0.23, 6.17] and 0.68 [0.12, 1.24] respectively), and increasing sibling number was associated with lower internalising behaviour (adj. mean diff. (95%CI) = -4.13 [-6.34, -1.91]).
Conclusions: In contrast to allergic disease, there was an absence of epidemiological evidence to support the association between these external microbial exposures and cognition and behaviour. Further studies are required to investigate a broader sweep of exposures which influence gut-microbial composition and cognition and behaviour.

The joint effects of direct and indirect adverse childhood experiences on the occurrence of asthma in adulthood

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Background/Aims: Adverse childhood experiences such as emotional and physical abuse, and family dysfunctions (e.g., intimate partner violence) have been individually linked to asthma development in adulthood. The combined effects of different types of ACEs on the likelihood of developing adult asthma have been seldom explored. This study evaluates associations between individual and combined exposures to direct childhood abuse, indirect household dysfunction and other adverse household experiences on the occurrence of asthma in adulthood.
Methods: This study is a secondary analysis of data from the 2013-Alberta Adverse Childhood Experiences Survey that gathered information about adversity during childhood and the risk of poor health outcomes in adulthood, including asthma, in a random sample of 1,207 subjects. We defined: direct childhood abuse (DCA) as physical, sexual or emotional experiences; indirect household dysfunction (IHD) as domestic violence or household substance use; and other adverse household experiences (AHE) as living with separate parents or with some family member with depression, other chronic disease or physical disability. We used multivariable logistic regression models to assess main and interaction effects of DCA, IHD, and AHE on asthma with adjustments by sex, education, income, and ethnicity. Odds ratios (OR) and 95% confidence intervals (CI) are reported.
Results: Among 1,207 study participants, 8.8% developed asthma; 27.3% experienced DCA; 26.4% experienced IHD,

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and 41.8% experienced AHE. Independent positive associations between DCA (OR: 2.26, CI:1.04-4.88) and OHD (OR: 1.82, CI:1.01-3.30) and the development of asthma later in life were observed. Combined exposures were not significant either in the additive and multiplicative scales.
Conclusions: Our study reinforced that direct childhood abuse is an important risk factor for asthma in adulthood. Moreover, it provides new insights into the effects of domestic dysfunction related to living with separated parents and adverse health conditions in the family on the likelihood of developing asthma in adulthood.

Dexamethasone induced syncytiotrophoblast cell apoptosis through blocking glucose transport in pregnant women with threatened preterm labor

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Abstract
Background and Objectives: Severely preterm infants may have underdeveloped lungs due to short of own surfactant and results in respiratory distress syndrome. To reduce this risk, dexamethasone (DEX) is often administered into pregnant mothers. However, preemies with low birth weight were caused by DEX. Therefore, the present study aimed to find the correlative therapeutic targets to reduce the side effects of DEX using the human placenta samples.
Methodology: Pregnant women with TPL were divided into DEX (6 mg of DEX through intramuscular injections every 12 h for 2 days was treated before 34 weeks' gestation, n=10) and control groups without DEX (n=10). Total RNA from placenta in the two groups was extracted, and then GLUT1, GLUT3, and GRα mRNA and protein expressions were detected using quantitative real time PCR and western blot, respectively. Cell nucleus was stained with Hematoxylin-eosin staining and human placenta lactogen (hPL) in placental lobules was detect immunohistochemical staining. Subsequently, the relevant study on cell apoptosis was performed using terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labelling assay.
Results: When compared with that of the control group, GLUT1, GLUT3, and GRα mRNAs and proteins expressions in DEX group were significantly decreased (P<0.05); Nucleus perimeter was increased in DEX group (P<0.01); hPL-positive cells were less than in DEX group. Additionally, cell apoptosis were increased in DEX group compared with the control group (P<0.01).
Conclusion: DEX suppressed the growth and development of fetus through GRα blocking glucose transport following by downregulating GLUT1 and GLUT3. It is significative for the side effects of DEX in treatment of pregnant women with threatened preterm labor.
Keywords: dexamethasone, glucocorticoids, glucose transporter, glucose transport, cell apoptosis.

Exploring Prenatal influences On Childhood Health (EPoCH): what role for mums and dads?

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Background/Aims: It is widely recognised that pregnant mothers can influence the health and characteristics of their children via non-genomic "maternal effects", but there are still gaps in our understanding regarding causality and the range and mechanism of effects. Consequently, current public health advice in pregnancy can be inconsistent, misleading and not based on robust, empirical evidence of causation. Additionally, there is increasing evidence that fathers can also exert "paternal effects" on the child health, but very little advice is currently offered to fathers-to-be. Funded by the UK Medical Research Council, I have established a research project (Exploring Prenatal influences On Childhood Health (EPoCH)) that aims to better understand whether and how both maternal and paternal health behaviours in the prenatal period causally influence offspring health outcomes in childhood.
Method: By combining existing questionnaire and 'omics data from six European birth cohorts, and "triangulating" evidence from multiple causal inference methods (Mendelian randomization, sibling comparisons, negative control designs), this project explores causal relationships and interactions between maternal and paternal prenatal health behaviours (smoking, alcohol, fat/sugar in diet, body mass index, caffeine and physical activity) and childhood outcomes including birth weight, cleft lip/palate, IQ and educational attainment. It also explores the role of DNA methylation as a potential molecular mediator of parental influences on offspring health.
Results: Through well-powered meta-analysis of epigenome-wide association studies, the project has already shown that maternal and paternal pre-pregnancy BMI are associated with offspring methylation to a similar degree, suggesting associations are better explained by genetic or shared environmental factors than a causal mechanism. The project is now exploring the other exposures and outcomes mentioned above.
Conclusions: Findings will identify the most appropriate prenatal targets (mothers, fathers, or both parents) for more effective public health to improve child health.

It's the mother! Recognising and addressing the imbalance of DOHaD research towards the study of maternal pregnancy exposures

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Background/Aims: DOHaD research has been more concerned with exposures in the *fetal* period than in any other window of development. This interest manifests as an abundance of studies on the potential effects of the health and lifestyle of mothers around the time of pregnancy on the health of their children.
Method: We reviewed all studies ever published in the Journal of the Developmental Origins of Health and Disease.
Results: Of 325 eligible articles, 274 (84%) describe studies of maternal exposures, with 214 (66%) describing studies of maternal exposures in isolation (i.e. these studies did not consider paternal, offspring or grandparental exposures). Maternal exposures *in pregnancy* were studied in 252 articles (77%), with 167 articles (51%) reporting on maternal pregnancy exposures in isolation. In stark contrast, only 12 articles (4%) described studies of paternal exposures (in any period) and only one study (0.3%) considered paternal exposures in isolation.
Conclusions: We argue that this focus reflects deeply-held assumptions, amongst researchers, clinicians, policy makers, the media and the public, that 1) causal early life exposures are primarily transmitted via maternal traits or exposures, 2) maternal exposures around the time of pregnancy and early infancy are particularly important, and 3) other factors, such as paternal factors and postnatal exposures in later life, have relatively little impact in comparison. These implicit assumptions about the "causal primacy" of maternal pregnancy effects set the agenda for DOHaD research and, through a looping effect, are reinforced rather than tested. We call for the DOHaD research community to recognise and challenge these assumptions.

Using genetic and epigenetic approaches to identify factors that influence paternal participation in birth cohort studies

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Background/Aims: Most birth cohorts recruit pregnant women initially, then ask these women to invite their partners. Accordingly, paternal involvement in birth cohorts is lower than that of mothers. As well as contributing to the focus on maternal effects in the DoHaD field, this can also bias estimates of paternal effects. A better understanding of the factors that influence paternal participation will improve the interpretation and conduct of analyses investigating paternal effects. It could also help in the development of strategies to increase paternal participation. Given the lack of data on non-participating partners, we can use data from enrolled mothers and offspring to identify factors that influence paternal participation.
Method: Using data from the Avon Longitudinal Study of Parents and Children (ALSPAC), we derived paternal participation based on whether the partner of an enrolled woman had completed at least one of two questionnaires administered during pregnancy. We first conducted epigenome-wide association studies (EWAS) of paternal participation using Illumina 450k DNA methylation data from mothers (n=895) and offspring (n=955). We then used the EWAS Catalog (a systematically compiled catalogue of published EWAS results) to identify CpGs where methylation is associated with each catalogued trait (n traits=165) and assessed enrichment of these sites in the paternal participation EWAS. We also used genotype data from the mothers (n=8,427) and their offspring (n=8,433) to conduct genome-wide association studies (GWAS) of paternal participation. Using GWAS summary statistics in the MR-Base database, we performed two-sample Mendelian randomization to identify traits (n traits>1000) which may be causally implicated in paternal participation.
Results: The paternal participation EWAS was enriched for CpGs that have previously been associated with traits related to smoking (serum cotinine and maternal smoking during pregnancy), mental health (PTSD, major depressive disorder and prenatal maternal stress), neurodevelopment (ADHD trajectories) and HDL cholesterol. In two-sample Mendelian randomization, activity levels and chronotype (morning preference) were positively associated with paternal participation while napping was inversely associated.
Conclusions: Using epigenetic and genetic data on mothers and offspring, we have performed a systematic evaluation of factors associated with paternal participation, some of which may be causal.

Glucose monitoring analysis identifies patterns specific to women with gestational diabetes

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Background/Aims: Continuous glucose monitoring (CGM) data have been used to unmask the complexity of glycemic

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patterns. The study aims to describe potential glycemic patterns in pregnant women who had gestational diabetes (GDM) from CGM data.
Method: The present study is embedded in the Born in Guangzhou Cohort Study, China. Pregnant women who had current GDM and underwent CGM for 5 to 14 days at around 29 gestational weeks (SD 3.5 weeks) were included. Glycemic signatures from CGM data were classified as low, moderate, and severe variability using spectral clustering method[1]. Individual glucose patterns were defined following the main variability signature that accounts for the largest proportion (over 1/3) of the monitoring time.
Results: A total of 97 women with GDM were included. Low, moderate, and severe variability signatures showed a progressive increase in glucose concentration and the magnitude and frequency of glycemic fluctuations (Figure 1). In the study population, 44 were classified as low (45.4%), 34 as moderate (35.1%), and 19 as severe (19.6%) variability pattern. The mean cumulative time spent in severe variability signature (in every 24 monitoring hours) for women with low, moderate and severe patterns were 3.1 ± 1.9, 5.5 ± 2.4, and 11.8 ± 2.4 hours, respectively. The fraction of time spent in severe variability was significantly associated with fasting glucose (r=0.3876, p=0.001), 2-hour glucose level (r=0.2656, p=0.0093), and pre-pregnancy BMI (r=0.2548, p=0.0118). There was an increasing trend in both fasting and 2-hour glucose across low, moderate and severe glucose patterns (fasting [mean ± SD]: 4.5 ± 0.4, 4.7 ± 0.4, 5.0 ± 1.0 mmol/l, p=0.0229; 2-hour [mean ± SD]: 9.0 ± 1.0 9.3 ± 1.3, 10.1 ± 2.0 mmol/l, p=0.0264).Women who had previous GDM or previously delivered a macrosomia, and who were multipara were more likely to have the severe pattern.
Conclusions: There are three glucose patterns in GDM women identified from CGM data—low, moderate, or severe variability. Nearly 1/5 of the GDM women experienced severe glucose variability in most of the time. Awareness is needed to manage the glucose dysregulation beyond the Oral-glucose-tolerance-test.
Reference: 1. Hall H, Perelman D, Breschi A, et al. Glucotypes reveal new patterns of glucose dysregulation. PLoS biology. 2018,16(7):e2005143.

Gestational diabetes is associated with change in the gut microbiota composition in second trimester of pregnancy

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Abstract
Background: Gestational diabetes mellitus (GDM) is a metabolic disease during pregnancy and imbalances of gut microbiota composition are associated with metabolic perturbations. In this study, we aimed to investigate the possible relationship between GDM and changed gut microbiota in second trimester of pregnancy.
Methods: Pregnant women with GDM (n = 80) and normal pregnancy (n = 240) were recruited in second trimester of pregnancy at Women's Hospital of Nanjing Medical University. Gut microbiota profiles were assessed by 16S rRNA amplicon Illumina sequencing of the V3-V4 region.
Results: Compared with normal pregnancy, lower observed_species were detected in the GDM group. Principal coordinates analysis based on the Bray-Curtis distance and unweighted unifrac distance showed that microbial communities were significantly different between the two groups. *Firmicutes* at phylum level had a lower abundance in the GDM group. Lefse analysis demonstrated a higher abundance of two genera from *Proteobacteria* phylum, i.e., *Burkholderia* and *Xenorhabdus* and an unclassified genus of the *Chloroflexi* pylum in women with GDM. Meanwhile, seven genera were enriched in the normal pregnancy group and four of them belonged to *Firmicutes* phylum.
Conclusions: Our results show changed gut microbiota composition in second trimester of pregnancy in pregnant women with GDM. Further prospective studies are needed to explore whether such microbiota disruption conveys risk of developing long-term metabolic disease in GDM women and their children.
Keywords: gestational diabetes mellitus; gut microbiota; second trimester of pregnancy

Prenatal exposure to lipopolysaccharide alters inflammatory responsiveness by LPS-challenging in offspring

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Background/Aims: Excessive inflammation by infections during pregnancy results in the pathogenesis of intrauterine growth restriction, preterm labor, and miscarriage. In addition, prenatal exposure of inflammation have profound long-lasting effects on the immune and reproductive functions of offspring. The aim of this study was to investigate the effect of maternal lipopolysaccharide (LPS) exposure during pregnancy on growth and function of offspring and the impact of LPS challenging to mature male offspring.
Method: To induce maternal inflammatory response, pregnant ICR mice were injected saline (n=6) or LPS (i.p., n=5, 0.1 mg/kg) at gestational days 14 and 15. After birth, the body weight of offspring was measured every week. At 8 weeks of age, male offspring were randomly injected saline or LPS (i.p., 0.5 mg/kg), and tissues (testis, spleen, and liver) were collected 24 h after administration.
Results: Administration of LPS significantly inhibited body weight of mother at gestational days 15-17, there was no difference in day of delivery. The body weight of offspring at birth in LPS group was significantly lower than those in control group. However, the body weight of offspring in LPS group was significantly higher during 1-3 weeks age. Testis weight and plasma testosterone levels were low in adult offspring born from mothers who received LPS. LPS injection to mother led to the decrease of testis weight and the increase of spleen weight at 8 weeks age male offspring. LPS administration to male offspring born in both dams significantly increased plasma CCL2 and IL-10 concentrations. In liver, LPS challenging to

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male offspring significantly increased cytokine production and mRNA expression (CCL2, TNFa, and IL-1b) in both groups, these increased levels were significantly lower in offspring lf LPS-treated dams compared to control dams.
Conclusions: Maternal inflammatory response during pregnancy may have potential to influence immune and reproductive functions in offspring.

Impact of Food Environment on Prevalence of CVD Risk Factors of Employed Adults in Urban Delhi, India

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Background: Unhealthy food environment can deteriorate health and make one susceptible to overweight, obesity and other cardio-vascular risk factors. The relationship between the food environment and overweight/obesity and cardio-vascular diseases (CVDs) is complex. CVD risk factors like hypertension, type 2 diabetes, abnormal triglyceride, low HDL, abdominal obesity, high body mass index contributes to morbidity, mortality and economic burden. This study aims to estimate the impact of food environment and prevalence of CVD risk factors among employed adults of urban Delhi, India.
Methods: A cross sectional study was carried out among 455 apparently healthy employed adults of urban Delhi, India. Different worksites from public and private sectors were selected to conduct the study. Using a pretested questionnaire information about family history of CVD, tobacco and alcohol use, dietary patterns, total physical activity was collected. Blood pressure, anthropometric and metabolic parameters were measured. Subjects were identified for metabolic syndrome as per NCEP ATP III Guidelines. Checklist for Health Promotion Environments at Worksites (CHEW) was used to assess the built and nutrition environment of the selected worksites. The scoring system for CHEW signified the degree to which a work environment is healthy, partially healthy or unhealthy.
Results: Based on the findings of the CHEW only one of the seven selected worksites had a healthy environment. Two worksites had partially healthy and four had unhealthy environment. The overall CHEW scores of the worksites was 19.8 ± 7.9. Nutrition (CHEW score: 13.4 ± 7.2) and physical (CHEW score: 6.45 ± 3.3) environment of theses worksites were unsupportive of health resulting in prevalence of CVD risk factors like low high-density lipoprotein (HDL) (62.9%), abdominal obesity (39.3%), overweight (20.9%), obesity (42.6%), hypertension (56.3%), elevated blood glucose (16%) and high triglyceride (61.1%). It was found that sedentary lifestyle among working adults was one of the significant risk factors for the prevalence of CVDs (32.3%, $p<0.04$) along with family history (74.9%), smoking (17.6%) and drinking (37.8%). Low physical activity was negatively correlated with increased body mass index ($p<0.005$) and high waist circumference was positively correlated with low HDL levels ($p<0.00$).
Conclusion: Employed adults spend majority of their time confined in offices, exposed to unhealthy built and nutrition environment limiting their access to healthy foods and minimal physical activity resulting in increased CVD risk factors. Findings of this study emphasizes and urges the need to implement food environment health programs and policies at community as well as worksite levels to prevent the ongoing CVD epidemic in India.

Effect of Maternal Diet High in Linoleic Acid on Maternal Lipid Metabolism and Endocannabinoid Signalling in Fetal Heart in rat model

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Background/Aims: Linoleic acid (LA) is a major omega-6 fatty acid which is critical for cellular function and signalling. It has vital roles during pregnancy for fetal growth and development. In modern diet, due to increased use of vegetable oils, the consumption of LA has been increasing gradually. Previous studies have reported the pro-inflammatory properties of increased LA, however, adverse effect of high LA intake in human's health is controversial. The effect of high intake of LA during pregnancy in mother's health and fetal programming is unknown. The aim of the present study is to explore whether maternal diet high in LA influences maternal metabolic health, fetal growth and endocannabinoid signalling in fetal heart.
Method: Female Wistar Kyoto rats were fed with diet low in LA (LLA-1.44% of energy) or diet high in LA (HLA-6.21% of energy) with matched omega-3 (0.3% of energy), for 10 weeks before and during gestation. Rats were sacrificed at E20, and maternal and fetal organs were collected for analysis.
Results: Total cholesterol, LDL-cholesterol and HDL- cholesterol were decreased in the maternal plasma from rats fed with HLA. The relative mRNA expression of sterol regulatory element binding transcription factor 1 (*SREBF-1*) was decreased in the maternal white adipose tissue from the rats fed with HLA. There was no changes in maternal circulating cytokines, however, TNF-α and IL-7 levels were increased in the maternal liver from HLA rats. Further, in fetal heart, mRNA expression of cannabinoid receptor 2 (*CB2*) was decreased in both sexes from mothers fed with HLA diet. NAPE-PLD, a key enzyme involved in endocannabinoid synthesis, was decreased in female fetal hearts in HLA group.
Conclusions: HLA diet before and during pregnancy alters maternal lipid profile, liver cytokines and endocannabinoid

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signalling in fetal heart suggesting that the amount of LA intake should be considered during pregnancy.

Retinoic Acid Deficiency Leads to Reduced Nephron Endowment in Offspring Exposed to Maternal Diabetes

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Background: There is growing evidence that offspring of mothers with type 1 diabetes are more prone to develop hypertension and chronic kidney disease in adulthood, which may be related to low nephron mass. During mammalian embryogenesis, all-*trans* retinoic acid (RA) is crucial for nephrogenesis. Our preliminary findings showed that there was a significant reduction of RA synthesizing activity and RA concentration in the kidneys of mouse embryos exposed to streptozotocin-induced maternal type 1 diabetes or high glucose conditions. We therefore hypothesize that RA deficiency in the kidneys of embryos exposed to a maternal diabetic or hyperglycemic milieu leads to reduced nephron number.
Methods: To test our hypothesis, we used an *in vitro* and *in vivo* approach to determine whether supplementation of RA could restore nephrogenesis in embryos exposed to hyperglycemic or diabetic conditions. First, we cultured kidneys explanted from mouse embryos in medium containing 30 mM (high) or 5 mM (normal) D-glucose with co-addition of varying concentrations of RA or pan-RA receptor agonist (TTNPB), or the solvent control. Next, we orally fed RA or the vehicle as control to diabetic or non-diabetic pregnant mice at gestational day 12 and 13, at which the kidneys exhibited RA deficiency.
Results: Supplementation with RA upregulated the mRNA expressions of genes that are downstream targets of RA signaling crucial for kidney development, and increased ureteric branching and nephrons generation in embryonic kidneys exposed to high glucose *in vitro* or *in vivo*. Similar effects were found in kidney explants exposed to TTNPB.
Conclusions: Perturbation of RA signaling in diabetic or hyperglycemic conditions leads to reduced nephron number.
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Is Dental Caries In Children Causally Associated With Altered Body Mass Index? Applying Twin Analyses to Infer Causation From Cross-Sectional Data

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Background/Aims: Obesity and dental caries are both highly prevalent conditions with significant short and long-term implications for the health and development of children. The aim of this study was to explore the relationship between body mass index (BMI) and dental caries and test whether the observed associations were consistent with causation using data from twin children.
Method: We measured BMI and cumulative dental caries at six years-of-age in a cohort of 344 twin children. Dental caries in primary teeth were categorised into 'any' or 'advanced' and BMI was analysed as both a continuous and categorical variable. Multiple logistic regression models were fitted using generalised estimating equations to adjust for twin correlation and known risk factors such as sex, age, diet, tooth brushing, community water fluoridation and socio-economic status. Within/between-pair analyses were adjusted for known and unknown shared factors and non-shared factors such as diet and sex. The within-pair effects for monozygotic (MZ) and dizygotic (DZ) twins were compared to determine whether unknown factors (including genes) might explain an apparent causal relationship.
Results: A total of 172 twin pairs, 101 DZ and 71 MZ, participated in the study. There was no association between 'any' dental caries experience and BMI, neither overall nor in within/between pair analyses. However, 'advanced' dental caries at six years was associated with a within-pair difference in BMI of -0.55 (95% CI 0.99, -0.11, p=0.015). A within-pair increase of 1 kg/m^2 in BMI was associated with a lower within-pair risk of advanced dental caries (OR 0.68, 95% CI 0.52, 0.90, p=0.007).
Conclusions: Using within/between-pair analyses to adjust for the effect of many shared known and unknown as well as known non-shared factors such as diet and sex revealed that a causal relationship is possible between lower BMI and dental caries. As dental outcomes were only measured at one time-point, it is not possible to determine the direction of this relationship.

Novel Insights Into Epigenetic Differences In Childhood Dental Disease

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Background/Aims: Oral disease is a common cause of pain, infection and hospitalisation in childhood and has been linked with chronic diseases in adulthood such as cardiovascular disease and diabetes. The most common dental conditions in childhood, dental caries and hypomineralisation, are increasingly recognised to have multifactorial aetiologies that could include epigenetic changes. Our aim was to estimate associations between epigenetic marks of DNA methylation in cord blood leucocytes at birth and dental caries and Hypomineralised Second Primary Molars (HSPM) at six years of age.
Method: This study was nested within a prospective study of 500 twin children, recruited from pregnancy. Genome-wide analysis of DNA methylation was performed on a subset of 27 twin pairs (54 individuals) using the Illumina Infinium MethylationEPIC BeadChip array with DNA from cord blood collected at birth. The presence/absence of 'any' dental caries, 'advanced' dental caries and HSPM were determined by dental examinations conducted at six years of age. There were 19, 15 and 18 individuals with 'any' caries, 'advanced' caries and HSPM, respectively. Linear regression was used to adjust the methylation values for birth weight, sex, maternal smoking, cell counts and batch effects. Residuals from this model were then inverse-normalized and used as the dependent variable in linear regression models in which each dental outcome was the independent variable and which accounted for correlation between twins in a pair.
Results: Applying a false detection rate (FDR) of 0.05, 'any' and 'advanced' dental caries were associated with 39 and five differentially methylated probes (DMPs) respectively. Genes implicated by these probes included *BCL2A1* and *SHANK2* for any caries and *MMP28* and *PRDM16* for advanced caries. No DMPs were found for HSPM.
Conclusions: The findings of this first, exploratory, epigenetic study of dental caries has identified several differentially methylated genes at birth associated with disease risk in childhood.

Acanthosis Nigricans: a Predictor of Developing Type 2 Diabetes in a High Risk population?

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Background/Aims: Indigenous Australians are at an increased risk of developing type 2 diabetes at a younger age, contributing significantly to the mortality gap present between Indigenous and non-Indigenous Australians. Acanthosis nigricans (AN), once considered a rare paraneoplastic dermatosis, has been shown to be associated with insulin resistance. It is being proposed as an easily identified, early clinical marker of diabetes risk.
Method: Established longitudinal birth cohorts, Indigenous (n 686) and non-Indigenous (n 196) with follow-ups at age 18yrs (adolescence; n=665) and 25yrs (adulthood; n=576). Face-to-face examination including presence of acanthosis nigricans (AN), height & weight used to calculate body mass index (BMI), and biomarkers including HbA1c. Diabetes (DM) was defined as HbA1c≥6.5% and prediabetes as HbA1c 5.8-6.4%. BMI categorised as underweight ≤18.5, normal 18.6-24.9, overweight 25-29.9, obese ≥30. Complete data available for 302 Indigenous & 91 non-Indigenous participants.
Results: At adolescence, low levels of DM were present (Indigenous 1, non-Indigenous 1). AN rates were higher in Indigenous (219 vs 2). Of those with AN, 208 had a normal HbA1c and 21 prediabetes. By adulthood, DM increased to 14 (Indigenous 13, non-Indigenous 1) and AN decreased (Indigenous 177, non-Indigenous 0), with AN no longer present in 74/221. Of those with DM in adulthood, AN was present in 10/14 in adolescence and 11/14 in adulthood. At adolescence, no relationship between AN and BMI category was seen; AN present in 37/68 of underweight, 65/182 of normal, 50/96 of overweight & 25/48 of obese. However, in adulthood, current BMI was associated with DM; odds ratio 5.9 (CI: 1.2-30; p .031) in overweight and 12.8 (CI: 2.5-66; p .002) in obesity compared to normal BMI.
Conclusions: AN was common in this high risk population, present at a young age. The proportion of people with AN was higher it adolescence. Of those who developed Type 2 DM by adulthood, 79% (11/14) had AN. However, 85% of adolescents with AN had a normal HbA1c up to 7 years post AN diagnosis: only 2/221 had DM at that time and <1% developed DM by adulthood. In this high risk population, the presence of AN was not a good predictor of current, or future, diabetes risk.

Growth Trajectory of Australian Indigenous and Non-Indigenous Fetal Growth Restricted Babies: Adolescence to Young Adulthood

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Background/Aims: Obesity is a major risk factor of chronic disease risk. However, being underweight also detrimentally affects physical and psychological health. Underweight women are at an increased risk of pregnancy complications and giving birth to fetal growth restricted (FGR) babies. Babies born FGR have an increased risk of developing chronic disease; this risk is magnified in those who become obese. Indigenous people in the Northern Territory, Australia have high rates of FGR at birth and are at increased risk of chronic diseases like diabetes, renal and cardiovascular disease later in life.

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Method: Two distinct but complementary longitudinal studies assessing the risk of chronic disease across the life course; Aboriginal Birth Cohort (urban and remote Indigenous) and Top End Cohort (urban non-Indigenous). Detailed anthropometric data was collected at birth, in adolescence (mean 18 years) and young adulthood (mean 25 years).
Results: Significantly higher rates of FGR (<10th percentile) were present in Indigenous compared to non-Indigenous (28 vs 7%). Risk factors for FGR in Indigenous babies included maternal smoking, undernutrition and young age. Those born FGR were smaller on all anthropometric measures in adolescence and young adulthood; being significantly shorter, weighed less, had a lower BMI, smaller mid upper arm, waist and hip circumferences, and lower waist to height and waist to hip ratios than non-FGR babies. By young adulthood rates of overweight/obesity (BMI≥25 kg/m^2) were increasing, highest in urban Indigenous (61% men: 52% women) compared to urban non-Indigenous (40% men: 34% women) and remote Indigenous (26% men: 38% women). However, underweight levels remained high in remote Indigenous young adults (22% men: 29% women).
Conclusions: Rates of obesity are increasing with age, with chronic disease markers increasing with current BMI. The lowest rates of obesity were seen in FGR babies and may explain the lack of association seen with FGR and chronic disease markers seen here. The risk factors for FGR (young maternal age, maternal smoking and undernutrition) still remain in this generation of remote women.

Epigenetic Aging in Newborns – Risk Factors and Associations with Cardiovascular Phenotype

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Background/Aims: Epigenetic aging is a potential mechanism driving risk of non-communicable diseases. There are limited studies on epigenetic aging in the newborn, and it is unknown whether epigenetic aging is associated with early life markers of cardiovascular health. We sought to investigate the associations between early life exposures and newborn epigenetic age, and whether epigenetic age is associated with age-appropriate markers of cardiovascular health at birth.
Method: Epigenetic age in 169 newborns was measured using the Horvath age calculator, and categorized as positive or negative epigenetic aging. Aortic intima-media thickness (an age-appropriate marker of atherosclerosis) and heart rate variability (a marker of autonomic activity) were assessed at birth. Maternal diet during pregnancy was assessed using food frequency questionnaire.
Results: Neonatal characteristics associated with higher prevalence of positive epigenetic aging included female sex (odds ratio 2.57 [95%CI 1.36, 4.85]), and preterm birth (odds ratio 5.70 [95%CI 1.43, 22.69]). Neonates with positive epigenetic aging had higher body fatness (11.7% body fat) than neonates with negative age acceleration (10.0% body fat; P=0.04), and were less likely to be small-for-gestational age (P=0.02). Maternal characteristics associated with epigenetic aging were age (0.7 weeks epigenetic age acceleration per 1 year higher maternal age [95%CI 0.0, 1.4]; P=0.04), total omega-3 fat intake (-15.6 weeks epigenetic age acceleration per 1% fat as omega-3 fat [95%CI 28.3, -2.9]; P=0.02), and iron supplementation during pregnancy. Newborn epigenetic age was not associated with markers of newborn vascular health or autonomic activity.
Conclusions: Maternal and newborn characteristics identify neonates with accelerated epigenetic aging. Modifiable lifestyle factors associated with lower epigenetic aging include a maternal diet rich in omega-3 fatty acids and iron supplementation during pregnancy, suggesting potential intervention strategies to prevent accelerated epigenetic aging.

