

Focusing on Multiple Micronutrient Supplements in Pregnancy: Second Edition

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Editors

Dr. Klaus Kraemer

Managing Director

Sight and Life Foundation

Rebecca Olson

Nutrition Specialist

Sight and Life Foundation

Communication consultancy, project management and text writing

Jonathan Steffen Limited

Cambridge, UK

Layout and artwork

Gregory van der Donk

Chamonix, France

Proofreading

Rosemary Boddington

Cambridge, UK

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Sight and Life Foundation

PO Box 2116,

4002 Basel, Switzerland

Phone +41 (0) 61 815 8756

Email info@sightandlife.org

sightandlife.org

ISBN 978-3-9525058-6-1

Contributor List

Abel Ntambue, **University of Lubumbashi School of Public Health**

Abraham D Flaxman, **University of Washington**

Abraham Sanga, **United Nations Children’s Fund (UNICEF)**

Ahmad Makuwani, **Ministry of Health Tanzania**

Aimerance Kabena, **Helen Keller International**

Aishwarya Panicker, **Vitamin Angel Alliance**

Aissata Ba, **Jhpiego**

Akhir Riyanti, **University of Indonesia (Faculty of Public Health)**

Akihiro Seita, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**

Alison Bowman, **University of Washington**

Anirudh Poddar, ***Sight and Life* Foundation**

Anne Hyre, **Jhpiego**

Ashutosh Mishra, **Vitamin Angel Alliance**

Augustin Kamanda, **Ministry of Health**

Democratic Republic of Congo

Auliya Suwantika, **Universitas Padjadjaran**

Basuki Imanhadi, **University of Indonesia (Faculty of Public Health)**

Beatrice K Tshiala, **Ministry of Health**

Democratic Republic of Congo

Benson Sanga, **Mbeya Region Secretariat Tanzania**

Bruno Bindamba, **Ministry of Health**

Democratic Republic of Congo

Budi Utomo, **University of Indonesia**

(Faculty of Public Health)

Casimir Alfred, **Haitian Health Foundation**

Charity Zvandaziva, **United Nations**

Children’s Fund (UNICEF)

Christle Grace Cubelo, **World Vision**

Christopher R Sudfeld, **Harvard T H Chan**

School of Public Health

Clayton Ajello, **Kirk Humanitarian**

Danielle Porfido, **Eleanor Crook Foundation**

Davidson Mamboleo, **Vitamin Angel Alliance**

Dev Priya Toor, **Sight and Life**

Duong T Tran, **National Institute of Nutrition Vietnam**

Elan Ebeling, **PATH**

Endang L. Achadi, **University of Indonesia (Faculty of Public Health)**

Erick Killel, **Tanzania Food and Nutrition Center**

Esther Elisaria, **Africa Academy of Public Health; Ifakara Health Institute**

Evi Martha, **University of Indonesia (Faculty of Public Health)**

Felix Bundala, **Ministry of Health Tanzania**

Filomena Gomez, **Micronutrient Forum**

Fitri Nandiaty, **University of Indonesia**

(Faculty of Public Health)

Florentine Oberman, **DSM**

Geoffrey Mchau, **Tanzania Food and Nutrition Center**

Germana H Leyna, **Tanzania Food and**

Nutrition Center

Holis A. Holik, **Universitas Padjadjaran**

Hou Kroeun, **Helen Keller International**

Jack Clift, **Eleanor Crook Foundation**

Jarno de Lange, **Vitamin Angel Alliance**

Jennifer Busch-Hallen, **Nutrition**

International

Jillian Emerson, **Vitamin Angel Alliance**

John B Atwater, **Ataqua Regulatory Services**

Joseline Marhone-Pierre, **Haitian Ministry of**

Public Health and Population

Kalpna Beesabathuni, ***Sight and Life***

Foundation

Katharine D Shelley, **PATH**

Kimberly Mansen, **PATH**

Keith P West Jr, **Johns Hopkins Bloomberg**

School of Public Health

Kiersten Israel-Ballard, **PATH**

Klaus Kraemer, ***Sight and Life* Foundation**

Kristen M Hurley, **Vitamin Angel Alliance;**

The Johns Hopkins Bloomberg School of Public Health

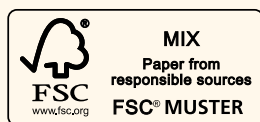
Kusyanti Febriani Hapsari, **Vitamin Angel**

Alliance

Latifah Farsia, **University of Indonesia**

(Faculty of Public Health)

Carbon-neutral production



- Lisa Noguchi, **Jhpiego**
- Ludvine Mbalá, **United Nations Children's Fund (UNICEF)**
- Lui Al-Khatib, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Mandana Arabi, **Nutrition International**
- Markus Puthut Harmiko, **Vitamin Angel Alliance**
- Marti J van Liere, **Micronutrient Forum**
- Martin N Mwangi, **Micronutrient Forum**
- Mary Sando, **Africa Academy of Public Health; Ifakara Health Institute**
- Masako Horino, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Maulana Hasan, **Vitamin Angel Alliance**
- Megan Bourassa, **Micronutrient Forum**
- Megan Parker, **PATH**
- Meredith Jackson-deGraffenried, **Helen Keller International**
- Minaud Dacius, **Vitamin Angel Alliance**
- Molly Russ, **Vitamin Angel Alliance**
- Monica Fox, **Johns Hopkins Bloomberg School of Public Health**
- Moniruzzaman Bipul, **Global Alliance for Improved Nutrition**
- Moshiur Rahman, **Social Marketing Company**
- Mulamba Diese, **Vitamin Angel Alliance Multiple Micronutrient Supplementation in Pregnancy Technical Advisory Group (MMS TAG)**
- Nancy Kosasih, **University of Indonesia (Faculty of Public Health)**
- Nandita Perumal, **Harvard T H Chan School of Public Health**
- Ngan TD Hoang, **National Institute of Nutrition Vietnam**
- Nicole Bennett, **Jhpiego**
- Nicole Young, **University of Washington**
- Nilima Azad, **Global Alliance for Improved Nutrition**
- Nurul Dina Rahmawati, **University of Indonesia (Faculty of Public Health)**
- Patrick Codjia, **United Nations Children's Fund (UNICEF)**
- Patricia S Coffey, **PATH**
- Peter Kaswahili, **Ministry of Health Tanzania**
- Peter J Winch, **Johns Hopkins Bloomberg School of Public Health**
- Philip T James, **Emergency Nutrition Network**
- Puja Peyden Tshering, **Sight and Life Foundation**
- Otte Santika, **Vitamin Angel Alliance**
- Quinn Harvey, **Vitamin Angel Alliance**
- Raphia Ngoutane, **Pennsylvania State University**
- Ramadhani Mwiru, **United Nations Children's Fund**
- Ramadhani Noor, **United Nations Children's Fund**
- Rami Habash, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Ray Masumo, **Tanzania Food and Nutrition Center**
- Rebecca Olson, **Sight and Life Foundation**
- Reed Atkin, **Micronutrient Forum**
- Robert E Black, **Johns Hopkins Bloomberg School of Public Health**
- Rolf Klem, **Helen Keller International**
- Rudaba Khondker, **Global Alliance for Improved Nutrition**
- Sadaf Khan, **PATH**
- Salam Ghanem, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Salum Manyatta, **Mbeya Region Secretariat Tanzania**
- Sarah Gibson, **Children's Investment Fund Foundation**
- Sarah Rowe, **Nutrition International**
- Sarah Straatsma, **DSM**
- Saskia JM Osendarp, **Micronutrient Forum**
- Satya Sadhu, **Summit Institute of Development**
- Sauli Epimack, **Tanzania Food and Nutrition Center**
- Shabina Raza, **Nutrition International**
- Shahidul Alam, **Social Marketing Company**
- Shannon E King, **Johns Hopkins Bloomberg School of Public Health**
- Shashank Sarvan, **Sight and Life Foundation**
- Spencer Kirk, **Kirk Humanitarian**
- Srujith Lingala, **Sight and Life Foundation**
- Stephen R Kodish, **Pennsylvania State University**
- Sufia Askari, **Sight and Life**
- Swald Msuya, **Ministry of Health Tanzania**
- Tamara Hani, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Tanuja Rastogi, **Micronutrient Forum**
- Tareq Hasan, **Global Alliance for Improved Nutrition**
- Tarej Al-Jilani, **United Nations Relief and Works Agency for Palestine Refugees in the Near East**
- Tiara Amelia, **University of Indonesia (Faculty of Public Health)**
- Tika Rianty, **University of Indonesia (Faculty of Public Health)**
- Tiny Rose Santos, **World Vision**
- Toslim Uddin Khan, **Social Marketing Company**
- Trisari Anggondowati, **University of Indonesia (Faculty of Public Health)**
- William Moore, **Eleanor Crook Foundation**
- Yashodhara Rana, **Eleanor Crook Foundation**
- Zoe Escalona, **PATH**

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Glossary

Anemia

A condition in which levels of red blood cells in the blood (or hemoglobin in the red blood cells) are lower than normal, such that red blood cells are not able to supply enough oxygen to all the tissues in the body. It is most commonly caused by nutritional deficiencies (iron, folate, vitamins B₁₂ and A); hemoglobinopathies; and infectious diseases (e.g., malaria, tuberculosis, HIV, and parasite infections).¹

Antenatal Care

Antenatal care (ANC) can be defined as the care provided by skilled healthcare professionals to pregnant women and adolescent girls to ensure the best health conditions for both mother and baby during pregnancy.

Bioavailability

The rate and extent to which an active ingredient in a supplement or food is absorbed and becomes available for use at a particular site. This estimation informs the amount of the ingredient that is absorbed and available for utilization or storage.²

Cost per Disability-Adjusted Life Years (DALYs) Averted

An increasingly popular means of assessing the cost-effectiveness of strategies to improve population health.

DALY (Disability-Adjusted Life Year)

One DALY represents the loss of the equivalent of one year of full health. DALYs for a disease or health condition are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population.³

Dietary Reference Intake (DRI)

Quantitative values that estimate nutrient intakes that are useful for planning and assessing diets for healthy people, including: the Estimated Average Requirement, EAR (an intake value estimated to meet the nutrient requirements of half of all people); Recommended Dietary Allowance, RDA (a dietary intake level that is sufficient to meet the nutrient requirements of most people); Adequate Intake, AI (a recommended nutrient intake that meets or exceeds the amount needed to maintain adequate nutrition in most people); and Tolerable Upper Intake Level, UL (the largest daily intake of a nutrient that is considered unlikely to cause harmful side-effects for most people).⁴

Essential Medicines List (EML)

A list of the minimum medicines needed for a basic healthcare system, detailing the most efficacious, safe, and cost-effective

medicines for priority conditions. MMS was added to the WHO EML in 2021.

Folate

A water-soluble B vitamin (vitamin B₉) that functions in nucleic acids (e.g., DNA and RNA) synthesis and amino acid metabolism. Folate is naturally present in many foods, including vegetables, fruits, nuts, beans, peas, grains, and animal-based foods, especially liver.⁵ Folate recommendations are made in dietary folate equivalents (DFE). The RDA for pregnant women is 600 µg DFE.

Folic Acid

The fully oxidized form of folate (vitamin B₉) that is synthetic, or manufactured, and used in supplements and fortified foods.⁶ 1 µg of folic acid equals 1.67 µg DFE.

Food/Dietary Supplement

A product that is intended to be added to the diet, containing one or more ingredients (e.g., vitamins, minerals, herbs, botanicals, amino acids, or their components) with a product label and intended to be taken by mouth as a pill, capsule, tablet, or liquid.⁶

Food Label

Any tag or other descriptive matter that is marked or attached to a food or product.⁷ It acts as an informational tool which helps consumers consider the nutritional content and health benefits of packaged foods and products.⁸ When referring to dietary supplements, information includes a descriptive name of the product, stating that it is a “supplement” as well as the name and place of business of the manufacturer and all ingredients contained in the product.

Formative Research

Evaluation activities that are conducted within a project to assess whether the objectives are being met and, if not, to modify the direction to ensure that they are met.⁹ Formative research is a process in which researchers, public health practitioners, etc. define a population of interest, determine how to access them, and describe the relevant characteristics of the population in relation to a specific public health issue and its solution.¹⁰

Fortification

Evidence-informed intervention that consists of intentionally increasing the content of one or more vitamins and/or minerals in a food, beverage or condiment to improve the nutritional quality of the food supply and deliver a public health benefit. Fortification contributes to the prevention, reduction and control of micronutrient deficiencies. For example, salt is fortified with

the micronutrient iodine and is said to be “fortified with iodine, or iodized”.¹¹

Hemoglobin

A protein found in red blood cells that carries oxygen to the tissues in the body. Optimal levels are required for the physiologic needs and vary by factors such as age, sex, pregnancy, lifestyle and environment. Reduced levels of hemoglobin in red blood cells is associated with anemia.¹

Implementation Research

An integrated investigation combining research and practice to accelerate the development and delivery of public health solutions and involving the application of knowledge to delivery of health policies and programs. Formative research is an important component of implementation research. It uses many disciplines and methods through partnerships to enhance equity, efficiency, scale-up, and sustainability of public health.¹²

Iron

A trace element (mineral) that is needed in the body and is an essential component of hemoglobin (red blood cell protein that transfers oxygen from the lungs to the tissue) which is important for physical growth, neurological development, cellular functioning, and hormone synthesis. Dietary iron has two main forms: one found in animal-based food called heme, and the other found in plants and iron-fortified foods, called non-heme or ionic iron.¹³

Low Birth Weight

Weight at birth of less than 2,500 grams.¹⁴ Babies with low birth weight (LBW) are at risk of sudden infant death syndrome (SIDS), infections, delayed development, learning disabilities, breathing problems, cerebral palsy, heart disorders, and other health conditions, and have a predisposition for noncommunicable diseases in adulthood.⁸

Macronutrients

Nutrients including proteins, carbohydrates and fats that provide calories or energy and are required in large amounts to maintain body functions.

Malnutrition

An excess or deficiency in nutrient intake, imbalance of essential nutrients, or impaired nutrient utilization.¹⁵ Malnutrition includes undernutrition (wasting, stunting, underweight, micronutrient deficiencies), overweight, and obesity, including diet-related noncommunicable diseases (heart disease, stroke, diabetes, etc.).¹⁶

Meta-analysis

A statistical method to combine results of different studies, especially those with a small sample size or with conflicting results. It is often an important component of a systematic review, a survey in which the results of the studies included in the review are statistically similar and are combined and analyzed as if they were one study.¹⁷

Micronutrients

Vitamins and minerals that are essential and needed by the body in very small quantities.¹⁸

Micronutrient Deficiency

Shortage of a vitamin or mineral needed by the body.¹⁹

Mineral

A nutrient that is needed in small quantities to keep the body healthy, including calcium, magnesium, iron and zinc.²⁰

Multivitamin

A product that is meant to supplement the diet. Multivitamins contain a variety of vitamins (and often minerals). The number and amounts of nutrients can vary substantially by product.²¹

Perinatal

A term referring to the time spanning from 22 completed weeks of gestation and ending seven completed days after birth.²²

Postnatal

A term referring to the time beginning immediately after the birth and extending up to six weeks (42 days) after birth of the baby.²³

Pre-eclampsia

An episode of hypertension (high blood pressure) occurring during pregnancy that is persistent (diastolic blood pressure ≥ 90 mm Hg) and associated with substantial proteinuria (high protein in urine > 0.3 g/24 hours).²⁴

Prenatal

A term referring to the time during pregnancy and before birth. Also called antenatal.²⁵

Recommended Dietary Allowance (RDA)

Average daily level of intake sufficient for meeting the nutrient requirements of 97–98% healthy individuals and a measure typically used to create nutritionally adequate diets.²⁶ RDAs are developed by the Food and Nutrition Board at the Institute of Medicine of the National Academies and vary by age, gender, pregnancy and breastfeeding. For example, the RDA for vitamin C is 80 mg/day for a pregnant teenaged woman and 90 mg/day for men.⁸

Systematic Review

A structured research method that consists of rigorously identifying, selecting and analyzing appropriate data to answer a specific question.⁸

UNIMMAP

UNICEF/WHO/United Nations University International Multiple Micronutrient Antenatal Preparation.

Vitamin

A type of nutrient that the body needs in small amounts to function and maintain health. Vitamins are micronutrients.

Examples include vitamins A, C and E.⁸

Vitamin A

A micronutrient and general term for a group of compounds that includes provitamin A carotenoids, which are found in plant-based foods, and retinol, which is preformed vitamin A found in animal-based foods. The body can use retinol to make retinal and retinoic acid, other forms of vitamin A, which support vision, bone growth, reproduction, immunity, cell development and skin health, and are found in certain foods (e.g., eggs, liver, fortified milk, cheese, leafy green vegetables, broccoli, dark orange fruits and vegetables, and red bell pepper).⁸

Vitamin B₁₂

Vitamin forms (vitamers) that contain cobalt and are needed for certain chemical reactions in the body. Vitamin B12 helps maintain healthy nerve cells and red blood cells, is needed to make DNA, and is required for the metabolism of carbohydrates, fats and proteins. Also referred to as cobalamin.⁸

References

- 1 Anaemia. Accessed March 28, 2023. <https://www.who.int/health-topics/anaemia>
- 2 Bioavailability and Bioequivalence Studies Submitted in NDAs or INDs – General Considerations. Published online 2014.
- 3 WHO Global Health Observatory. Indicator Metadata Registry List: Disability-adjusted life years (DALYs). <https://www.who.int/data/gho/indicator-metadata-registry/imr-details/158>
- 4 Board I of M (US) F and N. What Are Dietary Reference Intakes? National Academies Press (US); 1998. Accessed March 28, 2023. <https://www.ncbi.nlm.nih.gov/books/NBK45182/>
- 5 Office of Dietary Supplements - Dietary Supplements: What You Need to Know. Accessed March 28, 2023. <https://ods.od.nih.gov/factsheets/WYNTK-Consumer/>
- 6 Office of Dietary Supplements - Folate. Accessed March 28, 2023. <https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/>
- 7 Food Labelling. Food and Agriculture Organization of the United Nations. Accessed March 28, 2023. <http://www.fao.org/food-labelling/en/>
- 8 Office of Dietary Supplements - Dictionary of Dietary Supplement Terms. Accessed March 28, 2023. <https://ods.od.nih.gov/HealthInformation/dictionary.aspx>
- 9 Zimmerman M, Steckel L. Formative research: pretesting, revising, and more pretesting. *Dev Commun Rep.* 1985;(51):9, 12.
- 10 nhbs-msm4-formativeresearchmanual.pdf. Accessed March 28, 2023. <https://www.cdc.gov/hiv/pdf/statistics/systems/nhbs/nhbs-msm4-formativeresearchmanual.pdf>
- 11 Food fortification. Accessed March 28, 2023. <https://www.who.int/health-topics/food-fortification>
- 12 Theobald S, Brandes N, Gyapong M, et al. Implementation research: new imperatives and opportunities in global health. *The Lancet.* 2018;392(10160):2214-2228. doi:10.1016/S0140-6736(18)32205-0
- 13 Office of Dietary Supplements - Iron. Accessed March 28, 2023. <https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/>
- 14 Low birth weight. Accessed March 28, 2023. <https://www.who.int/data/nutrition/nlis/info/low-birth-weight>
- 15 Nutrition. Introduction. World Health Organization - Regional Office for the Eastern Mediterranean. Accessed March 28, 2023. <http://www.emro.who.int/health-topics/macronutrients/introduction.html>
- 16 Malnutrition. Accessed March 28, 2023. <https://www.who.int/health-topics/malnutrition>
- 17 Romm A, Ganora L, Hoffmann D, Yarnell E, Abascal K, Coven M. CHAPTER 3 - Fundamental Principles of Herbal Medicine. In: Romm A, Hardy ML, Mills S, eds. *Botanical Medicine for Women's Health.* Churchill Livingstone; 2010:24-74. doi:10.1016/B978-0-443-07277-2.00003-9
- 18 Micronutrients. Accessed March 28, 2023. <https://www.who.int/health-topics/micronutrients>
- 19 Definition of deficiency - NCI Dictionary of Cancer Terms - NCI. Published February 2, 2011. Accessed March 28, 2023. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/deficiency>
- 20 Definition of mineral - NCI Dictionary of Cancer Terms - NCI. Published February 2, 2011. Accessed March 28, 2023. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mineral>
- 21 Office of Dietary Supplements - Multivitamin/mineral Supplements. Accessed March 28, 2023. <https://ods.od.nih.gov/factsheets/MVMS-Consumer/>
- 22 Perinatal conditions. Accessed March 28, 2023. <https://platform.who.int/mortality/themes/theme-details/topics/topic-details/MDB/perinatal-conditions>
- 23 WHO Technical Consultation on Postpartum Care. World Health Organization; 2010. Accessed March 28, 2023. <https://www.ncbi.nlm.nih.gov/books/NBK310595/>
- 24 WHO_RHR_14.17_eng.pdf. Accessed March 28, 2023. https://apps.who.int/iris/bitstream/handle/10665/119627/WHO_RHR_14.17_eng.pdf
- 25 Definition of prenatal - NCI Dictionary of Cancer Terms - NCI. Published February 2, 2011. Accessed March 28, 2023. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/prenatal>
- 26 Office of Dietary Supplements - Nutrient Recommendations and Databases. Accessed March 28, 2023. <https://ods.od.nih.gov/HealthInformation/nutrientrecommendations.aspx>

Editorial

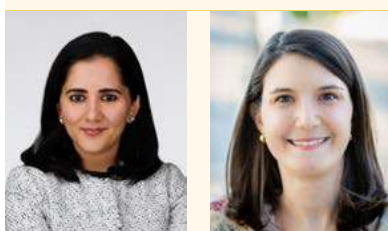
Klaus Kraemer, Rebecca Olson

Sight and Life Foundation, Basel, Switzerland



Yashodhara Rana, Danielle Porfido

Eleanor Crook Foundation, Washington, DC, USA



Introduction

Malnutrition plagues every country in the world, bearing adverse consequences in the short and long term that hinder communities and entire countries from reaching their fullest potential. If properly addressed, good nutrition has the power to develop healthy, prosperous and thriving communities and countries.

Micronutrient deficiencies are often referred to as ‘hidden hunger’ because they develop gradually, and the consequences are only seen once irreversible. A recent article in *The Lancet Global Health* estimates that 57% of preschool-age children and 74% of non-pregnant women of reproductive age are deficient in one or more of the three ‘core’ micronutrients (iron, zinc and vitamin A for preschool-age children; iron, zinc and folate for non-pregnant women of reproductive age).¹ *The Lancet* also identified women’s nutrition as a neglected area.

“The next decade is a new frontier for MMS”

High rates of micronutrient deficiency in women combined with inaction and neglect have perpetuated the cycle of malnutrition: malnourished women become pregnant and give birth to malnourished children. Multiple micronutrient supplements (MMS) containing 15 essential vitamins and minerals are proven to be safe and effective in improving the nutrition of pregnant women and reducing poor birth outcomes. There is consensus among the scientific community that MMS has a similar impact to iron and folic acid supplements on anaemia but performs better in preventing babies from being born too early

and too small, helping the next generation to survive and thrive. Yet today, only about 5% of women in need of MMS are receiving it.²

The overwhelming evidence of the benefits of MMS has propelled progress on MMS over the last decade. In just the last three years, since the launch of the first *Sight and Life* Foundation MMS Special Report, the World Health Organization (WHO) has updated antenatal care (ANC) guidelines with a conditional recommendation of MMS and has added MMS to the Essential Medicines List (EML). Many countries are now implementing or completing formative research on MMS, making the case for MMS as the standard of care for prenatal vitamins.

The work is far from complete, however. The next decade is a new frontier for MMS, and with the right support from countries, donors and other stakeholders, MMS will save lives and change futures. Ensuring women everywhere have access to the supplements they need during pregnancy will require renewed global ambition. Here’s where we should start:

First, WHO should revisit the evidence on MMS. The 2020 WHO Antenatal Care Recommendations for a Positive Pregnancy Experience only recommends the use of MMS in the context of rigorous research. WHO’s previously raised concerns regarding effectiveness, safety and cost-effectiveness have been addressed by the MMS Technical Advisory Group. The responsibility now lies with WHO to re-evaluate the evidence. In doing so, we call on WHO to be transparent about their concerns and next steps.

Second, supply and demand issues need to be further examined and addressed. The demand for MMS is growing every day, and women’s demand for MMS is expected to double by 2025, but there are still very few suppliers that produce the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS formulation, considered as the gold standard due to its clinical testing. Further, accepted supply standards are lacking, and this compromises the ability to ensure full access and equity in the delivery of MMS.

Third, every pregnant woman deserves access to high-quality ANC services that include comprehensive prenatal supplements. Globally, only two-thirds of pregnant women are accessing at least four ANC visits.³ Of the women that are receiving ANC, even fewer are receiving the highest quality prenatal vitamins. It’s clear: the world’s women deserve a paradigm shift in the delivery of antenatal care. The switch to and scale-up of MMS can serve as a catalyst to change the way women access and experience health and nutrition services.

Achieving these objectives will require political leadership. The world is currently experiencing multiple, overlapping crises that further exacerbate malnutrition, and women in low-and-middle-income countries are being hit the hardest. Maintaining the status quo for prenatal vitamins in the face of great need is an affront to women’s rights and an issue of equity. Twenty years of

evidence has made it clear that MMS delivers superior results to IFA. That these inferior supplements are the standard of care in low- and middle-income countries remains a double standard.

“The world’s women deserve a paradigm shift in the delivery of antenatal care”

This double standard in care should not be allowed to remain, and it doesn’t need to. Amid decades of research and evidence, it’s time to make sure that MMS is in the hands of every pregnant woman that needs it. We stand ready to drive significant, sustainable impact that will transform the lives of pregnant women, their families and communities.

The *Sight and Life* Foundation MMS Special Report 2.0 has compiled and curated the latest evidence, country experiences and implementation tools. It aims to serve as a resource for decision-makers and implementers to drive the scale-up of MMS globally. We are deeply grateful to all who have contributed to this

Special Report. A particular thank-you goes to Kirk Humanitarian, and specifically to Spencer and Kristen Kirk, for making this publication possible.

Correspondence: Dr Klaus Kraemer, President, *Sight and Life* Foundation, PO Box 2116, 4002 Basel, Switzerland
Email: klaus.kraemer@sightandlife.org

References

- 1 Stevens GA, Beal T, Mbuya MNN, Luo H, Neufeld LM; Global Micronutrient Deficiencies Research Group. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health*. 2022 Nov;10(11):e1590-e1599.
- 2 Ajello C, Suwantika A, Santika O, King S, de Lange J. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. Kirk Humanitarian, November 2022.
- 3 UNICEF. UNICEF Global Database 2022. Accessed 13 March 2023.

Foreword: Accelerating Multiple Micronutrient Supplement Supply Today to Meet Future Demand

Spencer Kirk

Kirk Humanitarian, Salt Lake City, UT, USA



Since the last *Sight and Life* Foundation Special Report on Multiple Micronutrient Supplementation (MMS) in pregnancy was published in April 2020, the world has changed in many ways. The COVID-19 pandemic has claimed millions of lives and exposed long-standing fragilities in our health systems; armed conflicts and climate shocks have continued to intensify around the world; and we are now contending with an escalating global food and nutrition crisis that threatens the health, wellbeing and future of millions. In just a few short years, we have seen decades of progress on global health and nutrition threatened with erasure.

During this same period, consensus has emerged among maternal health and nutrition experts on the evidence-based interventions that are proven to fight malnutrition and its harmful consequences in a safe, cost-effective and affordable manner. **MMS is among those proven interventions, and is now recognized as an untapped opportunity to address malnutrition in pregnant women.** Research and collective advocacy efforts have led to a policy framework – culminating in 2021 with inclusion of MMS in the World Health Organization’s Model List of Essential Medicines – that supports the introduction of MMS into antenatal care services as a critical intervention for pregnant women.

“This *Sight and Life* MMS Special Report 2.0 is a critical resource for the community working to introduce and scale up MMS in LMIC”

This *Sight and Life* MMS Special Report 2.0 is further proof of the global momentum around MMS, strengthened by increased dialogue and partnership among stakeholders. It contains the latest evidence showing the unequivocal benefits of the globally

recognized MMS formula known as United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP). And it shares how momentum is continuing to build at the national level, with at least 20 low- and middle-income countries (LMIC) currently introducing or exploring use of UNIMMAP MMS, with many more countries expected to soon follow.

While this is all progress worth celebrating, there is a great deal of work still to be done to reach all pregnant women in need. We are in a crucial phase for introduction and scale-up of MMS globally, but greater investment and actions are needed, including the following:

- **We must urgently support continued investment in national introduction of UNIMMAP MMS using an implementation science (IS) approach.** Many countries are already moving forward and successfully using IS to understand the barriers and enablers of supply, demand and delivery and to design and test strategies to deliver MMS effectively in their national context. This *Sight and Life* MMS Special Report 2.0 is a critical resource for the community working to introduce and scale up MMS in LMIC. Importantly, it provides learnings based on individual country experiences that point to a way forward to accelerate introduction of UNIMMAP MMS. These valuable evidence-based learnings, practical tools and resources can be used now by decision-makers actively exploring or just beginning the introduction of UNIMMAP MMS. However, because of the context-specific nature of introduction, continued investment in IS is needed to help each country identify effective strategies for integrating UNIMMAP MMS into their national health services, while continuing to facilitate cross-country learnings.

As more countries move to introduce UNIMMAP MMS, demand is expected to rise significantly in the next few years. Yet our current global supply and manufacturing capacity is not equipped to handle this surge. This report sounds an alarm bell on supply issues. By 2030, without action, the projected supply of UNIMMAP MMS will support just 30 million pregnant women each year. This means that at our current pace, only 13% of the 228 million women who become pregnant every year in LMIC will have access to this essential intervention. **We must work together to build global and regional manufacturing capacity and coordinated procurement and deployment of MMS, as well as to support national production where feasible.**

“UNIMMAP MMS is now positioned to become the standard of care for women globally”

Kirk Humanitarian is a private family foundation dedicated to improving global health through a focus on women’s nutrition during pregnancy. Since 2002, we have focused our efforts on building manufacturing capacity for high-quality, low-cost UNIMMAP MMS and supporting evidence-based national introduction of UNIMMAP MMS in LMIC by donating MMS supplies at zero cost and supporting IS efforts. At the end of 2022, we had reached more than 29 million women worldwide with a halal-certified product that meets internationally recognized quality standards as certified by the United States Pharmacopeia (USP). And by the end of 2023, we expect to have reached an additional 10 million pregnant women with our donated UNIMMAP MMS. Simultaneously, through our efforts to engage manufacturers and purchase product at high volume, we have been able to benchmark UNIMMAP MMS at cost parity with iron-folic acid (IFA), the current standard of care. Nevertheless, providing enough UNIMMAP MMS product to support the pregnancies of 228 million women annually in LMIC requires more investment that must be a shared responsibility.

Though we face complex challenges and circumstances, it is important to recognize that we – the MMS movement – have momentum. UNIMMAP MMS is now positioned to become the stan-

dard of care for women globally. Its introduction is supported by a policy guidance framework, and a growing number of countries are exploring or already transitioning from IFA to MMS. **But two areas need more attention and resources. First, we need to ramp up investments in manufacturing and procurement of UNIMMAP MMS to ensure there is something to place into a pregnant woman’s hands; and we must expand investments in national introduction initiatives using an IS approach to ensure UNIMMAP MMS supplies and delivery strategies are synchronized.** Solving global MMS supply and delivery issues requires governments, UN agencies, private donors, manufacturers and NGOs to come to the table and work together. Timing becomes even more critical given that it takes 4–5 years for an established manufacturer to produce a high-quality MMS product in volume and for national governments to build an effective strategy to ensure that UNIMMAP MMS is delivered to every pregnant woman that needs it.

We must act now.

Spencer Kirk

Managing Director, Kirk Humanitarian

Correspondence: **Spencer F. Kirk**, Managing Director, Kirk Humanitarian, 2755 E Cottonwood Pkwy, Salt Lake City, UT 84121, USA

Email: skirk@kirkhumanitarian.org

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The Evidence Base



Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements

The Multiple Micronutrient Supplementation in Pregnancy Technical Advisory Group (MMS-TAG)

Key messages:

- Prenatal multiple micronutrient supplements (MMS) provide a variety of vitamins and minerals to fill the gap between the typically low micronutrient intakes observed in low-resource settings and the higher requirements imposed by pregnancy.
- Various meta-analyses demonstrated that MMS containing iron and folic acid resulted in a consistent relative risk reduction for several outcomes, including low birthweights, small-for-gestational-age births, preterm births and stillbirths, over and above the benefits provided by iron and folic acid supplements (IFA).
- The benefits of MMS (when compared to IFA) are even greater among anemic and underweight pregnant women, those who initiate supplementation earlier, and those with higher adherence.
- MMS is a cost-effective intervention that brings additional benefits for the health of the mother, from improved micronutrient status to adequate gestational weight gain.
- MMS is safe, meaning that there is no evidence of harm or hypervitaminosis-related adverse effects.
- The research gaps identified in the 2020 WHO update of the MMS recommendation have now been addressed with recent meta-analyses and should be considered in future convenings of the WHO guideline development group.

Introduction

Vitamins and minerals, often referred to as micronutrients, are essential nutrients required in small amounts for healthy development, disease prevention and wellbeing across all life stages. During pregnancy, they have a particularly important role in all phases of fetal development, from the implantation and vascularization of the placenta, to the organ and neurological development, tissue deposition and body composition of the offspring.¹

Recent global estimates indicate that two-thirds of non-pregnant women of reproductive age worldwide have micronutrient deficiencies.² In pregnant women of low- and middle-income

countries (LMICs), the prevalence is likely to be higher, not only because nutrient-poor diets are common among women in resource-poor settings but also because requirements for several vitamins (e.g., B₁, B₂, B₃, B₆ and B₉) and minerals (e.g., zinc, iodine and iron) are increased by up to 50% to accommodate maternal and fetal demands (Table 1).¹ The well-documented consequences of micronutrient deficiencies during this critical stage of life include impaired fetal growth (low birthweight [LBW], being born small for gestational age [SGA]), preterm birth, perinatal mortality, maternal and child cognitive impairment, premature rupture of membranes, insufficient gestational weight gain, and birth defects.^{1,3}

While pregnant women should be supported and encouraged to receive adequate nutrition through consumption of a healthy, diverse and balanced diet,^{4,5} this is rarely available or else not affordable in resource-poor settings. Thus, prenatal MMS (multiple micronutrient supplements) were designed to fill the micronutrient gap between the increased requirements and the typically low intake of these essential nutrients observed during pregnancy in LMICs. In 1999, the United Nations Children's Fund (UNICEF), along with the World Health Organization (WHO) and the United Nations University, created the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP)⁶ to provide the recommended daily allowance (RDA) of 15 micronutrients. Table 1 shows the RDAs for these 15 vitamins and minerals in non-pregnant and non-lactating women⁷ as well as in pregnant women,⁷ the composition of the UNIMMAP MMS formulation,⁶ and the composition of the most commonly used formulations of iron and folic acid supplements (IFA) in LMICs.

An overview of the effects of MMS vs IFA on birth outcomes

MMS has been recommended by WHO, the World Food Programme, and UNICEF since 2007 for pregnant women in emergency settings, even in the presence of fortified rations,⁸ and by WHO since 2013 for pregnant women with active tuberculosis.⁹

In 2016, WHO launched guidelines on routine antenatal care (ANC) for pregnant women and adolescent girls, including 49 recommendations, of which 14 are related to nutrition.^{4,5} Daily IFA containing 30–60 mg of elemental iron and 400 µg of folic acid was widely recommended to prevent maternal anemia.⁴ In 2020, WHO updated the recommendation to include the use of MMS in the context of rigorous research.¹⁰ This recommendation was

TABLE 1: Recommended dietary allowances (RDA) for 15 micronutrients in non-pregnant and non-lactating women as well as in pregnant women, the composition of the UNIMMAP MMS formulation, and the composition of the most commonly used formulations of iron and folic acid supplements

Micronutrient	RDAs for non-pregnant and non-lactating (NPNL) women ⁷	RDAs for pregnant women (% increase from NPNL women) ⁷	UNIMMAP MMS formulation ⁶	Iron and folic acid supplements (common formulations) ⁴
Vitamin A	700 µg RAE	770 µg RAE	800 µg	-
Vitamin B₁ (thiamine)	1.1 mg	1.4 mg (+27%)	1.4 mg	-
Vitamin B₂ (riboflavin)	1.1 mg	1.4 mg (+27%)	1.4 mg	-
Vitamin B₃ (niacin)	14 mg	18 mg (+28%)	18 mg	-
Vitamin B₆ (pyridoxine)	1.3 mg	1.9 mg (+46%)	1.9 mg	-
Vitamin B₉ (folate)	400 µg DFE	600 µg DFE (+50%)	400 µg	400 µg
Vitamin B₁₂	2.4 µg	2.6 µg (+8%)	2.6 µg	-
Vitamin C	75 mg	85 mg (+13%)	70 mg	-
Vitamin D	600 IU	600 IU	200 IU	-
Vitamin E	15 mg	15 mg	10 mg	-
Copper	900 µg	1,000 µg (+11%)	2 mg	-
Iodine	150 µg	220 µg (+47%)	150 µg	-
Iron	18 mg	27 mg (+50%)	30 mg	30 – 60 mg
Selenium	55 µg	60 µg (+9%)	65 µg	-
Zinc	8 mg	11 mg (+38%)	15 g	-

RAE: Retinol activity equivalents; DFE: Dietary folate equivalents

“Various meta-analyses demonstrated that MMS containing iron and folic acid resulted in a consistent relative risk reduction for several adverse birth outcomes”

based on the evidence generated by an updated Cochrane review, which evaluated the benefits of providing MMS (UNIMMAP or other formulations) vs IFA (or iron alone) in 19 trials with 141,447 women conducted in LMICs.¹¹ However, WHO only considered

16 of these 19 trials when updating the MMS recommendation in 2020 (10 trials that used the UNIMMAP MMS formulation and 6 that used other MMS formulations). In addition, a comprehensive individual participant data (IPD) meta-analysis from 17 trials with 112,953 pregnant women established a better understanding of the modifiers of the effect of MMS vs IFA on birth and infant outcomes, and further underscored its safety.¹²

Table 2 provides an overview of the overall effects of MMS on birth outcomes, in comparison with iron (with or without folic acid) in LMICs based on the IPD meta-analysis,¹² Cochrane Review¹¹ and WHO analyses¹⁰ (analyses including all types of MMS providing between 13 to 15 micronutrients, and analyses including the UNIMMAP formulation only).

Overall, these meta-analyses show a consistent relative *risk reduction* for: LBW (varying from 12% in most analyses to 14% in the

random effects model of the IPD meta-analysis), SGA births (varying from 2% in the WHO analyses for all types of MMS to 9% in the same analyses limited to the trials that used the UNIMMAP MMS formulation), preterm births (varying from 6% in the WHO analyses to 8% in the fixed effects model of the IPD meta-analysis), very preterm births (varying from 13% in the IPD meta-analysis to 19% in the Cochrane review), and stillbirths (where a significant reduction of 8% was observed in the fixed effects model of the IPD meta-analysis). Variations in estimates were expected due to the differences in the number of trials included in each analysis and their methodology, but it is important to note the consistent findings demonstrating risk reduction for several birth outcomes. Moreover, a 12% risk reduction in LBW observed with MMS has the potential to benefit an estimated 2.2 million infants in LMICs annually, given the recent global estimates of 20.5 million live births with a birthweight of less than 2,500 g, of which 91% occur in LMICs.¹³ There were no significant differences identified for other maternal or infant outcomes assessed, e.g., maternal anemia in the third trimester, delivery via a cesarean section, congenital abnormalities, neonatal mortality, perinatal mortality, or infant mortality.

In 2021, MMS for pregnant women were added to WHO's 22nd Essential Medicines List, as discussed in more detail in another article of this Special Report (p. 47).

Greater benefits of MMS among anemic and underweight pregnant women, those who initiate supplementation earlier, and those with higher adherence

The 2017 IPD meta-analysis¹² conducted 26 subgroup analyses to identify individual characteristics that may modify the effect of MMS on several outcomes as compared with IFA alone. Importantly, these subgroup analyses based on individual participant data are more robust than the simple population means from the Cochrane Review,¹¹ and confirmed and expanded crucial findings from the trials themselves.¹⁴ The subgroup analyses¹² showed larger benefits of MMS among:

- anemic women (hemoglobin <110 g/L), compared to non-anemic women:
 - reduction of low birthweight by 19% versus 9%, respectively
 - reduction of SGA by 8% versus no effect, respectively
 - reduction of 6-month infant mortality by 29% versus no effect, respectively
- underweight women (BMI <18.5 kg/m²), compared to non-underweight (BMI ≥ 18.5 kg/m²)
 - reduction of preterm birth by 16% versus 6%, respectively
- women who started supplementation before 20 weeks of gestation, compared to at or after 20 weeks

TABLE 2: Effect of MMS vs IFA on birth outcomes, presented as Risk Ratios (RR) and the 95% confidence interval

	2017 IPD meta-analysis (Smith 2017) ¹²		Cochrane review (Keats 2019) ¹¹	2020 WHO guidelines ¹⁰ (all MMS formulations)	2020 WHO guidelines ¹⁰ (UNIMMAP MMS formulation)
	fixed effects model	random effects model	random effects model	random effects model	random effects model
Low birthweight (<2,500g)	17 trials 0.88 (0.85–0.90)	17 trials 0.86 (0.81–0.92)	18 trials 0.88 (0.85–0.91)	16 trials 0.88 (0.86–0.91)	10 trials 0.87 (0.81–0.94)
SGA birth (<10th percentile)	17 trials 0.97 (0.96–0.99)	16 trials 0.94 (0.90–0.98)	17 trials 0.92 (0.88–0.97)	15 trials 0.98 (0.96–1.00)	9 trials 0.91 (0.85–0.98)
Preterm birth (<37 weeks)	16 trials 0.92 (0.88–0.95)	16 trials 0.93 (0.87–0.98)	18 trials RR 0.95 (0.90–1.01)	16 trials 0.94 (0.88–1.00)	10 trials 1.00 (0.96–1.03)
Very preterm birth (<34 weeks)	14 trials 0.87 (0.79–0.95)	Not reported	4 trials 0.81 (0.71–0.93)	Not reported	Not reported
Stillbirth	16 trials 0.92 (0.86–0.99)	16 trials 0.97 (0.85–1.11)	17 trials 0.95 (0.86–1.04)	15 trials 0.98 (0.87–1.10)	10 trials 1.00 (0.86–1.17)

SGA: Small for gestational age

- reduction of preterm birth by 11% versus no effect, respectively
- women who started supplementation at or after 20 weeks of gestation, compared to before 20 weeks
 - reduction of SGA by 9% versus no effect, respectively
- women who had higher supplement adherence (95% or higher), compared to lower adherence (<95%)
 - reduction of neonatal mortality by 12% versus no effect, respectively
 - reduction of infant mortality by 15% versus no effect, respectively

Benefits of MMS vs IFA on gestational weight gain

An adequate gestational weight gain was not explored in any of these three meta-analyses, despite excessive weight gain being listed as an outcome of interest in the 2020 WHO guidelines.¹⁰ In 2022, an IPD meta-analysis of 14 studies conducted in LMICs explored the effect of MMS vs IFA on gestational weight gain.¹⁵ Percentage adequacy of gestational weight gain and total weight gain at delivery were calculated according to the Institute of Medicine 2009 guideline.¹⁶ Results show that, compared to IFA, MMS resulted in a greater percentage adequacy of gestational weight gain (weighted mean difference of 0.86%; 95% CI: 0.28% to 1.44%), higher gestational weight gain at delivery (weighted mean difference of 209 g; 95% CI 139 to 280 g) and a 2.9% reduced risk of severely inadequate gestational weight gain; importantly, it did not increase the risk of excessive gestational weight gain.

Benefits of MMS vs IFA in adolescent pregnant women

Pregnant adolescents are a particularly nutritionally vulnerable group because of the increased nutritional demands imposed by the fetus coupled with those required for growth during adolescence, and every year they account for 7.3 million births in LMICs.¹⁷ A recent IPD meta-analysis of 13 trials with 15,283 adolescents and 44,499 adult women in LMICs showed that adolescents who received MMS (vs those who received IFA) had a significantly reduced risk of low birthweight by 19%, preterm births by 14%, and SGA births by 14%.¹⁸ The group of adolescent women (<20 years old) had greater reduction of SGA births in comparison with the group of older women (≥ 20 years old).¹⁸ This review confirms that MMS also has benefits and does not evidence any harm to adolescent mothers or babies in LMICs. As such, new MMS programs should consider this vulnerable population group.

Epidemiology and physiological pathways that underpin the benefits and absence of harm

The physiological pathways that may explain the benefits of MMS stem from the complex interplay of multiple micronutrients in various stages of fetal development¹ which have been identified in some studies. For example, research from Priliani et al.^{19,20} showed that MMS, in comparison to IFA, stabilized mitochon-

drial DNA copy number, which was associated with improved birthweight and indicated more efficient energy metabolism and reduced oxidative stress. And a ten-year follow-up showed MMS decreased metabolic risk through decreased inflammatory biomarker profiles for the mother and child. Christian et al.²¹ observed that MMS enhanced erythropoiesis (the process by which red blood cells are produced) and reduced maternal stress during pregnancy, as women receiving MMS had lower levels of cortisol (a stress hormone) – two pathways that could influence birth size and gestational duration.

All the meta-analyses found no harm associated with the use of MMS with respect to mortality outcomes, specifically perinatal, neonatal, 6-month, or infant mortality; they rather showed benefits for these outcomes in certain subgroups. In addition, despite potential concerns that MMS paired with other micronutrient interventions may lead to hypervitaminoses or micronutrient toxicity,²² this has not been observed, as explained below.

First, in 2019 an analysis examined the risk of exceeding the tolerable upper intake level (UL), as set by the National Academy of Medicine, of any micronutrient in the UNIMMAP formulation if it was consumed with a nutritionally adequate diet (i.e., already including the recommended intake of the 15 micronutrients). The results revealed that for most micronutrients, this combination was substantially below the UL, and for the three micronutrients that met or exceeded the UL (folate, iron and niacin), health risks associated with these levels* were unlikely.²³

Second, the existing MMS trials conducted in LMICs showed that while MMS compared to IFA improved birth outcomes and ameliorated maternal micronutrient deficiencies (of vitamins B₂, B₆, B₁₂, D and folate in Nepal,²⁴ and of vitamins B₁₂, A, D and zinc in Bangladesh²⁵ – which was associated with improved micronutrient status of Bangladeshi newborns²⁶), it failed to eliminate them, suggesting that preconception MMS or higher micronutrient doses may be required in these nutritionally vulnerable populations. Even in high-income countries where complete, balanced diets are widely available, it has been shown that a significant number of pregnant women are not meeting recommendations for several micronutrients (vitamins D, C, A, B₆, K, and E, folate, choline, iron, calcium, potassium, magnesium, and zinc), even with the use of prenatal supplements.²⁷

Third, a variety of MMS formulations have been studied in the MMS vs IFA trials, and some²⁸⁻³¹ included doses of several mi-

*There are no health risks associated with the three micronutrients [folate, iron and niacin] meeting or exceeding the UL, because: 1) for niacin, 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, 2) for folic acid, 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], and 3) for iron, 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 and would be a concern for both MMS and IFA [which is recommended to provide 30 to 60 mg of iron].

micronutrients equivalent to multiple levels of RDAs established for pregnancy, with no evidence of harm. In fact, there is one trial that suggests additional benefits on birthweight with higher levels of micronutrients.²⁸ This trial included three arms: MMS providing 1 RDA of 15 micronutrients (UNIMMAP formulation), MMS providing 2 RDAs of the same 15 micronutrients (except for iron levels that remained at 30 mg per tablet), and IFA (control). The mean birthweight of the infants in the group that received 1 RDA of micronutrients in MMS was 53 g higher than the control group, and this value almost doubled (95 g) in the group that received 2 RDAs of MMS.²⁸

The optimal dose of micronutrients in MMS deserves further research, although this should not prevent countries from transitioning from IFA to MMS and benefitting from this cost-effective intervention. There is a planned superiority trial** comparing MMS with 30 mg iron, 45 mg iron and 60 mg iron among pregnant women in Tanzania looking at maternal anemia as the primary outcome.

