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Multiple Micronutrient Supplementation in Pregnancy TECHNICAL ADVISORY GROUP

Micronutrient FORUM

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Multiple Micronutrient Supplementation in Adolescents in Low-and Middle-Income Countries

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Key Messages

Multiple micronutrient supplementation (MMS) is beneficial and safe for women during pregnancy, and global guidance supports its use in women, including adolescent girls, who are pregnant or breastfeeding, particularly in humanitarian settings.

For menstruating adult women and adolescent girls, the current guidelines recommend daily iron (30-60 mg) or weekly iron (60 mg) and folic acid (2.8 mg) supplementation (IFA) to prevent anemia in settings where anemia prevalence is high (> 40% or > 20%, respectively).

Countries are seeking guidance about whether existing programs providing preventive iron or IFA to adolescent girls should transition to MMS instead.

To help inform these decisions, the global MMS Technical Advisory Group (MMS TAG) assessed the evidence on the benefits and safety of MMS in adolescents: pregnant, menstruating girls, and boys and girls.

The MMS TAG's recommendation is informed by the following points:

Among adolescent girls who are pregnant, a solid body of evidence shows MMS (compared to IFA) results in improved birth outcomes, similar to what is observed in adult pregnant women, supporting its use in this vulnerable population.

Among adolescent girls who are not pregnant, as well as adolescent boys, a few studies indicate that (UNIMMAP) MMS, compared to IFA, can improve adolescent micronutrient status and does not differ in its impact on reducing anemia, although results may vary according to doses, frequency, duration of supplementation, baseline anemia status, sex, and location. Further clinical and implementation research is needed before firm recommendations can be made, particularly comparing daily MMS with weekly IFA. Notably, providing weekly MMS would not fulfill the folic acid requirements of adolescent girls who might subsequently become pregnant.

Given the limited evidence on the benefits of MMS in non-pregnant and non-lactating adolescent girls and the limited global MMS supply, which should be reserved for pregnant women and adolescent girls in low- and middle-income countries (LMICs), currently the MMS TAG does not recommend universally transitioning from existing IFA to MMS programs in this population.

Introduction

Multiple micronutrient supplements (MMS) are a cost-effective intervention designed to meet the increased micronutrient requirements during pregnancy.[1,2] The most extensively studied formulation - UNIMMAP MMS - contains 15 essential vitamins and minerals.[3] Global guidance supports the use of MMS not only in adult women but also in adolescent girls who are pregnant or breastfeeding in humanitarian contexts.[4,5]

If all adolescents had access to varied and high-quality diets, supplementation would only be required in very particular cases. However, the low-quality and monotonous diets frequently observed among adolescents in LMICs, paired with the elevated nutritional requirements necessary to support their growth and development during puberty, make this population a nutritionally vulnerable group.

Adolescent girls are especially vulnerable because their increased iron requirements due to menstruation place them at a higher risk of iron deficiency and anemia, which can negatively impact their physical and cognitive health.[6] Deficiencies of other micronutrients, such as iodine, zinc, folate, and vitamins A and D, are also prevalent among adolescents in LMICs.[7,8]

Current World Health Organization (WHO) guidelines[9] recommend implementing effective actions for improving adolescent nutrition, including:

- **Daily iron supplementation** (30-60 mg iron for 3 consecutive months) for **menstruating adult women and adolescent girls** who live **in settings where anemia prevalence is 40% or higher,**[10] **or**

- **Weekly iron and folic acid supplements** (IFA), containing 60 mg iron and 2,800 µg of folic acid (e.g., provided for 3 months, followed by 3 months of no supplementation), for **all menstruating adolescent girls and adult women** living **in settings with an anemia prevalence of 20% or higher,** to improve their hemoglobin concentrations and iron status and reduce their risk of anemia.[11]

Intermittent supplementation with IFA reduces the risk of anemia by a third in menstruating adolescent girls.[12]

However, WHO emphasizes that evidence remains limited for some questions, including the optimal dose, schedule, and duration of iron and IFA supplementation, the optimal interval between supplementation periods, as well as the effects of other vitamins and minerals on hematological, nutritional and other health outcomes.[10,11]

Given the evolving global interest in MMS, many stakeholders are now asking whether existing programs that provide preventive iron or IFA to adolescents, in particular adolescent girls, in LMICs should transition to MMS instead.

