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Abstracts

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Maternal Vitamin D Status and Perinatal Outcomes in Twin Pregnancy

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Introduction: Vitamin D plays an essential role in regulating cell proliferation and apoptosis and has been linked to several obstetric complications. The aim of the study is to assess whether vitamin D dosage and supplementation can improve perinatal outcomes in twin pregnancy that is at high risk per se. *Materials and methods:* This retrospective study included twin pregnancies followed by the Twin Pregnancy Care Unit of Sant'Anna Obstetric-Gynecological Hospital in Turin between 2020 and 2023. In one group serum vitamin D was measured in the first trimester and, if needed, supplementation was administered. In the second group vitamin D was not measured nor supplemented. First, we compared perinatal outcomes between the two groups. Then, we assessed whether vitamin D status (insufficient, deficient, sufficient) in the first trimester could influence pregnancy outcomes. *Results:* Serum vitamin D was dosed (and, if appropriate, supplemented) in 146 of the 278 twin pregnancies included in our study in the first trimester. Pregnancies in which vitamin D was not dosed had a higher incidence of hypertensive disorders of pregnancy (HDP, 22.7% vs. 16.7%, $p = .042$) and birth weight discordance (11.4 ± 8.4 % vs. 7.3 ± 4.2 %, $p = .036$), while no difference was found between the two groups in mode of delivery, gestational age at birth, neonatal birth weight, incidence of IUGR and gestational diabetes. Vitamin D status in the first trimester was significantly associated to a higher rate of HDP: incidence of HDP was 29.4% in insufficient women, 25.3% in deficient ones and 16.0% in sufficient ones ($p = .045$). *Conclusions:* Assessment of vitamin D status and subsequent supplementation is associated to a reduction in the incidence of HDP and a decreased birth weight discordance in twin pregnancy. Vitamin D status in the first trimester appears to be significantly related to incidence of HDP later in pregnancy.

Chronic Widespread Musculoskeletal Pain and Atheroma Share a Highly Heritable Latent Pathway; A Study from TWINSUK

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Introduction: Chronic widespread pain (CWP) is prevalent and associated with reduced life expectancy. Coronary artery disease (CAD) is one possible mechanism for this. The purpose of this study was to examine the association of CWP with arterial stiffness and plaque to determine if shared environmental or genetic factors might account for any observed association. *Materials and Method:* TwinsUK cohort participants with CWP and carotid-femoral pulse wave velocity (cfPWV) as an index of arterial stiffness, carotid intima-media thickness (cIMT), and carotid plaque measurements were considered. The association between CWP and cfPWV, cIMT, and plaque was determined using generalised estimating equations controlling for sex, age, body mass index, mean arterial pressure, and twin relationship. UK Biobank (UKB) data were utilised to replicate the association analyses for cfPWV and cIMT. Cholesky decomposition and multivariate pathway twin models were examined in twin data showing significant epidemiological associations. *Results:* TwinsUK participants ($n = 3302$) demonstrated a significant association between CWP and increased cfPWV consistent with arterial stiffening ($OR = 1.35$, p value = .012), as well as the presence of carotid plaque ($OR = 1.45$, p value = .8×10-5). Association of CWP and cIMT showed borderline significance ($OR = 1.25$, p value = .04). Furthermore, the association between PWV and CWP for females over 50 years old was replicated using UKB data ($\beta = 0.27 \pm 0.09$, p value = .006) and was also seen for males under 50 years old ($\beta = 0.86 \pm 0.18$, p value = 0.3×10-6). The twin modeling showed a common latent component and pathway underlying CWP to cfPWV and carotid plaque, with genetic factors accounting for around 68% and 90% of the latent factor variation, respectively. *Conclusion:* This study found those with CWP have increased risk of arterial stiffness and atherosclerosis and suggests possible mechanisms by which people with CWP are at increased risk of coronary artery disease.

Comparison Between Different Delivery Methods in Twin Pregnancies

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Introduction: Vaginal birth (VB) is the modality of delivery associated with fewer maternal and fetal complications compared to cesarean section (CS), both short- and long-term. The route of delivery in twin pregnancies represents a challenge for obstetricians, although different studies say that the VB in twin pregnancies is possible and safe. Despite these data the CS rate remains high for patients with twin gestations, due to lack of training skills within clinicians. *Materials and methods:* A retrospective study with data collected from 2017 to 2024 (first trimester), with vital twin pregnancies (BCBA and MCBA) delivered at 34 gestational age and above, in a second level hospital. In 2021, a different clinical direction and physicians expert in twin and breech delivery started working in this center and clinicians and midwifes did periodic training about these

topics. Data collected until March 31st 2024, include 231 patients, and it is split in two groups: first one (before training) is from January 1st 2017 to December 31st 2020 with 124 patients, and second one is from January 1st 2021 to March 31st 2024 with 107 patients. The object is to evaluate maternal and neonatal outcomes. *Results:* From 2017 to 2020, 124 twin patients delivered in our Unit. 6 (4.8%) underwent VB, having 26 a planned VB (21.0%). From 2021 to 1st trimester 2024, 106 twin patients delivered in our Unit. 22 (20.7%) underwent VB, either natural and operative (n. 2) (p = .000234), with 33 having a planned VB (31.1%). The incidence of conversion in the period time changed from 77% to 33% (p = .000872). Albeit a significant increase in VB, maternal and neonatal outcomes were not statistically different between the two periods. *Conclusion:* Safety delivery and better outcomes are expected in larger number. Our population study is limited in number and we cannot highlight correlation to parity, previous CS and so forth. The mainstay of our data collection is that skill improvements are necessary to reach this challenge.

Identifying a Birth Cohort of Twins From Linked Administrative Data — Challenges And Opportunities

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Introduction: In the absence of *accurate* perinatal records, identifying and differentiating twins in administrative records is difficult because of their similarity; they share surnames, dates of birth, and residences. In administrative databases, events within twin pairs are often incorrectly identified as being from one individual, representing a threat to data accuracy. An inability to identify twins in administrative data precludes applying powerful twin-based causal inference methods to understand health and social wellbeing. *Materials & Methods:* We developed an algorithm using linked administrative birth, perinatal, emergency department, and hospital records in Victoria, Australia from 1 January 1993 to 31 December 2023. We probabilistically linked a sample of 1434 'known' twin pairs from the Australian Twin Registry to validate the sensitivity of our algorithm. We calculated specificity using a sample of non-twins derived from linked data. *Results:* Our algorithm identified 37,900 twin pairs, 75,800 twin individuals, in the Victorian linked dataset. The accuracy of our ascertainment of twins by key characteristics will be presented and discussed. *Conclusions:* The birth cohort we have generated is one of the largest twin cohorts in the world with unprecedented granularity in longitudinal health and social data. Our algorithm improves the accuracy of administrative data repositories and linkage, providing novel information on where errors in previous linkages have occurred due to limited familial or intergenerational information. Our large population-based birth cohort of twins can be used to investigate the familial and nonfamilial determinants of health using advanced causal inference which leverages the natural similarity between twins.

Skin Microvascular Function Assessed By Laser Speckle Contrast Imaging in Twin Pregnancies

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Introduction: In singleton pregnancies, microvascular reactivity improves from the first to the third trimester. However, data on endothelial function in multiple pregnancies are scarce.
This study aims to evaluate changes in microvascular function using laser speckle contrast imaging (LSCI) throughout twin gestation, and to compare these measurements with those of singleton pregnancies. *Materials & Methods:* 18 women carrying a twin gestation were enrolled. Skin microvascular blood perfusion was recorded using LSCI coupled with post-occlusive reactive hyperemia. Skin perfusion was recorded before (baseline flux) and after (peak flux) a 3-minutes arterial occlusion. The percentage increase from baseline to the maximal hyperemic response (base-to-peak flux) was calculated. The test was performed in the second (T2) and in the third trimester (T3). The longitudinal assessment was then compared with measurements from singleton controls, matched for gestational age. *Results:* 18 women with twin gestation underwent the test at T2; 16 of them completed the T3 assessment. In the twin cohort, the mean peak flux decreased from 162 perfusion units (PU) in T2 to 146 PU in T3 (p = .016), and the mean base-to-peak flux declined from 301% to 260% (p = .006). These findings differ from those in the singleton cohort, in which the microvascular reactivity was highest at T3. The base-to-peak flux at T2 was significantly higher in twins than in singletons (302.4% vs. 247.8%, p .004), and similar at T3 between twins and singletons (260% vs. 264.6%). *Conclusions:* Microvascular endothelial adaptation shows different dynamics throughout twin gestation compared to singletons. Twin pregnancies have enhanced microvascular function in T2 and, unlike singletons, deteriorated reactivity in T3 compared to T2. This novel finding may shed light on the increased incidence of placenta-related disorders in twin pregnancies, where endothelial dysfunction plays a central role.

New Approaches to Research In Facial Recognition and Police Identification in Twins Within The Context of Artificial Intelligence

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Introduction: Advancements in artificial intelligence (AI) have opened new avenues for research in facial recognition and police identification, particularly in cases involving twins. This research explores innovative methods and technologies for distinguishing between identical twins using AI algorithms. *Materials and Methods:* We present a simplified automation process to assist in the comparative identification of dental patients using panoramic radiographs, combining image segmentation techniques, feature extraction, and machine learning. The sample consisted of 50 pairs of twin images. We employed image segmentation, feature extraction, and machine learning techniques. The Python 3.10 language was used, utilizing the Google Colab application (version 3.7.13). Additional language packages included Numpy, Matplotlib, and

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CV2. *Results:* The proposed program displays the main image and comparison images, presenting the degree of similarity. The photographs are shown side by side, and matching colorations indicate similar features. In the process, using 50 pairs of twin images, the average similarity with image of the same individual but at a different time was 90.3%. The similarity between images of different individuals averaged 10.8%. *Conclusions:* The application demonstrates consistent potential to optimize the workflow of Facial Recognition and Police Identification in the practice of Official Forensics.

DNA Methylation Links Life Events to Environmental Breast Cancer Risk: Follow-Up From the Finnish Twin Cohort

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Introduction: While environmental exposures contribute to breast cancer (BC) risk, the mechanisms remain elusive. This study explores the links between stressful life events, DNA methylation (DNAm), and BC risk. Our studies show a long-term increased risk of BC after exposure to stressful events, such as loss of close person, divorce, or loss of job. In a previous study using twin pairs discordant for BC, we identified 212 DNA sites (CpGs) in blood associated with BC risk. Notably, 198 of these remained associated within the MZ twin pairs, suggesting links to environmental risk factors. Here we studied if stressful life events assessed in the 1981 survey are associated with these 212 CpGs. *Materials & Methods:* To investigate the association between BC-associated DNAm and exposure to stressful life events, within-pair differences in DNAm for twin pairs discordant for BC were linearly regressed over the within-pair differences in their life event exposure. Life event assessment was on average 15.8 years ($SD = 5.3$) prior to DNA sampling and DNA sampling was on average 11.3 years ($SD = 6.4$) prior to BC diagnosis. At first, we analyzed a set of 27 MZ and 58 same-sex DZ twin pairs, controlling for shared familial factors. For 17/212 CpGs the BC-associated DNAm patterns correlated with within pair differences in life events. Furthermore, a total of 172/212 CpGs showed consistent effect direction with BC-associated DNAm (binomial-test $p <$ 1e-20). To examine the impact of genetics, we re-ran the analysis on the 27 MZ twin pairs alone. *Results:* While only 1/212 CpG was validated, the effect direction in 128/212 CpGs still concurred with Bode et al. (2024) (binomial-test $p < .003$). *Conclusion:* This study suggests that DNAm patterns associated with BC not only predate the diagnosis but also persist long after exposure to stressful life events. This implies a potentially long-term impact of stress on DNAm as a mediator or indicator of BC development.

Epigenome-Wide Association Study Identifies Novel Loci Associated With Generalised Anxiety Disorder in a General Population Twin Cohort of Young Adults

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Introduction: Generalized Anxiety Disorder (GAD) is a prevalent psychiatric condition with significant impact on individuals' quality of life. Epigenetic modifications, particularly DNA methylation, are potential mediators linking genetic and environmental factors to psychiatric disorders, including GAD. This study aimed to identify epigenetic loci associated with GAD through an epigenome-wide association study (EWAS). *Materials & Methods:* We conducted an EWAS on a cohort of 1621 individuals from the Environmental Risk (E-Risk) study, comprising cases diagnosed with GAD and age-matched controls. GAD diagnoses were based on DSM-IV criteria assessed during participants' age 18 home-visit interview. DNA samples were extracted from peripheral blood and analysed using the Illumina Infinium Human Methylation 450 BeadChip. Quality control measures were implemented to ensure data reliability. Associations between DNA methylation levels at over 450,000 CpG sites and GAD were examined using linear regression models. We adjusted for age, sex, batch (plate), and estimated cell proportions (Granulocytes, Monocytes, B-cells, CD8+ T-cells, CD4+ T-cells, NK cells). *Results*: We reported a significant association with GAD that survived Bonferroni adjustment for multiple testing at a single CpG site located in upstream of a gene involved in the immune system regulation. Several differentially methylated loci were also associated with GAD at the discovery p-value threshold. *Conclusion:* This is, to our knowledge, one of the largest EWAS in GAD conducted to date. Our findings highlight the potential significance of epigenetic factors in the study of psychiatric conditions and may inform the development of biomarkers for GAD. Future research should aim to replicate these findings in independent cohorts and further explore the causal relationships between methylation changes and GAD.

Twin Pair Analysis Uncovers Novel Links Between DNA Methylation, Mitochondrial DNA Quantity And Obesity

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Background: Alterations in mitochondrial metabolism in obesity may indicate disrupted communication between mitochondria and nucleus, crucial for adapting to changing metabolic demands. This interplay can be subject to epigenetic regulation, such as DNA methylation, but remains poorly understood. This study aimed to identify DNA methylation sites associated with mitochondrial DNA quantity (mtDNAq) in adipose tissue, and to investigate their implications in obesity. *Materials and Methods:* We utilized data from the subcohort of the Finnish Twin Cohort (n = 173; 86 twin pairs) that includes comprehensive measurements of obesity-related traits, mtDNAq and nuclear DNA methylation levels. We performed an EWAS to identify mtDNAq-linked DNA methylation sites, and applied ICE FALCON, a method for inferring causality from examination of familial confounding, to analyze the potential causal relationship between DNA methylation, mtDNAq, and obesity. *Results:*

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We identified one CpG site, *cg19998400*, associated with mtDNAq in adipose tissue (FDR < 0.05), annotated to *SH3BP4* gene. Further, 14 out of the available 35 obesity-related traits were significantly associated with both *cg19998400* methylation and mtDNAq. Our data suggested that mtDNAq, insulin sensitivity and certain body fat measures were causal to *cg19998400* methylation. The relationship between mtDNAq and obesity-related traits suggested causation from mtDNAq to obesity but could not be distinguished from potential unmeasured within-individual confounding. *Discussion:* This study highlights changes in adipose tissue DNA methylation and gene expression at the *SH3BP4* gene, which may be influenced by mtDNAq and specific obesity-related traits. The detailed role of *SH3BP4* in obesity remains unclear, although it has been previously associated with adipogenesis. To gain comprehensive insights into causal pathways of these associations, a larger sample size and additional approaches, such as longitudinal study designs, would be beneficial.

Investigating the Relationship of Intrauterine Head Growth Rate With DNA Methylation at Birth and Beyond Using Twin Model

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Introduction: Optimal intrauterine head growth rate (IHGR) is crucial for later neurodevelopmental outcomes which may be mediated by epigenetic mechanisms such as DNA methylation (DNAm). No study has yet explored the association of IHGR with DNAm. Thus, we will investigate the relationship between IHGR and DNAm at birth, 18 months, 6 years, and 11 years using data from the Peri/Post-Natal Twin Study (PETS). *Methods:* Twin regression model/models will be used to test for CpGs and regions at birth strongly associated with IHGR including the effect of sex, zygosity and chorionicity. Pathway enrichment will be performed on genes annotating to the CpGs (false discovery rate <0.05) associated with IHGR at birth. CpGs will be compared between timepoints by ranks based on methylation values. *Results:* Regression lines fitted in each timepoint revealed that IHGR is linear in mid-gestation and slows down in late gestation with increasing discordance between twins. *Conclusions:* This study is the first to explore the longitudinal relationship between IHGR and DNAm. Results may elucidate critical epigenetic pathways related to IHGR.

Effects of Estimated Fetal Weight Dissertation on Neonatal Outcomes in Twin Pregnancies: A Cohort Retrospective Study

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Introduction: Assessing fetal growth in twin pregnancies is crucial, especially when discrepancies in estimated fetal weight (EFW) could influence neonatal health. This study investigates how significant EFW dissertations, categorized as either under 20% or over 20%, affect various neonatal outcomes. *Materials and methods:* A retrospective cohort analysis was conducted on twin deliveries at the 1st Department of Obstetrics and Gynaecology of the Medical University of Warsaw, with two groups based on prenatal EFW dissertation predictions: over 20% (LOW group, n = 13 twin pregnancies) and under 20% (HIGH group, n = 130 twin pregnancies). All patients received their prenatal care at our facility, and post-pregnancy outcomes were collected via a phone survey. *Results:* The LOW group had an average APGAR score of 9.20, similar to the HIGH group's 9.06. Both cohorts showed comparable use of antibiotics (8% LOW vs 7.69% HIGH) and similar birth timing (35 + 2.5 LOW vs. 35 + 5 HIGH). However, the LOW group required more respiratory support (48% vs. 29.62%, 95% CI, RR 1.62, p = .029), and also had higher ICU admission rate (48% vs. 29.23%, CI 95%, RR 1.64, p = .026). Nonphysiological jaundice occurred more frequently in the LOW group (48% vs. 20%, CI 95%, RR 2.40, p < .001). In the LOW group, 53.85% of pregnancies resulted in a birth weight discordance greater than 20%, consistent with the difference observed in prenatal ultrasounds, and there was one (n = 13) instance of intrauterine fetal demise in the third trimester. In contrast, only 13 pregnancies (10%) in the control group exhibited a significant postnatal weight difference. Differences in chorionicity were observed, potentially influencing these outcomes. *Conclusions:* EFW dissertations over 20% are associated with an increased need for respiratory support, ICU admissions, and a higher incidence of jaundice. This confirms the need to perform mandatory ultrasound examinations in multiple pregnancies, especially in the assessment of EFW.

Monochorionic Diamniotic (MCDA) Twins: What Prospective Parents Want To Know and The Influence Of Social Media

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Introduction: Parents actively seek information and support online, often through social media. We explore how online groups influence shared decision-making and informed consent. *Materials and methods:* In late 2021, an online survey targeted English-speaking adults with an MCDA pregnancy in the past five years. Participants shared how social media influenced their pregnancy. Data were analyzed using both qualitative and quantitative methods. *Results:* Our research found that 69% of respondents used social media, with 48% reporting it impacted their pregnancy management. Most joined online groups, primarily MCDA-specific (44.2%). Social media influenced birth plans, patient advocacy, provider choice, and complications. It was used to bridge information gaps, provide support, and enhance advocacy, with many recommending online support groups for information. *Conclusions:* Given the rarity of MCDA pregnancies, many patients seek additional information outside office visits for informed decision-making and active care participation. Providers should recognize this, discuss potential complications early, discuss treatment options transparently, and leverage social media to ensure parents are well-informed of their diagnosis and options throughout the pregnancy.

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Umbilical Cord Insertions in Monochorionic Twin Placentas With Selective Fetal Growth Restriction

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Introduction: Monochorionic (MC) twins share a single placenta which can be unequally shared, leading to selective fetal growth restriction (sFGR). Limited data is available on the prevalence and clinical consequences of proximate cord insertion (PCI) in sFGR pregnancies. We aim to investigate the prevalence of PCI in MC placentas with and without sFGR and per type of sFGR. *Materials & Methods:* We included MC twin placentas evaluated at the University Hospitals Leuven (Belgium) and Leiden University Medical Center (the Netherlands) between 2002-2023. Primary outcome measures were the prevalence of PCI and type of cord insertions (concordant, intermediate, discordant). We compared the outcomes of sFGR placentas with uncomplicated MC placentas. *Results:* Of 813 placentas, 468 were uncomplicated and 345 were diagnosed with sFGR (187 type I, 41 type II and 117 type III sFGR). The prevalence of PCI in uncomplicated versus sFGR placentas was 3.8% (18/468) and 4.6% (16/345), respectively ($p = .58$). PCI in sFGR type I, II and III was detected in 0.5% (1/187), 0% (0/41) and 12.8% (15/117), respectively ($p < .001$). The prevalence of discordant cord insertions (velamentous-paracentral) in uncomplicated twin placentas and sFGR placentas was 19.9% (93/468) and 45.5% (157/345), respectively ($p < .001$). Fetal demise occurred in 12.5% (2/16) of pregnancies with PCI and 6.1% (20/329) of sFGR pregnancies without PCI ($p = .27$). *Conclusions:* sFGR type III placentas exhibit a high prevalence of PCI, requiring increased awareness due to the presence of larger AA anastomoses and a potentially higher risk of fetal demise.

Treatment and Outcome of 13 Cases With Spontaneous or Post-Laser Twin Anemia Polycythemia Sequence

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Introduction: Twin anemia polycythemia sequence (TAPS) is a rare complication of monochorionic pregnancy (MC), occurring in 3–5% of cases and 2–16% after laser surgery in twin-to-twin transfusion syndrome (TTTS). There is no optimal consensus on the management of TAPS. The aim of the study was to summarize the results of TAPS treatment in our hospital. *Materials and Methods:* We analyzed type of TAPS, gestational age at diagnosis and birth, TAPS stage, Apgar score. Data 2023–2024 years. *Results:* Among 13 cases of TAPS diagnosed prenatally, in one case we lost the follow-up. In 2 cases of TAPS treated with laser intrauterine fetal demise occurred. Postlaser TAPS was diagnosed in 3 MC pregnancies, spontaneous in 7 women. Spontaneous TAPS was diagnosed at an average of 21 weeks, postlaser TAPS at mean 25 weeks of gestation. Post-laser group: two cases required serial amnioreductions. The gestational age at delivery ranged from 29 to 33 weeks. In the spontaneous TAPS group, 3 patients were treated with the laser at 21st, 21st and 24th weeks of gestation and delivered at 26+4, 33+1, 36+0 weeks respectively. Laser-treated spontaneous TAPS resulted in an overall time to delivery of 11 weeks at mean; however, one case had preterm premature ruptures of membranes from 27 weeks of gestation. Women with spontaneous TAPS managed expectantly delivered at mean 32 weeks of gestation (from 29 to 34 weeks). One case needed intrauterine blood transfusion. Spontaneous TAPS managed expectantly resulted in 6 to 12 weeks' time from diagnosis to birth. Median birth weight of first twin 1495g with Apgar score of 6/10, second twin 1605g with mean Apgar 8/10. Postdelivery donor hemoglobin concentration was 9.1 g/dL (*SD* 3.24), recipient 20.6 g/dL (*SD* 4.1) $p < .01$. *Conclusions:* Perinatal morbidity was high in all treatment groups. Our results suggest than laser treatment is invasive and can have fatal outcomes. Expectant management can be beneficial if TAPS occurs later in pregnancy.

