

Lancet Article: Multiple Micronutrient Supplementation for Women During Pregnancy

Below is a summary of the just released Lancet article on Multiple Micronutrient supplementation (MMNs; prenatal multivitamin) for women during pregnancy. The study confirmed the previously reported effects of MMNs containing iron-folic acid on reducing the risk of low birthweight, preterm birth, and being born small for gestational age. The main contribution of this study, however, is the identification of several subgroups of mothers that might experience greater benefits from antenatal MMNs than from iron-folic acid (IFA) supplementation alone.

Overall, this study found that antenatal MMNs improved survival for female neonates and provided greater birth-outcome benefits for infants born to undernourished and anemic pregnant women. Early initiation in pregnancy and high adherence to multiple micronutrient supplements also provided greater overall benefits. The specific findings are reported next, and can be found in the attached.

Findings (all compared the use of MMNs containing iron and folic acid to the use of IFA alone; so the benefits from MMNs shown below are above and beyond the benefits that were found with IFA alone)

Anemic women: Compared to non-anemic women, in anemic women, MMNs resulted in greater reductions in risk of the following:

- low birthweight (–19%),
- small-for-gestational-age births (–8%),
- infant mortality at 6 months of age (–29%).

Underweight women: In underweight women (BMI <18.5 kg/m), MMNs:

- reduced the risk of preterm birth (-16%)

Initiation and adherence:

- initiation of MMNs before 20 weeks' gestation decreased the risk of preterm birth (–11%)
- initiation of MMNs after 20 weeks' gestation provided greater reductions in risk of small-for-gestational-age births (–9%)
- initiation of MMNs before or after 20 weeks' gestation conferred similar benefits in reducing the risk of low birthweight (-9%)
- high adherence to regimen (≥95%) decreased the risk of infant mortality (–15%).

Sex-specificity:

- female infants born to mothers who received antenatal MMNs had an approximately 15% reduction in mortality risk during the first year of life.
- This survival benefit was not significant in male infants.
- As indicated by the authors, the sex-specificity of effects needs to be confirmed and potential underlying biological mechanisms elucidated in future studies.

Additional findings:

- MMN and risk of mortality: MMN did not significantly increase the risk of stillbirth or neonatal, 6-month, or infant mortality, neither overall or in any of the 26 examined subgroups. Thus, the current study does not confirm the increased risk of mortality that has been reported previously.
- MMN mortality risk due to larger babies: MMN trial reports have raised concerns that increased birth size due to MMNs may increase the risk of cephalopelvic disproportion and neonatal asphyxia, particularly among women of small stature. The researchers found that MMNs indeed increased the risk of large-for-gestational-age births (as defined by the Intergrowth standard), which could hypothetically increase the risk of maternal-fetal disproportion and related birth complications. However, they found no indication that mothers who took multiple micronutrient supplements and whose height was less than 150 cm had increased risk of stillbirth or mortality at any time point.
- Amount of iron in MMN: The authors pointed out that some trials provided lower iron doses in the MMN group (≤ 30 mg elemental iron) than in the IFA (60 mg elemental iron) groups. The authors therefore did a sensitivity analysis, which revealed no significant harmful effects overall or in any subgroups among trials that used the same dose of iron in the MMN and the IFA groups. By contrast, in trials that used a lower iron dose in the MMN group, the risk of stillbirth and mortality was greater in some subgroups. The researchers thus recommend that “countries and programs considering implementation of MMN should use a formulation with an iron dose similar to what they currently use; for example, MMNs that contains 60 mg iron should be considered in settings where 60 mg iron-folic acid is currently implemented.”
- MMN and HIV: Researchers were unable to examine HIV as a potential effect modifier since only two trials included both HIV-infected and HIV-uninfected women. Nevertheless, there was no indication that the effect of MMNs varied by maternal HIV status in these studies

The results of this meta-analysis are important, as they guide researchers and policy makers on subgroups to be targeted by MMNs and other potential nutrient intervention strategies. The study provides further evidence on the additional benefits of MMNS containing iron-folic acid above iron-folic acid alone in women entering pregnancy with poor nutritional status. The authors stated that “this new evidence suggests that WHO should consider re-evaluating the balance of benefits and harms of universal multiple micronutrient supplementation in their antenatal care recommendations”.

Programs and low income and middle-income countries considering implementation of multiple micronutrient supplements have the opportunity to simultaneously expand coverage of early antenatal care attendance and multiple micronutrient supplements including iron-folic acid, while also improving the quality of antenatal care counselling and services to produce population-level infant health benefits, which might be greater than any of these strategies in isolation.