

WHO recommendations on antenatal nutrition: an update on multiple micronutrient supplements

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MICRONUTRIENTS AND PREGNANCY

Optimal maternal nutrition, including adequate intake of essential vitamins and minerals, is important for fetal development and longer term impacts on the child's health. Although pregnant women are considered to be at increased risk of micronutrient deficiencies due to increased maternal and fetal nutritional needs, there is some debate around how best to achieve an optimal diet with adequate and balanced intakes of the necessary nutrients during the antenatal period and before pregnancy.¹ The most common micronutrient deficiency in pregnancy that is known to impact maternal health is iron deficiency, due to increased iron demands. Iron deficiency is a common cause of anaemia, which is estimated to affect 40% of pregnancies globally, highest in South-East Asia (49%), Africa (46%) and the Eastern Mediterranean (41%) and lower prevalence in Western Pacific (33%), the Americas (26%) and Europe (27%).² Thus, iron supplementation has been recommended by WHO for all women during pregnancy since the 1950s. Current global nutrition targets call for a 50% reduction in anaemia among women of reproductive age by 2025, and the prevalence of anaemia in women aged 15–49 years, by pregnancy status, has now been proposed as an indicator for Sustainable Development Goal 2.³ In addition to routine iron and folic acid (IFA) supplementation, various other interventions have been proposed to increase the micronutrient intake before and during pregnancy, including food-based approaches.

INDIVIDUAL MICRONUTRIENTS RECOMMENDED BY THE WHO DURING PREGNANCY

The 2016 WHO recommendations on routine antenatal care (ANC) for pregnant women and adolescent girls provide

comprehensive guidance on the practice, organisation and delivery of ANC and prioritise woman-centred care to facilitate a positive pregnancy experience.⁴ Recognising that ANC provides a strategic platform for important healthcare functions including health promotion and disease prevention, 14 out of the 49 recommendations in the WHO ANC guideline relate to nutrition. Antenatal micronutrient interventions recommended in this guideline for pregnant women and adolescent girls include daily elemental iron (30–60 mg) and folic acid (0.4 mg) to prevent maternal anaemia; calcium supplementation (1.5–2 g daily) in populations with low dietary intake of calcium to prevent pre-eclampsia; and vitamin A supplementation (up to 10 000 IU vitamin A daily or up to 25 000 IU vitamin A weekly) in populations with a high prevalence of night blindness.⁴ Calcium supplementation is also recommended prior to pregnancy for the prevention of pre-eclampsia and its complications.⁵

The possibility of giving one supplement that contains all the micronutrients necessary for pregnancy appears desirable. In practice, however, it might not be this simple, as micronutrient intake and deficiencies vary across regions, countries and populations. Several different micronutrient formulations containing IFA have been studied in randomised trials conducted mainly in low-income and middle-income countries, including the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP).⁶ UNIMMAP contains 15 micronutrients including 10 vitamins and 5 minerals (zinc, iron, selenium, copper and iodine; [table 1](#)).

During the 2016 ANC guideline development process, data from a Cochrane review of the effects of providing multiple

Table 1 Vitamins and minerals included in the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation⁶

Micronutrient	Dose
Vitamin A	800 µg
Vitamin D	200 IU
Vitamin E	10 mg
Niacin	18 mg
Folic acid	400 µg (0.4 mg)
Vitamin B ₁	1.4 mg
Vitamin B ₂	1.4 mg
Vitamin B ₆	1.9 mg
Vitamin B ₁₂	2.6 µg
Vitamin C	70 mg
Zinc	15 mg
Iron	30 mg
Selenium	65 µg
Copper	2 mg
Iodine	150 µg

micronutrient supplementation (MMS) in pregnancy was evaluated by the Guideline Development Group (GDG),⁷ along with evidence on resource use, equity, acceptability and feasibility. The evidence on the relative effectiveness compared with daily IFA supplementation suggested that multiple micronutrient supplements might lead to a small reduction (11%) in the rates of low birth weight babies⁷; however, the lack of other demonstrable benefits, equivocal evidence on neonatal mortality related to the dose of iron (30 mg or 60 mg) used, the higher cost of MMS and concerns about feasibility led to it not being recommended for all pregnant women as part of routine ANC.⁴ In the remarks, it was noted that policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMS to outweigh the disadvantages and may choose to give them to pregnant women instead of IFA supplements only.

