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COMMENT

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Multiple micronutrient supplements (MMS) for adolescent girls: are we getting carried away by the hype?

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Abstract

Multiple micronutrient supplements (MMS) during pregnancy have gained attention in recent years due to growing evidence that they are more effective than iron and folic acid (IFA) supplements in preventing preterm birth and low birth weight. So, should MMS also replace weekly iron and folic acid supplements (WIFAS) for non-pregnant adolescent girls?

Keywords Adolescent, Multiple micronutrient supplements, Weekly iron and folic acid supplements

Main text

Teenage brains have more synaptic connections than adult ones, which makes them highly impressionable. However, when it comes to multiple micronutrient supplements (MMS), it appears that it is us nutrition and public health specialists who are impressionable.

Maternal MMS has been a 'hot topic' for the past few years, with debates abounding over whether MMS should replace iron and folic acid (IFA) supplements as standard practice. Although the World Health Organization (WHO) still only recommends that MMS replace IFA supplements for pregnant women in 'emergency contexts' and 'contexts of rigorous research', the evidence that MMS are superior to IFA supplements at preventing preterm births and low birth weight, and hence improving newborn survival, continues to mount [1–4]. MMS contain 13–15 micronutrients including iron and folic acid and are therefore designed to reduce the gap between the requirements for these essential nutrients and average intakes during pregnancy. Many countries have decided to implement MMS as the standard of care, despite the current lack of endorsement from the WHO [5]. MMS has been added to the WHO Essential Medicines List (EML), and 68 countries have added MMS to their national EML [6, 7]. In addition, UNICEF has endorsed the implementation of MMS in its country programmes, the 2024 World Bank Investment Framework for Nutrition ranked MMS as one of the top priorities for investment, and several publications have documented that MMS is cost-effective [2, 8, 9].

For non-pregnant women and adolescent girls, the WHO currently recommends weekly IFA supplements (WIFAS; 60 mg iron + 2.8 mg folic acid) in settings with an anaemia prevalence of 20% or higher; daily iron (30–60 mg) is recommended in settings with > 40% anaemia prevalence. This intervention aims to improve their haemoglobin concentrations, reduce their risk of anaemia, and reduce the risk of neural tube defects in their offspring if they were to become pregnant [10, 11]. Now that transitioning from IFA supplements to MMS for pregnant women has gotten so much traction, researchers,

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programmers and policymakers are also considering the replacement of WIFAS for non-pregnant adolescent girls with MMS [12]. Could MMS have superior outcomes to WIFAS for adolescent girls? Could they prevent anaemia and neural tube defect-affected pregnancies better or the same as WIFAS, whilst also preventing other micronutrient deficiencies?

Limited research has been conducted on this topic, and the WHO has called for additional studies to clarify the optimal dose, regime, and formulation of MMS for menstruating adolescents and women [11]. At present, very few studies have examined MMS among adolescents; one large study in Burkina Faso comparing WIFAS and daily MMS to controls found that neither WIFAS nor MMS were especially effective at preventing anemia among adolescent boys and girls, potentially due to low adherence in both arms [13]. A study from Bangladesh found that twice weekly MMS reduced iron deficiency as effectively as twice weekly IFA, but it also improved Vitamin A, B_2 and C status in school girls [14]. However, this study targeted non-anaemic schoolgirls, limiting its relevance to high-anaemia settings where WIFAS are indicated. There have also been some studies of preconception MMS in women and girls; a meta-analysis of existing data found that daily MMS supplementation was no better than daily IFA supplementation in improving newborn anthropometric parameters [15, 16]. These studies focus narrowly on pregnancy outcomes and infant growth, overlooking key outcomes for adolescents themselves such as micronutrient status, physical growth, cognitive development and learning. More research is needed that prioritizes adolescents' own health and wellbeing, not just their future role in reproduction.