Ideal number of tablets of MMS and time of initiation

MMS should be initiated as soon as the pregnancy is identified and efforts should be taken to maximize adherence,³² as early initiation in pregnancy and high adherence to MMS were associated with greater benefits.¹² It has not yet been determined what is the minimum number of MMS tablets pregnant women should take to receive full benefits in order to reduce adverse birth outcomes, which is a question frequently raised by the global nutrition community. The contribution of the timing of initiation, adherence and total number tablets on the impact of MMS on birth and infant outcomes is being studied by an ongoing IPD meta-analysis.³³

As the evidence presented until now focused on the assessment of the effect of MMS vs IFA during pregnancy, and women included in those trials initiated supplementation after the first trimester, less is known about the potential benefits of starting MMS before and just after conception, or continuing during lactation. A recent trial (JiVita-5)³⁴ assessed the effect of starting MMS preconceptionally through the first trimester of pregnant Bangladeshi women (covering the periconceptional and embryonic period) on birth and pregnancy outcomes, and demonstrated a reduction of early pregnancy loss.³⁵

Clinical research priorities identified in the 2020 WHO update of the MMS recommendation

In the 2020 WHO update of the MMS recommendation,¹⁰ two clinical research priorities were identified: (1) more evidence is needed on the effects of switching from IFA with 60 mg of iron to MMS containing 30 mg of iron, particularly in settings with high

anemia prevalence, and (2) future trials should assess gestational age with ultrasound because of the differences in the effects on LBW, preterm birth, and SGA that were perceived as conflicting and confusing by the Guideline Development Group. Recent meta-analyses of the MMS Technical Advisory Group addressed both research gaps.^{36,37}

Regarding the first research gap, a comprehensive iron dose analysis of all trials that assessed third trimester maternal anemia included in the 2019 Cochrane review showed that, when compared to IFA, MMS results in comparable hemoglobin concentration and protection against anemia during pregnancy, independently of iron dose.³⁶ For the main comparison of interest (MMS with 30 mg of iron versus IFA with 60 mg), 5 trials with 4,677 participants with high mean baseline anemia levels (from 27% to 49%) showed no differences with respect to third trimester maternal anemia (RR 0.99; 95% CI: 0.92–1.07).³⁶ These analyses are described in detail in another article of this Special Report (p. 32).

Regarding the second research gap, a comprehensive analysis of all the 16 trials that contributed to the estimates of low birthweight, preterm and SGA in the 2020 WHO update of the MMS recommendation showed that most trials used high-quality methods for gestational age assessment, and effect estimates on birth outcomes were generally consistent across methods. Seven trials (44%) assessed gestational age by ultrasound between 9 and 17 weeks (consistent with the WHO recommendations to perform one ultrasound scan before 24 weeks of gestation³⁸), four trials (25%) assessed gestational age by prospective collection of last menstrual period and pregnancy urine test (a validated method³⁹), and five trials assessed gestational age by recall of date of last menstrual period. The meta-analysis suggests that the effect of MMS vs IFA on birth outcomes does not differ across the three assessment method groups, and when limited to the seven trials that used ultrasound, the magnitude of the beneficial effect of MMS was higher for all birth outcomes including: birthweight (RR 0.87; 95% CI 0.78–0.97), preterm birth (RR 0.90; 95% CI 0.79–1.03), and SGA (RR 0.90; 95% CI 0.83–0.99).³⁷ Based on this new important research, the MMS Technical Advisory Group challenges the need for additional efficacy trials in which early pregnancy ultrasound is used to determine effects on preterm births or SGA because this has already been demonstrated with existing trials.

MMS as a cost-effective intervention

Several studies have demonstrated the cost-effectiveness of MMS compared to IFA: in three South Asian countries (Pakistan, India, and Bangladesh),⁴⁰ in Bangladesh and Burkina Faso⁴¹ and then in 12 countries.⁴² The results are consistent across all the modeled scenarios, demonstrating that even with a small incremental cost for MMS compared with IFA because of the additional micronutrients, it was highly cost-effective, with positive health outcomes for both infants and pregnant women.

**This trial is being led by Dr Emily R Smith at The George Washington University, in collaboration with partners from Ifakara Health Institute, Muhimbili University of Health and Allied Sciences, and the Africa Academy of Public Health in Tanzania and Harvard University. The trial is expected to be completed in late 2025.

A more recent analysis in India, Pakistan, Mali and Tanzania showed that, while supplying balanced energy protein supplementation (containing MMS) universally to women at ANC has the greatest impact on child health outcomes, a targeted approach of providing balanced energy protein supplementation for underweight women and providing MMS to women with an adequate BMI is more cost-effective than supplying MMS alone.⁴³

Conclusion

The effects of MMS vs IFA during pregnancy have been extensively studied in 19 trials with 141,447 women conducted in LMICs over more than 20 years,¹¹ showing consistent risk reductions for LBW, SGA, and other adverse birth outcomes, with even greater benefits in underweight or anemic women. Additional recent research has demonstrated impactful benefits on birth outcomes of adolescent mothers. Moreover, specific physiological pathways have been identified that mediate the MMS effects. Overall, MMS is a safe, efficient and cost-effective intervention that brings additional benefits for the health of the mother, from improved micronutrient status to an adequate gestational weight gain. Recent analyses addressed the clinical research priorities identified in the 2020 WHO update of the MMS recommendation, demonstrating that a transition from IFA with 60 mg of iron to MMS with 30 mg of iron would not adversely affect maternal anemia, and no additional large clinical trials are needed to assess gestational age with ultrasound. All these new analyses generated since 2020 strengthened the evidence in favor of MMS and should be considered in future convenings of the WHO guideline development group.

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Correspondence: Dr Filomena Gomes, The Micronutrient Forum, Washington, DC, USA
Email: filomena.gomes@micronutrientforum.org

References

- Gernand AD, Schulze KJ, Stewart CP, West KP, Christian P. Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. *Nat Rev Endocrinol.* 2016;12(5):274-289. doi:10.1038/nrendo.2016.37
- Stevens GA, Beal T, Mbuya MNN, Luo H, Neufeld LM, Global Micronutrient Deficiencies Research Group. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Heal.* 2022;10(11):e1590-e1599. doi:10.1016/S2214-109X(22)00367-9
- Bourassa MW, Osendarp SJM, Adu-Afarwuah S, et al. Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Ann N Y Acad Sci.* 2019;1444(1):6-21. doi:10.1111/nyas.14121
- World Health Organization. World Health Organization Recommendations on Antenatal Care for a Positive Pregnancy Experience.; 2016. <https://www.who.int/publications/i/item/9789241549912>
- Tuncalp Ö, Rogers LM, Lawrie TA, et al. WHO recommendations on antenatal nutrition: an update on multiple micronutrient supplements. *BMJ Glob Heal.* 2020;5(7):e003375. doi:10.1136/bmjgh-2020-003375
- World Health Organization, UNICEF, United Nations University. Composition of a Multi-Micronutrient Supplement to Be Used in Pilot Programmes among Pregnant Women in Developing Countries: Report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO) and United Nations University Workshop.; 1999. <https://apps.who.int/iris/bitstream/handle/10665/75358/UNICEF-WHO-multi-micronutrients.pdf?sequence=1&isAllowed=y>
- Institute of Medicine. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements. (Otten J, Hellwig J, Meyers L, eds.). National Academies Press; 2006.
- World Health Organization, UNICEF, World Food Programme. Preventing and controlling micronutrient deficiencies in populations affected by an emergency. *Bull World Heal Organ.* 2007;1:5-6.
- World Health Organization. Guideline: Nutritional Care and Support for Patients with Tuberculosis.; 2013. http://apps.who.int/iris/bitstream/10665/94836/1/9789241506410_eng.pdf
- World Health Organization. WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy.; 2020. <https://www.who.int/publications/i/item/9789240007789>
- Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2019;2019(3):CD004905. doi:10.1002/14651858.CD004905.pub6
- Smith ER, Shankar AH, Wu LSF, 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. *Lancet Glob Heal.* 2017;5(11):e1090-e1100. doi:10.1016/S2214-109X(17)30371-6
- Blencowe H, Krusevec J, de Onis M, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. *Lancet Glob Heal.* 2019;7(7):e849-e860. doi:10.1016/S2214-109X(18)30565-5
- SUMMIT, Shankar AH V, Jahari AB, et al. Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet.* 2008;371(9608):215-227. doi:10.1016/S0140-6736(08)60133-6
- Liu E, Wang D, Darling AM, et al. Effects of prenatal nutritional sup-

- plements on gestational weight gain in low- and middle-income countries: a meta-analysis of individual participant data. *Am J Clin Nutr.* 2022;116(6):1864-1876. doi:10.1093/ajcn/nqac259
- 16 Rasmussen KM, Yaktine AL. Weight Gain During Pregnancy: Reexamining the Guidelines. (Rasmussen KM, Yaktine AL, eds.); 2009. doi:10.17226/12584
 - 17 United Nations Population Fund. Motherhood in Childhood - Facing the Challenge of Adolescent Pregnancy.; 2013. <https://www.unfpa.org/sites/default/files/pub-pdf/EN-SWOP2013.pdf>
 - 18 Keats EC, Akseer N, Thurairajah P, Cousens S, Bhutta ZA, Group GYWNI. Multiple-micronutrient supplementation in pregnant adolescents in low- and middle-income countries: a systematic review and a meta-analysis of individual participant data. Ali H Ashorn U, Belizan J, Black RE, Christian P, De-Regil LM, Dewey K, Dibley MJ, Fawzi W, Friis H, Gomo E, Huybregts L, Jayatissa R, Kaestel P, Khatry SK, Kolsteren PW, Labrique AB, McCauley M, Oaks BM, Piwoz E, Shaikh S, Soekarjo DD, Sudfeld CR, Urass EAS, ed. *Nutr Rev.* 2022;80(2):141-156. doi:http://dx.doi.org/10.1093/nutrit/nuab004
 - 19 Priliani L, Prado EL, Restuadi R, Waturangi DE, Shankar AH, Malik SG. Maternal Multiple Micronutrient Supplementation Stabilizes Mitochondrial DNA Copy Number in Pregnant Women in Lombok, Indonesia. *J Nutr.* Published online June 9, 2019. doi:10.1093/jn/nxz064
 - 20 Priliani L, Oktavianthi S, Prado EL, Malik SG, Shankar AH. Maternal biomarker patterns for metabolism and inflammation in pregnancy are influenced by multiple micronutrient supplementation and associated with child biomarker patterns and nutritional status at 9-12 years of age. *PLoS One.* 2020;15(8):e0216848. doi:10.1371/journal.pone.0216848
 - 21 Christian P, Nanayakkara-Bind A, Schulze K, Wu L, LeClerq SC, Khatry SK. Antenatal micronutrient supplementation and third trimester cortisol and erythropoietin concentrations. *Matern Child Nutr.* 2016;12(1):64-73. doi:10.1111/mcn.12138
 - 22 Kurpad A V, Sachdev HS. Precision in prescription: multiple micronutrient supplements in pregnancy. *Lancet Glob Heal.* 2022;10(6):e780-e781. doi:10.1016/S2214-109X(22)00207-8
 - 23 Gernand AD. The upper level: examining the risk of excess micronutrient intake in pregnancy from antenatal supplements. *Ann N Y Acad Sci.* 2019;1444(1):22-34. doi:10.1111/nyas.14103
 - 24 Christian P, Jiang T, Khatry SK, LeClerq SC, Shrestha SR, West KPJ. Antenatal supplementation with micronutrients and biochemical indicators of status and subclinical infection in rural Nepal. *Am J Clin Nutr.* 2006;83(4):788-794. doi:10.1093/ajcn/83.4.788
 - 25 Schulze KJ, Mehra S, Shaikh S, et al. Antenatal Multiple Micronutrient Supplementation Compared to Iron-Folic Acid Affects Micronutrient Status but Does Not Eliminate Deficiencies in a Randomized Controlled Trial among Pregnant Women of Rural Bangladesh. *J Nutr.* 2019;149(7):1260-1270.
 - 26 Schulze KJ, Gernand AD, Khan AZ, et al. Newborn micronutrient status biomarkers in a cluster-randomized trial of antenatal multiple micronutrient compared with iron folic acid supplementation in rural Bangladesh. *Am J Clin Nutr.* 2020;112(5):1328-1337. doi:<https://dx.doi.org/10.1093/ajcn/nqaa223>
 - 27 Bailey RL, Pac SG, Fulgoni VL 3rd, Reidy KC, Catalano PM. Estimation of Total Usual Dietary Intakes of Pregnant Women in the United States. *JAMA Netw open.* 2019;2(6):e195967. doi:10.1001/jamanetworkopen.2019.5967
 - 28 Kaestel P, Michaelsen KF, Aaby P, Friis H. Effects of prenatal multi-micronutrient supplements on birth weight and perinatal mortality: a randomised, controlled trial in Guinea-Bissau. *Eur J Clin Nutr.* 2005;59(9):1081-1089. doi:10.1038/sj.ejcn.1602215
 - 29 Fawzi WW, Msamanga GI, Urassa W, et al. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. *N Engl J Med.* 2007;356(14):1423-1431.
 - 30 Ashorn P, Alho L, Ashorn U, et al. Supplementation of maternal diets during pregnancy and for 6 months postpartum and infant diets thereafter with small-quantity lipid-based nutrient supplements does not promote child growth by 18 months of age in rural Malawi: A randomized controlled trial. *J Nutr.* 2015;145(6):1345-1353. doi:10.3945/jn.114.207225
 - 31 Adu-Afarwuah S, Lartey A, Okronipa H, et al. Lipid-based nutrient supplement increases the birth size of infants of primiparous women in Ghana. *Am J Clin Nutr.* 2015;101(4):835-846. doi:10.3945/ajcn.114.091546
 - 32 Gomes F, King SE, Dallmann D, et al. Interventions to increase adherence to micronutrient supplementation during pregnancy: a systematic review. *Ann N Y Acad Sci.* 2021;1493(1):41-58. doi:<https://doi.org/10.1111/nyas.14545>
 - 33 Smith ER, Gomes F, Rana Z, Caniglia EC, Bourassa M, Sudfeld C. Contribution of the timing of initiation, adherence and total dose to the impact of MMS on birthweight and key outcomes: Protocol for an individual patient data meta-analysis. PROSPERO 2022 CRD42022319207. Published 2022. Accessed January 27, 2023. https://www.crd.york.ac.uk/prospéro/display_record.php?RecordID=319207
 - 34 West KP. Micronutrient Supplementation Before and During 1st Pregnancy to Improve Birth Outcomes (JiVitA-5). *ClinicalTrials.gov.* Published 2019. Accessed February 6, 2023. <https://clinicaltrials.gov/ct2/show/NCT03921177>
 - 35 West KJ, Ali H, Alland K, et al. Periconceptional multiple micronutrient supplementation reduces risk of early pregnancy loss in rural Bangladesh: the JiVitA-5 trial. In: IUNS, 22nd International Congress of Nutrition. ; 2022.
 - 36 Gomes F, Agustina R, Black RE, et al. Multiple micronutrient supplements versus iron-folic acid supplements and maternal anemia outcomes: an iron dose analysis. *Ann N Y Acad Sci.* 2022;1512(n/a):114-125. doi:<https://doi.org/10.1111/nyas.14756>
 - 37 Gomes F, Askari S, Black R, et al. Antenatal multiple micronutrient supplements versus iron-folic acid supplements and birth outcomes: analysis by gestational age assessment method. *Maternal & Child Nutrition.* e13509. <https://doi.org/10.1111/mcn.13509>
 - 38 World Health Organization. WHO Antenatal Care Recommendations

- for a Positive Pregnancy Experience. Maternal and Fetal Assessment Update: Imaging Ultrasound before 24 Weeks of Pregnancy.; 2022. <https://www.who.int/publications/i/item/9789240046009>
- 39 Gernand AD, Paul RR, Ullah B, et al. A home calendar and recall method of last menstrual period for estimating gestational age in rural Bangladesh: a validation study. *J Health Popul Nutr.* 2016;35(1):34. doi:10.1186/s41043-016-0072-y
- 40 Kashi B, M Godin C, Kurzawa ZA, Verney AMJ, Busch-Hallen JF, De-Regil LM. Multiple Micronutrient Supplements Are More Cost-effective than Iron and Folic Acid: Modeling Results from 3 High-Burden Asian Countries. *J Nutr.* 2019;149(7):1222-1229.
- 41 Engle-Stone R, Kumordzie SM, Meinzen-Dick L, Vosti SA. Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness. *Ann N Y Acad Sci.* 2019;1444(1):35-51. doi:10.1111/nyas.14132
- 42 Nutrition International. Cost-Effectiveness Analyses for the WHO Review on Multiple Micronutrient Supplements during Pregnancy: Technical Report.; 2020.
- 43 Young N, Bowman A, Swedin K, et al. Cost-effectiveness of antenatal multiple micronutrients and balanced energy protein supplementation compared to iron and folic acid supplementation in India, Pakistan, Mali, and Tanzania: A dynamic microsimulation study. *PLoS Med.* 2022;19(2):e1003902-e1003902. doi:10.1371/journal.pmed.100390

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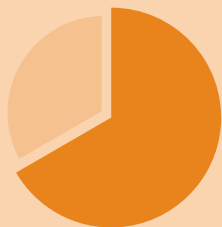
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Update on MMS Evidence

Key messages



Two-thirds of non-pregnant women of reproductive age worldwide have micronutrient deficiencies, and for pregnant women in low- and middle-income countries (LMIC) the prevalence is likely to be higher, resulting in adverse pregnancy and birth outcomes.



Recent evidence shows **consistent risk reductions** for low birth weight (LBW), small for gestational age (SGA), and other adverse birth outcomes, over and above the benefits provided by iron and folic acid supplements (IFA) alone.

Benefits of MMS on Birth Outcomes (over and above IFA alone)*

8%
in stillbirths

2%–9%
in SGA births

6%–8%
in preterm births

13%–19%
in very preterm births

12%–14%
in LBW

With even greater benefits for underweight and anemic women

19%
in LBW

29%
in infant mortality

16%
in preterm birth

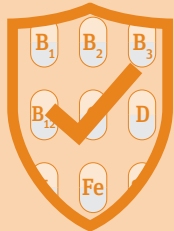
Adolescent girls who receive MMS also benefit substantially

19%
in LBW

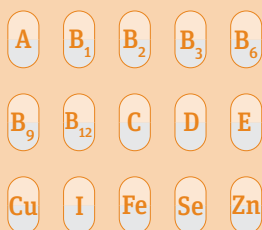
14%
in SGA births

14%
in preterm births

A **12% risk reduction** in LBW observed with MMS has the potential to benefit an estimated **2.2 million** infants in LMIC annually, given the recent global estimates of 20.5 million live births with a birth weight of less than 2,500 g, of which 91% occur in LMIC.



MMS is safe meaning that there is no evidence of harm or hypervitaminosis-related adverse effects (even when paired with balanced diets, which are rarely available or not affordable in LMICs).



Prenatal multiple micronutrient supplements (MMS) provide **15 vitamins and minerals** that are critical for a healthy pregnancy and to fill the gap between the higher nutrient requirements imposed by pregnancy and the typical low micronutrient intakes often found in LMIC.

Early start of supplementation and high adherence also produce greater benefits in terms of preterm births and neonatal and infant mortality

Recommended dietary allowances (RDA) for 15 micronutrients in non-pregnant and non-lactating women as well as in pregnant women (showing increases of micronutrient requirements by up to 50%), the composition of the UNIMMAP MMS formulation (designed to meet the needs of 15 micronutrients in pregnant women), and the composition of the most used formulations of iron and folic acid supplements (which only offer 2 micronutrients).

Micronutrient	RDAs for non-pregnant and non-lactating (NPNL) women	RDAs for pregnant women (% increase from NPNL women)	UNIMMAP MMS formulation	Iron and folic acid supplements (common formulations)
Vitamin A	700 µg RAE	770 µg RAE	800 µg	-
Vitamin B₁ (thiamine)	1.1 mg	1.4 mg (+27%)	1.4 mg	-
Vitamin B₂ (riboflavin)	1.1 mg	1.4 mg (+27%)	1.4 mg	-
Vitamin B₃ (niacin)	14 mg	18 mg (+28%)	18 mg	-
Vitamin B₆ (pyridoxine)	1.3 mg	1.9 mg (+46%)	1.9 mg	-
Vitamin B₉ (folate)	400 µg DFE	600 µg DFE (+50%)	400 µg	400 µg [†]
Vitamin B₁₂	2.4 µg	2.6 µg (+8%)	2.6 µg	-
Vitamin C	75 mg	85 mg (+13%)	70 mg	-
Vitamin D	600 IU	600 IU	200 IU	-
Vitamin E	15 mg	15 mg	10 mg	-
Copper	900 µg	1,000 µg (+11%)	2 mg	-
Iodine	150 µg	220 µg (+47%)	150 µg	-
Iron	18 mg	27 mg (+50%)	30 mg	30–60 mg
Selenium	55 µg	60 µg (+9%)	65 µg	-
Zinc	8 mg	11 mg (+38%)	15 g	-

[†]MMS contains 400 mcg folic acid. 1.67 mcg DFE is the same as 1 mcg of folic acid
1 mcg DFE = 0.6 mcg folic acid from fortified foods or dietary supplements consumed with foods
RAE: Retinol activity equivalents; DFE: Dietary folate equivalents

* Variations in estimates were expected due to the differences in the number of trials included in each analysis and their methodology, but it is important to note the consistent findings demonstrating risk reduction for several birth outcomes.

Accelerating the Delivery and Use of MMS in Humanitarian Contexts

Marti J van Liere, Martin N Mwangi

Micronutrient Forum, Washington, DC, USA

Philip T James

Emergency Nutrition Network, Kidlington, Oxfordshire, UK

Key messages:

- Huge gaps exist in the knowledge, research, programmatic guidance, and actions to concretely protect women's and girls' nutrition in humanitarian settings.
- International guidelines for women's and girls' nutrition in humanitarian contexts are not consistently translated into relevant national policies, guidance and implementation.
- Despite international recommendations on the use of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS⁴) formulation in humanitarian contexts, actual distribution remains fragmentary.
- Nutrition partners and national governments need to prioritize women's and girls' nutrition and invest in targeted nutrition guidance, implementation, and product supply and utilization for protecting their health.

Introduction

Food security and nutrition status of women and girls are disproportionately affected by crises and shocks due to COVID-19, climate change, and conflict.² Women not only have increased nutritional needs compared to other populations but are also more vulnerable because of cultural, social and economic inequities. In emergencies, they are confronted with disrupted health services and reduced access to support systems, especially antenatal, postnatal and obstetric care, further exacerbated by heightened insecurity. Malnutrition among women leads to a tremendous loss of human capital as it also impairs the future health and productivity of their children and their communities.³

While the information on women's and girls' nutritional status in humanitarian contexts is limited, recent surveys have shown a high prevalence of wasting and anemia in pregnant and lactating women and girls and a growing burden of overweight children.^{4,5} A recent Lancet Global Health publication⁶ estimated that micronutrient deficiencies in women are much more frequent than previously thought. Globally, two out of three non-pregnant women aged 15–49 years – that is, 1.2 billion – suffer from at least one micronutrient deficiency.

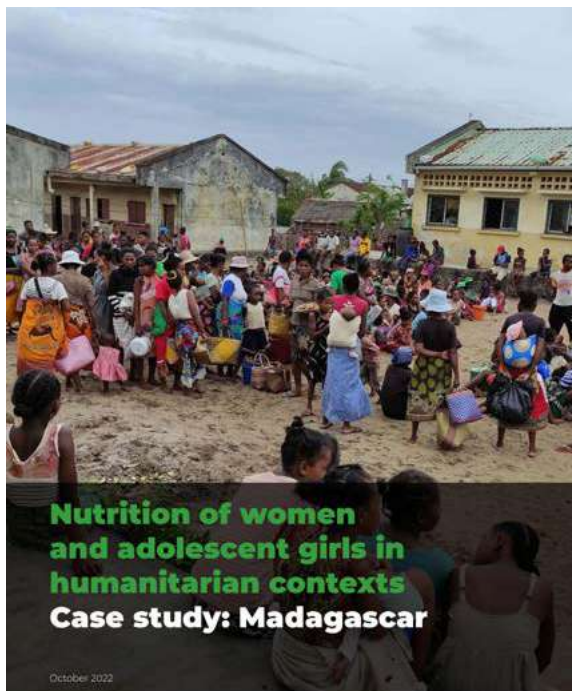
While WHO, WFP, and UNICEF published guidance on the use of multiple micronutrient supplementation (MMS) for pregnant and lactating women in emergency settings as early as 2006, it remains challenging for governments to adapt their national protocols and operationalize this guidance in humanitarian contexts.^{7,8}

The Emergency Nutrition Network (ENN), with support of the Healthy Mothers Healthy Babies (HMHB) Consortium, the Government of Ireland and UNICEF, recently published a state of play on the nutrition of women and adolescent girls in humanitarian contexts (**Figure 1**) and a case study on the use of MMS in humanitarian contexts in Madagascar (**Figure 2**), leading to a roundtable discussion in late 2022.^{9,10} See also **Box 2**.

FIGURE 1: Nutrition of women and adolescent girls in humanitarian contexts (2022)



This article summarizes the lessons learned, highlights the challenges to implementing MMS, and provides recommendations to safeguard the nutritional status of adolescent girls and adult women, notably pregnant and lactating women, in humanitarian contexts.

FIGURE 2: Madagascar case study (2022)

“Women not only have increased nutritional needs compared to other populations but are also more vulnerable because of cultural, social and economic inequities”

The state of women’s nutrition in humanitarian contexts

In 2022, an estimated 326 million people needed humanitarian assistance and protection – a significant increase from the estimated 274 million in 2021.^{11,12} The impacts of the converging food, climate and conflict poly-crises are disproportionately felt by women and girls, who account for 60% of the chronically food-insecure globally.¹³ The United Nations Population Fund offered services to a total of 30 million women of reproductive age in humanitarian emergencies in 2022.¹⁴

Yet, the burden of malnutrition in women and girls in humanitarian settings, especially micronutrient malnutrition, remains undefined. Surveys mainly collect data on children under five years, sometimes pregnant and lactating women, but rarely on non-pregnant women and girls.

Policies and guidance on women’s nutrition in humanitarian contexts

Despite the general availability of international guidelines and policies for women’s and girls’ nutrition, operationalizing them in humanitarian contexts appears to be challenging. Existing guidelines are spread out over various documents, not easy to find, and not always aligned. Guidelines include recommendations to provide MMS for pregnant and lactating women, weekly iron and folic acid (IFA) supplementation for non-pregnant women and girls in contexts of high anemia prevalence and the provision of balanced energy protein (BEP) supplementation for pregnant women in undernourished populations.¹⁵

Furthermore, the existence of international guidelines (**Box 1**) does not always equate to the adoption of policies, recommendations, planning and implementation at the national level.⁹

BOX 1: A detailed summary of the below guidelines and more is provided in ENN’s state of play (2022)⁹

WHO, WFP and UNICEF (2006). Micronutrient deficiencies in emergency contexts⁵

WHO (2016, updated 2020). Antenatal care guidelines¹⁵

WHO (2019). Essential Nutrition Actions

WHO (2022). Postnatal care guidelines

MMS in humanitarian contexts: what is happening in practice?

Peer-reviewed evidence regarding the delivery and impact of women’s nutrition interventions in humanitarian contexts is extremely limited. Given the methodological and security challenges of doing research in a crisis context, most information comes from case studies published in grey literature and key-informant interviews.

A recent systematic literature review found that most published studies about nutrition in conflict settings focused on children, whereas only 30% focused on pregnant and lactating women.⁹ General food distribution, micronutrient supplementation and nutrition education were the three most frequently reported interventions targeting women.

Huge gaps exist in the knowledge, research, programmatic guidance and actions to concretely protect women’s and girls’ nutrition in humanitarian settings.

For example, the use of MMS – a proven, safe, affordable, and cost-effective intervention to improve maternal micronutrient status and reduce adverse birth outcomes – largely appears to be limited to demonstration pilots or situations in which MMS is provided through private donor support.

The exact number of women reached with MMS in humanitarian contexts is not known. Though the UNIMMAP formulation was specifically created in 1999 for use in emergency situations, we estimated that in 2022, only 2 organizations provided MMS to at

least 3 million pregnant women: Kirk Humanitarian donated 2.9 million bottles and WFP donated 100,000 bottles.¹⁶ MMS availability and programming remain extremely limited compared to the overall need.

Participants in the previously mentioned roundtable highlighted the following challenges related to the delivery and use of MMS in humanitarian contexts:

1) Funding challenges

Insufficient funding from donors and governments significantly hinders progress in research and programming for women's and girls' nutrition in humanitarian contexts. While the needs of women and adolescent girls are recognized, overall demand for funding is so high that children under two years are prioritized, followed by pregnant women and adolescent girls.

2) Challenges with guidelines and protocols

The global guidelines on nutrition interventions for women and girls, for instance regarding implementation of MMS in an emergency setting, need more specificity on selection, monitoring and follow-up criteria. Moreover, there is an urgent need to translate global guidelines more effectively into national guidance. Where MMS is not included in the national or federal list of essential medicines or national nutrition protocols, it is challenging for national authorities to decide in favor of MMS distribution, despite the joint UN statement⁸ being in place.

3) Coordination and operationalization

The distribution of MMS, as with any other nutrition intervention, is not a stand-alone activity. It requires cross-sectoral collaboration across the health system, specifically with antenatal care (ANC) services, to ensure that the capacity and capability to provide nutrition services to women is available. Greater coordination is needed between health, nutrition and food system/security agencies and sectors on MMS and other interventions. This is particularly important in humanitarian settings where fragile health systems may further deteriorate, and humanitarian clusters take on a coordination role. For instance, in some countries, such as Yemen, micronutrient supplements for pregnant women are distributed through sexual and reproductive health teams yet reporting maternal nutrition outcomes falls to the nutrition cluster; this requires robust coordination.

4) Supply of commodities

Overall, supply chain management in the health system has multiple weaknesses, resulting in late and incomplete deliveries. These issues are exacerbated in emergencies, with the further disrupting of infrastructure, transportation and production systems. For instance, in the recent flooding in Pakistan, MMS was only available in a few districts thanks to a demonstration pilot project which had started before the crisis. A private foundation donated additional MMS supplies to cover flood-affected districts during the rehabilitation period.



Women and girls are disproportionately affected in humanitarian crises

BOX 2: Overcoming MMS supply chain issues during humanitarian crises: A case study from Madagascar¹⁰

Humanitarian responses focus on maintaining or extending national health guidelines and services, and few affected countries currently distribute MMS during humanitarian crises. National micronutrient supplementation guidelines mostly recommend iron and folic acid (IFA). MMS has been included alongside IFA supplementation as part of the ANC service package in Madagascar's National Nutrition Action Plan (2017–2021), with an aim to transition to MMS within routine ANC services at the national level. This would allow for the sustained implementation of MMS during the recurring humanitarian crises experienced in Madagascar. MMS has been piloted in two districts in Madagascar, providing lessons to inform scale-up, including in humanitarian contexts.

Health centers in Madagascar commonly experience difficulties receiving adequate MMS supplies due to inaccessibility and remoteness, which are exacerbated in humanitarian crises. Hence, the pilot project has incorporated community-based distribution and uptake models and mobile services that consider the safety of the health workforce and the women and adolescent girls accessing services. Two distribution levels are being used: the first runs between national and community levels, and the second between national level and health centers. Within the community-based distribution model, community members take turns retrieving supplements from a supply point. This aims to overcome issues of inaccessibility and remoteness, which prevent women from receiving adequate antenatal care, and to ensure the continuity of MMS supply chains at the community level. However, retrieval of supplies may still be restricted by work demands in the field and by the recent passage of cyclones, leading to further breaks in the supply chain.

Overall, the distribution of MMS by community health workers has been prioritized in landlocked and remote regions and works well. However, there is a need to strengthen the delivery of MMS to women who access supplements from community sites near health centers, where very little distribution has been recorded.

“Huge gaps exist in the knowledge, research, programmatic guidance and actions to concretely protect women’s and girls’ nutrition in humanitarian settings”

Supply of relatively new products, such as MMS, faces additional challenges. There has yet to be an established supply chain; there is only a handful of mainly global, certified suppliers, and products are often not included in the national essential medicines list.

“The momentum around women’s and adolescent girls’ nutrition should specifically be taken forward in humanitarian contexts”

Conclusions and recommendations

To protect women and adolescent girls, particularly in times of crises, we recommend the following:

- 1. More and better-quality data are required** to assess women’s and girls’ nutrition status. Including anthropometric and dietary diversity indicators for women and girls in SMART surveys should become standard practice.
- 2. Better documentation and dissemination of actual experiences** of MMS supplementation in humanitarian settings is needed, as well as the contextualization of global guidance into national guidelines, summarizing lessons learnt and challenges, and targeted active engagement with national and international nutrition actors in humanitarian contexts.
- 3. More and sustained advocacy** is needed to address the importance of good nutrition for women and adolescent girls. Their already high nutritional vulnerability is exacerbated in humanitarian settings, increasing the numbers of women suffering from one or multiple micronutrient deficiencies. Furthermore, specific advocacy messages should target building the supply chain capacity, adapting policy changes and scaling up the distribution of MMS to pregnant and lactating women and adolescent girls.
- 4. Clearer guidance is required on implementing MMS** in humanitarian contexts, notably in settings where MMS is not yet an integrated intervention within ANC services through health systems. This should also include guidance on selection criteria to target women who most require MMS and on the better integration of MMS interventions within health systems.
- 5. Better coordination and alignment** between the health, nutrition and food security clusters active in humanitarian contexts is also required, especially where ordering and distributing micronutrient supplements are within the mandate of the health clusters.
- 6. Alternative supply and distribution mechanisms** must be explored to avoid gaps due to broken-down transportation systems and health supply chains. Community supply reserves,

community-based social support networks, and the distribution of larger containers requiring less frequent contact should be considered.

7. Governments and other nutrition partners are called upon to invest in protecting and improving women's and girls' nutrition by ensuring the wide availability of MMS as an integral part of a more robust women's nutrition intervention package in humanitarian settings.

The momentum around women's and adolescent girls' nutrition should specifically be taken forward in humanitarian contexts. International recommendations on evidence-based interventions need to be implemented by national governments and international partners. Results are promising, for instance, acceptance and compliance with MMS are high in countries that have piloted the use of MMS including in areas of high food insecurity. However, providing MMS to countries experiencing shocks due to conflicts, climate change and the after-effects of the COVID-19 pandemic cannot fall upon one entity alone. Ninety-six percent of MMS supply for global humanitarian relief come from Kirk Humanitarian. There is an urgent need for more partners – including foundations, NGOs, and governments agencies – to support pregnant women in countries dealing with emergency and humanitarian crises.

Women's nutrition, and specifically distribution of the highly cost-effective MMS to pregnant women, should be prioritized in

this era of poly-crises, as the gap between funding needs and requirements increases with more people needing humanitarian assistance.

Correspondence: **Marti J van Liere**, Micronutrient Forum, 10th Floor, 1201 Eye St, NW, Washington, DC 20005-3915, USA

Email: Marti.vanLiere@micronutrientforum.org

References and notes

- 1 The term MMS in this article refers to the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP)
- 2 Kalbarczyk A, Aberman N, van Asperen BSM, Morgan R, Bhutta Z, Carducci B, Heidkamp R, Osendarp S, Kumar N, Lartey A, Malapit H, Quisumbing A, Fabrizio C. COVID-19, nutrition, and gender: An evidence-informed approach to gender-responsive policies and programs, *Soc. Sci. Med.* 2022;312(115364). <https://www.sciencedirect.com/science/article/pii/S0277953622006700?via%3Dihub>.
- 3 O'Leary M, Margolis E, Holte-McKenzie M, Kendall E, Israeloff-Smith M, Ben Ameer, A. Gender and nutrition at the United Nations Food Systems Summit and Nutrition for Growth Summit. *UN Nutr. J.* 2022;1:164-167. <https://www.fao.org/documents/card/en/c/cc2805en>.
- 4 Lebanon Nutrition Cluster. Nutrition in Times of Crisis: Lebanon National Nutritional SMART Survey Report (August - September 2021). Reliefweb.int. <https://reliefweb.int/report/lebanon/nutri->



Protecting women's nutrition should be prioritized in humanitarian contexts.

- tion-times-crisis-lebanon-national-nutritional-smart-survey-report-august. Accessed 30 November 2022.
- 5 Action Against Hunger. *Integrated Nutrition and Mortality SMART Survey Final Report, Bamyan Province, Afghanistan April 2021*. Reliefweb.int. <https://reliefweb.int/report/afghanistan/integrated-nutrition-and-mortality-smart-survey-final-report-bamyan-province>. Accessed 30 November 2022.
 - 6 Stevens GA, Beal T, Mbuya MNN, Luo H, Neufeld L, on behalf of Global Micronutrients Deficiencies Research Group. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health* 2022;10:e1590–99. [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(22\)00367-9/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00367-9/fulltext).
 - 7 World Health Organization, United Nations University & United Nations Children's Fund (UNICEF). *Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries: report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO) and United Nations University workshop*. WHO.int. 1999. Accessed 21 November 2022. <https://apps.who.int/iris/handle/10665/75358>.
 - 8 WHO, WFP, UNICEF. *Preventing and controlling micronutrient deficiencies in populations affected by an emergency – Multiple vitamin and mineral supplements for pregnant and lactating women, and for children aged 6 to 59 months*. WHO.int. April, 2006. <https://www.who.int/publications/m/item/WHO-WFP-UNICEF-statement-micronutrients-deficiencies-emergency>. Accessed 21 November 2022.
 - 9 Lelijveld N, Brennan E, Akwanyi B, Wrottesley SV, James PT. Nutrition of women and adolescent girls in humanitarian contexts: current state of play. ENNonline.net. October 2022. <https://www.ennonline.net/humanitariannutritionforwomen>. Accessed 21 November 2022.
 - 10 Wrottesley SV and Akwanyi B. Nutrition for women and adolescent girls in humanitarian contexts. Case study: Madagascar. ENNonline.net. October 2022. https://www.ennonline.net/humanitariannutritionforwomen_madagascar. Accessed 21 November 2022.
 - 11 The Global Humanitarian Overview 2022. Humanitarian InSight. <https://hum-insight.info/>. Accessed 21 November 2022.
 - 12 The Global Humanitarian Overview 2022. UNOCHA.org. <https://gho.unocha.org>. Accessed 21 November 2022.
 - 13 Food Security and Gender Equality: A synergistic understudied symphony. Care.org. <https://www.care.org/wp-content/uploads/2022/08/Final-Version-Food-Security-and-Gender-Equality.pdf>. Accessed 21 November 2022.
 - 14 Humanitarian Emergencies Dashboard. UNFPA.org. <https://www.unfpa.org/data/dashboard/emergencies>. Accessed 21 November 2022.
 - 15 WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: multiple micronutrient supplements during pregnancy (2016, Updated July 2020). WHO.int. <https://www.who.int/publications/i/item/9789240007789>. Accessed November 21, 2022.
 - 16 Information was requested and received from partners between 15 December 2022 and 31 January 2023.

Prenatal Supplements and Maternal Anemia: Is more iron better?

Iron dose analyses comparing multiple micronutrient supplements with iron and folic acid supplements

Filomena Gomes

The Micronutrient Forum, Washington, DC, USA; Universidade NOVA de Lisboa, Lisbon, Portugal

Megan Bourassa

The Micronutrient Forum, Washington, DC, USA

Key messages:

- A comprehensive analysis of the existing evidence was conducted to examine the effect of prenatal multiple micronutrient supplements (MMS) versus iron and folic acid (IFA) supplements on third-trimester maternal anemia and iron status outcomes, based on the different doses of iron provided by each supplement; a similar analysis was also conducted for the neonatal mortality outcome.
- The goal of both studies was to address potential concerns that the lower dose of iron in MMS containing 30 mg of iron may not be as effective as IFA supplements containing higher doses (60 mg) of iron.
- These analyses demonstrated that providing MMS with 30 mg of iron during pregnancy is comparable to IFA with 60 mg of iron in terms of preventing maternal anemia and deaths during the neonatal period.
- The results provide evidence to decision-makers in low- and middle-income countries (LMICs) that they can safely proceed with the transition from IFA supplements to MMS programs without increasing the iron dose.

Iron content of prenatal micronutrient supplements

Prenatal multiple micronutrient supplements (MMS) are a cost-effective intervention to fill the gap between the typical low micronutrient intakes in low-resource settings and higher requirements during pregnancy,¹ resulting in improved pregnancy and birth outcomes.²⁻⁴ In most MMS, including the widely used United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) comprising 15 vitamins and minerals, the amount of elemental iron provided in each tablet is 30 mg.⁵ The Recommended Dietary Allowance for non-pregnant and non-lactating

women between 19 and 50 years of age is 18 mg of iron/day. During pregnancy, this value increases to 27 mg/day⁶ to accommodate the maternal and fetal requirements, and the amount of iron provided daily by UNIMMAP MMS (i.e., 30 mg) was designed to meet these needs.⁵

The World Health Organization (WHO) recommends prenatal iron and folic acid (IFA) supplements providing 30–60 mg of elemental iron to prevent maternal anemia;⁷ in populations where anemia is a severe public health problem (i.e., affecting at least 40% of pregnant women), WHO states that a daily dose of 60 mg of iron is preferred, though it is not fully recommended due to the lack of a strong evidence base.^{7,8}

In 2020, WHO updated the recommendation related to the use of MMS, where this intervention became “recommended in the context of rigorous research.”⁹ This conditional recommendation requested two areas of clinical research. In these additional analyses, we aimed to address one of them, specifically that “...more evidence is needed on the effects of switching to a 30 mg dose of iron from a higher dose of iron (e.g., 60 mg), particularly in settings where higher doses of iron are routinely used due to a high anemia prevalence or other reasons.”⁹ Thus, the MMS in Pregnancy Technical Advisory Group (MMS-TAG) determined that additional analyses of the large body of evidence comparing the effects of MMS versus IFA supplements should be conducted to address the possible concerns related to the switching of IFA supplements with 60 mg of iron to MMS with 30 mg of iron, with regard to maternal anemia outcomes in low- and middle-income countries (LMICs).¹⁰

“The MMS-TAG determined that additional analyses of the large body of evidence comparing the effects of MMS versus IFA supplements should be conducted”

Addressing a clinical research gap identified in the WHO 2020 guidelines: maternal anemia

The 2020 WHO guidelines were informed by a Cochrane review published in 2019,² which included 19 studies comparing the effect of MMS versus IFA supplements on maternal, fetal and infant health outcomes. The levels of iron provided in the IFA arms of these 19 trials varied from 27 mg to 60 mg, and in the MMS arms they varied from 20 mg to 60 mg. In the analyses carried out by the MMS-TAG, the effect of MMS versus IFA supplements on maternal anemia outcomes was stratified by different doses of iron in both formulations, and assessed in relation to maternal baseline anemia levels (using meta-regressions).¹⁰

The 19 trials included in the Cochrane review² were screened to determine if they met the following inclusion criteria for the iron dose analyses by the MMS-TAG: 1) trials conducted in LMICs; 2) with daily supplementation regimens; 3) with MMS arms providing between 30 and 60 mg of iron (as 20 mg is not relevant to the comparison of interest); and 4) assessing outcomes of interest during the third trimester of gestation: prevalence of maternal anemia, prevalence of iron deficiency anemia, and mean hemoglobin concentrations.

From the screened trials, 11 were included, and these contributed to the analyses of the three outcomes of interest. **Table 1** shows

the country where the trial was conducted, iron doses in MMS and IFA arms, and the proportion of anemic women at baseline (varying between 5% and 46.8%) in the 11 included studies.

Data from these 11 trials were extracted from existing publications or obtained directly from the study authors. The 11 trials were divided into three subgroups according to daily total supplemental iron intake: IFA supplements with 60 mg of iron versus MMS with 60 mg of iron; IFA supplements with 30 mg of iron versus MMS with 30 mg of iron; and IFA supplements with 60 mg of iron versus MMS with 30 mg of iron – the main comparison of interest.

These subgroup analyses showed no differences between MMS and IFA supplements in any of the subgroups, for the three outcomes (**Table 2**). In the main comparison of interest, MMS containing 30 mg of iron did not increase the risk of maternal anemia or iron deficiency anemia and did not decrease hemoglobin levels. Of note, the five trials that showed comparable effects between MMS with 30 mg of iron and IFA supplements with 60 mg of iron on anemia-related outcomes had high levels of baseline anemia (from 29% to 47%), suggesting that even in areas with high prevalence of anemia, it is safe to transition to MMS programs with 30 mg of iron. In addition, meta-regressions showed that the baseline anemia prevalence was not associated with the overall effect of MMS versus IFA supplements on any of the outcomes.¹⁰

TABLE 1: Overview of included studies in the iron dose analysis related to maternal anemia outcomes

Study author, year	Country	Iron dose in MMS arm (mg)	Iron dose in IFA arm (mg)	Mean proportion of anemic women at baseline (%)
Christian, 2003 ¹¹	Nepal	60	60	33.3
Liu, 2013 ¹²	China	30	30	5.0
Moore, 2009 ³³	The Gambia	60	60	36.4
Osrin, 2005 ¹⁴	Nepal	30	60	38.0
Ramakrishnan, 2003 ³⁴	Mexico	60	60	14.2
Roberfroid, 2008 ¹⁵	Burkina Faso	30	60	46.5
SUMMIT, 2008 ¹⁶	Indonesia	30	30	46.8
Sunawang, 2009 ¹⁷	Indonesia	30	60	37.5
Tofail, 2008 ¹⁸	Bangladesh	30	30 and 60 (two arms)	28.5
West, 2014 ¹⁹	Bangladesh	27*	27*	21.7
Zeng, 2008 ²⁰	China	30	60	Not reported

MMS = multiple micronutrient supplements; IFA = iron and folic acid supplements
 *Both arms of the West 2014 trial received a supplement that was intended to contain 27 mg of iron. However, the analysis of chemical composition of MMS and IFA tablets showed that the amount of iron in MMS varied from 28.4 mg to 30.2 mg of iron, and between 26.2 mg and 29.8 mg in IFA. Thus, for the purpose of our subgroup analyses by iron dose, we considered this study as providing 30 mg of iron in each study arm.

TABLE 2: Summary of results: effect of MMS versus IFA on maternal anemia, iron deficiency anemia and hemoglobin levels, according to supplemental iron dose in each arm

Outcome: Maternal anemia (third trimester)			
<i>Hemoglobin < 110 g/L for most studies</i>			
Subgroup analysis by iron dose	n comparisons	Risk Ratio (95% CI)	p value (subgroup differences)
MMS 60 mg iron vs IFA 60 mg iron	3	1.06 (0.82, 1.37)	
MMS 30 mg iron vs IFA 30 mg iron	4	0.99 (0.88, 1.12)	0.89
MMS 30 mg iron vs IFA 60 mg iron	5	0.99 (0.92, 1.07)	
Outcome: Maternal iron deficiency anemia (third trimester)			
<i>Hemoglobin < 110 g/L and serum ferritin < 12 µg/dL for most studies</i>			
Subgroup analysis by iron dose	n comparisons	Risk Ratio (95% CI)	p value (subgroup differences)
MMS 60 mg iron vs IFA 60 mg iron	3	1.18 (0.94, 1.48)	
MMS 30 mg iron vs IFA 30 mg iron	2	0.91 (0.43, 1.93)	0.76
MMS 30 mg iron vs IFA 60 mg iron	2	1.31 (0.66, 2.60)	
Outcome: Hemoglobin (third trimester), g/L			
Subgroup analysis by iron dose	n comparisons	Risk Ratio (95% CI)	p value (subgroup differences)
MMS 60 mg iron vs IFA 60 mg iron	3	-0.68 (-3.56, 2.20)	
MMS 30 mg iron vs IFA 30 mg iron	4	0.14 (-0.71, 0.99)	0.78
MMS 30 mg iron vs IFA 60 mg iron	4	-0.26 (-1.41, 0.89)	

*MMS = prenatal multiple micronutrient supplements; IFA = iron and folic acid supplements

Rationale for the comparable effect of 30 mg of iron in MMS vs 60 mg of iron in IFA supplements in preventing maternal anemia

These findings are consistent with the results of trials designed to determine the lowest dose of iron to prevent iron deficiency.^{21,22} There are also physiological mechanisms that may explain why 30 mg of iron involved in a matrix of other micronutrients is enough to prevent anemia:

1. the presence of other micronutrients (especially vitamins A, B₂ and C) can improve the absorption and/or utilization of iron compared with the iron alone;
2. MMS can help prevent other nutritional causes of anemia e.g., anemia caused by deficiency of vitamins A, B₉ and B₁₂,^{23,24} and
3. iron doses ≥ 60 mg have been shown to trigger a transient increase in circulating hepcidin that can inhibit iron absorption, a phenomenon not seen with iron doses ≤ 40 mg.²⁵

It is noteworthy that MMS and IFA supplements are designed for the prevention of maternal anemia and not for the treatment of anemia. If a pregnant woman is diagnosed with anemia, it is important to conduct additional clinical assessments to determine the cause of anemia and establish if there is a need for additional iron supplements, which would not justify the discontinuation of MMS. It is estimated that approximately half of anemia cases are caused by iron deficiency, while the remaining cases have other causes that would not benefit from additional iron, such as other micronutrient deficiencies, genetic hemoglobin disorders, inflammation and infectious diseases (e.g., tuberculosis, HIV, and parasitic infections).^{26,27} In these cases, additional iron has the potential to be harmful.²⁸⁻³¹

“The transition is encouraged because of the well-documented benefits of MMS on the reduction of poor birth outcomes”

Addressing another concern identified in the WHO 2020 guidelines: neonatal mortality

Although not identified as an area for further research, the 2020 WHO guidelines noted that “when compared with IFA supplements containing a higher dose of iron (60 mg), MMS may be less effective in reducing neonatal mortality”. This statement was not based on the overall analyses, rather it was based on a sensitivity analysis limited to the trials that provided 400 µg folic acid in the IFA group. This resulted in the removal of the Sunawang 200917 trial in which the control group received 250 µg of folic acid, and removal of the largest trial (West 2014 trial¹⁹) with 44,567 pregnant women in which MMS and control group received 600 µg of folic acid.