CONTEXT OF, AND EVIDENCE FOR, AN UPDATED RECOMMENDATION ON THE PROVISION OF MULTIPLE MICRONUTRIENT SUPPLEMENTS DURING PREGNANCY

As part of the WHO's normative work on supporting evidence-informed policies and practices and its living guidelines approach,⁸ on the advice of the Executive Guideline Steering Group, WHO prioritised the updating of the recommendation on MMS on the basis of additional trials published after the release of the 2016 ANC guideline.⁹ In addition, an individual participant data meta-analysis was published in 2017,¹⁰ which led to a call for WHO to review the multiple micronutrient recommendation.¹¹

For the updated recommendation, data on effectiveness were derived from the updated Cochrane review, which included 20 trials (4 more than the 2015 version).⁹ Of the review's 20 trials, 4 did not meet the criteria for the WHO analysis, which considered studies of supplements containing 13–15 micronutrients including IFA, compared with IFA supplements only. All analyses conducted to address the prioritised guideline question, in participant, intervention, comparison, outcomes (PICO) format, are available in the WHO guideline document.¹² The resulting evidence on effectiveness was found to be largely similar to that evaluated during the 2016 guideline development process, showing an average 12% (9%–14%) reduction in low birth weight with MMS but little difference in effects on low birth weight's component parts (preterm birth or being small for gestational age). When analyses were limited to the 10 trials comparing UNIMMAP MMS with IFA supplements, low birth weight was reduced by 13% (95% CI, 6% to 19%) and small for gestational age was reduced by 9% (2% to 15%) on average. New evidence on cost effectiveness prepared for the update process by Nutrition International,¹³ suggesting that switching from IFA supplements may be cost-effective in some countries, as well as relatively favourable equity, acceptability and feasibility considerations led to a decision to recommend MMS in the context of rigorous research (box 1).

There are two critical research implications underlining this updated recommendation. Evidence on the effects of MMS on the component parts of low birth weight is inconsistent and controlled clinical trials are needed in which early pregnancy ultrasound is used to establish gestational age with certainty, to understand where the effect on low birth weight is derived. In addition, in settings where the provision of MMS is being considered, implementation research is needed to establish the impact of switching from IFA supplements to MMS, including evaluation of sustainability and cost effectiveness. Most of the evidence on effects was derived from studies comparing daily MMS containing 30 mg of elemental iron with daily IFA supplements with an equivalent amount of elemental iron. National policies in low-income and middle-income countries commonly recommend the 60 mg dose of elemental iron,¹⁴ where the higher dose of iron may be indicated due to a high anaemia prevalence. Therefore, more research is needed on the effects of switching from daily IFA supplements containing a 60 mg dose of elemental iron to daily MMS containing a lower dose (30 mg) of elemental iron in these settings. As evidence on the effects of MMS was mainly derived from low-income and middle-income countries, its applicability to high-income countries or to populations not at risk of micronutrient deficiencies, for example, due to an adequate diet and the implementation of food fortification of various staple foods (ie, wheat flour, maize meal, rice) with IFA, remains unclear.

Box 1 Updated multiple micronutrient supplementation (MMS) recommendation and other recommended nutritional interventions in the WHO antenatal care (ANC) guideline

Updated MMS recommendation

A.6: Antenatal multiple micronutrient supplements that include iron and folic acid (IFA) are recommended in the context of rigorous research.*

Remarks

- ⇒ This recommendation updates and supersedes the WHO recommendation found in the WHO ANC guideline.¹
- ⇒ The recommendation is based on evidence derived from trials using MMS containing 13–15 micronutrients (including IFA) and the widely available UNIMMAP, which contains 15 micronutrients, including 30 mg of iron and 0.4 mg of folic acid; see [table 1](#).
- ⇒ As the evidence was mainly derived from low/middle-income countries, its applicability to high-income countries or to populations not at risk of micronutrient deficiencies—for example, due to an adequate diet and food fortification programmes—is unclear.
- ⇒ Research in this context includes:
 - ⇒ Controlled clinical trials in which early pregnancy ultrasound is used to establish gestational age with certainty,† with assessment of critical maternal and perinatal outcomes, and follow-up of infants sustained into childhood.
 - ⇒ Where programmes of MMS are being considered, implementation research to establish the impact of switching from IFA supplements to MMS, including evaluation of acceptability, feasibility, sustainability, equity and cost-effectiveness.
- ⇒ Most MMS, including UNIMMAP, contain 30 mg of elemental iron. WHO recommends antenatal supplements containing 60 mg of elemental iron in populations where anaemia is a severe public health problem (a prevalence of 40% or higher).² Therefore, countries should consider their population magnitude and distribution of anaemia, and its nutritional determinants (ie, iron deficiency), as well as the magnitude and distribution of the complex low birth weight and its component parts (ie, preterm, small for gestational age (SGA) or a combination of these),³ when undertaking any research in the context of this recommendation.
- ⇒ Pregnant women should be supported and encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet consistent with guidelines on healthy eating.⁴