While there are still large data gaps with regard to the effectiveness of MMS vs. IFA for adolescents, we must also consider important practicalities such as supply chains, intervention coverage and adherence. There is currently no recommended supplementation regime for how often MMS should be provided for non-pregnant adolescents and MMS are not recommended for adolescents by WHO, nor are they included on the EML for menstruating adolescents or women. One weekly tablet is more feasible to distribute and will likely illicit better adherence than a daily tablet [17]. However, this requires the dosage of the supplement to be specifically formulated for weekly consumption. The current UNIMMAP MMS formulation ("The United Nations International Multiple Micronutrient Antenatal Preparation" is the most widely available formulation containing 15 micronutrients) is designed to meet the daily micronutrient needs of pregnant women. When given once weekly, MMS do not provide adequate iron, with only half of the recommended amount (30 mg) that is in WIFAS (60 mg), and contain insufficient folic acid to prevent neural tube defects in cases of pregnancy, containing only 14% (0.4 mg) of the WHO recommended weekly dose (2.8 mg) [18] (See Annex Table 1 for a summary of which supplements meet the recommended daily allowance (RDAs) for adolescents). It also means that adolescent girls are 'in competition' with pregnant women for the same product, which would mean that overstretched programmes have to prioritise one group over the other.

It is worth noting that many WIFAS programmes currently use IFA tablets that are designed for daily consumption by pregnant women, which pose the same challenges as above [19]. However, a specific formulation of WIFAS was recently (2023) added to the WHO EML and also the UNICEF supply catalogue (2019) [20]. This marks a key step toward improving production, importation, and access to appropriately formulated WIFAS for adolescent girls [20]. Despite requiring only weekly delivery, rather than daily delivery, WIFAS programme coverage remains relatively low. Still, it has increased substantially over the past decade with an estimated annual reach of over 20 million girls and expanding [21]. In addition, programmes that do deliver WIFAS to adolescent girls often only capture the lower end of the 10–19 years age range due to increasing school dropouts with age, and a focus only on primary and lower secondary schools in some contexts. These coverage challenges would persist if there was a transition from WIFAS to MMS, and could potentially be exacerbated if delivery of MMS needed to be daily. In many of the contexts currently providing WIFAS, anaemia rates would be high enough (> 40%) to meet the public threshold for considering daily supplementation for the same groups [22]; however, the cost, feasibility and likely adherence challenges of daily delivery make WIFAS, at present, the intervention of choice for programs at scale.

On the positive side, the additional micronutrients provided by an MMS product over WIFAS could have benefits for health, growth and development, by filling additional nutrient gaps for adolescents. However, these more functional outcomes have not been studied, nor has an appropriate dosage of the other micronutrients been explored in relation to adolescent needs. Other prevalent and concerning micronutrient deficiencies in adolescents, besides anaemia, include iodine, zinc, vitamin A, vitamin D, and calcium. Calcium and zinc requirements are greater during puberty and adolescence than any other population age group except during pregnancy, and these are important nutrients for bone development, growth, and maturation [23, 24]. However, the lack of field-friendly, functional biomarkers for many of these micronutrients makes it harder to assess and communicate the full benefits of MMS. Additionally, just like WIFAS, the UNIMMAP MMS formulation contains no calcium, highlighting yet another unmet

need in addressing the specific nutritional requirements of adolescents (Annex Table 1). The recommended calcium requirement in adolescent is 1,300 mg/day, given substantial bone accretion during this period, and yet it is thought that many adolescents in low- and middle-income countries (LMICs) do not meet this. For example, calcium intake in Malaysian adolescents has been reported to be as low as 377 mg/day and calcium deficiency may affect up to 99% of adolescent girls in Nigeria [23, 25, 26]. Preconception calcium levels are also important for preventing pre-eclampsia during pregnancy [27]. To inform the most effective approach for adolescent supplementation, research in LMIC is needed to evaluate how different micronutrient combinations and dosages influence both health and/cognitive/educational outcomes. Adherence should also be carefully considered and measured since it is thought that the lower dosage of iron (30 mg) in MMS may increase adherence when compared to the IFA dosage of iron (60 mg), which has some reported negative side effects when consumed daily.