The MMS-TAG determined that a reanalysis of the neonatal deaths data stratified by iron dose in each supplement would be useful.³² In this reanalysis, the effect estimates of MMS versus IFA supplements on neonatal mortality were calculated in four subgroups according to supplemental iron dose, and it included studies that had been excluded in the analyses of 2020 WHO guidelines. In particular, the MMS-TAG determined that the two trials from Sunawang¹⁷ and West¹⁹ should be included in the analyses because the variations in folic acid dose are likely to have little clinical significance. Importantly, most of these trials initiated supplementation in the second trimester of pregnancy – not at the beginning of the pregnancy, when folic acid supplementation is recommended and has a critical role in the neural tube development.

The reanalysis showed that neonatal mortality did not differ between MMS and IFA supplements, regardless of iron dose in either supplement.³² In comparison with IFA supplements containing 60 mg of iron, MMS with 30 mg of iron was associated with a non-significant risk ratio of 1.12 (95%CI 0.83 to 1.50), suggesting no difference between both supplements on deaths during the neonatal period.³²

Iron dose analyses on other outcomes beyond hematological outcomes and neonatal mortality

The iron dose analyses performed by the MMS-TAG were focused on hematologic outcomes and neonatal mortality. Keats et al. performed similar iron dose analyses for other birth outcomes, preterm births, small for gestational age and perinatal mortality (stillbirths and early neonatal deaths).² The analyses did not find significant differences among subgroups of iron dose in MMS and IFA. In the analyses from Keats et al. from the 2020 WHO guidelines,^{2,9} UNIMMAP MMS (with 30 mg of iron) significantly reduced the risk for small-for-gestational-age infants by 11% (RR 0.89, 95% CI 0.81 to 0.97) and low birthweight by 16% (RR 0.84, 95% CI 0.75 to 0.94), in comparison to IFA with 60 mg of iron.

Conclusion

These analyses demonstrate that the transition from programs of IFA providing 60 mg of iron to programs providing MMS with 30 mg of iron would not have a negative impact on anemia or neonatal/perinatal mortality. Instead, the transition is encouraged because of the well-documented benefits of MMS on the reduction of poor birth outcomes, such as low birthweight and small-for-gestational-age births. Moreover, anemic pregnant women have even greater benefits of MMS (i.e., greater reductions of low birthweight, small-for-gestational-age births and 6-month mortality) in comparison with non-anemic pregnant women,³ justifying the continued use of MMS in anemic women while the cause of anemia is investigated and the appropriate treatment is administered.

Correspondence: Dr Filomena Gomes, The Micronutrient Forum, Washington, DC, USA

Email: filomena.gomes@micronutrientforum.org

References

- 1 Gernand AD, Schulze KJ, Stewart CP, West KP, Christian P. Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. *Nat Rev Endocrinol.* 2016;12(5):274-289. doi:10.1038/nrendo.2016.37
- 2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2019;2019(3):CD004905. doi:10.1002/14651858.CD004905.pub6
- 3 Smith ER, Shankar AH, Wu LSF, 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. *Lancet Glob Heal.* 2017;5(11):e1090-e1100. doi:10.1016/S2214-109X(17)30371-6
- 4 Engle-Stone R, Kumordzie SM, Meinen-Dick L, Vosti SA. Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness. *Ann N Y Acad Sci.* 2019;1444(1):35-51. doi:10.1111/nyas.14132
- 5 World Health Organization, UNICEF, United Nations University. *Composition of a Multi-Micronutrient Supplement to Be Used in Pilot Programmes among Pregnant Women in Developing Countries.*; 1999. <https://apps.who.int/iris/bitstream/handle/10665/75358/UNICEF-WHO-multi-micronutrients.pdf?sequence=1&isAllowed=y> Accessed 22 December 2022.
- 6 Institute of Medicine. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements.* (Otten J, Hellwig J, Meyers L, eds.). National Academies Press; 2006.
- 7 World Health Organization. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience.*; 2016. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/ Accessed 22 December 2022.

- 8 Organization WH. *Nutritional Anaemias: Tools for Effective Prevention.*; 2017. <https://apps.who.int/iris/bitstream/handle/10665/259425/9789241513067-eng.pdf> Accessed 22 December 2022.
- 9 World Health Organization. *WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy.*; 2020. <https://www.who.int/publications/i/item/9789240007789>
- 10 Gomes F, Agustina R, Black RE, et al. Multiple micronutrient supplements versus iron-folic acid supplements and maternal anemia outcomes: an iron dose analysis. *Ann NY Acad Sci.* 2022;n/a(n/a). doi:<https://doi.org/10.1111/nyas.14756>
- 11 Christian P, Khatry SK, Katz J, et al. Effects of alternative maternal micronutrient supplements. *Br Med J.* 2003;326:571-577. doi:10.1136/bmj.326.7389.571
- 12 Liu J meng, Mei Z, Ye R, Serdula MK, Ren A, Cogswell ME. Micronutrient supplementation and pregnancy outcomes: double-blind randomized controlled trial in China. *JAMA Intern Med.* 2013;173(4):276-282. doi:10.1001/jamainternmed.2013.1632
- 13 Johnson W, Darboe MK, Prentice AM, Moore SE, Nshe P. Association of prenatal lipid - based nutritional supplementation with fetal growth in rural Gambia. 2017;(March 2016):1-13. doi:10.1111/mcn.12367
- 14 Osrin D, Vaidya A, Shrestha Y, et al. Effects of antenatal multiple micronutrient supplementation on birthweight and gestational duration in Nepal: double-blind, randomised controlled trial. *Lancet.* 2005;365(9463):955-962. doi:10.1016/S0140-6736(05)71084-9
- 15 Roberfroid D, Huybregts L, Lanou H, et al. Effects of maternal multiple micronutrient supplementation on fetal growth: a double-blind randomized controlled trial in rural Burkina Faso. *Am J Clin Nutr.* 2008;88(5):1330-1340. doi:10.3945/ajcn.2008.26296.1
- 16 SUMMIT, Shankar AH V, Jahari AB, et al. Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet.* 2008;371(9608):215-227. doi:10.1016/S0140-6736(08)60133-6
- 17 Sunawang, Utomo B, Hidayat A, Kusharisupeni, Subarkah. Preventing low birthweight through maternal multiple micronutrient supplementation: a cluster-randomized, controlled trial in Indramayu, West Java. *Food Nutr Bull.* 2009;30(4):S488-95. <http://www.ncbi.nlm.nih.gov/pubmed/20120790>
- 18 Tofail F, Persson LÅ, Arifeen SE, et al. Effects of prenatal food and micronutrient supplementation on infant development: A randomized trial from the Maternal and Infant Nutrition Interventions, Matlab (MINIMat) study. *Am J Clin Nutr.* 2008;87(3):704-711. doi:87/3/704 [pii]
- 19 West KP, Shamim AA, Mehra S, et al. Effect of Maternal multiple micronutrient vs iron-folic acid supplementation on infant mortality and adverse birth outcomes in rural Bangladesh: The JiVitA-3 randomized trial. *JAMA - J Am Med Assoc.* 2014;312(24):2649-2658. doi:10.1001/jama.2014.16819
- 20 Zeng L, Dibley MJ, Cheng Y, et al. Impact of micronutrient supplementation during pregnancy on birth weight, duration of gestation, and perinatal mortality in rural western China: Double blind cluster randomised controlled trial. *Bmj.* 2008;337(7680):1211-1215. doi:10.1136/bmj.a2001
- 21 Milman N, Bergholt T, Eriksen L, et al. Iron prophylaxis during pregnancy -- how much iron is needed? A randomized dose-response study of 20-80 mg ferrous iron daily in pregnant women. *Acta Obstet Gynecol Scand.* 2005;84(3):238-247. doi:10.1111/j.0001-6349.2005.00610.x
- 22 Zhou SJ, Gibson RA, Crowther CA, Makrides M. Should we lower the dose of iron when treating anaemia in pregnancy? A randomized dose-response trial. *Eur J Clin Nutr.* 2009;63(2):183-190. doi:10.1038/sj.ejcn.1602926
- 23 Behere R V, Deshmukh AS, Otiv S, Gupte MD, Yajnik CS. Maternal Vitamin B12 Status During Pregnancy and Its Association With Outcomes of Pregnancy and Health of the Offspring: A Systematic Review and Implications for Policy in India . *Front Endocrinol .* 2021;12:288. <https://www.frontiersin.org/article/10.3389/fendo.2021.619176>
- 24 Oregon State University. Micronutrient Needs During Pregnancy and Lactation. Pregnancy and Lactation. Published 2016. Accessed April 8, 2021. <https://lpi.oregonstate.edu/mic/life-stages/pregnancy-lactation#reference63>
- 25 Stoffel NU, von Siebenthal HK, Moretti D, Zimmermann MB. Oral iron supplementation in iron-deficient women: How much and how often? *Mol Aspects Med.* 2020;75:100865. doi:10.1016/j.mam.2020.100865
- 26 Karakochuk CD, Whitfield KC, Barr SI, et al. Genetic hemoglobin disorders rather than iron deficiency are a major predictor of hemoglobin concentration in women of reproductive age in rural prey Veng, Cambodia. *J Nutr.* 2015;145(1):134-142. doi:10.3945/jn.114.198945
- 27 Safri S, Kolahi AA, Noori M, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. *J Hematol Oncol.* 2021;14(1):185. doi:10.1186/s13045-021-01202-2
- 28 Fischer JAJ, Pei LX, Goldfarb DM, et al. Is untargeted iron supplementation harmful when iron deficiency is not the major cause of anaemia? Study protocol for a double-blind, randomised controlled trial among non-pregnant Cambodian women. *BMJ Open.* 2020;10(8):e037232. doi:10.1136/bmjopen-2020-037232
- 29 Brannon PM, Stover PJ, Taylor CL. Integrating themes, evidence gaps, and research needs identified by workshop on iron screening and supplementation in iron-replete pregnant women and young children. *Am J Clin Nutr.* 2017;106(Suppl 6):1703S-1712S. doi:10.3945/ajcn.117.156083
- 30 Dewey KG, Oaks BM. U-shaped curve for risk associated with maternal hemoglobin, iron status, or iron supplementation. *Am J Clin Nutr.* 2017;106(Suppl 6):1694S-1702S. doi:10.3945/ajcn.117.156075
- 31 Zhang X, Wu M, Zhong C, et al. Association between maternal

- plasma ferritin concentration, iron supplement use, and the risk of gestational diabetes: a prospective cohort study. *Am J Clin Nutr.* 2021;114(3):1100-1106. doi:10.1093/ajcn/nqab162
- 32 Gomes F, Agustina R, Black RE, et al. Effect of multiple micronutrient supplements vs iron and folic acid supplements on neonatal mortality: a reanalysis by iron dose. *Public Health Nutr.* Published online April 2022:1-13. doi:10.1017/S1368980022001008
- 33 Moore, S.E., A.J.C. Fulford, F. Sosseh, et al. 2019. Thymic size is increased by infancy, but not pregnancy, nutritional supplementation in rural Gambian children: a randomized clinical trial. *BMC Med.* 17: 38
- 34 Ramakrishnan U, Gonzalez-Cossio T, Neufeld LM, Rivera J, Martorell R. Multiple micronutrient supplementation during pregnancy does not lead to greater infant birth size than does iron-only supplementation: a randomized controlled trial in a semirural community in Mexico. *American Journal of Clinical Nutrition.* 2003;77:720-5

The Potential Impact of Scaling Up Prenatal MMS on Human Capital Outcomes

Christopher Sudfeld, Nandita Perumal

Department of Global Health and Population,
Harvard T.H. Chan School of Public Health, Boston, MA, USA

Key messages:

- There is a growing interest in the potential impact of maternal and child nutrition on human capital across the life course.
- Scaling up maternal multiple micronutrient supplementation (MMS) to 90% coverage globally may result in substantial gains in schooling (5.0 million additional school years) and lifetime income (US\$ 18.1 billion) per 5-year birth cohort.
- Decision-makers considering expanding MMS coverage should bear these large potential human capital returns in mind in addition to direct maternal and child health benefits.

Introduction

Globally, there has been remarkable progress in improving child survival. The total number of deaths among children under 5 years of age has declined from 12.6 million in 1990 to 5.0 million in 2020, which represents a 60% decline in the mortality rate.¹ As a result, there has been a shift in commitment, including from the global nutrition community, to ensure that all children not only survive but that all children also have the opportunity to thrive. Accompanying this wider view, a rapidly growing area of contemporary research investigates how nutrition interventions may impact children's development, schooling, adult income, and other long-term outcomes across the life course – all of which are components of broader “human capital”.^{2,3} The World Bank defines human capital as “knowledge, skills, and health that people accumulate over their lives” and notes that greater human capital is associated with higher wage earnings for adults, increased income for countries, and better cohesion within societies.⁴

To measure global human capital, the World Bank developed the Human Capital Index (HCI). The HCI is a country-level metric that estimates the human capital that the average child in a country can expect to attain by 18 years of age, considering the variable health, nutrition, and education risks that may exist in each coun-

try.⁵ The HCI is based on multiple indicators including health/nutrition (under-5 child mortality and under-5 child stunting, as well as adult survival) and the quantity and quality of schooling (attainment and international test scores).⁵ The HCI ranges from a score of 0 to 1 and is estimated for a country in a given year. In terms of interpretation, if a country has an HCI of 0.5 in 2020, this means that on average a child born in 2020 in the country is estimated to be half as productive as compared to if the child had the opportunity to be in an environment with optimal health, nutrition, and education and to reach their full potential. In 2020, the regions with the highest average HCI were North America (HCI = 0.75; three-quarters as productive as compared to optimal) and Europe and Central Asia (HCI = 0.69), while the lowest average HCIs were for South Asia (HCI = 0.48) and sub-Saharan Africa (HCI = 0.40) regions.⁵ As a result, on average, a child in South Asia and sub-Saharan Africa born in 2020 may be reaching close to or less than half of their human capital potential as compared to if they had the opportunity to be in an environment with optimal health, nutrition and education. Notably, the average HCI estimates are below 1.0 in all world regions, indicating significant opportunities to promote equitable change and ensure that *all* individuals and economies can reach their full human capital potential globally.

“Studies have found that fetal undernutrition in utero is associated with suboptimal neuronal growth and synaptic connections in the brain”

The importance of nutrition on human capital outcomes

There is emerging and growing evidence on the relationship between maternal nutrition and birth outcomes, with a particular focus on how these contribute to human capital, including child development, schooling and lifetime earnings. The period between conception and the first two years of life – known as the ‘first 1,000 days’ – is well recognized as a sensitive period of rapid brain development.⁶ Studies have indicated that nutrients such as iodine, zinc, vitamin B₆ and docosahexaenoic acid (DHA) during pregnancy play an important role in fetal brain development.⁷

Substantial evidence has also shown that preterm birth and low birth weight (LBW), which are known to be affected by maternal nutrition, are associated with suboptimal child development outcomes.^{8,9}

Studies in animals and humans have found that fetal undernutrition in utero is associated with suboptimal neuronal growth and synaptic connections in the brain as well as decreased brain volume.⁷ In addition, epidemiologic studies from different contexts have consistently found preterm birth and LBW to be associated with suboptimal developmental outcomes during childhood and adolescence.^{8,9} For example, in a birth cohort study in Tanzania, we found that adolescents 11–15 years of age who were born with LBW had lower intelligence and executive function test scores and greater behavioral problems as compared to their adolescent peers who were not born with LBW.¹⁰ Taking it a step further to schooling, the COHORTS collaboration, which collectively analyzes the long-term outcomes of birth cohorts in Brazil, Guatemala, India, South Africa and Brazil, found that each standard deviation increase in birth weight was associated with 0.2 years more of schooling attainment.¹¹ In a meta-analysis including the COHORTS data and additional studies in high-income country settings, LBW infants are estimated to attain 0.29 fewer school years (95% CI: -0.48, -0.10 years) as compared to non-LBW infants.¹² Further, in terms of lifetimes earnings, a recent systematic review and meta-analysis found that each standard deviation increase in birth weight was associated with a 2.8% increase in adult annual earnings and that adults born LBW had on average 3.4% lower annual earnings as compared to non-LBW individuals after adjusting for potential confounding factors.¹³ While these annual percentages may seem small, it is important to note that they are compounded over an individual's total work years, with the potential to lead to substantial cumulative sums. For example, in a high-income setting like the United States, one standard deviation increase in birth weight would be associated with additional total lifetime earnings of US\$ ~30,000 over 40 years of work. Overall, there is relatively robust evidence to suggest that improvements in maternal nutrition and birth outcomes contribute to improvements in development, schooling, and ultimately human capital.

“Decision-makers do not have decades to wait for direct evidence on human capital outcomes”

The effect of MMS on child development

It is well recognized that multiple micronutrient supplementation (MMS) in pregnancy can reduce the risk of adverse birth outcomes as compared to iron-folic acid supplementation (IFA) from randomized trials, but there is limited direct evidence from trials on

the effect of MMS on child development (an intermediary for adult human capital outcomes) and no data on the direct effect of MMS on schooling attainment and adult income. In the most recent Cochrane Review (2019), MMS was found to reduce the risk of LBW by 12% (95% CI: 9–15%) and reduce the risk of small-for-gestational-age births by 8% (95% CI: 3–12%) as compared to IFA.¹⁴ A few MMS trials have followed up individuals into childhood and adolescence and assessed child development outcomes. A large follow-up study of the SUMMIT randomized trial in Indonesia found that among children 9 to 12 years of age, children who had mothers that were randomized to MMS had higher procedural memory as compared to children whose mothers received IFA, and there was a beneficial effect of MMS on general intelligence scores among children whose mothers were anemic.¹⁵ A study in rural China also found MMS had beneficial effects on intelligence quotient (IQ) and verbal comprehension at 14 years of age.¹⁶ However, it is also important to note there are trials such as those conducted in Nepal, Ghana, Malawi, and Tanzania that have found no effect of MMS on developmental outcomes among children.¹⁷⁻¹⁹ There is also no data on the direct effect of MMS on adult human capital outcomes due in part to the substantial resources and a time-frame of decades required to follow up individuals born in pregnancy trials. Individuals born in MMS trials conducted in the early 2000s are just now approaching or are in their early twenties. Therefore, the strongest evidence we have is for the effect of MMS on birth outcomes, which are known to be associated with human capital outcomes, namely schooling, but the direct evidence on child development and economic benefits is limited and developing. Nevertheless, it is important to continue the ongoing policy and programmatic determinations on MMS, and therefore decision-makers do not have decades to wait for direct evidence on human capital outcomes to accumulate to inform their decision-making.

The Thrive Model

To meet the need and to inform the potential of MMS and other maternal nutrition interventions on human capital outcomes, we developed the ‘Thrive Model’. The goal of the Thrive Model was to estimate the potential human capital gains of scaling up MMS, IFA, calcium and other nutritional interventions in 132 low- and middle-income countries (LMICs).¹² Figure 1 presents a diagram of how the Thrive Model works. The model first estimates the impact of scaling up MMS, IFA, and calcium supplementation on the prevalence of low birth weight or preterm births in a country. It then translates this into years of schooling gained and, ultimately, increases in lifetime earnings at the country level.

The results of the Thrive Model have recently been published in the *American Journal of Clinical Nutrition*.¹² Figure 2 presents a country-level example of how the Thrive Models estimates scaling up MMS to 90% in Bangladesh, where an estimated 14.7 million births occur every 5 years and the prevalence of LBW is 27.8%. The

Thrive Model scales up MMS to 90% coverage and estimates that the low birth weight prevalence will decrease by ~5.9% or avert ~869,000 LBW births in the country. On average, each averted LBW child will attain 0.29 additional years of schooling, which translates into a total of 224,930 school years gained at the population level. In the context of Bangladesh, each additional year of school is associated with 7.1% higher returns in annual income and the estimated average annual wage is US\$ 668 (2010 constant). Therefore, scaling up MMS to 90% for 5 years is estimated to increase lifetime earnings by US\$ 290.8 million.

In terms of the global estimates for schooling years gained, we estimated that scaling up MMS to 90% coverage for 5 years in all 132 countries would lead to 5.0 million additional school years (95% uncertainty intervals [UI]: 1.1, 11.0 million), with the largest absolute gains in schooling attainment estimated to be for countries in South Asia and sub-Saharan Africa, in part due to the large population sizes and high burden of LBW in these countries. India (1,700,000 school years), Pakistan (420,000 school years) and Bangladesh (230,000 school years) were the three countries with the largest number of school years gained. In sub-Saharan Africa, Nigeria (208,000 school years) and Ethiopia (192,000

FIGURE 1: Thrive Model pathways to estimate the impact of maternal prenatal nutrition supplements on education attainment and lifetime income

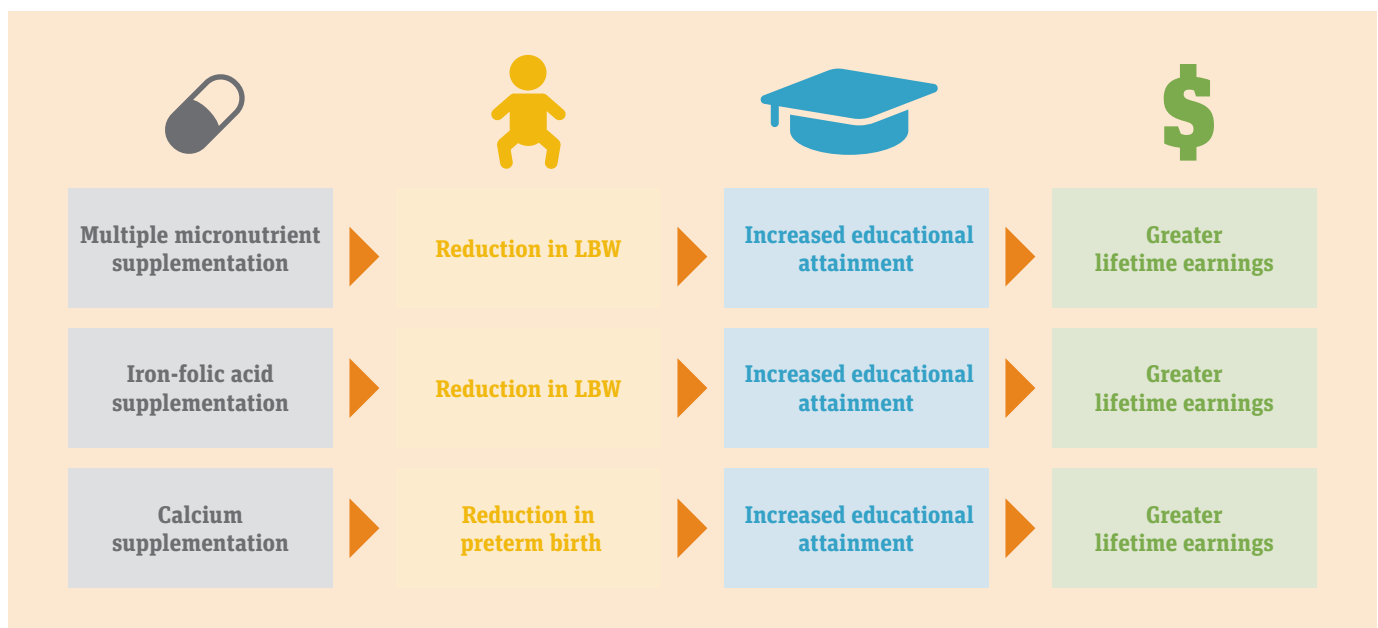
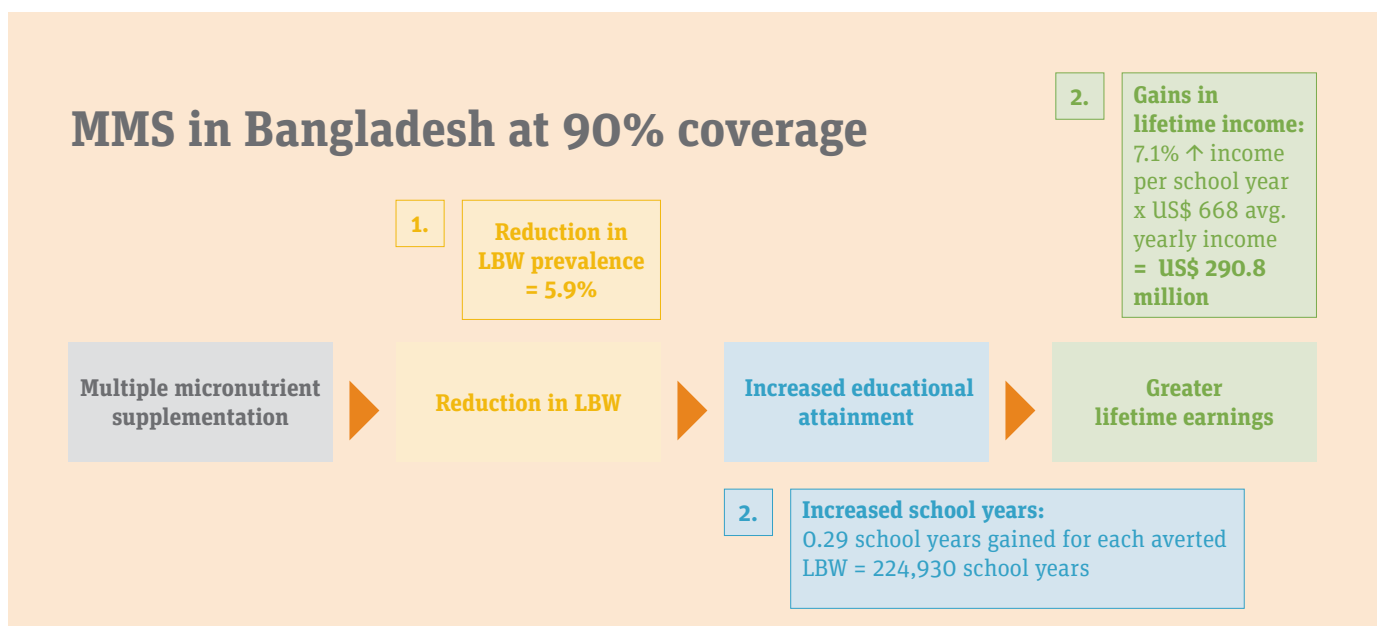


FIGURE 2: An example of the Thrive Model pathways to estimate the impact of scaling up MMS to 90% coverage in Bangladesh



school years) had the largest estimated number of school years gained from scaling up MMS to 90% coverage.

The Thrive Model then translates the additional years of schooling into increases in annual wages. We estimated that scaling up MMS to 90% coverage in all 132 countries would result in US\$ 18.1 billion in lifetime wages gained every 5 years (95% UI: 3.9 to US\$ 39.1 billion). The three countries with the largest absolute expected economic returns to lifetime income for scaling up MMS to 90% were India (US\$ 4.3 billion), Brazil (US\$ 1.72 billion) and Mexico (US\$ 1.10 billion). Notably, countries in Latin America rose on the list for gains in lifetime income, since on average these countries have higher returns to education for each additional year of schooling as well as higher average annual income as compared to countries in South Asia and sub-Saharan Africa. Nonetheless, estimated gains remain large for countries in South Asia and sub-Saharan Africa; for example, Pakistan had an estimated gain of US\$ 694 million, Ethiopia US\$ 203 million and South Africa US\$ 883 million.

Millions of additional school years and billions of US dollars in wage gains are difficult to conceptualize in terms of magnitude. As such, we compared the MMS estimates to those for scaling up IFA and calcium supplementation to 90% coverage in the same 132 LMICs (Figure 3). Compared to scaling up MMS, scaling up IFA to 90% coverage was estimated to result in roughly half of the estimated school years and lifetime earnings: 2.3 million additional school years and US\$ 8.3 billion. Scaling up calcium supplementation in pregnancy to 90% coverage was estimated to result in similar gains to MMS at 4.1 million years of schooling and US\$ 18.9 billion. Therefore, scaling up MMS and calcium supplementation may produce equally large gains in human capital and the magnitude of these gains are estimated to be greater than scaling up IFA.

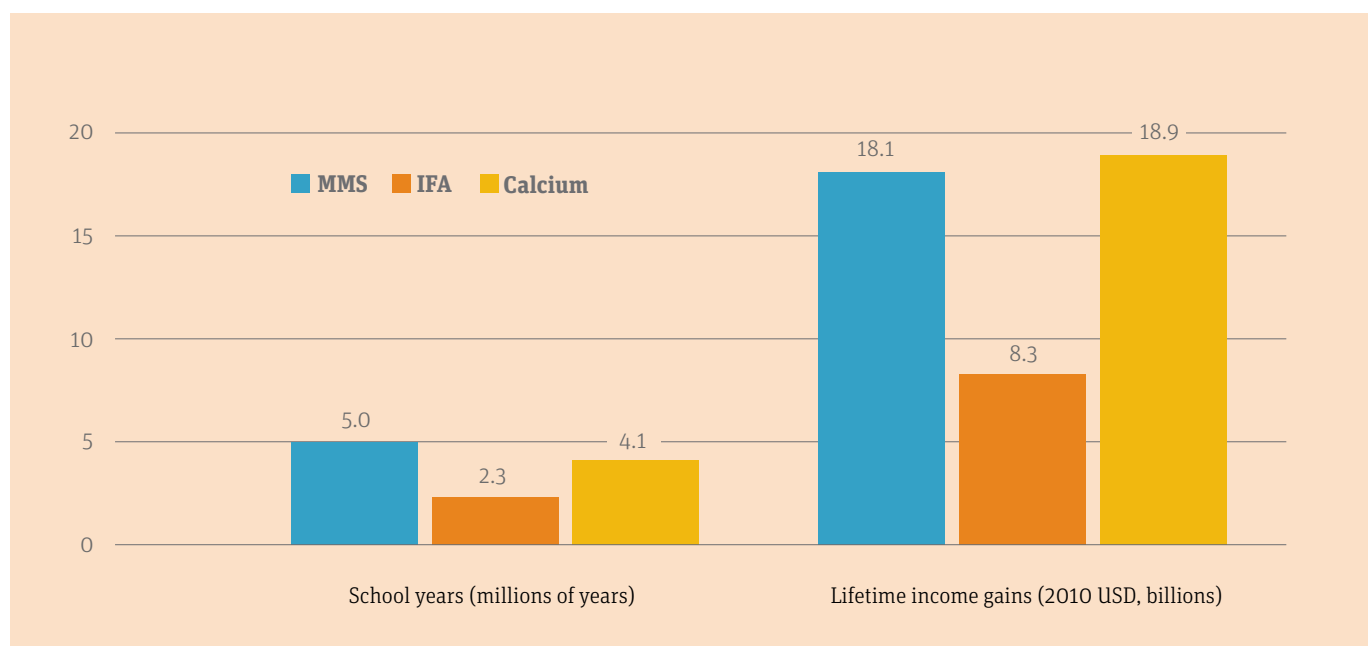
“MMS is in no way a ‘magic bullet’; rather, it should be considered as just one important intervention in a much larger effort”

The Thrive Model is the first to quantify the potential human capital benefits of scaling up MMS, but the model does come with important limitations. First, due to the lack of evidence from randomized controlled trial of MMS on schooling and adult earnings outcomes directly, the model used LBW as a mediator. The links connecting LBW to schooling and adult earnings were therefore all based on observational evidence, which is not immune from the risk of confounding and selection bias. In the future, as MMS trial cohorts age, we may be able to model the direct effect of MMS on schooling and adult income. Further, there were large variances (95% confidence intervals) in the effect sizes from observational data and therefore all our estimates had wide uncertainty intervals. Last, we estimated the potential benefits of MMS on human capital by one specific pathway – reductions in adverse birth outcomes – and gains in educational attainment, and therefore may have still underestimated the overall benefits that may occur by other pathways.

Conclusions

Overall, the potential human capital gains to scaling up MMS globally are likely to be substantial. The Thrive Model estimated that US\$ 18.1 billion in lifetime income gains equates to a return of US\$

FIGURE 3: Estimated gains in scaling up MMS to 90% coverage as compared to IFA and calcium supplementation to 90% coverage



~32 for each pregnant person who receives MMS. This is roughly a 2x return on investment based on an estimated MMS cost of US\$ 16.86 per pregnancy considering the supplement, program and patient costs.²⁰ Therefore, greater investment in MMS today is likely to result in large returns in the future. Policy and program decision-makers should consider these large potential human capital returns in addition to the maternal and child health benefits when considering the benefits of scaling up MMS. Nevertheless, it is important to note that MMS is in no way a ‘magic bullet’; rather, it should be considered as just one important intervention in a much larger effort across the life course to increase human capital globally and support the opportunity for all people to *thrive*.

Correspondence: Dr Christopher Sudfeld, Harvard T.H. Chan School of Public Health, 665 Huntington Ave, Boston, MA 02116, USA
Email: csudfeld@hsph.harvard.edu

References

- UNICEF. United Nations Inter-Agency Group for child mortality estimation (UN IGME). 2021. <https://data.unicef.org/resources/levels-and-trends-in-child-mortality/> Accessed 28 November 2022.
- Martorell R. Improved nutrition in the first 1000 days and adult human capital and health. *Am J Hum Biol.* Mar 2017;29(2)doi:10.1002/ajhb.22952
- Black MM, Walker SP, Fernald LCH, et al. Early childhood development coming of age: science through the life course. *Lancet.* Jan 7 2017;389(10064):77-90. doi:10.1016/s0140-6736(16)31389-7
- World Bank. *The Human Capital Project*. World Bank; 2018. <https://openknowledge.worldbank.org/handle/10986/30498> Accessed 28 November 2022.
- World Bank. *The Human Capital Index 2020 Update : Human Capital in the Time of COVID-19*. World Bank; 2020. <https://openknowledge.worldbank.org/handle/10986/34432> Accessed 28 November 2022.
- Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. *Lancet.* Jan 6 2007;369(9555):60-70. doi:10.1016/s0140-6736(07)60032-4
- Prado EL, Dewey KG. Nutrition and brain development in early life. *Nutr Rev.* Apr 2014;72(4):267-84. doi:10.1111/nure.12102
- Gladstone M, Oliver C, Van den Broek N. Survival, morbidity, growth and developmental delay for babies born preterm in low and middle income countries - a systematic review of outcomes measured. *PLoS One.* 2015;10(3):e0120566. doi:10.1371/journal.pone.0120566
- Sania A, Sudfeld CR, Danaei G, et al. Early life risk factors of motor, cognitive and language development: a pooled analysis of studies from low/middle-income countries. *BMJ Open.* Oct 3 2019;9(10):e026449. doi:10.1136/bmjopen-2018-026449
- Perumal N, Manji KP, Darling AM, et al. Gestational Age, Birth Weight, and Neurocognitive Development in Adolescents in Tanzania. *J Pediatr.* Sep 2021;236:194-203.e6. doi:10.1016/j.jpeds.2021.04.036
- Adair LS, Fall CH, Osmond C, et al. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet.* Aug 10 2013;382(9891):525-34. doi:10.1016/s0140-6736(13)60103-8
- Perumal N, Blakstad MM, Fink G, et al. Impact of scaling up prenatal nutrition interventions on human capital outcomes in low- and middle-income countries: a modeling analysis. *Am J Clin Nutr.* Nov 8 2021;114(5):1708-1718. doi:10.1093/ajcn/nqab234
- Lambiris MJ, Blakstad MM, Perumal N, et al. Birth weight and adult earnings: a systematic review and meta-analysis. *J Dev Orig Health Dis.* Jun 2022;13(3):284-291. doi:10.1017/s2040174421000404
- Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* Mar 14 2019;3(3):Cd004905. doi:10.1002/14651858.CD004905.pub6
- Prado EL, Sebayang SK, Apriatni M, et al. Maternal multiple micronutrient supplementation and other biomedical and socioenvironmental influences on children's cognition at age 9-12 years in Indonesia: follow-up of the SUMMIT randomised trial. *Lancet Glob Health.* Feb 2017;5(2):e217-e228. doi:10.1016/s2214-109x(16)30354-0
- Zhu Z, Cheng Y, Zeng L, et al. Association of Antenatal Micronutrient Supplementation With Adolescent Intellectual Development in Rural Western China: 14-Year Follow-up From a Randomized Clinical Trial. *JAMA Pediatr.* Sep 1 2018;172(9):832-841. doi:10.1001/jamapediatrics.2018.1401
- Dulal S, Liégeois F, Osrin D, et al. Does antenatal micronutrient supplementation improve children's cognitive function? Evidence from the follow-up of a double-blind randomised controlled trial in Nepal. *BMJ Glob Health.* 2018;3(1):e000527. doi:10.1136/bmjgh-2017-000527
- Prado EL, Adu-Afarwuah S, Lartey A, et al. Effects of pre- and post-natal lipid-based nutrient supplements on infant development in a randomized trial in Ghana. *Early Hum Dev.* Aug 2016;99:43-51. doi:10.1016/j.earlhumdev.2016.05.011
- Sudfeld CR, Manji KP, Darling AM, et al. Effect of antenatal and infant micronutrient supplementation on middle childhood and early adolescent development outcomes in Tanzania. *Eur J Clin Nutr.* Sep 2019;73(9):1283-1290. doi:10.1038/s41430-019-0403-3
- Kashi B, C MG, Kurzawa ZA, Verney AMJ, Busch-Hallen JF, De-Regil LM. Multiple Micronutrient Supplements Are More Cost-effective Than Iron and Folic Acid: Modeling Results from 3 High-Burden Asian Countries. *J Nutr.* Jul 1 2019;149(7):1222-1229. doi:10.1093/jn/nxz052

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Experience from the Field



World Map of Multiple Micronutrient Supplementation (MMS) Activities

Maintained by the Healthy Mothers Healthy Babies (HMHB) Consortium

Martin N Mwangi

Micronutrient Forum, Washington, DC, USA

The interactive world map of MMS activities (the ‘map’), designed and maintained by the Healthy Mothers Healthy Babies (HMHB) Consortium, is meant to provide a one-stop window depicting global MMS activities (see **Figure 1**). It summarizes the situation related to impact studies, implementation research, demonstration pilots, cost-benefit analyses, and scaling-up activities by various partners at the country level. The map is updated on an annual basis. According to its current version, an estimated 1,784,524 women are targeted to receive MMS through the mapped activities. However, this is an underestimate, as the current data is from 2021–2022; thus, the map is currently being updated to include ongoing activities for 2022–2023.

“The map is meant to provide a one-stop window depicting global MMS activities”

Partners and implementing agencies that have introduced MMS in national delivery platforms have, in general, followed a three-phased approach:

1. **The Exploration phase** aims to prepare an enabling environment for introducing MMS. This may consist of a landscape analysis to understand the specific context and feasibility of introducing MMS, advocacy activities leading up to MMS policy recommendations, and a consensus on the need for, and feasibility of, introducing MMS at a small scale.
2. **The Implementation phase** entails the actual introduction of MMS to demonstrate its feasibility through a pilot in a specific context.
3. **The Scale-up phase** occurs when policymakers decide to scale up MMS implementation at the national or sub-national level.

The map, therefore, classifies countries into four categories:

- Category 1:** highlights countries where an MMS impact study has taken place but where (exploration of) MMS introduction still needs to happen.
- Category 2:** highlights countries taking the first exploratory step to build the enabling environment for MMS.
- Category 3:** includes countries where initial implementation has started.
- Category 4:** includes countries in the final step to scale up the delivery of MMS to pregnant women with poor diets and high maternal malnutrition.

“Do you or your organization have ongoing MMS work that you would like included in the world map of MMS activities?”

Updating the MMS world map

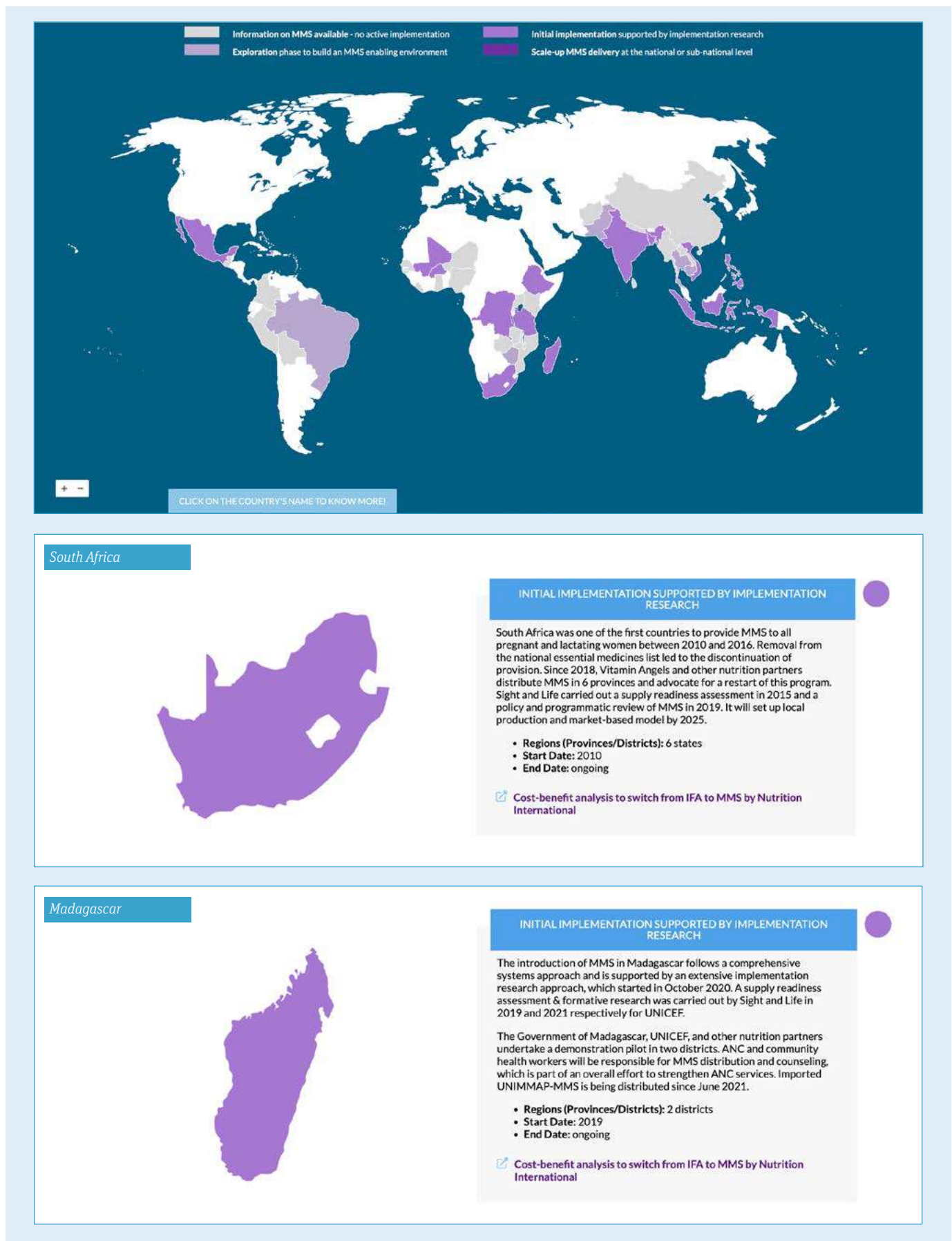
The HMHB consortium aims to annually update the map based on new information from partners and developments/activities from existing partners. The information/data is collected via a survey of ongoing activities. When the partner organization sends the requested information to the HMHB secretariat, the data is curated and formatted to upload to the online map.

Do you or your organization have ongoing MMS work that you would like included in the world map of MMS activities? Please email the HMHB secretariat at HMHB@micronutrientforum.org.

Correspondence: **Martin N Mwangi**, PhD, Micronutrient Forum, 10th Floor, 1201 Eye St, NW, Washington, DC 20005-3915, USA

Email: martin.mwangi@micronutrientforum.org

FIGURE 1: World map of MMS activities showing examples of typical country information – South Africa and Madagascar – obtained from clicking these countries on the map (Source: www.hmhbconsortium.org/world-map/)



The Inclusion of MMS on WHO's Essential Medicines List: Implications for scaling up MMS globally and at the country level

Megan Bourassa, Reed Atkin

The Micronutrient Forum, Washington, DC, USA

Key messages:

- Multiple micronutrient supplements (MMS) are now included on the World Health Organization's List of Essential Medicines (known as the EML).
- This is an important step forward in the procurement and use of MMS globally and nationally, and several countries are now considering adding MMS to their national EML.

The importance of MMS and its inclusion on the WHO EML

In 2021, the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS) formulation for pregnant women was added to the World Health Organization's (WHO) 22nd Essential Medicines List (EML). This marked an important milestone for transitioning supplementation programs for pregnant women with micronutrient-poor diets from iron and folic acid (IFA) supplements to MMS.¹ The WHO EML is updated every two years and is used by more than 130 countries as the basis for their national EMLs or drug formularies and to guide purchasing decisions.² Currently 479 medications, including MMS, are in the EML, based on efficacy, safety and cost-effectiveness data, because they are considered essential from a public health perspective.

It is now well documented that MMS reduces the risk of low birthweight (LBW), small for gestational age (SGA), and preterm birth when compared with IFA alone. MMS also has an even greater impact on anemic and underweight women and female infants for several pregnancy outcomes.^{3,4} Given the high rates of LBW and preterm birth in many low- and middle-income countries (LMICs), and the increased risk of mortality and morbidity associated with these outcomes, MMS has the potential to save and improve lives in a highly cost-effective way.^{5,6}

The 2020 *World Health Organization (WHO) Antenatal Care Recommendations for a Positive Pregnancy Experience*⁷ recom-

mends the use of MMS containing IFA in the context of rigorous research, rather than a full recommendation. Despite other guidelines from WHO, UNICEF and WFP recommending MMS, this is seen by some national-level stakeholders as a barrier to the implementation of MMS programs. The process for adding medications to the EML, however, is separate from those of the guideline development group, and many stakeholders regard this as an important step in advancing MMS as an efficient, safe and cost-effective pregnancy intervention. As many countries model their own EMLs off the WHO EML, its addition could support the procurement and use of MMS in many settings that would benefit from the intervention. It is important to note that other nutritional supplements, including IFA (for pregnancy), are already on the list, and micronutrient powders (MNP) were added in the previous revision of the WHO EML.

At the national level, additional benefits of the inclusion of MMS on the EML include:

1. Contributing to the achievement of global and national targets such as the Sustainable Development Goals (SDGs) 2 and 3 and the World Health Assembly (WHA) global nutrition targets;
2. Facilitating the integration of nutrition interventions into the health system;
3. Increasing accessibility, lower costs, and reducing restrictions on importing and/or local MMS production;
4. Assisting in changing perceptions around MMS and contributing to raising awareness of prenatal supplementation; and
5. Supporting the inclusion of a dedicated budget line to ensure the availability of MMS.

“It is now well documented that MMS reduces the risk of low birthweight, small for gestational age and preterm birth”

The process to include MMS on the WHO EML

With the support of many stakeholders, the New York Academy of Sciences and the Micronutrient Forum wrote and submitted the 63-page application for MMS in late 2020 for consideration by the Expert Committee on Selection and Use of Essential Medicines.⁸ The application included information on the importance of micronutrients during pregnancy and the high rates of deficiency around the world. It also pooled the available evidence from the more than 20 efficacy trials, as well as information on safety and cost-effectiveness.

Importantly, at the time of the submission, 68 countries already included some type of MMS (not just for pregnant women, and not necessarily the UNIMMAP MMS formulation) on their EML. Data from UNICEF's NutriDash survey also showed that 18 LMICs had already implemented MMS policies and 38 had procured MMS for pregnant women. The application suggested the UNIMMAP MMS formulation while leaving room for modifications in case new evidence becomes available.

Each application for consideration on the EML is published online for a public comment period during which anyone can submit a response to the application (either in support or in opposition).⁹ During the public comment period, WHO submitted a letter expressing concern about the inclusion of MMS. However, the MMS application also received 20 support letters from individuals, organizations and ministries of health, which demonstrated the broad recognition of the benefits of MMS and of its value as a key intervention during pregnancy. Many of these support letters cited the need for more effective interventions to improve pregnancy outcomes, ongoing activities to implement MMS, its role in achieving the SDGs, and the detrimental impact of the pandemic on nutritious diets.