Intergenerational Transmission – Maternal Anthropometry & Newborn Cardiometabolic Health

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Background/Aims: The children of women with obesity are more likely to develop obesity during childhood and cardiovascular disease in adulthood. It remains unclear as to whether this is due to a direct influence of maternal adiposity on offspring health or a shared obesogenic environment.
We sought to determine associations of maternal adiposity with newborn offspring cardiometabolic health.
Method: 209 mother-child pairs at RPA Women & Babies Hospital, Sydney. Birth weight, body fatness (air displacement plethysmography), aortic intima-media thickness (age-appropriate marker of atherosclerosis), and heart rate variability (marker of cardiac autonomic activity) were assessed at birth. Maternal anthropometric measures (height, weight) were assessed clinically at their first antenatal appointment, and BMI calculated.
Results: 153 women had BMI <25 kg/m^2, 38 were classified as overweight, and 18 with obesity. Maternal BMI was not associated with offspring birth weight (r = .066, P = .17) or body fatness (r = .067, P = .17); however, maternal weight was associated with offspring birth weight (r = .171, P = .01) and body fatness (r=.131, P= .03). Maternal height was strongly associated with offspring birth weight (r = .279, P < .0001) and body fatness (r = .188, P = .003).
Maternal BMI was the strongest predictor of offspring heart rate variability (r = -.191, P = .01). Maternal anthropometric

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measures were not associated with offspring aortic intima-media thickness ($P > .05$).
These results were similar in multivariable linear regression models adjusting for gestational age, physical activity, energy intake and newborn sex.
Conclusions: Maternal weight is associated with offspring adiposity, although this is due to maternal height, not maternal adiposity. These results suggest that maternal obesity is unlikely to directly influence fetal body fatness. However, higher maternal adiposity is associated with poorer autonomic activity in neonates. This is consistent with a higher risk of developing hypertension and cardiovascular diseases in adulthood as a direct result of these intrauterine exposures.

The promotion of nurturing care through routine antenatal services

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Background/Aim: South Africa (SA) acknowledges the importance of the first 1000 days for a child's future wellbeing. Efforts to promote nurturing care (NC) through the health system in SA are currently focused on routine postnatal services. This study explored how NC can be promoted during pregnancy, taking advantage of WHO's (2016) and SA's (2015) recommendations for routine ultrasound scan (US) <24 weeks. This is the first such study we identified in a lower resourced setting.
Method: Focus group discussions and interviews with pregnant women and their partners at Baragwanath Hospital in Soweto informed a 3-arm randomised trial to test the effects of messages about foetal development during US to pregnant women and their partners on infant development, parental mental health, parent-infant attachment and infant feeding. The three arms are: routine US; US <24 weeks with messages, US <24 and <34 weeks with messages.
Results: Emerging themes helped refine messages which aimed to: 1) improve relationships with health care staff (e.g. most women are not shown their baby during US); 2) reduce relationship anxiety by inviting partners to accompany women; 3) increase partner involvement and 4) provide information and reassurance about their infant's development and early care. One hundred pregnant women in each of three groups are being enrolled. Women (and their partners) and infants are followed up 6 weeks and 6 months postnatally.
Conclusions: Pregnancy is a period of heightened receptivity when information and support can increase parental investment in pregnancy and child wellbeing. Routine antenatal services, including eight visits and especially visualisation during US, can be better utilised to improve maternal knowledge and reduce anxiety, increase partner involvement in pregnancy and childcare and transform the focus of health professionals to support every child to survive and thrive.

Relationships between linear and abdominal pre- and postnatal growth and vascular structure and function in 8-9 year-old children

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Background/Aims: Low birth weight and later adiposity is associated with risk of adult cardiovascular disease (CVD). Blood pressure (BP), carotid intima-media thickness (cIMT), carotid-femoral pulse wave velocity (cfPWV) and measures of endothelial function are early vascular CVD risk markers in adults. We examined whether conditional linear and abdominal circumference (AC) growth from early pregnancy until age 8-9 years are associated with these vascular CVD risk markers in children.
Method: In the UK Southampton Women's Survey mother-offspring cohort, anthropometric measurements were collected at ten time-points from 11 weeks' gestation (wg) to 8-9 years. From these, conditional variables were calculated, representing growth velocity between time-points independent of earlier growth. Associations were examined using linear regression in 728 children that had growth measures from all time-points and vascular measures at 8-9 years.
Results: Prenatal linear- and AC-growth were not associated with systolic BP or cfPWV at age 8-9 years, while postnatal linear and AC growth were positively associated, especially accelerated AC growth between ages three and six years (1.96 mmHg higher systolic BP (95% CI: 0.88, 3.04) per 1SD greater AC-increase). In contrast, faster AC gain before 19 wg was associated with higher cIMT at age 8-9 years (0.009 mm greater cIMT (95% CI: 0.004, 0.015) per 1SD larger AC at 19 wg). We found no strong associations between conditional growth and measures of endothelial function.
Conclusions: Mechanisms affecting vascular structure and function in children operate very early in life, and are related to pre/postnatal patterns of both linear and soft tissue growth. Monitoring these may be important for targeting preventive interventions.

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Increased maternal fructose alters milk composition, offspring plasma free fatty acids and hepatic lipid deposition

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Background/Aims: Globally, dietary fructose is a major public health concern. Fructose can contribute to insulin resistance, hepatic *de novo* lipogenesis, hypertriglyceridemia and obesity. Since diet during pregnancy can influence fetal growth and later-life disease predisposition. Little is known regarding the effects of fructose during pregnancy and the influence on offspring development and predisposition to later-life disease.

Method: Female guinea pigs were randomly allocated to control (CD) or fructose (FD) (10% in drinking water) groups. Following 60 days of fructose intake, guinea pigs were mated. Pregnant dams continued *ad libitum* access to fructose water throughout pregnancy. Oral Glucose Tolerance Tests (OGTT) were performed prior to fructose feeding at 12 weeks of age, 60 days after fructose feeding and at mid-gestation day 35. Following birth, all litters were standardized to 4 pups/litter. Offspring groups were weighed daily and underwent blood collection on day 0, 7, and 14. On day 21 offspring underwent an OGTT and post-mortem tissues were also collected.

Results: Maternal response to glucose was significantly increased in the FD group (P>0.05). Significant increases in milk pentadecanoic(P>0.01), vaccenic (P>0.01), cis-vaccenic (P>0.01) and palmitoleic acids (P>0.08) were observed. At day 7 offspring plasma glucose was significantly increased in FD males and females. Likewise, free fatty acids were increased in offspring plasma, Total saturates (P=0.01), C18:0 (P=0.02), C16:0 (P=0.002). Metabolomics and proteomics are currently being analysed.

Conclusions: Increased maternal dietary intake of fructose causes a reduction in gestational length by ~1.5 days (~1-week human gestation) and significant elevation of free fatty acids in dams' milk. Offspring of fructose dams were observed to have significantly elevated plasma glucose and free fatty acids without consuming increased dietary fructose themselves.

The Influence Of Bariatric Surgery On Maternal Periconception Health: A Systematic Review

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Background/Aims: Maternal periconception health is crucial for embryonic and fetal development, affecting health in later life for both future mother and her offspring. The worldwide obesity epidemic has resulted in more frequent bariatric surgery (BS) in women of reproductive age over the past decades. BS can lead to maternal vitamin deficiencies and possibly an increased risk of prematurity and fetal growth restriction. However, the influence of BS on periconception health itself has never been reviewed systematically. The aim of this review is to investigate the evidence of possible associations between BS and measures of maternal periconception health such as hormonal status, fertility, menstrual irregularities, vitamin status, miscarriage and congenital malformations.

Method: Embase, Medline, PubMed, Web of Science and Cochrane database were used for the literature search until December 2018. The ErasmusAGE quality score was used to score the studies.

Results: 44 articles could be included in the analysis. 11 articles described menstrual irregularities after BS: 1 article showed an increase, 1 described no change and 9 described a significant decrease in menstrual irregularities. 10 articles described hormonal status after BS (AMH, LH, FSH, estradiol, SHBG, testosterone free androgen index and Müllerian inhibiting substance). The majority (8 out of 10) of these articles described a change indicating improved fertility, while 2 articles described no change. 15 articles described fertility outcome after BS. 10 of these described an increase in fertility, 2 described an increased use of fertility treatments, only 1 described less use of infertility services and 2 described no change in fertility. 11 articles reported on the change in miscarriage rate after BS. 4 articles described a decrease, 5 described no change and 2 described an increase. 7 articles described the difference between the rate of congenital malformations before and after BS and none found a significant change. 9 articles described maternal vitamin status during the first trimester after BS. All of these described an increased rate of deficiencies in vitamins B1, B9, B12, C, D, folic acid and retinol status except for one article that suggested increased folic acid serum levels.

Conclusions: This systematic review provides evidence of decreased maternal periconception health after BS due to nutritional deficiencies. This overview underlines the importance of adequate preconception care and close preconception monitoring of the vitamin status in these women.

Maternal Obesity Affects the Protective Role of Adipokines in Controlling Oxidative Stress Damage During the Third Trimester of Pregnancy

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Background/Aims: Pregestational obesity is associated with systemic inflammation and oxidative stress (OE) and affects the secretion of adipokines involved in maternal and fetal metabolism control. OE modulates metabolic health in fetuses and newborns supporting the hypothesis of developmental origins of health and disease (DOHaD). To date, it has not been evaluated the effect of pregestational body mass index (p-BMI) on adipokines and oxidative stress markers levels. The aim of this research was to evaluate the effect of p-BMI on adipokines and oxidative stress markers levels in the third trimester of pregnancy.
Methods: Seventy-four healthy adult women in the third trimester of pregnancy were recruited at the National Institute of Perinatology following written informed consent and categorized by p-BMI according to WHO criteria (normal weight n=27, overweight n=23, and obesity n=24). Adiponectin, leptin and 8-oxodG levels were analyzed by ELISA whereas lipohidroperoxides (LOOH), malondialdehyde (MDA) and carbonylated proteins (PC) were quantified by El-Saadani, Gerard-Monnier and Dalle-Done methods, respectively. One-way ANOVA with DMS post hoc test was used to analyze differences by p-BMI categories, and Spearman correlation was performed to study the association between adipokines and oxidative stress markers (IBM SPSS v22 software).
Results: Obese women had significantly lower concentrations of adiponectin (p=0.028) and higher concentration of LOOH (p<0.001), MDA (p<0.001) and CP (p<0.001) than normal weight women.
Adiponectin concentrations in normal weight women had a positive correlation with 8-oxodG (r=0.585; p=0.002) and had a significant negative association with LOOH (r=-0.389; p=0.040), whereas obese women lacked of the protective effect associated to adiponectin.
Conclusion: Adiponectin in pregnant women with normal p-BMI could be involved in the control of OE while in obese women decreased adiponectin levels are associated with increased oxidative stress markers.
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Characteristics and risk factors of gestational diabetes mellitus of women in the second pregnancy with normal blood glucose in the first pregnancy

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Background/Aims: To explore the characteristics of multiparous women in two pregnancies, and discuss the risk factors of gestational diabetes mellitus in the second pregnancy.
Method: Medical records of 2 242 women who gave birth twice in the First Hospital of Peking University from January 2005 to December 2017 were collected retrospectively, these women were non-GDM in their first pregnancy. According to the blood glucose level during the second pregnancy, the multiparous women were divided into non-GDM group and GDM group, and the clinical data of the two deliveries, such as age, pre-pregnancy body mass index, weight gain during pregnancy, OGTT blood glucose level, weight retention, inter-pregnancy interval, macrosomia percentage were analysed. T test, Chi-square test and logistic regression were used for statistical analysis.
Results: In 2 242 cases of women, compared with non-GDM group(1 792 cases), GDM group(450 cases) had higher age in second pregnancy, pre-pregnancy body mass index in first and second pregnancy, weight gain during pregnancy in first pregnancy, OGTT blood glucose level in first and second pregnancy, macrosomia percentage in first pregnancy, weight retention and inter-pregnancy interval. Non-GDM group had higher weight gain during pregnancy in second pregnancy. No significant difference overserved in the two groups in macrosomia percentage in the second pregnancy. Logistic regression analysis showed that longer inter-pregnancy interval will be a risk factor for GDM (OR=1.006,95%CI 1.000-1.011,P=0.032).
Conclusions: Although none of these women were diagnosed with GDM in their first pregnancy, the women diagnosed with GDM in their second pregnancy were already different from the women diagnosed with non-GDM in their second pregnancy as early as the first pregnancy. During the second pregnancy, the weight gain of GDM women during pregnancy was lower than that of non-GDM women, and the macrosomia percentage was not different from that of non-GDM women, which was considered to be related to blood glucose management during pregnancy. Prolonging the inter-pregnancy interval was a risk factor for GDM in the second pregnancy.

Placental and intra-amniotic inflammation are common in low-risk pregnancies and are associated with altered fetal immune responses at birth

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Background/Aims: Placental and intra-amniotic inflammation are typically associated with preterm birth and poor neonatal outcomes. However, recent reports suggest that low-grade placental inflammation is common in uncomplicated

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pregnancies. The relationship between placental inflammation and fetal immune programming remains speculative. Here, we sought to identify any association between placental inflammation and fetal immune responses.
Method: Cord blood samples collected from elective Caesarean section deliveries (n = 44) were exposed to various immune challenges (resiquimod, LPS, PGN, poly (I:C), cGAMP, and 5'ppp-dsRNA) and production of inflammatory mediators (G-CSF, IFN-γ, IL-1β, IL-6, IL-8, IL-10, and TNF-α) was measured by multiplex assay. Hospital histology reports were used to assess the extent of inflammation in the placenta. Amniotic fluid inflammation was measured by multiplex assay for IL-6, IL-10, CXCL10, and G-CSF.
Results: Almost half (47.7%) of placentae examined here showed histological evidence of inflammation. Different types of inflammatory lesions were associated with distinct fetal immune response profiles. In particular, fetuses with evidence of chorioamnionitis and fetal inflammatory reaction in their placentae had significantly increased immune responses to cGAMP and 5'ppp-dsRNA (ligands for STING and RIG-I, respectively) and significantly decreased immune responses to poly (I:C) (a TLR3 agonist). Interestingly, STING, RIG-I, and TLR3 are all involved in viral response pathways, suggesting that fetuses exposed to chorioamnionitis or fetal inflammatory reaction might respond differently to viruses postnatally.
Conclusions: Exposure to inflammation *in-utero* is associated with aberrant immune reactions at birth.

Reduced Maternal Glucocorticoid Clearance is Associated with Higher Serum Cortisol and Reduced Offspring Birthweight

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Background/Aims: Glucocorticoids play a critical role in directing fetal maturation. High levels of maternal cortisol, measured in serum or saliva, are associated with offspring growth restriction. After adrenal release most cortisol is metabolised and excreted in urine. We hypothesised that variation in this peripheral metabolism and excretion influences maternal serum cortisol levels, and fetal growth.
Method: 151 women with mean age 30.5 ± SD 5.0 years and BMI 27.6 ±.7.1 kg/m^2, performed 24 hour urine collections in the 2nd and 3rd trimesters at gestational ages (GA) 17.3 ± 2.4 and 33.9 ± 1.2 weeks. Maternal serum was sampled at GA 16.7 ± 2.4 and 33.3 ± 1.1 weeks. 24 hour-total urinary glucocorticoid metabolites (TUG) were measured by gas chromatography triple quadrupole mass spectrometry. Associations of log-transformed TUG with serum cortisol and offspring birthweight Z-score were tested with Pearson's correlation and linear regression adjusting for potential confounders.
Results: 3rd trimester TUG and serum cortisol were negatively correlated (r= -0.179, p=0.029). 2nd trimester, 3rd trimester and mean TUG were positively associated with birthweight Z-score (Table 1).
Conclusions: Reduced TUG was associated with both increased serum cortisol levels and reduced offspring birthweight. Variation in maternal peripheral metabolism and clearance of cortisol may serve as a novel mechanism influencing fetal glucocorticoid exposure and somatic growth.

Preterm Birth is Associated with Higher Evening Saliva Cortisol Levels Across the First Year of Life

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Background/Aims: Early exposure to extra-uterine life by preterm birth results in exposure to physiological and environmental stressors at a critical stage in development. Early-life stressors are associated with dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, a key hormonal axis underpinning the link between early-life development and later-life health. We hypothesised that there are differences in basal saliva cortisol levels in infants born at term and preterm across the first year of life.
Method: Saliva was collected during the morning (7:30-9:30), noon (10:00-12:00) and evening (19:30-21:30) across two successive days, monthly, until 1-year corrected age. Cortisol was quantified using a competitive radioimmunoassay. Cortisol values above 150nmol/litre were winsorized, with subsequent Ln-transformation for analyses. Cortisol levels from infants born at term (>37 weeks) and preterm (<32 weeks) was compared using repeated measures ANOVA, with separate analysis for morning, midday and evening values.
Results: 87 term and 33 preterm infants had morning, 78 term and 34 preterm had noon, and 76 term and 33 preterm infants had evening measurements across all study months. Diurnal cortisol secretion was observed in both groups with highest

2nd Trimester TUG		3rd Trimester TUG		Mean TUG across trimesters	
Unadjusted	Adjusted model	Unadjusted	Adjusted model	Unadjusted	Adjusted model
β=.221[2]	β=.199[1]	β=.169[1]	β=.192[1]	β=.258[2]	β=.312[2]

Table 1. [1] p≤ 0.05, [2] p≤ 0.01. Adjusted model variables: Gestation urine samples collected, ethnicity, smoking, maternal age, pre-eclampsia, hypertension, diabetes, maternal BMI, parity

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cortisol levels in the morning and lowest in the evening. In both groups morning cortisol values increased across the year (p<0.001). Evening cortisol was higher in preterm than term infants (estimated marginal mean ln-cortisol 0.318, 95% CI 0.025-0.612, p=0.034). Morning and noon cortisol values did not differ significantly between groups.
Conclusions: Preterm infants had higher evening cortisol values across the first year of life, consistent with a flattening of the diurnal rhythm, a pattern of secretion linked to other early life stressors and to later adverse health. Preterm birth may predispose infants to a different developmental trajectory of an important neuroendocrine system.

Birth order of twins and the risk of Special Educational Need at School: Retrospective Cohort study of 7421 schoolchildren

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Background/Aims: Recent studies have reported that second born twins have increased rates of perinatal mortality at term compared to first born twins. However, whether there is increased long term morbidity if the second twin survives is still to be determined. The aim of this study was to determine if birth order increases the risk of the child having special educational need (intellectual, physical or motor impairment) at school.
Method: We conducted a population-based, retrospective cohort study by linking school census data on 7421 eligible children to their routinely collected maternity records. Children who delivered preterm were excluded as prematurity is known to increase the rates of SEN. The risk of SEN in first and second twins was estimated using multivariable generalised estimating equation analyses.
Results: School census data was available for 7421 twin infants, of which 2217 were excluded as they delivered preterm (<37 weeks). SEN was recorded in 588 (11.30%) children. Overall there was no increased risk of SEN in second born twins (adj. OR 1.04, 95% CI 0.91-1.20). When we stratified by mode of delivery there was a trend towards an increased risk of SEN in second born vaginal twins but this was not statistically significant (adj. OR 1.18, 95% CI 0.97-1.45).
Conclusions: The second-born twin does not seem to be at an increased risk of special educational need at school when delivered at term compared to first born twins and this does not change according to the mode of delivery.

What do adolescents value and how do we use their values to maximise their engagement with health behaviour interventions?

Strömmer, ST[1,2], Shaw, SC[1,2], Jenner, S[1], Morris, T[1], Vogel, C[1,2], Lawrence, WT[1,2], Inskip,HM[1,2], Baird, J[1,2], Morrison, L[3,4], Barker, ME[1,2] and the EACH-B team.

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Background/Aims: Adolescence is an important lifecourse stage when many biological and cognitive functions mature. Intervening in adolescence represents an opportunity for triple benefit: to adolescent health now, to health in adulthood, and to the health of the next generation. Activating adolescent values can encourage better health behaviours. Little is known about adolescents' values in relation to diet and physical activity and how best to target them in interventions. This study explored key values in adolescents' lives and health behaviours.
Method: This qualitative study formed part of a person-based approach to develop an intervention targeting adolescents. We conducted 13 group interviews with adolescents 12-13 years old (n=54) to explore their perspectives on facilitators and barriers to healthy eating and physical activity, and ways to support adolescent health behaviours. Inductive thematic analysis was used to identify key underlying adolescent values for intervention design.
Results: The analysis identified four themes: (1) 'I do want to be healthy' where health behaviour for adolescents has a function in enabling them to feel good about themselves and to function well socially; (2) 'I do what others do' identifying families as role models, friends as key influencers, and celebrities as inspiration for adopting health behaviours; (3) 'This is my life' describing the effort and cost required for health behaviour change; and (4) 'I want healthy to fit into my life' denoting that adolescents want support for change that is fun, easy, engaging, and sociable.
Conclusions: Adolescents value being with their friends, doing things they enjoy, and being supported to achieve their goals. These values overlap with the three basic psychological needs outlined by Self-Determination Theory (SDT): autonomy, competence and relatedness. By aligning health agendas with adolescent values, interventions can support these psychological needs and optimise engagement with, and therefore effectiveness of, interventions.

Logic models in intervention development: an example from EACH-B, a health behaviour intervention in adolescents

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Background/Aims: Behavioural interventions require strong theoretical underpinning. Logic models are useful in intervention development, to define the needs and the approaches required to deliver the desired outcomes. The aim of this work was to develop logic models for the EACH-B intervention.
Method: EACH-B aims to engage adolescents in behaviour change. It builds on an existing intervention called LifeLab. It comprises an educational module focusing on the science behind the need for good health behaviours, and a visit to LifeLab in the University Hospital Southampton for an engaging science-based day to embed the health messages. EACH-B extends LifeLab by providing two additional types of support to the adolescents in embedding behaviour change in their lives: 1. Teacher support using Healthy Conversation Skills, previously successfully used by health workers, and 2. A digital game developed specifically for EACH-B. A logic model was developed for the EACH-B intervention, with the following areas addressed: the Problem, Needs, Evidence Base, Resources, Activities, Short-term outcomes, Medium-term outcomes, and Long-term outcomes. Each step was evidence-based, drawing on the literature. A further more detailed logic model was developed specifically for the digital game, based on psychological theory.
Results: The two logic models were developed successfully, underpinning EACH-B as a whole, and the digital game component. The EACH-B logic model was fundamental in clarifying thinking about the intervention and underpinned the successful funding application. The digital game logic model clarified the thinking on the development of the game and brought together researchers and game designers from widely different backgrounds.
Conclusions: Logic models are valuable in developing interventions, and assist in ensuring a strong theoretical underpinning to the intervention. They also ensure that all those working on the intervention from various backgrounds are clear in understanding the overall aims, what needs to be done and how it will be implemented.

Using creative methods in developing a complex intervention to engage adolescents in eating better and being more active: the EACH-B Programme

Strömmer, ST[1,2], Shaw, SC[1,2], Morris, T[1], Vogel, C[1,2], Lawrence, WT[1,2], Inskip,HM[1,2], Baird, J[1,2], Morrison, L[3,4], Barker, ME[1,2] and the EACH-B team.

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Background/Aims: Adolescence represents an opportunity for triple benefit to health: to adolescent health now, to health in adulthood, and to the health of the next generation. Little is known about how best to engage adolescents in health interventions and what strategies are effective. This study aimed to develop a complex intervention to deliver support to improve diet quality and physical activity levels in adolescents.
Method: The study used creative methods within an innovative Person-Based Approach to design format and content of an intervention targeting adolescents. We conducted small group interviews, active 'go-along' interviews, and creative workshops with adolescents 12-15 years old (n=450) to explore what motivates them to eat well and be active, what their aspirations are, and ways to support adolescent health behaviours. Inductive thematic analysis was used to analyse recordings and creative outputs to identify guiding principles for intervention design.
Results: From these data, three design objectives were distilled: (1) to make healthy eating and physical activity a positive experience with positive outcomes; (2) to enhance self-efficacy for healthy eating and physical activity and make them easy and fun to do; (3) to enable adolescents to seek support from their social network with healthy eating and PA (e.g. parents, teachers, peers). The design objectives guided the development of 15 distinctive intervention features.
Conclusions: An effective intervention to improve adolescent health behaviours must empower and motivate adolescents, provide an engaging, fun and easy-to-use resource for support, and enable connections with peers. Using a variety of creative methods to better understand the target population can help design interventions that are acceptable and engaging to them, and thereby improve the effectiveness of the interventions.

The Influence of Family Income on Anthropometry and Quality of Life of Preschool-Aged Children in Kupang City, East Nusa Tenggara, Indonesia

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Background/Aims: Studies revealed that the quality of life (QoL) of children can be affected by poverty. Family economic conditions greatly affect the availability of nutrition and education of their children, which can impact on long-term quality of life. This study assessed the effect of family income on anthropometry and quality of life of preschool-aged children in Kupang City of Nusa Tenggara Timur, which is one of the cities in Indonesia with low per capita income.
Method: A cross-sectional study was held in preschool-aged children. The family income was grouped into: below average,

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average, and above average according to households income per month. The Anthropometry of children was measured as weight, height, body mass index (BMI) and head circumference. The health-related quality of life (HrQoL) of children was obtained from parents proxy-report using Pediatric Quality of Life Inventory (PedsQL) for ages 2–18 years. Statistical analysis using Manova test, with p <0.05 being considered significant
Results: A total of 59 children were included with median of age was 65 (39-76) months. They divided into three differents family income groups: Below average 20 (33.9%), Average 23 (39.0%), and Above average 16 (27.1%) children. The family income significantly affect on body weight (P=0.040) and BMI (P=0.014), and also on Social functioning of QoL (P=0.045), which give a greatly impact on overall scores of PedsQL (P=0.026)
Conclusions: Efforts to increase family income is one of the effective entrances in order to improve child weight and quality of life of preschool-aged children especially in social functioning

Sex-stratified analysis of hemoglobin status and risk of behavior and psychosocial problems of preschool-aged children

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Background/Aims: Studies revealed that hemoglobin (Hb) level has correlation with behavior in children. Manifestations of behavior problems can be observed in the forms of hyperactivity, internalizing, externalizing, and attention behavior. However, the effect of sex differences must be taken into account. This study assessed the relationship between Hb levels and behavior in preschool-aged children by sex-stratified analysis.
Method: A cross-sectional study was held in 66 preschool-aged children at Kupang, East Nusa Tenggara, Indonesia. The Hb levels were taken from blood examination. The risk of behavior problems were assessed using Abbreviated Conner's Rating Scale (ACRS). The risk of psychosocial problems were evaluated using Pediatric Symptom Checklist 17 (PSC-17), and it was scored into 4 different subscales: Internalizing, Externalizing, Attention, and Total score. Sex-stratified statistical analysis was done in correlation test and significance is defined as two-tailed P value < 0.05. Ethical approval was obtained from the University of Nusa Cendana Kupang
Results: There were 40 (60.6%) boys and 26 (39,4%) girls children included, with the median of age was 71 months. The mean of Hb levels was 11,94 ± 0.99 gr/dl. The Hb levels was found to be not correlated with ACRS score (r=0,070; P=0,577) and PSC-17 score in subscale: Internalizing (r=0,146; P=0,243), Externalizing (r=-0,113; P=0,367), and Total score (r=-0,142; P=0,254). However, it was significantly inverse correlated with PSC-17 Attention subscale (r=-0,333; P=0,006), and this correlation was found to be stronger in the boys (r=-0,368; P=0,019) than in the girls group (r=-0,260; P=0,200)
Conclusions: Preschool-aged children who are at risk for behavioral psychosocial problems is recommended for Hb levels meassurement

Sex-stratified analysis of hemoglobin status and risk of behavior and psychosocial problems of preschool-aged children

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Conclusions: Preschool-aged children who are at risk for behavioral psychosocial problems is recommended for Hb levels meassurement

Growth of Extremely Preterm Infants till 3 Years of Birth in Japan

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Background/Aims: The aim was to study postnatal growth of extremely preterm infants till 3 years of birth born in Japan.

