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Hard facts and misfits: essential ingredients of public health nutrition research

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Policy decisions and the practice of public health nutrition need to be based on solid evidence, developed through rigorous research studies where objective measures are used and results that run counter to dogma are not dismissed but investigated. In recent years, enhancements in study designs, and methodologies for systematic reviews and meta-analysis, have improved the evidence-base for nutrition policy and practice. However, these still rely on a full appreciation of the strengths and limitations of the measures on which conclusions are drawn and on the thorough investigation of outcomes that do not fit expectations or prevailing convictions. The importance of ‘hard facts’ and ‘misfits’ in research designed to advance knowledge and improve public health nutrition is illustrated in this paper through a selection of studies from different stages in my research career, focused on the nutritional requirements of resource-poor populations in Africa and Asia.

Africa: Calcium: Evidence-based nutrition: Gambia: Vitamin D

Policy decisions and the practice of public health nutrition need to be based on solid evidence, developed through rigorous research studies where objective measures are used and results that run counter to dogma are not dismissed but investigated. Dr Elsie Widdowson, after whom this Nutrition Society Award was named, was a passionate advocate of this philosophy throughout her long career, and she has been an inspiration to me and many others engaged in public health nutrition research. These principles have been the bedrock of studies into the nutritional requirements of resource-poor populations

in Africa and Asia that I have conducted or been involved in over the years. A selection of these studies are described in this paper to illustrate the importance of ‘hard facts and misfits’ for research designed to advance knowledge and improve public health nutrition.

Lactational performance in poorly nourished women

The problem of infant growth faltering in resource-poor regions of the world has long been recognised^(1,2) and

Abbreviations: ART, antiretroviral therapy; SA-BMC, size-adjusted bone mineral content.

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remains an intense area of research and public health concern. In the past, because breast-feeding of infants was universally practised in these disadvantaged populations, it was assumed that growth faltering was a result of compromised pregnancy and lactation due to the mother's poor nutritional status. In the 1970s, Professor RG Whitehead, Director of the MRC Dunn Nutrition Unit in Cambridge, established an intensive series of programmes in Cambridge and The Gambia, West Africa, to provide the scientific evidence on which nutritional interventions to reduce infant growth faltering could be based. The Gambian research was based in the village of Keneba and its neighbouring villages in the province of West Kiang, a remote and resource-poor region of the country. This region had been the subject of longitudinal demographic and health surveys since 1950, primarily in connection with malaria research. In this rural Gambian society at that time, malnutrition and poor infant growth were already well documented, associated with marginal diets, seasonal food shortages and high infection rates⁽³⁾. Large family sizes were the norm and infants were customarily breast-fed for about 2 years with complementary foods introduced from about 4 months, making Keneba an ideal location for this research. In Cambridge, a much more affluent society, nutrition and health provision was generally good and breast-feeding, at least in the first year post-partum, was relatively common. Studies in Cambridge among pregnant and lactating women were conducted to provide comparative data for the Gambian studies.

The initial stages of the work involved establishing a small team of scientists, doctors and other staff in Keneba to create a rapport with the local community and develop culturally-sensitive research methods and protocols. This was especially important for the lactation studies in order to prevent any alteration in mother-infant behaviour that might interrupt breast-feeding, a problem that was suspected in many of the studies cited in the literature up to that time⁽⁴⁾. The ability to measure the breast-milk intake of babies in a non-intrusive manner was advanced by the development by the MRC Dunn Nutrition Unit scientists of innovative stable isotope methods using ²H oxide, and these were pioneered in the Gambian and Cambridge lactation studies^(5,6). Unexpectedly, these studies demonstrated that Gambian infants had similar breast-milk intakes to those in Cambridge in the first months after birth when they were exclusively or predominantly breast-fed^(4,7).