Brain Injury in Monochorionic Twins After Intrauterine Demise: A Multi-Center Restrospective Study (CITRUS Study)

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Introduction: Monochorionic (MC) twin pregnancies are considered high-risk pregnancies with significant perinatal mortality rates. In cases of single intrauterine fetal demise (sIUFD), the surviving co-twin risks death, brain injury and subsequent neurodevelopmental impairment, following acute exsanguination in the presence of large patent anastomoses. Precise data on these outcomes are limited due to small study populations and varying methodologies. The aim of this study is to describe the incidence of sIUFD in MC twin pregnancies including incidence, type, and severity of brain injury in surviving co-twins. Secondary aims include identifying perinatal risk factors for brain injury and examining neurodevelopmental outcome in relation to observed brain injury. *Materials & Methods:* We will perform an international multicenter retrospective cohort study. MC pregnancies with sIUFD between 2000-2025 are eligible for inclusion. Exclusion criteria are sIUFD after fetoscopic laser surgery, TAPS, selective feticide or congenital abnormalities. We will document brain injury identified through either ante- or postnatal neuroimaging (ultrasound and magnetic resonance imaging). To evaluate potential risk factors, obstetric and placental characteristics will be collected from medical records. If available, long-term neurodevelopmental outcome will also be recorded. *Results:* Currently, 11 centers are confirmed to participate in this study, and registration remains open for additional centers to participate. Data collection is scheduled from May 2024. *Conclusions:* By examining a large international cohort of MC pregnancies with sIUFD, we will enhance our understanding of the risk of brain injury in the surviving co-twin, identify potential risk factors for such injuries, and assess

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neurodevelopmental outcomes of surviving co-twins. Thereby, this research will aid in future counseling, early identification of infants at risk, and devising feasible management and treatment options.

Birth Weight Discordance and Adverse Neonatal Outcomes in Appropriately Grown Premature Twins

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Introduction: This study aimed to analyze the clinical characteristics of birth weight discordant twins (BWDT) who were premature and appropriate-for-gestational-age or large-for-gestational-age. Additionally, it assessed the impact of birth weight Journal Pre-proof discordance on the prognosis of appropriately grown premature twins, and investigated the effect of maternal factors on neonatal outcomes. *Materials & Methods:* This retrospective cohort study included twins who were born alive after preterm labor at the Nanjing Drum Tower Hospital from January 2018 to December 2021, along with their mothers. Twins were arranged into discordant and concordant groups according to intertwin birth weight discordance, followed by the analysis of the clinical characteristics of mothers and the prognosis of neonates. *Results:* A total of 585 mothers and 1170 neonates were included, with 47 mothers and 94 neonates in the discordant group. The incidence of birth weight discordance was 8.0% (94/1,170) in appropriately grown premature twins. The incidence of complications (43.2% vs. 21.8%) and transfer to the neonatal intensive care unit (NICU) (53.2% vs. 29.2%) was higher in the discordant group than in the concordant group ($p < 0.05$). Furthermore, the incidence of infectious diseases (36.7% vs. 19.4%), necrotizing enterocolitis (7.6% vs. 1.6%), and oxygen therapy rate (22.8% vs. 12.8%) were statistically significantly higher in the discordant group than in the concordant group ($p < .05$). *Conclusion:* Birth weight discordance remains a high-risk factor for complications and transfer to the NICU in appropriately grown premature twins. It is important to pay attention to birth weight discordance when the outcomes of twins are assessed.

White Matter and Heritability: A Preliminary Tract-Based Spatial Statistics (TBSS) Study on Italian Twins

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Introduction: Twin studies provided high heritability estimates for white matter (WM) connections, mainly based on fractional anisotropy (FA) in diffusion tensor imaging (DTI). However, mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) indices have not been investigated in depth. Therefore, in this preliminary twin study, we aimed to investigate WM heritability by considering FA, MD, AD and RD, and combining the Tract-Based Spatial Statistics (TBSS) with twin modeling. *Materials & Methods:* Among three different clinical centers, we acquired DTI images from 81 healthy twin pairs (33 monozygotic [MZ] and 48 dizygotic [DZ], age 8-32 years, 52% female), enrolled in the population-based Italian Twin Registry. By performing TBSS, we extracted FA, MD, AD and RD and corrected the multi-center effect. Age-adjusted twin correlations for each DTI index and each neuroanatomical atlas region were estimated. *Results:* Twin correlations varied considerably by brain region and DTI index, being overall higher in MZ than DZ twins. However, we found an opposite trend in some tracts, where correlations were higher in DZ than MZ and genetic effects faded out. *Conclusions:* Our results suggested high heterogeneity of genetic and environmental effects on WM integrity across brain regions and DTI indices, unveiling a crucial role of environmental factors in heritability of structural brain connectivity.

Diet and the Microbiome: Implications for Neurodevelopment in Early to Mid Childhood

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Introduction: The gut microbiome significantly influences immunity, metabolism, and neurodevelopmental and mental health risks. Despite its importance, the impact of early life factors, such as birth mode and breastfeeding, and the role of modifiable environments like diet remain unclear. This study aimed to map cross-sectional and longitudinal associations between microbiome composition and neurodevelopmental outcomes, determine the stability of the microbiome across ages, and identify dietary predictors of microbial and neurodevelopmental outcomes. *Methods:* Leveraging a cohort of 250 twin pairs followed from mid-gestation to 11 years, we collected comprehensive data on development, diet, cardiometabolic health, microbiome, and neurodevelopmental outcomes, including cognition, brain imaging, and behaviours. Metagenomic sequencing yielded a 98% read filter pass rate with a Q30 score of 89.95%. *Results:* Analysis revealed significant within-pair differences, including prorated full-scale IQ ($p = .011$) and cortical surface area ($p = .0011$), demonstrating the microbiome's association with key neurodevelopmental markers. *Conclusions:* Our findings will enhance our understanding of the interplay between diet, the microbiome, and neurodevelopment, providing insights for clinical trials of dietary and lifestyle interventions aimed at improving childhood outcomes.

Age Acquired Skewed X Chromosome Inactivation is Associated With Altered Inflammatory Markers: A Twin Study

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Introduction: X chromosome inactivation (XCI) silences one X chromosome to equalise the gene dosage between XX and XY cells. The choice of which X to silence is random, giving an expected 50:50 pattern of mosaicism within tissues. However, a significantly unbalanced ratio, termed XCI-skew, is common in blood cells and its prevalence increases with age: >30% of females over 60 yrs have

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an XCI ratio of 80:20 or greater. XCI-skew is associated with adverse health outcomes in humans, including cancer and autoimmunity. However, the reason XCI is associated with these diseases is poorly understood. Using a discordant twin pair approach, we assessed whether XCI-skew is associated with low-grade chronic inflammation, termed 'inflammaeging', as defined by cytokines IL6, IL8, IL18, IL10, TNF, and IFN-y. *Methods:* We assayed XCI in whole blood DNA in 35 female MZ twin pairs from TwinsUK. All volunteers were postmenopausal and had date-matched proteomic data. XCI was defined as a continuous variable with a range of 50–100%, with increasing values representing increasing skew. A difference in XCI between MZ twin pairs of >10% was defined as discordant. Protein levels were assayed using the OLINK platform and adjusted for BMI. Bonferroni correction was applied. *Results:* Of the 35 MZ twin pairs, 21 were concordant or XCI (mean difference XCI = 3%, mean age = 62 yrs) and 14 pairs were discordant (mean difference XCI = 21%, mean age = 66 yrs). Across the discordant pairs, IFN-y was significantly lower in individuals with higher XCI-skew compared to their co-twins (two-sided paired Wilcoxon test; Padj = .012). Across all 35 twin pairs, there was a significant correlation between intra-twin differences in XCI and IFN-y (Pearson's correlation; $p = .0076$; $r = -0.44$), confirming the directionality of the effect. *Conclusions:* Our results suggest XCI-skew could be a marker of age-related immune changes and should be investigated further to understand the molecular underpinnings of immune ageing.

Multi-Omic Associations of Epigenetic Age Acceleration are Heterogeneously Shaped by Genetic and Environmental Influence

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Introduction: Connections between the multiome and epigenetic age acceleration (EAA), and in particular whether these are influenced by genetic or environmental factors, remain underexplored. Therefore, we quantified associations between the multiome, consisting of four layers – proteome, metabolome, external exposome, and lifestyle – and six different EAA estimates in twins. *Materials and Methods:* Two twin cohorts were used in a discovery-replication design, comprising young ($N = 642$; mean age = 22.3) and older ($N = 354$; mean age = 62.3) twins from FinnTwin12 and the Older Finnish Twin Cohort (OldFTC), respectively. First, associations between EAA estimates and multi-omic factors were assessed in the FinnTwin12 sample using linear mixed effects models. Then, within-pair twin designs were used to assess genetic and environmental effects on the associations. Replication of associations with metabolites and proteins was performed in the OldFTC sample. *Results:* We identified 40 multi-omic factors associated with EAA, 28 of which were proteins, after adjustment for sex, smoking, and body mass index. Within-pair analyses showed that genetic confounding affected these associations heterogeneously. Six multi-omic factors remained significantly associated with EAA independent of genetic factors. Some associations identified in FinnTwin12 remained significant in older adults of OldFTC. *Conclusions:* Our study identifies a large number of multi-omic factors, including plasma molecules and exposures, associated with EAA. The twin designs suggest that genetics heterogeneously confounds these associations, with some associations remaining significant after controlling for all genetic and shared environmental effects.

A PRS-Informed BMI Approach Unveils Novel Insights in Epigenomic, Metabolomic, and Proteomic Changes in BMI-Discordant Twins

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Introduction: Genomewide association studies have identified numerous BMI-associated single nucleotide polymorphisms (SNPs), enabling the calculation of a polygenic risk score (PRS) for genetic BMI estimates. Lifestyle and environmental exposure, however, can create discrepancies between observed and predicted BMI. This study calculated a deviation score using PRS_{BMI} in twins from the Finnish Twin Cohort, to explore related DNA methylation, metabolomic and proteomic differences. *Materials & Methods:* Residuals were derived from a linear model between measured BMI and PRS_{BMI}, adjusted for age and sex. We compared the DNA methylation, metabolomic and proteomic profiles in BMI-discordant twin pairs where one individual is within their genetically predicted range, and the other is either above (Group 1, $N = 158$ pairs) or below (Group 2, $N = 141$ pairs) it. *Results:* Opposite DNA methylation pattern in MYO5C gene body were observed between two groups, linking MYO5C methylation to C-reactive protein abundance. Both groups exhibited epigenetic aging in the heavier twin, suggesting an overall aging effect from weight gain. LDL cholesterol increased more in the heavier twin in Group 2. Different protein pathways were enriched in the 2 groups. *Conclusions:* The results suggest that the discrepancy between observed and genetically predicted BMI is underpinned by distinct multiomics signatures.

Perinatal Outcomes of Twin Pregnancies

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Introduction: Twin pregnancies are a predictor of worse maternal and perinatal outcomes. Twins account for 10–14% of all perinatal mortality in Kazakhstan. The percentage of twin births in 2023 in Almaty increased by 2.7% compared to 2018. The research objective was to study twin pregnancies and their outcomes due to the twin pregnancies increasing number. *Materials and Methods:* This retrospective study was conducted at the Center for Perinatology and Pediatric Cardiac Surgery, Almaty. 959 birth records of twin pregnancies were analyzed from January 1, 2022, to December 31, 2023. The collected data was processed using clustering and descriptive statistics. To study the similarities and differences between various groups we used methods such as the Kruskal-Wallis test for examining several independent groups, ANOVA for comparing means, and the chi-square test for checking relationships in categorical data. To assess the degree of connection, we used correlation regression analysis. *Results:* According to the study, the average age of women in the group with IVF pregnancy was 31.31 years,

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and in the group with spontaneous pregnancy was 31.95 years. The average delivery time in the two groups was 35.6 weeks. Cesarean section was performed in 74.3% of cases. The arithmetic mean weight in both groups was borderline — 2427 gr. The survival rate in the neonatal period was higher in the IVF group — 98.6%, while in the spontaneous pregnancy group it was 97.02%. Twins in the spontaneous pregnancy group were more likely to require CPR, CPAP, and blood transfusions. *Conclusions:* Twin pregnancies are a risk factor for premature birth, as well as the birth of low-weight, premature children who require a prolonged stay in the Anesthesiology, Reanimation and Intensive Therapy Department or ICU ward and demand attention from medical personnel.

Analysis of Factors Associated With Individual Differences in Hemoglobin A1C for Personalized Medicine

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Introduction: Personalized medicine requires understanding of genetic and environmental influences on clinical measurements. We previously reported the heritability of various clinical measurements, but variability in susceptibility to environmental factors must also be considered. We hypothesized that this susceptibility is influenced by genetic factors. Focusing on HbA1c, we analyzed epigenetic factors as environmental influences within specific genetic backgrounds. *Materials & Methods:* We recruited 285 Japanese monozygotic twin pairs (76 male, 209 female) from the Center for Twin Research, Osaka University. SNP genotyping and CpG site DNA methylation levels were analyzed by microarray, while gene expression levels were assessed via RNA-seq. HbA1c was measured using the latex agglomerate turbidity method and categorized based on twin concordance. Statistical analyses were conducted using R-4.0.1 and PLINK. *Results:* We identified one SNP and several CpGs associated with HbA1c levels. Methylation levels of three CpGs were correlated with gene expression levels. Analysis of HbA1c concordance between twins revealed three SNPs and several CpGs associated with HbA1c levels, depending on specific SNP genotypes. These findings suggest genetic factors may modulate the impact of epigenetic factors on HbA1c levels. *Conclusions:* Variations in HbA1c levels may result from interactions between specific SNPs and CpG methylation. The susceptibility of HbA1c to epigenetic factors is likely influenced by genetic factors. Measuring these interactions holds potential for application in personalized medicine.

Speckle Tracking Echocardiography in Twin Pregnancies: A Systematic Review

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Introduction: Pregnancy complications related to twins are often associated with placenta insufficiency and hemodynamic changes in the fetal heart. Two-dimensional speckle tracking echocardiography (2D STE) is a relatively new ultrasound tool to evaluate fetal cardiac function. *Materials and Methods:* The aim of this study is to review systematically the current literature regarding global longitudinal strain, global longitudinal strain rate, peak systolic strain, and peak systolic strain rate assessed with 2D STE in twin pregnancies. *Results:* Seven articles met the inclusion criteria. All seven selected monochorionic diamniotic (MCDA) twins with TTTS as the study population. The control population was either MCDA twins without TTTS, or singletons, or an intrapair comparison was made. 2D STE assessment was shown feasible and reproducible in MCDA pregnancies. The global longitudinal strain in the right and left ventricle and the peak systolic strain in the right ventricle of the recipient MCDA twin is significantly decreased compared to the donor MCDA twin. Large heterogeneity in the control population, the technical characteristics, and varying gestational age between the articles induce inconsistent results. *Conclusion:* Overall, performing 2D STE is feasible in twin pregnancy, but the knowledge of the tool in twin pregnancy is very limited.

Diagnostic Accuracy of Estimated Fetal Weight Discordance in Predicting Birthweight Discordance In Monochorionic Twins

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Introduction: We evaluated the diagnostic accuracy of estimated fetal weight discordance (EFWD) ≥20% in predicting birthweight discordance (BWD) ≥20% in monochorionic (MC) twins. *Materials & Methods:* All uncomplicated MC twins and twins with sFGR born at our center between 2002–2023 were retrospectively included. EFW within 14 days of birth was documented for both twins, with the ultrasound closest to delivery being selected for analyses. Weight discordance was calculated as (weight larger twin–weight smaller twin)/weight larger twin x 100%. sFGR was diagnosed postnatally when the BWD was ≥20%. In a subgroup of sFGR twins in which EFW was available within 3 days of birth, the mean estimation error of the smaller and larger twin was calculated using the formula (birthweight – EFW)/birthweight x 100%. *Results:* In total, sonographic biometric measurements of 213 uncomplicated MC twin pairs and 134 twin pairs with sFGR were analyzed. Median gestational age at birth was 36.0 (33.6-36.4) weeks for uncomplicated twins and 32.7 (30.4–35.3) weeks for sFGR twins. The sensitivity and specificity of EFWD ≥20% within 14 days of birth in predicting BWD ≥20% were 84% (95% CI [76, 89]) and 85% (95% CI [79, 89]), respectively. Among twins with sFGR with available ultrasound within 3 days of birth (n = 47), the mean estimation error of EFW was 1.28% (*SD* 9.95) for smaller twin and -2.30% (*SD* 8.22) for the larger twin, indicating an underestimation of smaller twins and an overestimation of larger twins. *Conclusions:* We found a relatively high accuracy of EFWD ≥20% in predicting a BWD ≥20% in MC twins. However, there was a false-negative rate of 1 in 6 MC twins which should be taken into account in clinical practice. For research purposes, it is recommended to use actual BWD as diagnostic criterion for sFGR, if available.

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Amniocentesis and the Risk of Fetal Loss in Dichorionic Twin Pregnancies

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Introduction: There is a paucity of data regarding the risk of fetal loss due to invasive prenatal diagnosis in twins. Aim of the study is to assess the rate of amniocentesis-related fetal loss in uncomplicated dichorionic-diamniotic (DCDA) twin pregnancies. *Materials and methods:* Retrospective study. DCDA twin pregnancies who underwent amniocentesis between January 2010 and December 2023 at a single Centre formed the case group. The control group comprised DCDA twin pregnancies who did not undergo amniocentesis in the same period. Exclusion criteria were previous chorionic villous sampling, selective fetal reduction, elective termination of pregnancy, malformations, early intrauterine growth restriction, chromosomal aneuploidy. Primary outcomes of the study were miscarriage rate (<24 weeks), overall fetal loss and procedure-related fetal loss (loss of one or both fetuses < 4 weeks of the procedure; in the control group, 4 weeks after 16 weeks). Secondary outcomes were gestational age at birth and mode of delivery. *Results:* 220 women were included in the case group; the control group comprised 662 women. Women in the case group were significantly older (37.3 vs. 33.8 years, $p < .001$) and more frequently Caucasian (94.1% vs. 85.5%, $p < .001$). No difference in the primary outcomes was found: the fetal loss rate of one fetus was 1.8% in the case group and 2.1% in the control group, while of both fetuses it was 0.5% and 0.8% respectively ($p = .853$). Procedure-related fetal loss of one fetus was 0.9% in the case group and 1.1% in the control group, of both fetuses it was 0.5% in both groups ($p = .982$). No difference was found in secondary outcomes. Multivariate analysis confirmed the nonsignificant effect of amniocentesis on the risk of fetal loss, while it showed a significant influence of maternal age. *Conclusions:* Amniocentesis does not seem to increase the risk of fetal loss in uncomplicated DCDA twin pregnancies above the baseline risk of loss among twin gestations.

Prenatal Detection of Genetic Disorders in Twins

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Introduction: The invasive prenatal diagnostics is the most reliable method in detecting genetic fetal disorders. The risk of chromosomal abnormalities in twin gestations is higher than in the singleton pregnancies, thus, the frequency of invasive diagnostics is higher in the multiple pregnancies. *Materials & Methods:* A retrospective cross-sectional study was conducted at the 1st Department of Obstetrics and Gynecology, the Medical University of Warsaw between January and December 2023. The results of genetic testing of materials collected during chorionic villus sampling (CVS) or amniocentesis were analyzed. *Results:* Ten twin pregnancies were qualified for the study: One dichorionic (DC) and nine monochorionic diamniotic (MCDA). Indications for invasive procedures were as follow: six pregnancies with intrauterine twin-twin transfusion syndrome (TTTS), two cases with a high risk of aneuploidy and two patients diagnosed with fetal structural abnormalities. Chromosomal defects were found in two pregnancies (20%) with high-risk 1 trimester screening results; there were trisomy 18 in one of the fetuses in the DC pregnancy and trisomy 21 in the pregnancy in the patient MCDA. In two pairs of MCDA pregnancy the indication for amniocentesis were structural abnormalities; both patients had normal karyotype. *Conclusions:* A preliminary analysis of the results of genetic tests performed in twin pregnancies in the tertiary indicates that the main reason for karyotype determination are intrauterine treatment procedures for complications in MCDA pregnancies.

Assessment of Pulsatiility Index in Uterine Arteries and the Risk of Preeclampsia in Twin Pregnancies

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Introduction: Measuring the pulsatility index in the uterine arteries (UtA-PI) in the first trimester of pregnancy is necessary to stratify the risk of preeclampsia. The frequency of preeclampsia in multiple pregnancies is higher than in singleton pregnancies. The aim of the study was to determine the UtA-PI cut-off point indicating the increased risk of PE in multiple pregnancies. *Materials and methods*: We analyzed ultrasound examinations of 175 twin pregnancies performed in 2020-2023 at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw. This group included 57 DC, 97 MCDA and 6 MCMA pregnancies. 15 women were excluded from further analysis due to lack of complete data. In each case, the patient was contacted and interviewed regarding the course of pregnancy and its complications, mode and time of delivery and the neonatal out-come. Mean UtA-PI values were calculated according to FMF guidelines in the 1st trimester of pregnancy. *Results*: The average age of the mother at the time of the study was 31 years. 53% of the respondents were primiparas. In the study group, 4 women suffered from chronic arterial hypertension, 10 had PIH on average in the 29th week of pregnancy and 6 had PE — on average in the 32nd week of pregnancy. The average UtA-PI value in the first trimester of pregnancy was 1.59, which corresponds to 1.04 MoM. In women in twin pregnancies who developed preeclampsia, the mean MoM value was 1.1 MoM. *Conclusions:* Taking into account the average values of UtA-PI obtained in twin pregnancies, it seems that it would be justified to introduce a lower cut-off point than in singleton pregnancies. However, further studies on larger groups of women with multiple pregnancies complicated by preeclampsia are necessary to provide a clear answer.

Improving Multiple Birth Outcomes: What Role Could the European Standards of Care for Newborn Health Play?

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Introduction: The ESCNH aims to improve outcomes for multiple births by addressing challenges such as preterm birth, high NICU admissions, complications, and maternal issues. *Materials and Methods:* The ESCNH provide 11 standards topics and were

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developed by 220 professionals, from more than thirty countries, along with 50 parents and industry partners. For the purpose of this abstract, we will focus on two standards only: Infant- and Family-Centered Developmental Care, and Follow-up and Continuing Care and examined these standards from a multiple birth perspectives. *Results:* A holistic approach combining neurodevelopmental theories, parent-infant interaction, and environmental adaptation is beneficial for multiple births. Early bonding, continuous skin-to-skin contact, and additional NICU support are crucial. Preterm twins require multidisciplinary follow-ups, and ESCNH can be beneficial but requires expansion for specific multiple birth needs. *Conclusion:* The European Society for Neonatology (ESCNH) offers a comprehensive newborn care framework, but it lacks provisions for multiple births. Expanding the ESCNH to address multiple births can improve care quality and outcomes for families with twins, triplets, or higher-order multiples.