To help inform these decisions, the global MMS Technical Advisory Group (MMS TAG) assessed the evidence through a literature review on the benefits and safety of MMS in adolescents (defined as 10 to 19 years by WHO),[13] presented in this technical brief for pregnant girls, menstruating girls, and boys and girls in general.

Recommended Dietary Allowances (RDAs) and Tolerable Upper Intake Levels (ULs) for Adolescents

Table 1 presents the micronutrient requirements for adolescents, namely the Institute of Medicine's (IOM) RDAs and ULs, for 15 vitamins and minerals for non-pregnant and non-lactating adolescent girls and boys. It also presents the average daily intake if the target population consumes daily or weekly UNIMMAP MMS, or weekly IFA.

Taking a daily UNIMMAP MMS tablet would provide most of the requirements for the 15 micronutrients, without exceeding the ULs. The ULs represent the highest daily intake of a nutrient that is unlikely to cause adverse health effects for almost all individuals in a healthy population.[14]

Table 1 shows that the intake of all micronutrients provided by a daily tablet of UNIMMAP MMS formulation does not exceed the ULs set up for adolescents, either between 9 and 13 years of age or between 14 and 18 years of age. Furthermore, Appendix 2 demonstrates that, in the hypothetical scenario that adolescents were reaching the RDAs for the 15 micronutrients from adequate and complete diets and UNIMMAP MMS was consumed daily, the total amount of micronutrient intakes would be substantially below the UL for most micronutrients.

Taking a single UNIMMAP MMS tablet per week would provide a much smaller proportion of micronutrient requirements, including those for folic acid, which could be an issue if the adolescent girl subsequently becomes pregnant (Table 1).

Notably, the WHO-recommended weekly IFA intervention for menstruating adult women and adolescents supplies a larger dose (2,800 µg) of folic acid. Nonetheless, there are IFA programs providing only 500 µg of folic acid weekly to school-going adolescent boys and girls.[15]

Table 1 - Recommended Dietary Allowances (RDAs) and Tolerable Upper Intake Levels for 15 vitamins and minerals for non-pregnant and non-lactating adolescent girls and boys, and the assumed average daily nutrient intake with weekly and daily UNIMMAP MMS and IFA.[16,17]

Nutrient	RDAs (IOM)[16, 17]				Once daily UNIMMAP MMS formulation (average daily	Once weekly UNIMMAP MMS formulation (average	Once weekly IFA: 60 mg iron and 2800 µg of folic acid (average	ULs (IOM)[16, 17]	
	9-13 y Girls	9-13 y Boys	14-18 y Girls	14-18 y Boys				9-13 y	14-18 y
Vitamin A	600 µg	600 µg	700 µg	900 µg	800 µg	114 µg	-	1700 µg	2800 µg
Vitamin B1	0.9 mg	0.9 mg	1.0 mg	1.2 mg	1.4 mg	0.2 mg	-	N.A.	N.A.
Vitamin B2	0.9 mg	0.9 mg	1.0 mg	1.3 mg	1.4 mg	0.2 mg	-	N.A.	N.A.
Vitamin B3	12 mg	12 mg	14 mg	16 mg	18 mg	2.6 mg	-	20 mg	30 mg
Vitamin B6	1.0 mg	1.0 mg	1.2 mg	1.3 mg	1.9 mg	0.27 mg	-	60 mg	80 mg
Vitamin B9	**300 µg DFE**	**300 µg DFE**	**400 µg DFE**	**400 µg DFE**	**400 µg** (folic acid)	**57 µg** (folic acid)	**400 µg** (folic acid)	**600 µg** (folic acid)	**800 µg** (folic acid)
Vitamin B12	1.8 µg	1.8 µg	2.4 µg	2.4 µg	2.6 µg	0.37 µg	-	N.A.	N.A.
Vitamin C	45 mg	45 mg	65 mg	75 mg	70 mg	10 mg	-	1200 mg	1800 mg
Vitamin D	600 IU	600 IU	600 IU	600 IU	200 IU	29 IU	-	4000 IU	4000 IU
Vitamin E	11 mg	11 mg	15 mg	15 mg	10 mg	1.4 mg	-	600 mg	800 mg
Copper	700 µg	700 µg	890 µg	890 µg	2000 µg	286 µg	-	5000 µg	8000 µg
Iodine	120 µg	120 µg	150 µg	150 µg	150 µg	21 µg	-	600 µg	900 µg
Iron	**8 mg**	**8 mg**	**15 mg**	**11 mg**	**30 mg**	**4.3 mg**	**8.57 mg**	**40 mg**	**45 mg**
Selenium	40 µg	40 µg	55 µg	55 µg	65 µg	9.3 µg	-	280 µg	400 µg
Zinc	8 mg	8 mg	9 mg	11 mg	15 mg	2.1 mg	-	23 mg	34 mg