The fact that the lactational performance of these Gambian women did not appear to be compromised by their poor diet was underscored by the results of maternal supplementation trials conducted during lactation. These trials used a specially prepared energy-protein-rich biscuit, made locally, and a vitamin-fortified tea drink. These trials demonstrated that improving the diet of the mother had no effect on the breast-milk intake or growth of the infant⁽⁸⁾. There were increases in the breast-milk content of certain vitamins present in the supplement but only marginal effects on the macronutrient content⁽⁸⁾. The most noteworthy effects were in mothers, who gained weight and reported fewer episodes

of poor health. However, these women also had lower concentrations of several hormones associated with lactation, especially prolactin^(9,10). This suggested that the supplement had produced a relaxation from a state of high metabolic efficiency and that much of the additional energy derived from the supplement was wasted in less efficient metabolic processes⁽¹⁰⁾. Furthermore, the lower prolactin concentration of these mothers was associated with a shorter period of amenorrhoea⁽⁹⁾. Even greater effects on lowering prolactin and shortening the period of amenorrhoea were seen when the Gambian mothers also received the dietary supplement during pregnancy⁽¹¹⁾.

As part of these early investigations, detailed studies of breast-milk composition revealed that the Gambian women had consistently lower breast-milk calcium concentrations than women in Cambridge, by about 25%^(12,13). Breast-milk calcium concentration was shown to decrease as lactation progressed, tracking within individuals, and was independent of the volume of breast-milk consumed by the infant⁽¹³⁻¹⁵⁾. These findings indicated, therefore, that, on average, the Gambian breast-fed infants consumed considerably less calcium than their Cambridge counterparts during exclusive breast-feeding and after the introduction of complementary foods^(16,17). With the exception of certain water-soluble vitamins whose concentration in breast-milk depends on maternal dietary intake, few components of breast-milk had been found to vary to this extent between populations⁽¹⁸⁾. A comparison of breast-milk calcium concentrations from different regions of the world showed that women in populations with a high customary calcium intake, such as in the UK and North America, tended to have higher breast-milk calcium than in African countries with a much lower dietary calcium intake^(13,18). This led to the possibility that the calcium content of breast-milk might be dependent on the maternal intake.

Hard facts

The objective studies conducted in The Gambia provided the hard evidence that human lactational performance is little affected by maternal nutritional status, other than in severe malnutrition. Improvements in the diet of poorly nourished lactating mothers were shown to benefit the woman in terms of nutritional status and perceptions of well-being, but also to decrease the period of lactational infertility, which may not be to her advantage. These results ran counter to expectations at the time, but are now widely accepted and incorporated into textbooks and policy documents.

Misfits

The breast-milk calcium concentration of Gambian women was found to be considerably lower than that of women in Cambridge and other regions of the world. Since calcium is a primary bone-forming mineral and essential for infant skeletal growth and maternal bone health, this unexpected finding was noteworthy and indicated the need for more intensive studies into calcium nutrition in The Gambia.