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Method: All perinatal and anthropometric data were collected from database of Neonatal Research Network of Japan. The subjects were extremely preterm (24-27 gestational weeks) infants born, managed and followed up at level III perinatal centres in 2010 in Japan. Data on body weight (BW), body length (BL) and head circumference (HC) as well as derived parameters of body mass index (BMI) and corpulence index (CI) at birth, at discharge, at 1.5 corrected years and 3 chronological years of age were studied. They were categorised by gestational weeks and sexuality for analysis.
Results: A total of 396 infants (229 males/167 females) were extracted for analysis. Both BW and BL tended to be lower than normal at birth. The growth restriction progressed further after birth and maximized at discharge (mean z scores: BW -1.8, BL -2.5) and recovered afterwards. However, both BW and BL have not achieved a complete catch-up by 3 years. BMI showed a significant decrease down to ~80% normal at discharge but returned to normal level by 3 years. In contrast, CI kept within a normal range throughout infancy till 3 years.
Conclusions: Postnatal growth restriction peaks in early infancy, which corresponds to the critical period when both BMI and CI curves make a turn from upward to downward direction. It may well be concerning how this growth stunting in early life will impact on later growth, development and health.

What Proportion of Local Authorities in England have Plans to Tackle Childhood Obesity?

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Background/Aims: Local authorities (LAs) in England have a role in influencing the health of their population and are required to develop health and wellbeing strategies. In England 34.3% of 10-11 year olds are overweight or obese and the corresponding prevalence for adults is 61.3%. The UK government's ambition is to halve childhood obesity in England by 2030, necessitating action by local authorities. However there is no mandate for LAs to tackle obesity, and the proportion of English local authorities with plans in place to do so is not known. This study assessed the proportion of councils in England with accessible obesity policies/plans.
Method: An initial internet search followed by a search of councils' webpages was undertaken, using terms "healthy weight", "obesity" and "childhood obesity". For each search term the first 100 results from the council website were reviewed for up-to-date local plans, policies and strategies to tackle obesity in their area. This will be followed by interviews with a representative sample of LAs.
Results: In England 152 of the 353 councils (including 201 district councils covering smaller areas) have a public health function. Of these, only 51 (33.6%) had up-to-date and publicly accessible plans to tackle obesity. These included healthy weight, childhood obesity, whole systems approaches and healthy weight declarations. Councils without a plan may be taking action to tackle obesity, but within other public health or children and young people strategies.
Conclusions: Only one third of councils with public health functions had up-to-date and visible plans to tackle childhood obesity, which are required to translate priorities into action. If policies to address obesity in local government are included alongside other competing priorities rather than as a separate policy, it is unclear if childhood obesity in particular will be given the political commitment required to achieve national targets.

Paternal height has an impact on birth weight of their offspring in a Japanese population: The Japan Environment and Children's Study

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Background/Aims: This study examines the relationship between paternal height or body mass index(BMI) and birth weight in a Japanese general population. The sample included 33,448 pregnant Japanese women and used fixed data, including maternal, paternal, and infant characteristics, from the Japan Environment and Children's Study (JECS), an ongoing nationwide birth cohort study.
Methods: Relationships between paternal height or BMI and infant birth weight (i.e., small for gestational age (SGA) and large for gestational age (LGA)) were examined using a multinomial logistic regression model. Since fetal programming may be a sex-specific process, male and female infants were analyzed separately.
Results: Multivariate analysis showed that the higher the paternal height, the higher the odds of LGA and the lower the odds of SGA in both male and female infants. The effects of paternal BMI on the odds of both SGA and LGA in male infants were similar to those of paternal height; however, paternal height

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had a stronger impact than BMI on the odds of male LGA. In addition, paternal BMI showed no association with the odds of SGA and only a weak association with the odds of LGA in female infants.
Conclusion: This cohort study showed that paternal height was associated with fetal growth and had stronger effects than paternal BMI, suggesting that the impact of paternal height on fetal growth could be explained by genetic factors. The sex-dependent effect of paternal BMI on fetal growth may be due to epigenetic effects.

Influence of Maternal Genetic Determinants for Glycaemic Traits on Gestational Diabetes and Fetal Growth in Chinese Population

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Abstract
Background: The genetic basis for gestational diabetes mellitus (GDM) and its impact on fetal growth remains unclear. This study aims to evaluate the role of known genetic variants associated with type 2 diabetes (T2D) and glycaemic traits in affecting GDM and fetal growth.
Method: A total of 464 women with GDM and 1,211 controls were recruited from 3 independent cohorts in the Chinese population. GDM was diagnosed using the 2013 WHO definition. DNA samples were genotyped using the Illumina HumanOmniZhongHua-8 BeadChip, Human Omni2.5 Exome-8 BeadChip, or Global Screening Array. We imputed the genotypes using minimac 3, with 1000 Genome Project phase III data as reference panel. Using the variants identified in studies of non-pregnant individuals, we constructed five genetic risk scores (GRSs) for increased T2D risk, elevated fasting glucose and insulin, reduced insulin secretion and greater insulin resistance. In each cohort, we tested for their associations with GDM using logistic regression, with the adjustments for age, BMI and principal components (PCs). Results of individual studies were combined by meta-analysis. Associations between GRSs and neonatal traits (birthweight, birth length, ponderal index, head circumference, sum of skinfold, fat mass, cord blood glucose and c-peptide) were assessed by linear regression, adjusting for gestational age, offspring gender and maternal PCs in 954 mother-child pairs.
Results: All five GRSs were significantly associated with GDM in the meta-analysis, with a 1-unit increase in each score raising the odds of GDM by 5%–16% ($0.045 < P < 1.5\times10^{-12}$). A trend was observed for increased sum of skinfold with T2D GRS ($P = 0.0948$), but no association was observed for other neonatal traits with GRSs.
Conclusion: In conclusion, women carrying more risk alleles for glycemic traits are at higher risk for GDM. Our findings demonstrated evidence of shared genetic determinants for hyperglycaemia among pregnant and non-pregnant women.
Acknowledgement: Partially supported by the RGC Theme-based Research Scheme (T12-402/13N), Health and Medical Research Fund from the Research Fund Secretariat, Food and Health Bureau, the Government of the Hong Kong Special Administrative Region, China (Project no: 05161386), and the CUHK-SJTU Joint Research Fund.

Relationships between the perinatal factor, early child rearing environment at home, and later behavioral problem of children: a longitudinal cohort study

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Background/Aims: Children's behavioral problems are associated with their later social adaptation and well-being. In addition, many studies indicate the importance of long-term impact of perinatal risk on later health. To enhance the early support and appropriate follow up, this study aimed to clarify the relationships between perinatal risk, child rearing environment in infancy, and later behavioral problem of children by using longitudinal cohort data.
Methods: We conducted a prospective cohort study called "Community empowerment and care for well-being and healthy longevity" (CEC), which began in 1991, at a small village located in central Japan. Data were collected from 2005 to 2014, using professional assessment and caregiver-reported questionnaires. Statistical analyses including logistic regression analysis was used to examine the hypothesis. After explaining the objective and the process of this project to all participants, we obtained consent from them to participate in this investigation voluntarily. We collected the data anonymously with

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personal ID system, to protect the personal information of every participant. The Ethics Committee of the University of Tsukuba approved this study.
Results: There was a significant relationship between perinatal risk, early child rearing environment, and later behavioral problems in children. Gestational age (OR=1.3) was related to positive social stimulation to the child. Social stimulation (OR=3.3) and Parenting support (OR=2.1) were related to later prosocial behavior of children.
Conclusions: Regarding our findings, we can see that early parenting environment is associated with the later prosocial behavior and overall development. The results indicate that we can prevent behavioral problems in children's later development by providing a positive child rearing environment at home and appropriate follow-up from the perinatal stage.

The optimal anthropometric index to screen for metabolic syndrome in Chinese children and adolescents: a national cross-sectional analysis

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Background/Aims: As the growing epidemic of childhood obesity, pediatric metabolic syndrome (MetS) become a serious public health challenge, which defined as a cluster of abdominal obesity, glucose intolerance, hypertension, and dyslipidemia. Studies have indicated that pediatric MetS would predict adult MetS, cardiovascular disease, and type 2 diabetes, but limited research has been large enough to developed a convenient and reliable screening tool for pediatric MetS across a wide age span. We aimed to investigate the optimal anthropometric index to screen for metabolic syndrome (MetS) in Chinese children and adolescents among body mass index Z-score, waist circumference (WC) Z-score, waist-to-height, and waist-to-hip ratio, with the application of two different MetS definitions.
Method: This was a national survey involved 14932 children and adolescents aged 7-17 years from China. Anthropometric characters, blood lipids and serum glucose were measured, and dietary intake and physical activity information were collected. MetS definitions proposed by the International Diabetes Federation (IDF) and Cook et al. were adopted. The analysis of receiver operating characteristic (ROC) curve was performed and areas under the curve (AUCs) were calculated to decide the optimal index of MetS identification.
Results: Prevalence of MetS was significantly different between IDF definition and Cook's definition (2.2% vs. 8.8%, P<0.001), and higher in boys than in girls (P<0.01). The ROC analyses showed that WC Z-score performed better in screening for MetS than all other anthropometric index, regardless the definitions, and its screening accuracy was outstanding (AUC = 0.941 or 0.903, using IDF definition or Cook's definition, respectively).
Conclusions: WC Z-score was the optimal anthropometric index to screen for MetS in Chinese children and adolescents, and it can be a convenient and reliable screening tool for pediatric MetS.

Differences In Pregnancy Metabolic Profiles And Their Determinants Between White European And South Asian Women: Findings From The Born In Bradford Cohort

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Background/Aims: There is widespread metabolic disruption in women on becoming pregnant with this being more extreme in obese women. Variation in maternal pregnancy metabolic profiles, as well as ethnical differences may influence offspring risk of adverse cardiometabolic and congenital heart disease (CHD) outcomes. Our aim was to compare gestational metabolic profiles and their determinants between White European (WE) and South Asian (SA) women.
Method: We used data from the Born in Bradford (BiB) cohort to compare metabolic profiles and associations of maternal age, height, body mass index (BMI), parity, education, gestational diabetes (GD) and pre-eclampsia (PE) with 154 metabolic traits in WE (*N*=4,115) and SA (*N*=4,767) women. Metabolic traits, measured in fasting serum taken between 24-28 weeks gestation, were quantified by high-throughput nuclear magnetic resonance. We used linear regression with robust standard errors to examine associations and compared these between ethnic groups.
Results: Based on multiple testing corrections (P<0.003), distributions of 143 of the 154 gestational metabolic traits differed by ethnicity. WE women had higher levels of lipoprotein subclasses, cholesterol, and glycerides and phospholipids than SA women. Distributions were similar between the two groups for several high-density lipoprotein subclasses and fatty acids. In both ethnic groups, most metabolic traits increased with increasing maternal age. Several exposures related to traits differently in the two groups. For example, higher BMI and parity, GD and PE were associated with higher levels of very low-density lipoprotein (VLDL) subclasses, with stronger associations in WE women. BMI was associated with most of the metabolic traits and there was evidence that its associations with all lipoprotein subclasses, cholesterol, triglycerides and fatty acids differed by ethnicity (generally having more adverse associations in WE women). As an example, with adjustment for age, parity, and education difference in mean total lipids in small VLDL per standard deviation (SD) higher BMI in WE women was 0.18SD (95% CI; 0.15, 0.21) and in SA women was 0.07SD (95% CI; 0.04, 0.10), $P_{interaction} = 7x10^{-7}$).
Conclusions: We have shown differences in gestational metabolic profiles between WE and SA women and demonstrated that several associations of exposures with these metabolites

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differ by ethnicity. Ethnic differences in gestational metabolic traits and their determinants might relate to ethnic differences in offspring cardiometabolic or CHD risk.

Maternal Obesity in Pregnancy and Determinants of Cardiovascular Risk in infants

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Background/Aims: Several mother-child cohort studies have reported associations between obesity in pregnancy and adverse offspring cardio-metabolic outcomes. However, a causal relationship has yet to be established. To provide further insight, we explored associations of maternal obesity in pregnancy with cardiovascular parameters and adiposity in 3-4-year-old children. 60 mothers who were obese (BMI ≥30 kg/m2) in early pregnancy and their 3-4-year-old children were recruited from the UPBEAT cohort, a randomised controlled trial that examined the effects of a complex lifestyle intervention on the incidence of gestational diabetes and macrosomia. 48 lean controls (BMI 18.5-24.9 kg/m2) and their 3-4-year-old children were recruited for comparison and matched for maternal age and ethnicity.
Method: Measurements taken for each child included BMI and skin fold thicknesses, systolic and diastolic blood pressure (routine clinic BP measurements), heart rate variability (HRV, time and frequency domains) by electrocardiography and cardiac dimensions were obtained by echocardiography. Children's cardiovascular parameters for each maternal BMI category were compared by linear regression, adjusting for maternal ethnicity, maternal age at delivery, parity, pre-pregnancy smoking, mode of delivery, child's gender and current BMI.
Results: Obesity in pregnancy was significantly associated with a higher minimum and mean heart rate, lower SDNN (HRV), reduced low frequency power, and lower total power, shorter ejection duration (ED) and increased left atrial volume (LAV, $p<0.05$). Positive associations were also observed between obesity in pregnancy and child BMI and abdominal skin fold thickness ($p<0.05$). There were no associations between obesity in pregnancy and offspring systolic or diastolic blood pressure.
Conclusions: Children of obese mothers exhibit several markers of cardiovascular dysfunction, including altered autonomic function, indicating increased sympathetic and reduced parasympathetic tone, and alterations in cardiac structure, when compared with children of lean control mothers. Children of obese mothers also showed increased adiposity. Maternal obesity, therefore, appears to independently influence cardiac remodelling in the offspring, with no apparent change in blood pressure at age 3-4 years, but which may have cardiovascular consequences in later life.

DNA Methylation as a Potential Biological Mechanism in the Reduction of Risk for Obesity and Type-2-Diabetes (T2D) with Human Milk the First Years of Life

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Background/Aims: Worldwide obesity has nearly tripled since 1975, coincidently when breastfeeding rates were the lowest in history (WHO, 2018). A protective effect against obesity and type-2-diabetes is associated with longer duration of breastfeeding (Victora, 2016). Human milk provided during early life has been proposed as a potential epigenetic mechanism through gene methylation (WHO, 2013).
Methods: Methylation analysis using the Sequenom MassArray EpiTyper on 17 CpGs within 205 base pairs on the *CPT1B* gene located in the FAO pathway (Maples, 2015) were performed on the buccal DNA of 240 children enrolled in the Peri/postnatal Epigenetics Twins Study (PETS) at birth and 18 months of age, to investigate if there are any statistical differences in methylation levels between the breastfeeding groups and childhood growth parameters associated with obesity and T2D markers.
Results: Pending
Conclusions: Pending
References: -Maples, J. M., Brault, J. J., Shewchuk, B. M., Witczak, C. A., Zou, K., Rowland, N., . . . & Houmard, J. A. (2015). Lipid exposure elicits differential responses in gene expression and DNA methylation in primary human skeletal muscle cells from severely obese women. *Physiological genomics*, *47*(5),139. -Victora, C. G., Bahl, R., Barros, A. J., França, G. V., Horton, S., Krasevec, J., . . . & Rollins, N. C. (2016). Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet*, *387*(10017), 475-490. -WHO. (2018). *Obesity and overweight fact sheets.* https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight Accessed February 8, 2019. -WHO. (2013). *Long-term effects of breastfeeding: a systematic review.* ISBN 978 92 4 150530 7.

HIV and Lifestyle Diseases in Women

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Background/Aims: Sub Saharan Africa(SSA) is facing a rapidly growing number of people with chronic Non-

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Communicable Diseases (NCDs) while at the same time experiencing high death rates from infectious diseases e.g. HIV/AIDS, tuberculosis(TB) and malaria. Although this region comprises 10% of the world population, it carries the highest burden of diseases in the world. It is well known that some of the infectious diseases increase the risk of certain chronic diseases and the converse. The study aims to explore the relationship between HIV, its treatment and Lifestyle diseases

Method: Meta-analysis and scientific systematic literature review. Also I conducted individual interview with medical personnel at KCMC referral hospital.

Results: Introduction of Antiretroviral therapy(ART) in SSA having high prevalence of HIV has been recognized as a public health priority through reduction of its price, raised donor funding and enhanced political commitment e.g. WHO '3 by 5' initiative. This has been associated with an increased risk of developing metabolic syndrome. HIV has been linked with an increased risk of developing both diabetes and cardiovascular disease in women. The prevalence and incidence of gestational diabetes in pregnant women is markedly increasing in SSA compared to industrialized world due to increased use of ART.

Conclusions: The impact of these co-morbidities in SSA is likely to be large. Roll-out of ART coverage within the region is an essential response to the HIV epidemic; however it is likely to lead to a growing number of exposed women suffering adverse metabolic consequences. HIV disease requires a long-life treatment, meticulous adherence to ART and intensive clinical and laboratory monitoring. Therefore, robust and sustainable healthcare systems are needed to provide adequately trained staff, laboratory facilities and a reliable supply of effective drugs with fewer side effects

Neonatal vitamin D status and risk of asthma in childhood: results from the D-tect study

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Background/Aims: Asthma often develops early in childhood suggesting that the prenatal environment might play an important role for childhood asthma development. It has been suggested that prenatal vitamin D status can influence lung development and immune responses and thereby contribute to asthma development risk. The aim of this study was to assess the association between neonatal vitamin D status and asthma risk in childhood.

Method: We conducted a case-cohort study. The sub-cohort (n=1,423) was randomly selected from all children born in Denmark in 1992-2002. Asthma cases (n=911) were randomly selected from all cases of asthma first diagnosed at ages 3-9 years among all children born in Denmark in 1992-2002. Vitamin D status was assessed by measuring 25(OH)D concentrations from dried blood spot samples. We followed the children in the Danish National Patient Register from age 3-9 years to identify all children for their first diagnosis of asthma. We conducted a Cox regression analysis to assess the association between quintiles of 25(OH)D concentration and childhood asthma.

Results: The median 25(OH)D concentration was lower among the asthma cases (22.6 nmol/l, IQR 13.1-34.4) than among the sub-cohort (24.1 nmol/l, IQR 13.6-39.3). The hazard ratio for developing asthma at ages 3-9 years was lower for children in the highest quintile of neonatal 25(OH)D compared to children in the lowest quintile, both in the crude (0.61 95%CI: 0.46, 0.80) and adjusted (0.55 95%CI: 0.39, 0.77) model.

Conclusions: The results from our study suggest that higher neonatal vitamin D status reduces the risk of developing childhood asthma at ages 3-9 years.

Physical fitness in adults born preterm - a study of 80,000 young men

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Background/Aims: Individuals born preterm at <32 weeks or <1500 g report less physical activity and have lower cardiorespiratory and muscular fitness than their peers born at term. Whether this phenomenon extends to larger groups of adults born moderately or late preterm has been less studied. We aimed to study cardiorespiratory and muscular fitness in young men born preterm.

Method: We identified all men born in Finland between Jan 1987 and Sep 1990 through the National Medical Birth

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Register which included data on gestational age at birth (n=118 584). We linked these data with fitness test results of the Finnish Defence Forces (n=83 026): 12 min run (cardiorespiratory fitness), standing long jump (explosive leg power), and number of sit-ups (abdominal dynamic endurance) and push-ups (upper extremity dynamic endurance and trunk static endurance) in 60 s. We analysed data using linear regression.

Results: Fewer adults born preterm had fitness data (37.3% (<32 wks); 58.8% (32-33 wks); 67.6% (34-36 wks); 69.6% (37-38 wks, early term); 70.8% (39-41 wks). In the 12-min run, men born at <32 weeks had poorer performance (-66 m (95% CI -103 to -31). A dose-response relationship was observed between each week of shorter gestational length and lower performance in standing long jump (-0.43 cm (95% CI -0.53 to -0.33) and sit-ups (-0.09 (95% CI -0.14 to -0.05); even men born early term had lower performance than controls. Push-ups were not related to gestational age. When adjusting for maternal smoking, age, primiparity, and birth weight SD score, the associations remained unchanged.

Conclusions: Adults born preterm or early term have lower muscular fitness, at least in leg and abdominal muscles. Cardiorespiratory fitness was lower among those born at <32 weeks. Poorer availability of fitness data among preterm-born adults may indicate exemptions from military service due to health conditions. Therefore, our results represent a conservative estimate which can be generalised to apparently healthy young men.

Differences in Methylation of CpG and Non-CpG Sites Across Three Tissue Types

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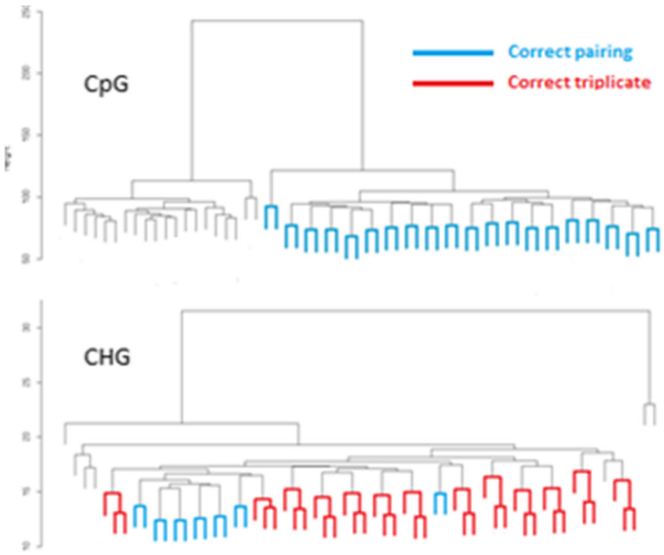
Background/Aims: Literature on human DNA methylation mostly describes CpG context, and knowledge regarding non-CpG methylation is comparatively poor. Non-CpG methylation still accounts for a significant proportion of methylation in the human genome (1). Our aim was to compare the DNA methylation profiles of CpG and non-CpG sites, and assess whether this differs by tissue type.

Method: Agilent SureSelect human methyl-seq array was used to interrogate 60 samples: 20 individuals were assayed in three tissue types each (umbilical cord, cord blood and 12yr peripheral blood). 1µg of DNA was used for analysis. High-quality, trimmed paired-end reads were aligned using ERNEbs2 and methylation percentage estimated using the erne.meth algorithm. Stata (15.0) and R (3.5.1) were used for production of statistics and hierarchical cluster analysis – using complete linkage methodology.

Results: Over 11 million sites had >30 read-depth across all 60 samples (CG=1,222,537; CHG=2,668,465; CHH=7,110,761 – where H represents A, C, or T). Median methylation levels in CHG and CHH sites (~2-3%) were significantly lower than in CpG sites (~50-66%) in all tissues. Using CpG sites only, cluster analysis grouped cord blood and 12yr peripheral blood samples together – within this, individuals clustered with their pair – while all umbilical cord samples clustered separately. Clustering on all non-CpG sites (CHG, CHH, or CHH+CHG) did not accurately differentiate by tissue type and group individuals. However using a subset of non-CpG sites where all 60 samples had non-zero methylation (CHG=208,884; CHH=462,867), cluster analysis accurately grouped pairs of individuals and also grouped multiple sets of triplicate samples from the same individual (see figure below).



Conclusions: Hierarchical cluster analysis suggests that methylation levels at commonly methylated non-CpG sites (especially CHG) vary more by individual than by tissue type, and that tissue type is more influential for CpG methylation than non-CpG methylation. It may follow that non-CpG methylation is more reflective of *cis* genotype and less responsive to cell fate.

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Supplementation of amino acids during pregnancy to prevent or treat fetal growth complications: a systematic review and meta-analysis of (pre)clinical studies

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Background: Complications of pregnancy that affect fetal growth may be related to the availability of amino acids (AAs). Oral AA supplementation could therefore form an interesting therapeutic or prophylactic approach. This systematic review combines data from human and animal studies to investigate the effect of AA supplementation on fetal growth restriction, preeclampsia, gestational hypertension, prematurity, (gestational) diabetes, and incidence of high birthweight.
Methods: PubMed, Embase and Cochrane libraries were searched to identify studies supplementing the following AAs during gestation: 1) nitric oxide metabolism related arginine, citrulline, glutamate, glutamic acid, and proline, 2) 1-carbon related methyl donors methionine, cysteine and choline, and 3) branch-chain AAs (iso-)leucine, and valine. Effects on birth weight, maternal blood pressure, maternal blood glucose and incidence of the before mentioned pregnancy complications were examined.
Results: A total of 19 human and 87 animal studies were included for analysis. Preliminary results with L-arginine supplementation based on 30 studies (12 human, 18 animal) showed increased fetal growth in growth restriction/preeclampsia compared to risk groups or healthy pregnancies (1.13 [1.09;1.7] vs. 1.04 [0.99;1.10] vs. 1.02 [0.99;1.04]; $p=1e^{-9}$). The effect was comparable between species, administration route and scheme. Administration in middle or late pregnancy appeared to be more effective than early or full gestation ($p=9e^{-10}$). Analysis on the other AAs related to nitric oxide metabolism, 1-carbon metabolism and insulin production are ongoing.
Conclusion: This integrated meta-analysis shows that prenatal supplementation with L-arginine improves fetal growth. L-arginine supplementation seems to be especially optimal for treatment rather than prevention of placental insufficiency. Further analyses is ongoing. Meta-analysis across species may provide a starting point to develop effective intervention strategies.

Preeclampsia Link to Hypoxic Pregnancy

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Aims: Preeclampsia remains a major pregnancy complication, affecting mother and offspring. Underlying mechanisms remain elusive, preventing plausible intervention. We investigated whether hypoxic pregnancy leading to fetal growth restriction (FGR) in sheep results in similar maternal cardiovascular and placental dysfunction as in preeclampsia.
Methods: Pregnant ewes were exposed to normoxia (N; n=10) or 10% hypoxia (H; n=7) from 105 to 138 days gestation (dGA; term 145 dGA) in isobaric chambers, after which placental and fetal biometry, placental stress and H_2S biology were assessed. Another cohort was instrumented at 120 dGA with catheters and uterine flow probes to record maternal cardiovascular data via a wireless data acquisition and exposed to N (n=5) or H (n=5) for 10 days.
Results: Hypoxic pregnancy led to FGR (3.7 *vs.* 2.7 kg, N *vs* H; $p<0.01$ Student's *t* test) and prevented the fall in uterine vascular resistance (Δ baseline -0.07 *vs.* -0.01 mmHg.(min.ml^{-1})$^{-1}$; $p<0.05$ RM two-way ANOVA) and in maternal blood pressure (Δ -6.3 *vs.* 0.3 mmHg; $p<0.05$ Student's *t* test). This was associated with increased placental stress, and unfolded protein response (UPR) activation (Table 1). It also lowered placental levels of the H_2S producing enzyme CSE and H_2S production (Table 1). UPR pathway activation correlated with asymmetric FGR (UPR^{Cyt} R=0.7, $p<0.01$; UPR^{ER} R=0.7, $p<0.01$; UPR^{mt} R=0.6, $p<0.05$; Pearson's correlation) and with decreased placental H_2S production (UPR^{Cyt} R= -0.6; UPR^{ER} R= -0.6; both $p<0.05$, Pearson's rank correlation).
Conclusions: Chronic hypoxia may provide a link between placental dysfunction, FGR and maternal cardiovascular dysfunction in adverse pregnancy, as in preeclampsia.
Supported by The British Heart Foundation and the Cambridge Centre for Trophoblast Research

DOHaD in developing nations: A systematic review exploring gaps in DOHaD population studies

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Background/Aims: The developmental origins of health and disease (DOHaD) paradigm asserts that early-life environmental factors can influence later chronic disease risk. The aim of this review is to identify where these investigations take place, and whether, given the burden of non-communicable diseases (NCDs) in lower-middle income countries, this focus is appropriate and ethical. Studies must investigate on the relationship between the early nutritional environment and later non-communicable disease risk in childhood, adolescence and adulthood.
Method: A systematic review was conducted covering publications up to 23 May 2018. A search for literature was conducted in three electronic databases: Medline, EMBASE (both accessed via Ovid) and Scopus. To be included, the studies must have been original, observational DOHaD studies published in academic articles that link maternal nutritional environmental

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exposures or birth factors to later NCD prevalence or risk. After full text reviews, 139 studies were included in the final review.
Results: Of the 139 studies included in this review, 48% were based on data from the Europe & Central Asia region, 21% in the East Asia & Pacific region, 15% within North America, 8% in Latin America & the Caribbean, 4% in South Asia, 3% in Sub-Saharan Africa and 0.6% from within the Middle East & North Africa. Additionally, this review found that only 6% of studies were based in lower-middle income countries, despite holding 80% of the non-communicable disease burden.
Conclusions: There is a disconnect between the regions highly burdened by NCDs and the areas where most of the DOHaD research occurs. As it stands, majority of research and funding is focused on high income countries with little emphasis given to lower income nations or indigenous populations whom have higher rates of NCDs and poor outcomes. To improve health for vulnerable communities in both developed and developing nations, there needs to be more resources put towards these burdened populations whom may benefit most from DOHaD research and related strategies.

DOHaD in the Pacific: Connecting early-life factors and current health in Rarotongan adolescents

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Background/Aims: The Cook Islands, a small island developing state in Oceania with a population of 14,800, carries one of the highest burdens of non-communicable diseases (NCDs) globally. 80% of deaths are attributable to NCDs and overweight/obesity in adults has reached 91%/72%. The developmental origins of health and disease (DOHaD) paradigm can be used to understand associations between adverse early-life environmental exposures, such as during preconception and pregnancy, and later-life NCD risk. In order to reduce the high NCD rates and promote good health for future generations in the Cook Islands, we must understand the health of adolescents as they are the next generation of parents. This study explored the health status and early-life factors of the Year 9 student cohort in Rarotonga, Cook Islands for three years.
Method: Annual school health assessments were undertaken from 2016-2018 with 403 Year 9 students in total, aged between 13-14 years. Measurements included weight, height, waist circumference, blood pressure, blood cholesterol and glucose levels. Based on adolescent cut offs, data were then categorised.
Results: Overall, 36% of Year 9 students had a healthy BMI and 64% were overweight/obese. In terms of other known risk factors, 43% had raised blood pressure, 43% were at risk for central obesity, 16% had raised total cholesterol levels and 7% had raised blood glucose levels. We also found associations between these health data and risk factors in the early-life stages via birth records.
Conclusions: This study highlighted several areas of concern for metabolic health in Rarotongan adolescents. As our future parents, it is crucial that we find ways to reduce risk not only for the individuals, but for the next generation. Future studies should build on this evidence and work towards supporting community empowerment to influence current and future health.