Epidemiology and Risk Factors Associated With Preterm Births in Twin Pregnancies: A Retrospective Cohort Study

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Introduction: In recent decades, the frequency of multiple pregnancies has increased, exposing them to a heightened risk of complications, particularly premature delivery (PPI) and other perinatal complications. This study aimed to analyze the epidemiology and risk factors of premature births in twin pregnancies, focusing on adverse maternal and fetal outcomes. *Materials and Methods:* A retrospective analysis was conducted on medical records of women with twin pregnancies who delivered at the 1st Department of Obstetrics and Gynecology of the Medical University of Warsaw between January 1, 2020, and March 8, 2024. Pregnancies beyond 22 weeks with complete data were included in the analysis. *Results:* Among 6814 deliveries, 414 (6.1%) involved twins, with 210 (51%) being monochorionic and 204 (49%) dichorionic. Premature delivery occurred in 356 (86%) cases, with 67% of vaginal deliveries being preterm. Premature births were significantly more frequent in monochorionic twins (205; 98%) compared to dichorionic twins (110; 54%), $p < .0001$. Low birth weight (<1500 g) was observed in 76 newborns (18%), and there were 18 perinatal deaths (4%). Perinatal asphyxia (Apgar score <7) occurred in 32 monochorionic (8%) and 19 dichorionic (5%) twins, $p = .03$. *Conclusions:* More than half of twin pregnancies result in premature delivery, significantly increasing the risk of neonatal complications, particularly in monochorionic pregnancies, where the incidence of preterm births approaches 100%.

Delayed Interval Delivery in Twin Pregnancy

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Introduction: Multifetal gestations might be complicated by spontaneous preterm birth. When this occurs, lower gestational age fetuses have high risk of hospitalization and mortality. Delayed-interval delivery is a method when the interval between firstborn and second born are over 24 hours. *Method:* This case-control study was organized in clinic 'Hera-2011' in Tbilisi; Georgia. *Result:* We present the case of a dichorionic-diamniotic twin pregnancy of 24 1/7 weeks. The premature delivery of the first twin had lethal outcome. The second twin was born after 10 days and survived. *Case report:* A 34-year-old woman presented to the hospital with stomach cramps, was hospitalized with diagnosis of premature rupture of membranes. As an obstetric background G5P4, she had three physiological labor, one C-section. Ongoing pregnancy was conceived by in vitro fertilization (IVF). Two days after being discharged, she delivered a 600g living preterm newborn. After delivery of the first fetus, she was examined vaginally and the cervix had closed. After discussion with the maternal-fetal medicine team, there was continued monitoring of pregnancy, regularly measuring her complete blood count, inflammatory markers, temperature daily and the fetal heart rate. At 25 3/7 weeks of pregnancy, she delivered a 950g living preterm newborn with positive outcome. *Conclusion:* In this case, we confirm that delayed delivery after premature delivery of the 1st twin is a key, which improves the survival rate of the second twin.

Cognitive Disengagement Syndrome, ADHD and Emotional Dysregulation: Exploring Their Relationships Via a Twin Study

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Introduction: Data on the etiological factors underlying the co-occurrence of cognitive disengagement syndrome (CDS) with attention deficit and hyperactivity disorder (ADHD) and emotional dysregulation (ED) are very limited. *Materials & Methods:* The present study aimed to determine the nature of the relationships between these phenotypes, evaluating the role of possible common etiological factors in explaining their observed comorbidity, in 400 Italian twin pairs aged 8–18. *Results:* Data showed moderate to high phenotypic correlations supporting constructs' psychometric separation with some interdependence. Variability in CDS was attributed to genetic (29%) and environmental factors (71%), with unique environmental influences larger than those for ADHD (55%) and ED (25%). The best-fitting model, highlighted that substantial co-occurrence between these phenotypes arises from common additive genetic and unique environmental factors, suggesting a shared liability grounded in both biology and the environment. *Conclusions:* Our results support the adoption of a broader view of the relationships between CDS, ADHD, and ED in childhood and adolescence for both clinicians and educators.

'You and Me': Asymmetry In Twins' Development and Their Dominance Relationship Dynamics Throughout Childhood

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Introduction: We investigated how nontypical development affects dominance in twin relationships. While dominance among siblings often arises from age or developmental gaps, little is known about dominance dynamic betweem twins, who share similar ages and

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contexts. *Materials & Methods*: A longitudinal study surveyed 1547 mothers and 536 fathers of 322 monozygotic (sharing nearly 100% genes) and 1199 dizygotic (sharing 50% genetic variance) twin pairs, at four measurement points (age 3, 5, 6.5, and 8-9). Mothers and fathers reported on the twins' relationships and whether they had a developmental condition. *Results*: No dominance difference was found in similar developmental conditions dyads, whether both twins shared typical or nontypical development. However, in dyads in which twins differed in their developmental condition, nontypically developed twins were less dominant than their typically developed co-twins. This dominance imbalance persisted throughout childhood even if initial developmental issues were resolved. *Conclusions*: Nontypical development does not in and of itself prevent children from demonstrating dominance behaviours in twinship, but it is more likely that the asymmetry in developmental conditions is associated with the relationship between the twins. Children with nontypical development paths might experience dominance asymmetry with a typically developed sibling, while demonstrating dominancy might be possible for them in other contexts, such as with peers in a similar developmental condition. Understanding these dominance dynamics in siblings and twins is vital for parents and educators, informing tailored parenting strategies and interventions to support the wellbeing of children.

Does Twin Pregnancy Affect Mental Wellbeing: Cross Sectional Study of Over 90 Patients

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Introduction: Pregnant women expecting twins are at greater risk of stress, which may affect the quality of life and the physical and mental development of the fetus. Our aim was to investigate the prevalence of anxiety and depressive symptoms. *Material and methods:* An anonymous survey was made available electronically in May 2024. The study included 90 women in twin pregnancy and 2939 women in single pregnancy. *Results:* The 90 women with twin pregnancies were at mean 24 weeks of gestation. During single and twin pregnancy women consulted with a psychologist regularly (6% vs. 7%, $p = .8$). 50% of participants noticed deterioration of their mental condition during twin pregnancy. Symptoms of anxiety were reported by 56% of pregnant women and were related to the fear of losing the pregnancy. Participants reported symptoms of depression, with anhedonia lasting longer than 2 weeks in 37% of women in twin gestation. Women with anhedonia were mostly under the age of 30, in their second or third pregnancy. 25/31 women with anhedonia also had sleep problems, mainly related to waking up at night. In contrast only 21% of women in single pregnancy reported anhedonia ($n = 585$, $p < .01$). Two women in a twin pregnancy had suicidal ideation; they were in a dichorionic pregnancy with no previous health problems. Surprisingly, almost 9% of study participants smoked cigarettes regularly; another 7% drank alcohol from time to time. Women in twin gestation more often resigned from sexual activity during pregnancy than women in single gestation (34% vs. 20%, $p = .02$). The study participants mainly used private medical care — 68%, but most of them chose public centers for childbirth — 80%. The lack of family support (29%), which affected their emotional wellbeing was reported by women in twin gestation. In contrast only 18% of women in single pregnancy reported this problem ($p = .045$). *Conclusion:* Twin pregnancy affects maternal wellbeing. We need to optimize the care for women in twin gestation.

The Effect of External Exposome on Separation Between Cotwins

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Introduction: Twin separation involved leaving close siblings and often the parental home to begin independent living, as a key transition. This study examines environmental influences on age at separation and interrelationships among environments, under the exposome framework. *Materials and Methods:* The observation unit was the twin pair. Age at separation was obtained from the national registry. Three external exposome blocks were analyzed: physical (25 exposures) and neighborhood social (47 exposures) at separation (mean year: 2005, IQR: 2004–2007), and for cotwins who relocated (Cotwin 1) or stayed (Cotwin 2) after separation. Exposures at separation were measured in 2006 and linked to cotwins' geocodes just before separation; post-separation exposures were measured in 2012 and linked to geocodes in 2012. Exposome-wide association analysis evaluated effects on age at separation, while multiblock sparse partial least squares (MB-sPLS) analysis explored interrelationships among the blocks. *Results:* Among 1,767 twin pairs, three neighbourhood social exposures at separation were significantly associated with age at separation: the proportion of residents aged 20–29 and unemployment rates for ages 18–24 and over 55 in the community. Only the unemployment rate for those over 55 remained significant in dizygotic pairs. MB-sPLS identified a cluster of greenness exposures from Cotwin 1 and 2 blocks. *Conclusions:* Our study offers insights into the environmental determinants of separation behaviour.

Developmental Patterns in Intelligence: Three Novel Twin and Twin-Like Couples Compared

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Introduction: Previous research shows that the IQ scores of MZ cotwins tend to become more similar over time. In contrast, the IQ scores of DZ twins and adoptive siblings become more dissimilar. The present study compared developmental patterns in general intelligence of three novel types of twin and twin-like couples. *Materials and method:* Participants included young adopted-apart MZ twins from the Fullerton Study of Chinese Twins Reared Apart and Together, adult reared-apart MZ twins from a Danish study, and young virtual twins (VT: same-age unrelated sibling raised together) from the Fullerton Virtual Twin Study. Participants completed the age-appropriate form of the Wechsler IQ test on two occasions. *Results:* Both reared-apart MZ twin samples showed score convergence over time, but the effect was more marked in the younger sample. The VT pairs were less similar at the second testing. *Conclusions:* The findings variously reflect the effects of increased genetic influence (reared apart twins; VTs), the greater effects of nonshared

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environments (VTs), and the reduced impact of shared environments (VTs). These results assist understanding of how/why MZ twins' intelligence levels may converge over time. The findings should be additionally useful to families and educators concerned with the developmental patterns of academic performance in children and pupils.

New Books on Twins

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Introduction: Twins have captivated the imagination of both scientists and the public for centuries, occupying a unique place in cultural and scientific history worldwide. New books on twins are published each year and deserve attention for their informative and entertaining qualities. *Materials and methods:* Three authors will present overviews of four new books that cover a wide range of twin-related topics. The authors and their books are: Will Viney—*Twinkind* (2024), which looks at twins in myth and legend, anatomy, sociology, and genetics, and as sources of spectacle, entertainment, and community. Nancy L. Segal—*The Twin Children of the Holocaust* (2023)—presents an annotated collection of photographs taken at the 40th anniversary reunion of the twin survivors of Dr Josef Mengele's brutal medical experiments at Auschwitz-Birkenau and at related events; and *Gay Fathers, Twin Sons* (2023) concerns a high-profile lawsuit against the U.S. State Department and Secretary of State for denying U.S. citizenship to one twin son. David Tarnoki (in lieu of editors): *Twin Studies in Social Science* (2023, Andras Pári et al., Eds.) brings together selected papers by students and researchers from a Twin Research Workshop in Hungary that covers many psychological and physical characteristics of twins. *Results:* Collectively, these four books remind us that twins are scientifically informative at many levels. Twin research has significant implications that concern us all. *Conclusions.* New areas for twin research are continually evolving. New books that describe the work in this area are vital for communicating this information to researchers and families.

Tattooing is Mainly Cultural: A Representative Twin Study of Tattooing Determinants

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Introduction: Tattooing has become increasingly common in recent decades, yet little is known regarding factors that influence tattoo behavior. *Materials and methods*: From the population-based Danish Twin Tattoo Cohort established in 2021, the study included 9173 randomly selected twins born 1920–2004. Among these were 4790 (52%) responders to a questionnaire on tattooing and lifestyle factors. There were 55% females, 22% were monozygotic twins, and the median age was 51 years. Familial influence of tattooing over time was assessed by comparing monozygotic and dizygotic twin pairs. *Results:* Responders were population representative on sex, age, and lifestyle factors. The cumulative incidence of being tattooed before age 25 years increased markedly from 6% (95% CI 4–7%) for males and 0% (0–1%) for females born in 1925–1960 to 30% (25–35%) for males and 41% (37–46%) for females born in 1981–2004. Also, more than half of both the tattooed males and females born in 1981–2004 were younger than 20 years old when they had their first tattoo. Tattooing was over twice as common among ever smokers compared to never smokers born in 1981–2004 (average smoking effect at age 25 years: 36% (29–43%)). The likelihood of a twin getting tattooed if the co-twin is tattooed, was 2.0 (1.4–2.6) and 1.8 (1.5–2.2) times higher, for monozygotic and dizygotic twins, respectively. The findings indicate that variation in the likelihood of becoming tattooed is primarily explained by shared environmental factors 65% (35–95%), and that genetic influences explained little of this variation. *Conclusions:* This study demonstrates that strong environmental exposures shared by twin siblings irrespective of degree of genetic relatedness drive the choice for getting tattooed. We conclude that tattooing is a cultural group clustering phenomenon that goes beyond genetically oriented behavioral characteristics.

Risk Factors for Maltreatment of Children At 3 Years of Age in Japan: A Community-Based Study

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Background: Child maltreatment is globally recognized as a serious health and social problem as it not only directly threatens a child's health and safety but can also result in lifelong impediments. In Japan, the number of child maltreatment consultations is constantly increasing despite a decreasing number of children due to the declining birthrate. Against this background, local governments should provide effective maternal and child healthcare services to prevent child maltreatment. We aimed to identify factors predisposing to maltreatment at 3 years of age in Japan. *Methods:* Records on child maltreatment and health check-ups for children aged 3 years at a Public Health Center between April 2007 and March 2011 (n = 17,631) were utilized. The associations of child maltreatment with potential risk factors were analyzed using the logistic regression model. *Results*: There were 76 documented cases of child maltreatment (4.31 per 1000 children), and in 75% of them, the biological mother was suspected. After adjusting the results for a number of potential biological and social risk factors, factors predisposing to child maltreatment were the mother's poor self-rated health (odds ratio [*OR*], 12.89; 95% CI [7.11, 23.35]), multiple birth (*OR*, 4.06; 95% CI [1.34, 12.29]), lack of an adviser for child rearing (*OR*, 3.29; 95% CI [1.20, 9.06]), lack of cooperation from other family members or relatives for child rearing (*OR*, 2.44; 95% CI [1.07, 5.55]), and maternal employment (*OR* 2.66; 95% CI [1.47, 4.84] for full-time and 2.94 [1.23, 7.04] for part-time employment as compared to non-employment). *Conclusion:* Mothers with poor self-rated health and multiple births have a higher risk of child maltreatment. Health care providers should be aware that these factors can place considerable stress on a family and should provide appropriate support and intervention, starting with recognizing that mothers with these factors are potentially a high-risk group.

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Evolution and Heritability of Xenophilia and Xenophobia

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Introduction: We argue that attitudes towards migration have evolutionary roots and that both xenophilia and xenophobia have been important for survival. *Materials and methods:* We used the Europ. Social Survey to study attitudes towards migrants, the MIDUS twins to study the heritability of ingroup/outgroup attitudes, the WLS study and the Brisbane twins to study the genetic consequences of these attitudes. *Results:* As assumed from evolutionary assumptions, we found that men are more xenophobic than women, who become more xenophobic after the first birth. We further found that the heritability of ingroup/outgroup attitudes ranges from 19% to 46%, and that strong ingroup preference may lead to a risk of inbreeding and thus homozygosity. *Conclusions:* We conclude that both xenophilia and xenophobia are heritable, both have evolutionary roots and had been important for survival in small scale societies.

The Birth of Twins at a Brazilian University Hospital, Types of Delivery, and Psychological Care for Mothers in the Neonatal Intensive Care Unit — NICU

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Introduction: Twin pregnancies are considered high risk and premature births. *Materials and Methods:* The study was carried out in a Brazilian University Hospital in 2023. The type of delivery, gestational age and weight of the newborns, the number of stillbirths and postpartum deaths and the length of stay of the mother and twin babies were analyzed. In addition, psychological consultations were carried out and analyzed with four puerperal women whose twin babies were in the neonatal NICU. *Results:* Several babies had low birth weights and were discharged after up to 104 days of hospitalization, but there were some deaths of one or both twins. Mothers who lost twin babies reported feelings of guilt, sadness and, occasionally, anger at the healthcare team. When one twin was discharged and the other remained in hospital, the mother experienced ambivalent feelings denoting a mixture of joy and psychological pain. *Conclusion:* The pregnancy and birth of twins require more intense care from both an obstetric and psychological point of view.

Using the MZ Differences Design to Explore the Relationship Between Hormonal Contraception and Depression

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Introduction: Hormonal contraceptives (HC) are widely used and among the most effective forms of contraception available. Despite the benefits of HC, some users report adverse side effects such as negative mood changes, depression and anxiety. Using longitudinal twin data, we sought to explore the relationship between HC and depression from adolescence to young adulthood. *Methods and materials:* Data from Twins Early Development Study (TEDS) were used — a cohort study of twins born in England and Wales. We analyzed self-reported depression symptoms using the MFQ when twins were 12, 16, 21 and 26 years old. HC use was self-reported at 26 years old. Univariate and bivariate genetic twin models were used to estimate the heritability of HC use and the etiological association between HC use and depression. Longitudinal associations between HC use and depression were explored using Generalised Estimating Equation (GEE) models and incorporated the MZ differences design. *Results*: Genetic (.69, 95% CI [.59, .78]) and nonshared environmental (.31, 95% CI [.22, .41]) influences explained variance in lifetime ever HC use. Longitudinal analysis suggested that HC use was associated with reduced symptoms of depression over time. However, MZ differences GEE models suggested that this effect was no longer significant once genetic/familial effects were accounted for. Lower depression symptoms were however evident in MZ twins who used HC for longer than their co-twin. *Conclusions:* Our results suggest that HC use is genetically influenced. For those who continue to use HC, there seems to be a positive effect on their depression symptoms. More research is needed in this area to help individuals make informed decisions about their contraceptive choices.

Stability and Change of Physical Activity: A Longitudinal Twin Study

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Introduction: Physical activity levels are generally below recommendations for health across the U.S. population. This study investigated the influence of genetic and environmental factors on physical activity stability and change in a large sample of twins. *Materials and Methods:* Data were obtained from 8839 monozygotic and 4080 same-sex dizygotic twin pairs from the Washington State Twin Registry (WSTR), with measures obtained 1-5 times over 10.8 years. Two measures of subjective physical activity were used: neighborhood walking and moderate-to-vigorous physical activity (MVPA). Both outcomes were moderately correlated with device-measured neighborhood walking (r = .47, 95% CI [0.38, 0.56]) and MVPA (r = .48, 95% CI [0.39, 0.57]) in the WSTR. We fit longitudinal genetic simplex models to both measures. *Results:* Individual differences in walking increased over time by 31% and were explained by a stable genetic component (25%), a nonshared environmental component transmitted across time (34%), and occasion-specific genetic (5%) and nonshared environmental (36%) variance. Increasing variability in walking over time was driven by increases in nonshared environmental contributions (b = 0.82, $p < .000$). Individual differences in MVPA decreased over time by 8% and were explained by a stable genetic component (29%), a nonshared environmental component transmitted across time (32%), and occasion-specific genetic (6%) and nonshared environmental (36%) variance. *Conclusions:* Nonshared environmental variance

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components accounted for stability and change in physical activity behaviors over time whereas genetic variance primarily accounted for stability.

Investigating Genetic and Environmental Substrates of the Relationship Between Positive Mental Health and Biological Aging

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Introduction: The Italian National Institute of Health (Istituto Superiore di Sanità) funded a 30-month project (July 2021–January 2024) to conduct a twin study of the relationships between Positive Mental Health (PMH) and cellular longevity. Only a few studies focused on aging biomarkers in relation to psychological well-being, and none of them exploited the potential of the twin design. *Materials & Methods:* Following the standard procedures of the Italian Twin Registry (ITR), 401 twins (32% male; 58% monozygotic (MZ); mean age: 51 years; age range: 19-81 years), resident in Rome and its province were recruited. A self-report psychological test battery was administered to participants to evaluate several PMH components. Blood samples were collected from participants and were processed to determine telomere length (TL) and mitochondrial DNA copy number (mtDNAcn). *Results:* TL was positively associated with mtDNAcn and it decreased with age at visit; furthermore, both TL and mtDNAcn were higher in females compared to males, independently of age at visit. TL was negatively associated with an anxious attachment style, while mtDNAcn was positively associated with having a purpose in life. *Conclusions:* Data analysis is still underway. However, preliminary results showed promising associations between mental and biological functioning, which will be presented in greater detail at the congress.

Investigating Genetic Predispositions to Internalizing Symptoms Within the HiTOP Framework: A Network Analysis Approach

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Introduction: This research employs network analysis to investigate genetic predispositions to internalizing disorder symptoms within the Hierarchical Taxonomy of Psychopathology (HiTOP) framework. *Materials and Methods:* Using advanced network modeling based on the Ising model, we analyzed a sample of 312 twins (240 females; *M* age = 25.14; *SD* = 7.81). *Results:* The analysis reveals significant associations between certain SNPs and internalizing symptoms, highlighting the gene-specific nature of these relationships. Specifically, the *COMT, DRD2,* and *HTR1A* genes show notable associations with particular symptoms, while *BDNF* and *TPH2* do not exhibit significant connections. The findings also uncover nonlinear associations between symptoms and specific gene risk variants, with central symptoms in the network linked to certain genetic factors. Strong genetic associations were found for symptoms of social phobia and agoraphobia, and PTSD symptoms were linked to the *DRD2* gene. *Conclusions*: This study underscores the importance of focusing on symptom-specific genetic pathways, enhancing the understanding of the biological foundations of psychopathological conditions and advocating for an integrative approach in genetic psychopathology research.

Heritability and Correlates of Subjective Traumatic Distress Among Italian Twins

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Introduction: The COVID 19 pandemic has exposed a large part of the world population to prolonged traumatic distress, with a burden that emphasized the need to explore the etiological mechanisms behind this phenotype. This study aimed to assess genetic and environmental influences on the variability of psychological distress (PD) and investigate the role of the candidate gene MECP2 and modifiable risk factors in PD expression. *Materials & Methods:*- Adult twins enrolled in the Italian Twin Register filled in an online survey regarding demographic and socioeconomic characteristics, as well as pandemic-related PD (Impact of Event Scale Revised). Genetic and environmental influences on PD variability was evaluated using biometric modelling. Regression models were applied to identify unique environmental exposures potentially related to PD. Association analysis of selected MECP2 polymorphisms were performed on a subsample of previously genotyped twins. *Results:* 2974 twins participated in the study (mean age 46, 64% female) and for 170 of these, information on selected loci in the MECP2 region was available. Twin correlation for PD was higher in MZ than in DZ pairs. Biometric modelling showed that PD variability was mainly explained by genetic (36%) and unshared environmental (60%) influences, with a negligible shared environmental role; however, gender differences in variance components were suggested. Financial difficulties, educational attainment, and symptoms of depression or hypochondria emerged as significant unique environmental exposures. Preliminary results indicate the possible effect of MECP2 genotypes on PD. *Conclusions:* This study highlights the contribution of both genetic and unshared environmental components to PD variability, and proposes a role of specific factors within both components of variance.