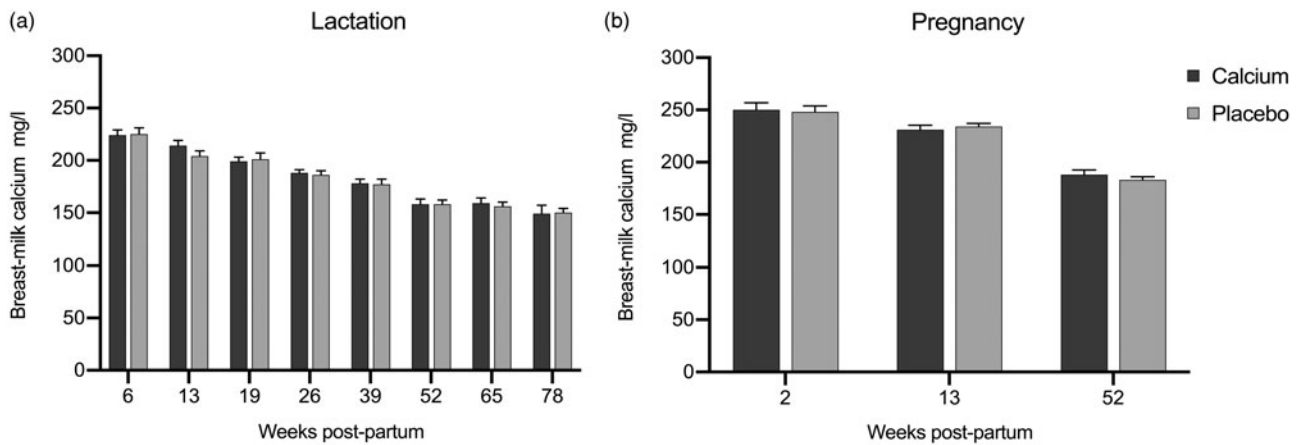


Fig. 1. Effects on breast-milk calcium concentration of maternal calcium supplementation during (a) lactation and (b) the preceding pregnancy. The data are expressed as mean (SE) concentration (mg/l) in breast-milk collected serially from 60 and 125 rural Gambian mothers respectively during randomised placebo-controlled trials of calcium carbonate supplementation (lactation trial = 1000 mgCa/d for 12 months; pregnancy trial = 1500 mgCa/d from 20 weeks gestation to delivery)^(22,23). Dark bars, calcium-supplemented group; light bars, placebo group. The numbers of women in the calcium and placebo groups respectively who participated in the sub-study of breast-milk calcium were: lactation trial 30, 30; pregnancy trial 61, 64. There were no significant differences between the groups at any time.

Dietary calcium intake and breast-milk calcium

The unexpected finding of low breast-milk calcium concentrations among Gambian women led to a more thorough exploration of dietary calcium intake in this population. The Gambian diet at that time was based predominantly on millet, sorghum and rice as staples, with groundnut (peanut)-, leaf- and vegetable-based sauces. Fish were eaten occasionally, often as dried ingredients in sauces, but the diet rarely included meat or milk. Dietary assessments were conducted, using detailed weighed intakes conducted by trained research assistants, combined with laboratory analysis of local foods and condiments. Potential hidden sources of calcium, such as flavourings, bush foods and pica, were also analysed and included in the estimates.

These studies demonstrated that the customary diet in rural Gambia was, and still is, very low in calcium throughout life^(19,20). This is largely ascribed to a lack of animal milk and milk products in the diet. Scrutiny of FAO balance sheets confirmed the much lower milk supply in The Gambia, and many other African countries, compared to the UK, Europe, Northern America and Australasia⁽²⁰⁾. These studies provided the estimates of average calcium intake of 300–400 mg/d in women and children, and 200 mg/d in infants^(17,19). These intakes are considerably lower than international dietary reference values and recommendations⁽²¹⁾. Such low intakes were surprising given that they are very close to the daily biological requirements for fetal growth, breast-milk production and childhood mineral accretion, even before making allowance for the reduced amount of calcium that can be absorbed from the diet⁽¹⁵⁾.

We conducted two randomised placebo-controlled supplementation trials to test whether raising the calcium intake of Gambian mothers would increase breast-milk calcium concentration and infant growth: the first during

lactation, the second during pregnancy. The mothers were supplemented with 1000 mg Ca/d from 2 weeks post-partum for 12 months in the lactation trial⁽²²⁾ and with 1500 mg Ca/d from 20 weeks gestation to delivery in the pregnancy trial⁽²³⁾. In both trials, the supplement was orange-flavoured, chewable calcium carbonate. The supplement was well accepted by the mothers and compliance was high. Breast-milk samples were obtained serially at specific times post-partum using carefully standardised collection and assay protocols⁽²⁴⁾. No significant differences were found between the calcium-supplemented and placebo groups in either trial (Fig. 1), thus demonstrating that breast-milk calcium concentration is not responsive to changes in maternal calcium intake. There was also no effect on the growth of the infants in terms of rates of increase in weight and length^(22,23,25). In addition, in the pregnancy trial, there were no differences in the mother's blood pressure between groups at any stage of pregnancy or lactation, nor was there an effect of the calcium supplement on infant birth size⁽²⁵⁾.