Amelioration Of Developmentally-Programmed Hepatic Steatosis With Tauroursodeoxycholic Acid, A Secondary Bile Acid; A Possible Involvement Of Chromatin Correction. *(Title should be no longer than 2 lines)*

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Background/Aims: We recently reported that treatment with tauroursodeoxycholic acid (TUDCA), a secondary bile acid, improved developmentally-deteriorated hepatic steatosis in mouse pups with undernourishment (UN) *in utero*. We herein attempted to elucidate the underlying molecular and epigenetic mechanisms.
Method: Livers and blood were obtained from pups with UN *in utero* (40% caloric restriction). A high-fat diet (HFD) was provided to pups (9-22 weeks) treated with TUDCA or vehicle (17-22 weeks). We performed a microarray analysis followed by an epigenetic analysis using DNA Methyl-binding domain sequencing and chromatin immunoprecipitation assays.
Results: We focused on two genes, Cell Death-Inducing DNA Fragmentation Factor-Like Effector A/C (*Cidea and Cidec*), because they are enhancers of lipid droplet (LD) sizes in hepatocytes, and showed the greatest increases in expression by UN that were completely recovered by TUDCA, concomitant with parallel changes in LD sizes. TUDCA remodelled developmentally-induced histone modifications (di-methylation of H3K4, H3K27, or H3K36), but not DNA methylation, around the *Cidea* and *Cidec* genes, leading to a heterochromatin structure, which contributed to the markedly down-regulated expression of their genes as well as hepatic fat deposition in UN pups only, even those under HFD.
Conclusions: TUDCA harmonized developmentally-programmed histone modifications around *Cidea* and *Cidec* gene expression and ameliorated hepatic steatosis. These results provide a novel concept for the future of precision medicine for

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developmentally-programmed hepatic steatosis by targeting chromatin reconstitution.

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Introduction: In this paper, the importance of the SLP's role in infant and paediatric feeding/swallowing will be discussed.
Research Aims: Research demonstrates the importance of early feeding skills and the correlation with successful feeding with positive feeding experiences. During early feeding, negative experiences can pave negative neuropathways for infants creating continuous feeding difficulties.
Methods: Using positive feeding experiences, shifting mind set of quality feeding versus quantity of feeds early on, and creating continuity of care with positive interdisciplinary interactions helps professionals and families create happy eaters and reduces risk of perpetual feeding difficulties in infants and paediatrics.
Results: The results of using the research available as evidence based practice, allows for earlier discharge, less medical expenses, more positive experiences for infants and families, and better outcomes for professionals.
Discussion: Feeding is the most complex task of infancy, even in term babies with no complications. There are many diagnoses, conditions, syndromes, and co-morbidities that can impact feeding in neonates, infants, and paediatrics. Early feeding experiences can shape the types of eaters that these children become. With early intervention, the SLP can help shape more positive feeding experiences with breast or bottle, and develop happier eaters across a lifespan. It is also our responsibility to continue to educate on the importance of quality feeding to help improve interdisciplinary relationships and create that continuum of care.
Conclusion: We are a social people. Our socialization and life experiences often are associated with eating. It is of utmost importance to allow little ones the best opportunities for successful feeding. As SLP's, it is essential that we assume the role as feeding experts and advocate for the assistance that is needed to create the most optimal opportunities. These strategies will transition across discipline and setting and can be incorporated no matter the family dynamic.

Neonatal overfeeding attenuates metabolic dysfunction of maternal organophosphate exposure in adult male offspring

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Abstract
Background/Aims: Evidence suggests that low concentration perinatal exposure to environmental contaminants, such as organophosphate (OP) is associated with later life insulin resistance and type 2 diabetes. The aim of this work was to investigate whether chronic maternal OP exposure may exacerbate the metabolic dysfunctions in early-overfed rats.
Methods: During pregnancy and lactational periods, dams have received OP by gavage. To induce neonatal overnutrition at postnatal day 3, pups were standardized in 9 or 3 per nest. At 90-day-old, glucose-insulin homeostasis and insulin release from pancreatic islets were analyzed.
Results: Unexpectedly, early overnutrition improved metabolic parameters and attenuated insulin release from isolated islets in presence of both glucose and antagonist muscarinic as well as slowed the increase of beta cell mass in adulthood offspring from mothers exposed to OP; whereas, rats from mothers exposed to OP alone presented a diabetogenic phenotype. In addition, high levels of butyrylcholinesterase and low levels of insulin in milk were detected at the end of suckling.
Conclusion: Our study show that maternal OP exposure may program to altered *in vitro* insulin release as well as endocrine pancreas structure, which reflects on metabolism at adulthood. However, postnatally overfed rats are less susceptible to long-term effects of maternal OP exposure.

Risk Factors Associated With Development of Post Lumbar Puncture Headache

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Abstract
Background: Post lumbar puncture headache (PLPH) is the most common adverse event to lumbar puncture. The incidence of PLPH range between (1-70 %) (1.2.3).The headache affects the patient, family, but also the ability to cope with quality of life and social life (4). The prevention and treatment of PLPH has until now been on an unsystematic basis (5).
Aim: The aim of this study was to examine risk factors, which could predict later development of PLPH.
Method: A case-control study was performed including 322 patients from a hospital in Demark in a period of two years. Factors that have been included are blood glucose and albumin levels, systolic -, diastolic – and mean arterial blood pressure (MAP). Statistical analysis as Student's t-tests, $\chi 2$ and logistic regression tests were performed.
Results: N= 38 patients later developed PLPH. Patients with PLPH compared with controls showed following: A lower glucose level (5.7 mmol in the case group versus 6.4 mmol /l in the

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control group and a lower systolic blood pressure were found in the case group 126 versus 137 mmHg among the control group. Finally, analysis of MAP showed 90 mmHg in the case group versus 96 mmHg in the control group. Logistic regression showed that lower systolic blood pressure (≤ 126 mmHg) significantly increased the risk of PLPH (0,977 (95 % CI 0,957-0,998)) compared with lower age (≤ 40 years).
Conclusion: This study showed that specific risk factors could contribute to later development of PLPH.
Further and larger studies are needed to explore risk factors of PLPH (6).

Dietary patterns of Malaysian pregnant women are associated with ethnicity and early pregnancy waist circumference: A prospective cohort study

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Background/Aims: Little is known about dietary patterns (DPs) of women over the course of pregnancy. The present study aied to identify DPs of Malaysian pregnant women and possible associations with socio-demographic, obstetrical, and anthropometric characteristics.
Method: This prospective cohort study included 737 participants enrolled between 2013 and 2015. Food consumption was assessed using a validated 108-food items semi-quantitative Food Frequency Questionnaire (SFFQ) at four time-points, i.e. pre-pregnancy and at each trimester (first, second and third). Principal component analysis (PCA) was used to identify DPs.
Results: Three distinct dietary patterns (DPs) were identified, i.e. DP1 (prudent diet, high in fruits, vegetables, nuts, seeds, legumes, eggs, milk and dairy), DP2 (high fat & energy, condiments), and DP3 (high protein & sugar, mostly plant & staple food-based). Women with higher education were more likely to have high adherence to DP1 up to the 3rd trimester. DP2 was more prevalent in Malays compared to non-Malays and showed high adherence over time. DP3 changed over time and during the 3rd trimester, adherence to DP3 was lower. DPs at pre- and during pregnancy were associated with ethnicity and early pregnancy waist circumference (WC). Women with a higher WC at booking, were more likely to have a high BMI, but less likely to show high adherence for DP2 and DP3 during 2nd and 3rd trimester, perhaps related to dietary counselling received to reduce gestational weight gain.
Conclusions: The DPs in the present study were substantially different from those reported in Western populations. Promoting healthy dietary behaviours before and during pregnancy is important to ensure overall health and well-being of pregnant women.

Targeted social care for highly vulnerable pregnant women: design of the Mothers of Rotterdam cohort study

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Background/Aims: Social vulnerability is known to be related to ill health. When a pregnant woman is socially vulnerable, the ill health does not only affect herself, but also the health and development of her (unborn) child. In Rotterdam a holistic care program was developed in close collaboration between the university hospital, the local government and a non-profit organization, to optimize care for highly vulnerable pregnant women and their unborn child. This program aims to organize and combine social and medical care from pregnancy onwards until the second birthday of the child.
In 2014, a pilot in the municipality of Rotterdam demonstrated the importance of this holistic approach for highly vulnerable pregnant women. In the "Mothers of Rotterdam" study, we aim to prospectively evaluate the effectiveness of this holistic approach, referred to as targeted social care.
Method: The Mothers of Rotterdam study is a pragmatic prospective cohort study, planning to include 1200 highly vulnerable pregnant women for the comparison between targeted social care and care as usual. Effectiveness will be compared on the following outcomes a) maternal mental health (is maternal distress reduced at the end of the social care program?) and b) child development (does the child show adaptive development at year 1?). Propensity scores will be used to correct for baseline differences between both social care programs. The study was approved by the Erasmus Medical Centre Ethics Committee (ref. no. MEC-2016-012).
Strengths and limitations of this study: The ecologically valid study design allows for the results to be directly generalizable to the actual population, but increases risks of true effects being masked by unmeasured differences in case mix and confounders. The maternal- and child-specific outcomes are measured through a multi-method approach of data collection: questionnaires, developmental and cognitive tasks, and video-observations in the home environment. The ultimate goal of this program and study is to support the healthy development of future generations through societal valorisation of knowledge

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within a valuable collaboration between academics, local government and a non-profit organization.
Conclusion: With this study we will gain unique insights into a notorious difficult-to-reach population of highly vulnerable pregnant women, their problems and the potential care pathways for dealing with these risks.

The relation between deprivation and healthcare costs in early childhood

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Background/Aims: One of the most detrimental factors influencing child development is growing up in poverty. According to the World Health Organization, extreme poverty is the leading cause of mortality and morbidity worldwide. Some children encounter more potentially detrimental and unhealthy circumstances than others, some already in the womb, increasing their risk for future health problems. Poor perinatal outcomes are more often observed in deprived neighbourhoods, with both more perinatal mortality and morbidity. Additionally, growing up in impoverished families exposes children to high levels of chronic stress, hindering optimal physical and behavioural development. These circumstances, alone and in combination, can potentially harm children's health. We assume that the poor health status of these children is reflected in higher healthcare expenses, since they require more medical care than their non-deprived peers. We aim to investigate the effect of deprivation on perinatal morbidity and healthcare costs of young children in the Netherlands.
Method: In this cross-sectional study, we combined data from several Dutch national registries of all children aged zero to three years old in 2014. Healthcare expenses included all health care resources covered by obligatory health insurance. Deprivation was studied at the individual and contextual level, where monthly household income per €1000 served as measure for the individual level and neighbourhood deprivation scores for contextual level deprivation. Perinatal morbidity was defined as prematurity (<37 weeks of gestation), small for gestational age (birth weight below 10th centile), or both. The final linear regression model was built for healthcare costs as function of both deprivation variables, perinatal morbidity, ethnicity and the two-way interactions between household income, neighbourhood deprivation and perinatal morbidity.
Results: A total of 482,966 children were included in the analyses. Mean healthcare costs were €1390, with a decrease of €0.36 for every €1200 euro's additional yearly household income, and an increase of €28.54 for every unit increase in deprivation. Stratified for perinatal morbidity, mean healthcare costs were €3516 when perinatal morbidity was present, and €1066 when it was absent. Secondly, for every €1200 additional yearly income, healthcare costs decreased €0.36 for presence of perinatal morbidity and an increase of €1.44 for absence respectively. Similarly, for every unit increase in deprivation, healthcare costs increased with €122.71 when perinatal morbidity was present, and €26.53 when it was absent.
Conclusions: This research sheds light on how income and neighbourhood deprivation contributes to differences in children's healthcare costs, already in early life. Mean healthcare costs triple when perinatal morbidity is present, while simultaneously the effect of deprivation on healthcare costs increases fivefold in this group as well. This inequality can have detrimental consequences since the gap between poor and rich is widening, not only regarding both income disparity and health inequality. More attention should be paid to impoverished populations in order to break through the perpetuating cycle of adversity and poor health.

Impact of a Blended Periconception Dietary and Lifestyle Approach Combining Face-to-Face Counselling with eHealth – Patient Adoption and Baseline Characteristics

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Background/Aims: Periconception dietary and lifestyle behaviour affects maternal, foetal, neonatal and transgenerational health outcomes. Lifestyle interventions during the periconception period have the potential to effectively target these behaviours, and thereby improve fertility, pregnancy outcome, and health later in the life course. Especially interventions that combine face-to-face visits and eHealth ('blended care') show promising results. We therefore developed and evaluated a blended, personalized care approach to periconception care, combining an outpatient lifestyle counselling service 'Achieving a Healthy Pregnancy' with the eHealth platform 'Smarter Pregnancy'.
Method: All couples contemplating pregnancy or already pregnant (≤12 weeks of gestation) visiting the outpatient clinics of the Department of Obstetrics and Gynaecology at the Erasmus Medical Centre (the Netherlands) between June and December 2018 were invited to participate. The approach, tailored to the individual patient, consisted of a face-to-face dietary and lifestyle counselling blended with the eHealth platform 'Smarter Pregnancy' and a (non-)medical risk assessment using 'ZwangerWijzer'. Counselling was provided at intake, where

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couples received personalised online coaching based on baseline screening on fruit and vegetable intake, folic acid supplement use, smoking and alcohol consumption for the following 26 weeks.
Results: A total of 539 women were screened for eligibility of whom 173 women were excluded, due to language barriers, logistical problems or absence of motivation for dietary and lifestyle counselling. In total, 366 women and 62 men received the blended periconception dietary and lifestyle approach. 264 women (72%) were contemplating pregnancy and 102 (28%) women were pregnant ≤12 weeks of gestation during the face-to-face counselling. The mean body mass index (BMI) at baseline was 26.6 kg/m^2 for women and 26.2 kg/m^2 for men, 105 women (29%) and 20 men (32%) were overweight and 80 women (22%) and 8 men (13%) were obese. At least one poor nutrition or lifestyle behaviour was present in respectively 84.3% and 95.1% of participating women and men.
Conclusions: The baseline results confirm the urgent need for a dietary and lifestyle intervention in both future parents. Moreover, results show that the majority of future parents are willing to participate in such an intervention. Since most couples are still following the 26 weeks eHealth coaching program 'Smarter Pregnancy, final results of this approach are expected in July 2019.

Using the CFIR Framework to Identify Implementation Determinants of a Blended Periconception Lifestyle Approach – Study Protocol

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Background/Aims: The detrimental effects of poor periconception nutritional and lifestyle behaviours on reproductive issues, pregnancy complications and future health are broadly acknowledged. Implementation of periconception care counselling offers a valuable opportunity to increase healthy behaviours and thereby improve fertility, but also maternal, foetal and neonatal outcomes as well as transgenerational health. Especially interventions that combine face-to-face visits and eHealth ('blended care') show promising results. However, evaluation of implementation processes is often lacking, which results in low effectiveness rates of new health care services after widespread implementation. Moreover, blended care is a relatively new treatment modality and its implementation process has not been evaluated so far.
Method/Results: We reviewed the literature to identify a suitable research framework, which enables the identification of context-driven and intertwined determinants of the implementation of a complex blended care approach. Data collection and analysis will take place between June 2018 and June 2019. A blended periconception dietary and lifestyle approach is being implemented at the outpatient clinics of the Department of Obstetrics and Gynaecology at the Erasmus Medical Centre, a tertiary care centre. The approach, tailored to the individual patient, consisted of a face-to-face dietary and lifestyle counselling blended with the eHealth platform 'Smarter Pregnancy' and a (non)medical risk assessment using 'ZwangerWijzer'. We aim to evaluate the local implementation of a blended periconception dietary and lifestyle approach using standardised questionnaires and the consolidated framework for implementation research (CFIR). CFIR will be used to guide systematic assessment of multilevel implementation contexts to identify determinants of implementation. Additionally, two (inter) national validated questionnaires will be used to assess potential determinants of healthcare professional implementation behaviour.
Discussion: Despite strong evidence of its benefits, delivery and uptake of periconception dietary and lifestyle counselling remain low. This study is the first to systematically assess the implementation process of a blended care approach and identify determinants of implementation. The results will provide insights on the development of effective strategies to improve the implementation process of periconception dietary and lifestyle counselling. The results of this implementation study can be expected in July 2019.

Cumulative Stress Exposure during Neonatal Intensive Care and Achievement of Independent Walking

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Background: The Neonatal Intensive Care Unit (NICU) is a stressful environment for preterm infants, involving stressors such as painful procedures, mechanical ventilation, medical treatments and complications. Cumulative stress exposure may be related to developmental outcome in early childhood.
Objective: To determine the effect of cumulative stress exposure during NICU stay on the attainment age of independent walking.
Methods: We included all preterm infants with a gestational age <30 weeks and/or a birth weight <1000 grams, who were admitted to our NICU, born in 2002-2003 and for whom the attainment age of independent walking was recorded (N=48). We determined cumulative stress exposure from

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birth till discharge, based on acute stressors (e.g. the amount of skin breaking procedures, number of intubations, spinal taps and x-rays) and chronic stressors (e.g. receiving respiratory support, phototherapy or suffering from infection). Achievement of independent walking was parent-reported in preventive child healthcare.
Results: The sample included 23 males (47.9%) and 25 females (52.1%), had a mean gestational age of 28 weeks and a mean birth weight of 1086 grams. The median cumulative stress score was 153 (interquartile range 75-312). The median attainment age of independent walking was 18 months (interquartile range 16-20 months). Higher cumulative stress scores correlated moderately with attainment age of independent walking (Spearman's rho=0.415, p=0.004).
Infants who walked late (i.e. top 25%) had higher cumulative stress scores (315 vs. 170, p=0.001). In reverse, the likelihood of late walking was higher for top-25% stress scores vs. the rest with an odds ratio of 5.56, 95%-confidence interval 1.15-26.8, p=0.033, adjusted for gestational age and birth weight.
Conclusion: Cumulative stress exposure during NICU stay is associated with attainment age of independent walking. Our study warrants further research into the effects of separate stressors and cumulative NICU stress on child development.

Maternal shift work exposure differentially affects singleton and twin pregnancy outcomes but has no effect on the metabolic health of adult progeny

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Background/Aims: Epidemiological studies have suggested a small but significantly increased risk of miscarriage, preterm birth and fetal growth restriction in pregnant women working night or rotating shift schedules. We have previously shown that maternal circadian rhythm disruption perturbs metabolic homeostasis in adult rat offspring, but the stage of gestation susceptible to this exposure is unknown. This study utilised sheep to assess the impact of varying duration of maternal simulated shift work exposure on pregnancy outcomes, metabolic homeostasis and body composition of adult progeny.
Method: Following estrus synchronisation, 65 Merino ewes were mated, and group housed in light-controlled sheds. Ewes were randomised to control (12h light: 12h dark) or simulated shift work conditions (SSW) for 1/3, 2/3 or throughout pregnancy. Following birth, ewes and lambs were returned to outdoor paddocks, with regular weight and body size measurements obtained until 12 months of age. Metabolic homeostasis of adult progeny was assessed by Dual-energy X-ray absorptiometry, intravenous glucose tolerance test (0.25 g/kg) and hyperinsulinaemic euglycaemic clamp.
Results: Gestation length was increased in twin pregnancies (+2.4 days, P = 0.032) and singleton lambs were lighter at a given gestational age if mothers were subjected to SSW in the first 1/3 of pregnancy (-476 g, P = 0.016). There were no adverse impacts of maternal SSW exposure on adiposity, glucose tolerance or insulin sensitivity of adult offspring, regardless of duration of exposure.
Conclusions: Exposure to shift work, even if only in early pregnancy, may adversely affect pregnancy outcomes (1). However, our data provide no evidence of perturbed metabolic health of adult offspring following maternal shift work exposure in a species which is similarly mature at birth as humans.
(1) Gatford KL, Kennaway DJ, Liu H, Kleemann D, Kuchel TR, Varcoe TJ. *Journal of Physiology* 2019; doi: 10.1113/JP277186.

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Pregestational and Gestational Diabetes affects ovarian function and Metabolic Profile of the female offspring at the moment of birth in a different manner

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Background/Aims: The effect of maternal diabetes on placental steroidogenesis and ovarian function of the female offspring is unknown. The aim of this study is to analyze the impact of maternal diabetes over placental steroidogenesis and ovarian function and metabolic profile of female newborns at the time of birth (TOB).
Method: A follow-up study of pregnant women with Type 2 diabetes (MT2D,n=24), gestational diabetes (MGD,n=26), and control (MC,n=25) during the second half of gestation were performed. Clinical assessment and a blood sample were drawn at V1 (24-28 weeks), V2 (32-34) and TOB (37-40). Clinical evaluation of their daughter (DT2D, DGD, and DC) and venous blood cord sample were drawn at TOB.

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Results: Testosterone levels were higher in the MT2D than in the MC group at V1[1.7 (0.4 - 4.2); 1.4 (3.5 - 4.5)], V2[3.1 (0.7 - 5.9); 2.1 (0.4 - 5.2)] and TOB [3.5 (1.0 - 6.2); 2.4 (1.0 - 4.2) nmol/l, P <0.05; respectively]. HOMA-IR was higher in MT2D than in the MGD and MC groups at V1, V2, TOB (P < 0.0001). When analyzing the female offsprings; higher HOMA-IR (1,3 ± 0.7; 0,8 ± 0.3; 0.5 ± 0.3 ng/ml, P<0.05, respectively], and higher IGF1 levels [145.0±26.1; 88.0±13.9; 84.2±9.8 ng/ml P<0.05; respectively] were observed in DT2D compared to DGD and DC. Higher AMH levels were found in DT2D compared to DGD and DC (P<0.05). Lower Adiponectin levels were observed in DT2D compared to GD and DC (34.6±3.3; 45.8±4.1; 45.9±2.1ug/ml; P<00.05).
Conclusions: Hyperandrogenemia and higher insulin resistance are observed in MT2D during pregnancy. DT2D have more insulin resistance, higher IGF-1, and AMH levels and lower adiponectin levels at birth, but in DGD. These data suggest that maternal T2D and DGD may impair ovarian function and metabolic profile of their female offspring in a different manner. FONDECYT No 11.12146.

Placental Leptin Receptor Gene Expression and Early Life Cardiometabolic Risk

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Background/Aims: Previous studies implicate both leptin signalling and an adverse *in utero* environment in the development of cardiovascular and metabolic (cardiometabolic) diseases in later life. However, the relationship between genetic variation in the leptin receptor gene (*LEPR*), *in utero* factors, and early cardiometabolic health, as well as their influence on *LEPR* expression remains unclear. Here, we aimed to examine the relationship between these factors in the placenta, which regulates exchanges between maternal and fetal circulations.
Methods: RNA was extracted from central villous tissue, from four pooled biopsies of each 854 placentae from the Barwon Infant Study (BIS). *LEPR* expression was measured using quantitative RT-PCR with Taqman chemistry. Genotypic data around *LEPR* were extracted from previously generated Global Screening Array data. Multivariable linear regression modelling was used to test associations between genotype, *in utero* factors, measures of cardiometabolic risk and placental *LEPR* expression.
Results: Two intronic SNPs of *LEPR* were independently associated with placental *LEPR* expression after adjusting for fetal sex, gestational age and maternal age. Maternal pre-pregnancy BMI, gestational diabetes mellitus, weight gain and smoking during pregnancy were not associated with placental *LEPR* expression. However, placental *LEPR* expression was negatively associated with levels of high sensitivity C-reactive protein (hsCRP), a biomarker of acute inflammation, in cord blood and positively associated with birth weight z-score, an indicator of fetal growth.
Conclusion: Genetic variation plays a key role in regulating *LEPR* expression in the placenta, with potential consequences on leptin signalling and function in early development. Future studies, encompassing other aspects of leptin signalling, including *LEP* gene expression and epigenetic regulation, are warranted to fully understand the role genetic and environmental variation in regulating this important pathway during *in utero* development.

Diabetes in Pregnancy among Métis Women in Alberta

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Background/Aims: Métis people make up one-third of the Indigenous peoples in Canada, however they are highly underrepresented in health literature. One important knowledge gap is the impact of diabetes in pregnancy among Métis women. The objective of this study is to evaluate the prevalence, maternal and perinatal health outcomes of diabetes during pregnancy among Métis women compared to non-Metis women in Alberta.
Method: A retrospective cohort study will be conducted using clinical and administrative health data in Alberta from April 1, 2006 to March 31, 2017. Deterministic linkage will be used to link data from the Alberta Perinatal Health Program (APHP) to administrative health databases. The Métis cohort will be identified by probabilistic linkage with the Métis Nation of Alberta Identification Registry. The primary outcome of the study is the prevalence of gestational diabetes mellitus (GDM) and pre-existing diabetes (type 1 or type 2) as defined by the APHP. Secondary outcomes include maternal outcomes (type of delivery, preeclampsia, maternal mortality, pregnancy type, GDM screening, labour type, induction of labour, obstetric haemorrhage and gestational hypertension), and perinatal outcomes (birth injury, stillbirth, congenital abnormality, neonatal death, NICU admission, gestational age at delivery, birth weight, birth weight in relation to gestational age, and preterm (spontaneous or induced)). Age adjusted annual prevalence estimates of study outcomes will be reported. Multivariable regression adjusting for important covariates will calculate odds ratios with 95% confidence intervals comparing outcomes of Métis women to non-Métis women.
Results: The Research Ethics office has granted ethics approval. Study data has been received from Alberta Health.
Conclusions: This will be the first study in Canada to examine the impact of diabetes in pregnancy among Metis women. The information from this study will be used by the Métis Nation of Alberta to inform the development of culturally appropriate health services.

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Left ventricular remodelling in preterm lambs exposed to intrauterine inflammation

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Background/Aims: Preterm birth occurs during a critical period of cardiac growth and maturation, that results in adaptive changes to the immature myocardium and which may programme long-term cardiovascular sequelae. Intrauterine inflammation, a common antecedent of preterm birth, may exacerbate the effects of prematurity on the heart. We aimed to investigate the effect of intrauterine lipopolysaccharide (LPS) exposure, a model of intrauterine inflammation, on postnatal cardiac growth and maturation in the left ventricle of preterm lambs.
Method: Pregnant ewes were randomised to receive either an intra-amniotic injection of LPS (n=9; 4mg, Escherichia coli) or saline (n=9), as an experimental control, 48 hours before preterm delivery. Lambs were delivered preterm at 128d gestational age (GA) (term is 150d GA), managed according to contemporary neonatal care and euthanised at 7d postnatal age. Age-matched fetal controls (n=7) were euthanised at 135d GA. Hearts were excised, weighed, sampled for molecular analyses and then perfusion fixed. Left ventricular tissue was sampled systematically for assessment of cardiomyocyte number, nuclearity and proliferation, myocardial extracellular matrix deposition and presence of inflammatory (CD45+) cells.
Results: The preterm myocardium had increased collagen deposition ($p<0.0001$) and presence of CD45+ cells ($p=0.0099$) compared to fetal controls, exacerbated by antenatal exposure to LPS ($p<0.05$). Cardiomyocyte endowment was reduced, cell size was increased and the majority of cardiomyocytes were binucleated in all preterm groups ($p<0.05$). Cardiomyocyte proliferation was only decreased in the preterm saline group ($p=0.0154$) compared to fetal controls. The mRNA expression of genes involved in cardiac metabolism and remodelling, and inflammation were upregulated in preterm lambs compared to fetal controls ($P<0.05$) but there was no effect of antenatal LPS exposure.
Conclusions: Preterm birth induces maladaptive collagen deposition, accelerated maturation of cardiomyocytes and upregulation of genes involved in cardiac dysfunction in the left ventricle. Intrauterine inflammation exacerbates the extracellular matrix remodelling and immune cell infiltration in the preterm myocardium. Inflammatory injury to the fetal heart coupled with preterm birth may have life-long consequences and contribute to the development of cardiovascular disease.

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Impact of Maternal Prenatal Psychological Distress on Newborn Microbiota

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Background/Aims: Maternal psychological distress during pregnancy is linked to allergic disease in offspring, possibly through dysbiosis of early gut microbiota. Little is known about the impact and timing of stress on human infant gut microbiota. In the sole study by Zijlmans et al of maternal prenatal stress, infant stool samples were profiled from 1 week to 4 months of age when gut microbiota are influenced by infant feeding, antibiotic use and other environmental factors. This study investigated the impact of prenatal distress on newborn microbiota soon after birth.
Method: In a subsample of 37 term-delivery newborns from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort, meconium (first stool) samples were collected and microbial taxa profiled with 16S rRNA sequencing. Maternal distress in the third trimester was ascertained by the 20-item CESD (Center of Epidemiologic Studies Depression) and the 10-item PSS (Perceived Stress Scale) scales. Negative binomial regression was employed to test associations between prenatal distress and taxon abundance adjusting for birth mode, maternal race, pre-pregnancy BMI and infant sex.
Results: One quarter of mothers experienced clinically-relevant depressive symptoms in the third trimester; this level of distress was associated with a substantial decrease (abundance ratio (AR) = 0.04, 95%CI: 0.01 - 0.23, $p = 0.0003$) in the meconium abundance of the order *Lactobacillales* (LAB, lactic acid bacteria). Unit increases in CESD scores were also associated with lower LAB abundance ($AR = 0.85$, $p < 0.01$). Higher maternal third trimester stress levels (> 12.96) and unit increases in the PSS score were also associated with lower LAB abundance.