Each application is reviewed by one or more experts to evaluate the application and the need for its inclusion on the EML. The two reviewers for the MMS application both stated that there was ample evidence for its inclusion.⁹ The official report from the Expert Committee cited the numerous support letters for MMS, the WHO, UNICEF, and WFP guidelines that recommend MMS, the large number of trials showing its effectiveness compared with IFA alone, and a lack of harm.¹⁰ While the antenatal care guidelines do not make a full recommendation for MMS due to some remaining questions – such as around the impact of switching from IFA to MMS – the committee concluded that adding MMS to the EML would not preclude answering such research questions.

“MMS is poised to become the standard care for pregnant women”

Conclusions

The accelerated action by number of engaged stakeholders supporting MMS transitions makes it difficult to attribute the direct

impact of the addition of MMS on the WHO EML, but there is little doubt that it was an important step in advocating for the switch from IFA to MMS. Since the addition of MMS to the WHO EML, several countries are considering adding it to their own national EML, and many partners who work at the country level have observed an improvement in advocacy discussions and manufacturing interests related to MMS. Now that MMS is on the WHO EML, the work is by no means done; but with continued national engagement and support from the global community, MMS is poised to become the standard care for pregnant women.

Correspondence: Megan Bourassa, The Micronutrient Forum, 1201 Eye St, NW, 10th Floor, Washington, DC, USA
Email: megan.bourassa@micronutrientforum.org

References

- 1 World Health Organization Model List of Essential Medicines – 22nd List, 2021.; 2021. <https://apps.who.int/iris/bitstream/handle/10665/345533/WHO-MHP-HPS-EML-2021.02-eng.pdf> Accessed 20 November 2022.
- 2 WHO. Application period now open for the 2023 update of the WHO Model Lists of Essential Medicines. <https://www.who.int/news/item/07-03-2022-application-period-now-open-for-the-2023-update-of-the-who-model-lists-of-essential-medicines>. Published March 7, 2022. Accessed 20 November 2022. <https://www.who.int/news/item/07-03-2022-application-period-now-open-for-the-2023-update-of-the-who-model-lists-of-essential-medicines>
- 3 Smith ER, Shankar AH, Wu LSF, 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. *Lancet Glob Health*. 2017;5(11):e1090-e1100.
- 4 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews*. 2019;(3).
- 5 Engle-Stone R, Kumordzie SM, Meinzen-Dick L, Vosti SA. Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost effectiveness. *Ann N Y Acad Sci*. 2019;1444(1):35-51.
- 6 Kashi B, M Godin C, Kurzawa ZA, Verney AMJ, Busch-Hallen JF, De-Regil LM. Multiple micronutrient supplements are more cost-effective than iron and folic acid: modeling results from 3 high-burden Asian countries. *J Nutr*. 2019;149(7):1222-1229.
- 7 World Health Organization. 2020. WHO antenatal care recommendations for a positive pregnancy experience: nutritional interventions update: multiple micronutrient supplements during pregnancy. World Health Organization.
- 8 *Essential Medicines List Application for Multiple Micronutrient Supplements During Pregnancy*; 2020.. https://cdn.who.int/media/docs/default-source/essential-medicines/2021-eml-expert-committee/applications-for-addition-of-new-medicines/a.22_multiple-micronutri-

ent-supplement.pdf?sfvrsn=55c7e988_4 Accessed 20 November 2022.

- 9 Multiple micronutrient supplement – antenatal supplement – EML Application, expert reviews and public comments. Published 2021. Accessed 20 November 2022. <https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/23rd-expert-committee/a22-multiple-micronutrient>
- 10 World Health Organization Model List of Essential Medicines – 22nd List, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.02). Licence: CC BY-NC-SA 3.0 IGO.

Implementation Research in Pakistan: Paving the way for a successful transition to multiple micronutrient supplementation

Jennifer Busch-Hallen, Sarah Rowe, Mandana Arabi

Nutrition International, Ottawa, Canada

Shabina Raza

Nutrition International, Islamabad, Pakistan

Key messages:

- Nutrition International, in collaboration with the Government of Pakistan, is undertaking implementation research to support the introduction of multiple micronutrient supplementation (MMS) in antenatal care (ANC) and identify effective program implementation solutions.
- The Advancing Maternal Health through MMS Implementation Research in Pakistan (AMMI) project will not only inform the introduction of MMS but also provide useful insights to tackle broader questions related to improving adherence to maternal supplementation and ultimately advancing maternal and newborn health outcomes.
- The AMMI project comprises several steps: (i) establishing and working with the Pakistan Technical Working Group, (ii) determining the priority research questions using a rigorous methodology, (iii) switching over from IFA to MMS in ANC, (iv) conducting the implementation research using mixed methods, and (v) undertaking knowledge translation to support real-time decision-making.
- Building on the approach in Pakistan, Nutrition International is working in partnership with the Government of Nigeria to conduct a new MMS implementation research project focusing on optimizing adherence to maternal micronutrient supplementation.

Introduction

Nutrition International, in collaboration with the Government of Pakistan (GoP), is undertaking implementation research on prenatal multiple micronutrient supplementation (MMS) to advance maternal and newborn health and nutrition. This work builds upon the findings from the MMS Cost-Benefit Tool¹ – an online tool developed by Nutrition International to assist governments in their

decision-making when it comes to switching from iron and folic acid supplementation (IFAS) to MMS. This tool found that MMS is more cost-effective than IFA for pregnant women in Pakistan.² Implementation research, as recommended by the World Health Organization (WHO),³ is a key step to inform the transition and successful scale-up of MMS within the antenatal care (ANC) platform, and to support a positive pregnancy.

The Government of Pakistan's commitment to maternal nutrition

Maternal and newborn health and nutrition needs in Pakistan are high. The neonatal mortality rate (estimated at 42 per 1,000 live births)⁴ and the prevalence of low birthweight (23% in 2018) are some of the highest in the world. According to the 2018 National Nutrition Survey, an estimated 14.4% of women of reproductive age are underweight, 41.7% suffer from anemia, 22.4% are affected by vitamin A deficiency, and 79.7% from vitamin D deficiency.⁵ An analysis of trends across Demographic Health Surveys shows that government support to ANC services is increasingly reaching more women and there have been some improvements in the uptake and use of these services, such as maternal IFA.⁴ However, there are several bottlenecks that are preventing the program from achieving its desired effectiveness.⁶

The GoP's five-year National Maternal Nutrition Strategy (2022–2027) outlines the government's renewed commitment to addressing the dire maternal nutrition situation in the country.⁷ This comprehensive strategy includes a recommendation to implement MMS as part of ANC services for pregnant women. Understanding the risks of scaling up a new intervention too quickly, particularly given the challenges of the current platform, the Nutrition Wing of the Ministry of National Health Services, Regulations and Coordination approached Nutrition International to undertake implementation research. This research is critical to exploring solutions to long-standing implementation issues and offers an opportunity to guide decision-making and ultimately a path to the scale-up of MMS. This collaboration builds upon Nutrition International's work with the GoP for more than two decades, serving as a technical nutrition ally in the areas of fortification, child survival, and maternal and newborn health.

“Increasing access to MMS will contribute to improving maternal nutrition, birth outcomes and reducing stunting, which are key objectives of Pakistan’s Stunting Reduction Strategy and part of the National Nutrition Program...This MMS implementation research project [...] is an important step towards potentially providing access to MMS to pregnant women across Pakistan, and I’m looking forward to the outcomes.”

Dr Abdul Baseer Khan Achakzai, Director General, Ministry of Health, Pakistan

Nutrition International and the Government of Pakistan collaborate on rigorous implementation research

The implementation research comprises several carefully designed steps, which are described in detail below.

1. Defining what implementation research means in the Pakistan context

To formally initiate the *Advancing Maternal Health through MMS Implementation Research in Pakistan* (AMMI) project (Figure 1), an evidence translation workshop was held with key stakeholders representing federal and provincial government and non-government organizations. During the workshop, the findings from Pakistan’s cost-effectiveness analysis were shared alongside the latest global effectiveness evidence and the 2020 WHO update.² The workshop provided a platform to discuss implementation research, explore its value for Pakistan, and galvanize commitment for MMS. It ultimately resulted in the creation of a Technical Working Group (TWG) to advise and oversee the research project.

2. Determining the implementation research questions

Recognizing there are many important implementation research questions related to the introduction of MMS in Pakistan, the GoP and the TWG, with the support of Nutrition International, employed the Child Health and Nutrition Research Institute (CHNRI) method to identify and prioritize research questions for this study. Working from an existing national IFA bottleneck analysis, TWG members participated in a workshop to identify MMS program challenges and opportunities that informed a consolidated list of 28 implementation research questions under seven thematic areas. Through an online survey, the broader TWG then scored these questions based on set cri-

FIGURE 1: Front cover of the technical brief for the *Advancing Maternal Health through MMS Implementation Research in Pakistan* (AMMI) project



More information about the AMMI project can be found in this technical brief: <https://www.nutritionintl.org/learning-resource/technical-brief-mms-implementation-research-pakistan/>

teria. Prioritization scores were calculated for each of the implementation research questions and then used to rank the questions. The primary research questions selected for this study focus on identifying approaches to improve the delivery of ANC nutrition services and introduce MMS, with a specific focus on nutrition counselling, the engagement of family, and healthcare provider capacity-strengthening (see Box 1). The secondary implementation research questions focus on the fidelity, acceptability, feasibility and cost-effectiveness of the enhanced implementation approaches, quality of care, enablers, and barriers to successful implementation.

BOX 1: Questions selected for the study

Primary questions:

1. What implementation approach(es)* could be used to enhance the delivery of ANC nutrition services and introduce antenatal MMS to replace IFA for pregnant women in Pakistan?
2. Does implementation of the enhanced approaches increase pregnant women’s adherence to MMS? If so, how?

*Focused on:

- Capacity-building and supportive supervision of healthcare providers, with emphasis on MMS and nutrition counselling
- Improved nutrition content and nutrition counselling tools and techniques integrated into ANC delivery
- Engagement of pregnant women’s family members in ANC

3. Introducing MMS into the antenatal care platform

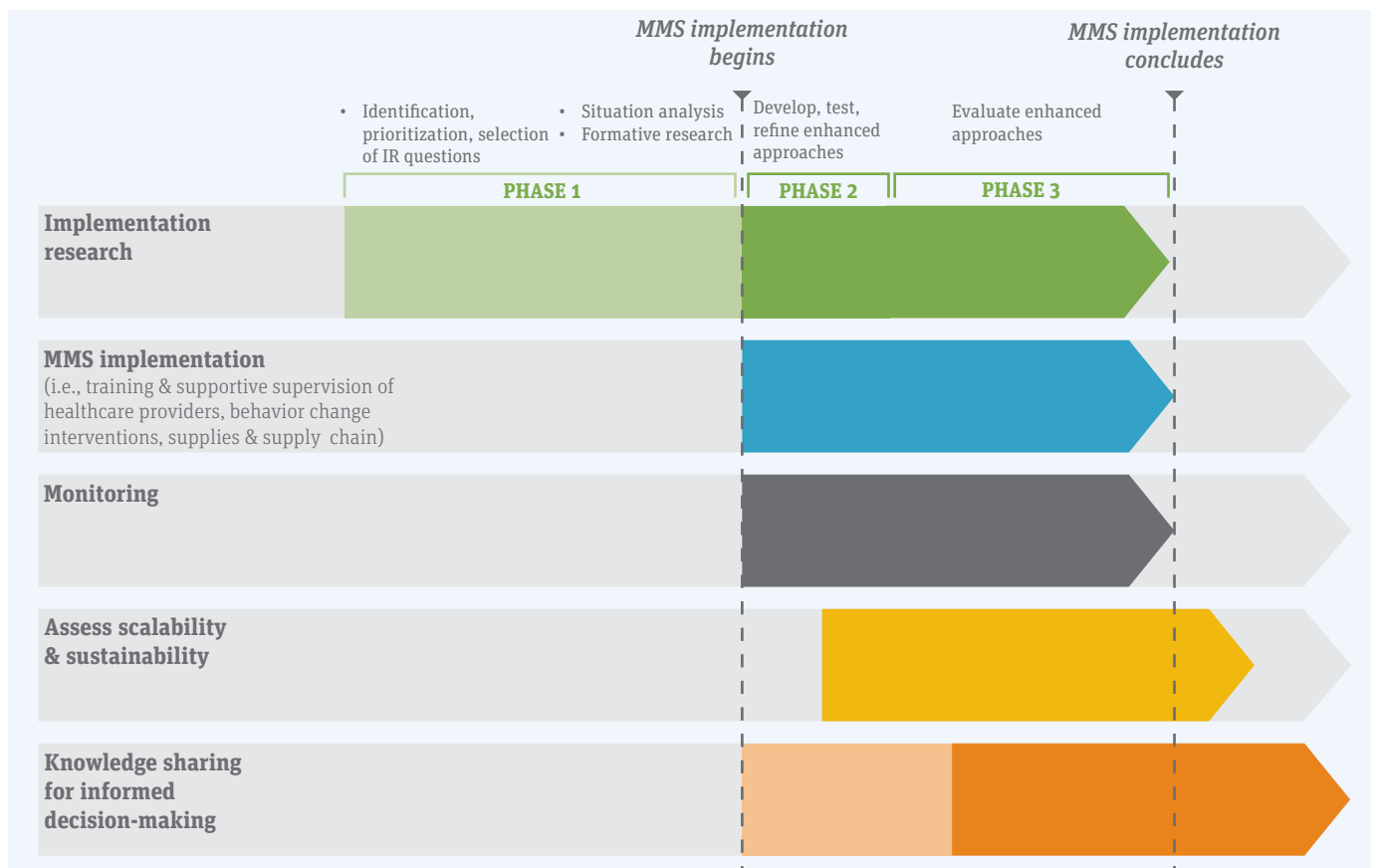
To study the selected research questions, MMS had to first be introduced into the ANC platform in place of IFA. Swabi district, located in Khyber Pakhtunkhwa province, was selected as the pilot area for the project. Beginning in April 2022, with the support of federal, provincial and district health officials and local stakeholders, all newly enrolled pregnant women accessing public ANC services in Swabi were offered two 100-count bottles of MMS over the course of their visits, whether at a government health facility or in the community from a Lady Health Worker or Community Midwife. To further support this transition from IFA to MMS, a ‘standard’ implementation package was developed (Figure 2). This included training for healthcare providers on MMS and the new standard operating procedures, a behavior change strategy and materials, a bolstered program monitoring system, and a strengthened supply chain.

Monitoring data and observations indicated a wide acceptance of the new MMS product among healthcare providers, pregnant women, and their influencers within the first month of the transition. Any programmatic issues that were identified during the initial roll-out were documented and corrected to improve the program and establish MMS as the new standard of care for preventative ANC services. In addition to ongoing course correction, a transition costing study is running parallel to this pilot project to generate a model for better capturing the true costs of moving from IFA to MMS.

FIGURE 2: ‘Standard’ transition package (counselling cards, factsheet, poster, standard operating procedures, Frequently Asked Questions, and modified monitoring forms)



FIGURE 3: Overview of implementation research process



4. Conducting the implementation research

Nutrition International and the GoP are deploying a phased approach using mixed methods to explore and answer the research questions (Figure 3).

Phase one (completed) included a situational analysis of existing ANC service delivery programming, platforms, stakeholders, and the supply of IFA supplements and MMS in Pakistan. Formative research was then conducted to better understand the current perspectives, experiences, and practices of key stakeholders, including pregnant women, their family members and healthcare providers. The insights learned during this phase subsequently informed the design of the pilot, the development of the transition package, and the other implementation research phases.

Phase two (completed) focused on the first research question, using a human-centered and participatory design methodology to develop, test, and adapt implementation research approaches that could be used to enhance the introduction of MMS and the delivery of ANC nutrition services. A modified Trials of Improved Practices (TIPs) was conducted with healthcare providers, pregnant women and their key influencers over several months. As a result, 'enhanced' implementation approaches focused on nutrition counselling tools and techniques and engagement of family members with a strong gender component were generated.

Phase three (in progress) focuses on evaluating the above approaches by not only testing the hypothesis that the enhanced implementation approaches will increase pregnant women's adherence to MMS, but also understanding how these approaches function. Outcome, process and cost-effectiveness evaluations are underway and



Lady Health Workers participate in a training on how to support the delivery of MMS to pregnant women in Swabi District, Khyber Pakhtunkhwa

are designed to answer this question in addition to the secondary implementation research questions. Together with the TWG, the results of this evaluation phase will be translated to inform decision-making and practices relating to maternal nutrition services and MMS in Pakistan, within Swabi district and beyond.



Formal launch of the AMMI project was in Islamabad in June 2022, in the presence of representatives from the TWG

The value of the MMS implementation research

This rigorous implementation research systematically explores what it would take to introduce and scale up MMS in Pakistan in a way that considers the realities of the existing ANC platform, the people who work within it, the needs of pregnant women and what influences their decision-making.

Building on its approach in Pakistan, Nutrition International is collaborating with the Government of Nigeria to conduct a new MMS implementation research project with funding from the Bill & Melinda Gates Foundation. Generating context-specific research is critical for country decision-making. Looking across the research also provides useful insights to tackle broader questions related to improving adherence to maternal supplementation and paving the way to better outcomes for women and their families.

Correspondence: Jennifer Busch-Hallen, Practice Area Director for Maternal and Newborn Nutrition and Health, Nutrition International, 180 Elgin Street, Suite 1000, Ottawa, Ontario K2P 2K3, Canada.

Email: jbuschhallen@nutritionintl.org

“Implementation research on MMS is shining a much-needed light on maternal nutrition. The global community needs to ensure that past mistakes are not repeated when introducing new nutrition products to the health system. When carried out effectively, implementation research can renew investment, interest and commitment to maternal nutrition and program effectiveness and provide a successful pathway to MMS scale-up.”

Jennifer Busch-Hallen, Practice Area Director for Maternal and Newborn Nutrition and Health, Nutrition International



Lady Health Worker providing MMS alongside antenatal counselling during a home visit in Swabi District, Khyber Pakhtunkhwa

References

- 1 Nutrition International. A tool to aid decision-making transitioning from IFAS to MMS. MMS Cost-Benefit Tool. Internet: <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>. Updated 2022. Accessed 30 November 2022.
- 2 Nutrition International. Cost-Effectiveness of Transitioning from Iron and Folic Acid to Multiple Micronutrient Supplementation for Pregnancy, Policy Brief: Pakistan. Nutrition International: Ottawa, Canada; 2020.
- 3 World Health Organization. WHO antenatal care recommendations for a positive pregnancy experience Nutritional interventions update: Multiple micronutrient supplements during pregnancy. World Health Organization: Geneva, Switzerland; 2020.
- 4 National Institute of Population Studies (NIPS) [Pakistan] and ICF. Pakistan Demographic and Health Survey 2017-18. NIPS and ICF: Islamabad, Pakistan, and Rockville, Maryland, USA; 2019.
- 5 Ministry of National Health Services, Regulations and Coordination, United Nations Children’s Fund (UNICEF), and Aga Khan University. Pakistan National Nutrition Survey 2018. Government of Pakistan: Islamabad, Pakistan; 2018.
- 6 Ministry of National Health Services, Regulations and Coordination, United Nations Children’s Fund (UNICEF), and Nutrition International. Iron Folic Acid (IFA) Bottleneck Analysis Report Pakistan. Government of Pakistan: Islamabad, Pakistan; 2022.
- 7 Ministry of National Health Services, Regulations and Coordination, United Nations Children’s Fund (UNICEF). Pakistan Maternal Nutrition Strategy 2022-2027. Government of Pakistan: Islamabad, Pakistan; 2022.

Galvanizing Partnerships to Accelerate Multiple Micronutrient Supplement Introduction

Marti J van Liere, Martin N Mwangi, Saskia JM Osendarp
Micronutrient Forum, Washington, DC, USA

Key messages:

- A greater sense of urgency is needed to empower and equip governments of low- and middle-income countries with tools and expertise to introduce the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS¹) formulation and strengthen other maternal nutrition interventions integrated into antenatal care (ANC) services.
- After 20 years of building the evidence base, new partnerships between key actors were instrumental to create momentum for the implementation of MMS for pregnant women and to align on priorities and accelerate collective action.
- Partnerships and collaborations need to be multisectoral to effectively tackle the barriers involved in the demand, supply, and delivery of MMS.

A quarter-century of solid evidence on the benefits of MMS

New and alarming global estimates for micronutrient deficiencies reveal the depth and breadth of hidden hunger globally, with two out of three women of reproductive age worldwide having at least one micronutrient deficiency.² Poor nutrition of women not only affects their health and wellbeing but also impairs future human capital.

In 1998 (25 years ago), experts in a workshop on ‘Micronutrients and Safe Motherhood’ discussed how micronutrient-poor diets of women in developing countries endanger the pregnancy process and outcomes. They urgently recommended improving nutrient intake through multiple micronutrient supplements (MMS). In 1999, the composition of a supplement for pregnant women was defined for use in effectiveness trials, and the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP MMS) was born.^{1,3}

Since then, a solid evidence base has been built, culminating in the publication of several meta-analyses confirming that MMS safely enhances maternal nutrition status and, in comparison with iron and folic acid (IFA), further reduces the risk of adverse birth outcomes such as preterm birth, stillbirth, low birth weight,

and small for gestational-age.^{4,5} Though MMS is not the only nutrition intervention for pregnant women, it is a proven, safe, affordable and cost-effective intervention for women who typically do not have access to a healthy diet. However, coordinated actions to expand the use of MMS have been lacking.



Micronutrient-poor diets endanger the pregnancy process and outcomes

Partnerships accelerate action

Twenty-five years and approximately 5.7 billion pregnancies in low- and middle-income countries⁶ later, the nutrition sector is finally witnessing momentum and action around MMS for pregnant women. Academic experts, implementing agencies and foundations are coalescing around one common agenda and voice on MMS.

The power of partnerships and collective action has been increasingly recognized in the international development and public health sectors, inspired by the African proverb, “If you want to go fast, go alone; if you want to go far, go together.” Global examples include the Global Fund and the Scaling Up Nutrition (SUN) movement.

Large-scale change requires broad cross-sector coordination to coalesce around one shared agenda that exceeds any individual organization’s reach. The key value of partnerships is that collective action leads to collective impact.⁷ Whereas previously, decision-makers preferred to select the one most effective organization to implement a solution, there is a growing recognition that stimulating collaboration and uniting intellectual forces will lead to more effective solutions and more rapid progress.

The Stanford Social Innovation Review defines five key conditions for collective impact: 1) a common agenda; 2) shared measurement systems; 3) mutually reinforcing activities; 4) continuous communication; and 5) the presence of a backbone organization. Critically, a backbone organization facilitates and strengthens these other conditions, provides the glue between the partners, and closes the gap between the common vision and collective action.⁷

A handful of deeply engaged donors and implementation agencies (including the Bill & Melinda Gates Foundation, the Children’s Investment Fund Foundation (CIFF), the Eleanor Crook Foundation, Kirk Humanitarian, Nutrition International (NI), *Sight and Life* Foundation, UNICEF and Vitamin Angels [VA]) recognized the need for collective action to accelerate the MMS agenda and decided to invest in evidence synthesis, implementation research, MMS manufacturing and supply, and the provision of support to backbone organizations to make it all happen.

“If you want to go fast, go alone; if you want to go far, go together”

Alignment of experts on the scientific evidence

Since 2017, scientific experts have come together in the MMS-Technical Advisory Group (MMS-TAG) hosted by the New York Academy of Sciences (NYAS) to synthesize the evidence base and respond to outstanding research questions.

The MMS-TAG’s key achievements include the publication of an interim country-level decision-making guidance document in 2020 as well as the successful application, together with the Micronutrient Forum, for the inclusion of MMS into WHO’s Essential Medicines List, which was approved in 2021.⁸ Key research areas on which the MMS-TAG has focused include a cost-effectiveness analysis, a risk assessment of exceeding Tolerable Upper Intake Level (UL) in combination with an adequate diet, an iron-dose comparison of 30 versus 60 mg iron, and a systematic review of interventions to increase adherence to micronutrient supplements.⁹⁻¹²

Furthermore, Nutrition International developed an evidence-based cost-benefit tool to aid countries’ decision-making.¹³ This tool uses a rigorous methodology to calculate the incremen-

tal benefits and costs of transitioning from IFA to MMS in various countries.

“The nutrition sector is finally witnessing momentum and action around MMS for pregnant women”

Advocacy to accelerate action

2019 was a pivotal year for MMS. Intense advocacy moments led to more interest, partnerships, and action. The ‘Power for Mothers’ initiated by *Sight and Life* Foundation event at the Women Deliver conference in June was the first step to raising awareness of maternal nutrition and MMS among women’s health and gender experts. In September, the Healthy Mothers Healthy Babies (HMHB) Accelerator¹⁴ was launched at the Bill & Melinda Gates Foundation’s Goalkeepers event, in which eleven *Accelerator Partners* committed to invest a total of US\$ 50 million in the introduction and scale-up of MMS over three years. These investments resulted in a stream of activities aiming to propel the adoption of MMS in country programs.

As a result of these commitments, just before the world entered major lockdowns due to the COVID-19 pandemic, two expert meetings were held, both sponsored by Kirk Humanitarian, a foundation that has dedicated its resources uniquely to MMS. A first meeting to discuss the UNIMMAP MMS Product Specifications was organized in November 2019 by NYAS and the Micronutrient Forum.¹⁵ That meeting was followed by the MMS Stakeholders’ Consultation hosted by the Micronutrient Forum in February 2020. This was the first time the main actors gathered to discuss implementation issues, experiences, gaps, and priorities.

Expanding on the Accelerator partnership, in early 2021, the HMHB Consortium was launched, bringing global and national MMS stakeholders together to accelerate action.¹⁶ Within 24 months, the Consortium has grown to a membership of over 100 organizations and individuals. Its ABC approach (Advocacy – Brokering knowledge – Convening) has driven both a global and a national advocacy agenda around maternal nutrition and MMS. In 2021, the year of the UN Food Systems and Nutrition for Growth



2019 HMHB Accelerator partners

(N4G) Summits, the Consortium advocated for the prioritization of MMS and maternal nutrition with relevant international health audiences. A timely Devex article published in advance of N4G positioned MMS as one of the best investments toward human and economic capital gains. Following the successful inclusion of MMS in WHO's Essential Medicines List, HMHB provided a range of advocacy tools and knowledge resources targeted for use by country-level actors.

“2019 was a pivotal year for MMS”

Collective national action to accelerate implementation

At the same time, momentum was building up at the national level. National MMS Taskforces or Technical Advisory Groups were set up in Indonesia and Bangladesh, bringing together local stakeholders to jointly address issues of national context, and connecting global and national expertise.

MMS introduction and demonstration projects launched a spur of implementation research. Vitamin Angels and Kirk Humanitarian supported nationally led programs in Indonesia and Haiti; UNICEF set up demonstration pilots in Bangladesh, Burkina Faso, Madagascar, and Tanzania with support of the Bill & Melinda Gates Foundation; and CIFF supported GAIN and the Social Marketing Company in Bangladesh and UNICEF in Ethiopia to develop a market-based approach to MMS. *Sight and Life* Foundation partnered with all these organizations to develop a rigorous supply-readiness and market analysis in over 20 countries.

More recently, awareness-raising, exploratory activities and implementation research are being undertaken in Cambodia, DRC, Ethiopia, Malawi, Mali, Mexico, Nepal, Nigeria, Pakistan, Philippines, South Africa, Thailand, Uganda, Vietnam, and Zambia.

During the initial two years of the COVID-19 pandemic, experience and knowledge-sharing regarding these efforts was restricted to online webinars and virtual conferences. For instance, two dedicated sessions to MMS were held at the Micronutrient Forum's 2020 CONNECTED Conference, and multiple webinars were organized or co-hosted by HMHB partners.

Participants of the first, in-person, MMS regional meeting in October 2022 were eager to share information and learn from their peers. This technical meeting offered an opportunity for representatives from Ministries of Health, national researchers and international implementation and technical agencies to connect in person and discuss challenges and solutions. Reinforcing the need for collaboration, the participants at this meeting requested a Community of Practice be established.

Public-private sector partnerships to meet demand

Key hurdles cited by national decision-makers regarding the intro-

duction of MMS in their country include the lack of product availability, accessibility and affordability, as well as regulatory issues and delivery challenges. Though importing MMS provides a short-term solution, either through government purchase or donations, a recent white paper by Kirk Humanitarian estimates the demand for MMS supplies will increase from 15.5 million pregnancies in 2024 to 61.8 million by 2030.¹⁷ To fulfil this anticipated future demand, better coordination and collaboration is urgently required among existing and new suppliers. Global consensus on UNIMMAP MMS product specifications is a prerequisite for ensuring product quality. Furthermore, advance market commitments by donors to existing and new manufacturers can support government decisions to introduce MMS; qualified global manufacturers or premix suppliers can support the capacity development of qualified regional and local companies.

“The HMHB Consortium aims to ensure that 75 million pregnant women annually will receive MMS by 2030”

A greater sense of urgency: Powering women's nutrition for promising futures

The launch of global and national collaborations and partnerships has dramatically advanced the MMS agenda in the past few years. Yet annually there are still 228 million underserved, pregnant women in low- and middle-income countries who need better access to proper nutrition.⁶

In 2022, the total number of donated or distributed MMS was only sufficient for 5% of them, or 11 million pregnant women. Sixty-two percent, or 6.8 million bottles, were donated by Kirk Humanitarian, 2 million by Vitamin Angels, 1.5 million by UNICEF, and 100,000 by World Food Programme, while the Social Marketing Company in Bangladesh sold MMS (in packs of 30 pills) to approximately 600,000 women.¹⁸

Hence, a greater sense of urgency is needed to invest in demand, supply, and delivery of MMS. The HMHB Consortium aims to ensure that 75 million pregnant women annually will receive MMS by 2030. To achieve this goal, we must collectively tackle barriers, including improving quality of and access to ANC services, integrating MMS with other maternal nutrition interventions, tackling supply chain issues, and resolving remaining (implementation) science questions.

We therefore need more and a wider range of partners at the table. Future partnerships and collaborations should be more multisectoral if we wish to effectively tackle the barriers, including issues related to the quality of delivery platforms.



Leveraging the power of multisectoral partnerships to achieving collective impact

We must develop partnerships and collaboration with government partners, not only with the nutrition divisions, but also with maternal health experts in the Ministries of Health or Family Welfare, as well as with Ministries of Finance.

We must develop partnerships beyond the nutrition sector: with academic experts and implementing agencies working in maternal health, health systems strengthening, humanitarian aid, financing mechanisms, implementation research, social and behavior change communication; and with private-sector manufacturers and distributors.

We must develop partnerships with advocacy experts to develop and implement a strategic and collective advocacy strategy to speak with one loud voice calling upon governments, bi-, and multilateral donors, and industry to invest in MMS and maternal nutrition.

We must develop partnerships with technical organizations to encourage and support more country governments in their decision to make MMS and maternal nutrition their priority.

We must develop partnerships with manufacturers and distributors to secure short- and long-term MMS availability, accessibility, and affordability, whether from national, regional, or global suppliers.

Most important of all, we must develop partnerships and collaboration between early-adopter countries and those interested and eager to learn from their peers. We specifically need to bring global, regional, and national experts together, stimulating dialogue and exchange across diverse perspectives and learning more from each other.

Powering women's nutrition for promising futures. It can be done, and it must be done together: more urgently and faster.

Correspondence: Marti J van Liere, Micronutrient Forum, 10th Floor, 1201 Eye St, NW, Washington, DC 20005-3915, USA

Email: Marti.vanLiere@micronutrientforum.org

References and notes

- 1 The term MMS in this article refers to the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP).
- 2 Stevens GA, Beal T, Mbuya MNN, Luo H, Neufeld L, on behalf of Global Micronutrients Deficiencies Research Group. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health* 2022;10:e1590–99. [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(22\)00367-9/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00367-9/fulltext).
- 3 World Health Organization, United Nations University & United Nations Children's Fund (UNICEF)(1999). *Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries: report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO) and United Nations University workshop*. WHO.int. <https://apps.who.int/iris/handle/10665/75358> Accessed 21 November 2022.
- 4 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst. Rev.* 2019;3:CD004905. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004905.pub6/full>
- 5 Smith ER, Shankar AH, Wu LS, Aboud S, Adu-Afaruwah S, Ali H, Agustina R, Arifeen S, Ashorn P, Bhutta ZA, Christian P, Devakumar D, Dewey KG, Friis H, Gomo E, Gupta P, Kæstel P, Kolsteren P, Lanou H, Maleta K, Mamadoultaiou A, Msamanga G, Osrin D, Persson LÅ, Ramakrishnan U, Rivera JA, Rizvi A, Sachdev HPS, Urassa W, West KP Jr, Zagre N, Zeng L, Zhu Z, Fawzi WW, Sudfeld CR. 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. *Lancet Glob. Heal.* 2017;5(11):e1090-e1100. <https://pubmed.ncbi.nlm.nih.gov/29025632/>
- 6 Sully EA, Biddlecom A, Darroch JE, Riley T, Ashford LS, Lince-Deroche N, Firestein L, Murro R. *Adding It Up: Investing in Sexual and Reproductive Health 2019*, New York: Guttmacher Institute, 2020. <https://www.guttmacher.org/report/adding-it-up-investing-in-sexual-reproductive-health-2019>. Accessed 21 November 2022.
- 7 Hanleybrown, F, Kania, J, Kramer, M. Channeling Change: Making Collective Impact Work. *Stanf. Soc. Innov. Rev.* 2012. Accessed 21 November 2022. https://ssir.org/articles/entry/channeling_change_making_collective_impact_work
- 8 Bourassa M, Atkin R. Including MMS on the World Health Organisation's Model Essential Medicine List. *Sight and Life Magazine* 2023.

- 9 Engle-Stone R, Kumordzie SM, Meinzen-Dick L, Vosti SA, Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness. *Ann N.Y. Acad. Sci.* 2019;1444(1):35-51. <https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14132>.
- 10 Gernand AD. The upper level examining the risk of excess micronutrient intake in pregnancy from antenatal supplements. *Ann N.Y. Acad. Sci.* 2019;1444(1):22-34. <https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14103>.
- 11 Gomes F, Agustina R, Black RE, Christian P, Dewey KG, Kraemer K, Shankar AH, Smith ER, Thorne-Lyman A, Tumilowicz A, Bourassa MW. Multiple micronutrient supplements versus iron-folic acid supplements and maternal anemia outcomes: an iron dose analysis. *Ann N.Y. Acad. Sci.* 2022 Jun;1512(1):114-125. <https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14756>.
- 12 Gomes, F, King, SE, Dallmann, D, Golan, J, da Silva, ACF, Hurley, KM, Bergeron, G, Bourassa, MW and Mehta, S. Interventions to increase adherence to micronutrient supplementation during pregnancy: a systematic review. *Ann. N.Y. Acad. Sci.*, 2021;1493: 41-58. <https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14545>.
- 13 Nutrition International. A tool to aid decision-making transitioning from IFAS to MMS. [nutritionintl.org](https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/). <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/> Accessed 21 November 2022.
- 14 Bill and Melinda Gates Foundation Goalkeepers Accelerators. Healthy Mothers, Healthy Babies. [Gatesfoundation.org](https://www.gatesfoundation.org/goalkeepers/the-work/accelerators/maternal-nutrition/). Accessed 31 January 2023. <https://www.gatesfoundation.org/goalkeepers/the-work/accelerators/maternal-nutrition/>
- 15 The Multiple Micronutrient Supplement Technical Advisory Group and the Micronutrient Forum. Expert Consensus on an Open Access United Nations International Multiple Micronutrient Antenatal Preparation – multiple micronutrient supplement product specification. *Ann. N.Y. Acad. Sci.*, 2020;1470: 3-13. <https://nyaspubs.onlinelibrary.wiley.com/doi/10.1111/nyas.14322>.
- 16 Healthy Mothers Healthy Babies Consortium. <https://hmhbconsortium.org/> Accessed 21 November 2022.
- 17 Ajello CA, Suwantika A, Santika O, King S, de Lange J. (2022). *UNIMMAP MMS for National Health Systems: Considerations for developing a supply strategy*. Kirk Humanitarian.org. https://kirkhumanitarian.org/wp-content/uploads/2022/11/UNIMMAP-MMS-Supply-Paper_Digital-Version-1-FINAL-1-1.pdf Accessed 21 November 2022.
- 18 Information was requested and received from partners between 15 December 2022 and 31 January 2023.

Multiple Micronutrient Supplements: Closing gaps and saving lives

Yashodhara Rana, Jack Clift

Eleanor Crook Foundation (ECF), Washington, DC, USA

Key messages:

- In many low- and middle-income contexts, women's and girls' diets often fail to provide minimum healthy levels of essential nutrients, due to lack of food access and affordability, socio-cultural norms, and gender inequality.
- While ensuring access to nutrient-rich foods is a critical long-term policy goal, supplementation is a necessity for pregnant women, who have higher needs.
- MMS represents a cost-effective investment for improving maternal and child health outcomes and is a step toward equity in access to a better standard of care.
- Renewed interest in prenatal supplementation with MMS provides an opportunity to address broader systems-level barriers.
- The Eleanor Crook Foundation (ECF), a private philanthropy focused on fighting global malnutrition, is committed to expanding MMS coverage through research and advocacy, with the goals of improving maternal and child nutrition, and saving lives.

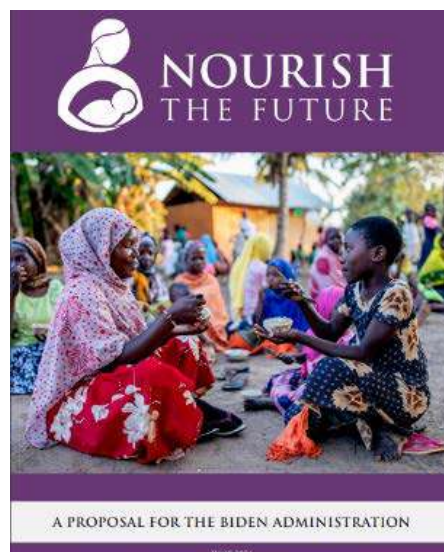
Despite being entirely preventable, malnutrition is a leading threat to child survival. According to the World Health Organization (WHO), nutrition-related factors contribute to about 45% of deaths in children under five years of age.¹ Almost 3 million children under five years of age die from malnutrition every year² and one in four children around the world are permanently impaired – both cognitively and physically. With a commitment to saving as many children's lives as possible, the Eleanor Crook Foundation (ECF) focuses on scaling proven interventions to address global malnutrition.

“MMS holds tremendous potential for improving maternal and child health outcomes”

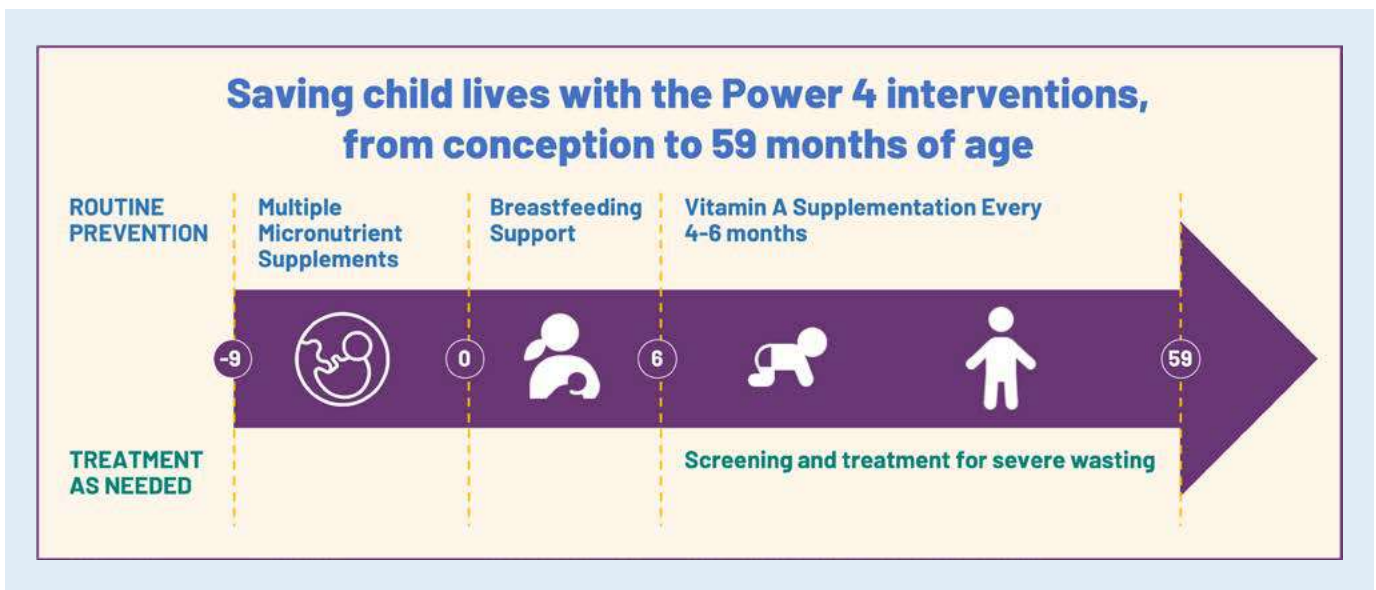
In 2019, ECF partnered with Johns Hopkins University (JHU) to identify the most cost-effective ways to reduce nutrition-related mortality through the scaling-up of priority high-impact malnutrition interventions. Four interventions emerged: multiple micronutrient supplements (MMS), breastfeeding support, vitamin A supplementation, and treatment of wasting with ready-to-use therapeutic foods (RUTF), also referred to as the *Power 4*.

Based on this research, ECF and a host of advocacy and technical nutrition groups partnered to develop a five-year plan for implementing the *Power 4* and creating the system changes needed to sustainably drive down malnutrition rates. The result is *Nourish the Future* (Figure 1), an evidence-based blueprint that would save 2 million lives, while markedly improving the quality of life for at least 500 million women and children.³

FIGURE 1: *Nourish the Future*, a blueprint for saving 2 million lives



Since launching *Nourish the Future* in October 2021, ECF has had a great deal of success raising awareness and funds for life-saving RUTF, the first of the *Power 4* interventions (Figure 2) on which the foundation opted to focus. In July 2022, United States Agency for International Development (USAID) Administrator Samantha Power announced a US\$ 200 million investment to scale up distribution of RUTF and called on other governments and philanthropic institutions to do the same.⁴ By October 2022, public and private donors, including ECF, had committed an additional US\$ 330 million.

FIGURE 2: The Power 4 interventions

While continuing the work to support RUTF scale-up, the foundation is now looking to leverage its success and expand efforts to the other Power 4 interventions. ECF chose MMS as the logical next step. By delivering necessary nutrients to women during pregnancy, MMS holds tremendous potential for improving maternal and child health outcomes.

MMS supports maternal nutrition and saves children's lives

Women and girls are the foundation of strong families and communities. Yet, in many contexts, women and girls eat less and are nutritionally vulnerable due to issues such as food access and affordability, socio-cultural norms, and gender inequality.⁵ A lack of nutrients causes severe outcomes, especially for pregnant women who need even higher levels of micronutrients than usual to support their health and fetal growth. Pregnant women with poor nutrition are at an increased risk of death from pre-eclampsia and postpartum hemorrhage and are more likely to experience stillbirths.⁵ Their babies are also more likely to be premature, born low birth weight, and small for their gestational age. These factors increase the risk of death during the first few months of life, morbidity, and the risk of diseases later in life.⁶

Increasingly, countries are moving towards the United Nations International Multiple Micronutrient Antenatal Preparation's (UNIMMAP) recommendation for MMS as an approach to meet the nutritional needs of pregnant women. There is clear evidence that MMS provides additional benefits over iron folic acid (IFA) supplementation in meeting the increased nutrient requirements of pregnancy, thus reducing adverse birth outcomes, particularly for anemic and underweight women.⁷ Nutrition International's MMS Cost-Benefit Tool⁸ demonstrates the role MMS could play in saving lives and reducing disability-adjusted life years (DALYs) in United States Government (USG's) priority geographies (**Table 1**).

The tool estimates that:

- More than 104,000 child deaths would be prevented and nearly 8 million DALYs averted if pregnant women who were already taking the recommended dose of IFA were switched to MMS;
- More than 200,000 lives would be saved if pregnant women who were receiving antenatal care were also given MMS; and
- As many as 368,944 lives would be saved if 95% of pregnant women in 13 USG priority geographies received MMS.

“There is clear evidence that UNIMMAP MMS provides additional benefits over iron folic acid supplementation”

MMS represents a good investment and a step towards equity in access to a better standard of care

Around the world, the overall quality of women's diets is poor, especially pregnant and lactating women in low- and middle-income countries (LMICs). Not surprisingly, recent analyses estimate that two-thirds of non-pregnant women of reproductive age worldwide suffer from micronutrient deficiencies.⁹ The state of nutrition is getting worse due to the disruptions to health and food systems caused by the COVID-19 pandemic, climate change and the global food crisis. While increasing access to nutrient-rich foods should be high on the policy agenda, most women will struggle to meet the higher nutrient needs of pregnancy through food consumption alone; supplementation with MMS is essential. A recent analysis conducted by the United Nations World Food Programme (WFP)

TABLE 1: The role MMS could play in saving lives and reducing disability-adjusted life years in USG’s priority geographies

Scale-up scenarios for MMS	Child deaths averted	DALYS averted
Switching to MMS among pregnant women who are already taking the recommended dose for IFA (90+ tablets)	104,794	8,614,852
Switching to MMS and improving coverage to those pregnant women who are already accessing antenatal care (ANC) services (4+ visits) but are not taking the recommended dose for IFA	204,665	16,341,298
Switching to MMS and improving coverage to reach 95% of pregnant women	368,944	29,087,229

Notes
 This exercise was done for USG’s 13 priority geographies: Burkina Faso, Democratic Republic of Congo, Mali, Nigeria, Niger, Senegal (Western and Central Africa), Ethiopia, Malawi, Mozambique, Tanzania, Uganda (Eastern and Southern Africa) and Bangladesh and Nepal (South Asia). The number of child deaths averted by transitioning from IFA to MMS includes stillbirth, neonatal mortality, and infant mortality. A DALY represents one lost year of perfect health. It is calculated by aggregating the effect of a health issue on mortality and morbidity.

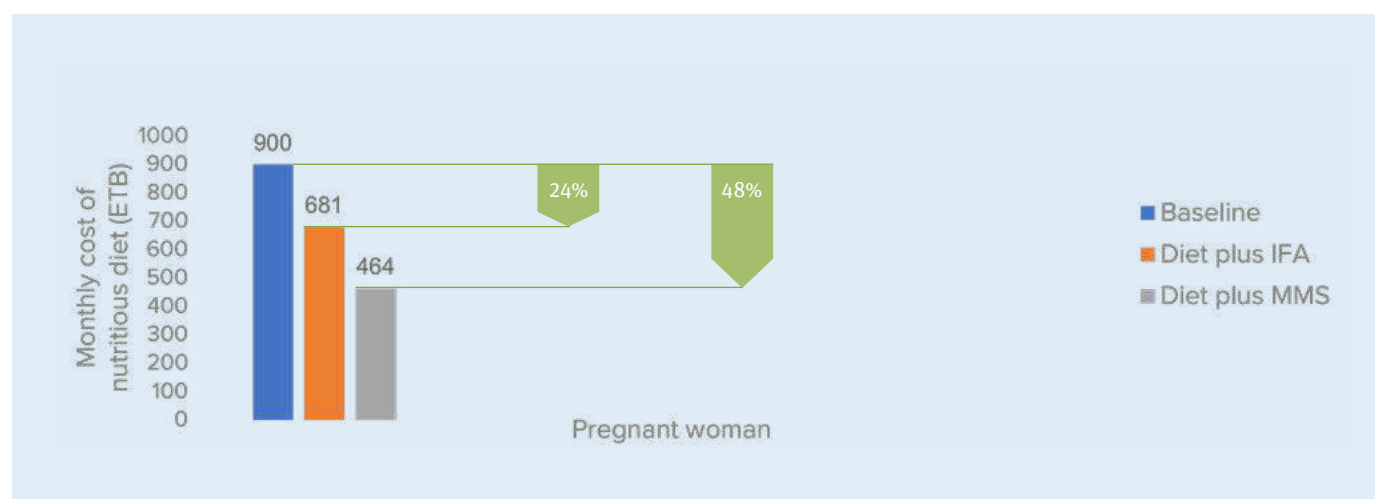
in Ethiopia found that MMS could reduce the cost of a nutritious diet by 48% for pregnant woman compared with a 24% reduction with IFA (Figure 3).¹⁰

In fact, MMS can help reduce the gap on maternal nutrition, especially for vulnerable pregnant women, while costing similar to the benchmark price of IFA. Currently, the leading UNIMMAP MMS supplier produces the supplement at less than US\$ 2.50 per woman per pregnancy,¹¹ which is close to cost parity with the historic price of IFA seen in the UNICEF Supply Catalogue.¹² It is also a social equalizer, given that doctors in high-income countries have long recommended multivitamins despite lower levels of

micronutrient deficiencies, while pregnant women in LMICs have been limited to a supplement containing only two nutrients – iron and folic acid. As a result of its cost-effectiveness, WHO added MMS to its Essential Medicines List (EML) in 2021.¹³

“MMS can help close the gap on maternal nutrition while being good value for money”

FIGURE 3: Reduction in the cost of a nutritious diet for pregnant women: MMS versus IFA



Renewed interest in prenatal supplementation with MMS provides an opportunity and obligation to address broader systems-level barriers

IFA has been a key component of antenatal care for pregnant women for decades, but implementation has been poor. Results for Development’s analysis of coverage of IFA programs in 14 USG priority geographies found that on average only 31% of pregnant women were taking the recommended dose (Figure 4). In addition, scale-up has been slow. Over the past decade, there has been a meager 1.6% increase in the availability of IFA in the eight countries where the data is available (Figure 5).