Hard facts

Contrary to common perceptions at the time, the Gambian studies demonstrated that breast-milk calcium content is not influenced by maternal calcium intake. This is now widely accepted and has largely stopped the practice of mothers with low calcium intakes being advised either not to breast-feed or to take calcium supplements in lactation in order to boost breast-milk calcium. The pregnancy trial also showed that the increase in calcium intake in these mothers did not produce benefits in terms of maternal blood pressure or fetal growth.

Misfits

These detailed studies showed that the customary diet in rural Gambia is very low in calcium, in common with many other resource-poor communities in Africa, at intakes very close to the biological requirement for bone mineral accretion and maintenance. This suggested that skeletal mineral content might be compromised in these populations during times of increased biological requirement, such as pregnancy, lactation and periods of rapid childhood growth.

Calcium requirements for maternal and infant bone health

During the 1980s, Dr Elsie Widdowson was awarded the prestigious Rank Prize in Nutrition, with which she endowed a fellowship at the MRC Dunn Nutrition Unit to work with me and the teams in Cambridge and Keneba to study the calcium requirements of mothers and children in Africa. This prompted the purchase of a single-photon absorptiometer, one of the first instruments designed to measure bone mineral content *in vivo* that could be used in healthy infants, children and adults. This was the start of the Nutrition and Bone Health Research Group based in the MRC Dunn Nutrition Unit and then in MRC Human Nutrition Research at the Elsie Widdowson Laboratory, and funds were obtained to set up parallel bone imaging facilities in Cambridge and The Gambia. The single-photon absorptiometer has been replaced over the years by new generations of bone scanning instruments as they became more sophisticated. Our more recent studies have predominantly used dual-energy X-ray absorptiometry and peripheral quantitative computed tomography.

To consider whether a low maternal calcium intake during lactation might necessitate mobilisation of skeletal calcium to support breast-milk production, we conducted a series of studies in Cambridge to investigate whether the bone mineral content of well-nourished breast-feeding mothers alters during and after lactation, and whether any changes are related to maternal calcium intake^(12–14,26,27). These studies demonstrated that measurable decreases in size-adjusted bone mineral content (SA-BMC) occur in the first few months of lactation, predominantly at the lumbar spine and hip, and that these are reversed in later lactation or after breast-feeding stops⁽²⁶⁾. The magnitude of the decreases after 3 months of exclusive breast-feeding was shown to vary between individuals, depending on the volume of breast-milk produced and other factors⁽²⁷⁾. However, no correlations with maternal calcium intake or breast-milk calcium concentration were found, despite the wide range of calcium intakes between the study participants⁽²⁷⁾.

To investigate this further, bone scanning was conducted to chart the skeletal changes during lactation in both the Gambian lactation and pregnancy calcium supplementation trials described earlier. The expectations were that the skeletal response to lactation would be less among women in the calcium-supplemented group