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Conclusions: LAB probiotics have shown efficacy in lowering risk of allergic disease in children. This is the first report of the impact of maternal distress on newborn LAB microbiota, and offers mechanisms by which prenatal distress increases risk for childhood atopy.

Intrauterine growth restriction as a consequence of increased maternal salt intake in mice

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Background/Aims: Low birth weight is associated with an increased risk for cardiovascular disease in later life. A restriction in intrauterine growth may be manifested by a stress factor like a high perinatal salt intake, as is typically seen in mothers consuming a "Western diet". With this study, we aim to establish a causative linkage between high salt consumption during the perinatal period and an elevated risk for cardiovascular disease in later life.
Method: Timed mating was performed between female C57Bl/6J mice at the age of 8-12 weeks and male Balb/c mice. Female mice were either fed normal-salt diet (NS, 2.2 g Na^+/kg) or high-salt diet (HS, 30 g Na^+/kg). The high-salt intake started with a successful mating (HS1) or 3 weeks before mating (HS2). At gestational day 13.5, the fetal and the placental weight were taken and analysed gender-specifically. Minimum litter size was defined as 7 fetuses per dam. The sex of the offspring was determined by polymerase chain reaction.
Results: There was no difference in litter size between treatment groups. Increasing perinatal salt intake significantly reduced fetal weights in male and female offspring in both experimental high-salt groups as compared with offspring from normal-salt diet fed dams (NS: 151.0±12.13 mg, n=159; HS1: 142.5±11.32 mg, n=115; HS2: 144.9±10.71 mg, n=96; $p<0.0001$ compared by 1-way ANOVA). Only in female offspring from the HS2 group, the placental weight was significantly reduced when compared to the placental weight of female offspring from normal-salt diet fed dams (NS: 83.78±12.69 mg, n=36; HS1: 77.33±11.54 mg, n=30; HS2: 75.13±7.075 mg, n=31 $p<0.01$ compared by 1-way ANOVA).
Conclusions: According to these data, an increased maternal salt intake during pregnancy leads to growth restriction in mice on gestational day 13.5. Perinatal salt intake has a higher influence on placental weight of female offspring. A reduced placental weight might be an indicator of placental malfunction with consequences on nutrition of the fetus. Whether litter is small for gestational age during the whole time of pregnancy, whether we can observe a reduction in birth weight and whether we find cardiovascular consequences in later life remains to be elucidated.

Perinatal high salt intake as a risk for the development of hypertension in later life

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Background/Aims: With a worldwide prevalence of 40%, meaning 1 billion affected people, hypertension is a global health burden causing 12.8% of all deaths worldwide. Nevertheless, in 85% of hypertensive patients, there is no identifiable cause for the disease. One risk factor for the development of hypertension in later life is low birth weight. High salt consumption influences body volume homeostasis and is therefore physiologically and via modulation of immune cells associated with an elevated blood pressure. We therefore suppose that a high salt intake in the perinatal period could be a challenge for the feto-maternal immune crosstalk, leading to intrauterine growth restriction and therefore an increased risk for development of hypertension in later life of the offspring.
Method: Female C57Bl/6J mice were either fed with normal diet (Altromin 1310 P, containing 0.2% sodium, NS group) or with corresponding high salt diet containing 3% sodium (HS group) from timed mating with a C57Bl/6J male until weaning of offspring. The offspring were separated from the mothers by end of weaning and from then on, were fed a normal diet. At the age of >1 year (55 to 79 weeks), mean arterial blood pressure (MAP), heart rate and activity were analysed with radiotelemetry.
Results: For male (n=6-12) and female (n=4-12) aged offspring, a typical day-night-rhythm pattern could be found for activity, heart rate and MAP. There was no difference in MAP between the perinatally normal salt (NS) fed and the perinatally high salt (HS) fed aged offspring neither at daytime (7:00-19:00) nor at nighttime (19:00-7:00). Heart rate and activity were also not different between corresponding NS and HS groups.
Conclusions: In the absence of additional hypertensive stimuli, we found no evidence for an increased risk for development of hypertension in the offspring when perinatally challenged with a high salt intake of the mother. Further analysis of blood pressure in the offspring under conditions of high dietary salt intake or increased angiotensin II levels remain to be performed. Analysis of the feto-maternal immune cross talk will enlighten the effects of perinatal high dietary salt intake on the immune system of mother and offspring.

Maternal Micronutrient Status in Pregnancy is Associated with Child's Adiposity at 18yrs of Age

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Table: Multivariate associations of maternal circulating nutrient concentrations during pregnancy and adiposity in the child at 18 yrs of age

	VAT (Visceral adipose tissue, MRI, cm^2)	SAT (Subcutaneous adipose tissue, MRI, cm^2)	Total fat mass (DXA, kg)
Vit B12 (pmol/l)	0.041	0.051	0.072
Erythrocyte folate (nmole/l)	0.164***	0.173***	0.173***
Vit D3 (nM/l)	–0.044	–0.152***	–0.133***
Ferritin (mcg/l)	0.004	0.011	–0.012

Values represent standardized ß,
*p<0.05, **p<0.01, ***p<0.001

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BACKGROUND/AIMS India is the world's capital of 'thin-fat' phenotype and young onset diabetes. Intra-uterine undernutrition and abdominal adiposity in later life are possible explanations. PMNS (Pune Maternal Nutrition Study) offers a unique opportunity to study the association between intrauterine nutrition and later adiposity.
METHODS PMNS is a preconceptional birth cohort set up in 1993 in six villages near Pune. Maternal circulating concentrations of vitamin B12, erythrocyte folate, ferritin and vitamin D3 were measured at 18 and 28wks of gestation. Children have been serially followed up. We measured total body fat (DXA), and visceral (VAT) and subcutaneous (SAT) abdominal adiposity by MRI at 18 years. We investigate the association between intrauterine micronutrient exposures and adiposity at 18 years of age.
RESULTS Adiposity measurements were available in 595 (308 boys) at 18 years of age. Half of them had a BMI < 18.5 kg/m2, 9.1% boys and 4.3% girls were overweight or obese. Body fat percent and abdominal fat were higher in girls; therefore, gender specific SD scores were generated. Multiple regression analysis showed that higher maternal erythrocyte folate concentration at 28 weeks of gestation was associated with higher VAT (ß=0.164, P>0.001), SAT (ß=0.173, P>0.000) and total body fat (ß=0.173, P>0.000) of the child. On the other hand, higher maternal Vit D3 was associated with lower SAT (ß= -0.152, P<0.002) and total body fat (ß= -0.133, P<0.004); vit B12 and ferritin were not related.
CONCLUSION We demonstrate that higher folate and lower vit D status in the mother during pregnancy are associated with higher adiposity in the child in later life. These findings provide an actionable target in pregnancy to influence the escalating epidemic of adiposity in Indians.

Protective role of physical activity and resilience in perinatal depression: a latent class analysis from a randomized controlled trial (IMPACT)

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Background: Almost one in four of the women during pregnancy experience at least one mental health problem. Half of women continue with these complaints into the postpartum period, affecting both mother and growth and development of her child. Few studies have explored the nature of perinatal depressive symptoms across pregnancy and postpartum. Drawing data from a longitudinal study, we aimed to 1) identify distinct patterns of maternal depressive symptoms at three time-points in the perinatal period; and 2) determine the relationship between physical exercise and psychological resilience and the trajectories of depression.
Method: A secondary analysis was conducted using data from 1789 mothers participating in a randomized controlled trial being implemented in Canada (IMPACT). Depression was measured using the EPDS scale. A distinct pattern of depression symptoms was identified by conducting longitudinal latent class analyses across three time-points in perinatal period in MPlus. Latent class membership was assigned and subseuently used in regression analyses to identify predictors of each trajectory identified including physical activity and resilience in SPSS.
Results: Three distinct trajectories of maternal depression over time were identified: low (63%), medium (29%) and high (9%). The predictors of the trajectories with high depression as compared to low depression showed that women who were 0-2

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times per week active during pregnancy were at a lower risk of being members of the high depression class [aOR: 0.36 (0.13-0.99)]. Similarly, women who had a level of resilience less than the mean resilience (M=74) were 6 times more likely to be members of the high depression class [aOR:5.96 (2.81-12.63)]. All analyses controlled for age, education, income, ethnicity, and marital status.
Conclusions: These analyses identified three patterns of depressive symptoms. Physical activity and resilience were identified as independent predictors of high depression indicating that moderate levels of physical activity and resilience are beneficial for improving high depressive symptoms in pregnant women.

Predictors of Trajectories of Childhood BMI: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC)

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Background: Childhood obesity has become a global epidemic irrespective of the socioeconomic status of a country or nation. Obesity increases the risk of various diseases in children. Available literature identify various risk factors. This analysis on longitudinal data adds to the existing evidence of predictors of childhood obesity. Drawing data from a longitudinal study, we aimed to 1) identify distinct patterns of childhood BMI at ten time-points in the postpartum period; and 2) determine the predictors of trajectories of childhood BMI.
Methods: A secondary analysis was conducted using data from more than 8,700 mother-child dyad participating in the Avon Longitudinal Study of Parents and Children (ALSPAC), a UK based birth cohort. The information on BMI was obtained from year 8 postpartum onwards. A longitudinal growth model was estimated followed by longitudinal growth mixture modelling to identify distinct trajectories of BMI in MPlus. Finally, predictors of trajectories of childhood BMI were determined by using logistic regression modelling in SPSS.
Results: Two distinct trajectories of childhood BMI over time were identified: Normal weight (94%) and overweight and obesity (6%). The predictors of the trajectories with overweight and obesity as compared to normal weight showed that 1 kilogram increase in mother weight caused mean increase in child BMI by 1.06 (95%: 1.05-1.07) in overweight and obese class. Similarly, never breastfed children were at a higher risk of being member of overweight and obese class [aOR: 1.24 (0.96-1.59)] controlling for other variables in the model.
Conclusions: These analyses identified two patterns of childhood obesity. Strict monitoring of mothers weight gain during pregnancy and initiating breastfeeding may reduce the risk of being obese in older years.

"When you are not pregnant it's easy. When you are pregnant it's not easy": a qualitative study of how women's lifestyles change when they become pregnant

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Background/Aims: Maternal lifestyle in the months leading up to conception and throughout pregnancy have both immediate and transgenerational impacts on offspring health. Aims were to explore how women's lifestyles change when they become pregnant, and their perspectives of the lifestyle advice they receive throughout pregnancy from health professionals and other sources.
Method: This qualitative study recruited pregnant women receiving maternity care at a large hospital network in Victoria, Australia. Semi-structured interviews with questions related to study aims were conducted between July and October, 2018. Data were thematically analysed and triangulated. Ethics approval was obtained from Monash Health Human Research Ethics Committee (Ref: RES-18-000-169A).
Results: Seventeen pregnant women participated (mean gestational age, 30.2±2.0 weeks). Emergent themes related to women's lifestyles before and during pregnancy, their advice-seeking behaviours, and the role of health professionals in providing advice. Maternal lifestyle during pregnancy was highly influenced by preconception lifestyle, the physiological demands of pregnancy and the pressures of daily life. Participants were active seekers of lifestyle advice from a range of sources but were passive recipients of lifestyle advice that was part of their routine maternity care. Participants appreciated the lifestyle advice they received from health professionals, despite acknowledging that they often received it only if they asked.
Conclusions: Women want lifestyle advice that supports positive lifestyle change during pregnancy and health professionals need to be proactive as they provide it. Other factors that impact on maternal lifestyle should be considered when providing advice that supports positive behaviour change.

Synthesizing a Map of the Human Methylome across the Life Course

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Background/Aims: Human development is tightly linked to epigenetic mechanisms, which can impact health and disease at all stages throughout life. However, we lack a clear understanding of what constitutes healthy patterns of epigenetic variation at each developmental period, and how these patterns change throughout the life course. To synthesise a life course methylome using multiple datasets, in conjunction with the CLOSER UK longitudinal study consortium, we developed methods to assess and minimize heterogeneity in methylomic data across cohorts. We then characterized the Human methylome at each developmental stage and describe changes across the lifespan. Finally, we developed an online, openly accessible resource, visualizing our findings.
Method: We obtained DNA methylation data from 7 cohorts across the UK (age 0 – 98 years; n=10,043 with an average of 60% females per cohort (range: 0-100%). Cohorts spanning several decades were split into 10-year age bins, resulting in 28 datasets. To assess cross-study heterogeneity, we used principal component analysis over eleven summary statistics (e.g, mean, standard deviation) on up to n=857,071 methylation probes. Epigenome-wide meta-regressions of age was carried out to assess changes in methylation across the lifespan.
Results: Principal component analysis showed that methylation measures of central tendency (e.g. mean) were more affected by study heterogeneity than others (e.g. variance in methylation). Based on meta-regression, we found age effects in 87% of methylation probes, but study heterogeneity was large (average I2 = 98%). Cross-harmonized summary data will be made openly available and will be linked to measures of health and disease across the life course.
Conclusions: Our analyses show that substantial heterogeneity between datasets can limit our ability to describe methylation patterns across the life course. Minimizing these effects through cross-cohort harmonization methods, we synthesized a map of the life course methylome. This may be used to highlight critical windows for healthy development or vulnerability to disease.

Maternal Diabetes Impairs Fetal Brown Adipose Tissue Development

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Background/Aims: Offspring of mothers with diabetes mellitus (DM) are more prone to develop obesity and related metabolic disorders. Brown adipose tissue (BAT) is important in adults for preventing obesity via dissipating energy as heat. We hypothesize that maternal diabetes impairs fetal BAT development, which renders the offspring more inclined to develop obesity in later life.
Methods: A mouse model of pregestational type 1 DM induced by streptozotocin was used in our study. BAT were collected from near-term fetuses of diabetic and non-diabetic mice and subjected to analysis of lipogenesis, mitochondria number and expressions of genes crucial for BAT development and function. Postnatal development was monitored and adult offspring were assessed for the susceptibility to develop obesity and type 2 DM.
Results: We found that in the BAT of near-term fetuses of diabetic mice, lipogenesis was impaired, as demonstrated by a significant suppression of lipogenic genes, and a prominent reduction in lipid accumulation and triglyceride content. Results of staining of mitochondrial membrane with prohibitin and measurement of mitochondrial DNA copy number revealed a marked reduction in mitochondrial mass. Notably, both mRNA and protein levels of uncoupling protein 1 (Ucp1), a BAT-specific protein crucial for the thermogenic process, were markedly reduced, which implicates impaired BAT thermogenic functions. The offspring of diabetic mice, despite having a lower birthweight, underwent rapid catch-up growth when fostered by a non-diabetic mother. Adult offspring of diabetic mice showed reduced ability to upregulate BAT-specific genes and maintain body temperature in the cold tolerance test. When challenged with a high-fat diet after weaning, they accumulated more subcutaneous and visceral fat, and were more prone to develop insulin resistance and glucose intolerance.
Conclusions: Offspring exposed to intrauterine type 1 DM exhibit impaired fetal BAT development and show increased risks to develop obesity and type 2 DM later in life.

Local RAS activation by fetal over-exposure to maternal glucocorticoid may participate in the intrauterine programming of adult osteopenia induced by prenatal caffeine exposure

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Background/Aims: Studies indicated that prenatal caffeine exposure (PCE) induced excessive maternal glucocorticoid and intrauterine growth retardation, and suppressed the bone development of the fetus. However, whether PCE suppresses the bone growth after birth and how it happens is still unclear.
Method: Pregnant rats were treated with 120 mg/kg.d of caffeine by intragastric administration from day 9 to day 20 after

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pregnancy. The offspring were sacrificed at day 20 after pregnancy and 2 weeks or 6 weeks after birth. Then, the length, microstructure and biomechanics of the bone, the local expression of glucocorticoid receptor (GR), CCAAT enhancer protein α (C/EBPα), members of the renin angiotensin systems (RAS) and biomarkers of the bone formation, as well as the DNA methylation of angiotensin converting enzyme in the long bone were detected. Then, in vitro model of bone formation based on rat bone marrow mesenchymal stem cells (BMSCs) were established, which was treated with exogenous corticosterone and/or mifepristone or enalapril expression level of genes mentioned above was detected.

Results: we observed a shorter long bone and primary ossification center in the PCE offspring from fetus to grown-ups, as well as less bone trabecular and poor biomechanical intensity. Meanwhile, local expression level of GR, CEBPα and angiotensin-converting enzyme (ACE) in the long bones was lower in PCE offspring, while the expression of bone gamma-carboxyglutamate protein (BGLAP), alkaline phosphatase (ALP) and bone sialoprotein (BSP) was higher, along with DNA hypomethylation of local ACE. Moreover, higher level (50 μM) of corticosterone suppressed the osteogenic differentiation of BMSCs and gene expression of BGLAP, ALP, BSP, but induced the expression of ACE mRNA and the hypomethylation of ACE DNA. Further, those changes were blocked by either mifepristone or enalapril in the BMSCs. Interestingly, corticosterone induced hypomethylation of ACE gene could be detected after 5 passages of the BMSCs.

Conclusions: Those findings indicated that PCE suppressed bone growth and induced adult osteopenia in the offspring, which might be trigger by the local activation of RAS induced by excessive maternal glucocorticoid, while the hypomethylation of ACE gene might be the key point of the sustained activation of the local RAS of the long bone.

Cord Blood Fetuin-A and Fetal Growth in GDM

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Objective: Fetuin A is a multifunctional glycoprotein produced by hepatocytes and has been associated with insulin resistance. It is unclear whether GDM may affect cord blood fetuin-A concentrations. We investigated the associations of cord blood fetuin-A levels with GDM and fetal growth.

Methods: In a nested matched case-control (1:1) study in the Shanghai birth cohort, we evaluated cord blood concentrations of fetuin-A and fetal growth factors in the neonates of mothers with GDM and euglycemic (n=153/153) pregnancies.

Results: Cord serum fetuin-A concentrations were not significantly different comparing the newborns of GDM (mean ±SD: 783.6±320.0 μg/ml) vs. euglycemic (738.9±274.2μg/ml) mothers, while IGF-1 (76.6±27.8ng/ml vs. 66.3±25.0 ng/ml, P=0.001) and IGF-2 (195.3±32.5 ng/ml vs.186.9±31.9 ng/ml, P=0.026) concentrations were significant higher. Cord blood fetuin-A was not significantly correlated with cord blood insulin, IGF-1 or IGF-II in GDM or euglycemic pregnancies. Cord blood fetuin-A was negatively correlated with birth length z score in GDM pregnancies (r=-0.218, P=0.026), but not in healthy pregnancies. Adjusting for maternal and delivery characteristics, the associations were similar.

Conclusion: In this largest study on cord blood fetuin A levels in GDM, we did not detect a significant difference between GDM and euglycemic pregnancies. Fetuin-A was negatively associated with fetal linear growth in GDM but not euglycemic pregnancies. This novel finding requires confirmation in other independent studies.

Inter-generational association between parental cardiovascular health status (Life's Simple 7) and blood pressure outcomes in their offspring

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Background/Aims: Childhood high blood pressure (HBP) has become major public health problem worldwide. The American Heart Association introduced the "Life's Simple 7" (LS7) concept of maintaining cardiovascular health, which is effective in adults. We assessed whether these positive effects would pass across generations.

Method: We studied 10 839 child-father pairs and 14 992 child-mother pairs from the baseline data of a Chinese national school-based multi-centered randomized trial conducted in 2012. Children's median age was 10.7 and 10.5 years. Each component of the parental LS7 was defined as ideal (1 point) or unfavorable (0 point) and then divided into 4 groups according to total score (0-3, 4, 5, 6-7). Children's blood pressure outcome was defined based on the Forth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. BP outcomes of each LS7 score category were calculated using logistic regression model and linear regression model, P for trend was also performed.

Results: With the healthiest group (LS7 score 6-7) as reference, decreased LS7 score led to higher HBP risk and BP level in both paternal and maternal subsets. The odds ratio for HBP ranged from 1.07 (0.89, 1.29) to 1.36 (1.08, 1.72) in paternal subset, and

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from 1.13 (0.91, 1.40) to 1.45 (1.07, 1.95) in maternal subset. P for trend were 0.004 and 0.465, separately.
Conclusions: Unfavorable parental cardiovascular health status is related to higher HBP risk in their offspring. These results suggest that parents should be involved in childhood HBP prevention strategies.

The effect of a hydrolysed infant formula with added synbiotics on growth, safety, and tolerance in healthy term Chinese infants: DRAGON study

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Background/Aims: Establishing a commensal microbiota in the gastrointestinal tract is important to provide the tolerogenic environment required for optimal immune system development. Disruption in gut microbiota balance known as dysbiosis is associated with an increased risk of food sensitization and atopic eczema [3]. New insights suggest dysbiosis could be prevented by symbiotic supplementation. However, data in the Chinese population are still lacking. If breastfeeding is insufficient or not possible for infants high at risk of developing allergies due to family atopic history, scientific organizations have recommended the use of hydrolysed formula in the first 4–6 months of life for the prevention of allergic diseases [1,2]. Apart from the importance to gain more insight into the effect on allergy risk reduction of hydrolysed protein formula with added synbiotics, it is also necessary to ensure healthy growth and nutritional adequacy in these formula-fed infants, especially in view of the variations seen in the composition of hydrolysed proteins and their macronutrient levels and sources. Recently it has been demonstrated that the addition of a specific synbiotic mixture to an infant formula also supports adequate infant growth [4]. The aim of this study is to prove equivalence in growth and to assess safety and tolerance of a partially hydrolysed protein (2.3 g/100kcal) infant formula supplemented with synbiotics (pHF synbiotics) compared to standard (intact cows' milk protein based) infant formula (2.0 g/100kcal) with prebiotics (IF prebiotics) in healthy term Chinese infants. In addition, the study is designed to assess specific immunological and microbial outcomes. The latter will provide an opportunity to explore the effects of pHF synbiotics on the prevention of allergy via early life nutrition through gut microbiota modulation in Chinese population.

Method: In a randomized controlled double-blind study, currently ongoing (NCT03520764), in total 224 healthy term Chinese infants are randomized to either pHF synbiotics or IF prebiotics. The intervention initiates before the infant is 28 days until 17 weeks of age. Maximal 112 (range 56-112) exclusively breastfed infants are included in the study as control group. After the intervention period anthropometric parameters, clinical data, and parents reported tolerance and allergy related outcomes are assessed until 12 months of age. Stool and saliva samples are collected before study product intake, at 17 weeks and 12 months of age. Blood sample are collected at 17 weeks and 12 months of age. Primary assessments up until 12 months of age include anthropometrics and safety via occurrence of adverse events. Secondary, parent-reported gastrointestinal tolerance, allergic symptoms and infection episodes are monitored. Liver and kidney function are assessed, and nutritional adequacy is determined by levels of vitamins and minerals in blood. Immunological parameters are measured in saliva, stool and blood. Microbial composition and activity is determined in stool in order to evaluate the impact of pHF synbiotics on gut microbiota and allergy prevention.

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DRAGON study team: Wei Cai, Ying Wang. Xinhua hospital, School of Medicine, Shanghai Jiao Tong University. Zailing LI, Peking University Third Hospital. Jieling WU, Guangdong Province hospital for maternal & child health care. Lili ZHANG, Wuxi People's Hospital. Min LIU, Shanghai Public Health Clinical Center.

Pre-pregnancy body mass index and the risk of cesarean section: a population-based cohort study

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Background: The substantially rising rate of caesarean sections is a growing public health burden. Pre-pregnancy body mass index, (BMI) was one of the modifiable risk factors. However, a recent meta-analysis indicated that the association between pre-pregnancy BMI and caesarean delivery was found in studies collecting information on pre-pregnancy BMI by recall during the first trimester, while such association was not found in studies measuring pre-pregnancy BMI before pregnancy. To assess the association between pre-pregnancy BMI and the risk of cesarean section in a large cohort study which measuring pre-pregnancy BMI before pregnancy.
Methods: A retrospective cohort study was conducted in the National Free-pregnancy Checkups (NFPC) from 31 provinces from 2010 to 2014. The baseline examination including pre-pregnancy BMI and the pregnancy outcomes. Log-binomial regression models were used to estimate the risk ratios of cesarean section for women with different BMI. Multivariable models were used and adjusted for potential risk factors for cesarean section. Sensitivity analyses adjusted for different covariates in the multivariable models. A total of 3,512,718 women who had singleton live births were included in this analysis.
Results: We found that the rate cesarean section was 30.04% (95% CI, 30.00%–30.09%). In the multivariable model, pre-pregnancy BMI was independently associated with increasing risk of cesarean section, after adjustment of socio-demographic characteristics, history of hypertension, diabetes mellitus and other chronic diseases, parity, delivery year, gestational week at delivery, offspring gender and birth weight. Compared with normal weight women, overweight women had a higher risk of cesarean section (adjusted risk ratio, 1.14; 95% CI, 1.14 to 1.15), and obese women had highest risk of cesarean section (adjusted risk ratio, 1.28; 95% CI, 1.28 to 1.29).
Conclusion: Our findings indicated that weight restrictions in overweight and obese women prior to pregnancy might be helpful to reduce the rate of cesarean sections.

Experience analysis of bundled management of safe delivery cycle in patients with the pernicious placenta previa accreta

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Aims: To assess the clinical guiding significance of implementing the whole-course safety management (bundle-model) measures for pregnant women with the pernicious placenta and placenta acrreta during the period of pregnancy and perioperative, the method of cross-sectional comparative analysis was used to determine the risk of pernicious placenta combined with placenta acrreta and improving maternal and infant outcomes after performing the bundle-model.
Method: Pregnant women with pernicious placenta combined with placenta acrreta who visited the Third Affiliated Hospital of Guangzhou Medical University from January 1, 2018 to December 31, 2018 were assessed and then included in the bundled-model management. The safe delivery full-cycle management bundle–model was detailly described as follows:**1. Patient and follow-up doctor bundle:** Patients in the diagnosis of pernicious placenta combined with placenta acrreta were evaluated for the condition, individualized treatment plan was developed, and emergency plans were prepared in the inpatient department and operating room. The follow-up doctors performed out-of-hospital follow-up;**2. Bind patients and hospitals:** All pregnant women who are managed by bundle-model can seek timely help from a doctor (They were asked to must live in a location that to in a 10-minute drive quickly reach the Third Affiliated Hospital of Guangzhou Medical University). These patients were required to perform outpatient checkup and blood matching to ensure the adequate reserve of blood produce every 2 weeks. Of note, the patients with active vaginal bleeding needed to be subjected with emergency treatment within 10 minutes. The emergency doctor would open the venous access and inform the blood bank and the operating room, and then directly enter into operating room in a rapid emergency passageway, initiating rapid response and multidisciplinary team treatment; **3. Building an obstetric rapid response team**:The rapid response depend on the whole team of doctor-nurse-patient trinity); **4. Implementation of controlled bleeding surgery:** The seamless cooperation between obstetrics-anaesthesiology, urology, surgery and nurse, transfusion department;**5. Before operation:** Before performing the operation, we made an adequate preparation of our team work, including a close communication between anaesthesiologists and transfusionists, ensuring sufficient blood products, making anesthesia plan, supplying sufficient physiological saline and balancing fluid before operation to reduce haemoglobin loss during operation. Notably, for those patients who exhibited a severity of implantation or the risk of ureteral injury prior to surgery, senior urologists were invited to perform cystoscopy and place double J tubes. **In surgery:** Generally, we mainly evaluated the area and depth of placenta implantation to control bleeding and then determined the retain of uterus according to the patient's bleeding volume and bleeding rate. After making a comprehensive assessment for the patient's condition and willingness, we provided an individualized treatment based on ensuring the patient's life safety. The program preserves the uterus possibly if such treatment cannot result in serious complications.
Results: Since 2018, the Third Affiliated Hospital of Guangzhou Medical University has made a great achievement through

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performing bundled management for pregnant women with the pernicious placenta and placenta acrreta. Compared with the outcome of patients with the same condition in our hospital in 2015, all the indexes determined were reduced significantly, including the bleeding amount of in operation, the rate of hysterectomy, the amount of blood transfusion, the rate of trans-surgical medicine, the ratio of neonatal to NICU, and the rate of intraoperative organ injury. In contrast,the former's gestational weeks, neonatal birth scores, and neonatal birth weight were all higher than the average amount in 2015.
Conclusions: The incidence of adverse outcomes in pregnant women with the pernicious placenta and placenta acrreta is remarkably reduced after performing the bundled-model management of safe delivery cycle.

