Antenatal multiple micronutrient supplementation: where are the long-term benefits?

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Bourassa et al. describe the work of a task force convened to consider whether antenatal Multiple Micronutrient Supplementation (MMS) should be offered to pregnant women.[1 2] They summarize a 2019 Cochrane review of antenatal MMS versus Iron and Folic Acid supplementation and an individual participant data analysis.[3 4] The Cochrane review found reductions in low birthweight and small-for-gestational age, but no effects on stillbirths, neonatal mortality, maternal anaemia, maternal mortality, or any other pregnancy outcome examined. Low birth weight was the only outcome for which authors had high-quality evidence of a reduction. On the basis of these mixed results, Bourassa et al. conclude that countries where women have insufficient micronutrient intakes should offer antenatal MMS to reduce the risk of adverse birth outcomes.

We have two concerns: the first is about the risks of relying on birthweight as the main measure of fetal health, and the second about the current lack of evidence for long-term benefits of antenatal MMS.

Birthweight is a proxy for a broad range of both positive and negative prenatal influences.[5 6] For this reason, interventions that seek to improve it may not always improve later health.[7] As early as 2003, a WHO-led consultation argued for a broader set of indices of fetal development including maternal body mass index, stillbirths, rates of prematurity, neonatal morbidity, perinatal, infant, and maternal mortality, anthropometry at birth and in childhood, and cognitive development.[8]

If we accept a broader view of fetal health – as the range of outcomes included in the Cochrane review suggests - it is important to look beyond birthweight to inform decisions about scaling up prenatal interventions, including MMS. In 2016, a systematic review of nine trials and 20 follow-up studies found no evidence of improved survival, anthropometry, body composition, or cardiovascular or respiratory health in childhood following antenatal MMS.[9] Bourassa et al. specifically highlighted findings from Indonesia suggesting that children whose mothers received antenatal MMS had better cognitive development at 3-4 years and improved procedural memory at 9-12 years.[10 11] To be precise, at 3-4 years of age, in a subsample of 1.9% of children (487/26228) alive at 12 weeks, Prado et al found improvements in motor ability only in a model adjusted for multiple covariates. There was no difference in any of the other four developmental domains studied. Similarly, at 9-12 years of age, in a subsample of 10.5% of children (2879/27356) alive at 12 weeks, procedural memory was improved by 0.11 standard deviations (95% CI 0.01, 0.20), but there was no difference in any of the six other developmental areas examined.[11] Such largely null results were replicated in other cognitive follow-up studies from China,[12 13] Tanzania,[14] and four separate studies from Bangladesh and Nepal.[15 16 17 18]

The large body of available empirical evidence has not shown that antenatal MMS leads to health benefits in childhood, including for cognitive development. Although such benefits may be more subtle and may subsequently come to light, theoretical future benefits should not supersede empirical evidence. This lack of long-term benefits should of concern for debates about scale up.

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