East Flanders Prospective Twin Survey From 1964 to 2024

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Introduction: The East Flanders Prospective Twin Survey (EFPTS) is a multiple birth register that was started in 1964 by Robert Derom and Michel Thiery at Ghent University Hospital. *Materials and Methods:* The population-based register includes prospectively all multiples born in East Flanders, Belgium. Basic data on the pregnancy, delivery, neonates, and placenta are collected, on top a placental biopsy has been saved at -80°C in the biobank since 1969. The collected perinatal data and placental biopsy allow researchers to conduct follow-up studies. *Results:* In 2024, EFPTS celebrates its sixtieth birthday. At present, more than 10,800 twin pairs and 300

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triplet sets are included in the register. In the past years, the researchers in the EFPTS group have successfully conducted several follow-up studies in different domains such as cognitive and behavioral development, stress and depression, air pollution, influence on cardiovascular phenotypes, etc. EFPTS also provided important insights into the origin and development of twins. Through the years, the register had some difficulties such as finding financial support for the daily operations, the introduction of an informed consent in 2019 and the change to digital communication canals. Apart from the difficulties, the register made also huge improvements in the daily working: a re-evaluation of the data collection, a new structured electronic database was created to improve the data collection, and we are planning to perform a quality assessment on the placental biopsies. *Conclusion:* After 60 years, EFPTS maintains its ability to prospectively collect perinatal and biological data at birth, alongside later-life phenotypes, enabling their correlation. Given the impossibility of retrospective placentation analysis and challenges in identifying multiples born after ovulation induction, EFPTS prioritizes investigating the impact of chorion type, pregnancy origin, and epigenetic factors on later-life phenotypes. This underscores EFPTS's role in exploring not just genetic determinants but also connections between the (epi)genome, intrauterine environment, air pollution exposure, and (sub)clinical outcomes.

Heritability of Education, Life Cycle Earnings and Employment in Italian Twins: Differences By Age

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Introduction: A higher rate of social mobility is associated with lower inequality in welfare. To understand how genes and environment shape the inequality of key socio-economic outcomes we focused on education, lifetime earnings and employment. In particular, we used data on educational attainments, lifetime earnings and employment to study correlations among adult Italian twins and to estimate heritability. The analysis is performed on three age groups (<37, 37-39, 40+ years). *Methods:* Twins are enrolled in the Italian twin register and data on lifetime earnings come from the record linkage with a database that routinely collects labour income from all workers (9722 twins). ACE decomposition models by age-group are used in the analyses. *Results:* The estimated heritability in educational attainment varies over cohorts. For the youngest cohort we estimate heritability at 44% while for the other cohorts our estimates are larger, especially for the intermediate one (63% and 51% respectively). As for life cycle earnings, for the oldest cohort there is a greater share of inequality that can be attributed to individual factors (49%) compared to education (27%), and symmetrically a lower share due to genetics (24%), while the impact of shared environment is similar (27% and 23%). For younger cohorts we see instead that shared environment does not contribute for labour market inequality, which is instead explained in equal proportions by the genetic (49%) and individual components (51%) in the case of earnings, and for the majority accounted for by individual variation the case of working time (54 and 55%). *Conclusions:* Results show that a more flexible institutional environment is associated with a greater relevance of genetic versus shared environmental determinants of inequality. This relevance suggests that labour flexibility has amplified the impact of inherent abilities and traits, partly determined by genetics, on labour market success and career progression.

Recurrent Monozygotic Twinning After ART: A Case Report

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Introduction: Assisted reproductive technology (ART) increases the risk of monozygotic twin (MZT) pregnancy. While elective single-embryo transfer (eSET) reduces multiple gestations, monozygotic splitting remains possible. *Materials & Methods:* In 2021, a 43-year-old Caucasian woman with primary infertility was referred to a local private fertility clinic. She underwent one in-vitro fertilization (IVF) cycle with oocyte donation from a 20-year-old donor, which resulted in a successful culture of two high-quality blastocysts. Vaginal progesterone 200mg/die and estradiol transdermal patch 25 μg/24h were prescribed as hormone replacement therapy. The following check-ups were performed at S. Croce e Carle Hospital in Cuneo, Italy. *Results:* After the first blastocyst transfer, 5-weeks transvaginal sonography revealed one gestational sac in the uterus. At 12 weeks' screening exam, no fetal heart rate could be detected with a CRL of 21.9 mm and the head of the fetal mass was V-shaped, suggesting the presence of parapagus dicephalus conjoined twins. Spontaneous miscarriage of conjoined twins was diagnosed and the patient underwent pharmacological treatment. The remaining frozen blastocyte was subsequently transferred; at 7 weeks' gestation exam, a monochorionic monoamniotic twin pregnancy was diagnosed with both fetuses showing a normal cardiac activity. At 11 weeks ultrasound, neither of the fetuses had cardiac activity with a CRL of 15.6 mm and 15.3 mm respectively and a second pharmacological treatment for spontaneous miscarriage was performed. *Conclusions:* To our knowledge, this is one of the few reported cases of recurrent monozygotic twinning in two subsequent pregnancies obtained via IVF with eSET.

Epigenetic Signature of Monozygotic Twinning: A Tool to Study Connection Between the Vanishing Twin Syndrome and Amyoplasia

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Introduction: Amyoplasia is a nongenetic form of arthrogryposis, characterized by multiple contractures of the joints. The frequency of monozygotic (MZ) twins is increased by 10-fold among patients. It has been hypothesized that MZ twinning could be the cause of amyoplasia. To test this hypothesis, we applied an MZT epigenetic signature. *Materials & Methods:* The study included 21 Amyoplasia patients (8 males, 13 females; aged 4 months to 61 years). Surveys were completed online, with parents assisting participants <18 years old, and buccal swab were collected at home. Buccal DNA methylation profiles for 15 patients were generated using the Illumina EPICv2 array. The control group comprised 1036 MZ and 201 dizygotic (DZ) twins from the Netherlands Twin Register.

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A one-sample *t*-test compared differences in MZT epigenetic scores. *Results:* Of the 21 Amyoplasia patients, 61% reported twinning-related issues, such as being an MZ twin (n = 4), being diagnosed with vanishing twin syndrome (n = 2), or having twins in the family (n = 9). MZT epigenetic scores classified 11 of 15 patients as MZ twins, including 3 born as MZ twins and 8 born as singletons. Comparison of MZT epigenetic scores between Amyoplasia patients and healthy controls showed no significant difference from MZ twins (p = .19) but a significant difference from DZ twins (p = .005). *Conclusions:* Amyoplasia is associated with familial twinning and possibly related to epigenetics. The MZT epigenetic scores of Amyoplasia patients suggest these patients may initially develop as twins.

An Update on the Genetics of Dizygotic Twinning

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Introduction: The propensity to give birth to DZ twins differs around the globe, is associated with body size, maternal age and smoking and runs in families. Heritability is between 8 and 20%. In 2016 Mbarek et al. identified the first two loci for a woman to have natural DZ twins. *Materials and methods:* We conducted a genomewide association meta-analysis (GWAMA) of mothers of dizygotic (DZ) twins (8265 cases, 264,567 controls) and of independent DZ twin offspring (26,252 cases, 417,433 controls). Participants were screened to exclude twins born after use of Medically Assisted Reproduction (MAR). Genetic association analyses by cohort for being a DZ mother and being a DZ twin were combined by fixed-effects inverse variance methods (METAL) meta-analysis. To predict the most likely effector gene in a locus we applied FLAMES. *Results*: By enlarging sample size, we identified four new loci, in addition to FSHB (follicle stimulating hormone subunit beta) and SMAD3 (SMAD family member 3). Two — GNRH1 (gonadotropin releasing hormone 1) and FSHR (follicle stimulating hormone receptor) — have well-established roles in female reproduction. The two further novel genes were implicated by gene level enrichment analyses. Both *ZFPM1* (Zinc Finger Protein, FOG Family Member 1) and *IPO8* (Importin 8) have not previously been implicated. Genetic correlations were seen for multiple aspects of female reproduction and body size and with a recent GWAMA of female infertility. *Conclusion:* Our studies only included European ancestry cohorts. The 26 top SNPs predicted the crude twinning rates in 47 non-European populations (r = .23 between risk score and population prevalence, p = .058) indicating that GWAS are needed in African and Asian populations to explore the causes of their high and low DZ twinning rates. About 1 in 40 babies born in the world is a twin and there is still much unknown why they run in families. We hope our results will inform investigations of female fertility and infertility.

The Relation Between DZ Twinning and Female Fertility

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Introduction: Natural DZ twinning results from a double ovulation, has a genetic component and has often been proposed as an indicator for super-fertility. However, the direct relation between DZ twinning and fertility remains unclear as several characteristics associated with DZ twinning, including smoking and obesity, also are associated with infertility. Here we aim to analyze the relationship between DZ twinning and female (in) fertility based on recent findings from large GWAS studies. *Methods:* We calculated genetic correlations between DZ twinning and recent GWASs into female fertility-related phenotypes. We compared the DZ twinning polygenic score (PGS) in mothers of naturally conceived DZ twins with other mothers in the Netherlands Twin Register (NTR) and the Norwegian Mother, Father and Child Cohort Study (MoBa). Finally, we performed Mendelian randomization based on GWAS summary statistics to understand the relationship between smoking, DZ twinning and infertility. *Results*: DZ twinning has a strong negative genetic correlation with female fertility-related phenotypes including anovulatory infertility (locally up to -0.85), PCOS and age at menopause. The PGS analyses showed that the PGS for DZ twinning is capable of distinguishing mothers of naturally conceived pregnancies, and mothers who received Medically Assisted Reproduction (MAR) treatments and can also distinguish between different MAR treatments. *Conclusions:* We find indications that female fertility is a genetic spectrum with anovulation/infertility on the one end and DZ twinning on the other end. This further supports the idea that DZ twinning is an important model for understanding female infertility. First results hint at a potential use of the DZ twinning PGS in clinical settings, but also highlight that larger sample sizes and the inclusion of other ancestries are required to optimize the potential of DZ twinning for fertility research.

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DNA Methylation Signature of Monozygotic Twinning: Investigating the Relationship With Medically Assisted Reproduction, Higer-Order Gestations, and Common Genetic Variants

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Introduction: Here, we study a DNA methylation signature of monozygotic twinning in relation to Medically Assisted Reproduction (MAR), higher-order gestations, and genome-wide common genetic variants. *Materials and Methods:* DNA methylation datasets (Illumina 450k/EPIC arrays) from the Netherlands Twin Register were analyzed. Buccal DNA methylation was compared between 934 naturally conceived and 43 monozygotic twins conceived with IVF/ICSI (mean age = 9), and between 59 triplets, 198 twins, and 119 siblings of twins in an independent buccal dataset (mean age = 15). A genomewide association study (GWAS) on the monozygotic twinning DNA methylation score was performed (Blood, $N = 2841$, mean age = 37, Buccal, N = 1150, mean age = 10). *Results:* 29 differentially methylated CpGs were detected between monozygotic twins conceived after IVF/ICSI compared to naturally conceived monozygotic twins. None of the 834 CpGs detected in our previous EWAS meta-analysis of monozygotic twinning were associated with MAR. The monozygotic twinning epigenetic signature showed similar performance in buccal DNA methylation data as previously observed (81% of monozygotic twins correctly classified). Sensitivity was highest for monozygotic triplets, but specificity remains moderate. GWAS analysis identified 3 genomewide significant loci in blood and none in buccal. The top SNP (rs76157694, MAF = 0.25) maps to TBX4; an embryonic transcription factor involved in hindlimb development. *Conclusions:* Monozygotic twinning and MAR show largely distinct DNA methylation signatures. Monozygotic triplets, like monozygotic twins, carry a comparable but stronger DNA methylation signature.

Mapping Multiple Birth Care During the First 1001 Critical Days: A World Café Method Study

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Introduction: The first 1001 days from conception to 2 years of age is a vital time for brain development of the child. Parents of twins, triplets or more (multiple birth families) face unique emotional and physical challenges during this critical time. Multiple birth families are often overlooked and unheard in policy and practice in the first 1001 days. Health professionals lack specific training on how to best care for multiple birth families, leaving them with unmet needs. This research in partnership with Twins Trust and the Institute of Health Visiting, funded by The Wellcome Trust through the British Academy/Leverhulme Small Research Grants Scheme, seeks to identify opportunities to improve care. *Materials and Methods:* A family friendly series of events will be held, bringing together multiple birth families and health professionals to capture their experiences of care. The World Café approach is an established method that enables the sharing of knowledge in a structured conversational way in small groups at several tables, like in a café. Events are planned for late 2024 and early 2025. *Results*: A professional facing document will be produced and a family facing parent stories resource to collectively drive improved multiple birth family care. This will include images captured by an illustrator in real time during the events. *Conclusions:* Using World Café methods, we will bring together professionals and parents to jointly discover 'quick wins' and further identify opportunities to improve the experience of care for multiple birth families.

Exploring the Experiences of Adolescent Identical Female Twins in the United Kingdom

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Introduction: This narrative inquiry study aimed to explore the experiences of adolescent identical female twins in the United Kingdom throughout their life course. *Materials and Methods:* The study involved 16 participants, in eight twin pairs, aged 10 – 17. Each participant was interviewed twice via Microsoft Teams, with the second interview also incorporating a photo-elicitation activity. *Results:* The study provided insight into evolution of the inter-twin relationship and the interaction between twins and their social surroundings. Generally, twins viewed their twinship positively, however, the perceptions of twins and twinship in wider society were challenging. *Conclusions:* Initial findings indicate a tension between the participants' positive perceptions of their twin relationship and the work to be seen as an individual within wider society.

Adverse Effect of High-Risk Fetal Ultrasound: Impacts and Implications of Monoamniotic - Monochorionic Twin Diagnosis

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This case report addresses the initial ultrasound diagnosis of a monomono twin pregnancy, its impact on the birth parents and birth maternal grandparents, and the lack of accessible, cost-effective delivery of nonpharmaceutical care to patients reporting adverse emotional responses to high-risk fetal diagnosis provided by specialized professionals within the OB-GYN clinic. With over 20 years as a sonographer in a high-risk perinatal unit and having acquired a PhD in fetal medicine, IEZ was the first to scan our 28-year-old daughter's first pregnancy verifying twins. Subsequent scans confirmed monoamniotic monochorionic twin pregnancy. Communication with our daughter became overt support and covert panic. My hair turned grey overnight. My daughter received excellent prenatal care resulting in a successful cesarian delivery at 34 weeks and discharge of twin boys at 38 weeks from NICU. The boys are 19 years old now and finished the first year of college. Although the literature with first-line interventions for emotional management relative to high-risk fetal ultrasound diagnosis is limited, existing evidence indicates maternal stress and anxiety can adversely influence fetal states, perhaps viability outcomes. Post-partum depression increasingly plagues our patient populations. Surprisingly, therefore, first-line management interventions to offset adverse responses to extreme

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levels of anxiety as demonstrated here are not yet part of the OBGYN standard of care. Assessment of accredited, evidence-based, non-pharmaceutical, accessible self-management techniques can provide cost-effective approaches to the maternal-fetal high-risk populations, thus providing not only maternal compliance and function, but ensuring skills that can offset postpartum depression and related comorbidities. Pivotal studies on first-line interventions noted here include the groundbreaking work of MFM physicians and their fellows in our department

Early Interaction During Multiple-Birth Pregnancy — View of the Mothers of Twins

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Introduction: Early interaction and bonding can be challenging for mother/parent when it is a question of more than one child at the same time. *Materials & Methods:* Research is part of the TWIN LIFE 2021-26 'Nurses' Competence in Multiple-Birth Family Nursing' project. The aim was to describe the early interaction from view of the twin pregnant mothers (n = 11). The data were collected by interviews and analyzed by content analysis. *Results:* Already during pregnancy, the confusion and anxiety, can affect to the early interaction. Mothers recognized the fetuses and interacted from each other in many ways. The most significant moment was when the mother felt their movements. Telling the fetuses as individuals becomes easier as pregnancy progresses, but half of the mothers felt that they were not able to tell the two fetuses apart. Early interaction support parenting growth and the role of parenting, but more than half of the mothers felt lack of support by health and social care professionals. *Conclusions:* A multiple-birth family is a special family with individual and specific needs. These needs are not yet recognized in family nursing care. Special knowledge needed to support mothers and parents with multiples during pregnancy and after birth. Education and training are needed to enable the development of multiple-birth family expertise. Further studies are required on early interaction and bonding, education, intervention, and impact.

Intrauterine Growth Restriction: Etiologies and Prognosis

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Introduction: Intrauterine growth restriction (IUGR) is a common condition. Early detection and diagnosis are essential for appropriate management, as IUGR is associated with significant fetal mortality and morbidity. Our study aims to investigate the etiological factors, diagnostic methods, and short-term neonatal prognosis of IUGR. *Materials and methods:* Our study examines 40 cases of newborns with IUGR at birth, born between January 2019 and December 31, 2021. *Results:* In our study, the ages of the patients ranged from 17 to 42 years, with a mean maternal age of 28 years. 23 patients were primiparous, representing 51.11% of our population. 15 patients had a history of IUGR (37%), 5 had at least two previous spontaneous miscarriages, 2 had a history of perinatal death, 3 had a history of gestational hypertension, 3 had a history of preeclampsia, and 1 patient had a history of HELLP syndrome. The average term for IUGR diagnosis was 30 weeks and 6 days. The etiologies of IUGR were distributed as follows: vascular in 42.5% of cases, chromosomal in 7.5%, uterine malformations in 7.5%, infectious in 2.5%, and unexplained in 40%. Cesarean delivery was performed in 60% of cases, with the most common indication being pathological fetal heart rate. The preterm birth rate was 33%, and the average birth weight was 2100 g. *Conclusion:* The detection of intrauterine growth restriction is crucial due to the associated high fetal mortality and morbidity. Vascular causes are the primary etiology, but idiopathic IUGR remains significant. For known vascular IUGR detected antenatally, appropriate monitoring is essential to identify severe signs and take necessary actions.

The Sri Lankan Twin Registry: The First and the Largest Twin Research Program in a Low- and Middle-Income Country

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Introduction: The Sri Lankan Twin Registry (SLTR), established in 1996 is the first-ever twin register in South Asia and a unique resource for twin and genetic research in a low-and-middle-income country (LMIC). It comprises a volunteer cohort of 7,060 pairs of twins and 119 sets of triplets, and a population-based cohort of 9,520 pairs of twins and 89 sets of triplets. *Materials & Methods:* The SLTR has contributed to several multi-component projects in Colombo, Sri Lanka. The Colombo Twin and Singleton Study (COTASS) is the first and largest South Asian twin prospective study. COTASS 1 (2005–2007) explored the prevalence and heritability of various psychiatric disorders and gene-environmental interplay. COTASS 2 (2012–2015) was a follow-up to assess the prevalence and interrelationship of metabolic syndrome and psychiatric disorders. Biospecimens were collected for clinical investigations and to develop the SLTR biobank. COTASS 2 also included two sub-studies which collected sleep, physical activity, and heart rate variability data. COTASS 3 (2021-2023) assessed the feasibility of using nutrition and dietary data within a Children-of-Twins design. In 2019 the SLTR was expanded by developing a twin register with infant, child and adolescent twins, and mothers pregnant with twins. *Results:* The SLTR biobank houses 3369 DNA and serum samples linked to longitudinal questionnaire data, clinical investigations, and anthropometric measurements, providing a unique resource for future research. Since its inception, SLTR has contributed to over 30 journal publications. *Conclusions:* SLTR is a classic showcase of successful North-South partnerships in building a progressive research infrastructure in an LMIC.

Cornual Placenta Acreta With Twin Intrauterine Pregnancy With Mini Modified B-Lynch Suture Resulting in a Successful Live Birth

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Introduction: This report discusses a case of cornual placenta accreta associated with a twin intrauterine pregnancy in a 24-year-old

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woman, highlighting the complexities of managing such a condition. We report a case of a 24-year-old G3P0 + 2, who presented to us with complaints of decreased fetal movements at 33 + 5 weeks gestation. She is a case of IVF conception of twin intrauterine pregnancy with a cornual heterotopic Ultrasound revealed a DCDA twin live intrauterine fetus with anterior and fundal placenta with first twin in transverse presentation and second twin in extended breech presentation. *Methods:* Initially managed conservatively with steroids for lung maturity, the patient's situation rapidly changed to require an emergency cesarean section due to preterm premature rupture of membranes and labor onset. During surgery, two healthy twins were delivered, weighing 1.8 kg and 1.6 kg. However, complications arose when substantial vascular invasion was found in the right cornual region of the uterus, leading to postpartum haemorrhage (PPH). Immediate management included the application of a modified B-Lynch uterine compression suture to control the bleeding, alongside administering blood transfusions for the PPH. Postoperative recovery was uneventful. *Results:* The report emphasizes the rising incidence of cornual pregnancies, particularly due to assisted reproductive technologies, and the high risk of maternal morbidity associated with these cases, including severe haemorrhage. Accurate ultrasound evaluation is crucial, but clinical risk factors are equally vital for diagnosis. The discussion also outlines how uterine compression sutures are pivotal in managing PPH, with the modified B-Lynch technique providing a solution to prevent sutures from slipping, thereby improving surgical outcomes. *Conclusion:* Overall, the case illustrates the potential for successful management of cornual pregnancies with timely interventions, highlighting the necessity for individualized treatment strategies to preserve intrauterine pregnancies while mitigating risks of severe complications. The complexities of diagnosis and management, and the need for vigilant monitoring underscore the challenges clinicians face with cornual heterotopic pregnancies, yet an effective approach can yield positive outcomes for both mother and infants.

The Influence of Parity in the Outcome of Twin Pregnancies

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Introduction: The aim of this study is to analyze the outcome of nulliparous women versus pluriparous women with twin pregnancies. *Methods:* We conducted a retrospective cohort study of twin pregnancies in our department between 2003 and 2009. Population characteristics, complications during pregnancy and delivery, and neonatal outcomes were assessed. Student's t-test and Fisher exact test, were used to examine the relationship between different variables, parity, maternal age, mode of conception, chorionicity, mode of delivery, total twin birth (TTBW). $p < .05$ was considered significant. *Results*: A total of 415 twin pregnancies were enrolled. Maternal age was statistically significant in the nulliparous versus pluriparous ($p = .007$) and also the TTBW ($p = .002$). Nulliparous have significant chance to have ART, *OR* 3.4 95% CI [1.9, 5.9]. *Conclusion:* Pluriparous women with twin gestation conceive more spontanously and the weight of their twins is increased comparing with nulliparous women. Nulliparous women with twin pregnancies are much younger than pluriparous and have more chances to conceive with assisted reproductive technology.