Other WHO recommendations on nutrition during pregnancy

- A.1.2: In undernourished populations, nutrition education on increasing daily energy and protein intake is recommended for pregnant women to reduce the risk of low-birth-weight neonates.
- A.1.3: In undernourished populations, balanced energy and protein dietary supplementation is recommended for pregnant women to reduce the risk of stillbirths and SGA neonates.
- A.2.1: Daily oral IFA supplementation with 30–60 mg of elemental iron and 400 µg (0.4 mg) of folic acid is recommended for pregnant women to prevent maternal anaemia, puerperal sepsis, low birth weight and preterm birth.
- A.2.2: Intermittent oral IFA supplementation with 120 mg of elemental iron and 2800 µg (2.8 mg) of folic acid once weekly is recommended for pregnant women to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in

Continued

Box 1 Continued

populations with an anaemia prevalence among pregnant women of less than 20%.

A.3.1: In populations with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of pre-eclampsia.‡

A.4: Vitamin A supplementation is only recommended for pregnant women in areas where vitamin A deficiency is a severe public health problem.§ to prevent night blindness.

A.5: Zinc supplementation for pregnant women is only recommended in the context of rigorous research.

A.10.1: For pregnant women with high daily caffeine intake (more than 300 mg per day),¶ lowering daily caffeine intake during pregnancy is recommended to reduce the risk of pregnancy loss and low-birth-weight neonates.

*The Guideline Development Group clarified that rigorous research includes implementation research using high-quality methods appropriate to the specific research questions.

†Gestational age accurately assessed by ultrasound emerged as an important feature of future trials because of the conflicting and confusing differences in intervention effects found on low birth weight and its component parts (preterm birth, and SGA).

‡Consistent with the updated living guideline, *WHO recommendation: calcium supplementation during pregnancy for the prevention of pre-eclampsia and its complications (2018)*.¹⁷

§Vitamin A deficiency is a severe public health problem if ≥5% of women in a population have a history of night blindness in their most recent pregnancy in the previous 3–5 years that ended in a live birth, or if ≥20% of pregnant women have a serum retinol level <0.70 µmol/L. Determination of vitamin A deficiency as a public health problem involves estimating the prevalence of deficiency in a population by using specific biochemical and clinical indicators of vitamin A status.

¶This includes any product, beverage or food containing caffeine (ie, brewed coffee, tea, cola-type soft drinks, caffeinated energy drinks, chocolate, caffeine tablets).

ADAPTING THE WHO ANC NUTRITION RECOMMENDATIONS TO HEALTH POLICIES AND PROGRAMMES

The WHO ANC guideline now includes five recommendations on antenatal micronutrients that are either recommended for all pregnant women (IFA supplements) or recommended in specific contexts, either for certain populations at risk (vitamin A and calcium supplements) or in a research context (zinc and MMS; [box 1](#).)

In considering the updated recommendation on MMS during pregnancy, it should be highlighted that coverage of IFA supplements remains an ongoing challenge in many countries.¹⁴ A review of IFA supplementation programmes in seven countries (Afghanistan, Bangladesh, Indonesia, Ethiopia, Kenya, Nigeria and Senegal) suggests that much remains to be done to improve uptake and adherence of essential nutritional supplements in pregnancy. Barriers to coverage include supply chain issues, lack of quality control and coordination, and inadequate staff training and patient counselling.¹⁴ Thus, the sustainability of transitioning from IFA supplements to MMS, which may suffer from similar barriers to coverage, or new barriers related to the added cost of MMS, needs careful consideration

by stakeholders considering making a programmatic switch. Populations affected by an emergency or humanitarian crisis, including pandemics like COVID-19, may be at a particular risk for micronutrient deficiencies due to loss of livelihoods and food crops, interruption in food supplies and outbreaks of infectious diseases and in these situations MMS may be considered for pregnant and lactating women.^{15 16}

CONCLUSION

WHO's living ANC guideline commitment aims to ensure that recommendations on routine ANC are based on the latest evidence and considerations to facilitate the strengthening of integrated, quality ANC services. Thus, the recommendation on MMS will be revisited in the future when more evidence of the nature recommended by the GDG becomes available. WHO nutrition recommendations for ANC highlight that pregnant women should be supported and encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet in the context of a healthy lifestyle that includes adequate exposure to sunlight and regular exercise. A key aspect of programmes to deliver micronutrient interventions at country level is effective communication with pregnant women, their families and communities regarding diet and healthy eating, including information on dietary sources of vitamins and minerals and dietary diversity and the importance of adhering to supplementation schemes. Effective implementation of these programmes will contribute to the achievement of the WHO global nutrition targets and sustainable development goals.

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