A renewed commitment to tackling long-standing barriers to nutrient supplementation for pregnant women (Figure 6) could help to overcome some of the challenges that implementing groups have faced in delivering IFA. First, in most settings, getting women

to start their ANC on time has been challenging due to both geographic accessibility and economic factors.¹⁴ Once a pregnant woman starts ANC, it is important that she receives high-quality health services. Yet several studies in multiple geographies have reported inadequate counselling and supplement supply, making it difficult for women to first initiate the use of IFA and then continue with the recommended dose.¹⁴⁻¹⁶ Finally, socio-ecological factors such as poor recognition of the harmful effects of micronutrient deficiencies on mothers and child’s health, forgetfulness, side-effects and social norms have hampered compliance levels.¹⁴⁻¹⁶ For these reasons, across the 14 USG priority geographies, there are pregnant women who are accessing some IFA but not the recommended dose (Figure 7). It is important to also note that a considerable proportion of pregnant women in countries like the Democratic Republic of Congo and Ethiopia are not accessing any IFA.

FIGURE 4: Coverage of IFA programs in 14 USG priority geographies

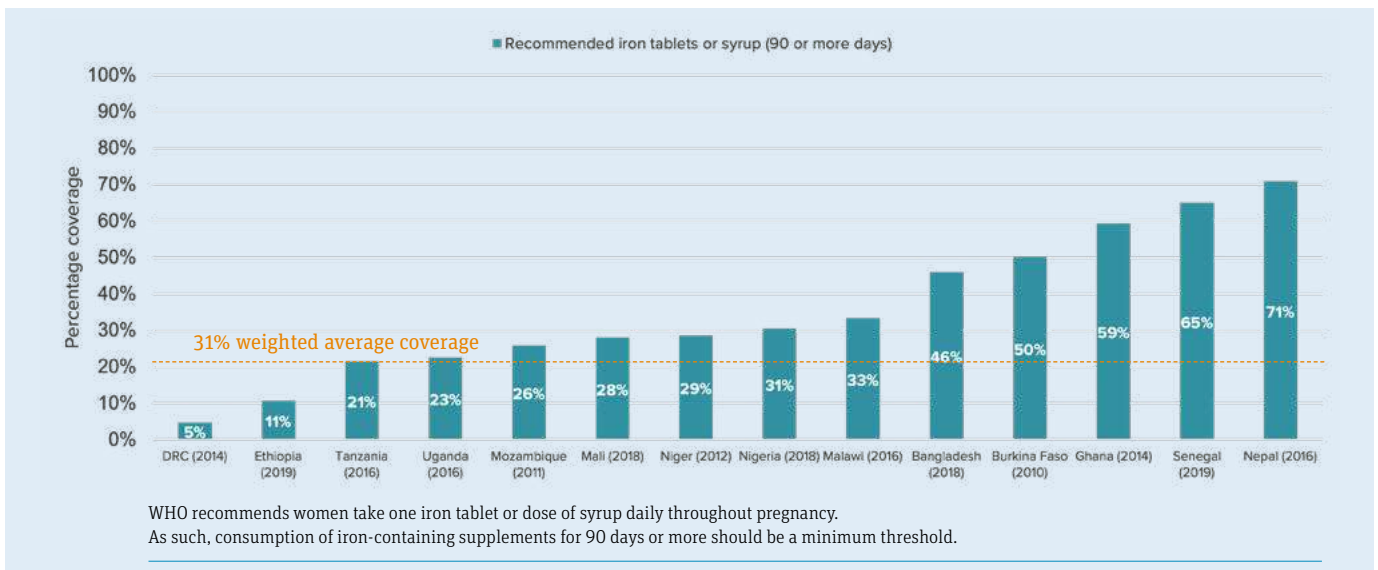


FIGURE 5: Trend in iron syrup or tablets (90+ days) for pregnant women from 2010 to 2020

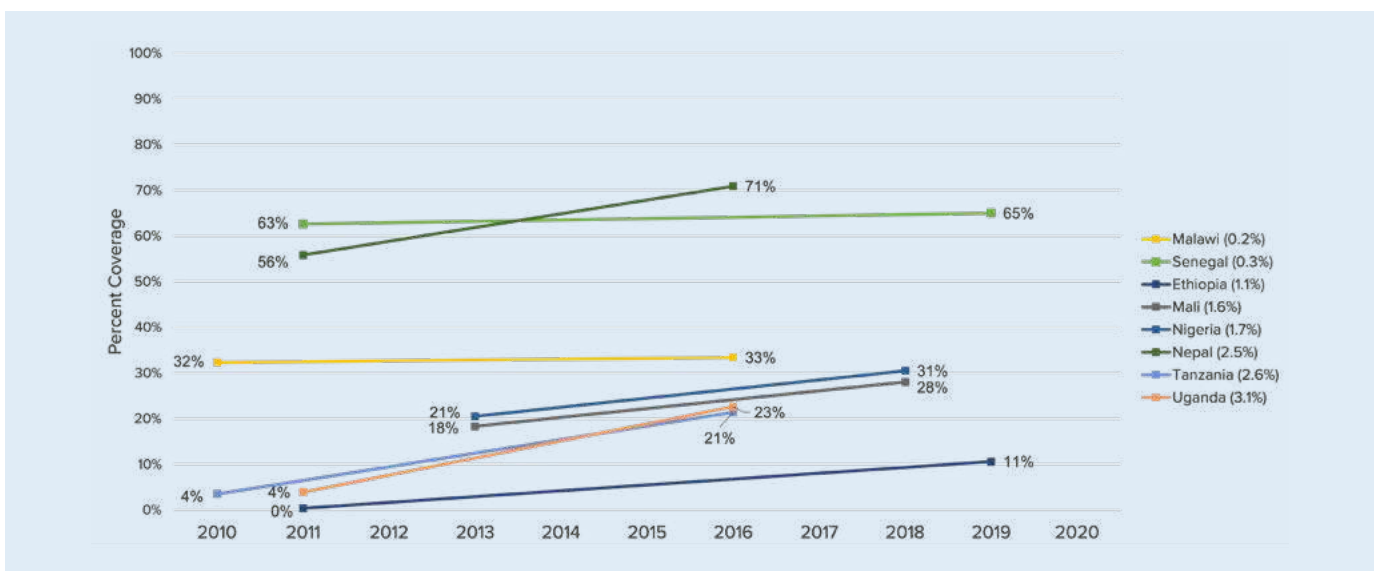


FIGURE 6: Tackling long-standing barriers to nutrient supplementation for pregnant women

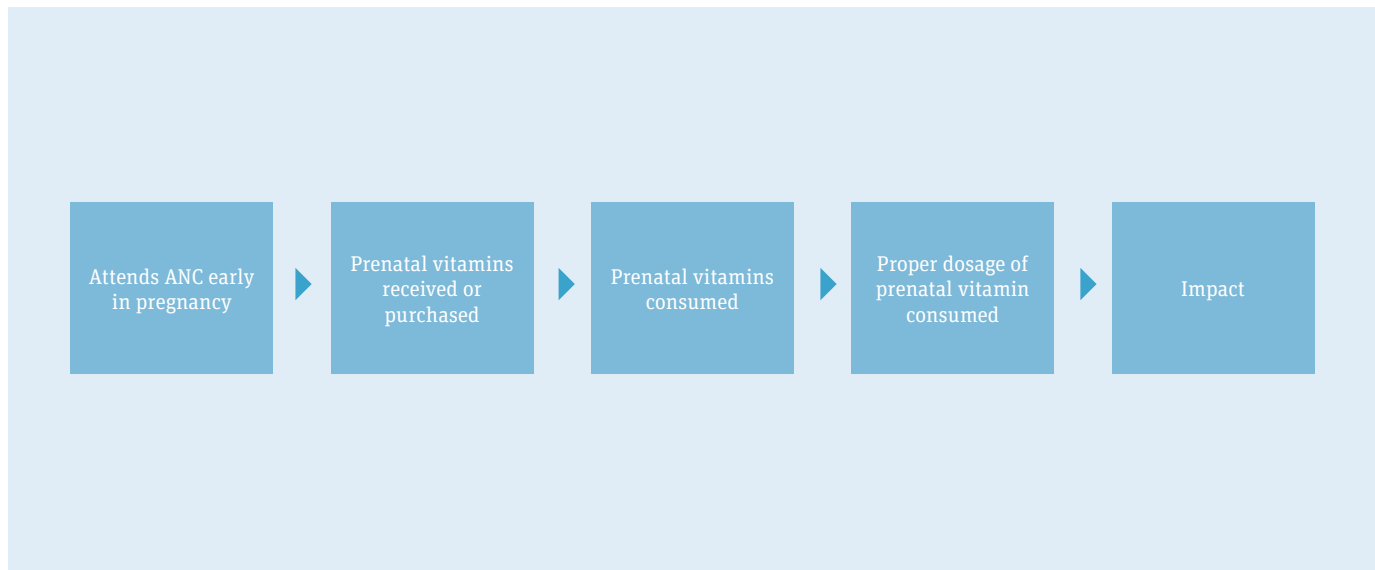
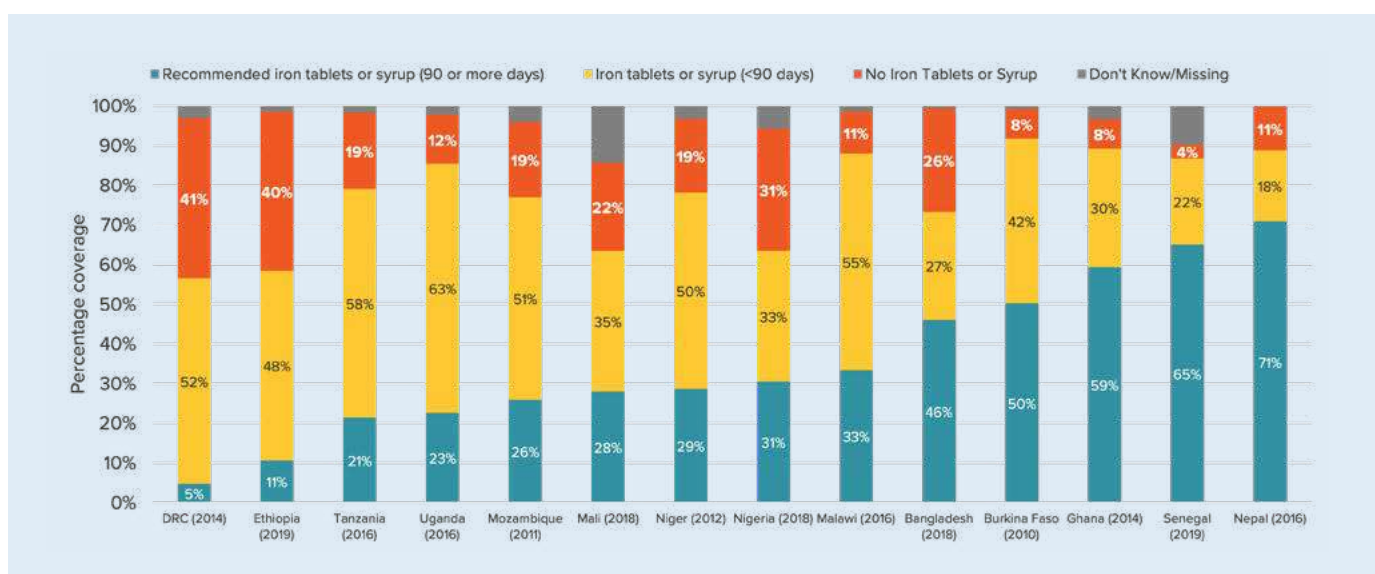


FIGURE 7: Access to and dosage of IFA among pregnant women in the 14 USG priority geographies



Today, amid growing awareness of the benefits of MMS, several groups are working on supply side issues to ensure high-quality UNIMMAP MMS is available and affordable to all pregnant women. There is also renewed interest in designing and testing new strategies to market MMS to women and improve adherence rates.

“Mothers and babies deserve nothing less”

ECF has a multi-pronged approach to supporting the scale-up of UNIMMAP MMS

Currently, there are a total of 15 countries globally in which MMS

is being introduced using an implementation science approach, while several more countries have expressed strong interest.¹⁷ ECF looks forward to partnering with other groups to support the scale-up of MMS, especially in geographies where country-level stakeholders have expressed strong interest and enthusiasm. To achieve sustainable distribution of the highest impact interventions, a range of players will need to work together to generate evidence, support global and national systems reform and secure increased financing.

Over the coming years, ECF remains committed to expanding MMS coverage through a two-pronged approach that includes research and advocacy. Through investments in research, ECF aims to identify barriers to MMS scale-up and generate evidence to inform service delivery. ECF is currently partnering with *Sight*

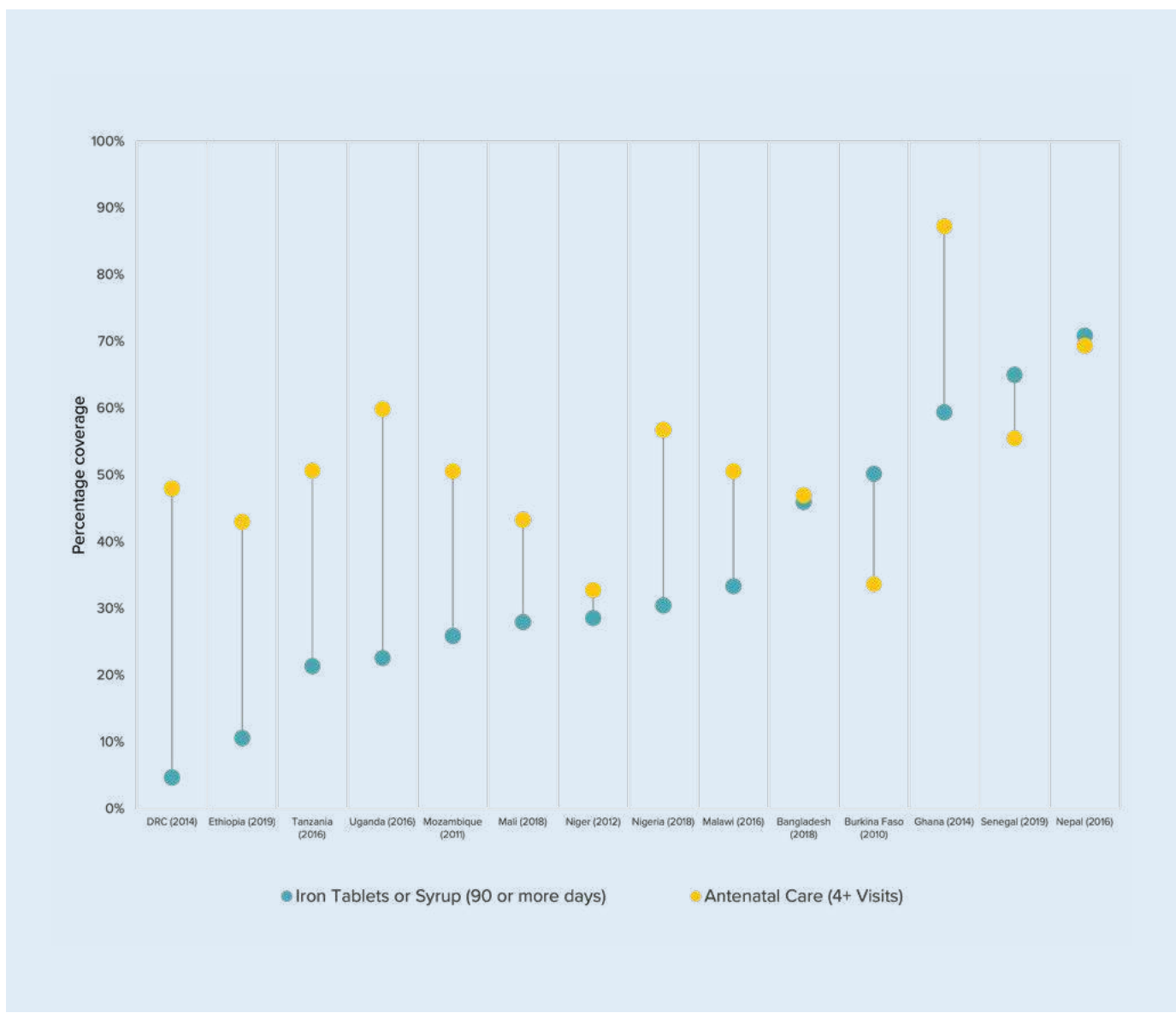
and Life Foundation to ensure local production and availability of MMS in Indonesia, Nigeria and South Africa by 2026. Similarly, in Ethiopia, we are supporting UNICEF to examine potential for local production, supply chain assessments and feasibility of market-based distribution to inform the Government of Ethiopia’s interest in MMS.

Alongside helping set up the supply infrastructure, ECF also looks forward to backing innovative research that encourages demand for, and adherence to, MMS. ECF is especially interested in supporting country-level stakeholders to make immediate progress, by ensuring that existing antenatal care services include the effective provision of MMS. As can be seen in the **Figure 8**, coverage of IFA, which is delivered through antenatal care, falls below the coverage of antenatal care in 11 of 14 USG priority countries. This denotes an opportunity to close the gap by targeting pregnant women who are already being reached through existing health services.¹⁸

In addition, ECF intends to support advocacy to inspire policy change and secure required financial investments. Ensuring that evidence generation and translation results in action requires advocacy for policy change, both globally and at the country level. Global advocacy could include urging WHO to update the relevant global guidelines on the use of MMS as well as mobilizing funders. ECF also intends to support local advocacy organizations and influential stakeholders to ensure inclusion of MMS in national guidelines and national EMLs.

ECF recognizes that a multitude of interventions spanning the health, food and social protection sectors are needed to address micronutrient deficiencies among pregnant women. MMS is a cost-effective tool that we already have for scale-up. Mothers and babies deserve nothing less.

FIGURE 8: Coverage of IFA versus coverage of antenatal care in 14 USG priority countries



Correspondence: Yashodhara Rana, Associate Director, Research, Eleanor Crook Foundation, Washington, DC, USA
Email: yrana@eleanorcrookfoundation.org

References

- 1 WHO. Children: improving survival and well-being. Published September 8, 2020. Accessed November 20, 2022. <https://www.who.int/news-room/fact-sheets/detail/children-reducing-mortality#:~:text=Malnourished%20children%2C%20particularly%20>
- 2 Lancet. Evaluation of maternal and child under-nutrition: Executive Summary of The Lancet Maternal and Child Nutrition Series. Published 2013. Accessed November 29, 2022. www.ennonline.net/evaluationofmaternalandchildundernutrition
- 3 Nourish the Future: A Proposal for the Biden Administration. Published online June 2021. Accessed November 14, 2022. https://www.endmalnutrition.org/img/nourishthefuture_paper_v13.pdf
- 4 USAID. Administrator Samantha Power delivers address on global food security titled, The Line between Crisis and Catastrophe. Published July 18, 2022. Accessed November 29, 2022. <https://www.usaid.gov/news-information/press-releases/jul-18-2022-administrator-samantha-power-delivers-address-global-food-security>
- 5 UNICEF. Maternal nutrition: Preventing malnutrition in pregnant and breastfeeding women. Accessed November 20, 2022. <https://www.unicef.org/nutrition/maternal>
- 6 Lopes K da S, Ota E, Shakya P, et al. Effects of nutrition interventions during pregnancy on low birth weight: an overview of systematic reviews. *BMJ Glob Health*. 2017;2(3):e000389. doi:10.1136/bmjgh-2017-000389
- 7 Smith ER, Shankar AH, Wu LSF, 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. *Lancet Glob Health*. 2017;5(11):e1090-e1100. doi:10.1016/S2214-109X(17)30371-6
- 8 Nutrition International. A tool to aid decision-making transitioning from IFA to MMS. Published July 20, 2022. <https://www.nutrition-intl.org/learning-resources-home/mms-cost-benefit-tool/>
- 9 Stevens GA, Beal T, Mbuya MNN, et al. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health*. 2022;10(11):e1590-e1599. doi:10.1016/S2214-109X(22)00367-9
- 10 Ethiopian Public Health Institute and World Food Programme. *Fill the Nutrient Gap - Ethiopia Summary Report – (English) | World Food Programme*. Ethiopian Public Health Institute and World Food Programme; 2021. Accessed November 14, 2022. <https://www.wfp.org/publications/fill-nutrient-gap-ethiopia-summary-report-english>
- 11 Kirk Humanitarian. Price Standards for MMS. Kirk Humanitarian. Accessed November 14, 2022. <https://kirkhumanitarian.org/why-mms/>
- 12 UNICEF. Iron, folic acid and combined iron and folic acid tablets – technical bulletin. Published December 2018. <https://www.unicef.org/supply/media/1431/file/Iron,%20folic%20acid%20and%20combined%20iron%20and%20folic%20acid%20tablets%20%E2%80%93%20technical%20bulletin.pdf>
- 13 New York Academy of Sciences. A Milestone: MMS Now On WHO's Essential Medicine List | The New York Academy of Sciences. [nyas](https://www.nyas.org/press-releases/a-milestone-mms-now-on-whos-essential-medicine-list/). Accessed May 11, 2022. <https://www.nyas.org/press-releases/a-milestone-mms-now-on-whos-essential-medicine-list/>
- 14 Siekmans K, Roche M, Kung'u JK, Desrochers RE, De-Regil LM. Barriers and enablers for iron folic acid (IFA) supplementation in pregnant women. *Matern Child Nutr*. 2018;14(S5):e12532. doi:10.1111/mcn.12532
- 15 Kavle JA, Landry M. Community-based distribution of iron–folic acid supplementation in low- and middle-income countries: a review of evidence and programme implications. *Public Health Nutr*. 2018;21(2):346-354. doi:10.1017/S1368980017002828
- 16 Desta M, Kassie B, Chanie H, et al. Adherence of iron and folic acid supplementation and determinants among pregnant women in Ethiopia: a systematic review and meta-analysis. *Reprod Health*. 2019;16(1):182. doi:10.1186/s12978-019-0848-9
- 17 Ajello, Clayton, Suwantika, Auliya, Santika, Otte, King, Shannon, Lange, Jarno de. *UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy*.; November 22.
- 18 Heidkamp RA, Wilson E, Menon P, et al. How can we realise the full potential of health systems for nutrition? *BMJ*. 2020;368:l6911. doi:10.1136/bmj.l6911

Fostering an Enabling Environment for UNIMMAP MMS for Pregnant Women: Progress and lessons learned from Cambodia and Vietnam

Ashutosh Mishra, Aishwarya Panicker

Vitamin Angel Alliance, Asia

Hou Kroeun

Helen Keller International, Cambodia

Meredith Jackson-deGraffenried

Helen Keller International, Asia

Ngan TD Hoang, Duong T Tran

National Institute of Nutrition, Hanoi, Vietnam

Rolf Klemm

Helen Keller International, USA

Monica Fox, Kristen M Hurley

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Quinn Harvey, Shannon E King, Clayton Ajello,

Kristen M Hurley

Vitamin Angel Alliance, USA

Key messages:

- The Vitamin Angel Alliance (VA), in partnership with Helen Keller International (Helen Keller) in Cambodia and the National Institute of Nutrition in Vietnam, conducted a comprehensive landscape analysis to better understand the context for introducing multiple micronutrient supplements (MMS) within the setting of strengthening antenatal care (ANC) services.
- A structured framework was used to conduct the landscape analysis which generated insights into the presence of maternal malnutrition, ANC systems and policies; and about regional similarities and challenges.
- A systematic approach to fostering an enabling environment is critical for successful MMS introduction as it encourages initial and continuous dialogue and discussion among key stakeholders and decision-makers.

Background

Introduction of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) multiple micronutrient

supplements (MMS) during pregnancy is supported by extensive research and work showing that it is efficacious, safe, cost-effective, and affordable.¹ The UNIMMAP MMS is an established formulation containing 15 vitamins and minerals, including iron and folic acid. When compared to iron and folic acid supplementation (IFA) alone, MMS is more effective in improving birth outcomes and has equivalent benefits in preventing maternal anemia.^{2,3} In 2020, the World Health Organization (WHO) recommended introducing MMS in the context of antenatal care (ANC) services informed by rigorous research, which includes implementation research to inform the transition from IFA to MMS.⁴ Unlike efficacy research, which demonstrates whether or not an intervention works in a highly controlled environment, implementation research (or more broadly, implementation science [IS]) is a systematic approach to understand and solve issues related to implementation within the context of real-world settings and programs.⁵

This IS approach often begins with efforts to understand contextual factors, barriers, enablers, and potential solutions to delivering and scaling an evidence-based intervention, like UNIMMAP MMS. To this end, systematic landscape analyses can be used to review existing literature on health and/or nutrition indicators in the country, map existing nutrition policies and programs, and conduct stakeholder interviews to help understand the barriers and opportunities related to introducing a new intervention within the context of national services and programs. During the landscape analysis and throughout the entire process, it is important to promote knowledge exchange, collaboration, and ownership among stakeholders to foster an enabling environment for the intervention. This can be achieved by raising awareness about the intervention and its supporting evidence, building consensus about the need and desire for the intervention, and engaging a broad coalition of multi-disciplinary stakeholders to provide periodic input throughout the process.

Given the clear evidence supporting the benefits of MMS relative to IFAS alone, the Vitamin Angel Alliance (VA), in partnership with Helen Keller International (Helen Keller) in Cambodia and the National Institute of Nutrition in Vietnam, conducted comprehensive landscape analyses to better understand the context for introducing UNIMMAP MMS against the backdrop of strengthening ANC services.

“The first step to exploring the introduction of a new evidence-based intervention often consists of fostering an enabling environment for that intervention”

Methods

In both countries, the landscape analyses included four components:

1. a comprehensive desk review of country-specific literature on maternal nutritional status and birth outcomes, existing programs, and policies related to improving maternal nutrition (including micronutrient supplementation in pregnancy), and the functionality of the ANC platform;
2. key-informant interviews and analyses to identify perspectives on UNIMMAP MMS among individuals belonging to four stakeholder groups including government, UN agencies, non-governmental organizations (NGOs), and donors;
3. consultative meetings with national government stakeholders and local manufacturers to explore supply chain context and readiness; and
4. a consensus-building workshop with officials from the Ministry of Health and other key stakeholders.

Results

Cambodia: Findings and recommendations from landscape analysis

Maternal undernutrition and multiple micronutrient deficiencies continue to be a public health problem in Cambodia, as indicated by the high prevalence of underweight (14% of women have a BMI <18.5 kg/m²) and mothers with folate deficiency (19%) and vitamin D deficiency (31%).⁶ In addition, maternal anemia is high, occurring in approximately half of the pregnant and non-pregnant women (53% and 45% respectively).⁶ However, iron deficiency anemia appears low among non-pregnant women (3%), suggesting that non-iron factors and deficiencies are contributing to the high prevalence of maternal anemia.⁷ In addition, 8% of maternal deliveries result in an infant born with low birth weight (LBW),⁶ and an estimated 18% are small for gestational-age (SGA).⁸ One of the key findings from Cambodia’s landscape analysis was that the data on broader micronutrient deficiencies in pregnancy is lacking.

In terms of national policies and programs, Cambodia currently has policies, for: (1) IFA in pregnancy and among women of reproductive age (WRA); (2) dietary counseling and weight gain monitoring in pregnancy; and (3) universal salt iodization. Programmatically, facility-based ANC services have the potential

to be an effective platform for delivering prenatal supplements, including UNIMMAP MMS, with a track record of high attendance and ability to promote adherence to interventions. For example, ANC attendance and IFA uptake is high, with nearly all (95%) pregnant women attending at least one ANC, the majority (76%) attending four or more ANC visits, and nearly all women (96%) taking iron-containing supplements during pregnancy.⁶

When investigating the supply context, government representatives and local manufacturers expressed interest in working towards immediate and long-term sustainable access to local UNIMMAP MMS supplies. Stakeholders suggested exploring both global and local production/procurement of UNIMMAP MMS with existing private-sector companies.

During the stakeholder workshop held on September 03, 2021, stakeholders agreed that UNIMMAP MMS is an efficacious, safe, and cost-effective intervention, but there is a need for implementation research (IR) to design and test implementation strategies in-country. In addition, there is a need for a national UNIMMAP MMS policy and a supply strategy to ensure a short-term (e.g., donated for IR) and long-term supply (e.g., locally manufactured and procured and/or procured globally) of UNIMMAP MMS.

Recommendations based on the findings of the landscape analysis included: (1) creating a national-level UNIMMAP MMS Steering Committee comprising technical stakeholders and influencers to provide advisory support and technical inputs for the UNIMMAP MMS initiative, and (2) creating policy briefs about the global MMS evidence and policies to support continued awareness-raising activities with decision-makers and planners. In addition, recommendations included the need for the creation of a roadmap (including a timeline, estimating total demand for MMS, and outline of resources needed) to transition from IFA to MMS that addresses national and subnational issues related to the following demand, delivery, and supply issues.

- **Demand.** Generate community awareness of UNIMMAP MMS, organizing national-level consultations with key stakeholders, and providing a platform for creating and passing a national UNIMMAP MMS policy for pregnant women.
- **Delivery.** Conduct a UNIMMAP MMS pilot program in line with the 2020 WHO context-specific recommendations for MMS in order to identify potential barriers and appropriate delivery strategies.
- **Supply.** Assess the potential capacity, cost, and regulatory issues related to ensuring a high-quality, affordable, and sustainable supply of UNIMMAP MMS, either through local, regional or international production and/or procurement.

Vietnam: Findings and recommendations from landscape analysis

In the last decade (2010–2020), Vietnam has experienced a reduction in anemia, zinc deficiency and vitamin A deficiency among pregnant and lactating women, as seen in [Table 1](#).⁹ How-

ever, while anemia prevalence overall has declined, iron deficiency anemia is still a public health issue, contributing to 37.7% of cases of anemia in non-pregnant women and 54.3% of cases of anemia in pregnant women in 2015.¹⁰

Vietnam has strong policies and guidelines for ANC services as well as micronutrient deficiency control. Some of these programs have been implemented through: (1) micronutrient supplementation for pregnant women; (2) large-scale food fortification with micronutrients; and (3) nutrition education and communication. Services that are included as part of ANC and covered by the national insurance scheme include provision of IFA, calcium, and vitamins A, B₁₂, C, D, E and K. These supplements are provided free of cost at antenatal health centers or can be bought from a pharmacy and reimbursed in cases where clinical evidence is available.¹¹ The annual report by the Ministry of Health Vietnam in 2020 indicated that approximately half of the pregnant women receive WHO-recommended standard prenatal screenings, and most (~70%) attend more than four ANC visits.¹²

While there are no policies that directly mention specific dose, composition or frequency of UNIMMAP MMS use for pregnant women, Vietnam has implemented UNIMMAP MMS for pregnant women in six provinces affected by salt intrusion and drought since 2016.¹³ By 2019, UNIMMAP MMS was provided to over 60,000 pregnant women in 85 poor districts through VA and UNICEF. Currently, along with UNIMMAP MMS supply, corresponding training & supervision, education & communication, and monitoring & evaluation activities are being planned. Women Unions and local government/village groups have been identified as potential partners of the program at the grassroots level.

Supply readiness: Government and civil society stakeholders have identified the need for a supply chain context assessment to understand the local UNIMMAP MMS manufacturing base in Vietnam and identify and test the potential for local manufacturing to secure a long-term supply of MMS. Currently, UNIMMAP MMS is not on Vietnam's essential medicine list (EML), and its uptake

is voluntary for pregnant women. There is, however, an opportunity within the structure of the existing Vietnamese healthcare system to accommodate UNIMMAP MMS into existing ANC services and on the national EML through continued advocacy and awareness-raising.

During a stakeholder workshop held on May 20, 2022, participants agreed that the revision of nutrition-related policies, guided by implementation research, is the next crucial step to enable UNIMMAP MMS introduction in Vietnam.

The key recommendations based on the findings of the landscape analysis in Vietnam include: (1) expanding the scope of the Nutrition Steering Committee to provide technical support for UNIMMAP MMS introduction and to act as a mechanism for creating a UNIMMAP MMS policy for all pregnant women; (2) introducing UNIMMAP MMS in select provinces through the existing ANC platform using IR; and (3) exploring financing options for UNIMMAP MMS introduction in Vietnam.

Similar to Cambodia, there was a recommendation to create a roadmap (including a timeline and outline of resources needed) to transition from IFA to MMS that addresses the following demand, delivery, and supply issues.

- **Demand.** Strengthen advocacy efforts to build awareness of global evidence on UNIMMAP MMS among policymakers, health workers and community members in Vietnam.
- **Delivery.** Conduct a systematic UNIMMAP MMS pilot program to train providers on UNIMMAP MMS and prepare for IR to examine the feasibility, acceptability of, adherence to, and cost of transitioning from IFA to MMS. There is also a need to consider the inclusion of UNIMMAP MMS in Vietnam's EML and health insurance program for pregnant and lactating women.
- **Supply.** Strengthen manufacturing capabilities and regulatory environment around UNIMMAP MMS and conduct additional supply context assessment to understand the local manufacturing base of UNIMMAP MMS in Vietnam.

TABLE 1: Anemia, zinc deficiency, and vitamin A deficiency, in Vietnam by year⁹

Indicator	2010	2015	2020
Anemia in pregnant women	36.5%	32.8%	25.6%
Zinc deficiency in pregnant women	90.0%	80.3%	63.5%
Low vitamin A concentration in breast milk in lactating women	35.5%	34.8%	18.3%

“Utilizing a systematic approach to fostering an enabling environment encourages dialogue and discussion among key stakeholders and decision-makers”

Summary of key lessons learned

Advantage of using structured frameworks to guide evidence-generation

Both countries utilized a structured (but adaptable) framework to conduct landscape analyses to understand the maternal nutrition situation in their national context, including into the status of maternal malnutrition, ANC systems and policies, and also about regional similarities and challenges. For example, strong maternal ANC policies and programs (including facility-based IFA programming) are in place in both countries, and both countries have the potential to effectively introduce and implement UNIMMAP MMS. However, existing challenges include the continued lack of awareness among key stakeholders related to the efficacy of MMS, the need for budget and cost-benefit analyses, and the need for a clear plan for local procurement and/or production.

Need for awareness-raising and consensus-building activities by and among local stakeholders

Consistent engagement with key government and other stakeholders and decision-makers has fostered an enabling environ-

ment for integrating UNIMMAP MMS into national ANC policy and programs in both Cambodia and Vietnam. Both countries have formulated a **UNIMMAP MMS taskforce or steering committee** to create and support a roadmap for existing and future MMS policy change, introduction, and scale-up.

The development of these national taskforces and advisory groups has helped ensure local ownership of efforts to transition from IFA to UNIMMAP MMS. A result of this engagement has been the continuous and growing interest of the Ministries of Health in both countries.

For example, in Vietnam, a country where UNIMMAP MMS is already provided within the context of emergency settings, continued efforts to raise awareness and build consensus provided the platform needed for advocating the inclusion of UNIMMAP MMS within the National Nutrition Policy.

Need for collaboration through partner dialogue and harmonization

Utilizing a systematic approach (as described above) to foster an enabling environment encourages initial and continuous dialogue and discussion among key stakeholders and decision-makers. As a result of the landscape analyses conducted in Cambodia and Vietnam, government agencies, in coordination with international NGOs (e.g., Helen Keller and VA that have local teams), academia and local manufacturers expressed interest in conducting short- and long-term activities and planning towards the introduction and scale-up of UNIMMAP MMS.



Participants of the May 2022 stakeholder workshop at the National Institute of Nutrition, Vietnam

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Conflict of Interest

Funding for the study described in this article was provided by Vitamin Angels. Dr Hurley is also seconded by Vitamin Angels and serves as Chief Nutrition Officer. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policies.

Correspondence: Dr Ashutosh Mishra, Senior Regional Technical Director, Vitamin Angel Alliance Asia Region, New Delhi, Delhi, India

Email: amishra@vitaminangels.org

References

- 1 Bourassa MW, Osendarp SJM, Adu-Afarwuah S, Ahmed S, Ajello C, Bergeron G, Black R, Christian P, Cousens S, de Pee S, Dewey KG, Arifeen SE, Engle-Stone R, Fleet A, Gernand AD, Hodinott J, Klemm R, Kraemer K, Kupka R, McLean E, Moore SE, Neufeld LM, Persson LÅ, Rasmussen KM, Shankar AH, Smith E, Sudfeld CR, Udomkesmalee E, Vosti SA. Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Ann N Y Acad Sci*. 2019 May;1444(1):6-21. doi: 10.1111/nyas.14121. Epub 2019 May 27. PMID: 31134643; PMCID: PMC6852202.
- 2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrients supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2019; 3:CD004905.
- 3 Smith ER, Shankar AH, Wu LS, Aboud S, Adu-Afarwuah S, Ali H, 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. *Lancet Glob Health*. 2017;(5):e1090–e1100.
- 4 WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: Multiple micronutrient supplements during pregnancy. Geneva: World Health Organization; 2020.
- 5 Peters DH, Adam T, Alonge O, Agyepong I A, Tran N. Implementation research: what it is and how to do it *BMJ* 2013; 347 :f6753 doi:10.1136/bmj.f6753
- 6 National Institute of Statistics, Directorate General for Health and ICF International. 2014 Cambodia Demographic and Health Survey Key Findings. Rockville, Maryland, USA: National Institute of Statistics, Directorate General for Health and ICF International; 2015. Accessed 10 December 2022. <https://dhsprogram.com/pubs/pdf/fr312/fr312.pdf>
- 7 Karakochuk CD, Whitfield KC, Barr SI, et al., Genetic Hemoglobin Disorders Rather Than Iron Deficiency Are a Major Predictor of Hemoglobin Concentration in Women of Reproductive Age in Rural Prey Veng, Cambodia, *The Journal of Nutrition*, Volume 145, Issue 1, January 2015, Pages 134–142, 2015.
- 8 Ota, E., Ganchimeg, T., Morisaki, N., Vogel, J. P., Pileggi, C., Ortiz-Panoso, E., Souza, J. P., & Mori, R. Risk Factors and Adverse Perinatal Outcomes among Term and Preterm Infants Born Small-for-Gestational-Age: Secondary Analyses of the WHO Multi-Country Survey on Maternal and Newborn Health. *PLoS ONE*, 9(8); 2014.
- 9 National Institute of Nutrition- Vietnam. Main findings of General Nutrition Survey 2019-2020. 2020. (Unpublished data)
- 10 National Institute of Nutrition- Vietnam. Micronutrient survey, 2014 - 2015; 2015. <http://vichat.viendinhduong.vn/103/print-article.html> Accessed 24 August 2022.
- 11 Ministry of Health, Vietnam. Circular No 30/2018/TT-BYT - List, cover rate, and conditions for liquidation of pharmaceutical drugs, biological products, radioactive drugs, and tracers covered by health insurance in Vietnam. Dated 30th October, 2018. Ministry of Health, Hanoi, Vietnam. (Unpublished data)
- 12 Ministry of Health, Vietnam. Summary of the achievements of the healthcare system in 2020; Responsibilities and solutions for 2021. (Unpublished data)
- 13 UNICEF Central Emergency Response Fund. Viet Nam: UNICEF's Humanitarian Coordinator Report On The Use Of Cerf Funds In Viet Nam: Rapid Response (pg. 9, 24). 2016. https://cerf.un.org/sites/default/files/resources/16-RR-VNM-20550-NR01_Viet%20Nam_RCHC.Report.pdf Accessed 24 August 2022.

Cost-effectiveness of Antenatal Multiple Micronutrient Supplementation Compared to Iron and Folic Acid Supplementation in India, Pakistan, Mali, and Tanzania: Results of a microsimulation study

Abraham D Flaxman, Alison Bowman, Nicole Young

University of Washington, Seattle, WA, USA

Key messages:

- We recently estimated the impact and cost of iron and folic acid (IFA), multiple micronutrient supplementation (MMS) and balanced-energy protein (BEP) supplementation in India, Pakistan, Mali and Tanzania by developing an individual-based dynamic microsimulation model of populations of newborns that tracked their health outcomes during the first two years of life.¹
- We found that MMS coverage of 90% of women who attend antenatal care (ANC) visits resulted in improving morbidity and mortality among children under 2 at an incremental cost of US\$ 52 per disability-adjusted life year (DALY) saved for Pakistan, US\$ 72 for Mali, US\$ 70 for India, and US\$ 253 for Tanzania.
- This supports the target of reaching high coverage of MMS for women through ANC as a cost-effective strategy to improve child health outcomes relative to the existing coverage and practice of providing only IFA.

Background

Without proper nourishment during pregnancy, the fetus may experience intrauterine growth restriction,² which can lead to babies born with low birthweight (LBW) and at increased risk of adverse neonatal child outcomes, chronic disease, diminished educational achievement, lower income, and lower weight of offspring

in adulthood.^{3,4} To address this, the World Health Organization (WHO) recommends multiple micronutrient supplements (MMS) containing IFA in the context of rigorous research.^{5,6} WHO also recommends balanced-energy protein (BEP) supplementation (foods in which protein provides less than 25% of the total energy content and which can come in various forms such as biscuits, beverages, or sachets made with locally sourced ingredients) in settings with high prevalence of undernourished pregnant women (more than 20%).^{7,8}

We modeled the impact on DALYs and the cost-effectiveness of supplementing 90% of pregnant women attending routine ANC with 1) universal MMS, 2) universal BEP, or 3) MMS + targeted BEP (where undernourished women receive BEP supplements containing MMS and adequately nourished women receive MMS). We used computer simulation to compare DALYs averted and incremental cost-effectiveness ratios in India, Pakistan, Tanzania, and Mali.

“Ensuring adequate maternal nutrition during gestation will have far-reaching benefits”

Methods

We developed a microsimulation model to compare the DALYs averted and incremental costs under various antenatal supplementation scenarios. We modeled the effect of pre-pregnancy BMI on birth weight and the effect of nutritional supplementation on birth weight. In our model, the effect of LBW acts directly on mortality and associated years of life lost (YLLs) in the neonatal period. Our model continued to track years lived with disability

(YLDs) due to protein-energy malnutrition, diarrheal diseases, measles, and lower respiratory infections, and YLLs due to all causes, until 2 years of age (Figure 1).

We compared DALYs from different intervention scenarios with the DALYs from the scenario with country-specific baseline coverage of IFA supplementation. For intervention scenarios, we scaled up supplementation coverage to 90%, where routine ANC attendees receive 1) universal MMS, 2) universal BEP, or 3) MMS + targeted BEP, in which attendees with low pre-pregnancy BMI below 18.5 kg/m² receive BEP containing MMS and

those with pre-pregnancy BMI above 18.5 kg/m² receive MMS (see Figure 2).

ANC, antenatal care; BEP, balanced energy protein (contains MMS); IFA, iron and folic acid; MMS, multiple micronutrient supplementation (contains IFA).

We calibrated our model to match estimates from the Global Burden of Disease 2017 study, as well as intervention effects on infant birth weight and costs per beneficiary from the literature (Table 1) and a population mean difference in birth weight of 138.46 g (95% CI: 102.25 to 174.68) between maternal BMI strata.¹

FIGURE 1: Conceptual model of the relationship between model components. The model captured morbidity due to lower respiratory infections, diarrheal diseases, measles, and protein-energy malnutrition and mortality from birth to 2 years of age.

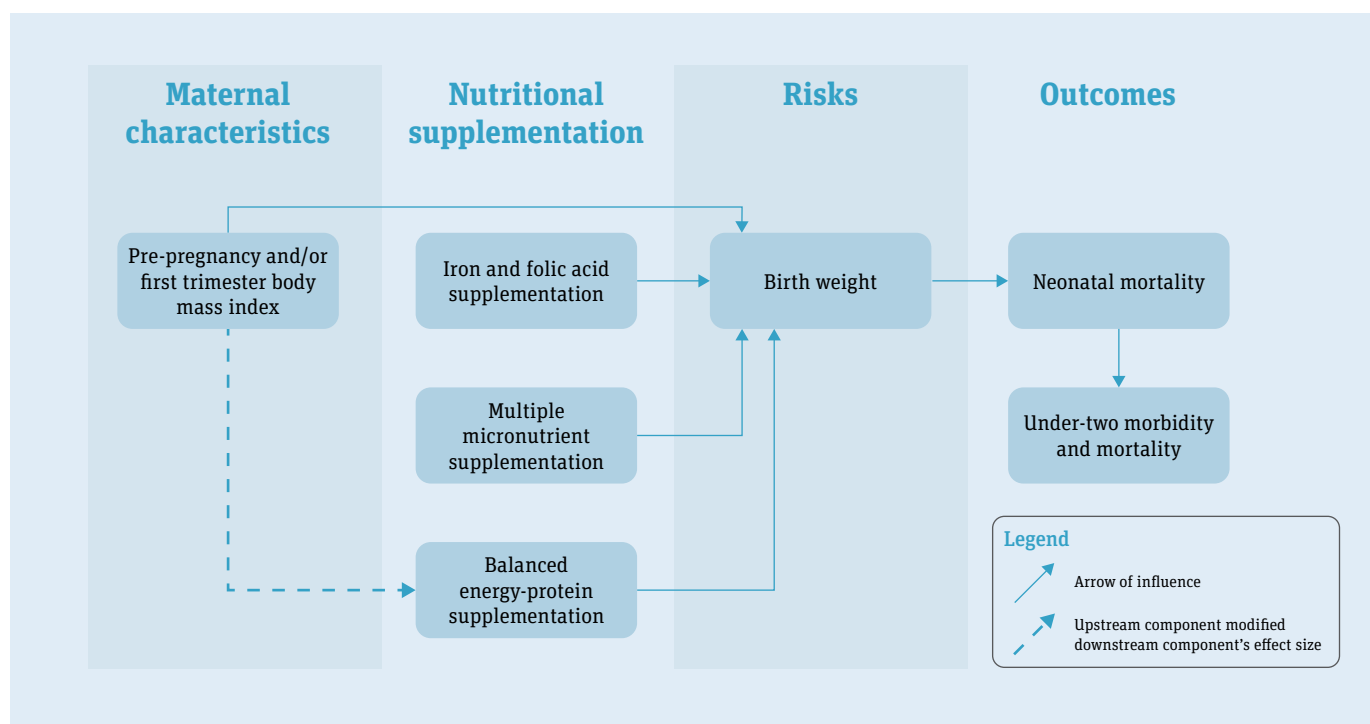
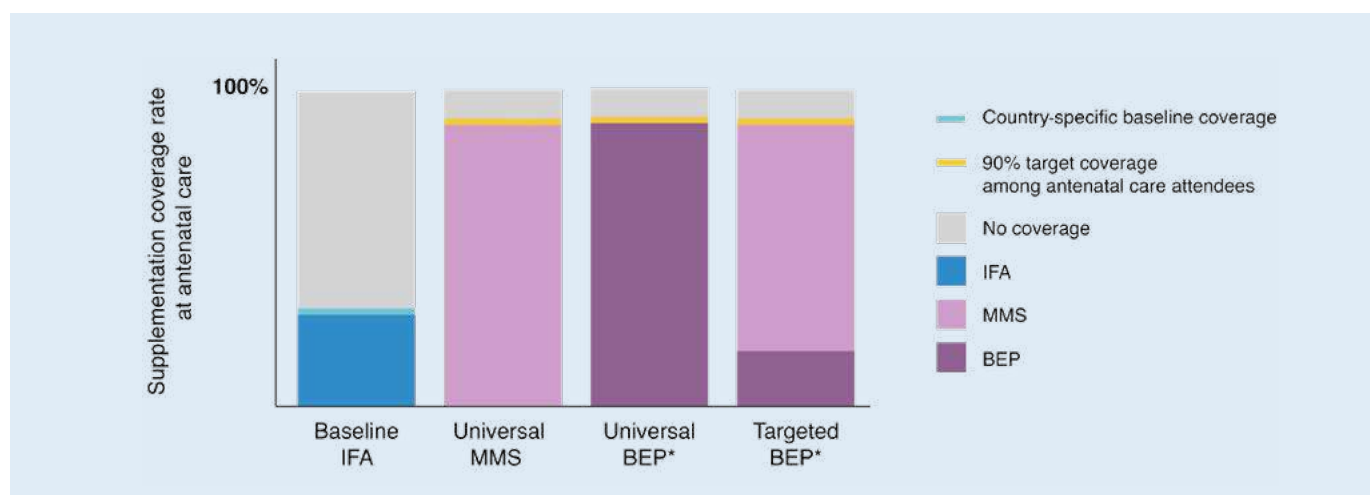


FIGURE 2: Supplementation coverage among those who attend antenatal care. In the targeted BEP scenario, 90% of antenatal care attendees receive BEP if undernourished and receive MMS if adequately nourished according to a pre-pregnancy body mass index threshold of 18.5 kg/m².