DNA Methylation Mediates Association Between Prenatal Exposure to The Chinese Great Famine and Adult Waist Circumference

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Background/Aims: To explore whether DNA methylation at *INSR*, a gene involved in growth and metabolism, mediated the association of prenatal exposure to the Chinese great famine with adult waist circumference (WC).
Method: A total of 174 subjects were selected into the study from famine striking areas in China through multi-stage clustered random sampling. DNA methylation at the *INSR* gene locus were assayed from peripheral white blood cells using the Sequenom's MassARRAY system. The "mediation" package of R was used to evaluate the mediation effect of DNA methylation at the *INSR* gene on the association between prenatal exposure to the Chinese great famine and adult WC. Bisulfite batch, province, gender, physical activity level, the frequencies of meat, vegetables, fruit, and milk consumption as well as smoking and alcohol use were adjusted in all analyses. Bonferroni correction was applied for multiple testing.
Results: DNA methylation was quantified at 8 CpG sites in the *INSR* gene. Prenatal famine exposure was significantly associated with higher overall methylation level of the *INSR* gene (d=5.0%; 95% confidence interval [*CI*]: 1.9-8.1; $P=9.0\times10^{-3}$) and larger WC (d=3.52 cm; 95%*CI*: 0.48-6.56; P=0.023), after adjusting for all covariates. Furthermore, famine significantly increased methylation levels at three CpG sites, including CpG1, CpG5 and CpG7, after Bonferroni correction. Methylation of the CpG7 site mediated 32.0% (95%*CI*: 5.0-100.0%, P=0.029) of the association between prenatal exposure to the Chinese great famine and adult WC.
Conclusions: Epigenetic changes to the *INSR* mediate the adverse effect of prenatal famine exposure on WC.

Using Mendelian randomization to disentangle maternal and fetal contributions to low birth weight and future risk of cardio-metabolic disease

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Background/Aims: Reduced intrauterine growth, as estimated by low birth weight, is robustly associated with poor perinatal outcomes and increased future risk of cardio-metabolic diseases, including type 2 diabetes and hypertension. However, it remains unclear which maternal exposures during pregnancy cause low birth weight (i.e. via intrauterine mechanisms) and whether reduced intrauterine growth causes increased risk of cardio-metabolic disease in later life.
Method: Mendelian randomization is an epidemiological method that uses genetic variants associated with a modifiable environmental exposure as instrumental variables to estimate the causal effect of the exposure on medically relevant outcomes. Several studies have used Mendelian randomization to investigate relationships with birth weight, however their interpretation is complicated by the correlation between maternal and offspring genotypes that threatens to reintroduce confounding into the analysis. We have developed a structural equation model that decomposes the genetic effect on birth weight into direct fetal and indirect maternal components. Using these fetal- and maternal-specific genetic effects in a Mendelian randomization framework enables us to disentangle the complex relationship between birth weight and future risk of cardio-metabolic disease.
Results: We will illustrate our framework using examples related to offspring birth weight and cardio-metabolic traits from the UK Biobank Study and the Early Growth Genetics (EGG) Consortium. For example, we find strong evidence to suggest that increases in maternal blood pressure cause decreased offspring birth weight. In contrast, we find no evidence that maternal genetic variants that decrease offspring birth weight are also related to increased offspring systolic blood pressure.
Conclusions: By successfully separating fetal from maternal genetic effects and using them in Mendelian randomization analyses we set a precedent for future studies seeking to understand the causal role of the intrauterine environment in later-life offspring health.

Antenatal Corticosteroids, Adiposity, and Adipokines in Young Adults Born Preterm

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	ANCS+, n=81	ANCS-, n=89	Adjusted Mean Difference*
Height, cm	166.2 ± 9.6	163.1 ± 9.8	3.8 (0.78, 6.9)§
Weight, kg	70.2 ± 20.7	73.1 ± 23.1	–2.3 (–9.0, 4.5)
Waist circumference, cm †	85.1 ± 15.6	88.9 ± 18.4	–4.63 (–10.14, 0.88)
Skinfold thickness sum, mm	38.3 ± 21.8	45.7 ± 23.4	–7.73 (–14.72, –0.73)§
BMI, kg/m^2	25.3 ± 6.9	27.3 ± 7.8	–1.9 (–4.3, 0.31)§
WHR †	0.51 ± 0.10	0.55 ± 0.11	–0.04 (–0.08, –0.01)
Leptin, ng/ml	25.7 ± 28.1	34.0 ± 28.6	–0.51 (–0.86, –0.17)‡§
HMW Adiponectin, ng/ml	4118.3 ± 3262.3	3753.4 ± 2242.1	–0.07 (–0.29, 0.15)‡
Resistin, ng/ml	7.38 ± 5.30	7.72 ± 3.52	–0.17 (–0.34, –0.003)‡ §

*Adjusted for matHTN and race; †n=77 ANCS+, n=87 ANCS-; ‡ln transformed, §p<0.05

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Background/Aims: Antenatal corticosteroids (ANCS) alter adiposity in animal models, but the effect of ANCS exposure on adiposity in humans is incompletely described. Our aim was to evaluate the effect of ANCS exposure on anthropometric measures and adipokine levels in young adults born preterm with very low birth weight (VLBW).
Method: In an observational study, we measured height, weight, waist circumference, triceps and subscapular skinfold thicknesses, plasma leptin, high-molecular-weight adiponectin, and resistin in 170 young adults age 18-22 years, born preterm with VLBW, and calculated body mass index (BMI), waist-to-height ratio (WHR), and the sum of skinfold thicknesses. Multivariable linear regression models were used to evaluate the associations of ANCS with the outcomes (anthropometrics and adipokines), adjusting for race and maternal hypertensive pregnancy (matHTN) and assessing for an interaction with sex. Natural log transformation was used as indicated to improve the distribution of continuous variables.
Results: There were no ANCS group differences in gestational age (mean ± SD; 27.9 ± 2.8 weeks), birth weight (1056 ± 274 g), birth weight z-score (-0.32 ± 0.84), or sex (51% ANCS+ vs. 38% ANCS-, male). The ANCS+ group was significantly more likely to have matHTN (46% vs. 28%) and non-black race (69% vs. 45%). Differences in the outcomes by ANCS status, expressed as mean ± SD and adjusted mean difference with 95%CI, are shown in the Table. We detected significant interactions between ANCS and sex, wherein the associations between ANCS and height and resistin were stronger in males.
Conclusions: Young adults born preterm with VLBW and exposed to ANCS were taller and had anthropometric measures and adipokine levels suggestive of decreased adiposity. The associations of ANCS to height and plasma resistin were stronger in males. Our results suggest that ANCS exposure may confer a protective effect against obesity in individuals born preterm with VLBW.

Community engagement to inform priority setting for mother and child nutrition: The Improved Nutrition Preconception Pregnancy Post-Delivery (INPreP^3) project in sub-Saharan Africa

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Background/Aims: Poor maternal nutrition, suboptimal infant and child feeding practices can have a profound impact on a child's development, and can lead to adverse economic, social and health consequences in the long-term. Characterized by rapid nutritional transition, countries such as South Africa, Ghana, and Burkina Faso face the increasing challenge of double burden of malnutrition, where undernutrition coexist with overweight and obesity. The INPreP^3 group aims to design and develop evidence-based context-appropriate interventions to optimise maternal and child nutrition targeting the first 1000 days of life.

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Method: As a sub-project, the study aims to modify a public engagement tool (CHAT) to facilitate the prioritization of cost-effective nutrition interventions that reflect local health needs, context and societal values. Critical in the modification process is qualitative data on communities' opinions and values, practices around nutrition that is being collected through focus groups. Female and male community members of 18-55 years are being invited to participate in focus group discussions in Nanoro, Burkina Faso; Navrongo, Ghana; and Soweto, South Africa alike. Qualitative data will be thematically analysed to produce a cross-country synthesis and findings from this analysis will be presented.
Results (expected): Themes will capture perceptions of the role nutrition has on a person's own and their future offspring's health in the short and long-term; and priorities and barriers related to a diverse and high quality diet. Ideas for the type and delivery of potential interventions to support and optimise nutrition will be explored.
Conclusions: Findings from this work will be triangulated with other INPreP[3] study results, including nutrition policy reviews, a systematic review of intervention studies, an economic investment case, expert consultations from the field of nutrition, and analysis of routine health and demographic surveillance data. The consolidation of the findings will facilitate the modification of the engagement tool and consequently enhance evidence-based policy making for improved nutrition.
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Weekly exercise frequency and maternal mental health symptoms during the perinatal period in the Mercy Pregnancy and Emotional Wellbeing Study

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Background/Aims: Randomised control trials have demonstrated exercise as an effective intervention for depressive and anxious symptoms in adults with mental health disorders. Although this has not been demonstrated in pregnant women, evidence has shown exercise to be safe in pregnancy, and there is recognition of the benefits of exercise for maternal, fetal and infant outcomes. In this study, we examine the longitudinal associations between weekly exercise frequency with maternal depressive and anxious symptoms during the perinatal period in an Australian pregnancy cohort.
Method: We have analysed the responses from 258 Melbourne women in the Mercy Pregnancy and Emotional Wellbeing Study (MPEWS), and published the findings in the Journal of Psychosomatic Research (2018, Vol. 111). There will be an additional 200 women completing measures at 12 months postpartum by April, 2019, and available for analysis (N=458). Exercise was measured using self-reported weekly frequency of 30-min bouts of moderate-to-vigorous exercise. The Edinburgh Postnatal Depression Scale and the State-Trait Anxiety Inventory were used to measure maternal mental health. The data were analysed using parallel-process growth modelling.
Results: In the 258 women, weekly exercise frequency during the perinatal period was negatively associated with women's mental health symptoms during the same period. Specifically, steeper reductions in exercise frequency during pregnancy and the postpartum were associated with steeper increases in both state anxiety and depressive symptoms during pregnancy and the postpartum. We will present the results of these model using the full sample (N=458) at the Congress.
Conclusions: Our study is the first to examine the longitudinal associations between exercise and mental health symptoms across the perinatal period and preliminarily demonstrate potential benefits of exercise for women's mental health during this period. The results support the need for randomised control trials to investigate the efficacy of targeted exercise interventions in reducing mental health symptoms in pregnancy women.

Preconception diabetes mellitus and adverse pregnancy outcomes in over 6.4 million women aged 20-49 years: a population-based cohort study

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Background/Aims: Diabetes mellitus (DM) is associated with a range of adverse outcomes, however, most of existing studies using DM status diagnosed according to blood glucose level during pregnancy. Seldom studies precisely focus on maternal blood glucose level prior to pregnancy. We aimed to evaluated the association between preconception blood fasting plasma glucose (FPG) level and subsequent pregnancy outcomes.
Method: We conducted a population-based retrospective cohort study with 6,447,339 women aged 20-49 years old, who participated in National Free Pre-Pregnancy Checkups Project and completed pregnancy outcomes follow up between 2010 and 2016 in rural China. Associations between preconception FPG level and substantial adverse pregnancy outcomes, including spontaneous abortion, preterm birth (PTB), macrosomia, small for gestational age infant (SGA), birth defect, perinatal infant death, and stillbirth, were examined by logistic regression models after adjusting for confounding variables.
Results: Of 7,094,807 registered women (age 20-49 years), 6,447,339 were included in analyses. The incidence of DM and IFG was 76,297 (1.18%) and 847,737 (13.15%), respectively. Only 917 (1.20%) women were aware that they had DM in rural China. The uncontrolled rate was 37.28% in those who were aware of their DM. A total of 1,005,568 (15.60%) women had adverse pregnancy outcomes. Compared to women with normal FPG, the multivariate odds ratios (ORs) of adverse pregnancy outcomes were 1.05 (95% confidence interval [CI]: 1.04-1.05) for women with impaired fasting glucose (IFG) and 1.16 (95%CI: 1.14-1.18) for women with DM. Among women without previously diagnosed DM, there was a positive linear association between FPG levels and adverse pregnancy outcomes (P for trend < 0.001).
Conclusions: DM is associated with an increased risk of maternal, perinatal and neonatal morbidity during pregnancy. The awareness rate of DM prevalence in rural China is extremely low. The management of DM is unsatisfactory in women diagnosed with DM. It is necessary to enforce pre-pregnancy examination on DM screening and implement effective glycemic control strategies in pregnant women in rural China. Meanwhile, the examination and treatment of DM for reproductive-aged women planning to conceive should be covered by medical insurance in rural China.

Telling the untold story: The economic and psychosocial impacts on families affected by intellectual disability

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Background/Aims: Data on the financial and psychosocial costs incurred by families affected by intellectual disability (ID) is scarce, thus limiting the capacity to value the benefits of diagnosing ID through the application of genomic testing. We report on the first large, in-depth study exploring the economic, psychosocial and potential reproductive impacts of whole genome sequencing (WGS) for ID.
Method: A survey instrument was developed to assess quality of life, psychosocial impacts, education, employment, income, wealth, welfare dependency, living arrangements, family out-of-pocket costs and family planning choices. Eligible families had WGS.
Results: Preliminary data showed combined costs to the Australian and State Governments, and private households totalled $13.1million per household up to the age of 69. Families bore a significant financial burden ($4.8million per household) mainly due to lost income and out-of-pocket expenses. Families were under enormous psychosocial strain and most carers reported significant quality of life impacts. Costs to Governments were $10.7million per household, with the main costs being for special education, residential care and welfare.
Conclusions: Families affected by ID experience a significant financial and psychosocial burden. This data is important for benchmarking the potential benefits of WGS in familial ID.

Determining the impacts of epigenetic modifying drugs on the female germline

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Background/Aims: Epigenetic modifications, including DNA methylation and histone modifications, regulate gene expression to facilitate the differentiation and maintenance of distinct cell lineages in multicellular organisms. Activity of the enzymes that mediate epigenetic modifications can be influenced by environmental factors such as drugs or diet. Polycomb

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Repressive Complex 2 (PRC2) is an essential epigenetic modifier that catalyses histone 3 lysine 27 trimethylation (H3K27me3) at developmental genes in many tissues, including the germline. Germ cells give rise to sperm and oocytes that transmit genetic and epigenetic information to offspring, and alterations in the germline epigenome can affect offspring development and health. Common dysregulation of epigenetic modifications in cancers has driven the development of drugs that inhibit epigenetic enzymes. For example, Tazemetostat inhibits EZH2, the catalytic component of PRC2, and is currently in phase I/II trials for treatment of tumours, including in patients of reproductive age. While epigenetic drugs have great therapeutic potential, they act systemically and may detrimentally affect the germline epigenome. Our past studies have demonstrated that PRC2 alters maternal epigenetic inheritance as offspring from oocytes lacking PRC2 function were overgrown, had increased fat and reduced muscle content and altered skeletal development.

Method: Using Tazemetostat inhibition of PRC2, we are examining how epigenomic drugs alter H3K27me3 and transcription of PRC2 regulated genes in growing oocytes and whether how this treatment affects offspring development.

Results and Conclusions: We show that oocytes are enriched with H3K27me3 during their growth and that treatment of adult female mice with Tazemetostat depletes H3K27me3 in growing oocytes, indicating that this drug will detrimentally affect offspring. We are examining the potential for tazemetostat to alter oocyte transcription as well as growth and development in offspring. We expect Tazemetostat to alter oocyte transcription and result in offspring outcomes that are similar to outcomes observed after deletion of PRC2 in oocytes.

Association of Early Life Growth Pattern with Body Composition and Metabolic Consequences in Sri Lankan Adolescents

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Background and Aims: Growth pattern in early life is recognized as a factor for obesity-related complications in later life. This study aimed to identify the association between growth pattern in the first year of life with body composition and metabolic consequences during adolescence.

Methods: A cross-sectional study was conducted in 366 urban school children (182 girls and 184 boys) aged 11-13 years selected through stratified-cluster sampling. Waist circumference (WC), height, blood pressure (BP), fasting blood sugar, fasting insulin (n=65), lipid profile, hs-CRP, serum leptin and AST/ALT were measured. Body composition was assessed using Bio-electrical Impedance Analysis using population-specific prediction equations. Fat-mass-index (FMI) and fat-free-mass-index (FFMI) were calculated. Birth weight and weight at 12-months were extracted from the Child-Health-Development-Record. An increase in weight SD score (SDS) by ≥0.67 between birth and 12-months was defined as accelerated growth.

Results: The mean age was 12.2 years (SD-0.87). One hundred and twelve (30.6%) had accelerated growth. Mean FMI (p=0.012), fat percentage (p=0.014), WC-SDS (p=003), systolic BP-SDS (p=0.045), diastolic BP-SDS (p=0.046), median leptin (p=0.032) and fasting insulin (p=0.046) were significantly higher in children who had accelerated growth. This significant difference in means persisted after adjusting for age, sex, pubertal status and birth weight of the child.

High birth weight (>3500g) showed significant associations with increased FFMI (p=0.000) and WC SDS (p=0.017).

Conclusions and Recommendations: Accelerated growth in early life, is associated with increased FM and metabolic consequences but not with increased fat-free-mass, in adolescence. Hence, it is important to ensure an optimum growth rate during first year of life.

The Prenatal Origins of Late-Life Cognitive Decline and Dementia: a Systematic Review

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Background/Aims: The significance of early life factors in age-related cognitive decline and risk of dementia has become increasingly clear. Because of its critical importance for brain development, the prenatal period might be especially important for later cognitive health. Studies in humans have associated several prenatal factors, like low birth weight and maternal hypertensive disorder, with age-related cognitive decline. However, a clear overview of these associations is lacking. With this systematic review, we aim to give an overview of prenatal factors associated, or not associated, with cognitive function, cognitive decline and dementia in older populations. Thereby, we want to shed light on the extent of the prenatal origins of late-life cognitive decline and dementia.

Method: We will perform an extensive search in MEDLINE, EMBASE and PsychINFO. We will include all cohort studies reporting on any prenatal exposures and aging-associated cognitive function (using cognitive tests), cognitive decline (using multiple time points or self-reported) or clinical diagnosis of dementia, all measured in an aging human population (≥95% should be above 50 years of age).

Results: At the time of submission, we have not yet finished the review search. However, we have already identified several studies meeting our inclusion criteria. Included studies found associations between birth size, birth weight, famine exposure,

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late preterm birth, economic recession during birth, prenatal sex hormone exposure, maternal hypertensive disorders during pregnancy and cognitive decline or dementia. However, the associations with birth weight and famine exposure were not replicated in all included studies. Furthermore, no association was found between prenatal pandemic influenza exposure and cognitive decline or dementia.

Conclusions: Our preliminary results suggest that some adverse events during pregnancy, depending on the nature of exposure and the setting, are associated with the rate of cognitive decline and risk for dementia at old age. We aim to present a description of the extent of the prenatal origins of late-life cognitive decline and dementia based on our full results at the DOHaD congress 2019.

Adolescence as a key point in the lifecourse to target health literacy interventions: A cluster randomised controlled trial of the LifeLab education intervention

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Background/Aims: Adolescence offers a window of opportunity during which improvements in health behaviour could benefit long-term health, and enable better preparation for parenthood, passing on better health prospects to children. We evaluated whether an educational intervention, which engages adolescents in science, can improve their health literacy and behaviours

Method: We conducted a cluster-randomised controlled trial of 38 secondary schools in Southern England. The intervention (LifeLab) drew on principles of education, psychology and public health to teach science focused on "Me, my health and my children's health". The programme comprised: 1) Professional development for teachers, 2) A 2-3 week module of work for 13-14-year-olds and 3) A "hands-on" practical health science day visit. The primary outcome was change in theoretical health literacy between baseline and 12 months post-intervention. This study is registered (ISRCTN71951436), and the trial status is complete.

Results: Data were collected from 2930 adolescents (aged 13-14 years) at baseline (control:intervention 1532:1398) and 2487 (84·9%) at 12-month follow-up (control:intervention 1336:1151). Participation in the educational intervention, LifeLab, was associated with an increased standardised total theoretical health literacy score (adjusted difference between groups = 0·27SDs (95%CI=0·12, 0·42)) at 12-month follow-up; intervention participants also showed a move to judgetheir own lifestyles more critically, with fewer reporting their behaviours as healthy (53·4%) than control participants (59·5%) (adjusted PRR=0·94 (0·87, 1·01)).

Conclusions: An interactive science education programme drawing on principles of science education, psychology and public health led to improved health literacy over 12 months. Adolescents demonstrated more critical judgement of health behaviour following LifeLab. Further work using digital technologies is being undertaken to translate this into sustained behaviour change.

Second-trimester Maternal Lipid Profiles Predict Pregnancy Complications in An Age-dependent Manner

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Background/Aims: Our objective was to investigate the combinatorial effect of maternal age and second-trimester maternal lipid profiles for pregnancy complications.

Method: With 1:4 matching, this retrospective study selected 499 advanced maternal age women and 1996 younger controls. Logistic regression analysis was used to estimate the correlation between second-trimester lipid profiles [total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)] and pregnancy complications [gestational diabetes mellitus (GDM), pregnancy-induced hypertension syndrome (PIH), preterm labor (PTL), macrosomia]. Optimal cut-off points were determined by receiver operating characteristic curve analysis.

Results: In women aged 20-34 years, TG was a risk factor for PIH [odds ratio (OR) 1.66, 95% confidence interval (CI) 1.32-2.09] and PTL (OR 1.38, 95% CI 1.10-1.73). LDL-C was positively associated with macrosomia (OR 1.25, 95% CI 1.06-1.48), while HDL-C was negatively with PIH (OR 0.46, 95% CI 0.25-0.84). The optimal cut-off points for TG predicting PIH and preterm birth were separately ≥2.135 and 2.335 mmol/L. The optimal cut-off point for HDL-C identifying PIH was ≤2.425 mmol/L and for LDL-C identifying macrosomia was ≥3.425 mmol/L. As for advanced maternal age, only HDL-C was an independent protective factor for macrosomia (OR 0.44, 95 % CI 0.21-0.95), and its optimal cut-off point was ≤2.275 mmol/L. And HDL-C could better predict macrosomia in those women with GDM.

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Conclusion: Second-trimester lipid profiles could predict pregnancy complications varied by maternal age. This suggested that individualized prenatal care strategies should be established for women in different maternal age to prevent pregnancy complications.

First-trimester GDM prediction: A clinical model based on deep learning and LR

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Background/Aims: Gestational diabetes mellitus (GDM) is a popular pregnancy-specific disorder and it is diagnosed since 24 gestational weeks. GDM could not only affect pregnancy outcome, but also the offspring's long-term health. However, there is no efficient early-phase GDM prediction and diagnostic method to reduce the incidence. The development of artificial intelligence (AI) inspires a new strategy to identify high risk women in the first trimester by establishing prediction model.
Method: We retrospectively collect the data of perinatal health record from the International Peace Maternity and Child Health Hospital to establish the data base. First-trimester clinical data including body weight, height, blood glucose, and other examination results were extracted from hospital electronic medical record system and women were divided into GDM group and non-GDM group. Women with diabetes were excluded. To obtain qualified dataset, we first filter samples and features/biomarkers whose missing value rate is >20%, and then z-standardized each feature and then normalized them so that each feature range from 0 to 1 across all the samples. To select a panel of features/biomarkers with best discriminative power in distinguishing GDM and non-GDM, we adopted a model-free sequential forward feature selection method that we developed before, in which we applied both five-fold and leave-one-out for cross validation and k-nearest-neighbour (KNN, k=20) and support vector machine (SVM) for classification. We then used logistic regression (LR) to further train and assign weight for each feature.
Results: After data curation and pressing, we obtained 2699 GDM samples and 14396 non-GDM samples (exclude pregestational diabetes mellitus), with 84 features/biomarkers which contains 24 basic clinical features, 52 molecular biomarkers, and 7 artificially created features. After training and testing in cross validation, we obtained a panel with 13 features based on which, the classification accuracy reaches 90% and area under ROC curve reaches 89%.
Conclusions: The new prediction model with 90% accuracy and 89% ROC area provides efficient technique to identify GDM patient in first-trimester. Utilizing this model throw a light on the early intervention strategy on GDM. It also proves the enormous utilization potential of combining clinical data and AI in medical field.

Associations between maternal leptin concentrations throughout pregnancy and gestational diabetes mellitus

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Background/Aims: The relation between longitudinal changes in maternal leptin concentration and gestational diabetes mellitus (GDM) remains unclear. This study aimed to find whether maternal leptin and its change throughout pregnancy were associated with GDM.
Method: This study is a nested case-control study from the Born in Guangzhou Cohort Study in Guangzhou, China. GDM was diagnosed using a 2-hour, 75-g oral glucose tolerance test (OGTT). A subset of GDM cases (n=198) and controls (n=192) were enrolled from the cohort during 2012 and 2015. Plasma leptin was measured at baseline (Mean: 20.2 weeks) and late pregnancy (Mean: 38.6 weeks) using an enzyme-linked immunosorbent assay. The change of leptin was defined as the ratio of level at late pregnancy to that at baseline. Logistic and general linear regression were used to assess the covariate-adjusted association between log2-transformed leptin concentrations (including the change) and GDM diagnosis and glucose levels in OGTT.
Results: Higher log baseline leptin levels were associated with higher risk of GDM (adjusted OR: 1.45, 95%CI: 1.08, 1.94), while the leptin changes were negatively associated with GDM (adjusted OR: 0.72, 95%CI: 0.58, 0.89). No association was found between leptin levels at late pregnancy and GDM. The log baseline leptin level had positive associations with fasting (β: 0.20, 95%CI: 0.05, 0.35), 1-hour (β: 0.07, 95%CI: 0.04, 0.11) and 2-hour (β: 0.06, 95%CI: 0.02, 0.11) glucose levels in multivariable regression models, while the log leptin at late pregnancy was negatively associated with 1-hour glucose (β: -0.06, 95%CI: -0.11, -0.01). The log leptin change had negative associations with 1-hour (β: -0.13, 95%CI: -0.18, -0.08) and 2-hour (β: -0.09, 95%CI: -0.15, -0.02) glucose levels.
Conclusions: Women with GDM had higher baseline leptin but less increase until late in pregnancy, suggesting an impaired

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compensatory response to the increasing insulin resistance during pregnancy.

The prevalence of insufficient physical activity in Chinese adolescents: a national survey in 2016

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Background/Aims: The prevalence of adolescent obesity has been increasing in China in the past decades. Insufficient physical activity (IPA) is an important factor contributing to the obesity epidemic. However, no nationwide data about the prevalence and distribution of IPA in Chinese adolescent has been reported.
Method: Participants came from a nationwide school survey conducted in 19 provinces in China. The survey adopted a multi-stage random cluster sampling procedure in each province. The IPA was defined according to WHO's cutoff point (<60 min/d of moderate and vigorous physical activity) and was measured by self-administrated international physical activity questionnaire short form (IPAQ-SF).
Results: A total of 138,950 adolescents aged 10-19 years old were surveyed in 2016. Among them, 138,787 (99.8%) adolescents had complete data of IPA (mean age 13.9 years; 50.3% female; 57.6% urban, 42.4% rural). The overall national prevalence of IPA was 72.0%, and it was adjusted to 73.8% after weighted by the provincial population. The prevalence was significantly higher in females compared to males (77.3% vs 66.7%). The prevalence increased significantly with age (78.8% in 15~19yrs; 67.2% in 10~14yrs) and grades (66.4% in grade1-6; 67.8% in grade 7-9; 79.3% in grade 10-12; 82.1% in college students). Nearly 90% of female adolescents aged 17~19 reported IPA. There was a small urban-rural disparity (71.7% vs 72.5%) in the prevalence. The provincial prevalences of IPA ranged from 64.3% in Beijing to 79.2% in Jiangxi. The provincial prevalences showed a significant negative correlation with local GDP per capita (Pearson correlation coefficient = -0.65, P<0.01).
Conclusions: IPA seems to be a very prevalent problem among Chinese adolescents, especially among female, elderly adolescents and those living in less developed provinces.

The status of Minimum Diet Diversity of children aged 6-23 months in China

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Aims: To assess the status of Minimum Diet Diversity (MDD) of children aged 6-23 months in China based on three different methods.
Method: Dietary intake of 1006 children aged 6-23 months was collected by using a 24-hour dietary recall method for three consecutive days from a nationwide survey in China. Dietary intake on the first day of the 3-day dietary recall was used to assess the MDD based on three methods, because MDD was not significant different among the 3-day ($p>0.05$). MDD was receiving foods from at least four food groups of the 7 food groups in the method 1. In the method 2, MDD was receiving foods from at least four food groups of the 7 food groups after excluding formula and breast milk. In the method 3, MDD was receiving foods from at least five food groups of the 8 food groups including breast milk.
Results: For children aged 6-8 months, 9-11 months, 12-17 months and 18-23 months, the MDD was 24.8%, 41.3%, 59.2% and 67.5% in the method 1, 18.3%, 28.3%, 48.0% and 57.9% in the method 2, and 20.1%, 28.1%, 40.4% and 36.1% in the method 3, respectively. For non-breastfed children, the density of vitamin A, calcium, iron, zinc, riboflavin and thiamine was significantly greater in the MDD group than below MDD group based on each of the 3 methods. However, for breastfed children only the density of calcium was significant greater based on either method 1 or method 3, and the density of vitamin A, calcium and thiamine were significant greater based on the method 2 between the two groups.
Conclusions: The MDD of children aged 6-23 months in China was not optimal based on either methods, of which the method 2 might perform better in assessing MDD.

Healthy Lifestyle To Prevent Obesity-Adiposity And Diabetes In Young Offspring Of Diabetic Mothers?

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Background: It's well known that maternal diabetes increases risk of obesity-adiposity and hyperglycemia in children. Few studies have explored the modifying influence of child's lifestyle (nutrition and physical activity, PA). Intensive treatment of GDM have not shown any protection against adiposity in the child. We assessed the current lifestyle in offspring of diabetic mothers (ODM) 2-26 years after birth and investigated its association with obesity-adiposity and hyperglycemia.
Methods: We studied 200 ODM and 177 offspring of nondiabetic mothers (ONDM, age and gender matched). Anthropometry, body composition (DXA) and blood glucose

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(capillary in <10y, 1.75g/kg OGTT in >10y) were measured. Overweight + obesity was classified by international standards [IOTF (≤18y), WHO (>18y)], glucose intolerance (ADA 2014). Dietary intake was assessed using food frequency questionnaire (preceding 6 months) and PA by recording time and frequency of vigorous, moderate, and sedentary activities. We studied the influence of diet and activity on risks of obesity-adiposity and hyperglycemia.