Acceptance of Vaginal Delivery During Twin Pregnancy

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Introduction: Twin pregnancies are on the rise worldwide due to the increase in assisted reproduction. The birth of twins can be the cause of difficulties and complications that can affect the maternal and neonatal state at the end of this delivery, for this knowledge of the criteria and limits of acceptance of vaginal delivery is necessary. *Materials and method:* Descriptive retrospective study conducted in the maternity department of Béja spread over 36 months including parturiants between 27 and 40 weeks of age with a twin pregnancy. 72 cases have been reported. *Results:* The mean maternal age was 30.41 years, delivery term 36SA+6d, 24.32% had dysgravidia (12.16% had PAH, 13.68% had gestational diabetes), 62 of the twin pregnancies were bichorionic biamniotic and 10 of the twin pregnancies were monochorionic of which 4 were biamniotic. On average, parturients were 2nd gesture. The vaginal approach was accepted from the outset in 38.8% of cases, the use of cesarean section in 61.2%.The indications were: uni-scarred uterus in labor in 22.7%, bi-scar uterus in labor in 9.1%, stagnation of dilation in 9.1%, primiparous patient with j1 site in 22.7%, transfusion syndrome transfused in 4%, twin pregnancy with preeclampsia in 9.1% and failure to induct in 18.18% of cases. For deliveries in case of d1 in breech presentation, the criteria that were respected are a PFE between 2500–3800 g, BIP < 98 mm and a well-flexed head. *Conclusion:* Twin pregnancy is responsible for the increase in caesarean section rates with all the risks incurred in subsequent pregnancies, A good knowledge of the indications for cesarean section can reduce this rate.

Exploring the Experiences and Needs of Multiple Birth Fathers During the Early Years Through Twins Trust's Charity Peer Support Service: A Project Justification

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Introduction: The first 1001 days of childhood are crucial for lifelong wellbeing, while the brain grows and develops rapidly. Primary caregiver relationships impact abilities to learn, work, and form relationships, and impact stress and disadvantage. Our recent rapid review found a pronounced lack of understanding about multiple birth fathers' perspectives during the early year. Exploring these needs will inform further research and supportive strategies, emphasised due to the UK's rising cost of living. In collaboration with Twins Trust's Peer Support Service for fathers, we aim to explore multiple birth fathers' experiences/needs during the early years and to review and report on the peer support service. Twins Trust is the leading UK charity providing multiple birth family support. *Materials and method:* The study will be a qualitatively driven multiple methods design, inspired by Morse and Cheek, 2014: Interviews with the peer support volunteers on their personal motivations for establishing the peer support service and experiences responding to fathers' needs; An anonymised open-ended survey distributed to the Twins Trust. Dads of Multiples Facebook Group, exploring lived experiences; Analysis of secondary data collected via an existing registration form. *Results:* Data collection: Sept 2024. Outputs: Journal and conference submissions; Findings will inform future applications, including international collaborations with Kristiina Heinonen, from University of Eastern Finland; A report for Twins Trust to

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inform their Impact Report; Summaries disseminated to appropriate networks. *Conclusion:* This pilot project will assist understanding of multiple birth fathers' experiences and needs informing further research and international collaboration. It will inform Twins Trust and early years services on how they can best support fathers during the early years.

Exploring Opinions Towards Interventions to Prepare and Support Siblings for Neonatal Journeys: Including the Views and Opinions of NICU Staff, Parents of NICU Siblings and Child Psychology Experts

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Introduction: Annually, around 1 in 7 UK babies are admitted onto neonatal units, with multiples at increased admission risk alongside additional complexities, like separation. Older siblings can experience negative outcomes, like anger and disrupted sleep and school behaviours within and after a neonatal experience. A 2020 review found that NICU sibling support remains lacking and under researched. This project gained insight into intervention approaches to support siblings of neonatal babies. *Methods:* Two online workshops (parents and professionals) utilised a modified nominal group technique, consisting of open-ended questions, a mind map, and a prioritisation exercise. Deductive content analysis followed SAGE's Guidebook and Elo and Kyngäs's (2008) phases of preparation, organizing and reporting. Ulrich's (1991) Theory of Supportive Design informed the themes. *Results:* Discussions covered both in-person and technological support approaches. Evidence was found in support of Ulrich's (1991) Theory of Supportive Design, alongside additional reflections on practical and ethical considerations. Frequently noted was the need for conveying information efficiently and from a child's POV, alongside the importance of reducing uncertainty about medical objects, the parents' behaviour, and the health of the babies. Various visual, audio, and interactive approaches were liked, particularly those with the flexibility to be made age-appropriate, engaging, and equitably accessible. The context of whole-family trauma was highlighted, alongside the use of milestone-led, narrative storytelling and trauma-informed principles. *Conclusions:* Parents and professionals highlighted a need for sibling support. Discussions backed the flexibility and equitability of technological interventions. Implementation challenges included nonlinear neonatal journeys, bereavement risks, inequitable provision, and variations in visitation and engagement.

A Danish National Twin-Family Study of COVID-19 Infection

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Introduction: The COVID-19 pandemic was characterized by highly variable SARS-CoV-2 infection susceptibility in otherwise comparable individuals. We aim to shed light on the underlying mechanisms. *Methods:* Through linkage of the Danish Twin Registry and the COVID-19 Surveillance Registry we mapped familial aggregation of SARS-CoV-2 infections in Danish adult twins and their spouses. *Results:* More than 96% of the study population was tested during the pandemic. Only 4% were tested positive during the two first waves. Spouses consistently showed the highest recurrence rates, followed by similar concordance rates for MZ and ssDZ twins, and lower rates for osDZ suggesting that social distance was the key determinant. The third and last wave of the pandemic had a very high infection rate (56%). The recurrence/concordance rates for spouses, MZ, ssDZ and osDZ suggested some genetic influence. *Conclusions:* The familial aggregation pattern of COVID-19 infections in the first two waves of the pandemic was compatible with the degree of contact being the main determinant of infection, while there was no indication of genetic influence. However, in the third wave with high infections rates, genetic influence was detectable in the Danish population.

Does Reproduction Come at the Expense of a Shorter Life?

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Introduction: Life history theory predicts that organisms face trade-offs between resources invested in reproduction versus somatic maintenance. In this context, aging is the price of natural selection for reproductive success. However, it remains unclear whether reproductive investment accelerates the rate of aging in itself. *Materials & Methods:* Here, we use a twin study design to revisit the most famous hypothesis of evolutionary biology: the trade-off between reproduction and lifespan. We assessed how the number and timing of pregnancies predicts lifespan and DNA methylation-based epigenetic age acceleration in the Finnish Twin Cohort, with women born between 1880-1958. Our approach accounts for not just the number but also the timing of childbirths by identifying latent reproductive patterns across 17,175 Finnish twins, bringing insight into female reproductive behavior in contemporary societies. *Results:* By adjusting for familial background and genetics as well as socioeconomic background and lifestyle, that early childbearing and increased number of lifetime pregnancies accelerates aging and increases mortality risk compared to women who have only fewer pregnancies later in life. *Conclusions:* Our results suggest lifelong reproductive investment might incur costs on one's aging rate that reflect the history of cellular stress and maintenance, which are stored as epigenetic patterns. However, as found in previous studies, women who never give birth exhibit the most accelerated aging and lowest survival, potentially due to confounding factors such as poor initial health. Our results support the theorized tradeoff between reproduction and lifespan, elucidating how reproduction underlies aging through the prism of evolutionary theories, ultimately deepening our understanding of the determinants of healthy aging.

Heritability of Children and Adolescents' Dietary Intakes and Physical Activity: A Twin Study in Iran

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Introduction: Besides the home environment, the resemblance in dietary intakes and physical activity between children and their parents might suggest a potential role for genetic factors. We aimed to investigate the relative genetic and environmental impacts on

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dietary intake and physical activity of Iranian children and adolescents. *Materials & Methods:* This cross-sectional analysis was performed on 566 (148 monozygotic and 428 dizygotic) pairs aged 2 to 18 years in the Isfahan Twin Registry (ITR). Dietary intake was evaluated using a validated food frequency questionnaire and physical activity was determined using International Physical Activity Questionnaire (IPAQ). DASH and Mediterranean dietary patterns were calculated. *Results:* After fitting structural equation models, the ACE model was the best-fitting model for total fat, saturated and poly unsaturated fatty acids while for the remaining CE model was the best-fitting model. Both MED and DASH scores were affected by additive genetic (24% and 12%) and the remained proportion of variance was defined by C as a shared environment effect (69% and 84%). Physical activity and all related domains were affected by genetic except for transportation that was strongly influenced by the shared environmental. *Conclusions:* Our results indicate that genetic factors have an important influence on determining fat intake and dietary patterns. Physical activity, but not transportation activities, are also influenced by genetic.

Radiomics Analysis of Carotid and Femoral Atherosclerotic Plaques in Twins

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Introduction: Atherosclerotic plaques frequently affect the vascular system. Analyzing plaque morphology and texture is essential for assessing plaque vulnerability, with progression marked by ulceration, rupture, neovascularization, and intraplaque hemorrhage, all closely linked to CVD. However, the association with cardiovascular risk factors remains limited. This study evaluated the correlation between the texture of femoral and carotid atherosclerotic plaques and the lipid panel, blood pressure, and arterial stiffness in a healthy twin population. *Methods:* We evaluated 85 healthy adult Caucasian twins (41 pairs and 1 triplet) from the Hungarian twin registry, excluding those with a history of cerebrovascular events. Of these, 46 patients (25 monozygotic, 21 dizygotic) with an average age of 60.3±10.1 years were analyzed for plaque texture. They underwent carotid and femoral artery ultrasound imaging, blood pressure, and body composition measurement. Atherosclerotic plaques were marked and delineated upon detection. Texture analysis with MaZda software generated 303 texture features. Correlative statistical analysis was performed between these features and physiological data. *Results*: Spearman correlation coefficients were calculated between 7 physiological parameters and 26 selected carotid and femoral plaque texture features. Significant correlations were found with diastolic blood pressure, LDL-cholesterol, arterial stiffness, and visceral fat percentage ($p < .04$). No significant correlations were observed with body fat percentage, serum HDL-cholesterol, total cholesterol, and triglyceride levels. *Conclusion:* Carotid and femoral plaque texture features are linked to certain cardiovascular risk factors, suggesting potential targets for future clinical studies on plaque risk management. Clinical trials on the effects of lipid-lowering or antihypertensive medications on plaque texture and progression could enhance atherosclerosis management.

Twin Pregnancy Following Assisted Reproduction and HELLP Syndrome: A Population-Based Study

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Background: The association between in-vitro fertilization (IVF), twin pregnancy, and HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets) is understudied. We compared the rates of HELLP syndrome in twin versus singleton pregnancies following spontaneous and IVF conception. *Methods:* All women with singleton or twin live birth or stillbirth in British Columbia, 2008/09-2020/21 were included; data were obtained from the British Columbia Perinatal Database Registry. We used logistic regression to adjust for potential confounders (e.g., maternal age, smoking, and body mass index), and to assess modification of the association between singleton/twin pregnancy by mode of conception. *Results*: Among 523,867 women, 16,707 (3.2%) women conceived using IVF. The proportion of twin deliveries was 14.7% (2455/16,707) among women who conceived by IVF, and 1.2% (5882/507,160) among women with spontaneous conception. Among women who conceived by IVF, the rates of HELLP syndrome in twin versus singleton pregnancies were 2.6% versus 0.6% respectively; among those who conceived spontaneously, HELLP syndrome rates were 2.3% versus 0.3% respectively. The adjusted odds ratio (AOR) for HELLP syndrome in twin versus singleton pregnancy in women who conceived by in-vitro fertilization was 3.83, 95% CI [2.76, 5.30]), while the AOR among women who conceived spontaneously was 8.34, 95% CI [6.98, 9.97]; *p* value for interaction. Results were similar in sensitivity analyses restricted to opposite-sex twin (dichorionic). *Conclusion:* Mode of conception modifies the association between twin versus singleton pregnancy and HELLP syndrome. The risk of HELLP syndrome in twin pregnancy (following either spontaneous conception or in-vitro fertilization) is substantially higher than the risk of HELLP syndrome among women who conceive singletons spontaneously. Our results inform preconception counseling and prenatal care for women who plan to conceive by IVF.

Perinatal Outcomes of Complicated Monochorionic Diamniotic Twins: A Single-Center First Three Years' Experience

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Introduction: Monochorionic diamniotic (MCDA) twin pregnancies are at increased risk for complications like twin-to-twin transfusion syndrome (TTTS) and selective fetal growth restriction (s-FGR). Fetoscopic laser coagulation (FLC) has been established as the treatment of choice for TTTS. *Material and Methods:* In this retrospective study, we included all complicated MCDA underwent FLC at our Center during 3 years. We analyzed perinatal outcomes comparing TTTS group and TTTS+s-FGR group, according to Delphi criteria. *Results:* Over a total of 150 cases of MCDA, 60 (40%) underwent

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FLC. In 20 cases the indication was TTTS only (33%) and in 40 was TTTS+s-FGR (66%). Most of cases underwent surgery had a Quintero stage 2 and 3 (33.3% and 56.6%). FLC was performed also in Stage 1 (8.3%) for obstetrical indication. Pre-FLC Doppler analysis showed donor umbilical artery (UA) absent-reverse end diastolic flow (ARED) in 10% of TTTS cases and in 68% of TTTS+s-FGR ($p < .0001$). The comparison of donor UA-PI between the two groups resulted significant ($p = .02$). No statistical difference emerged in recipient UA doppler. No difference emerged in ductus venosus at all. The survival rate at birth of at least one twin was 85% and 80% in TTTS and TTTS with s-FGR respectively ($p = .94$). Donor and recipient survival was significantly different between the two groups (donor: 94% and 65%, $p = .006$; recipient: 82% and 100%, $p = .01$). *Conclusions:* The coexistence of s-FGR with TTTS significantly worsens the donor survival after FLC.

Can PPROM in Monochorionic Twins With Discordant Amniotic Fluid Lead to Feto-Fetal Transfusion and TAPS: A Case Study

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Introduction: A case report of amniotic fluid discordance in MCDA twins with resultant reversal of inter-twin fluid discordance, intracranial hemorrhage (ICH) and anemia in co-twin following preterm PROM. *Materials & Methods:* A 33-year-old primigravida with MCDA twins was transferred to our perinatal centre at 26 weeks post PPROM. Pre-PPROM ultrasound (US) at 24 weeks showed Twin-A MVP 4.1 cm while Twin-B MVP 9.1 cm with normal MCA-PSVs. PPROM occurred at 25+4 weeks. At 26 weeks, US revealed twin A MVP of 11.9 cm, while twin B MVP 4.6 cm and anemia (MCA-PSV 1.86). ICH in co-twin A was noted along with a midline shift making assessment of MCA-PSV difficult. Fetal bradycardia of twin B prompted delivery at 26 weeks. Care was withdrawn due to poor response of both. Placental perfusion study confirmed Veno-Venous and Arterio-Arterial anastomosis. Post-mortem examination revealed appropriate growth parameters with cardiomegaly in twin A. *Discussion:* This case illustrates reversal in inter-twin amniotic fluid distribution following PPROM with acute TAPS leading to severe ICH in twin-A and anemia in co-twin. We speculate an evolving TTTS and subsequent hemodynamic compromise through shunt reversal. Reversal of TTTS has been previously reported following fetoscopy laser photocoagulation (FLP) of communicating vessels. Amnioreduction, has been rationalized to exert beneficial effects through decompressive effects on communicating vessels within the placental bed. Similarly, sudden decompression of intraamniotic pressure following PPROM in the recipient twin may have opened up compressed placental anastomosis leading to acute perfusion of previous donor, causing acute polyhydramnios, ICH and anemia in the previous recipient. *Conclusions:* Careful evaluation of MCDA twins with fluid discordance following PPROM should be assessed for individual amniotic fluid volumes, MCA-PSV and fetal well-being as feto-fetal transfusion can occur as a consequence of uterine decompression.

A Comparison of Maternal and Perinatal Outcomes in Selective Fetal Growth Restriction in Monochorionic Diamniotic Twins Diagnosed By the Traditional and Delphi Criteria

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Introduction: The purpose of this study is to compare the maternal and perinatal outcomes of selective fetal growth restriction (sFGR) in monochorionic diamniotic (MCDA) twins diagnosed using the traditional and Delphi criteria. *Materials and Methods:* This is a retrospective analysis of MCDA twins ≥ 20 weeks gestation, delivered at a single centre between June 2019 to December 2023. Antenatal ultrasounds were reviewed to extract parameters for diagnosis of sFGR using either the traditional criteria or the Delphi criteria. sFGR was diagnosed if either criteria was met at least once. Three groups of MCDA twins were compared: uncomplicated MCDA twins (group 1), sFGR via the traditional criteria (group 2) and sFGR via the Delphi criteria (group 3). Maternal and perinatal outcomes were assessed which included gestational age at diagnosis, percentage birth weight discordance, gestational age at delivery, cesarean section rates, and a composite of neonatal outcomes. *Results:* To date, 63 MCDA pregnancies were included in the study. Of these, 23 (36.5%) were assigned to group 1, 22 (34.9%) to group 2, and 18 (28.6%) to group 3. The mean gestational age at diagnosis of sFGR in groups 2 and 3 were 26.9 and 29.4 weeks respectively. The mean gestational age at delivery for groups 1,2 and 3 were 35.0, 28.6 and 35.4 weeks respectively. The cesarean section rates for groups 1, 2 and 3 were 26.1%, 86.4% and 55.6% respectively. The mean percentage birth weight discordance for groups 1, 2 and 3 were 10.98%, 31.35% and 16.14% respectively. Neonatal outcomes will be collected as data collection proceeds. *Conclusion:* Early analysis of MCDA twins with sFGR shows a lower gestational age at delivery, a higher cesarean section rate, and better correlation with discordance in actual birth weight in pregnancies meeting the traditional criteria compared to those diagnosed by the Delphi criteria. Data collection is ongoing to increase sample size and confirm currently observed differences.

Monochorionic Twin Pregnancies Complicated With Twin Reverse Arterial Perfusion Sequence: Comparing Different Management at a Single Center

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Introduction: Twin Reverse Arterial Perfusion Sequence (TRAPs) is a rare complication of monochorionic pregnancies, where an acardiac twin is perfused by the 'pump' twin, which has high risk of demise due to cardiac overload. This study evaluates perinatal outcomes in

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cases managed at our center. *Materials & Methods:* A 13-year retrospective observational study of monochorionic pregnancies complicated by TRAPs, treated with coagulation of the acardiac twin's artery using diode laser fiber, microwave (MW), or bipolar forceps under ultrasound guidance. *Results:* Sixty-four cases, diagnosed between 11 and 24 weeks, were included. Among 27 expectant cases, there were 2 miscarriages, 5 pump twin deaths, and 9 spontaneous acardiac twin demises with no consequences for the pump twin. MW coagulation (7 cases) showed the highest pump twin survival (87%), compared to laser (50%) and bipolar forceps (50%) and a longer procedure-delivery interval. Acardiac twin had shorter diameter in untreated cases(36 mm) compared to laser (67.5 mm) or MW (67 mm) groups. Neonatal mortality occurred only in the untreated group (13%) and 1 case of postnatal neurological delay was observed in both laser and MW group. *Conclusion:* TRAPs ceases spontaneously when acardiac size is shorter. When treatment is required, microwave coagulation offers the best survival outcomes according to our data.

Twin Simulation Training Evaluation Research: A Retrospective Evaluation of Obstetrical Outcomes Before and After Twin Simulation-Based Training

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Introduction: We developed a Simulation-Based Training (SBT) on twin pregnancies focussing on timing and mode of delivery, internal podalic version, breech extraction, (assisted) vaginal breech delivery, and recognition of abnormal cardiotocogram recordings, and trained all gynecologists in one hospital. In this study we analyse the effect of Twin-SBT on mode of delivery, labor management and neonatal and obstetric outcomes. *Methods:* A retrospective, single-center study compared neonatal and obstetric outcomes before (2015-2018) and after (2018-2023) Twin-SBT, with mode of delivery as the main outcome. *Results:* 250 women attempted vaginal delivery, 117 were in the pre-Twin-SBT group, and 133 in the post-Twin-SBT group. The combined delivery rate remained unchanged, 2.6% ($n = 3$) vs. 3.8% ($n = 5$), a*OR* 1.2 (95% CI [0.6, 2.4]). Primary breech extraction increased from 12% ($n = 14$) to 30.1% ($n = 40$), a*OR* 3.2. Epidural use rose from 55.6% ($n = 65$) to 85% ($n = 113$) ($p < .001$). The number of twins born within an interval > 30 minutes decreased from 23.1% ($n = 27$) to 10.5% ($n = 14$), a*OR* 0.5 (95% CI [0.2, 0.9]), oxytocin use during labor increased from 27.4% ($n = 32$) to 56.4% ($n = 75$) ($p < .001$). There were no changes in composite maternal or neonatal outcomes. *Conclusions:* Twin-SBT did not result in fewer combined deliveries. However, there was an increase in overall EDA use, breech extraction and fewer deliveries in which the interval between twins exceeded 30 minutes without any increase in either neonatal or obstetric outcomes. Further research is needed to better understand the value of a Twin specific Simulation Based Training.

Correlation Between Neonatal Complications and Neonatal Weight: A Retrospective Comparative Study of Eutrophic and Macrosomic Infants at the Sousse Maternity Hospital

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Introduction: Fetal macrosomia presents a significant challenge for obstetricians and pediatricians due to issues related to delivery and neonatal complications. The objective of our study is to investigate the correlation between birth weight and neonatal complications. *Materials and Methods:* This retrospective study includes 440 deliveries at the Sousse Maternity Hospital over a period of four months. *Results*: Of the newborns, 134 were macrosomic (birth weight > 4 kg), and 306 were eutrophic. The main complications observed were: Shoulder dystocia (SD): This was noted in 1.2% of cases. Although the difference between the two groups (macrosomic versus eutrophic) was statistically significant ($p = .007$), the correlation coefficient between neonatal weight and SD was negligible at 0.121. Hypoglycemia: The correlation coefficient was 0.175 ($p = .034$). Perinatal asphyxia: The correlation coefficient was negligible at 0.027, and the difference between the two groups was not significant ($p = .569$). Neonatal death: The difference between the two groups was statistically significant ($p = .02$), with a weak correlation coefficient of .109. *Conclusion:* In our series, fetal macrosomia did not increase the incidence of neonatal complications such as shoulder dystocia, hypoglycemia, and perinatal asphyxia.

Investigating MRI, Microbiome, and Blood Marker Differences in a Twin Pair Discordant for PSP: A Comprehensive Case Study

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Introduction: Progressive supranuclear palsy (PSP) is a rare neurodegenerative disorder characterized by tau protein accumulation in the brain, leading to diverse neurological symptoms. Diagnosis primarily relies on clinical signs and neuroimaging, but research into biomarkers and the gut microbiome's role is ongoing. This study

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aimed to identify potential blood biomarkers and observe gut microbiome variations in a monozygotic twin pair discordant for PSP. *Materials and methods*: We conducted broad assessment of a PSP-discordant twin pair, including neuropsychological and neurological examinations, blood analysis, brain MRI, also investigated the gut microbial composition and diversity. *Results*: Alpha-synuclein levels showed significant difference, moderate differences were observed regarding MMP-2, MB, Apo-A1, Apo-CIII, and Apo-H levels, only small differences in ApoA1/SAA and ApoB/ApoA1 ratios were seen. According to gut microbiome analysis, the affected twin exhibited relative dysbiosis. Brain MRI pointed out that the affected twin displayed midbrain and frontoparietal cortical atrophy, reduced overall brain volumes, and increased white matter lesions. Cognitive impairment consistent with PSP-related neurodegeneration were detected in the affected twin. *Conclusions:* Significant differences in blood biomarkers, gut microbiome composition, and brain structure were found between a PSP-affected twin and the unaffected sibling. Combining blood biomarkers, microbiome analysis, and neuroimaging could enhance PSP diagnosis and understanding.