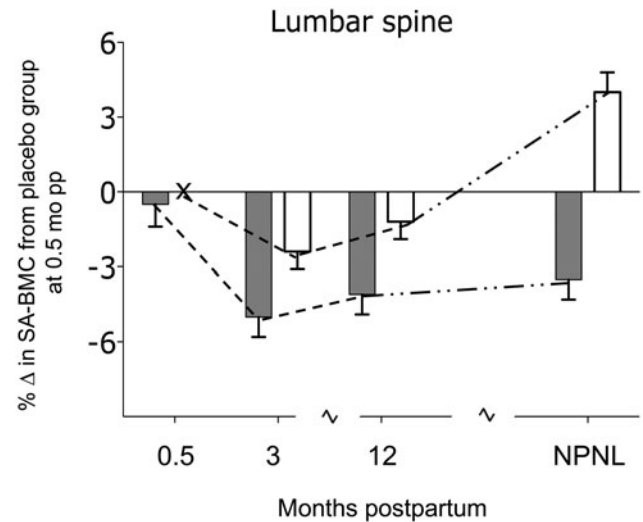


Fig. 2. Effects on size-adjusted bone mineral content (SA-BMC) of the lumbar spine (L1–4) of maternal calcium supplementation during pregnancy in Gambian mothers. The data are expressed as mean percentage difference (SE) relative to the placebo group at 0.5 months post-partum. The scans were obtained using dual-energy X-ray absorptiometry (DXA) as part of a randomised placebo-controlled trial of 1500 mgCa/d from 20 weeks gestation to delivery with follow-up. Measurements in the DXA sub-study were made serially on each individual during the index lactation at 0.5, 3 and 12 months⁽²⁸⁾ and approximately 5 years later at a time when the mother was neither pregnant nor lactating and at least 3 months since the end of a recent lactation period (NPNL)⁽³⁰⁾. The numbers of measurements at each timepoint for the calcium and placebo groups respectively were 0.5 months = 23, 27; 3 months = 29, 29; 12 months = 40, 39; NPNL = 31, 28. Dark bars, calcium-supplemented group; light bars, placebo group. The changes over time were significantly different between the two groups: in the index lactation *P* for interaction = 0.05; in the follow-up study *P* for interaction = 0.002.

than in the placebo group because the requirement to mobilise bone calcium to support breast-milk production would be lower, given the greater amount of calcium available from the diet. The results showed that this was not the case. In the lactation trial, which was performed at a time when only forearm scanning by single-photon absorptiometer was available, the expected decrease and reversal in SA-BMC was observed, but there were no significant differences between the groups⁽²²⁾. In the pregnancy trial, which was conducted several years after the lactation trial, whole-body and regional dual-energy X-ray absorptiometry scans were obtained to 12 months of lactation. The expected decrease in SA-BMC was observed in the first months of lactation but there was little sign of recovery of bone mineral by 12 months post-partum (Fig. 2)⁽²⁸⁾. The likely explanation for this was that, unlike most mothers in the Cambridge studies, all the mothers in the Gambian pregnancy trial were still breast-feeding on demand at 12 months and would not have begun to wean their infant from the breast. More surprisingly, and contrary to expectations, there were greater decreases in lumbar spine and whole-body SA-BMC in the mothers who

had been in the calcium-supplemented group during pregnancy than the mothers who had been in the placebo group (Fig. 2), and they also had lower hip SA-BMC throughout the 12 months⁽²⁸⁾.

Hard facts

These studies, plus data from other research groups around the world⁽²⁹⁾, demonstrated that skeletal mobilisation of bone mineral followed by restitution is a physiological aspect of lactation, and not a sign of calcium insufficiency.

Misfits

The accentuated skeletal response during lactation in those mothers who received the calcium carbonate supplement in pregnancy was an unexpected finding, contrary to the original hypothesis. This raised concerns that the pregnancy supplement may have disrupted the mother's ability to adapt to a low calcium intake, with potential health consequences for the bone health of herself and her offspring.

Follow-up studies of pregnancy calcium supplementation in The Gambia

Once the findings of the pregnancy calcium supplementation trial became apparent, those mothers who had been scanned during the trial were traced and invited to be scanned again. The time interval was approximately 5 years from their 12-month measurement; two-thirds of the women had had at least one more pregnancy-lactation cycle in the intervening years⁽³⁰⁾. The scans were conducted either when the woman had been breastfeeding her latest child for 12 months or when she was neither pregnant nor lactating and at least 3 months after having stopped the most recent lactation period. The neither pregnant nor lactating women who had been in the placebo group during the trial were found to have had similar increases in SA-BMC post-lactation to those observed in Cambridge women, while no such skeletal recovery was seen in those who had received the pregnancy calcium supplement (Fig. 2)⁽³⁰⁾. For those women in the follow-up study measured at 12 months lactation, the SA-BMC values in both groups were similar to their values at 12 months in the index lactation⁽³⁰⁾.