Results: ODM consumed sweets, milk and milk products, vegetables and salads more frequently and cereals less frequently than ONDM. Frequent consumption of 'healthy foods' and infrequent consumption of 'unhealthy foods' were associated with decreased risk for obesity-adiposity. Higher level of moderate PA (>60min/day) and lower sedentary PA (<480 min/day) were associated with lower obesity-adiposity in both the groups. Hyperglycemia was not affected. These effects worked across both groups, there was no interaction with maternal diabetes.

Conclusions: Healthy lifestyle (food and activity) is protective against obesity-adiposity but not against hyperglycemia in young Indian children (both ODM & ONDM). Our results suggest a need for a formal lifestyle intervention in children born in diabetic pregnancies for reduction in obesity-adiposity and hyperglycemia.

Changing Dietary Intakes And Body Composition In Rural Adolescents: The Pune Maternal Nutrition Study

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Background: We explored change in macronutrient intake from early and late adolescence and its association with body size and composition.

Methods: We followed 654(54% boys) children at 12 and 18 years. Dietary intake was recorded using a semi-quantitative food frequency questionnaire (FFQ) from which we estimated macronutrients and their density (percent calories from macronutrients). Body size was measured by anthropometry and body composition by DXA.

Results: Median calorie intake (Kcal/day) increased in boys (2030 to 2909, p<0.001) and girls (1853 to 2054, p<0.001) from 12 to 18 years as did that of protein, fat and carbohydrates (p<0.001 for all). Boys had a significant gain in BMI, waist circumference and lean mass (p<0.001 for all) while girls gained peripheral and central skinfolds fat (p<0.001 for all). Boys showed increase in each macronutrient intake and its density while girls showed increase in fat density. Increased intake of each macronutrient was associated with BMI gain (p<0.001 for all). Increase in protein (absolute intake and density) was associated with higher gain in height, lean mass (p<0.001), and lower prevalence of adiposity (16.8 vs. 31.9%) and central adiposity (19.2 vs. 31.9%). In contrast, increased fat density was associated with higher fat mass gain (p<0.05) while increased carbohydrate density was associated with increased central obesity prevalence (9 vs. 4%). Low birth weight boys showed a strong sensitivity to fat density of foods, higher density was associated with overweight and lower density with underweight which was not seen in those with normal birth weight.

Conclusions: Our observations highlight that increased dietary protein across adolescence supported height and muscle growth but increased fat density enhanced higher obesity especially among those who had low birth weight.

Excess maternal fructose-induced oxidative stress is caused by *Tfam* promoter methylation in the hippocampus of rat offspring.

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Background/Aims: Recently, it has been suggested that maternal fructose can alter the phenotype of the offspring through an unknown mechanism. The current study was performed to clarify the adverse transgenerational epigenetic effect of maternal fructose consumption on the hippocampus of rat offspring.

Methods and Results: Pregnant rats were fed a 20% fructose solution during gestation and lactation. Immediately after weaning, hippocampi were isolated from pups (21-d old). Consequently, hippocampal lipid peroxides were up-regulated in the offspring of fructose-fed animals, suggesting that maternal fructose induces oxidative stress in offspring. We focused on the effect of maternal fructose on hippocampal mitochondrial transcription factor A (TFAM) expression, which can protect against oxidative stress. Increased DNA methylation was observed in the hippocampi of offspring of fructose-fed animals compared to that in control offspring; reduced *Tfam* mRNA expression was also observed. To examine the effect of DNA methylation on *Tfam* mRNA expression, we measured *Tfam* promoter activity by performing luciferase assays after promoter methylation. Luciferase activity was significantly reduced by DNA methylation, indicating a direct association between *Tfam* transcription and promoter methylation level. Thus, maternal fructose-induced suppression of *Tfam* transcription might be regulated by altered DNA methylation of the promoter region. As a result, its anti-oxidative effect might be suppressed, resulting in oxidative damage to the hippocampus of the offspring.

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Conclusions: This study provides new insights into maternal high-fructose diet-induced genetic interactions, and specifically those regulated by epigenetic modifications, in the hippocampus of the offspring; this in turn could promote brain dysfunction.

Exercise Intervention During Pregnancy Induces Promoter, Methylation Changes In Cord Blood

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Background/Aims: Environmental events and nutritional conditions may induce permanent DNA methylation mark changes in utero during the sensitive period and these adaptive changes will be 'memorized' that may have a lasting impact on adult disease later. The potential plasticity of DNA methylation also enables reprogramming, depending on exposures to nutritional, chemical, and environmental factors. We here illustrate the role of epigenetic modifications in umbilical cord blood of offspring by altered intrauterine exposures induced by exercise.
Method: 24 overweight/obese pregnant women (body mass index $<28/\geq 28 kg/m^2$) who had an uncomplicated pregnancy at $<12^{+6}$ weeks of gestation were randomly allocated to either exercise (n=12) or a control group (n=12). Patients allocated to the exercise group were assigned to exercise 3 times per week (at least 30 min/session with a rating of perceived exertion between 12-14) via a cycling program begun within 3 days of randomization until 37 weeks of gestation. Maternal blood as well as umbilical cord blood samples from both groups were collected and DNA methylation levels were determined by Illumina MethylationEPIC microarray.
Results: Four specific genes in umbilical cord blood in exercise group were differentially methylated compared to the controls ($p < 0.01$). KEGG pathway showed the aldosterone synthesis and secretion was impacted.
Conclusions: The intrauterine environmental exposure induced by exercise is playing an important role in the fetal programming. The epigenetic mechanism is believed to provide an explanation for the phenomenon. The findings shed light on our understanding of long-term effects of in utero exposures.

Association between Exposure to Electronic Screens in the Early Stage of Life and Myopia among Preschoolers in Shenzhen of China: A Cross-sectional Study

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Background/Aims: The prevalence of myopia among preschoolers in urban areas increased quickly. And recently, children are more likely to be exposed to electronic screens at an early stage of life. Whether this exposure is associated with myopia in preschoolers remains unknown. Therefore, we conduct the study to resolve this issue in a kindergarten-based sample.
Method: 24,051 preschoolers were recruited from kindergartens located in Longhua District of Shenzhen, China. Data were collected with structured questionnaires concerning their sociodemographic characteristics, visual acuity and exposure to electronic screens during 0-3 years old and their parents' relevant information. A series of Cox regressions were employed to explore the association between exposure to electronic screens at an early age (0-3 years old) and myopia via the life course model.
Results: After adjusting for the sociodemographic factors, parents' vision and exposure to the other electronic screens, compared with preschoolers never exposed to handheld electronic screens for the whole 3 years, only those who were not only exposed in the first year had the increased risk of myopia, PR (95% CI) ranging from 2.08 (1.61-2.67) to 3.73 (2.24-6.22); compared to preschoolers never exposed to the TV screens for the whole 3 years, those exposed in the first year, irrespective of their exposure during 1-3 years old, showed considerably elevated risk of myopia, PR (95% CI) ranging from 1.40 (1.02-1.93) to 3.23 (2.02-5.16). Moreover, we reran the analysis in preschoolers of parents with good eyesight, and the trend of the results agreed with that of the former analysis.
Conclusions: Exposure to electronic screens in the early stage of life might be a risk factor for myopia among preschoolers, and the first postnatal year was possibly the sensitive period. Thus, we should reduce or avoid exposure to electronic screens during the early stage of life.

Retinol-Binding Protein 4, Fetal Overgrowth and Growth Factors

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Abstract
Objective: Retinol-binding protein 4 (RBP-4) is an adipokine associated with insulin resistance. Increased RBP-4 levels in maternal circulation have been associated with accelerated fetal growth, but whether there is a similar association for RBP-4 in fetal circulation remains unclear. We sought to assess cord

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blood RBP-4 in association with fetal overgrowth and the mediation effects of fetal growth factors.
Study Design: In a nested study of 125 LGA (birth weight > 90th percentile) and 125 optimal birth weight (25th–75th percentiles) control infants in the Shanghai Birth Cohort, we assessed cord blood RBP-4 in association with LGA, and the mediation effects of fetal growth factors (insulin, proinsulin, insulin-like growth factor 1 (IGF-1) and IGF-2).
Results: Cord blood RBP-4 concentrations were elevated in LGA infants (P=0.025), and positively correlated with birth weight z score (r=0.17, P=0.006), cord blood proinsulin (r =0.22, P=0.001), IGF-I (r =0.23, P=0.001) and IGF-2 (r=0.17, P=0.008). Each SD increase in cord blood RBP-4 concentration was associated with a 0.23 increase in birth weight z score (P=0.005). In the mediation analyses, cord blood IGF-1 and proinsulin could account for 39.1% and 26.1% respectively of the variation in birth weight z score related to RBP-4. The association between RBP-4 and birth weight (z) became non-significant after adjusting for both proinsulin and IGF-1.
Conclusion: LGA was associated with elevated cord blood RBP-4 levels. The association between RBP-4 and fetal growth appeared to be largely medicated by fetal growth factors.

Early life exposure to China Famine in 1959-1961 and adulthood Hypertension related conditions: a retrospective study in Hunan Province, China.

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Background/Aims: Numerous evidences have showed that there are significant associations between famine exposure and hypertension and cardiovascular diseases. But no paper demonstrated the effects of famine exposure on the subtypes of hypertension, such as hypertension with hyperuricemia or high homocysteine. The aim of the present study is to systematically analyse the associations between famine exposure with hypertension related conditions.
Method: Data were deprived from a cross-sectional study in Hunan Province of China, where is a central province greatly affected by the Famine from 1959-1961. A total of 1150 adults born from 1952 to 1964 were selected in the present study, 5 famine exposure cohorts were defined based on the birthdate: non-exposure (1962/10/01-1964/09/1964), fetal exposure (1959/10/01-1961/09/30), early childhood exposure (1956/10/01-1958/09/30), mid childhood exposure (1954/10/01-1956/09/30) and late childhood exposure (1952/10/01-1954/09/30). High homocysteine was defined as serum homocysteine > 15umol/L, and hyperuricemia was defined as serum uric acid >7.0 mg/dL in males and >6.0 mg/dL in females. All association analyses were conducted adjusting for covariates (sex, BMI, marital status, educational status, average annual family income, smoking and drinking) and treatment correction (+15/10mmHg for SBP/DBP in the presence of any antihypertensive medication).
Results: Participants exposed to famine in early life all had significantly higher risk of hypertension with hyperuricemia than the non-exposure participants, the OR are 2.06(0.96-4.41), 2.2(1.11-4.36), 2.27(1.15-4.5), 2.74(1.27-5.9) for exposure in fetal period, early childhood, mid childhood and late childhood, respectively. Participants exposed to famine in childhood all had significantly higher risk of hypertension than the non-exposure participants, the OR are 1.74(1.2-2.51), 1.64(1.14-2.37), 1.85(1.24-2.78) for early childhood, mid childhood and late childhood, respectively. Additionally, participants with exposure of famine in childhood reported a significantly higher rate of ischemic heart disease or stroke than control group, OR are 2.18(1.06-4.52), 3.07(1.56-6.03) and 4.76(2.38-9.53), respectively. However, the associations between famine exposure with hyperuricemia, high homocysteine or hypertension with high homocysteine are not significant.
Conclusions: Early life exposure to famine might linked to a higher risk of hypertension with hyperuricemia, hypertension, ischemic heart disease or stroke, especially in childhood.

Association of maternal preconception body mass index and glycemia with the risk of preterm birth: a population-based cohort study

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Background/Aims: Previous studies reported maternal abnormal weight and glycemia can increase preterm birth(PTB) risk. However, the association between preconception body mass index(BMI) or fasting plasma glucose(FPG) level as well as the combined effect and PTB risk were not well investigated. We aimed to evaluate the associations of preconception BMI, FPG alone and their combination with PTB.
Method: We conducted a population-based retrospective cohort study with 4876710 women aged 20-49 years old, who participated in National Free Pre-Pregnancy Checkups

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Project between 2013 and 2016 and had a singleton delivery before Dec 2017 in rural China. Logistic regression models and restricted cubic spline (RCS) models were used successively to estimate risk of PTB adjusted for confounding variables.
Results: A total of 328,394 (6.73%) women had preterm deliveries, with lowest PTB rate in women with preconception BMI of 22.0–22.9 kg/m^2 (6.57%) or FPG of 4.0–4.9 mmol/L (6.59%). The RCS result showed that the ORs of PTB keep an upward trend with the decreasing or increasing of BMI or FPG (U-shaped, $P_{nonlinear} < 0.05$), with lowest risk of PTB at BMI of 22.1 kg/m^2 or FPG of 4.5 mmol/L. Compared to women with BMI 18.5–24.9 kg/m^2 and FPG 2.8–5.5 mmol/L, the multivariate-adjusted ORs of PTB were 1.03 (95%CI: 1.02–1.05), 1.07 (95%CI: 1.06–1.08) and 1.13 (95%CI: 1.10–1.14) for those with abnormal weight (BMI<18.5 or ≥25.0 kg/m^2), abnormal glucose (FPG<2.8 or ≥5.6 mmol/L) alone and the combination of abnormal weight and glycemia, respectively.
Conclusions: U-shaped relationships between preconception BMI or FPG and PTB risk were identified. The risk of PTB was significantly associated with a synergistic effect due to abnormal weight and glycemia besides a conventional main effect derived from either of them. Achieving desirable weight and glucose control before conception should be advised considering available surveillance and feasibility.

Effects of paternal age on intellectual disability and autism spectrum disorder in offspring

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Background/Aims: The objective of this study is to verify the effects of advanced paternal age on intellectual disability (ID) and autism spectrum disorder (ASD), while taking into consideration the confounding factors such as maternal age, diseases at conception, and the socioeconomic status of the parents.
Methods: We performed a population-based cohort study of parent-offspring trios in South Korea during 2003-2015. We collected data for parental age, diseases at conception, and the socioeconomic status of the parents. We estimated the odds ratio (OR) of ID and ASD development in offspring. We estimated the odds ratio (OR) of ID and ASD development in offspring.
Results: Within the cohort of 3,869,860 parent-offspring trios, we identified 10,880 offspring with ID (0.2%) and 5,059 offspring with ASD (0.1%). Advanced paternal age linearly increased the OR of ID and ASD development in offspring up to 3.42 and 1.97, respectively. Beginning as young as 30 years of paternal age, the effects of advanced paternal age is independent of paternal diseases at conception. The maternal age of 30-39 years at childbirth significantly reduced the OR of ID development in offspring down to 0.88, while maternal age younger than 25 years at childbirth showed a significant OR increase in ID development in offspring up to 2.19. The maternal age at childbirth showed an OR of 1.12 of ASD development in offspring at the age of 35-39 years. Maternal diseases at conception have significant effects on the risk of development of ID and ASD in offspring, independent of maternal age. Better SES of parents significantly decreased the OR of ID development in offspring in a linear way.
Conclusions: These findings call for public awareness in regards to the biological implication of delayed fatherhood and the importance of maternal health at a fertile age.

Neonatal IL-4 Administration Decreases Body Fat Content And Weight And Also Improves Glucose Tolerance In Adulthood

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Background/Aims: Intrauterine growth restriction (**IUGR**) due to uteroplacental insufficiency is a common complication of pregnancy and leads to an increased risk for type 2 diabetes (**T2D**) in adulthood. We model IUGR by performing bilateral uterine artery ligation in pregnant rats at d18 of gestation (term 22 days). Offspring are growth restricted and newborn males, but not females have decreased ß-cell proliferation and impaired insulin secretion which is associated with inflammation and increased IL-4 levels. IUGR males develop obesity and insulin resistance in adulthood. Neutralizing IL-4 antibody given on postnatal days 1-6 normalizes hyperglycemia in adult IUGR animals. The aim of this study was to determine whether IL-4 is sufficient to recapitulate the IUGR phenotype.
Method: IL-4 (50ng or 100ng) or PBS was injected subcutaneously to normal newborn rat pups on postnatal days 1-6. IL-4 had no adverse effects on newborn rat pups and weights did not differ between the IL-4 and PBS injected pups (n=15). IL-4 was also detectable in the pancreas and significantly increased after injections (n=12).
Results: At 2 weeks and 10 weeks of age IL-4 injection had no effect on glucose stimulated insulin secretion as measured by both static incubation experiments and perifusion studies (n=6, n.s.). Surprisingly, neonatally IL-4 injected rats had decreased fasting blood glucose levels at 10 weeks of age (n=6-7; p=0.0055) suggesting improved glucose homeostasis. Therefore, we measured body fat content by Dexa. At P14, animals treated with IL-4 in the newborn period had decreased % fat mass (p=0.0173) and increased % lean mass (p=0.0173) compared to control (n=6). Further, at 7 weeks of age IL-4 injected rats weighed less than controls (n=3-7; p=0.00017) and that difference increased with age.
Conclusions: These results suggest that IL-4 is not sufficient to recapitulate the IUGR metabolic phenotype. However, IL-4

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administered transiently during the neonatal period has lasting effects in adulthood, decreasing fat content and improving glucose tolerance.

Interpreting the changing association between caesarean birth and neonatal death: a case study from Ethiopia

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Background: Both individual- and aggregate-level studies have yielded inconsistent results about the association between caesarean birth and neonatal mortality. We provide an interpretation of the changing association over time between caesarean birth and neonatal death using Demographic and Health Survey (DHS) data within the context of Ethiopia.
Methods: We used data from Ethiopian DHS in 2000, 2005, 2011, and 2016. We analysed the association between caesarean birth and neonatal death using log-Poisson regression models for each survey adjusted for potential confounders. We then applied the 'Three Delays Model' to provide an interpretation of the changing association between caesarean birth and neonatal death in Ethiopia.
Results: The adjusted prevalence ratios (aPR) for neonatal death among neonates born via caesarean section versus vaginal birth increased over time, from 0·95 (95% CI, 0·29, 3·19) in 2000 to 2·81 (95% CI, 1·11, 7·13) in 2016. The association between caesarean birth and neonatal death was stronger among rural women (aPR (95% CI) 3·43 (1·22, 9·67)) and among women from the lowest quintile of household wealth (aPR (95% CI) 7·01 (0·92, 53·36) in 2016. However, the aggregate-level analysis revealed that an increase in caesarean section rate is correlated with a decrease in the proportion of neonatal deaths.
Conclusions: The naïve interpretation of the changing association between caesarean birth and neonatal death from 2000 to 2016 is that caesarean section is increasingly associated with neonatal death. However, the changing association reflects improvements in health service coverage and a shift in the characteristics of Ethiopian women undergoing caesarean section after complicated labour or severe foetal compromise.

The impact of caesarean section on breastfeeding indicators in sub-Saharan Africa: a meta-analysis of Demographic and Health Surveys

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Background: The association between caesarean section and breastfeeding is poorly understood in sub-Saharan Africa. We aimed to examine the impact of caesarean section on breastfeeding indicators—early initiation of breastfeeding, exclusive breastfeeding, and ever breastfeeding—in sub-Saharan Africa.
Methods: We used the most recent data from 32 Demographic and Health Surveys (DHS) completed in sub-Saharan Africa. We analysed the data to examine the impact of caesarean section on breastfeeding indicators using log-Poisson regression models for each country adjusted for potential confounders. For each breastfeeding indicator, the within-country adjusted prevalence ratios were pooled in random effects meta-analysis.
Results: The within-country adjusted analyses showed, compared with vaginal birth, caesarean section was associated with adjusted prevalence ratios (aPR) for early initiation of breastfeeding that ranged from 0·23 (95%CI, 0·16, 0·31) in Tanzania to 0·81 (95%CI, 0·64, 1·02) in Cameroon. Similarly, the aPR for exclusive breastfeeding ranged from 0·57 (95% CI; 0·33, 0·99) in Senegal to 1·60 (95%CI; 1·07, 2·39) in Mali, while the aPR for ever breastfeeding ranged from 0·90 (95% CI, 0·82, 0·99) in Liberia to 1·02 (95%CI, 0·98, 1·06) in Guinea. Meta-analysis combining the adjusted effects from 32 countries showed that caesarean section was associated with a 47% lower prevalence of early initiation of breastfeeding (pooled PR, 0·53 (95%CI, 0·48, 0·58)), but not with exclusive breastfeeding (pooled PR, 0·93 (95%CI; 0·86, 0·99)) nor ever breastfeeding (pooled PR, 0·98 (95%CI; 0·98, 0·99)).
Conclusions: Caesarean section had a negative influence on early initiation of breastfeeding, but showed little difference in exclusive- and ever-breastfeeding between infants born by caesarean versus vaginal birth in sub-Saharan Africa.

Low Birth Weight is Associated With Diabetes Mellitus In Japanese Adult: The Toon Health Study

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Background/Aims: Many studies have shown the association of low birth weight and type 2 diabetes. However, little is known about the relationship between birth weight and diabetes in Japanese population. Therefore, we investigated the association of birth weight with type 2 diabetes in a population-based study of Japanese.
Method: A cross-sectional study of 1078 middle- to old-aged Japanese men and women enrolled in the Toon Health Study from 2009 to 2017 was conducted. We performed a 75 g oral glucose tolerance test as a diagnostic test for diabetes mellitus. The participants responded to a questionnaire about their birth weights. The associations between birth weight and the prevalence of type 2 diabetes in their later life were examined using

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multivariable logistic regression analysis, adjusting for age, sex, body mass index, drinking status, smoking status, physical activity, family history of diabetes mellitus, premature delivery history, hemoglobin A1c, HOMA-IR, and so on.
Results: The odds ratios of type 2 diabetes were 2.57 (95% confidence interval, 1.23-5.39) for people with low birth weight (<2500 g) when compared with the reference group (2500-4000 g). There was no statistically significant relationship between high birth weight (>4000 g) and diabetes.
Conclusions: Low birth weight is associated with diabetes mellitus in Japanese adult. Further study is required to reveal the association between birth weight and diabetes by age.

Fruits and vegetables consumption during early pregnancy and the risk of low birth weight in Japan: The Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study

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Background/Aims: Low birth weight (LBW) is a serious problem in Japan, where the prevalence of it is higher than other developed countries. To our knowledge, 12 studies on the relationships of fruits and vegetables consumption to the risk of LBW have been reported, whose results were inconsistent, and no such a study has been conducted in Japan. Therefore, we investigated those relationships in Japan.
Method: A total of 23,493 pregnant women were recruited between July 2013 and September 2016 in the Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study in Japan. For analysis, we excluded women without live-born, singleton, full term deliveries and with lack of information on birth weight or following confounders: maternal age, pre-pregnancy BMI, income, education, parity, smoking, consumption of alcohol, folate supplement, and food groups. Fruits and vegetables consumption was evaluated by food frequency questionnaire at first-trimester. Birth weight was obtained from the obstetrical and gynecological medical record. LBW was defined as a birth weight of less than 2,500 g. Relationships among them were analysed using logistic regression and multiple liner regression.
Results: Among 8,786 infants, 475 infants were LBW. In logistic regression model, women in the highest quartile of fruits consumption had lower odds of having a LBW infant than women in the lowest quartile (OR: 0.729; CI: 0.554-0.961; P-trend: 0.013), on the other hand, there was no relationship between vegetables consumption and the risk of LBW. In multiple liner regression model, fruits consumption was positively associated with birth weight (β= 0.13, p= 0.0001), but vegetables consumption was not associated with it (β= -0.058, p= 0.21).
Conclusions: Our findings revealed that higher consumption of not vegetables but fruits during early pregnancy is associated with higher birth weight and reduced risk of LBW.

Placental endocrine malfunction programs reproductive defects in female murine offspring

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Background/Aims: The endocrine placenta is a major regulator of fetal growth. Moreover, the intrauterine environment has profound programming effects on long-term offspring health. Our previous study demonstrated that placental endocrine malfunction, induced by placental endocrine zone deletion of the paternally expressed imprinted *Igf2* gene, caused growth restriction *in utero* and insulin resistance in adult female murine offspring (Placenta 2018; 69:e60-61). However, the impact on female offspring reproductive capacity is unknown. We thus aimed to investigate the consequences of placental endocrine malfunction on reproductive parameters in female murine offspring.
Method: Litters with placental endocrine malfunction were generated by crossing *TpbpaCre* females with Igf2-floxed males. Female offspring were weaned at 3 weeks of age and monitored for vaginal opening to indicate pubertal onset. Estrous cycles were tracked by daily vaginal smears for 2 weeks from 8 weeks of age. Female offspring were mated with wildtype males at 12-13 weeks of age and time to pregnancy (defined as the day a copulatory plug was observed) was recorded. Mice were then killed on day 16 of pregnancy to assess pregnancy outcomes. Offspring of the reverse genetic cross, with normal placental endocrine function, served as controls. Significance was set at $p<0.05$ and determined by t-test. Data are representative from $n \geq 6$ litters.
Results: Compared with controls, female offspring exposed to placental endocrine malfunction entered into puberty about a week earlier (malfunction:4.2±0.1 weeks versus controls:5.1 ±0.1 weeks). They also displayed longer estrous cycles due to a prolonged estrus stage (malfunction:1.7±0.2 days versus controls:0.8±0.1 days). However, time to pregnancy was twice as long in offspring exposed to placental endocrine malfunction (median time of 6 days to pregnancy compared to 3 days in controls). Fetuses of female offspring with placental endocrine malfunction were also approximately 10% lighter than those of controls (malfunction:373.6±13.6mg versus controls:412.2±9.0mg).
Conclusions: Therefore, placental endocrine malfunction induces defects in the reproductive capacity of female offspring,

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and has detrimental consequences on the growth of the next generation.

Interactions between Vitamin D and Selected Maternal Characteristics on The Risk of Gestational Diabetes Mellitus (GDM): Findings of the SECOST Project

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Background/Aims: Vitamin D is widely used for bone growth and normal insulin secretion; however, the association between vitamin D status and the risk of gestational diabetes mellitus (GDM) is controversial. This study aims to determine the association between maternal serum 25(OH)D level in early pregnancy and the risk for GDM, as well as its interaction effects with selected maternal characteristics on GDM.
Method: This study was part of the Seremban Cohort Study (SECOST) in which a total of 259 pregnant women were recruited. Blood samples were taken at < 14th weeks of gestation for serum 25(OH)D level and a standard 75g Oral Glucose Tolerance Test (OGTT) was performed between 24 – 32nd weeks of gestation. Serum 25(OH)D level was categorized as severe vitamin D deficiency (VDD) (< 25 nmol/L), mild deficiency (25 – <50 nmol/L), insufficiency (50 – < 75 nmol/L) and sufficiency (≥ 75 nmol/L). Logistic regression was performed to estimate odds ratios of the risk of GDM.
Results: About 13.9% of pregnant women in the present study were diagnosed with GDM. The mean maternal serum 25(OH)D was 32.83 ± 11.37 nmol/L. The prevalence of severe VDD, mild VDD and insufficient were 23.2%, 68.3%, and 8.5%. None showed sufficient serum 25(OH)D levels. There was no significant association between serum 25(OH)D on the risk of GDM, but significant interaction effects were found between pre-pregnancy body mass index (BMI), history of GDM and serum 25(OH)D on the risk of GDM.
Conclusions: The present study showed a high prevalence of VDD among pregnant women in Malaysia, but vitamin D status was not associated with GDM. Further study is needed to confirm the study finding as well as to determine the mechanism by which the effect of personal characteristics and vitamin D status on the risk of developing GDM.

Association Between Cesarean Section And Constipation In Infants: The Japan Environment And Children's Study (JECS)

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Background and Aim: There have been increasing reports on the association between cesarean section (C-section) and the subsequent development of diseases in infants. C-section affects the diversity of microbiota in the infant's gut. Abnormal intestinal flora may be associated with functional gastrointestinal disorders, such as constipation, in infants. In the present study, we investigated the association between infants delivered by C-section and the development of constipation at 1 year old due to altered gut microbiota using data from the Japan Environment and Children's Study (JECS).
Methods: This cohort study (n = 83,019) used data from JECS, an ongoing cohort study which began in January 2011. Data on bowel movement and potential confounding factors were recorded. A log-binomial regression model was used to estimate the risk of C-section, and the results were expressed as risk ratios and their respective 95% confidence intervals. Constipation was defined as chronic fecal retention characterized by defecation frequency of <3 per week at 1 year old.
Results: C-section-delivered infants (n=15,515) had younger gestational age and lesser birth weight than those of vaginally

Table: Crude and adjusted risk ratios for constipation

	Crude (n=83,019)			Adjusted (n=71,489)		
	OR	(95% CI)	p value	OR	(95% CI)	p value
Cesarean delivery	1.09	(0.94, 1.28)	0.26	0.94	(0.79, 1.13)	0.51

CI: confidence interval, OR: Odds Ratio

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delivered infants (n=67,504). However, the frequency of bowel movements was almost similar between the two, independent of the mode of delivery. The prevalence of constipation in the entire infant was 1.37%. No significant differences were observed for C-section in crude and adjusted risk ratios for constipation (Table).
Conclusion: C-section has no effect on the development of constipation at 1 year old.