Exploring Cortical Morphology in Twins: Genetic and Environmental Impacts

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Introduction: The cerebellum, brainstem, and cortical structures are critical for sensorimotor, cognitive, and social functions. This study examines the genetic and environmental influences on brain morphometry and compares these to white matter hyperintensity (WMH) heritability. *Methods:* We analyzed T1-weighted MRI data from 118 healthy adult twins from the Hungarian Twin Registry using the volBrain pipeline for morphometric measurements. *Results:* MZ twins displayed higher resemblance than DZ twins in brainstem and cerebellar volumes, with significant heritability (A: 90.5-92.6%) and minimal environmental effects (E: <1%). Supra-tentorial volumes (e.g., frontal and temporal lobes) exhibited high heritability (A: 74.5-92.4%), while frontal lobe thickness was influenced more by environmental factors (C: 63-66.5%; E: 33.4-37%). *Conclusions:* Genetics strongly influence infra-tentorial and cortical morphology, particularly the parietal lobe. Environmental factors are more significant in frontal and temporal regions. These findings highlight the importance of region-specific strategies for promoting brain health and resilience.

The OMICS of Twinning

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Introduction: Recent genetic and epigenetic studies identified genes associated with DZ twinning and hundreds of differentially methylated sites in MZ twins. To gain further functional insight, we asked if these results are accompanied by (1) differences in other omics and (2) if the epigenetic signature of MZ twins is present in earlier development. *Methods:* (1) We compared 42,663 RNA transcripts from the Affymetrix U219 array in 1453 MZ twins and 1294 DZ twins from the Netherlands Twin Register (NTR), followed by sex-stratified analyses. The 5% transcripts with the lowest p values were selected for replication in 217 MZ and 158 DZ twins from the older Finnish Twin cohort (FTC). We meta-analyzed 169 serum metabolites from an NMR platform in 2797 MZ and 2040 DZ twins from the NTR, FTC and FinnTwin12 (FT12). (2) We will generate DNA methylation array data on cord blood and placental samples from twin pairs in the PANDA obstetrics biobank and in multiple tissues from twins in the Dutch Fetal Biobank. *Results*: (1) We identified one differentially expressed RNA transcript of the protein-coding PURG gene in NTR. Replication in FTC ($N = 367$) of the top 5% most discriminant RNA transcripts revealed 19 differentially expressed transcripts after correcting for multiple testing, none of which have been implicated for twinning before. Enrichment analyses showed differences in expression in the WNT pathways and cell adhesion processes, which were previously indicated with MZ twinning, and the TGF-B pathway known to be associated with DZ twinning. No differences were observed between metabolite levels in the MZ and DZ twins. (2) We identified 50 twins in the PANDA obstetrics biobank and 20 twins in the Dutch Fetal Biobank. Zygosity assessment by genotyping and epigenetics are in progress. *Conclusions:* We identified novel transcriptomics biomarkers of twinning and provided partial converging evidence for multiple pathways previously identified in the GWAS of DZ and EWAS of MZ twinning.

The Emotional Impact of Loss for Multiple Birth Families: A Systematic Mapping Review

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Introduction: Multiple birth pregnancies carry increased risks that can result in the death of one or more babies. While research has examined the emotional impact of singleton deaths, understanding the specific emotional impact for multiple birth families is crucial for providing appropriate support. *Materials & Methods:* A mapping review examined evidence on the emotional impact of multiple birth loss, including selective termination and multifetal pregnancy reduction, during the perinatal period. Literature published between 2013-2023 was searched across MEDLINE, APA PsycINFO, CINAHL Ultimate, ASSIA, and Web of Science databases. Fourteen identified studies were coded and mapped for data extraction. *Results:* The review showed the complexity of loss and its emotional impact on multiple birth families, including single twin loss, loss from multifetal pregnancy, loss of both twins, twin-to-twin transfusion syndrome (TTTS) losses, and multifetal pregnancy reduction. Research gaps

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were identified in several areas: emotional impact on fathers, higher-order pregnancies, selective termination, studies in low/middle-income countries, understanding trauma after loss, and longitudinal research. *Conclusions:* The emotional impact of multiple birth loss is complex and requires further research, particularly in under-studied areas, to better inform support strategies. Multiples-specific education and interventions are needed across all healthcare services to support families through the perinatal period and beyond.

Perinatal Outcomes in Patients With Monochorionic Twins and Selective Intrauterine Growth Restriction Type III Managed With Expectant

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Objectives: To evaluate the prognosis of monochorial pregnancies with selective intrauterine growth type III restriction under expectant management. *Methods:* Methods: Double monochorionic diamniotic twin pregnancies with selective type III intrauterine growth restriction were evaluated, and classified based on umbilical artery Doppler and weight difference between twins greater than or equal to 20% in whom conservative management was decided. Adverse perinatal outcomes were included such as prematurity, perinatal death, main indications for the term of pregnancy, and most frequent neonatal complications. *Results:* We included 34 cases to follow up with a diagnosis of selective intrauterine growth restriction type III, follow-up appointments were scheduled for an average of 2 weeks. The venous duct represented the most important vessel in this follow-up. The main indications for delivery include hypertensive states associated with pregnancy, hemodynamic changes in one fetus, and spontaneous labor. The time of delivery was 32.3 weeks. A case of fetal intrauterine death occurred at follow-up, and two newborns died because of neonatal sepsis, with a total survival of 65/68 twins,(95.5%), hyperbilirubinemia (57.1%), and cerebral hemorrhage (28.5%).The birth weight of the small baby was from 450 to 800 g, and in the big baby from 950 to 1750 g. *Conclusion:* The expectant management of monochorionic pregnancy with selective intrauterine growth restriction type III has presented a higher survival rate, however, prematurity continues to be the most important factor against this, derived from multiple pathologies that affect pregnancy evolution.

Maternal, Perinatal and Neonatal Outcomes of Triplet Pregnancies According to Chorionicity: Our 13-Year Experience at Careggi University Hospital in Florence, Italy

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Introduction: Triplet pregnancies are associated with a higher risk of fetal and maternal morbidity and mortality compared to twins and singletons. Chorionicity has been proposed as a major determinant of perinatal and maternal outcomes in triplet pregnancies, although further evidence is needed to clarify the extent and real influence of this factor. Thus, the goal of this study was to evaluate the effect of chorionicity on maternal, fetal and neonatal adverse outcomes in triplet pregnancies. *Materials & Methods:* A retrospective observational study was carried out on triplet pregnancies that were delivered between 2010 and 2023, in Careggi University Hospital in Florence, Italy. A total of 79 pregnant women and 215 newborns were analyzed. Of these triplet pregnancies, 32.9% were nontrichorionic. We analyzed maternal characteristics and obstetric, fetal, perinatal and neonatal complications based on their chorionicity by comparing trichorionic to nontrichorionic triplet pregnancies. In addition, we conducted several multivariate logistic regressions to deepen our understanding of the most relevant complications that can be associated to the chorionicity. *Results:* Pregnant women with nonchorionic triplet pregnancy face a higher risk of giving birth at lower gestational age, presented greater prematurity under 34 weeks, and more probability to have post-partum hemorrhage, and fetus with intrauterine growth restriction. On the other hand, newborns with a nontrichorionic component had a lower birth weight, greater probability of birth weight under 2500 g and an APGAR score below 7 at 1 min after birth, more respiratory distress syndrome, higher requirement of reanimation and neonatal intensive care therapy, as well as, the development of hypoglycemia and Icterus (p <.05). *Conclusion:* Triplet gestations with a nontrichorionic component present a higher risk of obstetric, fetal and neonatal complications.

Genetic Etiology of Agenesis of the Corpus Callosum: A Retrospective Single-Center Cohort Analysis of 114 Fetuses

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Introduction: The identification and prognosis of the agenesis of the corpus callosum (ACC) for prenatal consultation are complex and currently unclear. This study aims to explore the correlated genetic mutations of prenatal ACC. *Materials and Methods:* We retrospectively analyzed 114 prenatal cases of ACC. All cases (n = 114) were subjected to chromosomal microarray analysis (CMA), and 66 CMA-negative cases underwent prenatal exome sequencing (pES) for further analysis. *Results:* CMA was diagnosed positively in 15/114 (13.2%) cases and pES was diagnosed positively in 24/66 (36.4%) CMA-negative cases. The detection rate of genetic causes between complete and partial ACCs was not significantly different (p > .05). Between isolated and nonisolated (other anomalies present) ACCs, the diagnostic rate of pES in nonisolated cases was significantly higher (p < .001), while CMA results did not differ (p > .05). The diagnostic rate of CMA was significantly increased in cases combined with intracranial and extracranial malformations (p =.014), while no CMA positive was detected in cases combined with only intracranial malformations. The detection rates of pES increased when ACC was combined with cerebellar hypoplasia (p = .121) or with intracranial hemorrhage (p = .020) compared to isolated ACC. In cases of ACC combined with a single extra-CNS system anomaly, fetuses with skeletal dysplasia were more likely to have a positive result from CMA (p = .001). Families with nonisolated or complete ACC were more inclined to terminate the pregnancy (p = .001 and p = .027). Among the live birth cases in our study, the postnatal neurodevelopmental prognosis between isolated versus nonisolated or complete versus partial ACC seemed no significant difference (p > .05). *Conclusion:* For fetuses with prenatal

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ACC, further pES analysis should be recommended after negative CMA results. Chromosome abnormalities are less likely to occur when ACC with only intracranial malformations combined.

Dichorionic Twin Pregnancies: Comparison Between the Use of Singleton Curves and Twin-Specific Curves for the Identification of SGA Fetuses

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Introduction: Twins have a growth trajectory in utero that differs from singletons starting from 28-30 weeks. However, there is currently no agreement on the use of twins-specific growth curves, and standards for singletons continue to be used, potentially leading to an overdiagnosis of small for gestational age (SGA) fetuses, an increased number of check-ups and unnecessary interventions. We aimed to compare the incidence and accuracy of the diagnosis of SGA fetus using twin-specific growth standards compared to singleton standards in dichorionic (DC) twin pregnancies, and to compare perinatal outcomes. *Materials & Methods:* A retrospective study was carried out on DC twin pregnancies that received care in a tertiary care hospital between 2017 and 2023. Estimated fetal weight centiles were calculated using twin-specific growth standards and singleton standards. Cases of major fetal malformations, double SGA, miscarriage, or selective termination were excluded. *Results:* Out of 453 DC twin pregnancies, using the twin-specific growth standards, 28 fetuses (6.2%) were classified as SGA, compared to 76 fetuses (16.7%) using singleton standards ($p < .001$). Twin-specific curves were more specific (99% vs. 92%) and had a greater PPV (96% vs. 64%) for birth weight <10th centile compared to the singleton standards, with similar sensitivity (42% and 40%) and NPV (84% and 81%). Among SGA fetuses diagnosed with the twin-specific standards, a significantly higher incidence of intrauterine fetal death (21.4% vs. 6.5% $p = .03$), preterm birth <34 weeks (42.8% vs. 21.0% $p = .03$), low birth weight (1100g +/- 510 vs. 1730g +/- 560 $p < .001$) and admission to NICU (82.1% vs. 40.7% $p \leq .001$) was observed, compared to SGA diagnosed with singleton standards. *Conclusions:* Twin-specific growth standards reduce the number of twins diagnosed as SGA, are more accurate in predicting low birth weight, and identify the SGA fetuses with a greater incidence of adverse perinatal outcomes.

Role of Ultrasound in the Prenatal Diagnosis of Cystic Hygroma of the Neck: A Report of 25 Cases

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Introduction: Cystic hygroma of the neck (CHN) is a congenital malformation of the lymphatic system, characterized by fluid-filled formations in the retro and lateral cervical regions, often bilateral and associated with lymphedema. It is the primary fetal anomaly detected by ultrasound in the first trimester of pregnancy and frequently indicates associated chromosomal abnormalities, present in 70% of cases. This study aims to highlight the role of ultrasound in the prenatal diagnosis of CHN and compare ultrasound findings with fetopathological examinations. Currently, medical termination of pregnancy is not systematic and depends on fetal karyotype results, the resolution of CHN, the absence of other malformations, and particularly the normality of the fetal heart. *Materials and methods:* A retrospective study of 25 cases of CHN collected in our department over a period of 4 years. *Results:* The average age of the patients was 32 years with an average parity of 1.2. Consanguinity was noted in 20% of cases. The average term for ultrasound detection was 15 weeks of gestation. The average size of the CHN was 5.8 cm. The thickness of the septum defined the type of hygroma as uni-, bi-, or multilocular. Karyotyping was performed in 80% of cases, revealing normal karyotypes in 50% of these. The main chromosomal abnormalities were free trisomy 18 (2 cases) and Turner syndrome (monosomy XO in 6 cases and mosaic in 2 cases). Comparison with fetopathological examination was conducted in 80% of cases, confirming the ultrasound diagnosis and correcting it in 40% by identifying additional malformations. Five pregnancies were carried to term, resulting in four live births with no morphological anomalies or chromosomal abnormalities. *Conclusion:* Prenatal ultrasound is essential in diagnosing cystic hygroma, as it is one of the earliest indicators of chromosomal abnormalities. The decision to terminate or continue the pregnancy depends on karyotype results, the presence of associated anomalies,

Fetal Akinesia: A Report of 4 Cases and Literature Review

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Introduction: The term 'fetal akinesia sequence' defines a syndrome of malformations resulting from reduced or absent fetal movements. These movements, which appear very early in the embryo, are essential for the harmonious development of the fetus throughout intrauterine life. The suppression of these movements can lead to significant developmental issues. *Materials and methods:* We report a series of 4 cases of fetal akinesia collected in the Department of Gynecology and Obstetrics of the University Hospital Farhat Hached, Sousse, Tunisia. *Results:* In all 4 cases, the parents were consanguineous, and the diagnosis was made via ultrasound, indicated by reduced fetal movements in the third trimester. Two patients delivered vaginally, with one requiring forceps due to expulsion failure. Confirmation was made through fetopathological examination, providing proof of the condition and detailing the extent of the lesions. *Conclusion:* Fetal akinesia syndrome is a sequence characterized primarily by fetal immobility, regardless of the underlying cause. Understanding its etiopathogenic mechanisms is crucial for effective genetic counseling, improving prenatal screening, and implementing effective prevention strategies.

Trisomy 18: The Importance of Prenatal Diagnosis

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Introduction: Trisomy 18, or Edwards syndrome, is a rare aneuploidy caused by the presence of an extra chromosome 18. Infants with trisomy 18 have a high mortality rate due to the lethal malformations associated with this syndrome. The aim of this study is to determine the prevalence of ultrasound anomalies found in fetuses with trisomy 18. *Materials and methods:* This retrospective study includes cases of trisomy 18 diagnosed prenatally in our maternity ward over a period of 3 years. We analyzed the main ultrasound findings. *Results:* Nine

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cases were diagnosed prenatally. The average age of the patients was 35 years, ranging from 20 to 46 years. The diagnosis was confirmed by fetal karyotype analysis. Various indications led patients to undergo fetal karyotyping, such as the discovery of ultrasound markers in 86.6% of cases, a positive result for Trisomy 21 screening in 6.3% of cases, or a history of the condition in the patient in 0.5% of cases. The cytogenetic study results were as follows: the majority of complete trisomy 18 cases were free and homogeneous: 47,XY,+18 or 47,XX,+18 (77.7% of cases), with one case of mosaic trisomy 18 and one case of trisomy 18 with an extra Y chromosome. A female predominance was observed (6 female fetuses and 3 male fetuses). In the first trimester, increased nuchal translucency was detected in 60.6% of trisomy 18 fetuses, sometimes associated with generalized edema in 31.5% of affected subjects. After the first trimester, the most common anomalies found were limb anomalies (28.3%), digestive anomalies (26.9%), CNS anomalies (23.7%), intrauterine growth restriction (23.3%), and cardiac anomalies (20.5%). Therapeutic termination of pregnancy was performed for all patients with their consent. *Conclusion:* Trisomy 18 is a condition with a poor prognosis. Ultrasound detects 80% of trisomy 18 cases, although none of the detected anomalies can be considered pathognomonic for the syndrome. Postnatal care is limited to comfort measures.

Preterm Birth Affects the Gut Microbiota, Metabolome and Health Outcomes of Twins At 12 Months Of Age

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Introduction: Perinatal factors can influence gut microbiota, adversely impacting infant health outcomes. However, little is known about the combined effect of preterm birth and chorionicity on gut microbiota, metabolism, physical and neurobehavioral development for twin infants. *Methods and materials*: We profiled and compared the gut microbial colonization of twins aged 12 months from 143 families. Twins were divided into four groups based on their gestational age at birth and chorionicity as dichorionic-diamniotic full-term birth group, dichorionic-diamniotic preterm-birth group, monochorionic-diamniotic full-term birth group, and monochorionic-diamniotic preterm birth group. Gut microbiota diversity and fecal metabolic alterations at 12 months old were determined by 16S rRNA gene sequencing and untargeted metabolomics, respectively. Wilcoxon's rank-sum tests, the general linear models, and the twin-based ACE model were used. *Results*: We found that preterm birth and chorionicity dominated genetics in altering the composition of gut microbiota and abundance of metabolites over 12 months of age. The influence of genetic factors differed between preterm and full-term births. There were 16 gestational age and chorionicity specified gut microbiota genera and 285 group-specified metabolites. Association analysis filtered 7 microbiota genera and 19 metabolites associated with twins' physical and neurobehavioral development. Three metabolites, N-Oleoyl dopamine, Ecgonine, and Methyl jasmonate participated in the neuroactive ligand-receptor interaction pathway, tropane, piperidine, and pyridine alkaloid biosynthesis pathway, and alpha-Linolenic acid metabolism and biosynthesis of secondary metabolitesrespectively. *Conclusion*: Preterm birth is associated with dysbiotic microbiota profiles and significant metabolic alterations, which may eventually influence physical and neurobehavioral development.

Comparison of Different Ultrasound Parameters for the Prediction of Preterm Birth in Twin Pregnancies

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Introduction: The incidence of preterm birth (PTB) due to cervical insufficiency in twin pregnancies is significantly higher than in singletons. Cervical length (CL) is considered the most reliable parameter to screen both single and twin pregnancies for PTB, with different cut-offs. *Materials & Methods:* This study aims to evaluate the reliability of alternative ultrasound cervical parameters to increase the detection rate of twin pregnancies at risk of preterm delivery. A population of 36 twin pregnant women was subjected to longitudinal transvaginal ultrasound cervical evaluation during II and III trimesters. Uterocervical angle (UCA), hardness ratio (HR), elasticity contrast index (ECI), internal os strain (IOS), external os strain (EOS), and cervical length (CL) have been collected at every scan. Ultrasound mean measurements of women (n 24) who delivered at term (after 37 weeks for dichorionic twin pregnancies, after 36 weeks for monochorionic) were compared to those who delivered before the planned date (n 12). ROC curves were calculated for every parameter to find the best predictor for preterm birth for twins. *Results:* Baseline characteristics or neonatal outcomes showed no differences between the groups. The only statistically significant difference was found comparing UCA ($p = .001$) and IOS/EOS ratio ($p = .031$) between the two groups, but not for the CL ($p = .128$). UCA showed a better performance in predicting PTB (AUC 0.771) than the CL (AUC 0.354) universally considered the gold standard in PTB screening, A wider angle between the cervix and the uterus resulted in a higher risk of PTB. *Conclusions:* Alternative ultrasound cervical parameters represent promising tools for the prediction of PTB in twin pregnancies. The CL showed poor performance, unlike singleton ones. The UCA and the cervical strain could represent indirect signs of the overdistension of the uterus typically present in twin pregnancies. Evaluating longitudinal changes in UCA can be helpful in the screening of twin gestations at risk of PTB.

Epidemiology and Risk Factors of Preterm Birth in Twins Pregnancies: Beja Maternity Experience

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Introduction: Prematurity is a major public health issue at the global level, it is the most feared cause of perinatal morbidity and mortality. The most common etiology of prematurity in twin pregnancies is the threat of premature delivery. Through our study, we proposed to synthesize knowledge on the incidence and on certain risk factors of prematurity and describe neonatal morbidity and mortality. *Materials and methods:* This was a descriptive retrospective study, spread over 36 months in our maternity hospital in Beja, including patients between 27 and 40 weeks of amenorrhea (WA) with twin pregnancy. We have collected 72 cases. *Results:* The prevalence of

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preterm delivery was 50% of cases, of which 89% of these preterm births were associated with threat of premature delivery, and 16% of which were associated with preterm premature rupture of the membranes. The average age was 33 years. The time between spontaneous entry into labor and the consultation was 6 hours, the average term of pregnancy at the time of delivery was 35 weeks. Tocolysis was opted for in 59% of cases (n = 44/74). The mean latency period was 2.67 days from labour to delivery. A cesarean delivery was seen in 68.4% of the patients. Expectancy was correlated with an increase in the prevalence of vaginal delivery in the three days following the onset of UC. At the fetal level, weight gain without an increase in the risk of neonatal respiratory distress in the event of tocolysis was observed. The mean neonatal weight was 2900 g. The Apgar score was greater than or equal to 7 in 63.5% of cases (n = 46/72). 60% of mortalities and 50% of neurological sequelae occurring in children born before 32 weeks of amenorrhea. *Conclusion:* The obstetric strategy for the management of threat of premature delivery in twin pregnancy is a collegial decision that takes into consideration several factors in order to determine an appropriate term and the path to delivery. It is a balance between maternal risk and fetal risk.

Gene–Environment Interaction Between Gaming Addiction and Perceived Stress in Late Adolescents and Young Adults: A Twin Study

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Introduction: The study aimed to investigate the underlying mechanism of the relationship between gaming addiction (GA) and perceived stress (PS). *Materials & Methods:* In total, 1468 twins (mean age = 22.6 ± 2.8 years) completed an online survey including the GA and PS scales. The bivariate G x E model-fitting analyses were performed. *Results*: Additive genetic, shared environmental, and nonshared environmental effects were 0.70 (95% CI [0.61, 0.77]), 0.00, and 0.30 (95% CI [0.26, 0.33]) for GA, and 0.38 (95% CI [0.24, 0.55]), 0.35 (95% CI [0.18, 0.51]), and 0.22 (95% CI [0.20, 0.26]) for PS. Model-fitting analysis supported the diathesis-stress model, where genetic influences on GA were greater in high levels of PS, whereas environmental influences on GA were small and constant across levels of PS. *Conclusions:* PS exacerbated genetic vulnerability to GA, which was consistent with the etiology of many forms of psychopathology.