Although the growth of the infants was not significantly affected by the maternal pregnancy supplement, there was an indication that the bone mineral accretion rate was lower in the offspring of mothers in the calcium-supplemented group⁽²³⁾. To investigate the possibility that the maternal supplement had influenced the skeletal growth of the offspring, regular follow-up measurements throughout childhood were introduced. dual-energy X-ray absorptiometry scans were possible once the children were 8–12 years old, an age which in rural Gambia represents late childhood but pre-puberty⁽²⁰⁾. Unexpectedly, these studies demonstrated sex-specific effects of the pregnancy supplement, such that girls

whose mothers had been in the calcium group were shorter, lighter and had smaller bones with less bone mineral than girls whose mothers had been in the placebo group⁽³¹⁾. The opposite effects were seen in the boys; those whose mothers had been in the calcium group tended to be larger with greater bone mineral than boys whose mothers had been in the placebo group⁽³¹⁾. A similar pattern was also seen in insulin-like growth factor 1 concentrations measured in plasma samples collected when the children were approximately 7 years old⁽³²⁾.

Hard facts

The follow-up studies of the placebo group from the pregnancy calcium supplementation trial demonstrated that Gambian mothers are able to replenish bone mineral post-lactation, despite their customary low calcium intake. This added to the evidence that multiple cycles of pregnancy and lactation in African women with low calcium intakes are not associated with skeletal mineral depletion⁽³³⁾.

Misfits

The calcium carbonate supplement consumed in pregnancy by Gambian mothers, rather than confer a benefit on the women, was shown to have increased bone mineral mobilisation during lactation and inhibited skeletal recovery post-lactation. In addition, the calcium supplement was found to have altered the growth of the offspring during childhood in a sex-specific manner. These surprising findings suggest that the pregnancy supplement had altered maternal bone metabolism in such a way that the deficits in SA-BMC were still observed after 5 years, and may also have altered the *in utero* programming of the growth hormone-insulin-like growth factor 1 axis in the offspring. Further investigations are in progress to determine whether these effects persist long-term, by follow-up studies of the women in mid-life and the children during adolescence.

Calcium requirements in childhood and adolescence

One interpretation of the sex-specific effects noted in the offspring of mothers in the Gambian pregnancy trial is that the calcium supplement had increased the growth trajectory towards puberty faster in boys and more slowly in girls. This has resonances with the results of follow-up studies from our earlier calcium supplementation trial of prepubertal children in the same region of The Gambia. These children were 8–12 years of age and supplemented with 1000 mg Ca/d as calcium carbonate or placebo, 5 d weekly for 12 months. The calcium supplement increased forearm SA-BMC and decreased the bone turnover marker osteocalcin but with no increase in height or bone dimensions⁽³⁴⁾. Follow-up studies, however, demonstrated sex-specific effects on the passage through puberty for these children, such that the boys who had been in the calcium group entered their pubertal height spurt earlier than boys who had