Results

Our model found that universal BEP averts the most DALYs, followed by MMS + targeted BEP, and then universal MMS. The intervention effects per 100,000 live births were largest in Pakistan, followed by Mali, India and Tanzania. This follows the pattern in LBW prevalence and percentage of baseline DALYs attributable to LBW. DALYs averted as well as total supplementation costs relative to baseline levels of IFA supplementation are shown in **Figure 3**.

Discussion

Inadequate nutritional intake during pregnancy is a major contributor to poor birth outcomes.¹² To improve birth outcomes, WHO recommends antenatal supplementation with multiple micronutrients containing IFA in the context of rigorous research¹³ and BEP in populations with more than 20% burden of undernourished pregnant women.⁷ As countries consider investing in MMS, there are opportunities to integrate supplement delivery with optimized formulations of BEP containing MMS, so that micronutrient and energy deficits can be met within a single vehicle. While

TABLE 1: Intervention parameters

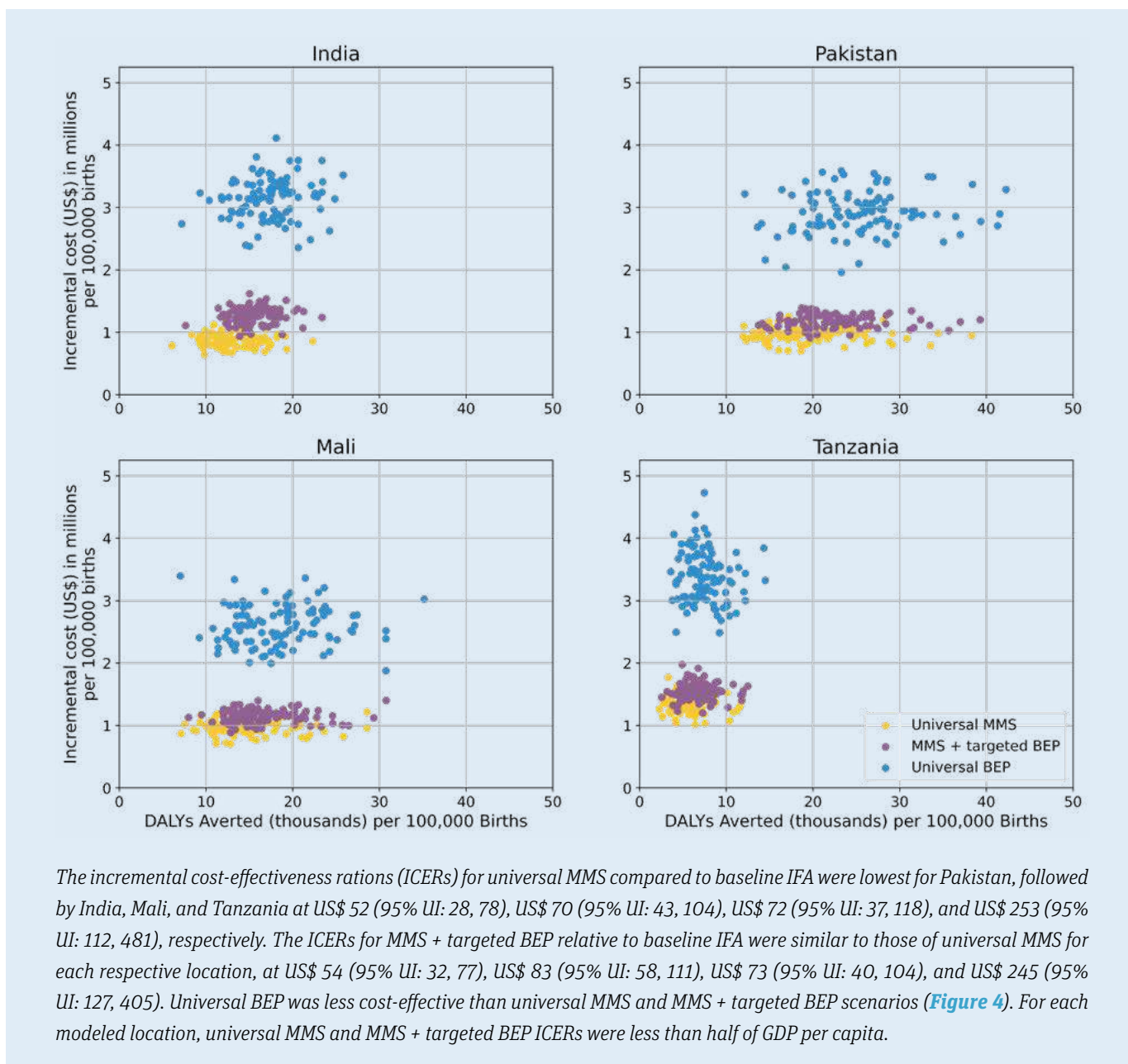
Intervention	Birth weight mean difference in grams (95% CI)	Cost per beneficiary in 2021 US\$ (95% CI)
Iron and folic acid supplementation	+57.53 (7.66 to 107.79) relative to no supplementation ⁹	32.8%
Multiple micronutrient supplementation	+45.16 (32.31 to 58.02) relative to iron with or without folic acid ^{1*}	80.3%
Balanced energy-protein supplementation		
Undernourished mothers	+66.96 (13.13 to 120.78) relative to control or no intervention ^{8**}	India: 47.88 (38.30 to 57.46) ¹¹
		Pakistan: 45.96 (36.66 to 55.15) ¹¹
Adequately nourished mothers	+15.93 (-20.83 to 52.69) relative to control or no intervention ^{8**}	Mali: 41.20 (32.96 to 49.44) ¹¹
		Tanzania: 41.90 (33.52 to 50.28) ¹¹

CI: confidence interval; US\$: United States dollar.

* Effect size obtained from a meta-analysis of 13 trials¹ (see supplement) obtained from an existing meta-analysis of MMS on the risk of low birth weight.⁵

** The trials from the 2015 Cochrane review compared a range of comparison groups. We interpreted the effect size as that of balanced energy plus vitamins and minerals versus vitamins and minerals.

FIGURE 3: Disability-adjusted life years (DALYs) averted in the first 2 years of life and incremental costs per 100,000 live births in each modeled location for each simulated scenario relative to the baseline scenario

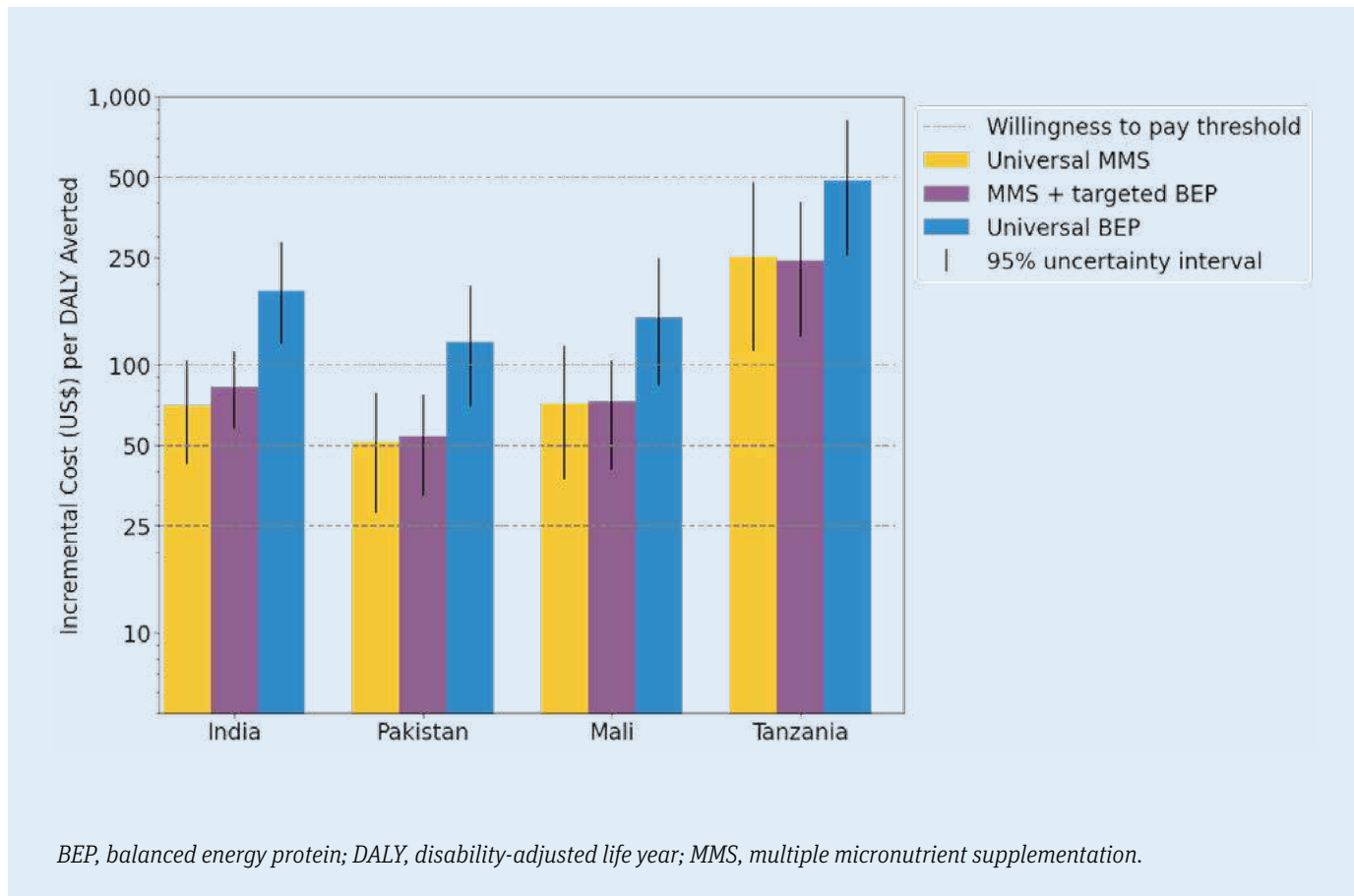


some cost-effectiveness analyses have shown that switching from IFA to MMS is very cost-effective in some countries,^{10,14-16} there are no detailed studies, to the best of our knowledge, estimating the cost-effectiveness of BEP or comparing the cost-effectiveness of MMS and BEP. Our study modeled the currently available evidence from Cochrane Systematic Reviews on antenatal IFA, MMS, and BEP supplementation as well as hypothesized effects of BEP as suggested by some evidence in a best-case scenario. We explored the impact of targeting undernourished women for BEP and found that MMS + targeted BEP averts more DALYs and remains cost-effective compared to universal MMS. Targeting may be an attractive and cost-effective strategy to consider, especially in countries that do not meet WHO's 20% undernourishment prevalence.

The strength of our approach came from using an individual-based microsimulation which we calibrated to match estimates from the GBD 2017 study. We used this to compare the impact of alternative supplementation scenarios on DALYs and costs. Our study provides decision-makers a side-by-side comparison of the incremental cost-effectiveness of scaling strategies for MMS and BEP compared to current baseline levels of antenatal IFA consumption in four countries with a considerable burden of undernourishment among pregnant women.

Our ICERs for universal MMS were greater than a recent cost-effectiveness analysis of antenatal MMS supplementation, which estimated US\$ 22.47, US\$ 22.64, and US\$ 61.82 per DALY for India, Pakistan, and Tanzania respectively (no data available

FIGURE 4: Incremental cost per DALY averted in the first 2 years of life in each modeled location for each simulated scenario relative to the baseline scenario (log-scale)



for Mali) using the MMS Cost Benefit Tool,¹⁵ which only considered commodity costs. Both studies showed an approximately three times greater cost per DALY averted in Tanzania than in India and Pakistan. These results may reflect the differences in baseline characteristics of the populations; since antenatal supplementation mainly affects birth weight, we expected the greatest gains in countries with higher baseline prevalence of LBW and higher percentage of DALYs attributable to LBW. Tanzania has an overall higher mean birth weight at baseline, which means additional improvement in birthweight from supplementation may not have as great an impact on averting DALYs.

“Our study indicates that universal MMS is cost-effective”

Limitations

Our study is limited by at least five key assumptions. First, we modeled supplementation to 90% of women who attend ANC, which may not be easy to achieve without substantial effort and costs, considering that only 20–40% of baseline women took antenatal iron for 90 days or more. Additionally, we applied

a fixed supplement duration of six months in our model and did not account for timing of ANC attendance, which also varies; those who attend late in pregnancy may not receive maximum benefit, which we did not account for. Further, our model does not consider differential utilization of ANC services by factors such as residency (urban versus rural) or maternal age, although such differences have been documented.¹⁷ If supplementation interventions do not reach higher-risk groups such as rural and/or young mothers, our model may overestimate their impact.

Second, differences in product formulation, duration of supplementation, timing of supplementation initiation, and comparison groups across trials may limit the generalizability of applying effect sizes of MMS and BEP from the published literature to local contexts.^{5,8}

Third, we model the impact of antenatal supplementation on birth weight at the individual level using population mean differences in birth weight and therefore do not model heterogeneity or stochastic variation of these effects at the individual level. Furthermore, while we considered uncertainty in the parameters used in this model, which are reflected in the UIs of our results, we did not attempt to quantify structural uncertainty regarding the relationships between parameters or heterogeneity at the sub-national level in our model.

Fourth, we only considered costs from a payer's perspective and did not consider other societal costs, such as time spent attending ANC for women.

Fifth, our model only considered how birth weight increases associated with antenatal supplementation affected neonatal mortality in the first 28 days of life (and associated ripple effects on DALYs in the first 2 years of life) and did not consider the potential impact of antenatal supplementation on outcomes such as maternal health or other downstream impacts on child health. If we had included such additional outcomes, we would likely have shown the interventions to be more cost-effective. Additionally, we model only a subset of causes of disability in our simulation. According to our model structure, including additional causes of disability may have slightly attenuated our estimates of DALYs averted due to additional YLDs experienced in the first 2 years of life among averted deaths in the neonatal period.

Conclusion

Our study indicates that universal MMS is cost-effective and shows that MMS in combination with targeted BEP averts more DALYs among children under 2 years of age than universal MMS while remaining cost-effective (under US\$ 100 per DALY for India, Pakistan, and Mali and under US\$ 250 per DALY for Tanzania). As countries begin to consider using MMS in alignment with recently updated WHO guidelines, targeted BEP could be considered as an additional cost-effective strategy to maximize benefit and synergize program implementation. Ensuring adequate maternal nutrition during gestation is a necessary and worthwhile investment that will have far-reaching benefits for current and future generations.

The text and figures in this chapter are based on Young, et al., *Cost-effectiveness of antenatal multiple micronutrients and balanced energy protein supplementation compared to iron and folic acid supplementation in India, Pakistan, Mali, and Tanzania: A dynamic microsimulation study*, <https://doi.org/10.1371/journal.pmed.1003902>.

Correspondence: Abraham D Flaxman, Associate Professor, Global Health; Associate Professor, Health Metrics Sciences; Adjunct Associate Professor, Paul G. Allen School of Computer Science and Engineering University of Washington, Institute for Health Metrics and Evaluation, 2301 5th Avenue, Suite 600, Box 358210, Seattle, WA 98121, USA
Email: abie@uw.edu

References

- 1 Young N, Bowman A, Swedin K, et al. Cost-effectiveness of antenatal multiple micronutrients and balanced energy protein supplementation compared to iron and folic acid supplementation in India, Pakistan, Mali, and Tanzania: A dynamic microsimulation study. *Myers JE, ed. PLOS Med.* 2022;19(2):e1003902. doi:10.1371/journal.pmed.1003902
- 2 Mandruzzato G, Antsaklis A, Botet F, et al. Intrauterine restriction (IUGR). *J Perinat Med.* 2008;36(4):277-281. doi:10.1515/JPM.2008.050
- 3 Institute of Medicine (US) Committee on Improving Birth Outcomes. *Improving Birth Outcomes: Meeting the Challenge in the Developing World.* (Bale JR, Stoll BJ, Lucas AO, eds.). National Academies Press (US); 2003. Accessed February 8, 2021. <http://www.ncbi.nlm.nih.gov/books/NBK222097/>
- 4 Victora CG, Adair L, Fall C, et al. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet.* 2008;371(9609):340-357. doi:10.1016/S0140-6736(07)61692-4
- 5 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2019;3:CD004905. doi:10.1002/14651858.CD004905.pub6
- 6 Tuncalp Ö, Rogers LM, Lawrie TA, et al. WHO recommendations on antenatal nutrition: an update on multiple micronutrient supplements. *BMJ Glob Health.* 2020;5(7):e003375. doi:10.1136/bmjgh-2020-003375
- 7 WHO recommendations on antenatal care for a positive pregnancy experience. Accessed February 8, 2021. <https://www.who.int/publications-detail-redirect/9789241549912>
- 8 Ota E, Hori H, Mori R, Tobe Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database Syst Rev.* 2015;(6). doi:10.1002/14651858.CD000032.pub3
- 9 Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T. Intermittent oral iron supplementation during pregnancy. *Cochrane Pregnancy and Childbirth Group, ed. Cochrane Database Syst Rev.* Published online October 19, 2015. doi:10.1002/14651858.CD009997.pub2
- 10 Kashi B, M Godin C, Kurzawa ZA, Verney AMJ, Busch-Hallen JF, De-Regil LM. Multiple Micronutrient Supplements Are More Cost-effective Than Iron and Folic Acid: Modeling Results from 3 High-Burden Asian Countries. *J Nutr.* 2019;149(7):1222-1229. doi:10.1093/jn/nxz052
- 11 Scott N, Delpont D, Hainsworth S, et al. Ending malnutrition in all its forms requires scaling up proven nutrition interventions and much more: a 129-country analysis. *BMC Med.* 2020;18(1):356. doi:10.1186/s12916-020-01786-5
- 12 Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet.* 2013;382(9890):427-451. doi:10.1016/S0140-6736(13)60937-X

- 13 Blencowe H, Krusevec J, de Onis M, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. *Lancet Glob Health*. 2019;7(7):e849-e860. doi:10.1016/S2214-109X(18)30565-5
- 14 Engle-Stone R, Kumordzie SM, Meinzen-Dick L, Vosti SA. Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness. *Ann N Y Acad Sci*. 2019;1444(1):35-51. doi:10.1111/nyas.14132
- 15 MMS cost benefit tool: integration of who meta-analyses draft technical report. Published 2019. Accessed February 15, 2021. <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>
- 16 Svefors P, Selling KE, Shaheen R, Khan AI, Persson LÅ, Lindholm L. Cost-effectiveness of prenatal food and micronutrient interventions on under-five mortality and stunting: Analysis of data from the MINIMat randomized trial, Bangladesh. *PLOS ONE*. 2018;13(2):e0191260. doi:10.1371/journal.pone.0191260
- 17 Langa N, Bhatta T. The rural-urban divide in Tanzania: Residential context and socioeconomic inequalities in maternal health care utilization. Amo-Adjei J, ed. *PLOS ONE*. 2020;15(11):e0241746. doi:10.1371/journal.pone.0241746

Formative Research: Barriers and enablers for successful implementation of antenatal MMS in Indonesia

Trisari Anggondowati, Evi Martha, Tika Rianty, Tiara Amelia, Basuki Imanhadi, Nancy Kosasih, Akhir Riyanti, Fitri Nandiaty, Nurul Dina Rahmawati, Latifah Farsia, Budi Utomo, Endang L Achadi

Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Otte Santika, Maulana Hasan, Markus Puthut Harmiko, Kusyanti Febriani Hapsari, Shannon E King, Quinn Harvey

Vitamin Angel Alliance, USA

Monica Fox, Kristen M Hurley

Vitamin Angel Alliance, Goleta, CA, USA; Center for Human Nutrition, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Key messages:

- In Indonesia, efforts are underway to understand how the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) multiple micronutrient supplements (MMS) formulation can be effectively introduced and scaled within the country's antenatal care system to support improved maternal nutrition.
- Formative research was conducted to understand contextual factors, enablers and barriers to UNIMMAP MMS use, and to inform the development of implementation strategies to achieve high MMS uptake and adherence in Indonesia.
- The formative research identified numerous enablers and barriers to prenatal micronutrient supplements introduction and scaling, which are described in the paper.

Introduction

Nearly half of the estimated 5.2 million pregnant women in Indonesia suffer from anemia,^{1,2} and adverse pregnancy outcomes associated with maternal anemia remain a public health problem. The prevalence of maternal mortality is high at 305 deaths per 100,000 live births, nearly 1 in 3 infants are born premature, and approximately 6% of infants are born with low birth weight (less than 2,500 g).¹

Since the 1990s, iron and folic acid (IFA) supplementation has been part of the antenatal care (ANC) system in Indonesia. The Indonesian IFA guidelines recommend that every pregnant woman receives at least 90 tablets of IFA during pregnancy beginning at the first ANC contact. IFA is delivered to pregnant women through primary health centers and its network of health outposts and outreach workers. Despite the decades-long implementation of the IFA program, there remains a wide gap between service delivery and the uptake and adherence by pregnant women, with a 2018 national survey showing that 87.6% pregnant women receive IFA, but only 51% received 90+ IFA tablets and only 38% consumed 90+ IFA tablets.¹ The country's maternal nutrition situation calls for more effective and comprehensive actions to strengthen nutrition service delivery within ANC and to explore the introduction of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) multiple micronutrient supplements (MMS) formulation in Indonesia.

Efforts to explore the introduction of UNIMMAP MMS in Indonesia

In an effort to foster an enabling environment for UNIMMAP MMS in Indonesia, a symposium was held at the Asian Congress of Nutrition conference in 2019, followed by a series of stakeholder meetings and consensus-building workshops with stakeholders. This resulted in consensus regarding the need for an MMS policy, a supply of MMS, and to conduct implementation research (IR) to increase MMS uptake and adherence. To support these actions, stakeholders agreed to the formation of an MMS Technical Advisory Group (TAG) in Indonesia.

Following the 2020 WHO recommendation to introduce MMS in the context of ANC, and informed by rigorous research,³ the University of Indonesia, Hasanuddin University, Airlangga University, the Center for Human Nutrition at the Johns Hopkins Bloomberg School of Public Health, and Vitamin Angel Alliance partnered to conduct IR across 25 districts across the country.

The IR objective is to ascertain how antenatal MMS can be effectively introduced and scaled within the country's ANC system to support improved maternal nutrition, with the goals of creating an enabling environment for MMS introduction; understanding contextual factors, enablers, barriers and potential solutions to

MMS introduction through formative research; designing and testing implementation strategies; and ultimately raising awareness through and among stakeholders for the investment of domestic resources to support MMS scale-up. At the same time, within the context of IR, efforts are underway to ensure a local supply of UNIMMAP MMS. For example, a supply context assessment (including cost-benefit and budget impact analyses, which is described in the MMS 2.0 Special Report in Supply Context Assessment [SCA] Tool for National Governments) has been conducted and efforts to build capacity for local manufacturing have been initiated, with local manufacturing available to the government by early 2025.

“The IR objective is to ascertain how antenatal MMS can be effectively introduced and scaled within the country’s ANC system to support improved maternal nutrition”

Formative research methods and results

This paper presents the results of the formative research that was conducted to understand the barriers and enablers to MMS coverage and adherence. The formative research involved multiple methods, including: 1) a desk review on the nutrition situation in the country; 2) a content analysis of existing IFA communication materials; 3) a quantitative electronic survey gathering data from primary health care (puskesmas) (n=103), health providers (n=380) and pregnant women (n=168); 4) qualitative interviews through in-depth interviews (IDIs, n=60) and group discussions (n=15) with key stakeholders from the community up to the central level; and 5) a co-design workshop with key stakeholders (n=17).

Desk review

We reviewed existing peer-reviewed and grey literatures on the existing IFA program, as well as barriers to and facilitators of adherence to IFA consumption. We also reviewed regulations and guidelines pertaining to the IFA program. The findings from the desk review were used to inform the development of formative research tools.

Content analysis and quantitative e-survey

The content analysis was used to identify what IFA-related communication materials exist and for what target audiences, and to assess the quality of existing communication materials to promote adherence to IFA, and ultimately MMS. Data on communication materials was extracted and coded by a trained team using the checklists related to material type (originating organization, intended audience[s] and topics covered) and quality (technical accuracy,

appropriateness, behavioral focus and persuasive appeals). In addition, an electronic survey among primary health care (puskesmas) (n=103 clinics) was used in relation to the content analysis to examine what communication materials were actually being used in the primary health care (puskesmas).

Through the content analysis, 83 IFA and anemia-related communication materials were identified. Most materials (>70%) provided technically accurate and appropriate messages about IFA but lacked a behavior change focus or persuasive appeal. Similarly, based on the electronic survey, we found that most clinics (97%) used the *Maternal and Child Health Booklet*, which includes information on IFA but also lacks behavioral change messages or counseling.

Qualitative interviews

The formative research included qualitative interviews and group discussions in six districts, which were selected based on socio-cultural diversity, variation of ANC coverage levels, and regions. We conducted in-depth interviews with the community (n=31), consisting of pregnant women, their husbands, mothers/mother-in-laws, kadres (community health volunteers), and community leaders, service providers (n=18), and ANC administrators (n=11), and small group discussions with district (n=3), provincial, (n=3) and national health officials (n=3), and with other professional organizations (n=2) and NGOs (n=4).

Human-centered co-design (HCD) workshop with key stakeholders

Key findings from the formative research (described below) were then used to facilitate a 3-day human-centered co-design workshop facilitated by the Johns Hopkins Center for Communication Programs (JHU-CCP) and the JALIN Foundation, and attended by pregnant women, midwives, and health officials from several districts ([see photo](#)). Based on the workshop, initial prototypes of different types of communication materials were developed and tested. The prototypes included a calendar for recording MMS consumption, cue cards, and the MMS bottle label.

“Progress in Indonesia has led to government commitment to work towards the transition from IFA to UNIMMAP MMS within the national health system”

Key Findings: MMS-Related Enablers

1. *Growing global and national commitment to introduce UNIMMAP MMS.*
2. *Women and families trust healthcare providers.* We often hear health providers say that women do not listen to them, but we found that women perceive them as the most trustworthy source of health information; and we did not find ta-



Human-centered design workshop in Indonesia

boo/traditional beliefs to be as prevalent as we would have expected.

3. *Providing MMS at ANC visits has the potential to result in high MMS coverage* as ANC services are widely available throughout Indonesia, including in rural and remote areas. The national survey showed that about 96% pregnant women had contact with a health provider in the context of ANC during their pregnancy.¹ The existing ANC system, including the various levels of care provided at outpost level in the village and at sub-village level, offers a strong platform for the introduction of MMS in Indonesia.
4. *Most pregnant women (86%) in Indonesia started ANC during their first trimester.*
5. *The idea of switching from IFA to MMS was well received* by women, their families, and health care providers.
6. *The introduction of MMS is supported by policymakers*, but nearly all raised issues related to scalability and sustainability, and emphasized the importance of local MMS production.
7. *Given technology advances in Indonesia, there is potential for the use of digital technology to promote MMS adherence.*
8. *Recent changes to IFA procurement regulation.* Beginning in 2022, the central government issued a new regulation that transfers responsibility for IFA procurement to the province level. The changes are expected to cut down the bureaucracy and make the procurement, distribution and monitoring of prenatal supplements more efficient.
9. *Introduction of IFA adherence into routine monitoring systems.* As part of the government regulations to reduce child

stunting, IFA adherence is required to be collected and reported through the existing health monitoring system. The government is currently exploring how to collect high-quality adherence data within the existing monitoring and evaluation system and the most substantive use of digital strategies to capture this routine health data. The addition of this indicator into the existing monitoring system should ultimately help monitor MMS adherence and support efforts to ensure that high uptake and adherence are achieved and maintained.

Key Findings: MMS Related Barriers

1. *Lack of clarity related to supplement dose.* Due to supplement stock-outs and varying provider implementation strategies, some pregnant women were not aware of the correct dosing regimens.
2. *Supplement side-effects.* Some pregnant women reported experiencing side-effects when taking IFA. Common side-effects included nausea, vomiting, and dizziness.
3. *Existing ANC practices.* Some providers reported not providing IFA early in the first trimester in order to prevent side-effects such as nausea.
4. *Limited counseling related to prenatal supplements in ANC* due to time constraints on the part of the midwife and limited guidelines, training and job-aids on the part of health providers (especially midwives).
5. *Existing stock shortage.* Within the existing IFA program, there are stock issues related to both shortage of stock and

uncertainty in the distribution schedule of the product to the district and health center level. The uncertainty of stock availability in some districts leads to health providers giving pregnant women less than the recommended amount of IFA tablets due to fear of experiencing a later shortage. Thus, pregnant women do not obtain a sufficient number of supplements to take for the recommended period of time.

6. *Low provider knowledge and some negative perceptions related to supplement use.* While most providers were aware of the benefits of prenatal supplements, some were not aware of the benefits for the offspring.
7. *MMS formulation, packaging, and tablet count.* Despite the proven efficacy of UNIMMAP MMS, some health providers remained concerned about the lower iron content in MMS (30 mg) compared to IFA (60 mg). In addition, the UNIMMAP MMS contains 65 ug of selenium which is currently higher than that mandated by the Indonesian FDA (currently 60 ug).
8. *Mixed views existed related to MMS packaging.* Health providers often shared that they preferred individually packaged pills (e.g., blister packs) for safety reasons, perceived ease of ensuring and monitoring adherence, and smaller facility storage requirements. Providers also expressed concern that giving too many pills at one time may reduce adherence and affect the quality of the product over time (i.e., lead to degradation). On the other hand, some pregnant women felt that bottles were better, and of higher quality given they resembled more expensive commercial products.

Progress and next steps

Efforts to foster an enabling environment for UNIMMAP MMS in Indonesia have led to national engagement and commitment towards MMS introduction within the context of implementation science – designed to systematically address issues related to MMS policy, delivery, and supply.

The formative research described in this article was the first step towards understanding the potential enablers (e.g., national commitment, etc.) and barriers (e.g., side-effects) of MMS introduction from the perspective of multiple sources, and has informed the development and testing of MMS behavior change and packaging strategies (i.e., 90-vs. 180-count bottle) in Indonesia.

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Conflict of Interest

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Correspondence: **Trisari Anggondowati**, Center for Family Welfare, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia
Email: trisarianggondowati@ui.ac.id

References

- 1 Riskesdas: Institute for Health Research and Development, Ministry of Health Republic of Indonesia. 2019. *Laporan Nasional Riskesdas 2018* [National Report of 2018 Basic Health Research]. Published by *Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan*, Jakarta. Retrieved from <http://repository.litbang.kemkes.go.id/3514/> Accessed 18 October 2022.
- 2 Profil Kesehatan: Ministry of Health Republic of Indonesia. 2019. *Profil Kesehatan Indonesia Tahun 2018* [2018 Indonesia Health Profile]. Published by Ministry of Health Republic of Indonesia, Jakarta. Retrieved from <https://www.kemkes.go.id/downloads/resources/download/pusdatin/profil-kesehatan-indonesia/profil-kesehatan-indonesia-2018.pdf> Accessed 18 October 2022.
- 3 World Health Organization (2020). WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy. Available for download at: <https://www.who.int/publications/i/item/9789240007789> Accessed 18 October 2022.

An Assessment of Barriers and Enablers to Uptake and Adherence of UNIMMAP MMS for Pregnant Women in Haiti

Minaud Dacius

Vitamin Angel Alliance, Haiti

Joseline Marhone-Pierre

Haitian Ministry of Public Health and Population,
Port-au-Prince, Haiti

Casimir Alfred

Haitian Health Foundation, Jérémie, Haiti

Shannon E King, Jillian Emerson, Quinn Harvey

Vitamin Angel Alliance, USA

Kristen M Hurley, Monica Fox

Vitamin Angel Alliance, USA; Center for Human Nutrition, Johns
Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Key messages:

- Formative research was used to understand the current perceptions, knowledge and experiences with antenatal care (ANC) services and prenatal multiple micronutrient supplements (MMS) in Haiti.
- The Socio-Ecological Model (SEM) provided the framework for the formative research design and analysis, allowing for influences at the individual, interpersonal, community, health system and policy level to be explored.
- This paper describes numerous multi-level insights into the barriers and enablers for ANC and MMS uptake and adherence in Haiti.

Introduction

A high number of women in low- and middle-income countries (LMICs) experience micronutrient deficiencies during pregnancy due to increased nutrient demands for both the mother and fetus.¹ In LMICs, supplementation with iron and folic acid (IFA) is the current standard of care for pregnant women. However, evidence from efficacy trials shows that the use of daily United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP multiple micronutrient supplements [MMS] containing 15 vitamins and minerals, including iron and folic acid) during pregnancy reduces the risk of poor birth outcomes above that achieved with IFA alone.^{2,3}

In 2020, the World Health Organization (WHO) recommended the introduction of MMS informed by rigorous research, including implementation research to support the transition from IFA to MMS.⁴ In line with this guidance, the Haitian Ministry of Public Health and Population (MSPP), in partnership with Haitian Health Foundation (HHF), Vitamin Angel Alliance (VA), and the Johns Hopkins Bloomberg School of Public Health (BSPH), began to conduct implementation research in 2019 to inform the introduction of MMS in Haiti. As part of the overall project, which has been described previously,⁵ the initial formative research aimed to assess the current perceptions, knowledge and experiences with ANC care and prenatal micronutrient supplementation in Haiti. Specifically, it aimed to i) understand the current knowledge and experiences of ANC and supplements among pregnant women, their families, and the broader community in Haiti, and ii) identify the barriers and enablers to uptake and adherence to ANC and prenatal supplements during pregnancy.

Methods

The formative research was conducted over a three-year period (2019–2021) due to political instability, natural disasters and the COVID-19 pandemic. It was conducted in five districts of the Grand'Anse department, selected based on high rates of maternal anemia, an existing ANC platform and ongoing distribution of IFA. The formative research included a literature review, stakeholder analysis (including an assessment of the nutritional situation) and a qualitative assessment. For the literature review, articles selected included: i) empirical research on prenatal supplementation, ii) research published in peer-reviewed English-language journals between 1996 and 2017, and research conducted in LMICs. Search terms included iron folic acid (or IFA), multiple micronutrient supplementation, pregnancy or prenatal supplementation, and LMICs. For the stakeholder analysis, a stakeholder mapping was conducted to identify people who hold influence and power in the areas of ANC and maternal nutrition. In addition, a PESTLHE tool (**Figure 1**) was used to engage stakeholders to better understand political, economic, social, technological, legal, health and environmental factors that might influence maternal ANC and supplement use and adherence.^{6,7}

FIGURE 1: PESTLHE (Political, Economic, Social, Technological, Legal, Health, and Environmental Factors) Tool describing factors that may affect behavior change communications (BCC) intervention

P	Political	Political campaigns / elections Expected change in government
E	Economic	Currency stability, food insecurity, poverty Social protection programs, links with other communities (i.e., trade, roads)
S	Social	Language, culture, religion, clan/ethnic considerations, gender relations, literacy, major public health/social marketing campaigns
T	Technological	Technology tools: mobile penetration, TV, radio coverage, access to internet
L	Legal	Policies (e.g., nutrition policy, code), institutional mandates, approval for communication
H	Health	Malnutrition prevalence, mortality, malaria, access to contraception Program coverage and use
E	Environmental	Harvest season, major drought, rainy season (cyclones, road/boat passage)

The qualitative assessment included: i) in-depth interviews (IDIs) with pregnant women and new mothers (had child within past 6 months), influential family members, community leaders, and health care providers, ii) focus group discussions (FGDs) with health care providers, and iii) an acceptability trial with pregnant women. (Table 1). IDI and FGD audio records were transcribed and translated from Creole to English. Inductive codes were generated using a subset of transcripts prior to coding of all transcripts. Dedoose software⁸ was used to facilitate data management, orga-

nization and coding. All transcripts were thematically analyzed. *Sight and Life* Foundation provided technical guidance in conducting the formative research.

Theoretical underpinnings

The Socio-Ecological Model (SEM) provided the guidance for the basis of the formative research study design and analysis (Figure 2).⁹ The SEM allowed for the capture of influences at the following levels: **individual** (i.e., pregnant women’s knowledge, atti-

TABLE 1: Participant sample for qualitative component of formative research

	District 1	District 2	District 3	District 4	District 5	Total
In-depth interviews (IDIs)						
Pregnant women / New mothers	4	4	2	2	2	14
Family members	2	2	2	2	2	10
Community leaders	3	2	2	2	1	10
Health care providers	3	8			3	14
TOTAL						48
Focus group discussion (FGDs)						
Health care providers	3	1	2	2	1	9
TOTAL						9
Acceptability trial						
Pregnant women	7	6	6	4	0	23
TOTAL						23

tudes, and behaviors); **interpersonal** (i.e., family, friends, social networks, and service providers); **community** (i.e., government [MSPP], NGOs, community leaders, etc.); **health system** (i.e., government [MSPP], NGOs, private sector, and other safety net programs); and the **policy environment** (i.e., national, state, and local policies and laws). The research received ethical approval from the Haitian MSPP Bioethical Review Committee and the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

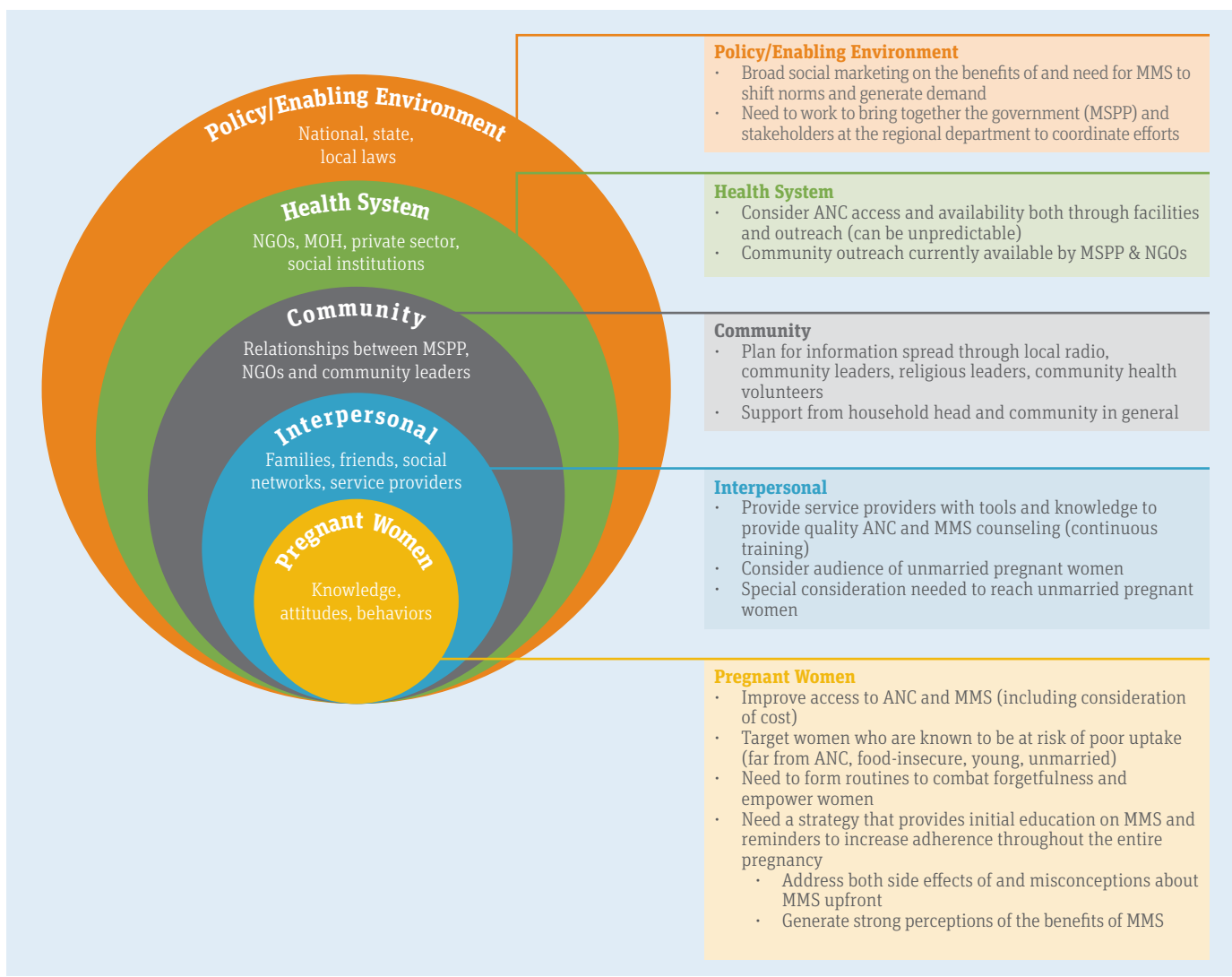
“The Socio-Ecological Model provided the guidance for the basis of the formative research study design and analysis”

Results

Literature review and stakeholder analysis

Forty-six unique articles were found that met selection criteria. Examples of key findings from the literature review and stakeholder analysis (**Figure 2**) are organized based on the SEM. At the **individual level**, findings suggest a need for improved access to ANC and prenatal supplement education, behavior change strategies, and commodities (including reducing client cost). Similarly, at the **interpersonal level**, equipping service providers with tools and knowledge that would enable them to provide quality ANC and prenatal supplement counselling was suggested. At the **community, health system, and policy level**, findings suggest a need for: i) a maternal messaging campaign using community health workers, radio, and community leaders; ii) increasing ANC access and availability through health facilities and community outreach; and iii) sharing evidence related to the benefits of MMS to decision-makers, respectively. Findings from the literature review were then further validated through stakeholder and/or PESTLHE tool interviews and analyses.

FIGURE 2: Theoretical framework, analysis and results⁹



Qualitative assessment

A total of 48 IDIs and 9 FGDs were conducted with pregnant women / new mothers, family members, community leaders and health care providers. In addition, 23 pregnant women completed a two-week acceptability trial, in which they were provided UNIMMAP MMS and asked to take them each day for two weeks. The acceptability trial aimed to understand women's perceptions and experiences taking the supplement. (Table 1).

Perceptions of pregnant women

When interviewed, pregnant women / new mothers and family members often placed emphasis on wanting to be a good mother combined with little control over life choices or activities and described predominately negative pregnancy experiences and lack of support.

"I hope that she/he is [BORN] healthy, alive. I hope that God gives him/her a good memory so that he/she can learn well." [pregnant mother]

"Her parents are giving her hard time, she is crying sometimes ... Some people say that she is too young to have a baby, they will not help her. I tell her that's nothing; she just has to rely on God." [sister of pregnant woman]

Perceptions of health care providers

Respondents, including pregnant women, family members and health care providers, frequently described having trust in the health care system combined with some key pain points.

"If you follow their [HEALTH CARE WORKER] advice everything will be alright." [husband of pregnant woman]

"One of the problems we face in our work is when the pregnant woman come for check-ups, and we refer her to the hospital for tests and she refuses to go." [health care provider]

Perceptions surrounding pregnancy and supplement use

Many respondents (from pregnant women to health care providers) perceived that both acceptable and unacceptable behaviors exist during pregnancy, and that there is a perceived difference between medicines and nutrition supplements.

"For myself there is nothing I do not eat. I simply don't smoke, I don't drink." [new mother]

"The [MMS] increases appetite. Don't take it if you do not have food to eat." [health care worker]

"They say that they [SUPPLEMENTS] protect you like; if you

are anemic, they protect the baby you're carrying." [pregnant woman]

Enablers: ANC and prenatal supplements

Key enablers to ANC and prenatal supplement use and adherence occur at the interpersonal, community and health system level (Figure 3). Key themes around enabling ANC and prenatal supplements included: i) family support (e.g., some provide reminders to take supplements and help with transportation and fees related to ANC visits), ii) community awareness and prevalence of varying communication channels (i.e., mothers and adolescent groups that encourage and support healthy pregnancy behaviors), iii) trust in the health care system, iv) belief in benefits of good nutrition and supplements, especially to prevent anemia, and v) satisfaction with existing ANC access and quality (e.g., education and counseling on potential side-effects related to supplement use and how to reduce them without discontinuing supplement intake).

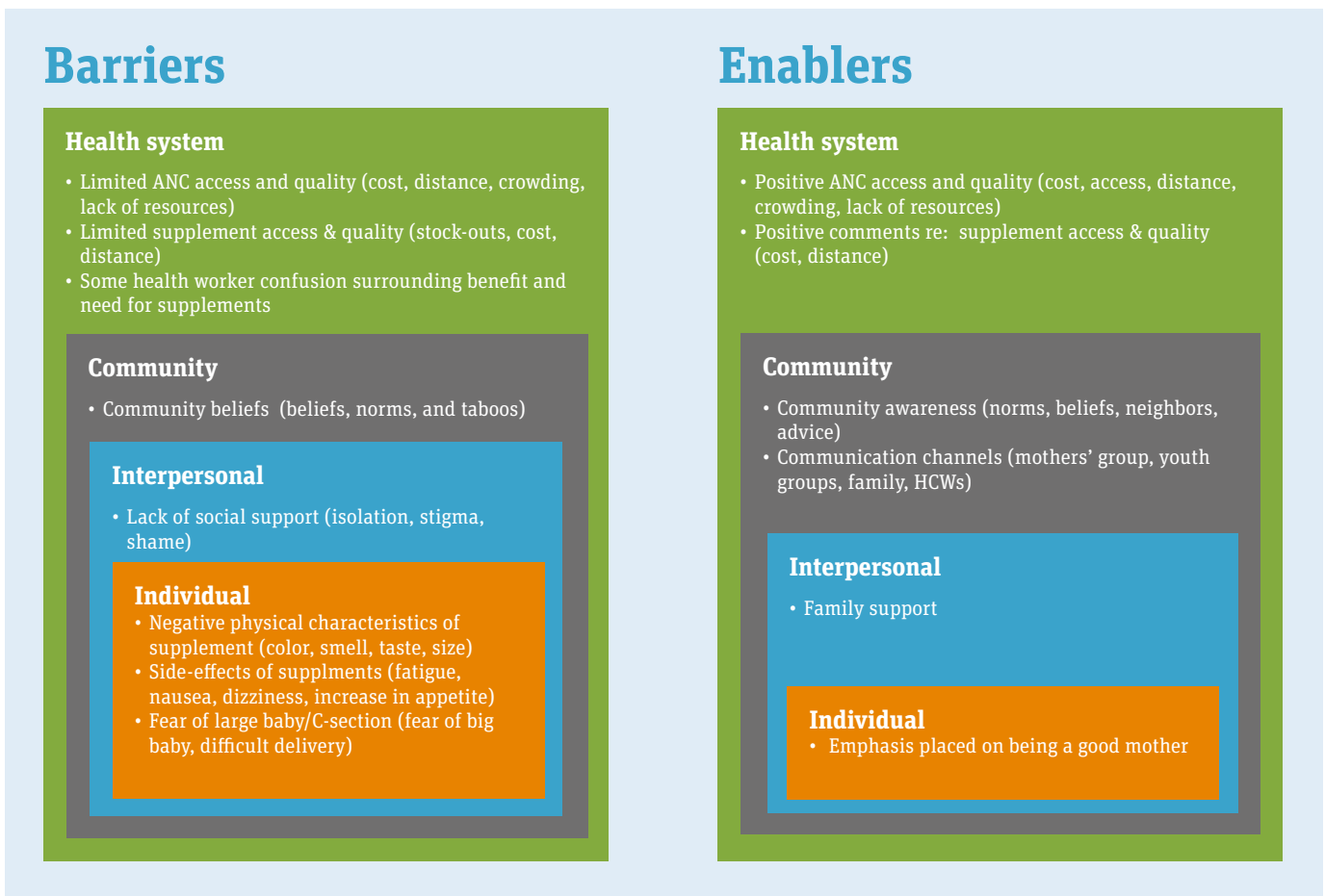
"When I come to the rally post, they talk about it; and I used to go to the mother's group, they talk about it there too." [new mother]

"She should take it [PRENATAL SUPPLEMENTS] for anemia so that her blood can speed up, to have more appetite, to have more strength to deliver a good baby." [pregnant woman]

Barriers: ANC and prenatal supplements

Key barriers to ANC and prenatal supplement use and adherence occur at the individual, interpersonal, community and health system level (Figure 3) and key themes include: i) supplement characteristics and side-effects, ii) confusion about MMS vs IFA (i.e., IFA is considered a medicine to treat anemia whereas MMS a vitamin, with some perceiving MMS as unnecessary if diet is adequate), iii) fear of large baby or C-section (often referred to as "sister of death", given constraints of local obstetric system), iv) tendency for some women to hide pregnancy (especially if the woman is young or already has multiple children), v) lack of family support (e.g., either discouragement from using health services or consumption of supplement by non-pregnant family members), vi) community beliefs and taboos (e.g., fear that something negative might happen to fetus/baby if community is aware of pregnancy, especially in the first trimester – sometimes causing delay in accessing ANC services), vii) limited access to ANC or prenatal supplements combined with poor-quality health services (e.g., some women walk long distances to attend ANC and receive supplements), and viii) poverty (e.g., some women reported not attending ANC due to visit fees and/or not taking prenatal supplements due to lack of food to consume with the supplement or due to fear of increased appetite with supplement use in the context of food insecurity).