DFE = Dietary Folate Equivalents; IFA = Iron and Folic Acid; IOM = Institute of Medicine; IU = International Units; N.A. = Not available; RDA = Recommended Dietary Allowances; UL = Tolerable Upper Intake Levels; UNIMMAP MMS = The United Nations International Multiple Micronutrient Antenatal Preparation

MMS in Pregnant Adolescent Girls in LMICs

Pregnancy during adolescence creates exceptional nutritional challenges as the girl must fulfill both her own developmental nutritional needs and those required to support fetal growth. Annually, approximately 7.3 million births occur among adolescent girls in LMICs, and 70,000 girls die from complications related to pregnancy and childbirth.[18]

A 2022 individual participant data (IPD) meta-analysis evaluated the effect of MMS in pregnant adolescents.[1] This review, which included 13 trials, demonstrated that daily MMS, when compared to daily IFA supplements, reduced the risk of low birthweight by 19%, preterm births by 14%, and small for gestational age (SGA) births by 14% among pregnant adolescents.[1]

The MMS TAG concludes that MMS is equally beneficial for pregnant adolescents as for adult pregnant women in LMICs, justifying its use in this vulnerable population.

MMS in Non-pregnant Adolescents in LMICs

Several systematic reviews examined the effect of nutritional interventions (e.g., supplements with a single or multiple micronutrients, micronutrient fortified foods and beverages, etc.) in adolescents and school-aged children.[19–24] However, none of them assessed the isolated effect of UNIMMAP MMS in adolescents.

We identified four published randomized controlled trials among adolescents that assessed the effect of UNIMMAP MMS compared to IFA or standard of care,[25–28] along with an additional trial for which results are currently available only in a preprint.[29]

These five studies are described in detail in this section and summarized in Appendix Table 1; three studies were conducted in postmenarchal adolescent girls, and two were conducted in adolescent boys and girls.

There was considerable heterogeneity in study design regarding target population, baseline anemia status, comparison group, and supplementation frequency, dose and duration (varying from 10 to 52 weeks).

In all trials, supplements were provided on the school premises under close supervision of fieldworkers or teachers, which could explain the observed high levels of compliance. All trials assessed anemia (hemoglobin) and/or nutritional status (iron, vitamins A, B2, B12, C, and folic acid) and no studies examined cognitive outcomes.

MMS (UNIMMAP) in Non-pregnant, Postmenarchal Adolescent Girls in LMICs

Among postmenarchal **anemic girls** in Bangladesh, **twice weekly UNIMMAP MMS**, compared to **twice weekly IFA (providing 30 mg iron and 400 µg folic acid in each IFA tablet)**, improved the status of vitamins A, C, and B2. However, it was not more efficacious in improving prevalence of anemia, i.e. the prevalence of anemia decreased significantly in both treatment groups after 12 weeks of supplementation, without significant differences between groups.[25] Two trials compared **twice weekly IFA (providing 60 mg iron and 400 µg folic acid each) vs. once weekly double UNIMMAP MMS vs. twice weekly double UNIMMAP MMS, for 52 weeks.**

Among **anemic** Bangladeshi **girls,**[26] hemoglobin and serum ferritin concentrations increased significantly from baseline in all three groups. Once-weekly double MMS, twice-weekly double MMS, and twice-weekly IFA were equally efficacious in maintaining hemoglobin concentrations and preventing anemia. Both MMS arms significantly improved micronutrient status in comparison to IFA; twice-weekly MMS was more efficacious than once-weekly MMS in improving iron, vitamins A, B2, and folate status.

