Transient benefits in young children of a nutrition intervention during pregnancy

In this issue of *The Lancet Global Health*, Delan Devakumar and colleagues report on the follow-up of children aged 8·5 years in southern Nepal whose mothers participated in a randomised controlled trial of multiple micronutrient supplementation during pregnancy. Control mothers received standard doses of iron and folic acid supplements. The offspring of mothers in the intervention group had significantly higher birthweights and higher weights and lower systolic blood pressures at age 2·5 years than the offspring of control mothers. However, at age 8·5 years, no difference was detected in weight-for-age, height-for-age, body-mass-index-for-age, and systolic blood pressure. This finding is consistent with those of other studies cited by Devakumar and colleagues in Burkina Faso, China, and Bangladesh.

The findings add to the mosaic of evidence on the effectiveness of interventions to prevent child undernutrition. Multiple micronutrient supplements during pregnancy were recommended in *The Lancet’s* Series on maternal and child nutrition in June, 2013, in which a meta-analysis was cited that found that such supplements led to a 12% reduction in intrauterine growth restriction.

What might explain the findings that the benefits of the intervention at birth and early childhood were no longer apparent in mid-childhood? There was 30% loss to follow-up between enrolment in the randomised controlled trial and 8·5 years. Although lost children were more likely to be urban and their mothers more educated, there was no difference between the intervention and control groups. The use of different reference populations at 2·5 and 8·5 years might have affected the values of anthropometric indices. Perhaps Devakumar and colleagues could reanalyse the data at 2·5 years using the most recent WHO reference population to determine whether the convergent trend stands. Finally, the follow-up study was not powered to detect differences in weight of less than 800g; however, as Devakumar and colleagues point out, the clinical significance of lower differences is uncertain.

The slower growth velocity in the intervention children between ages 2·5 and 8·5 years might be due to environmental influences that have not been identified in this study, such as child feeding practices or other family-based lifestyle factors, which could be clustered by community. This potential clustering effect of nutrition behaviours was not analysed in the study.

Another possibility lies in the fact that growth rates are relatively slow in pre-adolescent children and differences between the intervention and control groups could re-emerge during the adolescent growth spurt. This possibility suggests the need for further follow-up during early adolescence.

Do the findings of this study call for a review of current recommendations? Certainly not, given that a number of randomised controlled trials have shown that multiple micronutrient supplements in pregnancy are associated with reduced rates of low birthweight, and low birthweight is a strong predictor of child survival. A study in Indonesia found that multiple micronutrient supplements in a large sample of pregnant women led to an 18% reduction in early infant mortality compared with infants of women given iron and folic acid.

But this study does challenge some of the assumptions underlying the current global focus on nutrition interventions during the “first 1000 days” between conception and a child’s second birthday. Although the evidence to support this approach remains solid, Devakumar and colleagues’ paper suggests that there is a need to look at continuing nutritional support into childhood and adolescence. Studies that can pinpoint other factors, beyond dietary behaviours and biological markers, that affect children’s growth velocity into adolescence are urgently needed.

The paper also challenges us to re-evaluate the assumptions underlying the “Barker hypothesis”—that babies who have a low birthweight are at greater risk of developing cardiovascular disease in adulthood. The finding that there was no difference in systolic blood pressure between the intervention group and the control group suggests that other factors, not measured by the study, might be at play. A significant number of girls aged 8–11 years will have experienced puberty. So one would expect that those who initially benefited as a result of the intervention might experience
some rebound at this age. Further follow-up of these Nepalese children in adolescence could shed more light on this issue.

*Michael J Toole, Andre Renzaho
Burnet Institute, Melbourne, VIC 3184, Australia (MJT, AR); Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia (MJT, AR); and School of Social Sciences and Psychology, University of Western Sydney, Sydney, NSW, Australia (AR)
toole@burnet.edu.au

We declare no competing interests.

© Copyright Toole at al. This is an open access article published under the terms of CC BY-NC-SA.