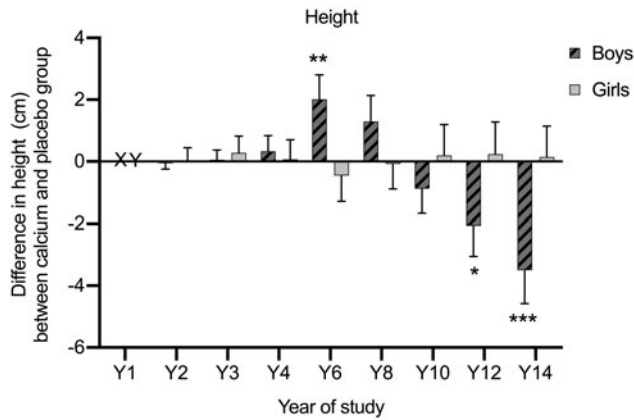


Fig. 3. Effects on height of calcium supplementation in pre-pubertal Gambian children. The data are expressed as the mean (SE) difference in height between the calcium and placebo groups by year of the study obtained from regression models after adjustment for height and age at Y1. The measurements were made serially during adolescence in 160 children (80 boys, 80 girls) who had participated in a randomised placebo-controlled trial of 1000 mg Ca/d, 5 d weekly for 12 months at the age of 8–12 years⁽³⁵⁾. The average age (years) of the boys at each measurement timepoint was approximately Y1 = 10.5; Y2 = 11.5; Y3 = 12.5; Y4 = 13.5; Y6 = 15.5; Y8 = 17.5; Y10 = 19.4; Y12 = 21.5; Y14 = 23.5. The average age of the girls was approximately 0.5 years younger at each timepoint. The supplementation was commenced after the Y1 measurement (baseline) and ceased after the Y2 measurement. The numbers of boys in the calcium and placebo groups respectively were: Y1–6 = 40, 40; Y8 = 39, 39; Y10 = 37, 39; Y12 = 34, 30; Y14 = 29, 25. The numbers for the girls were Y1–4 = 40, 40; Y6 = 38, 39; Y8 = 39, 40; Y10 = 29, 25; Y12 = 33, 30; Y14 = 25, 29. On the graph, XY = baseline for boys and girls respectively; significance of difference between the groups in boys * P = 0.04; ** P = 0.01; *** P = 0.002. There were no significant differences between the groups in girls at any time.

been in the placebo group and reached peak height velocity approximately 7–8 months earlier⁽³⁵⁾. These boys were taller in mid-adolescence, but they stopped growing earlier and were shorter by an average of 3.5 cm in young adulthood (Fig. 3). Similar effects were seen in the boys on the timing of skeletal development and mineral accretion during adolescence measured by dual-energy X-ray absorptiometry⁽³⁶⁾. There was no discernible effect on growth or skeletal development in girls (Fig. 3)⁽³⁵⁾.

These findings raise the question whether shortening the period of pre-pubertal growth by increasing the calcium intake of prepubertal Gambian boys to values closer to those recommended internationally confers a health or social benefit in the long-term, indeed the slightly shorter adult stature might be considered a disbenefit. However, the low calcium intake of young children in regions of Africa and Asia has been implicated in the aetiology of nutritional rickets that is not due to primary vitamin D deficiency^(37–39) and, in rural Gambia, there is a higher prevalence of nutritional rickets among boys⁽⁴⁰⁾. This indicates that such low calcium intakes can be limiting for some children during periods of bone growth and development. However, other factors, such as iron deficiency and environmental contaminants, and secondary

disturbances in the metabolism of phosphorus and vitamin D, have also been implicated in nutritional rickets, along with a very low calcium intake⁽³⁸⁾. Furthermore, most studies have been conducted in children with active rickets or rickets-like bone deformities, and little is known about the predisposing factors that underlie the development of the condition. This includes whether or not the customary calcium intakes of affected children were lower before they developed rickets than those of their unaffected contemporaries⁽³⁸⁾.

Hard facts

Evidence from the Gambian calcium carbonate supplementation trials of mothers and children raises questions about the balance of benefits and disbenefits of supplementing populations with a low customary calcium.

Misfits

A very low calcium intake has been associated with nutritional rickets in certain parts of Africa and Asia when vitamin D deficiency is not indicated. However, little is known about whether this is the principal causal factor in the development of the condition. Carefully-designed, long-term studies are required in populations vulnerable to nutritional rickets to determine the benefits, and any potential unforeseen consequences, of supplementing or fortifying the diets of children with calcium alone.