Among **non-anemic** Bangladeshi **girls**,[27] all three treatments reduced iron deficiency with no reported differences across the three groups. Compared to twice weekly IFA, both MMS treatments significantly improved micronutrient status of vitamins A, B2 and C. No differences in hemoglobin levels were observed, except at 26 weeks, when twice-weekly MMS reduced the risk of anemia compared to twice weekly IFA.

Similar to the study conducted among anemic girls, [26] once-weekly MMS was less effective than twice-weekly MMS in improving iron, vitamins A, B2 and folic acid status,[27] in the long-term trial conducted among non-anemic girls. Notably, despite being conducted among non-anemic girls, the trial was conducted in a country where the prevalence of anemia in women of reproductive age is 38%.[30]

MMS (UNIMMAP) in Adolescent Boys and Girls

Only two trials assessed the effect of MMS in a group of adolescent boys and girls. One trial was conducted in Burkina Faso in a study population with 31% prevalence of anemia[28] and another trial was conducted in Tanzania, in a study population with 53% prevalence of anemia, for which the results are available only in a preprint.[29]

Both trials compared two treatment arms of **weekly IFA (providing 60 mg iron and 2800 µg folic acid each) and daily UNIMMAP MMS with standard nutrition and health education (comparison arm)**, for two supplementation periods (10 and 16 weeks in Burkina Faso or 17 weeks each period in Tanzania) separated by a period of no supplementation (20 weeks in Burkina Faso and 6 months in Tanzania).[28,29]

The trial conducted in Burkina Faso found that, compared to no supplementation, weekly IFA supplementation resulted in higher hemoglobin levels in the overall group (over the full study period) while daily UNIMMAP MMS resulted in higher hemoglobin (and lower risk of moderate or severe anemia by 68%) among boys, but not among girls (where no differences were observed).[28]

The trial conducted in Tanzania found that, compared to standard nutrition education (control group), daily UNIMMAP MMS reduced the risk of moderate or severe anemia by 37% in the overall group, and by 73% among boys. Among girls, no differences were observed. In the overall group, weekly IFA had no impact on anemia or hemoglobin; when disaggregating results by sex, boys, but not girls, in both the IFA and UNIMMAP MMS arms had significantly higher hemoglobin levels across the full study period, compared to the control group.[29]

Notably, the effect of IFA compared with MMS was not assessed in either trial - a gap that should be addressed in future research on adolescent boys and girls.

In summary, a limited number of studies suggest that MMS, compared to IFA or standard of care, **can improve adolescent micronutrient status and seems to have similar effects on anemia, although results vary according to doses and frequency of MMS, anemia status at baseline, sex, duration of intervention and location.**

Acceptability of MMS

A recently completed study[31] showed that acceptability of UNIMMAP MMS among adolescents was very low. Notably, the product label states "for pregnant and breastfeeding women" (personal communication with study investigators), suggesting the need to adapt labels of UNIMMAP MMS to this population, should MMS be used for non-pregnant adolescents. Additionally, the study showed that there is a high stigmatization of pill distribution in communities, and also pills were not preferred by the adolescents themselves.

Other types of MMS

Other trials have compared a UNIMMAP-like formulation (i.e., a tablet containing 13 micronutrients closer to the RDAs, given every school day) and anthelminthic therapy with placebo (with participants randomized to receive MMS, anthelminthic therapy, both, or neither intervention) to assess their effects on hemoglobin and serum retinol in Kenyan adolescents.[32,33] These trials found no interaction between MMS and anthelminthic treatment, and indicated that MMS (compared to placebo) increased hemoglobin and serum ferritin, irrespective of their baseline levels.[32,33]

Future Research

While daily UNIMMAP MMS appears to be a non-inferior alternative to IFA, i.e. a reasonable substitute for weekly IFA supplementation where these programs exist, this information is based on a very limited number of trials with different study designs. Further research is needed, particularly in the following areas:

Explore the potential effects of UNIMMAP MMS supplementation on outcomes beyond nutritional status and anemia, such as growth and cognitive performance.