Twins' Attachment Scale: Secondborn's Version (TAS-s)

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Introduction: Through this research effort, we aim to develop and validate the Twins' Attachment Scale-Secondborn (TAS-s). *Materials and Methods:* More specifically, we assessed the proposed factor structure, reliability and construct validity of the Twins' Attachment Scale. The item selection was based on the previous work by Waters (1987). *Results:* A total number of 176 parents of twins participated in the study. First, the exploratory factor analyses (maximum likelihood) with promax rotation suggested a two-factor solution assessing F1: Secure attachments with parent, F2: Insecure-avoidant attachments with parent, and a two-factor solution assessing F3: Secure attachments with sibling, and F4: Insecure-avoidant attachments with sibling. Kaiser-Meyer-Olkin measure of sampling adequacy for the first two-factor solution was formed at .788 and Bartlett's test of sphericity was significant, $\chi^2(136) = 807.554$, $p = .000$. While for the second two-factor Kaiser-Meyer-Olkin measure of sampling adequacy was formed at .753 and Bartlett's test of sphericity was significant, χ^2 (171) = 908.014, $p = .000$). CFAs confirmed the proposed factor structure in both cases. ΔCFIs and ΔRMSEAs were estimated and the model with the best fit was the four-factor. No floor-ceiling effects were observed. *Conclusions:* Assessment of measurement invariance across fathers and mothers provided us with strong evidence that the proposed structure is both meaningful and valid in the above groups, as well. Consequently, the TAS-s is an easily applied and comprehended research tool which could be used to assess attachment in a valid and reliable manner.

Updates on the Twin Education Website

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Introduction: TwinEducation.org is a website designed to address the educational needs of families with twins/multiples. It is a continuation of the work of David Hay and Pat Preedy's earlier website. This presentation discusses the challenges and opportunities the current site offers for parents, teachers, school administrators, and supportive twin/multiple organizations. *Materials and Methods:* Electronic means were used to collect information and communicate with visitors to the site. *Results:* There remains a need for this web resource for teachers and parents, especially. However, it is evolving into other forms as challenges arise. *Conclusions:* Although the website is important and useful, there remain obstacles to overcome. It is necessary to think how such information can be available in other formats.

A Twins and Education Course for Teachers: Progress and Feedback

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Introduction: There is a need to help teachers better understand the issues and needs of twins and multiple-birth students in public schools. This presentation reports on the effectiveness of one such course designed as an online professional development course for teachers. *Materials and Methods:* The course was developed and implemented in 2022 and monitored over the last two years. The course included data collection, quiz scores, and final project with attached survey. *Results:* The results indicate the need is still great for such a course, as many of the participants reported increasing their knowledge and attitude toward the educational needs of twins/multiples. *Conclusions:* Teachers report finding the course useful, especially the interviewing and practical application of survey and inventory tools designed to work with parents and school-age twin siblings.

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Growth Path From Birth to School-Age Among Twin Children

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Introduction: Low birth weight is a proxy for intrauterine growth restriction and may influence later-life outcomes, including education and earnings. Prospective studies on child development based on early twin observations are valuable but limited in Brazilian research. This study aimed to evaluate birth weight's role in the physical development of twins from birth to school age, focusing on z scores of twins born in São Paulo. *Materials and Methods:* We analyzed data from 138 healthy twins (M = 9.2 years; SD = 2.3), comparing birth and school-age weights to singleton growth curves. *Results:* Statistical analysis revealed a significant reduction in the proportion of z scores below the median from birth (98.1%) to school age (30.3%; McNemar $\chi^2 = 95.01$, $p < .001$). At birth, 99% of female and 97% of male twins had z scores below the median, which decreased to 29% and 32%, respectively, by school age. Monochorionic twins exhibited greater variability in z scores below the median at birth than dichorionic twins (2.1273 vs. 1.7067; Fligner-Killeen $\chi^2 = 3.97$, $p < .05$), but this difference was not observed at school age. 71% of twins improved their weight development, and none deteriorated *Conclusion:* These findings suggest that, despite lower birth weights characteristic of multiple pregnancies, twins demonstrate significant growth catch-up, eventually resembling singleton children. This highlights the resilience of twin growth trajectories and underscores the importance of monitoring their early development.

Genetic and Environmental Factors Impacting Quality of Life: Insights from the Isfahan Twins Study

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Introduction: HRQoL is a complete concept covering physical, mental, and social well-being, offering valuable insights into the overall effects of health conditions on individuals' daily functioning and life satisfaction. *Materials & Methods:* In this substudy, participants aged 6 years and above were enrolled. A self-administered questionnaire consisting of 26 questions was utilized. WHOQOL-BREF evaluates an individual's perceptions (for those older than 18 years) of their health and well-being. Conversely, for subjects under 18 years old, the PedsQL measurement model encompassed 23 items to assess health-related inputs and relied on self-reporting by children and young individuals. *Results:* The mean age of survey participants was 8.71 ± 1.61, 13.91 ± 1.91, and 30.02 ± 8.99 years for the 6–12, 12–18, and above 18 age groups respectively. The structural equation model found moderate heritability (51.0%) for academic factors in the 6–12 age group, and a high heritable influence (80%) for the physical domain in the 12–18 age group. In adults, genetic effects accounted for 61% and 65% of the influence on the physical and environmental domains, respectively. The second age group and the first one showed the highest and lowest variance components in the total score respectively. *Conclusion:* Investigating the differences in HRQoL between MZ and DZ twins provides valuable insights into the relative contributions of genetics and environment in shaping HRQoL outcomes. While genetic factors may contribute to certain aspects of HRQoL, the influence of environmental factors should not be underestimated.

Multidisciplinary Management and the Effects on Surviving Twins

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Introduction: Newborns, in the event of perinatal bereavement in twin pregnancies, are more vulnerable due to parental relationships burdened by psychosocial risk factors and psychopathologies. The child participates in a series of syndromes: maternal anxiety about his health and survival, fear of responsibility for caring for the child, delusions or obsessions about the child or disturbances in the relationship with the fetus and the child, in particularly emotional rejection and pathological anger. *Materials and methods:* The research was conducted on a sample of 24 women with twin pregnancies who shared the presence of a stillbirth between 15 and 25 years old. Standardized tools and interviews were used to evaluate women's representations and maternal experiences, allowing screening to be carried out already during pregnancy on some specific psychopathologies such as peripartum anxiety and depression. *Results:* The data obtained from the research indicate that in twin pregnancies resulting in MEF of one of the two fetuses, 64.9%, if not treated in the acute moment and after birth, develop important symptoms of depression, anxiety and relationship disorders with the child survivor. Conversely, only 4.7% of women followed and treated in the acute moment of pregnancy according to the multidisciplinary path and subsequently followed with specific psychological support developed psychopathological symptoms. *Conclusions:* Research has shown that the constant presence of a dedicated psychologist and a multidisciplinary approach allows the transition from 'curing' to 'taking care', reducing the development of maternal and relational psychopathologies. Paying attention to the health, including psychological health, of family members and not only to the characteristics of medical care, allows you to manage a variety of problems that can only and exclusively be mitigated by a Family Care approach in hospital which also continues outside the facilities.

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Interaction in Multiple-Birth Families Requires More Attention From Health and Social Care Professionals in Nursing Care

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Introduction: Interactions between twins already occur during pregnancy when the babies share their mother's womb, and these interactions continue after birth in intertwin relationship. *Materials & Methods:* This research is part of the TWIN LIFE 2021-26 'Nurses' Competence in Multiple-Birth Family Nursing" project and concentrates to the interaction in multiple-birth families in intertwin relationship. The aim of this cross-sectional study was to evaluate nurses', working at maternity and child health clinics, knowledge of multiple-birth families. The data wascollected in 2022 using a questionnaire with Likert-scale statements and open-ended questions. *Results:* These show that nurses need more knowledge on intertwin relationships in the situation of growing up as a multiple. Dominance, submissiveness, and speaking role appear in those children's behavior, and they can interact as either being brave and visible or withdraw into the background. When one twin is without their co-twin, the roles they assume can be different and they can more easily be themselves. The quality of intertwin relationships manifest in daily lifesituations, which are excellent opportunities to guide and support the children's individuality and balance the intertwin relationship. It is important that parents are aware of the intertwin relationship because they have an important role in influencing the relationship. *Conclusions:* Education and training are needed to enable the development of multiple-birth family expertise. Further studies are required on intertwin relationships and into education, intervention, and impact.

Eating Disorders and Emotional Regulation: A Literature Review in a Twin Studies Perspective

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Introduction: Food has always held numerous significances, including psychological ones. Eating behaviour is often investigated to understand how much psychological factors can influence food choices, and difficulties in emotion regulation appear to be an aspect associated with eating disorders (ED). The aim of this literature review is to explore the relation between ED and emotional regulation in twins, emphasizing possible susceptibilities and implications. *Materials and Methods:* A literature review of twin studies on ED and emotional dysregulation was implemented with a doubleblind approach, and was conducted to draw a summary of the published works in the field of emotional regulation and ED. *Results:* Literature on twin studies related to ED is limited. However, some researchers refer to the construct of emotional dysregulation. This review explores relationships, major themes, and any critical gaps in the research expressed in the field, and helps to re-design some specific questions on the nature of covariation between ED and emotional regulation. *Conclusions:* This review suggests that there is the need to fill the gap between emotional regulation and ED in a behavioral genetics and twin studies perspective, particularly with longitudinal designs and multivariate approaches.

Basal Metabolic Rate and Dietary Habits in Twin-Pregnancies: The Venere Study

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Introduction: Unlike single pregnancies, limited studies on nutritional factors in twin-pregnant women prevent us from addressing their needs and risks. The VENERE study examined the basal metabolic rate (BMR) and dietary habits of twin-pregnant women across all trimesters. *Materials and Methods*: Data were collected at Careggi University Hospital, Florence, October 2022-December 2023. BMR was estimated with both indirect calorimetry and predictive equations. Nutritional intake and adequacy were evaluated with a 7-day food diary. *Results*: The study included 32 twin-pregnant women with an average pre-pregnancy BMI of 24.1±3.9 kg/m2, and a weight gain of 12.2±3.9 kg at delivery. BMR measured by indirect calorimetry increased from 1479±196.1 kcal in the first trimester to 1571±186.5 kcal in the second and 1732.8±223.8 kcal in the third. Estimation of BMR using predictive equations showed Hronek's equation as the most accurate and reliable compared to indirect calorimetry, in the first (ICC = 0.77; $p < .001$), second (ICC = 0.70; $p < .001$) and third trimester (ICC = 0.79; $p < .001$). Nevertheless, the equation under- or overestimated BMR in 33% of the evaluations. Daily energy intake increased by approximately 140 kcal from the first to second trimester (1660.2±244.2 vs 1801±263.5 kcal) and 90 kcal from the second to third trimester (1888.8±262.4 kcal). On average, intake was ~40% below recommendations, with all women reporting insufficient macro- and micronutrient intake. *Conclusions*: Hronek's predictive equation showed the greatest reliability with indirect calorimetry in the assessment of BMR. Twin-pregnant women reported lower dietary intakes compared to current recommendations.

A Replication Twin Study of Breast Cancer Risk Factors

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Introduction: Hamilton et al. found that breast cancer risk factor associations differed according to a woman's personal and family history. In their co-twin control study, disease-discordant pairs allowed for inference about risk for controls who, by definition, had a family history, while in disease-concordant pairs, the case was the first diagnosed and the inference was about women with both

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a family history and a diagnosis themselves, and likely increased genetic susceptibility. We conducted a study of 574 breast cancer-affected female twin pairs and replicated the previous analyses. *Methods:* Twin pairs with one or two women with breast cancer were recruited through twin registries in the USA and Australia. *Results:* The mean age at diagnosis was 50.5 years (*SD* = 10.3). The adjusted odds ratios from conditional logistic regression of the first-to-diagnosis (outcome) among 65 disease concordant pairs (20 DZ, 45 MZ) were >1 for age at first menarche, breast development, first menstrual period and an early-puberty-index, consistent with Hamilton et al., though none were nominally significant. There was no evidence of increased breast cancer risk from analyses of 509 disease-discordant pairs. *Conclusions:* We found some albeit weak evidence to support hereditary breast cancer being potentially due to unusual sensitivity to pubertal hormones

Environmental and Genetic Determinants of Three Epigenetic Aging Clocks Across the Lifespan

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Introduction: Epigenetic aging clocks such as GrimAge2, PhenoAge, and DunedinPACE are crucial biomarkers for health outcomes. Unlike the well-studied Horvath clock, which is predominantly influenced by environmental factors with a familial cohabitation-dependent pattern, the genetic and environmental determinants of these newer clocks across lifespan remain unclear. *Materials and Methods:* We analysed genome-wide DNA methylation (DNAm) data from 3,888 participants (aged 0-92 years) across 10 studies, including monozygotic (MZ) and dizygotic (DZ) twin pairs, and non-twin sibling pairs. DNAm age was assessed using GrimAge2, PhenoAge, and DunedinPACE. Familial correlations and variances were estimated using a multivariate normal model. *Results:* The correlation with chronological age was .04-.82 for GrimAge2, .01-.82 for PhenoAge, and .01-.19 for DunedinPACE. Across the three epigenetic aging clocks, MZ twins exhibited higher correlations than other pairs, while DZ twins showed higher correlations than non-twin siblings, but the difference was nonsignificant ($p > .05$). The best-fit models of familial correlations were different across the clocks. For GrimAge2, there was a linear increase in MZ pairs, a linear increase before 18 years but a linear decrease thereafter in DZ pairs, and a linear decrease in non-twin sibling pairs. For PhenoAge and DunedinPACE, the best models were both when the constant correlations in MZ pairs were twice the correlations in DZ pairs. Accordingly, for GrimAge2, the additive genetic variance was 0.02 (*SE*: 0.30), and the common environmental variance within MZ twin pairs showed a linear decreasing pattern starting from 0.57 (*SE*: 0.30), while nondetected at birth for DZ pairs, increased before age 18 and decreased thereafter, and a linear decrease starting from 0.21 (*SE*: 0.52) for sibling pairs. For PhenoAge and DunedinPACE, no evidence for additive genetic variance or changes was found ($p > .05$), and the common environmental variance was .43, .26 and .00 for MZ twins, DZ twins and non-twin siblings respectively; for PhenoAge, was .54, .26, and .00 for DunedinPACE respectively. *Conclusions:* GrimAge2, PhenoAge, and DunedinPACE exhibit unique familial and environmental influences, providing valuable insights into their determinants and potential implications for health outcomes. GrimAge2 is more likely to have a cohabitation pattern within families, especially in DZ twins. PhenoAge and DunedinPACE, no evident change with cohabitation was observed, while the common environmental variance is more shared within MZ twin pairs. These findings underscore the significance of environmental factors over genetic contributions in shaping these epigenetic aging clocks, offering opportunities for targeted interventions to modulate biological aging.

Genetic Impacts on Early and Late Onset of Menarche: Insights From Four Twin Cohort Studies

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Introduction: The age at menarche (AAM) has shown a declining trend over the last century. Existing studies have predominantly explored the determinants of early menarche. In contrast, this research endeavors to expand the understanding by evaluating both early and delayed onset, differentiating between genetic and environmental contributions, alongside intrafamilial and interfamilial variations. *Materials and Methods:* We examined the genetic and environmental influences on AAM throughout the puberty period, using 4 twin cohort studies of multiple populations. We also estimated the relative importance of within- versus between- family variation, and differences in AAM within twin pairs. *Results*: The heritability increased as the increase in AAM. Late menarche showed higher heritability (0.709, 95% Cis [.686, .732]) than early menarche (0.463; 0.332 0.594). Early menarche, but not late menarche, had meaningful shared environmental effects. Within-family variation was generally larger than between-family for both monozygotic and dizygotic twins except Koreans. The relative importance of within-family variation holds regardless of obesity. The differences in AAM within twin pairs were globally observed, with 2/3 of monozygotic twin pairs showed >1 year. *Conclusion:* Our study suggests that comprehensive determinants of AAM would be better identified by incorporating both early and delayed AAM. Risk factors that are appropriate for 'within-family variation' and 'cotwin difference' have been largely neglected, but need to be more emphasized. Further genetic studies need to consider the variants responsible for interactions between genes and environments.

Associations Between Cord Serum Antibodies Against Phosphorylcholine and Neonatal Bacterial Infections: A Prospective Cohort Study in Singletons and Twins

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Introduction: Antibodies against phosphorylcholine (anti-PC) are reported to protect against infection. This study aimed to investigate these associations among both singletons and twins. *Materials & Methods:* A total of 1007 neonates (329 singletons and 678 twins) within the hospital-based Shenzhen Baoan Birth & Twin (SZBBTwin) cohort were included in this study. Levels of IgM anti-PC, IgG anti-PC, as well as IgM, IgG, and IgA in cord serum were measured by enzyme-linked immunosorbent assay. Diagnoses of bacterial infections were identified within 0-27 days after birth. Multivariable logistic regression with propensity score adjustment was performed to assess the associations between levels of antibodies and neonatal bacterial infections. *Results*: The mean (standard deviation) levels of IgM and IgG anti-PC were 46.68

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(14.15) ng/ml and 73.68 (30.44) ng/ml, respectively. Neonatal bacterial infections were diagnosed in 24 singletons (7.29%) and 48 twins (7.08%). A higher level of IgM anti-PC was associated with a lower risk of neonatal bacterial infections in the analyses of singletons (*OR* 0.64, 95% CI [0.41, 0.99]) or discordant twin pairs (concerning bacterial infection) (*OR* 0.44, 95% CI [0.20, 0.95]). *Conclusions:* A higher cord serum level of IgM anti-PC is associated with a lower risk of bacterial infections in neonates.

Twin Pregnancy: Maternal and Fetal Prognosis

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Introduction: Twin pregnancies are high-risk pregnancies, and twin deliveries pose various challenges due to the complexity of obstetrical mechanics and the frequency of dystocic presentations. Twin pregnancies are a significant public health issue and contribute to a high rate of perinatal mortality. The objective of this study is to report the epidemiological, clinical, therapeutic, and developmental aspects of newborns from twin pregnancies. *Materials and Methods:* This is a retrospective study based on the records of patients with twin pregnancies over a period of 2 years. Data from 48 newborns from twin pregnancies were collected. *Results:* The average maternal age was 28 years. The average term of delivery was 35 weeks. Prematurity was noted in 28 newborns (58% of cases). Twin-to-twin transfusion syndrome was observed in 4 cases. IUGR was present in 19 cases (40%). Neonatal infection was found in 28 newborns (58%). Congenital malformations were found in only 2 cases. The mortality rate was 43%. The most commonly used antibiotic therapy was a combination of third-generation ceftriaxone and an aminoglycoside. Phototherapy was used for 6 newborns; invasive ventilation for 11 newborns, and 19 newborns received CPAP. *Conclusion:* Efforts must be made to prolong gestational age, increase birth weight, and optimize the mode of delivery. Under optimal conditions, a target gestational age of 37-38 weeks should be the goal before delivery to reduce perinatal morbidity and mortality in twin pregnancies.

Twins and Twin Studies: The Science and the Fascination

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Introduction: Twins and twin studies are universally fascinating for scholars in the scientific community and for members of the general public. Why this is so has never been adequately addressed, but several explanations will be suggested. *Materials:* Based on the extant twin literature and ongoing research, an overview of compelling variations in twinning that exist among both MZ and DZ twin pairs are presented. Examples include twins discordant for medical conditions, the so-called 'biracial twins', and twins with different fathers; illustrative cases will be presented. Some novel, twin-like couples will also be described, due to their being scientifically informative across a arrange of behavioral and physical characteristics. Examples include virtual twins, unrelated look-alikes, and switched-at-birth twin pairs. *Results:* Twin research continues to expand and to develop as more twins and higher multiples are being born, and researchers representing diverse disciplines, such as politics, religious studies, economics, space science, and molecular genetics, are utilizing a twin-based approach to assess their observations. *Conclusion:* There are many ways in which unusual pairs can be used to inform various twin-related topics. The next few years promise to be an exciting time in this expanding field.

Documentary Films Tell Twins' Stories: Identical Colombian Twins Doubly Switched at Birth and Identical Dutch Twins Reared Apart

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Introduction: Twins have been central figures in books, plays, and paintings. Twins have also figured prominently in films. *Materials:* The first documentary film to be shown in this session, Hermanos por Accidente (Accidental Brothers), was directed and produced by Alessandro Angulo Brandestini. It tells the compelling story of doubly-switched Colombian monozygotic (MZ) male twins. One infant twin in each pair was accidentally switched with an infant twin in another pair, yielding two identical sets of 'fraternal' twins. One pair was raised in the lively capital city of Bogotá, while the other pair was raised in the tiny rural town of La Paz, approximately 100 miles away. The stunning truth was revealed when the four young men turned 25 years of age. Some of the twins will be available for discussion; their story is also told in the book, Accidental Brothers (2018). The second documentary film of this session, Peter and Erik, traces events leading to the separate lives of Dutch MZ male twins and their reunion at age 17. The film is organized into two parts: 'A New Brother' and 'They Thought They Were God'. Many unsettled questions surround the reasons for their separation, possibly orchestrated by psychologists with colleagues in America who were linked to the controversial 1960s' New York City study of adopted-apart babies. This film will be presented by producer and co-director, Myrthe Buitenhuis. *Results:* These two films capture significant aspects of twins and twin-related issues. The first film can be viewed on Netflix. The second film can be viewed on Dutch television as a documentary series, 2024. *Conclusion:* Both films are available for viewing throughout the ISTS conference. More about reared-apart twins is available in Segal's books, Born Together-Reared Apart (2012) and Deliberately Divided (2021).

Hungarian Twin Studies in Neurological Disorders

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Introduction: Recent studies have revealed the potential role of the gut microbiota and microbial metabolites in modulating mild cognitive impairment (MCI) and Alzheimer's disease (AD) via the gut-

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brain axis. However, this relationship has not been studied in monozygotic twins yet. *Materials and methods:* Among the 10,007 twin members of the population-based Hungarian twin registry, we invited twins with a history of multiple sclerosis, Alzheimer's disease, and Parkinson's disease, as well as all identical twin pairs over the age of 68. 113 identical twins were examined who underwent carotid and femoral ultrasound, liver ultrasound elastography, cerebral MRI, arterial stiffness, body composition measurement, lifestyle and neurological questionnaires, blood sampling with complete lipid profile analysis, and intestinal microbiome analysis. *Results*: 7 twin pairs discordant for Addenbrooke's cognitive questionnaire test (ACE) score and 15 twin pairs discordant for Montreal Cognitive Assessment (MoCA) score were analysed separately. Albeit no significant difference was found in the alpha and beta diversity based on separate microbiota, genus and family level, ANCOM analysis confirmed a lower abundance of Lachnospiraceae family and Alphaproteobacteria class in ACE discordant twins in a $p<0.01$ level. We found a correlation between cognitive functions and amygdala volume, with left-sided dominance. Cognitive functions were associated with ApoJ, ApoC2 (straight correlation) and amyloid-beta 42 (inverse correlation). A strong correlation was found between the visceral body fat percentage, serum LDL-cholesterol level and the texture features of the atherosclerotic plaques ($p < .001$ and $p < .01$). *Conclusions:* Dysbiosis and individual bacteria may contribute to the development of MCI. Visceral body fat and serum LDL-cholesterol level is associated with some carotid plaque ultrasound features.