Intergenerational influence of paternal running on juvenile offspring fear memory processing

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Background/Aims: There is growing evidence that paternal health factors such as stress and diet, exert transgenerational influences on offspring behavior and physiology. One paternal lifestyle factor that has been considered is exercise. In a mouse model of paternal high fat diet, exercise prevented negative intergenerational effects manifesting in male and female offspring (Stanford et al., 2018). However, a separate study previously reported that paternal exercise yielded offspring at greater risk for obesity and diabetes (Murashov et al., 2016). Our lab had previously reported that preconception paternal exercise alters fear memory reinstatement of juvenile male offspring (Short et al., 2017), in association with altered sperm tRNA content. Interestingly, this behavioral phenotype was not observed in female offspring. We have extended on that initial examination by characterizing the spontaneous recovery of fear memory and associated cellular substrates.
Method: Offspring of free wheel-running and control male C57Bl/6 breeders were obtained through paired-matings with naïve females. On post-natal day 15, offspring were subject to fear conditioning and extinction as per our published protocol (Short et al., 2017). One week after, spontaneous recovery of fear memory was assessed. PFA-fixed brains were collected for cellular studies in the infralimbic cortex and the dorsal hippocampus.
Results: Paternal exercise did not alter the rate of fear conditioning, confirming our previous results. Interestingly, paternal exercise appears to be associated with an increased rate of fear extinction during the early phase. This was only observed in male offspring, but not in females. Ki67-positive cell counts in the hippocampus indicate an unaltered capacity for cellular proliferation at this early age.
Conclusions: This study provides additional evidence that paternal exercise modifies fear memory processing of male juvenile offspring. There could be intergenerational implications for the susceptibility for anxiety disorders and PTSD-like conditions associated with the physical fitness of the parental generation.

Influence of maternal ethnicity on neonatal outcomes of babies born small

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Background: Australia has an ethnically diverse population. Maternal ethnicity has been linked to differences in neonatal outcomes of premature babies. However, the relationship between ethnicity and neonatal outcomes of small for gestational age (SGA) babies is not clear.
Methods: Retrospective cohort study comparing neonatal outcomes of babies born SGA to mothers born in Australia, New Zealand (ANZ) to those born SGA to mothers born in South Asia (SA) from a large metropolitan hospital network between 2013-17. Univariate and multivariate analysis of neonatal outcomes between groups was conducted.
Results: 1018 SA and 959 ANZ SGA babies were included. SA babies were significantly older (median (IQR) 39(38-40) weeks) and heavier (2590(2310-2780) grams) compared to ANZ babies (38 (37-40) weeks) and 2480 (2059-2740) grams; $p<0.001$ for both). There was no difference in perinatal mortality (0.5% vs 0.9%; $p=0.2$). After correction for differences in maternal and infant demographics, SA SGA babies were 1.5 times more likely to develop hypothermia (CI 1.1 to1.8, $p=0.001$); but 2.5 times less likely to be born with a major congenital malformation (CI 0.2 to 0.6, $p=0.001$) and 1.5 times less likely to need gavage feeding (CI 0.4 to 0.9, $p=0.02$) as compared to ANZ SGA babies. No significant differences in any other neonatal outcomes were observed, though there were trends towards less need for resuscitation, and need for respiratory support in SA SGA babies.
Conclusions: Babies born SGA to SA mothers have a different neonatal outcome profile as compared to babies born SGA to ANZ mothers. Further research into the influence of maternal ethnicity on placental structure and function, organogenesis and body composition (fat stores) of SGA babies may be warranted.

Association between maternal glycaemia during pregnancy and carotid intima-media thickness, pulse wave velocity, augmentation index, and blood pressure in 6-year-old Singaporean children

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Background/Aims: In women without pre-existing diabetes, little is known about the consequences of hyperglycaemia during pregnancy for the offspring's cardiovascular structure and function. We investigated the association between maternal glycaemia during pregnancy and childhood cardiovascular risk markers.
Methods: Analyses were conducted on 462 mother-child dyads from the multi-ethnic GUSTO cohort study. At 26-28 weeks, a 75g oral glucose tolerance test was used to measure fasting and 2-h postprandial plasma glucose concentrations (mmol/L). Gestational diabetes mellitus (GDM) was defined using WHO 1999 diagnostic criteria. At age 6 years we measured the child's carotid intima-media thickness (cIMT), carotid-femoral pulse wave velocity (cfPWV), aortic augmentation index (AIx) and AIx normalized for a heart rate of 75 bpm (AIx@75)). Associations between maternal glycaemia during pregnancy and cIMT, cfPWV, AIx, AIx@75 were analysed using multiple linear regression, adjusted for study site, child's sex, paternal hypertension and maternal age at delivery, ethnicity, educational attainment, pre-pregnancy BMI, pre- or hypertension before 20 weeks of gestation, and smoking and environmental tobacco exposure during pregnancy. Associations between maternal glycaemia and child's blood pressure (mmHg) were limited to a subsample (n=436).
Results: Higher 2-hour postprandial glucose at 26-28 weeks gestation (but not fasting glucose) was associated with higher cIMT, cfPWV, AIx and AIx@75 at age 6 years (adjusted β [CI 95%], cIMT: 0.02, by 10mm increase [0.00; 0.03]; PWV: 0.08 m/s [0.01; 0.16]; AIx: 0.79 %[0.15; 1.43]; AIx@75: 0.87 %[0.24; 1.50]].GDM was also associated with higher AIx and AIx@75. No association was found between maternal glycaemia during pregnancy and offspring blood pressure.
Conclusions: Among mothers without pre-existing diabetes, postprandial hyperglycaemia during pregnancy was associated with structural cardiovascular risk markers and greater conduit arterial stiffness in their children.

Ouabain decreases the risk of kidney disease and hypertension in later life of IUGR offspring rats through rescuing nephrogenesis

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Background/Aims: Intrauterine growth restriction(IUGR) is associated with Low birth weight, resulting the reduction of the nephron endowment and increasing the risk of kidney disease and hypertension in later life. We found that low-dose ouabain could increase the number of rat nephrons under serum deprivation condition in *vivo* study. The aim of this study is to investigate whether low-dose ouabain can reduce the risk of kidney disease and hypertension in later lifr of IUGR offspring rats.
Method: Pregnant SD rats were divided into three groups: control group(Con), low protein group(Lp) and low protein + ouabain group(Oua). At GD20, some fetuses were taken out to weigh the body mass, placenta and kidney. After birth, the newborn rats were weighed every three days in the first month. At 5 mo, some rats were killed randomly, their kidneys were weighed and nephron numbers were counted. The remaining rats were followed up, the blood pressure, the serum creatinine and urea nitrogen were measured. At 24mo, urinary microalbumin was measured, then rats were killed, the kidneys were weighed.
Results:1.The incidence of IUGR in Lp was 96.20%, Oua was 75.90%. 2. the fetuses body mass and the placental weight in Lp and Oua were lower than Con At GD20. The body weight of Lp was also lower than Oua and Con within 30 days after birth. 3. The kidney weight in Lp and Oua were lower than Con at GD20, At the age of 5 mo, compared with Con, the weight of two kidneys in Lp and Oua increased, showing a catch-up pattern, there was no significant difference among the three groups. At the age of 24 months, the weight of two kidneys in Lp was even slightly higher than that in Con and Oua. 4. The nephron numbers of LP were lower than Con and Oua at the age of 5 mo. 5. At the age of 15 and 18 mo, the level of blood urea nitrogen and the serum creatinine level in Lp was higher than Con and Oua. The urinary microalbumin of 24-month-old female rats in Lp was significantly higher than con and Oua, while there was no significant difference between male rats. 6. The systolic and diastolic blood pressures of rats in Lp were higher than Con and Oua at the age of 5, 10, 15 and 18 months,
Conclusions: Low dose ouabain can decrease the incidence of IUGR, rescue nephrogenesis, decrease the risk of kidney injury and hypertension.

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Maternal Rat Docosahexaenoic Acid (DHA) Supplementation Prior to and During Pregnancy and Lactation Prevents Anxiety and Cognitive Deficits in Male Offspring (F1) of Obese Mothers

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Background/Aims: Maternal obesity (MO) increases F1 risk of developing metabolic, affective, and cognitive disorders. DHA is a structural constituent of membranes especially in the central nervous system. Adequate DHA intake is required for optimal brain development and function. Few studies address whether maternal DHA supplementation can prevent harmful effects of MO on F1 anxiety and cognition. We aimed to determine if maternal DHA supplementation in MO pregnant rats prevents affective (anxiety) and cognitive deficits (recognition memory) in adult male F1.

Method: From weaning throughout pregnancy and lactation female rats ate control (C - 5% fat) or obesogenic diet (MO - 25% fat). At postnatal day (PND) 90, one month before mating and during pregnancy and lactation, half of the females from each group received 400 mg/kg/day of DHA (CDHA and MODHA) by gavage and remained on their respective diet. F1 were weaned onto C diet. At PND 120, one male from each litter was tested in the elevated plus maze (EPM) and open field (OF) and activity analysed by video. At PND 130, learning and memory capacities in male F1 was evaluated in the novel object recognition (NOR) task. During 3 consecutive days, F1 were placed in a testing arena to evaluate spontaneous locomotor activity (area recognition session). On the fourth day two identical objects were introduced (object habituation session). At 2, 24 and 48 h post-training one item was replaced (short or long-term memory retention) to evaluate for 7 minutes the time spent exploring either the novel or familiar object. We evaluated the discrimination Index= (exploring time for novel object - familiar object)/total time exploring for both objects) *100.

Results: In the EPM test, MOF1 had fewer entries, spent less time and covered less distance in the open arm vs C. No differences were observed in total distance travelled. In the OF test, MO F1 decreased the number of entries in the centre zone in comparison with C, indicating more anxiety. In the NOR task, spontaneous locomotor activity and exploration time of both objects were similar among groups. At 2 h, no differences were observed in short memory retention. However, at 24 and 48 h post-training (long-term memory retention), MOF1 spent less time exploring the novel object, resulting in a decreased discrimination index compared with C, indicating impaired recognition memory. Maternal DHA administration increased the number of entries and the time spent in the EPM open arms in MO+DHA F1 in comparison with MOF1, without changes in overall distance travelled. In the OF and NOR, MO+DHA F1 showed a greater number of entries and increased novel object exploration time and a restored discrimination index vs MOF1.

Conclusions: MOF1 showed increased anxiety t behaviour in EPM and OF tests and displayed decreased approach behaviour with subsequent learning impairment and long-term recognition memory retention in the NOR task. Maternal DHA administration prevents the innate tendency to explore novel environments (less anxiety) and learning and memory deficits. Further studies are needed to evaluate the neural mechanisms involved. ANR-CONACyT 2015-16-273510.

Maternal Obesity (MO) in the Rat Affects Milk Composition: Benefits of Docosahexaenoic Acid (DHA) Intervention Prior and During Pregnancy and Lactation.

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Background/Aims: Breastfeeding protects against rapid neonatal weight gain and later susceptibility to obesity and plays an important role in preventing and reducing children's behavioural disorders. In previous studies we have published that in rats, MO induced by an obesogenic diet affects maternal milk nutrient concentrations, specially it increases milk fat content and alters long-chain polyunsaturated fatty acid composition (1). Therefore, we aimed to determine if maternal DHA intervention in obese mothers improves milk content.

Method: From weaning throughout pregnancy and lactation female rats ate control (C - 5% fat) or obesogenic diet (MO - 25% fat). At postnatal day (PND) 90, one month before mating and during pregnancy and lactation, half of the females from each group received 400 mg/kg/day of DHA (C+DHA and MO+DHA) by gavage and remained on their respective diet.

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At 20 days of lactation, mothers received 0.8 U oxytocin (ip) and were milked 15 minutes later. Milk nutrient composition (water – gravimetric, fat – Folch, protein – Bradford, AA (arachidonic acid), EPA (eicosapentaenoic acid) and DHA by gas chromatography) were determined.
Results: The milk of MO mothers contained less water and higher fat content in comparison with C. In the MO+DHA group, maternal DHA intervention did not increase water and fat content. Milk protein content was similar among groups. The milk from mothers fed with the obesogenic diet (MO group) had more AA and less EPA and DHA content compared to C. In the milk from t MO+DHA mothers, maternal DHA administration reduced AA and increased DHA content compared to MO; while EPA was similar to MO group. In milk from the C+DHA group, water, fat, protein, AA and EPA was similar to C, but DHA content was higher than C.
Conclusions: MO induced by an obesogenic diet affects milk composition. In previous studies we reported that offspring from obese mothers have cognitive deficits in adult life (2), which could be caused in part by the reduction in milk DHA content, since DHA plays an essential role in brain development. Maternal DHA intervention in obese rats prior to and throughout pregnancy and lactation improves milk composition, specially DHA content. Further studies are needed to evaluate the benefits of DHA supplementation as well as the mechanisms involved. ANR-CONACyT 2015-16-273510. References: 1) Br J Nutr. 2016;115:538, 2) Int J Dev Neurosci. 2012;30:75.

High-Fat Diet Consumption by Male Rat Offspring of Obese Mothers Accentuates Body Fat Accumulation and Metabolic Alterations in Adult Life

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Background/Aims: Obesity rates, including those in pregnant women and young children, are increasing exponentially, due in large part to the adoption of a lifestyle with increased energy intake and reduced physical activity. We have previously reported that maternal obesity (MO) induced by an obesogenic diet predisposes offspring development of obesity and metabolic dysfunction. However, a question that needs to be clarified is when offspring follow the same dietary patterns as their mothers, will it also stimulate offspring development of obesity in adult life. We aimed at determining if a high-fat (HF) diet consumption from early childhood to adulthood in MO offspring accentuates the body fat accumulation and the metabolic alterations.
Method: Control female Wistar rats (C) ate normal chow (5%-fat) while MO females ate a HF diet (25%-fat) from weaning through pregnancy and lactation. After weaning male offspring (F1) ate either chow or HF diet (CHF and MOHF). At postnatal day 110 male F1 were euthanized. Body weight was recorded, and fat depots excised and weighed to determine adiposity index (AI). Serum was obtained to determine glucose (enzymatically), leptin and insulin (radioimmunoassay) levels as well as insulin resistance index (IRI).
Results: C and MO body weight were similar. HF diet increased body weight in CHF vs C and MOHF vs MO. Total fat and AI were higher in all experimental groups (CHF, MO and MOHF) compared to C; but this increase was much higher in MOHF F1. Serum glucose concentration was only increased in MOHF. Serum leptin and insulin levels as well as the IRI were similar between CHF and MO but higher than C. In the MOHF they were much higher in comparison with all groups.
Conclusions: The pre-existing fat accumulation and metabolic dysfunction in male MO offspring was accentuated by high-fat diet consumption from weaning to adulthood. We conclude that by both intra-uterine and postnatal environmental factors can contribute to an obese phenotype. This work was supported by the Newton Fund RCUK-CONACyT (FONCICYT/49/2016).

Lipid Levels in Normal Pregnant Women with Macrosomia

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Background/Aims: To retrospectively analyze the lipid profiles in normal pregnant women with macrosomia and explore the independent factors for macrosomia.
Method: 7310 normal pregnant women were divided into macrosomia group (n=413) and control group (n=6897), and then we compared their second and third-trimester lipid levels and other obstetrical characteristics. Logistic regression analysis was applied to estimate the risk factors of macrosomia.
Results: Second and third-trimester triglyceride (TG) levels, maternal age, gestational weight gain (GWG) and gestational weeks at delivery in macrosomia group were significantly higher than control group, while high-density lipoprotein cholesterol (HDL-C) level was lower (all $P<0.05$). In addition, maternal age [odds ratio (OR) 1.072, 95% confidence interval (CI) 1.040-1.105], GWG (OR 1.108, 95% CI 1.083-1.134), gestational weeks at delivery (OR 1.676, 95% CI 1.521-1.847), third-trimester TG (OR 1.067, 95% CI 1.011-1.127) were independent positive factors for macrosomia, while third-trimester HDL-C level was an independent negative factor (OR 0.496, 95% CI 0.372-0.660).
Conclusions: The maternal age, GWG, gestational weeks at delivery, and hypertriglyceridemia were associated with macrosomia.

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Transgenerational Obesity and Alteration of ARHGEF11 in Rat Liver Induced by Intrauterine Hyperglycemia

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Background/Aims: Intrauterine hyperglycemia increases the risk of obesity and diabetes in offspring of consecutive generations, but its mechanism remains obscure. This study aimed to establish an intrauterine hyperglycemia rat model to investigate the growth and glycolipid metabolic characteristics in transgenerational offspring, and the mechanism of Rho guanine nucleotide exchange factor 11 (ARHGEF11) with PI3K/AKT signaling pathway in offspring development.
Method: The sever intrauterine hyperglycemia rat model was caused by STZ injection before mating, and the two generations of offspring were observed for their development and glycolipid metabolism. The expression of ARHGEF11, ROCK1, PI3K and AKT was tested in liver and muscle of F2 offspring.
Results: The results showed severe growth restriction in F1 offspring, and obesity, fatty liver and insulin resistance in female F2 offspring, especially the offspring with female intrauterine hyperglycemia exposure parent (F2G♀C♂) and both (F2G♀G♂). The expression of ARHGEF11 and ROCK1 was significantly increased, PI3K and phosphorylation of AKT were significantly decreased in liver tissue of F2G♀C♂ and F2G♀G♂.
Conclusions: Our study revealed that intrauterine hyperglycemia could cause obesity and abnormal glycolipid metabolism in female transgenerational offspring, the programming effect of the intrauterine environment could cause more obvious phenotype in the maternal line. The mechanism exploration suggested that increased expression of ARHGEF11 and ROCK1, and the decreased expression of PI3K and phosphorylation of AKT in the liver could be responsible for the abnormal development in F2 offspring.

Longer breastfeeding duration is associated with favourable growth trajectories in early childhood

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Background/Aims: Emerging research highlights the programming effects of infant feeding in childhood obesity. This study aimed to examine the influence of breastfeeding duration and timing of solids introduction on trajectory of body mass index z-scores (BMIz) in early childhood.
Method: Secondary analyses of data from the Melbourne InFANT Program (n=542), a prospective cohort with follow-ups at birth, 3, 9, 18, 42 and 60 months, were conducted. Linear spline multilevel model with adjustment for child (sex, birth weight, gestational age) and maternal (maternal education, country of birth and pre-pregnancy BMI) factors was performed.
Results: Differences in growth rates were observed from birth to 3 months and 9 to 18 months by breastfeeding duration ($\geq$ 6 versus < 6months) and timing of solids introduction (before versus after 6 months). Children who were breastfed for $\geq$ 6 versus < 6months, had similar BMIz at birth, but lower BMIz at all ages from 3 to 60 months. The difference remained after adjustment for child and maternal factors, and the adjusted mean difference at 3, 9, 18, 42 and 60 months was -0.34, -0.44, -0.13, -0.19, and -0.23, respectively. In contrast, children who received solids before 6 months versus after 6 months had higher BMIz at 18 and 42 months, but these differences were attenuated after adjustment for child and maternal factors.
Conclusions: Longer breastfeeding duration was associated with lower BMIz to five years of age. The findings provide further support for infant feeding guidelines to prolong breastfeeding duration for overweight and obesity prevention.

The Influence of The Interval between Laparoscopic Sterilization and IVF-ET on Ectopic Pregnancy: A Case Control Study

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Background/Aims: To investigate the influence of the time interval between laparoscopic sterilization and IVF-ET on ectopic pregnancy.
Method: A total of 171 patients undergoing IVF-ET after laparoscopic sterilization and known pregnancy outcome in the third affiliated hospital of Guangzhou Medical University from Apr. 2008 to May 2016 were divided into two groups according to the time interval between laparoscopic sterilization and IVF-ET:group A, within 240 days; group B, beyond 240 days. The ectopic pregnancy rate between two groups were compared.
Results: In a total of 171 patients, the pregnancy outcomes included term birth(83 cases), premature birth (41 cases),

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ectopic pregnancy (40 cases), abortion (6 cases), and stillbirth (1 case). In group A, there were 31 patients with ectopic pregnancy, accounting for 31.3%; in group B, there were 9 patients with EP, accounting for 12.5%. The difference was statistically significant between group A and group B (P<0.05).
Conclusions: The ectopic pregnancy rate can be significantly decreased when the time interval of laparoscopic sterilization and IVF-ET is beyond 240 days.

Influence of severe preeclampsia with different blood pressure circadian rhythms on perinatal outcomes

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Aims: To explore the influence of severe preeclampsia with different blood pressure circadian rhythms on perinatal outcomes.
Method: 173 cases who were diagnosed with severe preeclampsia in The Third Affiliated Hospital of Guangzhou Medical University from January 1st, 2014 to April 30th, 2018 were divided into 3 groups according to blood pressure circadian rhythms, including group I (dipper type blood pressure) 30 cases, group II (non-dipper type blood pressure) 106 cases, group III (reverse-dipper type blood pressure) 37 cases, comparing perinatal outcomes among the three groups.
Results: (1)Maternal outcomes: The preterm birth rate (79.8% (respectively 73.3%, 76.4%, 94.6%)), the retinopathy rate (31.2% (respectively 46.7%, 23.6%, 40.5%)), and the rate of HELLP syndrome (6.9% (respectively 3.3%, 4.7%, 16.2%)) were all associated with elevated blood pressure (P<0.05). The average amount of postpartum hemorrhage was respectively (327.53±78.211)ml, (366.52±195.595)ml, (429.76±410.544) ml, increased with the growing blood pressure at night, but the differences weren't statistically significant (P>0.05). The cesarean section rate (91.9%), the postpartum anemia rate (20.2%), the average prenatal and postpartum hemoglobin value had no statistical significance (P>0.05). There were no maternal deaths in all the three groups. (2)Neonatal outcomes: The rate of low birth weight infants was 75.1% (respectively 83.3% 67.9% 89.2%), and the mean birth weight of newborn was respectively (1755.93±774.53)g, (1838.25±808.50)g, (1403.46±485.13)g. The rate of fetal growth restriction was 32.9% (respectively 50.0%, 25.5%, 40.5%). They were all related to abnormal blood pressure (P<0.05). The fetal distress rate (15.6%), the neonatal asphyxia rate (8.7%), and the neonatal mortality rate(8.1%), as well as the average of Neonatal Apgar's score, weren't statistically significant (P>0.05).
Conclusions: Variations in the circadian rhythm of blood pressure were associated with the occurrence of poor perinatal outcomes in severe preeclampsia.

The Role of Education in Persistent Postpartum Depression Among Different Ethnic Groups: A Cross-Sectional Study in Rural Western China

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Background/Aims: Our study aimed to focus on persistent postpartum depression (persistent PPD) among different ethnic groups in rural western China and explore possible reasons for the difference of persistent PPD risk among different ethnic groups.
Method: A cross-sectional survey was conducted in 20 rural counties of 8 provinces in Western China. The mothers of children under five and more than six months postpartum were included, and their persistent PPD status was assessed by the Chinese version of Edinburgh Postpartum Depression Scale. Univariate and multivariate logistic regression models were used to analyze the risk factors of persistent PPD. Two multivariate logistic regression models that separately containing and not containing the factor of educational level were used to explore the role of education in persistent PPD to explain the risk difference among different ethnic groups.
Results: 2732 mothers were finally included and the total persistent PPD rate was 16.0%. The Yi showed significantly higher persistent PPD rate (23.6%) and lower educational level compared with other ethnic groups. In multivariate analysis, educational level of primary school and below (adjOR1: 1.51, 95%CI: 1.09-2.11) and diarrhea of youngest child in past two weeks (adjOR1: 1.32, 95%CI: 1.02-1.72) remained as independent predictors of persistent PPD after adjusting all the factors significant in univariate analysis. If educational level was not adjusted in above model, woman from Yi ethnic group (adjOR2: 1.49, 95%CI: 1.08-2.05) would additionally become a significant predictor of persistent PPD.
Conclusions: The ethnic difference in persistent PPD rate was largely due to the ethnic difference in educational level. To reduce the risk of developing persistent PPD, the government should attach importance to the popularization of nine-year compulsory education among the people living in remote and resource-poor areas with low education, such as the ethnic minorities living in rural minority autonomous areas, like the Yi people.

Associations Among Childhood Abuse, Neuroticism, Social Support, Coping Style and Depressive Symptoms.

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Background: Exposure to childhood abuse has been identified as a salient risk factor for the development of depression. However, there is a long time interval between childhood abuse and adult depressive symptoms. The mediating factors that affect the development and severity of depressive symptoms after childhood abuse exposure has not been sufficiently elucidated. This study aims to investigate the mediating effects of neuroticism, social support, and coping style between childhood abuse and depressive symptoms in population covering general adults, depressed patients, bipolar disorder patients, and high risk population for depression.
Methods: This is a cross-sectional study. Five validated questionnaires were used to measure the psychological outcomes (Childhood Trauma Questionnaire CTQ-SF, Eysenck Personality Questionnaire EPQR-S, Simplified Coping Style Questionnaire SCSQ, and Patient Health Questionnaire-9 PHQ-9) in 312 subjects in tertiary hospitals. Multiple regressions and structural equation modeling (SEM) were used to conduct data analysis.
Results: Multiple regression analysis and structural equation modeling showed a significant association between childhood emotional abuse and depression symptoms. The standardized indirect path coefficient of predictors on depressive symptoms were: emotional abuse 0.208, P=0.001 (mediated by neuroticism, active coping, use of social support), EPQR-S neuroticism 0.065, P=0.002 (mediated by use of social support and active coping), the use of social support 0.086, P=0.002 (mediated by active coping score). The R2 for our model was 0.456., indicating that 45.6% of the variability in depressive disorders can be explained by the model.
Conclusions: This study suggested that neuroticism, active coping and use of social support paly important role in mediating the effects of childhood abuse on adult depressive symptoms successively.

Brain Gray and White Matter Abnormalities in Preterm-Born Adolescents: a Meta-analysis of Voxel-based Morphometry Studies

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Abstract
Background. Studies using voxel-based morphometry report variable and inconsistent abnormalities of gray matter volume (GMV) and white matter volume (WMV) in brains of preterm-born adolescents (PBA). In such circumstances a meta-analysis can help identify the most prominent and consistent abnormalities.
Methods. We identified 9 eligible studies by systematic search of the literature up to October 2017. We used Seed-based d Mapping to analyze GMV and WMV alterations between PBA and healthy controls.
Results. In the GMV meta-analysis, PBA compared to healthy controls showed: increased GMV in left cuneus cortex, left superior frontal gyrus, and right anterior cingulate cortex; decreased GMV in bilateral inferior temporal gyrus (ITG), left superior frontal gyrus, and right caudate nucleus. In the WMV meta-analysis, PBA showed: increased WMV in right fusiform gyrus and precuneus; decreased WMV in bilateral ITG, and right inferior frontal gyrus. In meta-regression analysis, the percentage of male PBA negatively correlated with decreased GMV of bilateral ITG.
Conclusions. PBA show widespread GMV and WMV alterations in the default mode network, visual recognition network, and salience network. These changes may be causally relevant to socialization difficulties and cognitive impairments. The meta-regression results perhaps reveal the structural underpinning of the cognition-related sex differences in PBA.

Early-life exposure to the Chinese famine is associated with higher methylation level in the INSR gene in later adulthood

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Background/Aims: As the largest famine in human history, the China famine have provided many important evidences for the hypothesis of DOHaD, however, underlying mechanisms were still unclear. We examined the association between the China famine exposure in early life and DNA methylation of INSR (hg18, chr19:7110130-7110574) and CPT1A (hg18, chr11: 68286513-68286952) related to growth and metabolism in 235 subjects selected from two provinces in China.
Method: The subjects were categorized into prenatal famine-exposed group and non-exposed group based on their birthdates. DNA methylation at the INSR gene locus was assayed from peripheral white blood cells using the Sequenom's MassARRAY system. Two dependent samples t-test was used to compare the difference between the exposed group and non-exposed group.

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Results: DNA methylation level of INSR was higher among individuals who exposed to the China famine in the fetus than that of non-exposed group (d = 3.3%, P = 0.006). A significant interaction between famine exposure and province was observed for INSR (Pinteraction < 0.001). DNA methylation level of INSR was positively associated with triglyceride (β = 0.011, P = 0.021), and negatively associated with high-density lipoprotein cholesterol (β = −0.039, P = 0.021). Moreover, exposed group had higher meat consumption than non-exposed group in severe exposure area.
Conclusions: Prenatal exposure to the China famine plus later life eating habits might regulate epigenome.

Is there an association between the family meal frequency of toddlers and maternal anxiety and depression symptoms?

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Background/Aims: Diet in the first years of life is important for growth, development and long-term health. In toddlerhood, higher dietary quality is reported among those who eat meals together with their family. Maternal depression and anxiety are related to feeding practices. There is, however, limited research on the association between maternal anxiety and depression symptoms and frequency of shared family meals among toddlers. The aim of this study was to explore the association between frequency of shared family meals among toddlers and maternal anxiety and depression symptoms.
Method: Cross-sectional data from 455 maternal-child dyads from a Norwegian randomized controlled trial after an intervention was used to assess maternal anxiety (4 items) and depression (4 items) (categorized in high and low levels) using The (Hopkins) Symptoms Checklist (SCL-8), and toddler participation in family meals (seldom (< 3 times/week) or often (≥ 4 times/week)) (dependent variable). Logistic regression analyses adjusting for child gender and intervention group were performed using SPSS 25.0.
Results: The percentage of 12 months olds eating breakfast (64%), lunch (42%), dinner (79%) and supper (32%) together with family often, varied according to meals. Maternal anxiety and depression symptoms were reported by 17 and 24 percent, respectively. Children with mothers with higher scores of anxiety had lower odds of eating breakfast often with their family (OR:0.656, p=0.049) and children with mothers of higher depression scores had lower odds of eating lunch often with their family in the adjusted model (OR: 0.580, p=0.015).
Conclusions: Maternal anxiety and depression was associated with frequency of toddler attending family breakfast and lunch. Further exploration of this relation is needed.

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