While a 2025 meta-analysis showed that the provision of micronutrients (in tablets, or fortified foods/beverages) vs. placebo has the potential to increase height in older children/young adolescents, this has not been assessed in the main comparison of interest, i.e., UNIMMAP MMS vs. IFA.[24]

Determine the optimal UNIMMAP MMS supplementation regimen for adolescents, i.e., dose, frequency, and duration.

This may include a non-inferiority trial directly comparing daily (or 5 x/week, if more feasible) UNIMMAP MMS with weekly IFA, along with additional trials comparing daily UNIMMAP MMS with daily IFA using biomarkers of nutritional deficiencies beyond anemia and iron status. The ideal duration of supplementation is likely to be similar to the current practices of weekly IFA, where those programs exist.

Evaluate different distribution/delivery platforms.

All studies presented in appendix Table 1 delivered MMS in schools. However, there are programmatic challenges of delivering daily MMS in schools, such as lack of intake supervision during weekends, holidays, and school breaks. To reach vulnerable groups, such as out-of-school adolescents, other concomitant delivery platforms, such as distribution through community-based health workers would likely be needed.

In addition, other effective and cost-efficient mechanisms need to be explored to reach adolescent girls.

Assess co-interventions.

For example, in Malawi, researchers are assessing the effect of ibuprofen and UNIMMAP MMS on menstrual blood loss and iron stores in menstruating adolescent girls.[34,35] In Burkina Faso and in Pakistan, researchers are assessing the effect of co-administration of calcium supplements and MMS (vs taking both supplements at separate times) on maternal and newborn hemoglobin levels.[36]

Study the cost-effectiveness of MMS programs compared to IFA.

While MMS has been shown to be a highly cost-effective intervention in pregnancy,[37,38] this has not been demonstrated in non-pregnant adolescents.

Final Considerations

Due to the existing limited evidence on the benefits of MMS for adolescents and the limited global supply of UNIMMAP MMS that should be prioritized for women and adolescents who are pregnant, **currently, the MMS TAG does not recommend universally transitioning from existing IFA programs to MMS for adolescents who are not pregnant or breastfeeding.**

If MMS were to be considered for non-pregnant adolescents, the middle or late adolescent girls (e.g., over 14 years old) would likely benefit the most, due to the increased iron needs from menstruation and a higher risk of becoming pregnant.

Daily MMS would likely improve hemoglobin and micronutrient status without causing harm from overdosing. In cases where long-term and broader interventions (such as school meal fortification) are effectively implemented, MMS would only be advisable for adolescent girls who become pregnant, although prevention of early pregnancy should be prioritized.

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Appendices

Appendix 1 – Table: Summary of trials providing UNIMMAP MMS to adolescents in LMICs