Calcium, vitamin D and osteoporosis risk

The complexity of issues surrounding the prevention and treatment of nutritional rickets is a reminder of the intimate inter-relationships between calcium and vitamin D metabolism and bone health⁽⁴¹⁾. The extent to which increasing dietary calcium intake and/or vitamin D supplementation in adults reduces the risk of osteoporosis and fracture risk in later life has been much debated⁽⁴¹⁾. It has long been recognised that the age-adjusted incidence of hip fracture in Africa is considerably lower than in Westernised countries, despite the lower calcium intakes throughout life⁽⁴²⁾. Why this is the case is not known; detailed studies examining potential reasons, for example, higher physical activity, fewer environmental trip hazards and anatomical differences such as shorter hip axis length, have generally not provided clear answers, or have provided unexpected results^(42–45). For example, our studies in The Gambia have shown that adult bone mineral density and bone mineral loss during menopause and ageing are very similar to Western countries^(43,44) and that circulating concentrations of parathyroid hormone and bone turnover markers are greater⁽⁴⁶⁾, factors that are generally considered to be risk factors for osteoporosis and fracture.

It has been suggested from studies in Western countries that vitamin D deficiency resulting from increased metabolism might be responsible for the bone mineral loss seen in people living with HIV, especially in those receiving antiretroviral therapy (ART), and that supplementation might be beneficial⁽⁴⁷⁾. The bone loss is



particularly marked when the ART includes tenofovir disoproxil fumarate⁽⁴⁷⁾. In Eastern and Southern Africa, where tenofovir disoproxil fumarate-based ART is commonly prescribed, women have the highest burden of HIV infection and, because of ART, women living with HIV are now likely to live into and beyond the menopause. Our recent study in Soweto, South Africa, among women with good vitamin D status, showed the expected bone mineral loss in those living with HIV after the initiation of ART⁽⁴⁸⁾. However, we found no evidence of an effect on their vitamin D status. This suggests that vitamin D supplementation would be unlikely to provide any benefit for these women in terms of ameliorating the ART-related bone loss, although a randomised trial would be needed to confirm that finding.

Hard facts

Studies in Africa have demonstrated that the presumption that a low customary calcium intake is a predisposing factor for osteoporosis and fracture in later life does not hold true across all populations.

Misfits

Common aetiological factors implicated in poor bone health, i.e. low bone mineral content/density, bone loss, and elevated parathyroid hormone and bone turnover, are present among people in Africa, where ART-related bone loss also occurs among people living with HIV. These findings are ones that require further research as a matter of priority. As African nations transition towards a more affluent diet and lifestyle along with urbanisation and expanding numbers of older people^(49,50), there is a growing concern that the incidence of osteoporotic fractures will increase rapidly, compounding the health, societal and economic problems of these regions⁽⁵⁰⁾.

Conclusions

These research experiences from different stages of my research career exemplify the importance to public health nutrition of robust, objective studies, conducted among different populations, cultures and ethnicities, in partnership with local communities. Very few of these studies demonstrated the outcomes that had been hypothesised, and, in some, there were unexpected findings that could be a cause for concern. These experiences, along with examples in the literature from other research groups, show that without firm evidence based on studies that have considered a range of secondary outcomes over an extended period, the instigation of well-intentioned dietary interventions may have unforeseen consequences. In recent years, enhancements in study designs, and in methodologies for systematic reviews and meta-analysis, have improved the evidence-base for nutrition policy and practice, and assisted decision-making by scientific advisory committees and other authoritative bodies⁽⁵¹⁾. However, this still relies on a full appreciation of the strengths and limitations of the measures on which

conclusions are drawn, and on the thorough investigation of outcomes that do not fit expectations or prevailing convictions. Folklore, anecdote and conjecture have dogged public health nutrition for decades, and 'fake news' about diet and nutrition is commonplace. Dr Elsie Widdowson recognised the importance of 'hard facts' and 'misfits' during her illustrious research career, and these continue to be essential ingredients of all research studies aimed at improving public health nutrition.

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Conflict of Interest

None.

Authorship

The author had sole responsibility for all aspects of preparation of this paper.

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