

# Multiple micronutrient supplementation (MMS) for pregnant women

The World Health Organization (WHO) currently recommends providing Iron and Folic Acid supplementation (IFA) for women during pregnancy as part of the routine antenatal care (WHO 2012). In recent years – culminating with the recent publication of a Cochrane Review<sup>1</sup> and a Lancet article<sup>2</sup> – it has become clear that the evidence pertaining to the provision of MMS for women starting early in pregnancy provides clear benefits for both women and their unborn and newborn infants, beyond IFA supplementation alone. Please note that when MMS is referenced in this document, these supplements contain iron and folic acid, in addition to 13-15 different micronutrients, while IFA alone contains only iron and folic acid.

## WHO recommendation (2016)<sup>3</sup>

### RECOMMENDATION A.6: Multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes. (Not recommended)

#### Remarks

- There is some evidence of additional benefit of MMN supplements containing 13–15 different micronutrients (including iron and folic acid) over iron and folic acid supplements alone, but there is also some evidence of risk, and some important gaps in the evidence. Although the GDG agreed that overall there was insufficient evidence to warrant a recommendation, the group agreed that **policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMN supplements on maternal health to outweigh the disadvantages, and may choose to give MMN supplements that include iron and folic acid.**
- More research is needed to determine which micronutrients improve maternal and perinatal outcomes, and how these can be optimally combined into a single supplement.



Similar to IFAs, MMS reduces the rate of maternal anemia. Since the WHO recommendation in 2016, additional research has been published showing the positive effects of MMS in improving birth outcomes, above the improvements from IFA alone, including:

- Reduction in low birthweight in infants
- Reduction in small for gestational age (SGA) in newborn infants
- Decrease in infant mortality at 6 months of age

Based on the strength of the research, the World Bank, Results for Development Institute (R4D), and 1,000 Days, with support from the Bill & Melinda Gates Foundation and the Children’s Investment Fund Foundation (CIFF) conducted an in-depth costing analysis and developed an investment framework for achieving four of the six global nutrition targets.<sup>4</sup>

According to this analysis, pregnant women should receive MMS for about 180 days per pregnancy, delivered as a part of antenatal care (Table 3).

TABLE 3: TO MEET THE TARGETS

Intervention and target addressed*	Description and assumptions
<b>For pregnant women and mothers of infants</b>	
  Multiple micronutrient* supplementation for pregnant women (stunting and anemia)	Includes iron-folic acid, and at least one additional micronutrient, for approximately 180 days per pregnancy. Delivered as part of antenatal care.

	Summary of study & findings	Conclusions
<p><b>Cochrane Review</b></p> <p>Multiple-micronutrient supplementation for women during pregnancy (2017)<sup>1</sup></p>	<p>This review included data from 17 trials involving 137,791 women.</p> <p>When compared with IFA supplementation, MMS resulted in a significant decrease for newborn infants in:</p> <ul style="list-style-type: none"> <li>• Low birthweight (LBW) (-12%)</li> <li>• Small-for-gestational age (SGA) (-8%)</li> </ul> <p>No statistically significant differences were shown for other maternal and pregnancy outcomes including:</p> <ul style="list-style-type: none"> <li>• preterm births</li> <li>• stillbirth</li> <li>• miscarriage</li> <li>• risk of delivery via a caesarean section</li> <li>• maternal anemia in the third trimester</li> <li>• maternal mortality</li> <li>• perinatal mortality</li> <li>• neonatal mortality</li> </ul>	<p>The authors' findings support the effect of MMS with iron and folic acid in improving some birth outcomes.</p> <p>Overall, pregnant women who received MMS had fewer LBW babies and SGA babies.</p> <p>These findings provide a basis to guide the replacement of iron and folic acid with MMS for pregnant women in low and middle-income countries.</p>
<p><b>Lancet Global Health</b></p> <p>Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality (2017)<sup>2</sup></p>	<p>This two-stage meta-analysis of individual patient included data from 17 randomized controlled trials done in 14 low-income and middle-income countries, which compared MMS containing iron-folic acid versus iron-folic acid alone (IFA) in 112,953 pregnant women.</p> <p><i>Benefits from MMS shown below are above and beyond the benefits that were found with IFA alone.</i></p> <p><b>Anemic women:</b> Compared to non-anemic women, in anemic women, MMS resulted in greater reductions in risk of the following:</p> <ul style="list-style-type: none"> <li>• Low birthweight (-19%),</li> <li>• Small-for-gestational-age births (-8%),</li> <li>• Infant mortality at 6 months of age (-29%).</li> </ul> <p><b>Underweight women:</b> In underweight women MMS:</p> <ul style="list-style-type: none"> <li>• Reduced the risk of preterm birth (-16%)</li> </ul> <p><b>Initiation and adherence:</b></p> <ul style="list-style-type: none"> <li>• Initiation of MMS before 20 weeks' gestation decreased the risk of preterm birth (-11%)</li> <li>• High adherence to regimen (≥95%) decreased the risk of infant mortality (-15%).</li> </ul>	<p>Antenatal MMS improved survival for female neonates and provided greater birth-outcome benefits for infants born to undernourished and anemic pregnant women.</p> <p>Early initiation in pregnancy and high adherence to MMS also provided greater overall benefits.</p>
<p><b>World Health Organization (WHO)</b></p> <p>The Global Prevalence of Anaemia in 2011 (2015)<sup>5</sup></p>	<p>This report provides estimates of the prevalence of anemia in 2011 in several population groups, including pregnant women.</p> <ul style="list-style-type: none"> <li>• In 2011, the global prevalence of anemia for pregnant women was 38.2%, and for all women of reproductive age was 29.4%; thus, hemoglobin concentrations in pregnant women were lower than in non-pregnant women.</li> <li>• These prevalence translate to 496.3 million non-pregnant women, and 32.4 million pregnant women with anemia worldwide in 2011.</li> <li>• In developing regions, maternal and neonatal mortality were responsible for 3 million deaths in 2013 and are important contributors to overall global mortality.</li> </ul>	<p>Anemia resulting from iron deficiency during pregnancy may be associated with low birth weight and increased risk of maternal and perinatal mortality.</p> <p>According to the Lancet, pregnant women who are anemic experience even greater benefits from MMS, therefore there is a lot to be gained when looking at the prevalence of global anemia.</p>