Trial	Population	Intervention	Control	Findings
Trials conducted in menstruating adolescent girls (anemic or in settings with high prevalence of anemia)				
Ahmed, 2005[25]	Anemic girls, Bangladesh Age: 14-18 y n=178	UNIMMAP MMS twice weekly Duration: 12 weeks	IFA twice weekly (30 mg iron and 400 µg folic acid) Duration: 12 weeks	MMS improved the status of vitamins A, C, and B2, compared to IFA, but was not more efficacious than IFA alone in improving anemia status.
Ahmed, 2010[26]	Anemic girls, Bangladesh Age: 11-17 y n=223	1. Double* UNIMMAP MMS weekly + placebo 2. Double* UNIMMAP MMS twice weekly Duration: 52 weeks	IFA twice weekly (60 mg iron and 400 µg folic acid) Duration: 52 weeks	Once-weekly MMS, twice-weekly MMS and twice weekly IFA are equally efficacious in maintaining hemoglobin concentrations and preventing anemia. While both MMS arms significantly improved micronutrient status in comparison to IFA, twice-weekly MMS is more efficacious than once weekly MMS in improving iron, vitamins A, B2, and folic acid status.
Ahmed, 2012[27]	Non-anemic girls, Bangladesh Age: 11-17 y n=246	1. Double* UNIMMAP MMS weekly + placebo 2. Double* UNIMMAP MMS twice weekly Duration: 52 weeks	IFA twice weekly (60 mg iron and 400 µg folic acid) Duration: 52 weeks	All treatments reduced iron deficiency effectively. MMS (weekly and twice weekly) vs IFA significantly improved micronutrient status of vitamins A, B2 and C (with no differences in hemoglobin, except at 26 weeks where twice weekly MMS vs IFA reduced risk of anemia). Once-weekly MMS was less effective than twice-weekly MMS in improving iron, vitamins, A, B2, and folic acid status.
Trials conducted in adolescent boys and girls (anemic or not)				
Cliffer, 2023[28]	Boys and girls (31% anemic), Burkina Faso Age: 10-18 y n=3123	1. Weekly IFA (60 mg iron and 2800 µg folic acid) 2. Daily UNIMMAP MMS Duration: two periods (10 weeks, then 16 weeks) separated by 20 weeks without supplementation	Standard nutrition and health education	Overall, IFA significantly increased hemoglobin levels compared to control (but no effects for MMS). Among boys, IFA and MMS were associated with significantly higher hemoglobin levels and MMS reduced the risk of moderate or severe anemia by 68%, compared to control, with no significant effects observed in girls.
Cliffer, 2024[29] (PREPRINT only)	Boys and girls (53% anemic), Tanzania Age: 10-17 y n=2480	(1) Weekly IFA (60 mg iron and 2800 µg folic acid) (2) Daily UNIMMAP MMS Duration: two 17-week periods between May-October, in 2022 and 2023	Standard nutrition education	Participants receiving MMS had a 37% lower risk of moderate or severe anemia compared to controls, with no differences observed for IFA versus control. When disaggregated by sex, IFA and MMS significantly increased hemoglobin in males. Boys receiving MMS had a 20% reduction in the risk of anemia and 73% reduction in the risk of moderate or severe anemia compared to controls.

* double dose of the UNIMMAP formulation of all 15 micronutrients except folic acid, which was kept at 400 µg
IFA = Iron and Folic Acid; UNIMMAP MMS = The United Nations International Multiple Micronutrient Antenatal Preparation

Appendix 2 – Intake of 15 micronutrients from daily UNIMMAP and a complete diet

In the hypothetical scenario that adolescents were reaching the RDAs for the 15 micronutrients from adequate and complete diets, if UNIMMAP MMS was consumed daily, the total amount of micronutrient intakes would be substantially below the UL for most micronutrients.

For the four micronutrients that met or exceeded the UL (niacin, folate, iron for older adolescent girls, zinc for younger adolescents), health risks associated with these levels were unlikely.

For niacin, the total intake would be 30 mg for younger adolescents, 32 mg for older adolescent girls and 34 mg for older adolescent boys. The UL is based on the side-effect of flushing and only occurs with the synthetic form nicotinic acid, which is not used in dietary supplements.

For folic acid, the total intake would be 700 ug for younger adolescents and 800 ug for older adolescents. There are no known side-effects for reaching the UL; the UL is set based on the risk of masking the diagnosis of pernicious anemia, which can happen with vitamin B12 deficiency, but MMS contains vitamin B12, which mitigates this risk. In addition, the same issue would apply in programs of weekly IFA with 2800 ug of folic acid.

For iron, the total intake would be 45 mg for older adolescent girls. The UL is 45 mg/day, based on gastrointestinal side-effects, which are most commonly reported when a supplement is consumed on an empty stomach.

Zinc could only reach the UL in younger adolescents (with a total intake of 23 mg), because the UL for this age group (of also 23 mg) is low, but this is also not the main target population among adolescents. Excessive zinc intake can interfere with copper absorption, potentially leading to copper deficiency, but MMS contains copper.

Scan for Translations

About HMHB

The Healthy Mothers Healthy Babies Consortium (HMHB), hosted by the **Micronutrient Forum,** is a growing collective of over 400 individuals and organizations dedicated to improving maternal nutrition. We work collaboratively to advance evidence-based interventions such as multiple micronutrient supplementation (MMS) and balanced energy and protein (BEP) dietary supplementation during pregnancy in low- and middle-income countries. HMHB also convenes Technical Advisory Groups (TAGs) on **MMS** and **BEP**, bringing together experts in nutrition, maternal health, and public health to interpret evidence, identify knowledge gaps, and provide guidance to governments, NGOs, and partners.

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