FIGURE 3: Key barriers and enablers influencing use of supplements for pregnant women



“For me to get to the post for prenatal care, I just can’t walk. The child goes down to my lower abdomen, which makes me unable to walk. I take it slowly ... And when I get to the post, I sit down and receive the care I need, then I go home.” [new mother]

“She did not come to the appointment because she did not want the neighbors to know about this pregnancy. She knows that she has five children already, so she is blaming herself.” [health care provider]

“So they [MY FRIENDS] warn me about the negative effect of the multivitamins on the baby’s weight which could lead to C-section. They told me to take little from the package... if they gave me 30 pills, I should take 10.” [pregnant woman]

Summary and next steps

The formative research provided numerous insights into the barriers and enablers for ANC and MMS uptake and adherence. The findings were validated and used during a co-design workshop with pregnant women and other community-level stakeholders to design social and behavior change MMS implementation

strategies. The next step is to get feedback on the strategies from government officials and policymakers, and then pilot MMS implementation strategies.

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Correspondence: Shannon E King, Implementation Science Manager, Vitamin Angel Alliance, 6500 Hollister Ave Suite 130, Goleta, CA, 93117, USA
Email: sking@vitaminangels.org

References

- 1 Bhutta ZA, Das JK, Rizvi A, Gafey MF, Walker N, Horton S, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet*. 2013;382(9890):452–77. 02.
- 2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2019 Mar 14;3:CD004905. 03.
- 3 Smith ER, Shankar AH, Wu LS, Aboud S, Adu-Afarwuah S, Ali H, 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. *Lancet Glob Health*. 2017;(5):e1090–e1100. 04.
- 4 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. World Health Organization; 2016. Internet: <https://apps.who.int/iris/bitstream/handle/10665/250796/9789241549912-eng.pdf;jsessionid=C318150B4AD16B3EF60DFED8EF6A216A?sequence=1> (Accessed 3 October 2019).
- 5 Dacius M, King SE, Harvey Q, Marhone-Pierre J, Hurley KM. Ensuring effective implementation of MMS for pregnant women in Haiti. *Sight and Life Magazine*. <https://doi.org/10.52439/YFUR3152>
- 6 SocioCultural Research Consultants. Dedoose Version 8.0.35 [Internet]. Los Angeles; CA: SocioCultural Research Consultants, LLC. Available from: <https://www.dedoose.com/home/features>
- 7 *Sight and Life* Foundation. Behavior Change Communication Webinar. *Sight and Life*; 2018. Internet: https://sightandlife.org/blog/news_posts/sight-and-life-webinar-series-on-behavior-change-communication/ (accessed 2 March 2020).
- 8 King SE, Harvey Q, Ajello C, Dacius M, Marhon-Pierre J, Hurley KM. Increasing Adherence to MMS among Pregnant Women in Haiti: Experiences using *Sight and Life's* process for designing behavior change programs. *Sight and Life*. 2020;34(1):101–5.
- 9 Sallis JF, Owen N, Fisher EB. Ecological models of health behavior. In: Glanz K, Rimer BK, Viswanath K, eds. *Health Behavior and Health Education*. 6th ed. San Francisco: John Wiley & Sons; 2004:697–647.

Co-designing in Mali: A formative approach to optimizing uptake and adherence of multiple micronutrient supplements by pregnant women

Aissata Ba

Jhpiego, Bamako, Mali

Nicole Bennett, Anne Hyre, Lisa Noguchi

Jhpiego, Baltimore, MD, USA

Peter J Winch, Monica Fox, Kristen M Hurley

Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Shannon E King

Vitamin Angel Alliance, Goleta, CA, USA

Key messages:

- Images speak volumes, especially for illiterate populations.
- Husband and mothers-in-law are allies in encouraging MMS uptake; therefore all efforts should include their participation.
- Co-creating with beneficiaries, in this case Malian women, and leveraging their experience and knowledge is advantageous when designing interventions.
- Local understanding, perceptions and names must be considered in efforts to make MMS understood and accepted by the general population.

Introduction

Within the context of antenatal care (ANC), the current national policy in the Republic of Mali recommends that pregnant women should take daily iron and folic acid (IFA) supplements containing 60 mg of iron and 400 µg of folic acid starting at the first ANC contact and ending three months after delivery. However, recent data from the Demographic and Health Survey (DHS) indicates that IFA coverage for pregnant women for at least 90 days has remained suboptimal, and may be decreasing, with only 28% of women taking iron tablets for at least 90 days during their last pregnancy.¹ A 2020 update to the WHO ANC guideline now recommends the use of the United Nations International Multiple Micronutrient Antenatal Preparation

(UNIMMAP) multiple micronutrient supplements (MMS) formulation in the context of rigorous research.² Given the need for further evidence on strategies to optimize adherence to MMS during pregnancy, Jhpiego is collaborating with the Center for Vaccine Development in Mali (CVD-Mali), the Mali Ministry of Health, and Johns Hopkins Bloomberg School of Public Health (BSPH) to evaluate potential differences in adherence and acceptability associated with three different approaches to supplementation in pregnancy: i) routine standard of care (IFA dispensed as 30 tablets per month); ii) MMS dispensed as 30 tablets per month; and iii) MMS dispensed as 180 tablets once, with one refill if needed.

“Pregnant women, in particular, have difficulty distinguishing between different medicines of similar appearance”

Previous experience³ in Mali found that women use many terms to refer to medicines, and a single term may be used to refer to many different medicines. Pregnant women, in particular, have difficulty distinguishing between different medicines of similar appearance. To differentiate MMS from other medications, this study deemed it important to develop a distinctive name, packaging and set of counseling messages for MMS. Furthermore, it was critical to understand the Mali context so that this could be used to inform product testing, packaging features, and counseling strategies on MMS acceptability and adherence.

To tailor packaging and counseling strategies for the Mali context, we used a co-design process based on human-centered design principles,⁴ and engaged closely with pregnant women, mothers, midwives and graphic designers to create a local name, label, packaging approach, and set of counseling messages and images for MMS prior to introducing and evaluating MMS adherence.

TABLE 1: Workshop activities, description and results

Activity	Description	Result
Evaluating existing medications	<p>Jhpiego obtained samples of commonly prescribed drugs for pregnant women. After forming pairs, participants chose a drug and reported back to the larger group what the drug is and how they recognized it. The goal was to understand how:</p> <ul style="list-style-type: none"> • Women recognize drugs • The local name relates to packaging, and how this name helps women to identify it 	<p>Most women recognized folic acid as they recognized the package and knew it was used during pregnancy. The second most frequently chosen was a malaria drug, which was recognized because of the mosquito drawing on the package.</p> <p>Overall, these results suggested that the most important aspects in recognition of a drug product by pregnant women are images on the package and related messages.</p>
Fishbowl discussion with pregnant women	<p>Pregnant women sat inside a circle with facilitators, with other participants at a distance on the outside, and were asked:</p> <ul style="list-style-type: none"> • What is the most important thing for you when it comes to your pregnancy? • What is your experience with medications during pregnancy (e.g., fear, hope, side-effects, and support mechanisms)? • What motivated or inhibited your use of medications? • What did your midwife do or say that encouraged you to take a medication? What discouraged you? 	<p>Counseling should include strategies to avoid negative pregnancy outcomes. Keeping the medication bottle in a purse or drawer by the bedside was recommended to support remembering to take supplements. The most frequent place or object used during the day (such as drawers and purses, and above the fridge) was seen as the ideal reminder to take pills.</p>
Poster prompts with pregnant women	<p>Multiple posters with images conveying healthy pregnancy, eating, and emotional and mental wellbeing were shared with pregnant women participants, who then shared the rationale for their top choice of the images.</p> <p>In addition, pregnant women were shown posters with images that related to being healthy in pregnancy and asked to share opinions and perceptions, including how the images related to a healthy pregnancy, and which might be associated with better adherence. During the fishbowl, an impromptu roleplay was conducted about routines for taking medication.</p>	<p>The most important aspect that emerged from the poster discussion for pregnant women was emotional and mental wellbeing. From these states, it was thought that all other health outcomes emerge, e.g., adherence, healthy baby, etc.</p>

Activity	Description	Result
Fishbowl with midwives	Midwives were asked to discuss what is important for them in terms of being a midwife, their experience with counseling, barriers to counseling, and ways to encourage adherence.	The importance of short counseling sessions was raised, considering the busy context of ANC and the many tasks of midwives. Outlining paths to both positive and negative pregnancy outcomes during counseling was noted as important.
“My Ideal Package”: ‘Show & Tell’ session with graphic designers (Figure 2)	Based on what they learned about MMS, small groups of participants were asked to design an ideal MMS product package. Groups were provided with a kit of materials to use for their designs. They also were asked to name their ideal MMS package.	Proposed designs all had images of vegetables, meat, fish, fruits, and pregnant women, because they would be easy to understand regardless of education level, and because they depict the micronutrients in the supplement.
Rapid roleplays	For this activity, participants chose specific scenarios to act out related to MMS, including a positive counseling session with a midwife, an interaction with a rude pharmacist, and an interaction with a family member not familiar with MMS (e.g., husband, mother-in-law).	Positive and respectful counseling by midwives, along with supportive spouses, were perceived as being able to encourage MMS uptake and adherence. Emphasis was placed on explaining what MMS is, how it relates to healthy pregnancy, and the importance of a warm welcome and judgement-free interactions.
My ideal session skits	The goal was to create ‘ideal counseling sessions’ for different scenarios that focused on experiences with IFA and pregnancy. From there, messages focused on ensuring pregnant women understood what MMS is and how it is different from IFA. Also, the different micronutrients, their equivalent in local food, and what a good diet looks like were discussed.	Notes from each performance were refined and used to create counseling materials in addition to Vitamin Angel Alliance and NYAS’s materials.
Activity: MMS marketplace	During the marketplace activity, graphic designers created different options for the MMS package and counseling images for participants to evaluate. Participants had to rank the designs from most to least liked (1 being the most liked/first choice and 5 the least liked).	Participants favored designs with local fruits, vegetables, and pregnant women to whom the participants could relate in terms of skin complexion, outfits and mood.



Jhpiego staff testing the design; on the left is a pregnant woman attending ANC, with a Jhpiego consultant on the right



Group work on ideal package: a midwife, pregnant woman, and sexual and reproductive health specialist



Samples of ideal package designed by the group



Fishbowl with pregnant women

Design process

Co-design workshop

We conducted a two-day co-design workshop in July 2021 to develop a local name, label, package, and set of counseling messages to encourage women to take MMS daily. Participants included six midwives, seven women who were pregnant and/or mothers, and two graphic designers, as well as representatives of Jhpiego, the Ministry of Health, a local university, and a local youth health advocacy group.

To provide participants with an orientation to MMS, the Jhpiego team used the New York Academy of Sciences' (NYAS) documents.⁵ The presentation included content on MMS, prevalence of nutritional deficiencies in pregnant women in Mali, adverse pregnancy outcomes in LMICs, interventions to improve nutrition in pregnant women, and the role of micronutrients in pregnancy. The Jhpiego team then facilitated a range of workshop activities for participants. During these activities, the graphic designers observed participants and took note of what they said. Designers stayed alongside participants during the group work, and at the end of each activity the designers presented sketches of materials, which were then shared with participants for their feedback and suggestions. **Table 1** outlines activities included in the workshop.

In addition, during the co-design session, the following names from a local language (Bambara) were given as part of the “my ideal package session” (see **Table 2**):

TABLE 2: Proposed names

Name in Bambara	Meaning in English
<i>Lafia</i>	Peace of mind
<i>Sewa</i>	Joy, fulfillment
<i>Muso konoman djigui</i>	A pregnant woman's hope
<i>Konomaya sinsilan</i>	Strengtheners of pregnancy
<i>Den mokognuman</i>	Good growth of the baby
<i>Banque demelan</i>	Help for delivery
<i>Konomaya djigui</i>	Hope for pregnancy

“The program team worked with a photographer to document the experience of pregnant women taking MMS”

During the co-design workshop, participants voted for their favorite names. After the workshop, the program team computed scores for each name and visualized the results by comparing votes cast by pregnant women with votes cast by others (i.e., the midwives, or other administrators that were present). This showed some interesting differences. For example, although *Sewa* (Joy) was ranked highly by non-pregnant women, it was ranked low by pregnant women. The program team decided to pilot the name *Lafia* (Peace of Mind) because it was ranked moderately by pregnant women and highly by non-pregnant women and also *Djigui* (Hope) because the term (within a broader name) was ranked highly by both pregnant women (*Konomaya djigui*) and non-pregnant women (*Muso konoman djigui*). Ultimately, the name *Djigui* was selected as it scored highest during field testing with pregnant women. Scoring names was done by adding the number of votes per name and selecting the one with most votes.

Field testing of packaging and counseling materials

Once the co-design activity was finished, the graphic designers produced samples of all materials, including the external packaging for the MMS bottle, its name, label, counseling images, and an MMS adherence tracker. The final designs were brought into two community health centers and one district health center. In each of the sites, four pregnant women participated in the testing. The majority were self-identified homemakers and were not able to read.

Participants were asked to compare two different proposed mono carton designs and provide rationales for their top choice. Then the facilitator asked participants to share their perspective about what the mono carton could hold, just by looking at the designs. Once they shared, the facilitator explained its purpose – to package the MMS bottle. Participants were also asked to choose counseling images, messages, uptake tracker, and the name for MMS from those collected during the co-design workshop. Based on feedback, the women chose the name *Djigui* (Hope). For the images, women insisted on the woman holding the baby, but did not mention how the pregnant woman and the mother should be dressed or their age. However, they insisted the picture of vegetable and fruits should be like local ones, instead of cartoonish design or foods that are unknown to Malians.

Based on the participants' feedback, the graphic designers created final packaging designs (**Figures 1–4**). The program team developed a storyboard for the counseling messages using MURAL, a digital whiteboard. Then, after hearing the importance of using realistic images during counseling, the program team worked with a photographer to document the experience of pregnant women taking MMS. These images, with the consent of the individuals photographed, were featured in a pictorial-based job aid for midwives to use with pregnant women.

FIGURE 1: Final design of the label



FIGURE 2: Final design of the logo



FIGURE 3: Final design of the packaging



FIGURE 4: Final design of the uptake tracker

	SEMAINE 1	SEMAINE 2	SEMAINE 3	SEMAINE 4	SEMAINE 5	SEMAINE 6	SEMAINE 7	SEMAINE 8
1	1	1	1	1	1	1	1	1
2	2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3	3
4	4	4	4	4	4	4	4	4
5	5	5	5	5	5	5	5	5
6	6	6	6	6	6	6	6	6
7	7	7	7	7	7	7	7	7

Lessons learned during field testing

Lessons from the formative activities include the following:

Aspect of MMS for introduction in Bamako, Mali	Finding
Description (e.g., vitamin, medicine)	<ul style="list-style-type: none"> Ensuring that MMS is not promoted as a vitamin, because according to local beliefs, vitamins induce weight gain, hence the fear of having a macrosomic baby which may result in complications leading to C-section. Instead, use the local name <i>Djigui</i>.
Counseling approach and messages	<ul style="list-style-type: none"> Starting counseling by focusing on things women know, e.g., IFA/prenatal supplements, and then move to talking about MMS. Focusing on the health benefits of MMS, as these act as incentives for pregnant women wanting to have a healthy baby. However, also mentioning the reduced risk of negative outcomes is useful. Making sure that the stories and examples used during counseling paint a picture of happy people and outcomes. Midwives can be powerful agents in providing counseling and can positively affect adherence both of pregnant women and their influential family members (husband or mother-in-law).
Introduction as a new product	<ul style="list-style-type: none"> Ensure participants understand that the project is not intended to test the product for safety, but rather to gather information for programmatic reasons. Free product distribution may create suspicion, so this must be addressed in counseling. The reason for their being given free of charge should be stressed – e.g., donated to help pregnant women and their communities and also to compensate for their time in participating in the study.

“By listening to pregnant women and midwives, we were able to directly turn participant feedback and input into actionable implementation strategies”

Conclusion

Overall, we learned that creating an open and safe environment for creativity allowed for rich information to be conveyed that can directly impact the design of the MMS package and counseling strategies. By listening to pregnant women and midwives, we were able to directly turn participant feedback and input into actionable implementation strategies. These strategies are currently being tested through implementation research (IR) and, depending on the IR results, will ultimately be used and adapted to promote MMS adherence.

Correspondence: Aissata Ba, Program Manager, Jhpiego-Mali, Hamdallaye ACI 2000, rue 234, Porte 110, Bamako, Mali
Email: aissata.ba@jhpiego.org

References

- Institut National de la Statistique (INSTAT), Cellule de Planification et de Statistique Secteur SantéDéveloppement Social et Promotion de la Famille (CPS/SS-DS-PF) et ICF. 2019. . 2019. Enquête Démographique et de Santé au Mali 2018 : Rapport de synthèse. Bamako, Mali et Rockville, Maryland, USA : INSTAT, CPS/SSDS-PF et ICF"
- World Health Organization. WHO antenatal care recommendations for a positive pregnancy experience Nutritional interventions update: Multiple micronutrient supplements during pregnancy. Geneva: World Health Organization; 2020.
- Patterson, A, et al. Local terminology for medicines to treat fever in Bougouni District, Mali: implications for the implementation and evaluation of malaria treatment policies. Tropical medicine and International Health. Volume 11, Issue 10, 2006. <https://doi.org/10.1111/j.1365-3156.2006.01713.x>
- Stratos Innovation Group, 2016. Co-design: A Powerful Force for Creativity and Collaboration (<https://medium.com/@thestratos-group/co-design-a-powerful-force-for-creativity-and-collaboration-bed1e0f13d46>)
- Multiple Micronutrient Supplementation in Pregnancy- Technical Advisory Group. Technical Reference Material II, Generic Training Materials <https://www.nyas.org/media/19951/trm-ii-training-materials-complete-draft-1.pdf> Accessed 4 April 2021.

A Summary of Consumer Research Findings in Bangladesh, to Support the Case for MMS

Kalpna Beesabathuni, Anirudh Poddar, Srujith Lingala, Puja Peyden Tshering

Sight and Life Foundation, Basel, Switzerland

Toslim Uddin Khan, Shahidul Alam, Moshir Rahman

Social Marketing Company (SMC), Dhaka, Bangladesh

Rudaba Khondker, Moniruzzaman Bipul, Tareq Hasan, Nilima Azad

The Global Alliance for Improved Nutrition (GAIN), Geneva, Switzerland

Sarah Gibson

The Children's Investment Fund Foundation (CIFF), London, UK

Key messages:

- There is much scope for clarifying when to start taking multiple micronutrient supplements (MMS) during pregnancy, since an initial survey of knowledge, attitudes and practices (KAP) showed that most respondents did not see prenatal multivitamin supplements as something they needed to take before becoming pregnant or during their first trimester.
- MMS also needs to be prioritized during pregnancy, and the KAP study found that most of the providers agreed that pregnancy supplements are essential to a healthy pregnancy and a healthy baby. However, the belief that supplements can be substituted by a nutritious diet (comprising more fruits and vegetables) is high.
- The introduction of the FullCare MMS brand elicited overall positive reactions, one of them being that respondents saw it as a product that is good for both mother and child. Respondents suggested that the name FullCare itself can be further highlighted in the marketing to emphasize the message that it caters to both mother and child, hence heightening the appeal of the product.

Introduction

In low- and middle-income countries (LMICs) such as Bangladesh, micronutrient deficiencies are common in pregnancy, and inadequate maternal nutrition before and during pregnancy leads to adverse outcomes for mother and baby.¹ The International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation of Multiple Micronutrient Supplement (MMS) containing 15

vitamins and minerals has been proven effective in improving pregnancy outcomes and addressing this scourge of maternal micronutrient malnutrition.²

Despite various strategies, the prevalence of micronutrient deficiencies in Bangladesh remains high and is considered a significant public health problem.³ In 2011, the Bangladesh Demographic and Health Survey (BDHS) found that 49.6% of pregnant women and 47.8% of lactating women were anemic.⁴ Poor-quality diets are the major contributor to micronutrient deficiencies in the country.⁵ Other contributors include limited dietary diversity due to a low socio-economic status and household food insecurity, as well as low levels of knowledge about optimal diet and hygiene practices.^{6,7}

There are several prenatal multivitamin supplements available to purchase in Bangladesh, but currently, only one MMS is adherent to the UNIMMAP formulation. It is called FullCare and was introduced by Social Marketing Company in 2021 (SMC is a Bangladeshi non-profit organization that offers education and products for family planning as well as maternal and child health). It is the first and only MMS product produced with the recommended composition or ingredients of the UNIMMAP formulation available in Bangladesh.

“Despite various strategies, the prevalence of micronutrient deficiencies in Bangladesh remains high and is considered a significant public health problem”

This article presents findings from two consumer studies that informed the launch and post-launch marketing strategy of FullCare. The first study is a Knowledge, Attitudes, and Practices (KAP) quantitative survey, of which one part was conducted with pregnant women across different socio-economic classes and regions in Bangladesh, and the other part conducted with pharmacists and healthcare professionals (referred to as ‘providers’ in the following) within SMC’s pharmacy network in relation to prenatal multivitamin supplements. The survey explored barriers to uptake, potential gaps in the market, how MMS could be better positioned to increase adoption and usage, as well as reactions to a concept card outlining the FullCare value proposition. It also

assessed the 5 Ps (Product, Packaging, Promotion, Price, Place) for FullCare based on brief exposure to the FullCare product prototype. A total of 600 consumers (pregnant women) and 330 Providers were interviewed for the study.

The second study, a qualitative study with consumers and providers, was conducted seven months after the launch of FullCare in the market (within SMC's network) to assess how consumers were reacting to the produce and to gauge any elements for course correction to bolster the marketing strategy going forward. Here, also, the 5 Ps were examined in addition to understanding the FullCare user persona and journey with the category. The pregnant women interviewed included FullCare users, users of other prenatal supplements, and also 'lapsed' who had tried FullCare for at least 15 days but had stopped consuming it.

Findings from the KAP survey

Among the consumers, the KAP study found that most respondents did not see prenatal multivitamin supplements as something they needed to take before becoming pregnant or during their first trimester, and more than half of the respondents (56%) stated that a woman should start taking supplements 'after the first trimester'. This is an interesting finding, as other studies have highlighted the benefits of taking certain supplements while trying to conceive and during early pregnancy.⁸ These findings suggest the need for MMS to be promoted as a product that should be used throughout pregnancy and possibly when trying to conceive, while also tackling the myths and beliefs concerning when an expectant mother should attend antenatal care.^{9,10}

The study identified several barriers, including perceived lack of support from other family members (21.8%), highlighting the need to engage with other family members to increase the acceptability of MMS and communicate the importance of taking it. These conversations should be had with the extended family as well, and not only the husbands, as mothers-in-law have substantial influence within the family units.¹¹

In addition, the study found the need to promote the wellbeing of both mother and child, as the respondents often focused solely on either their own health or that of the babies. For instance, when asked about the benefits of taking supplements, more than half of the respondents (54.5%) stated, 'not falling sick' and 47% mentioned being 'able to do regular work'. On the other hand, only 29.5% stated that they believed the supplements helped their baby to grow well. Very few of the respondents considered the health of both the mother and the baby. This might suggest that mothers lack an understanding of how their health and their baby's health are interlinked.

Among providers, the study's findings showed that providers believed that pregnant women would benefit from taking supplements, and most of the providers agreed that pregnancy supplements are essential to a healthy pregnancy and a healthy baby (83%). However, the belief that supplements can be substituted by

a nutritious diet (comprising more fruits and vegetables) is strongly prevalent: of the respondents who believed there were substitutes available (61.5%, n=203), 'nutritious foods' was the most frequently given response, which shows that there is a need to also sensitize providers to prenatal supplementation. This is especially important due to the ongoing high rates of food insecurity within Bangladesh.¹²

“The study’s findings showed that providers believed that pregnant women would benefit from taking supplements”

The FullCare proposition (linking the health of the mother and the baby) garnered positive reactions

Overall, FullCare garnered positive reactions across the 5 Ps. In terms of the Product, respondents scored the tablet on average 7/10 on all core attributes such as product size, color and format (tablet/capsule). Importantly, respondents saw it as a product for both mother and child. This was driven by the information provided to them during the interview: *It aids healthy functioning of her body and prevents anemia when her diet is not sufficient and it helps to avoid her baby from being born too soon, too small, and reduces risk of mortality*. Respondents suggested that the name FullCare itself can be further highlighted in the marketing to emphasize the message that it caters to both mother and child, hence heightening the appeal for the product.

Non-users (pregnant women who were aware of prenatal supplements but had consciously never consumed), cited discouragement from husbands and elderly relatives as the primary barrier to the use of supplements.

On the *Packaging*, the tagline, “One tablet a day...a healthy baby on the way”, was seen as memorable and informative (i.e., “consume one tablet a day”). Consumers trust SMC to provide high-quality healthcare products and were pleased to see its logo on front-of-pack. Each of the attributes – color, size, quality, font, logo/image, overall design and tagline – scored 8 or more, with the tagline scoring the highest (9.1/10). The blister pack itself was also received, scoring 8 or more on attributes such as format, quality, color, and design. It was also preferred over the other formats such as bottles for two reasons: it was perceived as easy to dispense the most common purchase unit of 10 tablets at a time, and was seen to support compliance, as a consumer can easily check how much of a blister is empty.

A high score on *Promotion* was driven by the trust in SMC. Almost all the respondents (95%) reported trust in SMC and more than 80% feel that the SMC logo should be a key feature of promotion. More than one-third (77%) of pregnant women said that a

doctor’s recommendation could increase their motivation to start using FullCare. Further, showing both mother and child in advertising could help – almost all suggest featuring a baby – be it by means of TV, radio or billboard. This could be effective, as there is no supplement in the market that links the benefits accrued by the mother to the child in the womb.

For *Price*, the average price suggested by respondents was Bangladeshi Taka (BDT) 4.3/pc (0.041 US\$ per piece). This was benchmarked against current prices paid – BDT 2/pc for IFA, BDT 4/pc if zinc is added, BDT 7/pc for calcium and vitamin D. The willingness to pay could be even higher if the 15-micronutrient proposition is leveraged in the marketing, but given the target audience’s economic constraints, BDT 4/pc is reasonable. Providers confirmed the suggested price of BDT 4/pc of Fullcare as the ideal price.

As a *Place* for purchase, most preferred this to be a pharmacy/ dispensary, of which the preferred one would be a Blue Start or Green Star pharmacy.¹³

“Overall, FullCare is positively received by all”

Findings from the follow-up consumer study (post product launch)

The actual FullCare product delivers on its promise; highlighting the FullCare woman can expand this promise

In the post-launch study, when looking at the actual final FullCare product, the 5 Ps discussed earlier were validated. Overall, FullCare is positively received by all – even users of competitor products and ‘lapsers’ appreciated it. The packaging is appealing, the price sits well within the consumer’s willingness to pay for prenatal supplements, and the constant recommendation is for it to be available in every pharmacy, not just SMC’s network. Respondents felt that some things – such as the type and amount of micronutrients available in the product, the link with SMC, and the core benefits associated with the product, such as ‘mobility’ and ‘energy’ can be further emphasized to create greater appeal for the product.

Beyond validation, the post-launch study also offered insights into who the FullCare woman is, as well as her experience and journey with the product. The product does seem to appeal more strongly to women with a slightly different approach to pregnancy. For instance, values such as gratitude, confidence and optimism were noted by women taking the product, and they used words such as ‘grateful’, ‘looking forward’, ‘amazing’, ‘blessed’ and ‘relaxed’. One FullCare user mentioned, “I cannot express in words how amazing I feel right now while pregnant... I am blessed with the ability to give birth...”. While some women noted anxiety regarding the health of the baby, the delivery and their own health, it was noticeably less compared to how competition users and

lapsers see their pregnancy experience. For instance, one user recalled her experience of finding out she is pregnant, as follows: “When I learned I was pregnant, I felt joy, I didn’t have any worries. If I had to tell someone what it feels like to be pregnant, I would tell them that becoming a mother comes with pain, but it makes a woman complete.” Leveraging this aspirational persona across different marketing touchpoints can be effective for the brand.

When looking at the user’s journey with FullCare, it is clear that the women are typically not alone; the husband plays an important role, especially in determining which brand of prenatal supplements to obtain. Purchases are generally made on a monthly basis, taking multiple factors into account: ease of access, recommendations by the doctor and family/ friends, product content, price, etc. For FullCare, husbands seem to pay more attention to the fact that FullCare contains 15 micronutrients, which is an important differentiator. If the wife feels better after taking FullCare, the husband continues to buy the same supplement. If the wife faces issues, the husband usually consults with the doctor/ pharmacist and buys another brand.

Way forward

FullCare is just getting started in Bangladesh, as it is first UNIMMAP MMS product. The price (confirmed after the KAP survey) acts as a delight factor, since consumers expect a prenatal supplement that delivers more (15 micronutrients) to cost more. There is much that needs to be accomplished – first and foremost, getting both consumers and providers acquainted with MMS. Since FullCare MMS has been classified as a drug and not a food supplement, the demand creation activities have been heavily scrutinized and therefore focus more on providers, wherein close to 17,000 individuals from the SMC network as well as the medical fraternity have been sensitized to MMS and the need to switch to MMS from IFA. The consumer-facing demand creation activities largely adopt a holistic, pregnancy-care approach and will be ramping up this year, with an aim to link MMS as part of an effective pregnancy-care routine, along with regular ANC check-ups, healthy eating, and other tips.

“The consumer-facing demand creation activities largely adopt a holistic, pregnancy-care approach and will be ramping up this year”

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Correspondence: Puja Peyden Tshering, Senior Manager – Consumer Insights, *Sight and Life* Foundation, PO Box 2116, 4002 Basel, Switzerland
Email: puja.tshering@sightandlife.org

References

- 1 Arlappa, Nimmathota & Laxmaiah, Avula & Balakrishna, Nagalla & Harikumar, R & Kodavanti, Mallikharjun & Chitty, Gal Reddy & Saradkumar, S & Ravindranath, M & Brahman, Ginnela. (2010). Micronutrient deficiency disorders among the rural children of West Bengal, India. *Annals of human biology*. 38. 281-9. 10.3109/03014460.2010.536572.
- 2 World Health Organization. The global prevalence of anaemia in 2011 [Internet]. WHO Report. Geneva; 2015 [cited 2022, February 19]. Available from: http://apps.who.int/iris/bitstream/10665/177094/1/9789241564960_eng.pdf?ua=1.
- 3 Smith, Shankar, Wu, Aboud, Adu-Afarwuah, Ali 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. *Lancet Glob Health*. 2017;5(11):e1090–e1100.
- 4 Darnton-Hill I, Ahmed F & Samon S (2015) The impact of micronutrients on inflammation and health in low- and middle-income countries. In *Preventive Nutrition: The Comprehensive Guide for Health Professionals*, 5th ed., chapter 30, pp. 597–644 [A Bendich and RJ Deckelbaum, editors]. New York: Springer.
- 5 Government of the People's Republic of Bangladesh (2014) Millennium Development Goals: Bangladesh Country Report 2013. Dhaka, Bangladesh: Planning Commission, Government of the People's Republic of Bangladesh.
- 6 Jahan & Hossein (1998) Bangladesh National Nutrition Survey, 1995–96. Dhaka, Bangladesh: Institute of Nutrition and Food Science, University of Dhaka.
- 7 Institute of Public Health Nutrition (2015) National Strategy on Prevention and Control of Micronutrient Deficiencies, Bangladesh (2015–2024). Dhaka, Bangladesh: Institute of Public Health Nutrition, Ministry of Health and Family Welfare, Government of the People's Republic of Bangladesh.
- 8 Khatun W, Rasheed S, Dibley MJ, Alam A. Understanding maternal dietary behaviour and perceived attributes of foods in the context of food insecurity in rural Bangladesh: a qualitative study. *Journal of Global Health Reports*. 2020;4:e2020018. DOI:10.29392/001c.12326
- 9 Bourassa MW, Osendarp SJM, Adu-Afarwuah S, Ahmed S, Ajello C, Bergeron G, Black R, Christian P, Cousens S, de Pee S, Dewey KG, Arifeen SE, Engle-Stone R, Fleet A, Gernand AD, Hoddinott J, Klemm R, Kraemer K, Kupka R, McLean E, Moore SE, Neufeld LM, Persson LÅ, Rasmussen KM, Shankar AH, Smith E, Sudfeld CR, Udomkesmalee E, Vosti SA. Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Ann N Y Acad Sci*. 2019 May;1444(1):6-21. doi: 10.1111/nyas.14121. Epub 2019 May 27. PMID: 31134643; PMCID: PMC6852202.
- 10 Schaefer E, Nock D. The Impact of Preconceptional Multiple-Micronutrient Supplementation on Female Fertility. *Clin Med Insights Womens Health*. 2019 Apr 23;12:1179562X19843868. DOI: 10.1177/1179562X19843868. PMID: 31040736; PMCID: PMC6480978.
- 11 Siekmans, K., Roche, M., Kung'u, J. K., Desrochers, R. E., & De-Regil, L. M. (2018). Barriers and enablers for iron folic acid (IFA) supplementation in pregnant women. *Maternal & child nutrition, 14 Suppl 5*(Suppl 5), e12532. <https://doi.org/10.1111/mcn.12532>
- 12 Disha Ali, Kuntal K. Saha, Phuong H. Nguyen, Michael T. Diressie, Marie T. Ruel, Purnima Menon, Rahul Rawat, Household Food Insecurity Is Associated with Higher Child Undernutrition in Bangladesh, Ethiopia, and Vietnam, but the Effect Is Not Mediated by Child Dietary Diversity, *The Journal of Nutrition*, Volume 143, Issue 12, December 2013, Pages 2015–2021, <https://doi.org/10.3945/jn.113.175182>
- 13 A Blue Star Network consists of community level non-graduate health providers who are trained in family planning, reproductive and child health and nutrition with other public health priority areas to offer quality services to the community people, operating as attachments to pharmacies. A Green Star Network consists of non-graduate health care providers with at least 2 years of professional experience + pharmacists and drug sellers who own their own store. They are the primary point of contact at the community level for minor ailments, such as diarrhoea, cough, fever, weakness etc.

FullCare Case Study

**Shashank Sarvan, Anirudh Poddar, Puja Peyden
Tshering, Srujith Lingala, Sufia Askari,
Kalpana Beesabathuni**

Sight and Life Foundation, Basel, Switzerland

Toslim Uddin Khan, Shahidul Alam, Moshir Rahman
Social Marketing Company (SMC), Dhaka, Bangladesh

**Rudaba Khondker, Moniruzzaman Bipul, Tareq Hasan,
Nilima Azad**

The Global Alliance for Improved Nutrition (GAIN), Geneva,
Switzerland

Sarah Gibson

The Children's Investment Fund Foundation (CIFF), London, UK

Key messages:

- The “One MMS a Day and a Healthy Baby is on the Way” project enabled Bangladesh to become the first low- and middle-income country to produce UNIMMAP MMS locally and pilot a market-based model to tackle micronutrient deficiencies in pregnant women.
- This article briefly touches upon the elements and efforts that go towards the launch of such a project, including market study, product design, channel selection and pricing.
- The reach and sales from the proof-of-concept phase that followed the launch are covered in detail. Initiatives for demand generation to circumvent roadblocks in marketing and innovative feedback mechanisms through tele-counselling unique to the project's context are also discussed.
- The learnings from this project and the plans towards the sustainability of the project beyond the grant support can serve as a template for similar programs in other parts of the world.

Introduction

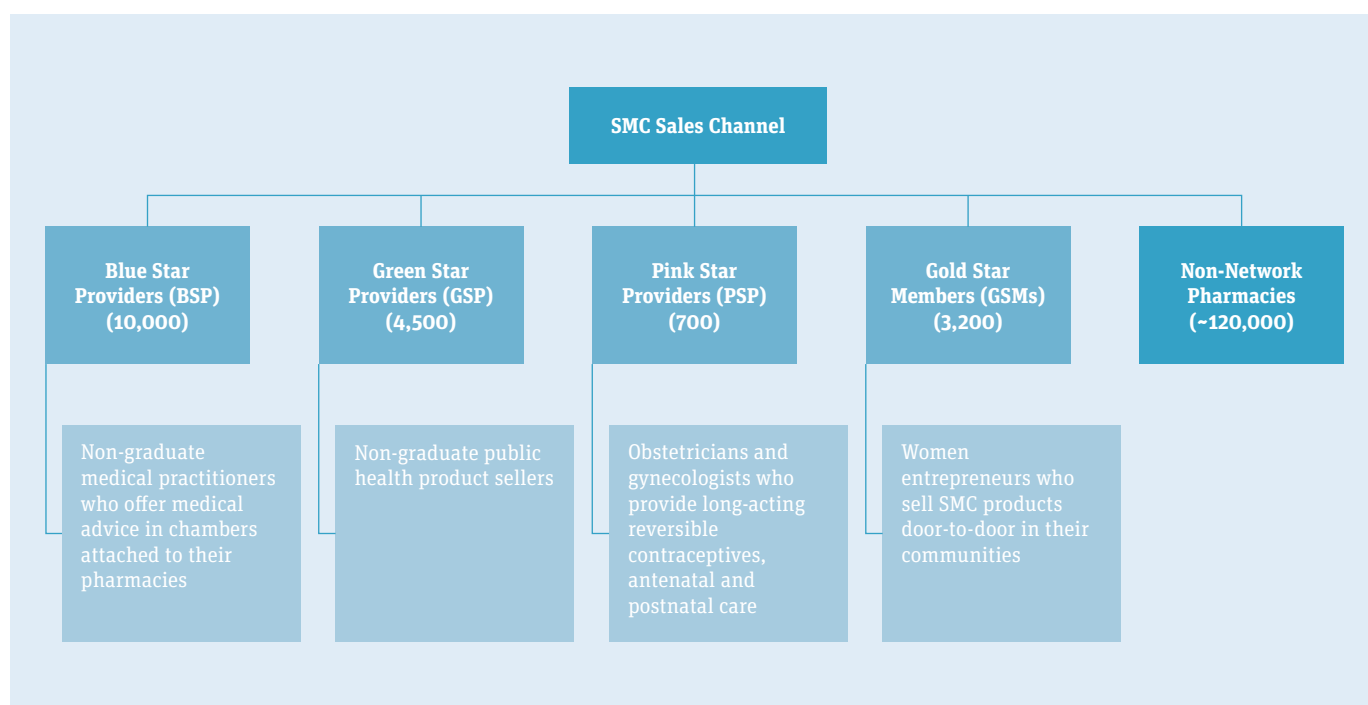
Vitamin and mineral deficiencies in pregnant women are a major risk factor for low birth weight (LBW) in their children and other adverse birth outcomes. Millions of pregnant women in Bangladesh suffer from micronutrient deficiencies, and, as a result, give birth to small babies. Bangladesh has the highest prevalence of LBW children in the world – at 28%.^{1,2} Multiple micronutrient supplements (MMS), containing 15 vitamins and minerals including iron and folic acid (IFA), are a low-cost, high-impact solution which can improve nutrient intakes of pregnant women where quality of diets is likely to result in maternal anemia, LBW and small-for-gestational-age (SGA) births.

Based on prior experience with the multiple micronutrient powders (MNP program and the evidence for MMS), the Government of Bangladesh decided to lead the pilot of MMS in the country. Two models of intervention were finalized: a pro-poor model supported by UNICEF in two target districts and a market-based model in the remaining 62 districts. “One MMS a Day and a Healthy Baby is on the Way” is a multi-sectoral collaboration assembled by CIFF that translated the market-based model for MMS into reality in Bangladesh. The project is supported by the Global Alliance of Improved Nutrition (GAIN) in coordination with Social Marketing Company (SMC), *Sight and Life* Foundation (SAL), along with strategic and technical direction provided by the National Nutrition Service (NNS) through the National Technical Committee (NTC). The article from the first *Sight and Life* Foundation Special Report on MMS captures the design of the model in detail and can serve as a pre-read.⁴ This article discusses the learnings and outcomes from the proof-of-concept phase of the program.

Pre-launch of the program

In many thriving marketplaces in low- and middle-income countries (LMIC) in Asia, pregnant women even from the lowest socio-economic segments seek care from private healthcare providers, and they purchase IFA from pharmacies. Bangladesh has a dense network of retail pharmacies across the country, which are the preferred first point of contact for most of the population and a familiar entity in community life. Currently, in Bangladesh, there are nearly 100,000 licensed retail pharmacies and approximately an equal number of unlicensed ones. It is, therefore, important to ensure that MMS is available in these stores for the market-based model to reach target segments.

Social Marketing Company (SMC) is a non-profit social enterprise and the largest social marketing company in Bangladesh. They have a portfolio of over 120 health products, ranging from contraceptives to packaged oral rehydration salts. Their products reach more than 50% of the pharmacies in Bangladesh. SMC operates a social franchising network of more than 15,000 community-level private medical practitioners and pharmacists who cater to the community (**Figure 1**). They not only sell SMC's products in various target segments; some – Blue Star Providers (BSPs) and Pink Star Providers (PSPs) – are also trained to provide medical care and advice. This helps SMC to inform and educate its customers as part of their consumer journey. SMC is an affordable and trusted brand for consumers, especially those at the base of the pyramid. In 2008, 60% of the oral saline produced in the Bangladeshi market was from SMC.³

FIGURE 1: SMC sales channel

Product

Sight and Life conducted a pre-launch market research and Knowledge, Attitude and Practices (KAP) survey. It was found that IFA and IFA+Zinc were the most prescribed supplements during pregnancy. They are priced in the range of BDT 2–7 per tablet (US\$ 0.02–0.07) (Table 1).

The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS formulation contains 15 micronutrients. It not only bridges the gap in delivering all essential micronutrients but could also increase consumers' willingness to pay through the influence of social marketing. Based on the KAP survey responses obtained from consumers as well as providers (within SMC's network), BDT 4/tab seemed the most reasonable pricing for the MMS product that was exposed as part of KAP survey. The brand name FullCare was chosen to connect the health of the mother to the child in the womb (evoking, as it does, complete, holistic care).

TABLE 1: Supplement pricing

Supplement	Price per tablet
Iron + Folic Acid (IFA)	BDT 2
Iron + Folic Acid + Zinc	BDT 4
Calcium + Vitamin D	BDT 7

FIGURE 2: FullCare blister and pack

An economically produced tablet is important if it is to be affordable to end-consumers. To reduce costs therefore, Renata, the fourth largest pharmaceutical company in Bangladesh, came on board as the manufacturing partner. They were able to produce tablets at prices that ensured sufficient margins for all actors in the supply chain while the retail price for the end-customer stayed at BDT 4/tab. A full course of FullCare (180 tablets) costs BDT 720 or US\$ 6.80 per pregnancy.

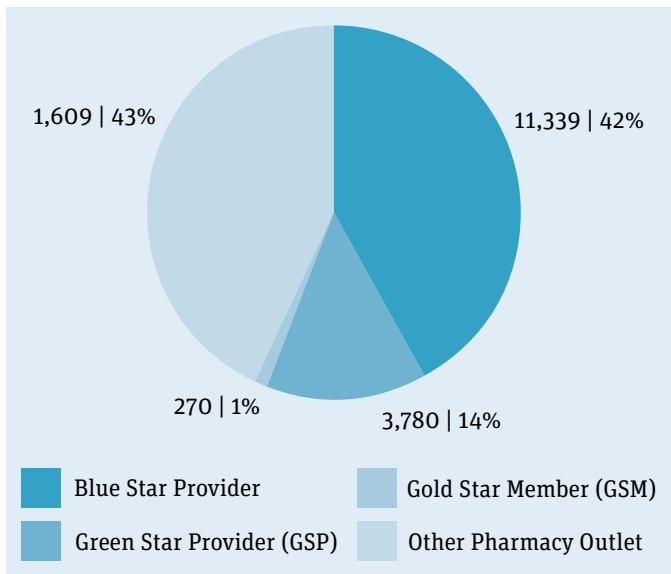
The Directorate General of Drug Administration (DGDA) approved the UNIMMAP formulation of the MMS tablet on 22 March 2021 with the brand name "FullCare". Renata started MMS production on 31 May 2021, conducted stability testing, and launched the first batch to SMC in June 2021 (with continuous monitoring of the product). FullCare was launched in July 2021.

Results from proof-of-concept phase

Sale and reach

As of December 2022, FullCare has been on sale in all districts of Bangladesh (except for two districts). The sales channel currently has 26,998 outlets, with half of them (57%) belonging to the SMC network and the rest to other pharmacies/NGOs.

FIGURE 3: Network coverage as of December 2022



Since its launch, the total number of tablets sold is 21.4 million (2.1 million blister packs of 10 tablets). SMC network providers contributed to the majority (81%) of total sales. The non-network pharmacies/NGOs covered the other 19%. The initial estimates of average purchase size per pregnant women vary from 50 to 5 tablets. This would put the estimated number of pregnant women reached at 280,000–430,000 between July 2021 and December 2022.

FullCare’s progress in a market setting should be compared with other brands that face similar market forces. There are more than 50 IFA-like supplement brands 90+ multivitamin brands in the market. In the year of 2022, FullCare sales were around 16.8 million tablets. Total annual prescription sales of IFA-like brands was 145 million tablets. FullCare ranks 5th among those brands. In the segment of multivitamin supplements brands selling 230 million tablets annually, FullCare ranks 6th.

Tele-counselling

In December 2021, SMC started a tele-counselling line called ‘Tele-jigyassa’, run by a dedicated, trained staff of five SMC tele-counselors. Pregnant women are registered using their phone numbers when they purchase FullCare at SMC network pharmacies. The Telejigyassa counsellors then reach out to the pregnant women via individual telephonic monthly counselling sessions. They educate their consumers on good practices to follow during pregnancy and follow up on any side-effects experienced while taking FullCare. The registered women are also sent SMS pregnancy care messages.

The data from the follow-ups are logged in a digital interface, and a dashboard helps summarize the findings (Figure 4). The platform enables SMC to track feedback from consumers more effectively. Between December 2021 and December 2022, about 17,900 pregnant women were counselled and more than 400,000 SMS messages were sent.

Demand generation and building capacity

A key roadblock in the demand generation activity was the categorization of FullCare as a drug. This greatly restricted Business-to-Consumer (B2C) marketing activities such as advertising in mass media. To circumvent this, a shift in focus towards training and dissemination of the benefits of MMS to pharmacists and health care providers was necessary.

FIGURE 4: Digital dashboard



The following is a brief look at the capacity-building and sensitization efforts made in the Business-to-Business (B2B) domain. Recognizing the weight a medical professional's prescription carries regarding MMS sales, the following was implemented:

- 16 seminars with obstetricians, gynecologists and graduate doctors, attended by 723 participants;
- 6 orientations with Pink Star Providers (PSP), attended by 338 PSPs;
- 65 *Upazila*-level Health Complex Seminars, attended by 1,573 graduate doctors and other health and family planning service providers;
- Special trainings regarding FullCare (MMS) for 9,250 Blue Star Providers (BSPs), 2,310 Green Star Providers (GSPs) and 2,480 Gold Star Members (GSMs);
- Refresher trainings in the five intervention *Upazilas*, in which BSP, GSP and GSM participated; and
- 40 talk shows broadcast on pregnancy care and MMS on national TV channels.

On the B2C side, the activities were designed to build awareness. A prime way of doing this was courtyard sessions, whereby SMC organized a gathering of pregnant women and invited obstetricians and gynecologists to provide advice on ANC and supplementation. As at December 2022, 345 sessions had been conducted, which were attended by 6,436 pregnant women.