There are potential benefits as well as risks to using one product for two different programs and population groups. Providing one product to both pregnant women and adolescent girls can have the benefit of streamlining supply chains, especially if accessing supplies is not easy. For example, during the besiegement in Gaza in 2024, UNICEF were providing MMS to pregnant women and planned to also provide them to adolescent girls to minimise the number of different products required for procurement and management [28]. In cases of humanitarian emergencies, UNICEF often adopts the term "iron-containing supplements" in its recommendations in order to allow for flexibilities of products, depending on availability.

However, there are also risks of stock-out, especially for maternal health programs when a commodity is used for additional programs. This is especially problematic given that there are currently only a handful of manufacturers and suppliers of UNIMMAP-MMS that meet quality standards, though supply capacity is beginning to improve. Joint and harmonized forecasting, procurement and supply chain management systems would be needed between maternal and adolescent programs using MMS, which would often involve multi-sectoral coordination and reporting mechanisms when adolescent supplements are primarily delivered in schools. Prior to the inclusion of WIFAS on the WHO EML, many countries used the same maternal commodity of IFA for both maternal (daily) and adolescent nutrition programs (weekly), and stock outs and supply shortages were very common. Even in 2024, UNICEF's NUTRIDASH data shows that they are supporting national WIFAS programming in 69 countries, and more than half of these use the IFA supplements designed for daily consumption by pregnant women [29].

An additional concern around using a maternal product for non-pregnant adolescents is that parents could perceive it to be a "reproductive" commodity for their daughters, creating further barriers to adherence [30]. Even if evidence end up supporting the use of the same antenatal MMS for non-pregnant adolescent girls, ideally the packaging and labelling should be specific to the adolescent population rather than an "off-label" use of an antenatal supplement for girls.

Building on the growing momentum around MMS for pregnant women, now is the perfect time to ask: "what would an ideal supplement for adolescent girls (10–19 years) look like?". To answer this question, both programmatic and scientific considerations are needed. Programmatically, would it be preferable to be a weekly or daily product? What packaging options would make sense for delivery in schools as well as in community or healthcare settings to reach non-school going adolescents? Scientifically, what would the ideal micronutrient content look like from a perspective of biological requirement, dietary deficiencies, and cost-effectiveness? And beyond haemoglobin and iron status, which outcomes truly capture improvements in adolescent health, development and wellbeing? Actionable research priorities could include: randomised controlled trials (RCTs) comparing weekly, adolescent-formulated MMS vs. WIFAS on haemoglobin, micronutrient status, and school performance; formulation studies to determine optimal weekly doses of iron, folic acid, zinc, and calcium for adolescents; and implementation research on delivery platforms (school vs. community) and youth-centred packaging.

It is also important that this research be undertaken without conflict of interest. Researchers and policymakers need to be acutely aware of potential pressures coming from industry who are producing MMS, WIFAS, or other commodities and may be interested in expanding markets for their products through national and WHO recommendations and programs.

Conclusions

In summary, while weekly MMS may be a practical option in some humanitarian contexts for adolescent girls (despite lacking adequate iron and folic acid dosage), at present WIFAS is still the relatively better evidenced and appropriate formulation of supplement for this population. New evidence is required to fill knowledge gaps around MMS and adolescents, and these studies should come from a perspective of practicality, need, feasibility of delivery, and cost-effectiveness to ensure that future solutions are both impactful and sustainable.

Abbreviations

WIFAS	Weekly iron and folic acid supplements
MMS	Multiple micronutrient supplements
IFA	Iron and folic acid
WHO	World health organisation
EML	Essential medicines list
RCT	Randomised controlled trial
LMIC	Low- and middle-income country
UNIMMAP MMS	The United Nations International Multiple Micronutrient Antenatal Preparation

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

NL and MR conceived the idea for the article; NL wrote the first draft. EK and MR reviewed and revised the manuscript. All authors have read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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