

Is now the time for revisiting supplements for pregnant women?



See [Articles](#) page e298

More than half of neonatal deaths are attributable to being born too soon or small; these infants are known as small vulnerable newborns.¹ Global estimates for 2020 suggest that 23.4 million neonates were born small for gestational age, 13.4 million were preterm, and 19.8 million had low birthweight. There are several reasons for babies being born small or early; high rates of protein and micronutrient deficiencies in pregnant people are some of the key factors. Small vulnerable newborns are at elevated risk of mortality, growth and cognitive faltering, and non-communicable diseases in later life.

In *The Lancet Global Health*, Dongqing Wang and colleagues² used an individual patient data meta-analysis to assess the effect of multiple micronutrient supplements (MMSs) and small-quantity lipid nutrient supplements (SQ-LNSs) on the ten different categories within the small vulnerable newborn group.²

This is a very timely publication as it reinvigorates the debate for revisiting the guidelines for antenatal supplementation, especially considering the long overdue debate to replace routine iron and folic acid with MMSs. WHO currently recommends iron and folic acid supplements for all pregnant people and balanced-energy protein supplements for pregnant people in undernourished populations. In the revised version of the antenatal care guidelines in 2020, WHO does recommend MMSs, but only in the context of rigorous research or humanitarian crises. There is still no universal recommendation for MMSs, as these guidelines concluded that “whilst the evidence suggests that there may be a limited benefit and little harm in replacing iron and folic acid supplements with MMS, the evidence on low birthweight and its component parts (preterm birth and small for gestational age) is difficult to interpret”.³ This interpretation by policy makers has been met with perplexity by many global experts.

The analysis by Wang and colleagues used individual participant data from 14 randomised controlled trials of MMSs (n=42 618) and four randomised controlled trials of SQ-LNSs (n=6246) in low-income and middle-income countries and demonstrated the benefits of prenatal MMSs in preventing small vulnerable

newborns, especially the subgroups that are at greatest risk of mortality.² SQ-LNSs, which are nutritional supplements that provide not only micronutrients but also energy and essential fatty acids, only reduced the risk of one of the ten subgroups of small vulnerable newborns.

This analysis further underscores the existing evidence, which have also concluded that there are significant benefits to MMSs for various mother and infant birth outcomes.⁴ The latest *Lancet Series on Maternal and Child Undernutrition in 2021* made a strong recommendation for the replacement of iron and folic acid in pregnancy with MMSs^{5,6} and balanced-energy protein supplements for women in food insecure households.⁵ SQ-LNSs have shown some benefits on the birth outcomes, but require further evidence, especially in comparison to MMSs.⁷ Consideration should also be given to research into the role of MMSs and SQ-LNSs in the preconception period and for non-pregnant adolescent girls and to research on how best to deliver such interventions.

Although the evidence of antenatal MMS is now quite clear, the task is far from complete, as only about 5% of women in need of MMSs are receiving them.⁸ The challenges cited for MMSs roll-out apart from the lack of global recommendations, are questions around its production, distribution, costs, and cost-effectiveness. There are still very few suppliers that produce the UN-recommended MMS formulation, but by enhancing the local production capacity, the availability, affordability, and programme ownership can be enhanced. MMSs should be recommended and included in national medicine formularies and local production can also help eliminate regulatory and logistical challenges. The cost-effectiveness of replacing iron and folic acid with MMSs have been evaluated and studies have suggested that MMSs are good value for money. Cost-benefit analyses across different settings consistently show a high return on investment; in Bangladesh, India, and Pakistan MMSs can avert 2–3 times more disability-adjusted life years than iron and folic acid and have a higher return on investment, ranging from a few hundred to a few thousand US dollars.⁹

Public health entities should now focus on not only updating the recommendations but also finding context-specific solutions for universal uptake. The ever-challenging and increasing threats of poly-crisis including escalating conflicts, political and social polarisation, inflation, and climate change currently risk undermining the small global gains we have made in nutrition. Therefore, there is an urgent need for holistic, dynamic, and context-specific strategies to tackle multifaceted and intergenerational forms of malnutrition, and its far-reaching repercussions.

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