Too much effort for too little effect: time to reconsider the merits of food supplementation programs?

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October has brought us The State of the World's Children report by UNICEF (United Nations International Children's Emergency Fund), an update on the global childhood nutrition state, which concludes that "more children and young people are surviving, but far too few are thriving" (1). Thus, the current issue of The Journal of Nutrition is timely; Mahfuz et al. (2) describe a meticulously conducted trial which set out to prevent stunting in children who were already below -1 SD for length, by supplying an egg, 150 mL of cow's milk, and a sachet of multiple micronutrient powder daily for three months. The title encouragingly suggests that this regimen 'increases linear growth', but this conclusion should be treated with caution, as there was no randomisation to treatment or control as this was thought to be unethical. The authors instead compared the treated children to another cohort, recruited in the same community, 5 years earlier. The cohorts are well matched for age and duration of follow up and adjustment for many potential confounders was considered. The authors observed a net decline by 0.14 in height z score in the comparison group and an increase of 0.9 n the intervention group, an overall difference of differences of 0.23. However, the prevalence of stunting in Bangladesh fell by around 10% points between 2009 and 2014 and this trend was projected to continue across the time period covered by this study (3). The later cohort would thus be expected to show less stunting, even with no intervention. Adjustment for wider environmental changes or improvements in public services is not possible.

Even if we accept that this difference was an effect of intervention, then the effect is still very small. These children were on average 2 standard deviations below the mean, yet the adjusted difference found was equivalent to only around a tenth of that deficit. A possible reason for this could have been the fact that the follow up period was only 3 months, and the authors acknowledge that this may be too short a time to achieve significant reversal of nutritional stunting. The supplementary foods supplied almost the entire daily requirement for children of this age for protein, as well as more than 100% of their daily requirements for folate, riboflavin, vitamins B12 and A. We cannot be so sure that they met their energy requirements, but the 24 hour recall data suggest that they exceeded it. The trial also supplied well over 200% of a child's requirements for iron and zinc, which may not be a good thing. Iron in the gut feeds pathogens, which may further compromise gut function, particularly if these children are suffering from compromised absorption due to an altered gut microbiome, resulting from environmental enteropathy(4). Some trials of iron treatment have found decreased growth or weight gain in the intervention arms (5) so it is possible that this oversupply of iron cancelled out any other nutritional benefits.

There was great excitement when Iannotti and colleagues reported much a large gain in height (0.61 SD) as a result of giving just one egg per day in Ecuador (6). Sadly, the effect of a daily egg could not be replicated in this trial in Bangladesh. It seems likely that this powerful effect, in a small

trial, was an outlier . Mahfuz's trial is the latest in a series of commendable efforts to find a solution to stunting. These are often complex trials of nutritional supplementation that result in small, or no effect. (7, 8). Compliance had been a concern in the past but, as in Mahfuz's trial, many recent trials have rigorously enforced compliance, yet increased supervision has not resulted in larger effect sizes (8). So even when the food is definitely taken, generally this has resulted in very little or no overall gain in height. This suggests that food insufficiency cannot, in fact, be the main or sole mechanism underlying stunting. There are other reasons to suspect this, notably the fact that most stunted children are not concurrently wasted or have been wasted previously (9).

We thus need to start thinking more broadly about what truly causes stunting and how it can be best prevented or treated in a cost effective manner. Firstly, it must be remembered that much stunting has its origin in utero, and thus at best can only be ameliorated by postnatal supplementation. A trial in Guatemalan infants showed no impact of meat and micronutrient supplementation on linear growth, compared to cereal based diets, but further analysis demonstrated that stunting was already well established by 6 months of age (10). Thus the life course approach has to be taken into consideration if the generational nature of the problem is to be addressed.

It has also been suggested that environmental enteropathy, arising from longstanding exposure to gut pathogens may be the underlying mechanism (4). It has been shown for example that chronic intestinal parasite infections limit the efficacy of protein supplementation, by increasing lysine requirements (11). However malabsorption cannot explain isolated stunting without wasting. It has been well shown in other settings that chronic inflammation supresses growth (12). If children are in a state of chronic inflammation due to repeated infections or intestinal parasites, might this directly suppress growth? Indeed, could chronic inflammation in their mothers during pregnancy also be the mechanism for intrauterine growth retardation and low birth weight?

Whatever the explanation, very large amounts are currently spent worldwide on buying and distributing supplemental foods (13). It is surely time to accept that food supplementation is just too expensive for too little gain, and to consider where that money might be better spent.

Determining an alternative approach is not straightforward – there is no obvious magic bullet. Trials of water and sanitation (WASH) interventions have so far been no more effective than food trials in impacting on stunting, but these trials have not had the resources necessary to effect meaningful environmental change(14). The huge improvements in public health in the 19th century in the United Kingdom were not achieved by digging wells and educating people to wash their hands, but by major infrastructure projects which provided mains drainage and piped clean water, none of which were ever subjected to a randomised trial. The Sustainable Development Goals are a good

indicator of the magnitude of compromise and change required to achieve sustainable improvements in stunting. Sadly, handing out food in the meantime seems not to be the answer.

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