Radiomic Study of Breast Cancer Discordant Twins

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Introduction: Previous twin studies show that genetic factors are responsible for 63% of the variability in breast density. Breast tumors are the most common malignant change in women and the leading cause of death from oncology in Europe. Breast tumor risk factors include a positive family history, breast tissue with increased density, as well as some known specific genetic mutations that significantly increase the chance of developing a breast tumor. However, the background of sporadic breast cancers is still not fully understood. *Materials and methods:* A total of 28 twins from the Hungarian Twin Registry between the ages of 38 and 75 participated (11 monozygotic and 3 same-sex dizygotic twin pairs, average age 54.2 ± 14.3 years, 72% female), of which at least one sibling has a history of breast cancer. Twins underwent mammography and ultrasound. We measured breast density using 3D Slicer software and analyzed the mammographic images of 9 discordant twin pairs for breast cancer. Genetic variants predisposing to breast cancer were also examined. The subjects also took part in a blood test (DNA test, epigenetics), filled out lifestyle questionnaires and provided a stool sample for microbiome testing. *Results*: One of the examined twin pairs had a BRCA2 mutation in both members. There was no significant difference between the mean values of breast density in the tumor and non-tumor groups ($p = .323$). In terms of parity and the presence of menopause, in the majority of twin pairs, we found no significant difference between the two members of the twin pair. We observed a dysbiosis in the breast cancer discordant twins. *Conclusions:* The average breast density showed no significant difference, which can be explained by the common genetic basis of breast cancer and breast density. Bacterial dysbiosis can be observed with the breast cancer affected twin. The combination of genetics and epigenetics with imaging can answer questions whether various imaging phenotypes can predict genetic and epigenetic modifications related to organ structure, function and metabolism, which impact disease risk and progression.

Impact of Maternal Smoking on Obstetric and Neonatal Outcomes in Twin Pregnancies: A Prospective Study

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Introduction: Maternal smoking during pregnancy adversely affects maternal and fetal health, with potential postnatal consequences. In twin pregnancies, which already carry a higher risk of perinatal complications, the impact of smoking remains underexplored despite evidence linking tobacco use to adverse outcomes in singleton pregnancies. *Materials & Methods:* A prospective study at La Fe University and Polytechnic Hospital, Valencia, Spain, examines maternal-fetal outcomes in twin pregnancies among active smokers ($n = 2$), passive smokers ($n = 2$), and nonsmokers ($n = 4$). Approved by the Ethics Committee, the study includes participants who provide informed consent. Exhaled carbon monoxide (CO ppm) and oxygen saturation (SatO2) are measured at 10, 16, 24, 28, and 32 weeks of gestation. Demographic, obstetric, and neonatal data are recorded. *Results:* The study includes 8 women with twin pregnancies (mean age: 32.57 years); 5 conceived through assisted reproductive techniques and 3 naturally. The cohort comprises 5 dichorionic-diamniotic, 2 monochorionic-diamniotic, and 1 monochorionic-monoamniotic pregnancies. No significant differences in SatO2 were found between groups. Active smokers exhibited higher CO ppm levels, which increased with gestational age. CO ppm levels in passive smokers were comparable to nonsmokers. *Conclusions:* Active smoking in twin pregnancies is associated with increased exhaled carbon monoxide, potentially leading to elevated obstetric and neonatal risks. This ongoing study seeks to enhance understanding of smoking's impact on twin pregnancies and inform targeted interventions to mitigate risks.

Predictive Value of First Amniotic Sac Il-6 and Maternal Blood CRP for Cerclage Success in Twin Pregnancies

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Introduction: Cervical insufficiency is a risk factor for preterm birth (PTB) in singleton and twin pregnancies. In cases of second-

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trimester cervical dilatation with bulging membranes, treatment options include expectant management or physical examination-indicated cerclage. While cerclage is effective in singleton pregnancies, its role in twin gestations remains controversial. Intra-amniotic inflammation (IAI), defined by amniotic fluid interleukin-6 (IL-6 ≥2.6 ng/mL), or infection, is a significant cause of cervical insufficiency and is associated with adverse pregnancy outcomes. Additionally, maternal blood factors such as C-reactive protein (CRP) may be elevated in the presence of intra-amniotic inflammation or infection. *Materials & Methods:* This prospective study included 28 twin pregnancies with bulging membranes admitted to La Fe Hospital (2012–2023). Amniocentesis was performed on the first sac to detect IAI, with 12 patients undergoing testing of both sacs. Patients with IL-6 <2.6 ng/mL received cerclage, while those with IAI were treated with intravenous antibiotics. CRP levels were analyzed as a prognostic marker. Ethical approval was obtained. *Results:* Among 28 patients, 18 (64.28%) had IL-6 ≥2.6 ng/mL. Cerclage placement in 10 patients with IL-6 <2.6 ng/mL resulted in delivery at 34 (±3) weeks versus 23 (±4) weeks for IL-6 ≥2.6 ng/mL ($p<0.001$). Latency to delivery was 88.1 (±31.56) days for IL-6 <2.6 ng/mL and 13.11 (±20.43) days for IL-6 ≥2.6 ng/mL ($p<0.001$). Elevated CRP levels (≥3.9 mg/L) were associated with worse outcomes, with delivery at 24 (±5) weeks and 21.95 (±30.97) latency days compared to 33 (±5) weeks and 86.5 (±44.88) days for lower CRP ($p < .01$). IL-6 levels correlated positively between both sacs (rho = 0.835, $p < .001$). *Conclusions:* Emergency cerclage is effective in twin pregnancies with bulging membranes without IAI. Amniocentesis is necessary only in the first sac. Maternal CRP levels could serve as a valuable predictor of cerclage prognosis.

Hungarian Twin Study on COVID-19 Infections and Vaccination Status

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Introduction: SARS-CoV-2 has resulted a devastating pandemic with serious social, economic and health disruptions globally. There have been over 750 million confirmed cases including almost 7 million deaths reported to WHO. Considering the high transmission and pathogenic potential of the virus, it is crucial to examine the characteristic of the disease and the willingness to vaccinate, understanding more the genetic susceptibility and the phenotype influenceability by external factors. We aimed to identify genetic and environmental factors and detect the vulnerable groups. *Materials and methods:* We performed a questionnaire based online survey to inquire about the impact, symptoms, and severity of COVID-19 disease in Hungarian twins among the members of the population-based Hungarian Twin Registry. *Results:* From July 2022 to April 2023, 813 twins filled the questionnaire form (608 female, 205 male subjects, 74.7% women; 460 monozygotic, MZ and 353 dizygotic, DZ twins, age range 19-84 years). 26 (16,3%) out of 160 MZ pairs, and 20 (21%) out of 95 DZ pairs were discordant for COVID vaccination. Getting vaccinated (C: 62.6%, 95% CI [48.0, 74.7]; E: 37.4%, 95% CI [25.3, 52.0]), undergoing COVID infection (C: 45.8%, 95% CI [30.3, 59.3]; E: 54.2%, 95% CI [40.7, 69.7]) were influenced by environmental factors. Vaccination willingness at the time when the vaccine first became available was not influenced by heritable factors. The feeling of being a test subject in the vaccination campaign (27.3%, 95% CI [11.1, 42.2]) and the opinion on that the vaccination should be obligatory (60.7%, 95% CI [49.0, 70.3]) was a heritable trait. *Conclusions:* More MZ twins were concordant in opinion of vaccination than DZ twins. COVID infection severity, willingness and opinion on the COVID vaccination was influenced by environmental factors, which underlines the importance of external communication channels.

The West Japan Twins and Higher Order Multiple Births Registry

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Introduction: The West Japan Twins and Higher Order Multiple Births Registry was established by recruiting young twins and multiples and referrals from public health centers in the 1990s. The goals of this registry are not only to research human genetics and maternal and child health but also to contribute to providing appropriate information for families with multiples. *Methods:* Twins, triplets, quadruplets, quintuplets and their family in this registry were recruited from several other sources, including mothers who responded to magazine articles featuring nursing guidance for families with multiple births, the various Japanese Mother's Organization for Twins and Higher Order Multiple Births, and referrals from several public health centers in west Japan. Follow-up questionnaire has been mailed out every 3 to 4 years in longitudinal survey studies. *Results:* The number of participants who take part in the survey is over 8,000 twins and over 4,500 higher order multiple births and their families. Public health centers have been collaborating with us to provide appropriate childcare information for families with multiples since 2002. Expectant mothers and fathers with multiples have been offered childcare information for families with multiples based on several articles. On the other hand, currently, it is difficult to get new subjects of multiples in general, because of the private information protection law in Japan. Referrals from public health centers are therefore important for this registry to keep getting new subjects. *Conclusions:* The goals of this registry are not only to research human genetics and maternal and child health but also to continue providing appropriate information for families with multiples in public health centers.

Guangzhou Twin Eye Study: 2024 Update

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The Guangzhou Twin Eye Study (GTES) has been a pivotal longitudinal research project since 2006, aimed at exploring the genetic and environmental influences on common eye diseases. Initially, approximately 1300 pairs of twins, aged 7–15 years, were enrolled, with annual data collection on various ocular and systemic phenotypes. By 2019, significant findings were made in understanding the heritability of ocular traits and the interplay between ocular and systemic conditions. In 2024, the GTES undertook a new follow-up with the now adult cohort, all participants being over 18 years old. This latest phase of the study expanded the scope to include comprehensive evaluations of both systemic and ocular traits. The systemic data encompassed metrics such as height, weight, waist-hip ratio, blood pressure, and blood composition, while ocular data included visual

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acuity, cycloplegic refraction, axial length, intraocular pressure, and advanced imaging techniques like OCT angiography. The 2024 update aims to provide a detailed analysis of the longitudinal changes in ocular and systemic traits from childhood to adulthood. By integrating multi-omic data and employing advanced statistical models, the study seeks to quantify the genetic and environmental contributions to these traits over time. The findings will enhance our understanding of the dynamic interactions between genetics, environment, and the development of eye diseases, contributing to more effective prevention and treatment strategies.

Maximising the Value of Twin Studies in Current Research

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Introduction: The classical twin design, introduced by Siemens in 1924 in the Netherlands, compares monozygotic (MZ) and dizygotic (DZ) twins to estimate genetic and environmental influences on traits. Siemens, a dermatologist who studied moles, ingeniously combined correlation (similarity) analysis and twin data, laying the foundation for thousands of twin studies exploring the genetic influences across a wide range of human traits and advancing our understanding of population variation. *Methods:* This review explores advancements in twin studies, focusing on new phenotypes, omics data, and global diversity in twin cohorts. *Results:* The twin design has also become a valuable tool for studying causality in the discordant twin design, intergenerational transmission when including parents or offspring of twins, comorbidity among multiple phenotypes, gene-environment correlation and interaction. Key findings highlight that genetic influences are not deterministic, as demonstrated by discordance in MZ twins for highly heritable traits. Twin studies underscore that genetic risk predictions are inherently limited by MZ concordance rates. Further, they provide valuable insights into diverse phenotypes and methods to address global underrepresentation in twin research. *Conclusions:* Twin studies remain invaluable for genetic and environmental research.

Modelling Monochorionic Twinning in Human Stem Cell-Based Embryo Models

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Introduction: The underlying causes and mechanisms of monochorionic twinning remain largely unknown. A widely accepted hypothesis to explain twin formation is that the inner cell mass (ICM) splits during the blastocyst stage, giving rise to a single trophectoderm cyst with two ICMs. However, due to limited availability and ethical concerns surrounding blastocyst research, mechanistic studies have been lacking. In the recent years, advances in the stem cell biology have resulted in stem cell based blastocyst models called blastoids. In our study, we have used blastoid cultures to develop a model for monochorionic twinning in vitro. *Materials & Methods:* We aggregated naïve pluripotent stem cells in microwell arrays to generate hundreds of blastoids. We optimized culture conditions to generate blastoids with two ICMs. We used scRNAseq, immunostaining, and morphological measurements to compare these structures to singleton blastoids and tracked the splitting of the ICM with live imaging. Moreover, we used an endometrium-on-chip platform to study the adhesion of twin blastoids. *Results:* We were able to reach a yield of 16% twin blastoids in our blastoid culture. Twin blastoids contained two opposed epiblast-like clusters, each adjacent to a distinct polar trophectoderm-like region within the shared trophectoderm-like cyst. Moreover, we observed the splitting of the ICM concurrent with cyst expansion. Transferring formed blastoids to the endometrium-on-chip showed a more efficient adhesion of twin blastoids compared to singletons. *Conclusions:* We have generated a model for monochorionic twinning. These models can be produced at large scale and thus provide an unprecedented opportunity for studying the mechanisms at play in twin formation.

The MELON Study: Monochorionic Twin Pregnancies with SinglE Intrauterine Fetal Demise: The LONg-Term Effects in Survivors

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Introduction: Monochorionic (MC) twins are at risk for complications, including twin–twin transfusion syndrome, twin anemia polycythemia sequence and selective fetal growth restriction. These complications may result in fetal demise. Single IUFD (sIUFD) can have significant consequences for the surviving co-twin, with a high risk of cerebral injury and subsequent neurodevelopmental disabilities due to acute exsanguination in the presence of large patent anastomoses. Yet, conclusive evidence on long-term outcomes of survivors of sIUFD is lacking. The main objective of the MELON study is to assess long-term neurodevelopmental outcome in a cohort of survivors of MC twin pregnancies with sIUFD. *Materials & Methods:* We will perform an observational cohort study. All survivors of MC twin pregnancies with sIUFD born in the LUMC or an affiliated hospital between 2002 and 2023 are eligible for inclusion. The survivors will be invited for a follow-up assessment, consisting of a standardized psychometric age-appropriate tests and a neurological examination. Long-term behavioral outcome, attachment, quality of life and school functioning will be documented using questionnaires. *Results:* The protocol for the MELON study is currently under review at our local medical ethical committee. The study is set to commence in the first quarter of 2025. *Conclusion:* Knowledge of long-term outcomes is essential both for adequate counselling of parents of these vulnerable patients and for early identification of children who will benefit from additional postnatal monitoring. Moreover, a better understanding of long-term outcome might aid in devising feasible management options in the future.

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CODATwins Project: International Comparisons Demonstrating the Importance of Collecting Twin Data in Populations With Different Macro-Environmental Exposures

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Introduction: Genetic and environmental variation can shed light on the mechanisms behind human diversity. The role of these factors can also vary between societies reflecting the influence of cultural differences. However, since this requires international comparisons, we collected an international database including height and weight measures from all available twin cohorts in the world. *Materials and methods:* We started data collection in 2013 by contacting all twin cohorts worldwide and requesting individual-level data. Currently, the database includes around 1 million height and weight measures from half a million twin individuals representing 24 countries. The data were analyzed using classical genetic twin modeling. *Results:* We found that mean height and body mass index (BMI) were largest in North America and Australia followed by Europe and were lowest in East Asia. For BMI, the differences in total variance were similar to those found in means whereas in height the variance was largely similar in these areas. Heritability estimates of BMI and height were roughly similar in all areas. *Conclusions:* We found that the macro-environment can affect not only the mean but also the variance of anthropometric traits, but these effects may be different for different traits. However, despite differences in means and total variances, heritability estimates were roughly similar in these geographic-cultural areas. These results demonstrate the need to collect measures on various traits in twins living in different macro-social contexts.

Epigenetic Aging and Personality Differences: Latent Change Analyses of Twin Data

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Introduction: Personality stability and change is not only attributable to both genetic and environmental factors but also to their complex interplay. So can environmental factors induce changes in the expressions of genetic factors underlying personality differences. These changes can be age-related (epigenetic aging) and individual differences in such epigenetic aging processes could account for variance in personality change over time. Reversely, personality differences could drive experiential differences that affect epigenetic aging. So far, such associations have not been investigated. The present study approached these associations using saliva-based DNA methylation and self-reported personality data from 1,088 early adolescent to young adult twins from the TwinLife Epigenetic Change Satellite Project. *Materials & Methods:* Using chronological and biological clocks as measures of epigenetic aging, we applied (biometric) latent change analyses to explore the patterns, sources, and links of epigenetic aging and Big Five personality traits across a 2-year time interval, coinciding with the COVID-19 pandemic. *Results:* Besides significant mean-level acceleration in epigenetic aging and decreases in all personality traits (except neuroticism), variance in change was mainly attributable to environmental factors. Accelerated epigenetic aging based on chronological clocks was associated with higher baseline levels of agreeableness and conscientiousness and with decreases in conscientiousness. Epigenetic aging based on biological clocks and conscientiousness were negatively linked at baseline. These links involving stable personality differences were rather genetically driven, whereas change correlations were primarily environmental. *Conclusions:* Findings suggest complex interplays between epigenetic aging and personality traits with evidence for differential roles of both genetic and environmental factors.

Parental Warmth and Self-Esteem in Early Adolescence: A Longitudinal Twin Study

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Introduction: Parenting relates to adolescent self-esteem, an effect typically viewed as unidirectional. We address the possibility that self-esteem predicts parenting through a longitudinal twin study. *Materials & Methods:* Israeli adolescent twins (N = 1155) filled the Rosenberg Self-esteem Scale, and parents reported warmth with the Parent Practices Questionnaire at ages 11 and 13. *Results:* Age 11 self-esteem predicted maternal and paternal warmth at age 13, but warmth did not predict self-esteem. Analysis of MZ and DZ twins suggested genetic contributions to both traits. *Conclusions:* Results highlight the need to view the family as a system of mutual influences. Genetic effects underscore the interplay between genetic and environmental factors in family relationships.

Effects of Estimated Fetal Weight Discordance on Neonatal Outcomes in Twin Pregnancies: A Cohort Retrospective Study

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Introduction: Accurate assessment of fetal growth in twin pregnancies is vital, particularly when estimated fetal weight (EFW) discordance might impact neonatal outcomes. This study examines how EFW discordance, categorized as either under or over 20%, affects neonatal health. *Materials & Methods:* A retrospective cohort analysis was performed on twin deliveries at the 1st Department of Obstetrics and Gynaecology at Medical University of Warsaw. Pregnancies were grouped based on prenatal EFW discordance: over 20% (LOW group, n = 13) and under 20% (HIGH group, n = 130). Data on prenatal care and neonatal outcomes were collected via medical records and post-pregnancy phone surveys. *Results:* The LOW group had an average APGAR score of 9.20, comparable to the HIGH group's 9.06. Antibiotic use and birth timing were similar between groups. However, the LOW group showed higher rates of respiratory support (48% vs. 29.62%, p = .029), ICU admissions (48% vs. 29.23%, p = .026), and nonphysiological jaundice (48% vs. 20%, $p < .001$). In the LOW group, 53.85% of pregnancies had a postnatal weight discordance exceeding 20%, aligning with prenatal predictions, compared to 10% in the HIGH group. One intrauterine fetal demise occurred in the LOW group. Differences in chorionicity may have influenced outcomes. *Conclusions:* EFW discordance over 20% is associated with increased respiratory support, ICU admissions, and jaundice, emphasizing the importance of routine ultrasound evaluations in multiple pregnancies to monitor EFW.

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Guinea-Bissau Twin Registry

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Introduction: In Africa, there is a high natural twinning rate, but also a very high mortality among newborn and young twins. Thus, it has been estimated that one in five twins dies during childhood, but reliable data is often lacking. *Materials & methods:* In 2009, we established one of the first twin registries in Sub-Saharan Africa at the Bandim Health Project in the capital Bissau, Guinea-Bissau. We aimed at characterizing twinning rate and mortality in a cohort of newborn twins, including mortality and hospitalizations. Second, due to lower twin birth weight, this could increase their risk of dysmetabolic disorders later. Yet, no such 'fetal programming' data have been available from African twins. In a cohort of young twins between 5-30 years we investigated this. *Results:* In Guinea-Bissau, twins accounted for 9% of all perinatal deaths, making it a high-risk group of substantial size. There was a low burden of metabolic syndrome and diabetes among young individuals, and twins were not at increased risk. Yet, fasting glucose was significantly higher for twins, despite significantly lower BMI. *Conclusions:* Newborn twins is Guinea-Bissau is a high-risk group, with significantly elevated mortality during the first three months of life. Any possible long-term metabolic risks for twins still need to be investigated further.

Enhancing Future Studies of the PETS Twin Birth Cohort Through Participant Engagement

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Introduction: The Peri/postnatal Epigenetic Twins Study (PETS) is a Melbourne-based twin birth cohort investigating early-life origins of cardiometabolic and neurodevelopmental outcomes. Despite 17 years of research, PETS lacked a Participant Advisory Group to enhance engagement and guide future studies. This study aimed to gather participant feedback and establish an advisory group. *Materials and Methods:* A participant experience questionnaire was sent via REDCap to PETS mothers and twins, followed by online workshops to discuss key themes. Basic statistical analyses were conducted, and interested participants were invited to join the discussions. *Results:* Participants were motivated by altruism and valued the research's personal and broader importance. They preferred brief online interactions, convenient visits, and debit card compensation. Most supported future data use without re-consent. Workshops highlighted the importance of including mental health, genetics, new technologies, and improved communication in future PETS waves. *Conclusion:* Altruism, convenience, and research relevance drive PETS engagement. Forming a Participant Advisory Group will be essential for optimizing future research efforts.

Genetic Impacts on the Skin Methylome In Healthy Older Twins

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Introduction: DNA methylation at CpG dinucleotides is a dynamic epigenetic mechanism that has been linked to a number of skin phenotypes and diseases. Previous studies in blood show that a substantial proportion of the human DNA methylome exhibits evidence for genetic influence. DNA methylation is a highly tissue-specific modification to the DNA, and no previous study has explored the genome-wide heritability of DNA methylation in the largest human organ, skin. *Materials and Methods:* Utilizing a twin-based heritability model, we estimated DNA methylation heritability using 414 bulk skin tissue samples from healthy older female twins from the TwinsUK cohort, profiled using the Illumina Infinium Human Methylation 450 BeadChip. *Results:* Over 8.2% of measured CpG sites showed evidence for strong heritability ($h2 > 0.4$), with a mean additive heritability estimate of 11.07% across all tested sites. Genome annotation analyses suggest that heritability of methylation in skin is highest in intragenic regions (mean additive heritability: 13.2%), compared to regions proximal to gene bodies and in regulatory elements (mean additive heritability: 10.5%). We observed that a greater proportion of the skin methylome is strongly influenced by the environment compared to previous reports in blood and adipose tissue, potentially reflecting a greater extent of environmental exposure in skin tissue. *Conclusions:* Our study is the first genome-wide DNA methylation heritability analysis of whole skin, giving insights into the regulatory landscape of epigenomic variation in skin.

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