## Frequently Asked Questions About MMS

### 1. What specific benefits are documented to accrue for the woman, the unborn child, and the newborn child that warrant consideration of MMS?

*Multiple micronutrient deficiencies co-exist among women and are increased in pregnancy, leading to potentially adverse effects on the mother and developing fetus.*

*Multiple micronutrient supplementation is demonstrated to significantly improve birth outcomes by reducing the occurrence of low birth weight, SGA, preterm births, and infant mortality at 6 months as compared to use of Iron/ Folic Acid (IFA) alone.<sup>1,2</sup>*

*While the benefits of the MMS on birth outcomes are found overall, women who are vulnerable, that is, women who are anemic and/or underweight during their pregnancy experience even greater benefits.<sup>2</sup>*

### 2. What is the best timing for initiating MMS in pregnancy to optimize the beneficial effects?

*Research suggests that early (< 20 weeks' gestation) and extended (> 20 weeks' gestation) adherence to a daily MMS regimen throughout the period of pregnancy decreases risk of preterm, small for gestational age, low birth weight, and infant mortality.<sup>2</sup> Thus, starting MMS as soon after conception as possible, and continuing use throughout the pregnancy is the most optimal pattern of use to encourage.*

### 3. Why does the UNIMMAP formulation contain only 30 mg of iron while IFA usually contains 60 mg of iron?

*The UNIMMAP supplement contains 30mg of iron (rather than 60mg) for the following reasons:<sup>6(p 12)</sup>*

- *Iron absorption in the UNIMMAP formulation is enhanced (as compared to the IFA) due to the inclusion of vitamin C, vitamin A, and riboflavin.*
- *Adherence is likely to be improved with lower iron due to decreased side-effects (e.g., constipation).*
- *Including 60mg of iron requires including at least 30mg of zinc in order to avoid possible negative influence of iron on zinc absorption. This increases the total amount of metals, which is likely to increase negative side-effects.*
- *Most pregnant women suffer from mild or moderate anemia, which can be addressed with 30 mg of iron.*

## Donations of MMS from Vitamin Angels

In order to achieve the greatest public health benefit, Vitamin Angels provides donations of MMS to underserved pregnant women, encouraging our partners to reach women as early in their pregnancy as possible. Donations from Vitamin Angels should be used to fill gaps in supply, thus increasing coverage. Given the strong evidence, we encourage governments to consider incorporating MMS for pregnant women into the national health policy.

For more information about receiving a donation from Vitamin Angels, please visit [www.vitaminangels.org/apply](http://www.vitaminangels.org/apply) or send an e-mail to [programs@vitaminangels.org](mailto:programs@vitaminangels.org).

#### Endnotes

<sup>1</sup> Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database of Systematic Reviews, 2017, Issue 4. Art. No.: CD004905. DOI: 0.1002/14651858.CD004905.pub5.

<sup>2</sup> Smith ER et al. Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries. The Lancet Global Health, 2017, Vol 5, Issue 11, e1090 - e1100

<sup>3</sup> World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. 2016.

<sup>4</sup> World Bank. 2016. Investing in nutrition: the foundation for development – an investment framework to reach the global nutrition targets (English). Washington, D.C. : World Bank Group. <http://documents.worldbank.org/curated/en/963161467989517289/Investing-in-nutrition-the-foundation-for-development-an-investment-framework-to-reach-the-global-nutrition-targets>

<sup>5</sup> World Health Organization. 2011. The Global Prevalence of Anaemia in 2011.

<sup>6</sup> UNICEF, WHO, UNU. Composition of a multiple-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries, 1999.