Follow-up consumer insights

In the post-launch study by *Sight and Life*, the insights captured were validated. Overall, FullCare is positively received by all – even users of competitor products and lapsers appreciated it. The packaging is appealing, the price sits well with the consumer's propensity to pay for prenatal supplements, and the constant recommendation is for it to be available in every pharmacy, not just SMC's network. Respondents felt that certain things – such as the type and amount of micronutrients available in the product, the link with SMC, and the core benefits associated with the product such as 'mobility' and 'energy' – could be emphasized more, to create greater appeal for the product.

Advocacy

GAIN played a pivotal role by helping establish the national-level taskforce (NTC) and also being actively involved in it. NTC is led by the National Nutrition Services (NNS), with representation from other relevant Line Directors of Ministry of Health and Family Welfare (MOHFW), BNNC, OGSB UNICEF, development organizations, professional bodies, researchers, and academia. The main objective of the committee is to act as an interface with the government to provide strategic and technical support to implement the FullCare program, including policy advocacy and eventual policy inclusion in national standard treatment guidelines.

Various partnerships have been developed leveraging NTC to help in advocacy for MMS ([Table 2](#)).



Courtyard gathering of pregnant women.

TABLE 2: Partnerships leveraging NTC to help in advocacy for MMS

Partner organization	Brief of partnership
National Nutrition Services (NNS)	Leading MMS demonstration program through NTC. Actively supported finalizing the National Maternal Nutrition Guideline to include MMS. Developed technical documents on maternal nutrition and MMS for Micronutrient Forum 2020, Devex video case study and International Federation of Gynaecology and Obstetrics (FIGO) World Congress 2021.
Multiple micronutrient supplementation	Supporting CCTN (Comprehensive Competency-based Training on Nutrition) to promote orientation on maternal nutrition including MMS. CCTN is basic nutrition training for all Health and Family Planning staff throughout the country.
Bangladesh National Nutrition Council (BNNC)	Advocate maternal nutrition services to support antenatal care with MMS. BNNC will advocate for MMS in different national platforms, seminars, workshops, national events, etc.
Obstetrical and Gynecological Society of Bangladesh (OGSB)	Capacity-building of doctors and private service providers with knowledge about MMS.

The Government of Bangladesh has endorsed MMS on multiple policies and plans, thereby demonstrating its commitment:

1. National Strategy on Prevention and Control of Micronutrient deficiencies (2016–2024).
2. Second National Plan of Action for Nutrition (2016–2025).
3. National Strategy for Adolescent Health (2017–2030).
4. The Operational Plan (OP) of NNS, Ministry of Health and Family Welfare (MOHFW) has included micronutrient supplementation.

Sustainability

SMC earns a small margin from public health goods such as FullCare: this margin is reinvested in running operations. SMC also created a for-profit subsidiary, SMC Enterprise Ltd (SMC EL), in 2014 to separate its profit-based activities from other public health programs. SMC EL manages more than 100 products that have a strong consumer pull. Examples of these products are ORS and contraceptives that have stabilized in the market and generate profits for the company. Some of the profits from SMC EL are funneled into supporting SMC's program products. In the context of unforeseen external pressures that can be caused by shocks such as floods, pandemic and inflation, SMC EL provides the necessary cushion to make sure programs remain unaffected.

SMC also owns and operates a pharmaceutical production company. Wherever feasible, the organization moves production from third-party to in-house manufacturing. This has given SMC better control over quality, ensuring steady supply and also higher margins. SMC EL and the in-house manufacturing company help

sustain programs beyond donor support. This was previously done with the ORS sachets and MNP products: FullCare could soon follow suit.

Conclusions

The project successfully enabled Bangladesh to produce a UN-IMMAP formulation of MMS and become the first low- and middle-income country to produce and sell MMS locally. The FullCare project is one of a kind: a sustainable, market-based model. The type of demand generation activities and tele-counselling augmented feedback systems demonstrate how the program adapted to its unique operational setting. Initial reach and sales data show the acceptance of the product in the segments it targets. The learnings and outcomes from this venture could educate and inform many interventions globally.

References

- 1 World Health Organization, *World Health Organization Model List of Essential Medicines – 22nd List*, 2021, Geneva, 2021.
- 2 United Nations Children's Fund (UNICEF), World Health Organization, *UNICEF-WHO Low birthweight estimates: Levels and trends 2000–2015*, Geneva: World Health Organization, 2019.
- 3 M. Zannat, "Saline price spikes on diarrhoea spurt", *The Daily Star*, 2008. <https://www.thedailystar.net/news-detail-33707> Accessed 20 January 2023.
- 4 S. Askari and S. Gibson, *One MMS a Day and a Healthy Baby is on the Way*, 2020. <https://sightandlife.org/article/one-mms-a-day-and-a-healthy-baby-is-on-the-way/> Accessed 15 January 2023.

A Social Marketing Approach to Introducing Multiple Micronutrient Supplements in the Filipino Context

Kalpna Beesabathuni, Anirudh Poddar, Dev Priya Toor, Puja Peyden Tshering

Sight and Life Foundation, Basel, Switzerland

Florentine Oberman, Sarah Straatsma

DSM, Heerlen, the Netherlands

Christle Grace Cubelo, Tiny Rose Santos

World Vision, Metro Manila, the Philippines

Key messages:

- Family and religion bolster a positive disposition towards life for Filipino women. Husbands are generally supportive and caring of pregnant women and even take up their wife's part of the household chores when possible.
- The pregnancy journey, which in low-income households across the world is generally associated with many concerns, is looked on as a blessing and a special journey from the Filipino woman's perspective. Despite facing challenges such as lack of mobility, drowsiness and body pains as part of her pregnancy experience, she embraces it all.
- Being pregnant does not lead to consumption of any special foods – nearly all consumers mention eating fruits (such as raw mango, banana, and apple) and vegetables (such as bitter melon, taro leaves, string beans and moringa leaves) to maintain good health, generically mentioning that the latter contain vitamins and minerals.

Introduction

Micronutrient malnutrition, or 'hidden hunger', is a one of the key nutritional challenges facing Filipino women and children. The 2019 Expanded National Nutrition Survey (ENNS) shows that anemia, in part caused by deficiencies in iron and vitamin A, is still a focus area, since 20% of pregnant women and 12% of lactating women have anemia.¹

Multiple micronutrient supplements (MMS) are a promising solution to improve birth outcomes of Filipino women and are proven to be a safe, effective, and affordable way to meet the nutrient demands of pregnant women. The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS formulation has been tested globally in low-resource settings and has shown itself to be superior to iron and folic acid (IFA) in improving pregnancy and child health outcomes.²⁻⁴

Joining Forces for Last Mile Nutrition (JF4LMN) is a public-private partnership among World Vision, *Sight and Life* Foundation and Royal DSM N.V. that aims to develop scalable and inclusive business models which increase the availability and consumption of nutritious foods and improve livelihoods at the last mile. The focus of JF4LMN is on a child's first 1,000 days – from pregnancy to their second birthday. The partnership's latest program is in the Philippines, where the aim is to strengthen the affordability and sustainability of the MMS value chain to improve the nutritional status of pregnant women in four pilot locations: Tacloban City, Bulan, Pio Duran, and Pasacao. This is translated into the co-creation of a viable, replicable, and scalable MMS project model by the JF4LMN partners with support from local and national Philippine Government bodies using pilot design and testing.

This pilot model, designed by World Vision Philippines, *Sight and Life* Foundation and DSM, intends to: (i) increase the availability of, and access to, MMS in a sustainable way; (ii) ensure adequate understanding and sustainable use of MMS through social marketing activities; and (iii) work closely with the DOH and Government Agencies on providing technical support for National Policy amendment on MMS, in line with the WHO guidelines and work of other partners. As a first step, a consumer research study was conducted. Its findings are captured in this article. They will inform the social marketing campaign to be launched during the pilot.

“To understand the Filipino mother, one must first understand the role of family in the Philippines”

Methodology

The qualitative consumer research study comprised 16 in-depth interviews (IDIs) and four focus group discussions (FGDs) with pregnant women aged 18–35 years and belonging to a lower socio-economic classification (SEC) in their second or third trimester of pregnancy. Half the women were current IFA users who had been consuming IFA regularly (they have not missed more than seven doses) in the previous three months. The other half were 'laspers' (pregnant women who stopped using IFA for reasons other than accessibility of supply). The study was conducted in four municipalities/cities across the Philippines: 1) Pio Duran Albay (rural); 2) Lagonoy, Camarines Sur (rural); 3) Bulan, Sorsogon (peri-urban/

urban); and 4) Tacloban City, Leyte (urban/peri-urban).

Key findings

1. Social life and identity of the audience is anchored in family

To understand the Filipino mother, one must first understand the role of family in the Philippines. The mother’s daily life revolves around taking care of her family, making the meals, cleaning the house, doing laundry, watching TV, etc. Recreational moments such as going to the beach or mall are also shared with family rather than friends. Beyond this, her aspirations are linked to the wellbeing of the family.

The Filipino mother largely feels inspired and empowered by her family. Almost all women look up to their own mothers as their role model, recalling how their mothers diligently and resiliently took care of the entire household while maintaining a kind, loving and joyful disposition. The husbands also generally play a supportive role, and often become like a ‘mother’ themselves; many women mention that their husbands have assumed responsibilities such as doing the laundry and cooking dinner to ease the burden on them during pregnancy. A ‘lapsesr’ in Lagonoy mentioned: “During pregnancy, my husband turned out to be like my mama. He cooks, cleans, and basically he made me feel like a princess.”

This sense of support underscores two truths. One, men are also excited about and invested in the idea and growth of the family. Two, gender equality in the Philippines is the highest in Asia,⁵ where a matriarchal system affords women an equal share in family inheritance and access to the use, control and ownership of assets.

Apart from family, religion bolsters a positive disposition to life. Many women are church-going and for them, faith in God enables hope and assurance that things will be fine despite seeming otherwise. This in turn allows them to be more resilient, as well as enabling positive values such as kindness and being respectful towards others.

2. Pregnancy is seen as a blessing; not many complaints arise

Nearly all women mentioned that they were happy and excited the first time they heard they were pregnant. The idea of growing the family and welcoming another member brings great joy to them, even if it is not a first-time pregnancy. Some of the high points of the pregnancy for nearly all women is when they experience the baby’s movement: either kicking, or when they hear its heart-beat via an ultrasound. Some worries, however, are voiced. Most women immediately mention not having a safe delivery as their

predominant concern. A ‘lapsesr’ in Bulan mentioned, “I think about the difficulty of delivery, if it’s going to be easy or not. In my first pregnancy, I had experienced dry labor. My water bag broke early. I had dextrose inserted...it was very difficult and painful.”

3. Pregnancy does not compel a radical change in health-related practices

The supreme importance given to pregnancy and growing a family puts the woman and her health at the center of things. Focusing on her health does not involve radically changing her lifestyle, however. For instance, her diet does not change before, during or after pregnancy. Nearly all consumers mention eating fruits (such as raw mango, banana, and apple) and vegetables (such as bitter gourd, taro leaves, string beans and moringa leaves) to maintain good health, generically mentioning that the latter contain vitamins and minerals. Specific benefits are not recalled for most of the foods. Further, any change that takes place, if at all, is reactive in nature. For instance, in response to fatigue, women reduce their workload (chores such as doing laundry).

This behavior could be explained by women’s view of health itself, which focuses much more on ‘what they can see’. **Table 1** outlines what women define as ‘good health’.

4. Midwives play a pivotal role in pregnancy care guidance

For most, the local *barangay* (the smallest administrative division in the country) health center plays a dominant role in guiding their nutrition and health practices during pregnancy, as it is the focal point for all questions and processes. As soon as a woman is pregnant, she goes to the *barangay* health center. It is generally the midwife or nurse that interacts with her, guides her regarding tests to undergo, and introduces her to prenatal supplements. In more urban locations, the *barangay* center is less relied upon as a key provider of pregnancy-related guidance. In Lagonoy and Tacloban (which are both relatively more urban), looking for information online is more common and regular than in Pio Duran and Bulan. There consumers mentioned following Facebook pages such as *Pregnant Mommies* and *Woop Mommyship*, YouTube pages of *Nurze Yeza* and the TikTok page of *Mommy Julie* are also mentioned.

5. Iron and folic acid (IFA) has low awareness and engagement; this category potential is untapped

Given that most women are largely content with their current diet and practices, and traditionally have been, it is no surprise that

TABLE 1: Parameters related to good health, as per the target audience

Physical	Cosmetic	Mental
Absence of sickness	Supple, clear skin	Peace of mind
Good energy levels	Looks like one is ‘blooming’ or ‘glowing’	Clarity of thought
Not too thin or too overweight		Positivity

most women did not have much prior knowledge about IFA before becoming pregnant. Further, most consumers were told by a midwife/health care worker in local health center that IFA would be good for their own and their baby's health. The link to a safe delivery, or to any other benefits (top concerns of the pregnant woman) was not made. For anemic consumers, however, the importance of taking the product was stressed more, along with the fact that taking it would be 'good for the blood'.

Due to lack of knowledge, consumption of the IFA is driven by faith in the midwife, rather than faith in the product itself. Despite this, we found that most women demonstrated diligence in taking the medication. Among these women, those that had a complication in an earlier pregnancy gave even more importance to taking the supplements. Mealtimes acted as anchors for taking supplements and, in many cases, husbands and even children regularly reminded the woman to take the medication. Only a few women used a daily alarm, while some marked their calendars.

'Lapsers' largely discontinued their use of IFA for one of two reasons: 1) The taste of supplement was acrid, sometimes leading to feelings of nausea and vomiting; and 2) IFA consumption was stopped when their midwife/doctor told them that it was no longer necessary (this was only noted in a few cases).

“Nearly all women mentioned that they were happy and excited the first time they heard they were pregnant”

6. *MMS is seen as an upgrade from IFA, and MMS packaging has great potential*

Most women had a positive reaction when shown the MMS product with a brief description (what it contains, recommended dosage, no side-effects) and an outline of its beneficial potential to improve birth outcomes. Overall, the presence of 15 vitamins and minerals was the biggest draw, linked with two core benefits: 1) *Increased efficacy*: multiple micronutrients cues increased efficacy, which itself is linked with an increased likelihood of being able to remain energetic and diligent; and 2) *Convenience*: the product comes across as an all-in-one supplement that provides many nutrients which would otherwise have to be accessed through different foods and supplements.

Some concerns, however, lingered around the flavor of the product. Consumers, especially 'lapsers' who lapsed out of taste, felt that the flavor (such as a strawberry or orange flavor) should match the appealing color (a purplish-pinkish color).

While still at an early stage, the packaging (an unlabeled white bottle containing 180 tablets) invited positive reactions. The bottle pack is novel, whereas blister packs – which consumers have been buying – are more familiar. Consumers see great potential in

designing an appealing and informative pack that clearly outlines each vitamin that the MMS contains, with its specific benefits. A bottle also does not cue medication as much as a blister pack. The inclination to buy a smaller unit is stronger, as consumers are willing to pay more for 30 tablets compared to a one-time purchase of 180 tablets. At an overall level, there is a general willingness to pay for the MMS product, and it is perceived as a product that would be available at local pharmacies and not just for free at the local health clinic. When asked where they could get such a product, MMS was not immediately associated with the *barangay* health center but more with private pharmacies – seen to be something one should pay for, not get for free or at a subsidized rate.

“There is a great opportunity to create an emotional appeal that will truly resonate with the Filipino woman”

What is our social marketing challenge?

The core challenge is to popularize MMS in the context of the Filipino pregnant woman who believes she has the support, and is doing enough, to manage her pregnancy. As such, the potential for prenatal supplements has not yet been unlocked. In this case, as a first step, both awareness and consideration regarding MMS need to be increased. In the other words, we must highlight *what the product is* and *how it helps* in a pregnancy. The secondary challenge is to prevent lapsing. Current and potential consumers need to have communicated to them to *how the product can be best consumed* and *the benefits of taking it for their entire pregnancy*.

In addition to highlighting rational/functional benefits, there is a great opportunity to create an emotional appeal that will truly resonate with the Filipino woman. One way to do this is to celebrate, across different marketing channels, the identity of the woman – family, love, warmth, support, and her relationship with her husband. Relevant and aspirational values for the woman can be highlighted – confident, resourceful, loving, humorous, takes everything in her stride. There are many possibilities for branding the MMS for women: The SuperMom, for example.

Including midwives, health workers and obstetricians are also important, as these are the most trusted sources of information during pregnancy. They should be equipped with messages as to the benefits of MMS, that MMS it is different from/superior to IFA and other prenatal supplements, and the recommended practices that promote regular use (e.g., taking MMS alongside meals or just before going to bed) and eating plenty of vegetables and fruits – all of which factors have been linked to reduced side-effects.^{6,7}

Correspondence: Puja Peyden Tshering, Senior Manager
– Consumer Insights, *Sight and Life* Foundation, PO Box 2116,
4002 Basel, Switzerland
Email: puja.tshering@sightandlife.org

References

- 1 Mbuya, N. V. N. (2021). *Undernutrition in the Philippines: Scale, scope, and opportunities for nutrition policy and programming*. Washington, DC, USA: World Bank Group.
- 2 Multiple Micronutrient Supplement Technical Advisory Group (MMS-TAG), Micronutrient Forum (MNF). Expert consensus on an open-access United Nations International Multiple Micronutrient Antenatal Preparation-multiple micronutrient supplement product specification. *Ann N Y Acad Sci.* 2020 Jun;1470(1):3–13.
- 3 Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2017 Apr 13;4:CD004905.
- 4 Smith ER, Shankar AH, Wu LSF, Aboud S, Adu-Afarwuah S, Ali H, 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* [Internet]. 2017 Nov [cited 2022 May 23];5(11):e1090–100. Available from: <https://jhu.pure.elsevier.com/en/publications/modifiers-of-the-effect-of-maternal-multiple-micronutrient-supple>
- 5 Mathkar M. (2019). 'Philippines leads Asia in gender equality'. *The Hindu*. <https://www.thehindu.com/news/international/philippines-leads-asia-in-gender-equality/article26351544.ece> Accessed 19 January 2023.
- 6 Bahati F., Kairu-Wanyoike S. and Nzioki J.M.. *Adherence to iron and folic acid supplementation during pregnancy among postnatal mothers seeking maternal and child healthcare at Kakamega level 5 hospital in Kenya: a cross-sectional study* [version 2; peer review: 2 approved]. *Wellcome Open Res* 2021, 6:80 (<https://doi.org/10.12688/wellcomeopenres.16699.2>)
- 7 Nasir B.B., Fentie A.M., Adisu M.K. (2020) *Adherence to iron and folic acid supplementation and prevalence of anemia among pregnant women attending antenatal care clinic at Tikur Anbessa Specialized Hospital, Ethiopia*. *PLOS ONE* 15(5): e0232625. <https://doi.org/10.1371/journal.pone.0232625>

Introducing MMS by Strengthening Community and Health Systems

Tanzania's experience in the context of implementation science

Geoffrey Mchau, Erick Killel, Sauli Epimack, Ray Masumo, Germana H Leyna

Tanzania Food and Nutrition Center (TFNC); Department of Epidemiology and Biostatistics; Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

Abraham Sanga, Ramadhani Mwiru, Ramadhani Noor, Charity Zvandaziva, Patrick Codjia

United Nations Children's Fund (UNICEF), Dar es Salaam, Tanzania; United Nations Children's Fund (UNICEF), ESARO, Kenya

Mary Sando, Esther Elisaria

Africa Academy of Public Health (AAPH); Ifakara Health Institute (IHI)

Peter Kaswahili, Swald Msuya, Ahmad Makuwani, Felix Bundala

Ministry of Health (MoH), Dodoma, Tanzania

Salum Manyatta, Benson Sanga

Mbeya Region Secretariate

supplementation, but several bottlenecks contribute to low coverage and uptake of essential health and nutrition services.

- The introduction of MMS represents an opportunity to generate adherence for ANC services, strengthen the health systems, and improve the delivery of nutrition services.
- Through the Improving Maternal Nutrition Project (IMAN), the Government of Tanzania is leading the implementation of an MMS demonstration project focused on the sustainable scale-up of MMS in Tanzania.
- Evidence generated from the demonstration project will inform the learning agenda and implementation of the NMNAP II strategy including addressing micronutrient deficiencies.

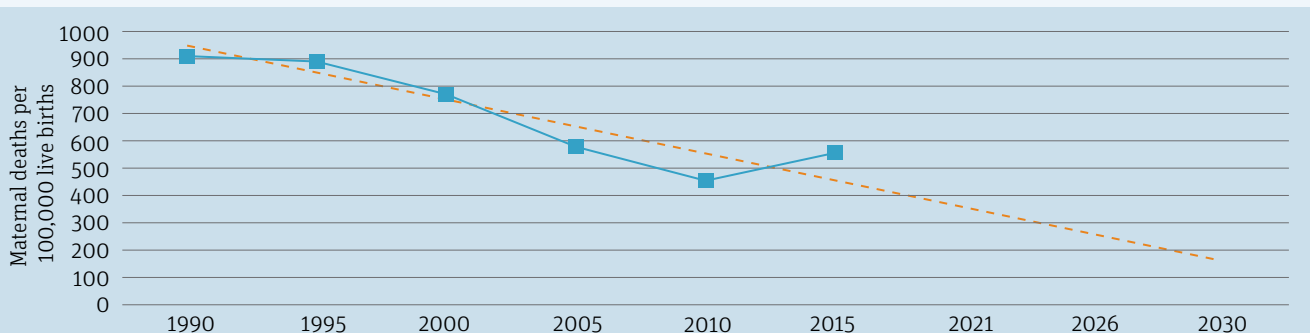
Introduction

The burden of malnutrition among women and adolescent girls in Tanzania is substantial. An estimated 45% of women of reproductive age (15 to 49 years) and 57% of pregnant women are anemic, and one in three women of reproductive age suffer from multiple micronutrient deficiencies, especially iron, iodine, and vitamin A.^{1,2} Maternal micronutrient deficiencies, and anemia in particular, are among the main causes of maternal mortality, with 20% of maternal deaths attributed to severe maternal anemia. The maternal mortality ratio (MMR) increased in recent years – from 454 deaths per 100,000 live births in 2010 to 556 deaths per 100,000 live births in 2015 (Figure 1).² In addition, Tanzania experiences high rates of adverse birth and early child development outcomes including low birth weight (10%), high rates of preterm birth (15.3%), and early-life mortality rates, with 54 deaths per 1,000 births occurring around the time of birth.^{1,2}

Key messages:

- Baseline study information collected was key for the proper design and implementation of an implementation science study on how to roll out a multiple micronutrient supplements (MMS) program.
- Implementation of the National Multisectoral Nutrition Action Plan (NMNAP) I and II prioritizes the use of globally recommended interventions for ANC, including micronutrient

FIGURE 1: Trends in MMR in Tanzania (DHS)



Despite the high coverage of antenatal care (ANC) services in Tanzania (98% for at least one ANC visit and 51% for the four recommended ANC visits), effective coverage of iron and folic acid (IFA) supplementation remains low (29% nationally).³ While IFA has long been the standard of care for pregnant women in low- and middle-income countries (LMICs), a greater range of vitamins and minerals should be considered to support a healthy pregnancy. Multiple micronutrient supplements (MMS), containing 15 vitamins and minerals, may fill this gap and has been demonstrated to be a safe, affordable, and effective intervention when it comes to improving maternal and child nutrition and health outcomes.⁴

“MMS have been demonstrated to be a safe, affordable and effective intervention”

Evidence from baseline studies in Mbeya

In the Mbeya Region of Tanzania, maternal underweight among young pregnant women (15–19 years) remains modest (11%), while multiple micronutrient deficiencies among pregnant women including anemia across all trimesters (25.5%) and 60% of anemic pregnant women presented with iron deficiency anemia (IDA). The prevalence micronutrient deficiencies was as follows; RBC folate (21.7%), vitamin B₁₂ (9.9%), iron (38.4%), vitamin A (9.8%) and median Urinary Iodine Concentration (UIC) was 279.4 µg/L. Persistent high rates of pregnant women who consume unhealthy refined grains (48%) with low consumption of green leafy vegetables (29.2%) also remain. Baseline analyses found that reported barriers to ANC use among pregnant women and adolescents include feeling shame around pregnancy, lack of support from a spouse in the case of unmarried women, economic difficulties, long waiting times for service, lack of

trained healthcare providers, mistreatment by health professionals (e.g., verbal abuse), and lack of education. Older women have reported additional barriers to accessing ANC including distance to the health facility and geographical location (mountainous), limited support from spouses/partners (especially in the case of single mothers), and traditional beliefs and social norms.

The Improving Maternal Nutrition Project (IMAN)

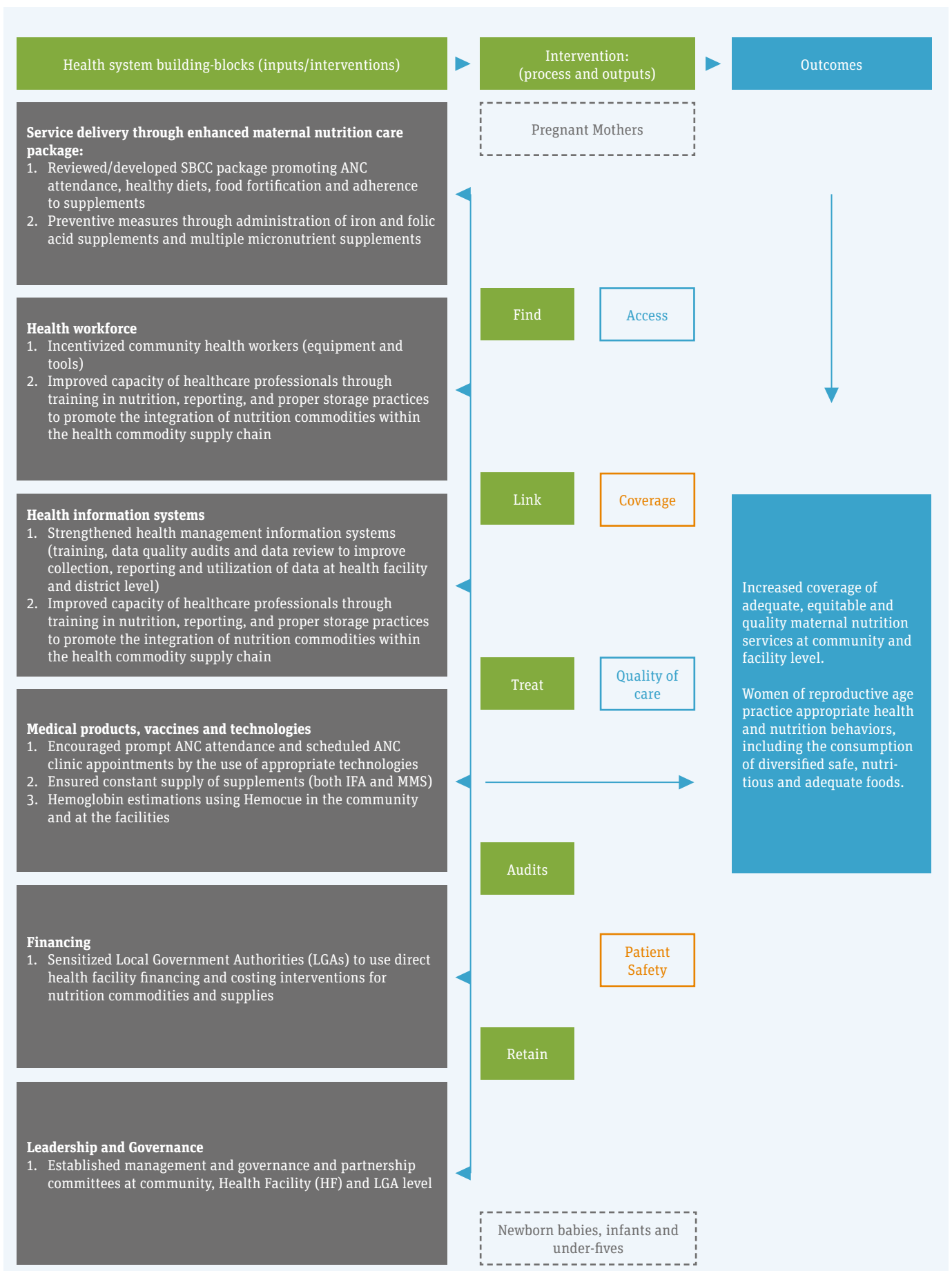
Tanzania’s nutrition agenda is guided by the National Multisectoral Nutrition Action Plan II (NMNAP II). During the mid-term review of the NMNAP I in 2018–19, the government proposed the need for a renewed approach to addressing maternal nutrition, and the Improving Maternal Nutrition project (IMAN) was born. As a first step, the Government of Tanzania recommended that the Tanzania Food and Nutrition Center (TFNC) should conduct a baseline survey to inform the design of the IMAN project. In collaboration with NGOs, academics and community-based organizations, with the support of UNICEF, a baseline study in the Mbeya region was conducted. The results were then used to inform the design of the MMS demonstration project, which aimed to document best practices in the transition from IFA to MMS. However, the feasibility of transitioning from IFA to MMS while utilizing the existing health platform in Tanzania was unknown. As such, a strengthened health system approach that addresses key barriers in the form of human resource capacity, supply chain issues, and cultural and social norms in the uptake of services was introduced. An implementation science research was designed to generate evidence on the capacity-building strategy with five (5) domains that can improve the delivery of quality maternal health and nutrition services. Beyond MMS, the project will also address issues of quality maternal nutrition counseling and promotion of the consumption of nutritious food during pregnancy, among other things.

Figures 2 and 3 demonstrate the design of Tanzania’s approach toward the implementation of the IMAN project in the Mbeya region.

FIGURE 2: Theory of change for the IMAN project in Mbeya

Impact	Reduced micronutrient deficiencies and adverse birth outcomes among pregnant women			
Outcome	1) Increased demand for ANC services 2) Coverage/delivery of nutrition services through ANC		3) Increased uptake / adherence to maternal nutrition services through ANC, including MMS	
Risk	Occurrence of natural disaster and climate change related shocks, political instability, reduced donor funding, high turnover of key staff in the government, occurrence of economic shocks, COVID-19 pandemic, change in political will regarding nutrition			
Assumptions	Government policies and regulations continue to support provision of maternal nutrition services, communication platforms are willing to support maternal nutrition promotions, community members are open-minded toward good maternal nutrition			
Outputs	1.1 Increased availability, accessibility and sustainability of maternal nutrition services at facility and community level	1.2 Improved enabling environment for maternal nutrition	2.1 Women of reproductive age have increased knowledge about diversified, safe, nutritious and adequate DIETS, improved access to these, and consequently improved uptake	2.2 Increased empowerment of adolescents, parents (men and women) and care-givers and consequent involvement regarding informed and appropriate health and nutrition behaviors
Strategies	Strengthening Health and Community Health Systems for Maternal Nutrition			

FIGURE 3: The intervention strategy ‘Find, Link, Treat, Audits and Retain (FLTAR)’ model linked with health system building-blocks



IMAN project design

The project is an implementation research project designed to strengthen the health system and community and framed as a *quasi-experimental pre- and post-intervention survey design*. This design allows a comparison of outcomes between the intervention and control arms without relying on random assignment, meaning that subjects are assigned to groups based on non-random criteria. The project has three major arms targeting pregnant mothers, as demonstrated in **Figure 4**.

“The project is framed as a quasi-experimental pre-and post-intervention survey design”

Supply chain management

The project used the existing supply systems with the Ministry of Health and local government authorities. Whereas the Chief

Pharmacist (CP) ensures policy, guidelines, and timely distribution of all medical and equipment supplies across all levels, the Medical Stores Department, by means of the Electronic Logistics Management System (ELMS), ensures proper storage, supplies, logistics and distribution based on the needs of each health facility. Moreover, the validation of commodities is carried out by Tanzania Medicine and Medical Devices Authority (TMDA). The IMAN project used the same system for the importing, validation and distribution of MMS in Tanzania.

IMAN coordination and partnership

The coordination of IMAN focuses on three key aspects: 1) the use of the existing NMNAP governance structure at all levels, 2) co-leadership with the regional and district authorities, and 3) engagement of an independent Technical Advisory Group (TAG) with comprehensive Terms of Reference. These measures enhance ownership and leadership by the Government of the study findings. **Table 1** demonstrates the roles and responsibilities involved in coordinating the IMAN project.

FIGURE 4: Implementation design and implementation phases

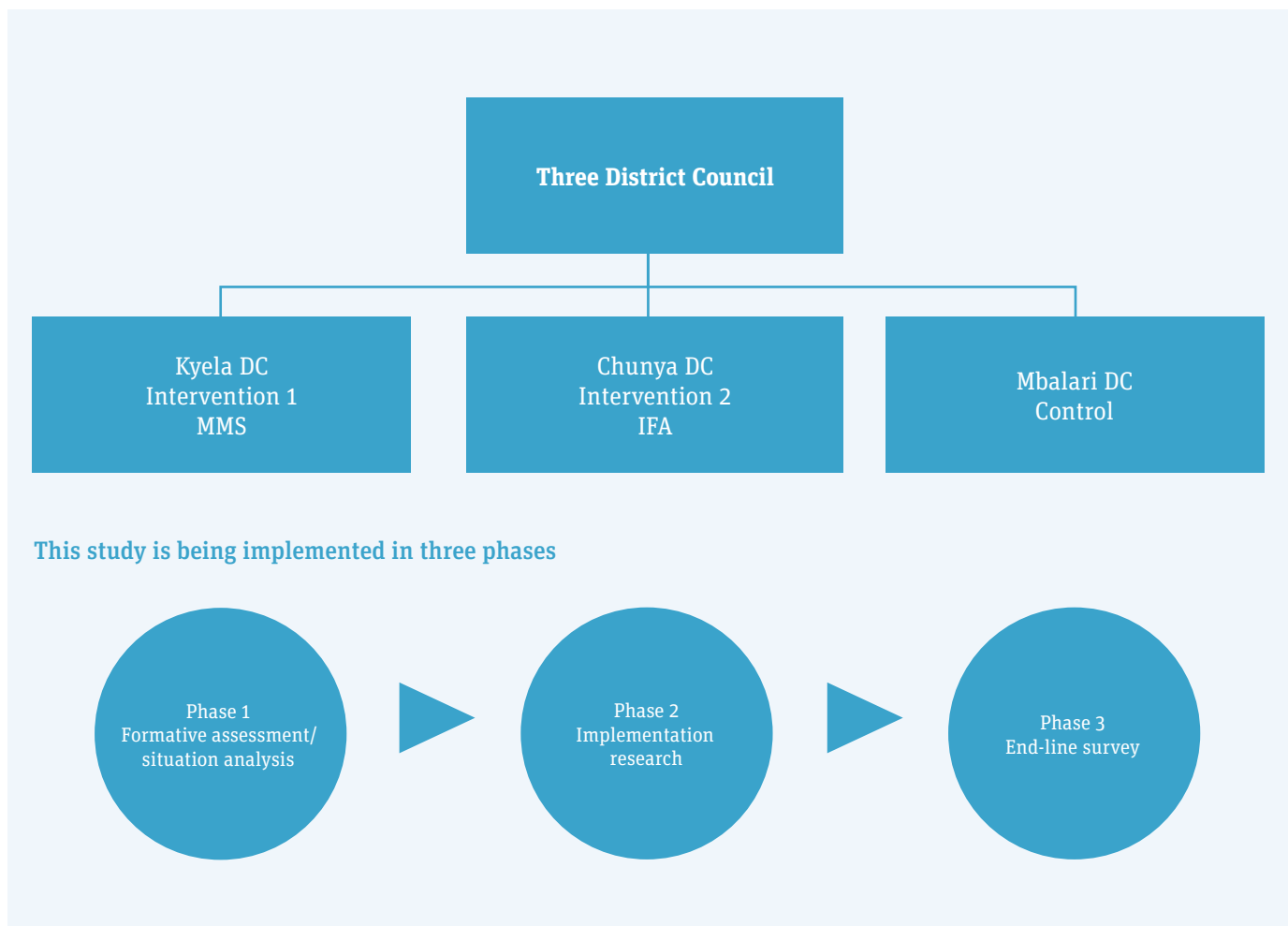


TABLE 1: Roles and responsibilities for coordinating the IMAN project

Partners	Roles
Ministry of Health (Nutrition, Procurement System Unit & Reproductive and Child Health)	<ul style="list-style-type: none"> • Technical leadership, development of policies and guidelines • Facilitate procurement of MMS and forecasting of supplies
Tanzania Food and Nutrition Center (TFNC)	<ul style="list-style-type: none"> • Overall coordination; micronutrient survey in Mbeya Region
President’s Office Regional Administrative and Local Government	<ul style="list-style-type: none"> • Overall guidance and supervision of project implementation
Mbeya Regional Secretariate and Local Government Authorities (Mbeya, Chunya, Kyela and Mbalari)	<ul style="list-style-type: none"> • Local coordination, training and mentorship of health service providers, supportive supervision • Implementation of project at health facility level; data collection, analysis and use for evidence-based planning and budgeting
CRS / COUNSENUTH	<ul style="list-style-type: none"> • Community Health Worker training and supervision, support for community activities implementation such as Village Health and Nutrition Days (VHNDs) and Counselling at Household (HH) level
Medical Store Department	<ul style="list-style-type: none"> • Logistics provision and distribution of supplies (IFA/MMS)
African Academy for Public Health (AAPH), Ifakara Health Institute (IHI)	<ul style="list-style-type: none"> • Conduct of studies and assessments including comprehensive situation analysis, baseline survey, barrier analysis, and formative monitoring
Technical Advisory Group (TAG)	<ul style="list-style-type: none"> • Review of evidence, feedback and guidance on project implementation
Sight and Life Foundation, Pharmaceutical Service Unit (PSU)	<ul style="list-style-type: none"> • Support with the analysis of procurement, production and distribution of supplies • Formative research for the introduction of multiple micronutrient supplements in Tanzania.
Nutrition International	<ul style="list-style-type: none"> • Support with the analysis of the cost-effectiveness of MMS
UNICEF (CO, RO, HQ) and Bill & Melinda Gates Foundation	<ul style="list-style-type: none"> • Overall technical and financial support

“The implementation of the IMAN project in Mbeya will help inform the best approach to introducing MMS within Tanzania”

Conclusion

Through the IMAN project, the Government of Tanzania is leading the implementation of a demonstration project focused on the sustainable scale-up model of MMS in Tanzania. It is strategically designed to (1) strengthen the health system (capacity-building

for human resources, commodities, and delivery platforms), and (2) improve the enabling environment (in terms of nutrition governance and information systems). The baseline information collected supported the design of the IMAN project across all levels (national and subnational), as well as allowing for the involvement of key stakeholders during each stage, which is critical for smooth implementation. The project offers the opportunity to generate demand for ANC, strengthen the health systems and improve the delivery of maternal health and nutrition services. Through rigorous measurement & evaluation and new feedback loops, the implementation of the IMAN project in Mbeya will help inform the best approach to introducing MMS within Tanzania, and across the region as a whole.

Acknowledgements

UNICEF, Bill & Melinda Gates Foundation, Catholic Relief Services (CRS), President's Office, Regional Administration and Local Government (POLARG), Ministry of Health (MOH), Health Promotion Section (HPS), Pharmaceutical Service Unit (PSU), Reproductive and Child Health (RCH) Nutrition International (NI), Ifakara Health Institute (IHI), Africa Academy of Public Health (AAPH), MBEYA Region Secretariate Council health management Team (CHMT) of Chunya and Kyela District.

Correspondence: **Geoffrey Mchau**, Tanzania Food and Nutrition Center (TFNC), 22 Barack Obama Drive, PO Box 977, Dar es Salaam, Tanzania
Email: gmchau@gmail.com

References

- 1 Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], Tanzania Food and Nutrition Centre (TFNC), National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS) [Zanzibar] and UNICEF. 2018. Tanzania National Nutrition Survey using SMART Methodology (TNNS) 2018. Dar es Salaam, Tanzania: MoHCDGEC, MoH, TFNC, NBS, OCGS, and UNICEF.
- 2 Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) [Tanzania Mainland], Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), and ICF. 2016. Tanzania Demographic and Health Survey and Malaria Indicator Survey (TDHS-MIS) 2015-16. Dar es Salaam, Tanzania, and Rockville, Maryland, USA: MoHCDGEC, MoH, NBS, OCGS, and ICF.
- 3 Moshi, F. V. (2021). Prevalence and factors which influence early antenatal booking among women of reproductive age in Tanzania: An analysis of data from the 2015-16 Tanzania Demographic Health Survey and Malaria Indicators Survey. *Plos One*, 16(4), e0249337.
- 4 Gernand, A. D., Schulze, K. J., Stewart, C. P., West, K. P., & Christian, P. (2016). Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. *Nature Reviews Endocrinology*, 12(5), 274-289.

Exploratory Efforts to Distribute UNIMMAP Multiple Micronutrient Supplements (MMS) in the Democratic Republic of the Congo

Mulamba Diese, Davidson Mamboleo

Vitamin Angel Alliance, Democratic Republic of the Congo

Bruno Bindamba, Augustin Kamanda, Beatrice K Tshiala

Ministry of Health, Kinshasa, Democratic Republic of the Congo

Abel Ntambue

University of Lubumbashi, School of Public Health, Lubumbashi, Democratic Republic of the Congo

Ludvine Mbala

UNICEF, Kinshasa, Democratic Republic of the Congo

Aimerance Kabena

Helen Keller International, Kinshasa, Democratic Republic of the Congo

Molly Russ, Quinn Harvey, Shannon E King,

Kristen M Hurley

Vitamin Angel Alliance, USA

Introduction

While rich in natural resources, the Democratic Republic of the Congo (DRC) remains one of the poorest countries in the world. Weak infrastructure, armed conflict and food insecurity all contribute to poor maternal health and birth outcomes. The country has a maternal mortality rate of 473 per 100,000 live births,¹ neonatal mortality of 27 deaths per 1,000 live births,² and under-five mortality estimated at 81 deaths per 1,000.³ Many (38%) pregnant women are anemic,⁴ the preterm birth rate is 4.8%,⁵ and the low birthweight rate is 10.8%.⁶

Since 2015, the Vitamin Angel Alliance (VA) has collaborated with the Ministry of Health (MoH), key public health nutrition stakeholders, and local non-governmental organizations (NGOs) in 15 of 26 provinces in the DRC. These collaborations are intended to help build capacity and expand coverage of evidence-based nutrition interventions (i.e., vitamin A supplementation, deworming, and United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) multiple micronutrient supplements [MMS]) to pregnant women, infants and young children in underserved communities. Additionally, VA and its local partners have engaged in awareness-raising and consensus-building events, the provision of technical assistance, and the donation of nutrition commodities to support MMS use to approximately 2 million pregnant women over the last 5 years. A multi-year process has been undertaken with several different policy and program activities to explore the introduction and scale-up of MMS in DRC (**Figure 1**).

The landscape for MMS in DRC

DRC's National Health Development Plan Nutrition Domain 2011–2015 recommended that pregnant women receive MMS to reduce micronutrient deficiencies associated with poor maternal and pregnancy outcomes.⁷ However, while an MMS policy and political will exist to implement MMS, this policy has not been fully implemented due to a lack of resources (supply) and capacity (demand and delivery of services within antenatal care [ANC] services), this policy has not been fully implemented.

Exploratory efforts to distribute MMS to pregnant women in the DRC

In 2018, in partnership with the MoH and 76 local NGOs, VA supported (via the provision of commodities and technical assistance) the exploratory distribution of MMS to pregnant women in

Key messages:

- The Government of the Democratic Republic of the Congo's (DRC) National Health Development Plan Nutrition Domain 2011–2015 recommended the use of multiple micronutrient supplements (MMS) for pregnant women.
- Since 2018, in coordination with the Ministry of Health and over 60 local non-governmental organizations, the Vitamin Angel Alliance has been supporting exploratory efforts to scale up MMS in the DRC.
- Key lessons learned include the value of strong local partnerships, investment in capacity-building among health care providers, and the use of community socialization to increase demand for MMS.

“VA partnered with a local researcher to conduct a landscape analysis in 2021”

the DRC. Program feedback suggested that MMS was accepted by healthcare providers and pregnant women, their communities, and their families alike. Throughout this period, demand for MMS increased among both pregnant women and healthcare providers, as the perceived benefits of MMS were numerous. This initial distribution period, along with successful awareness-raising efforts, led to the official launch of the MoH's MMS program in 2021.

To begin to better understand how to deliver MMS most effectively to pregnant women within the national context and system, VA partnered with a local researcher to conduct a landscape analysis in 2021. The landscape analysis reviewed existing literature on health and nutrition indicators in the country, mapped key nutrition policies and programs, and included stakeholder interviews to help understand the barriers and opportunities related to introducing a new intervention (e.g., United Nations International Multiple Micronutrient Antenatal Preparation [UNIMMAP] MMS) within the context of ANC services and programs. Awareness-raising and consensus-building efforts occurred simultaneously with landscaping efforts and have been used to inform next steps towards the introduction of the intervention.

The landscape analysis found that maternal anemia remains high (38%) and is primarily caused by iron deficiency in pregnant women and women of childbearing age.⁴ In addition, experiences with iron and folic acid (IFA) supplementation in the DRC suggested that the following barriers may also impede effective MMS programming: i) lack of training for healthcare providers, ii) limited product (i.e., UNIMMAP MMS) availability, iii) unwillingness of health providers to prescribe IFA because of its perceived intol-

erance by pregnant women, and iv) high cost of IFA, which is not available for free within the existing health system.

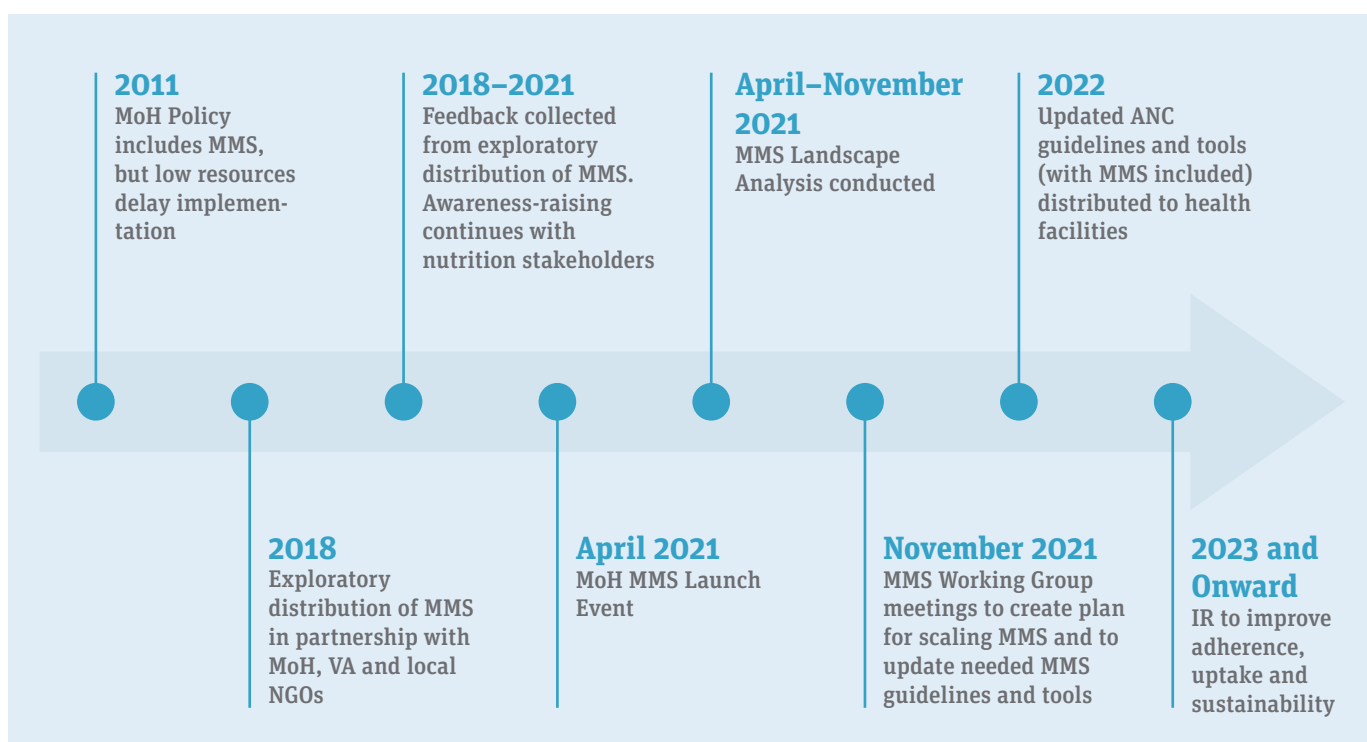
On 20 April 2021, the MoH officially launched an MMS program in the DRC. This event was attended by more than 100 participants from government and NGOs, including directors from the three key national programs: the Program for Nutrition, the Program for Reproductive Health, and the Program for Maternal, Neonatal and Child Health. The event resulted in strong consensus among stakeholders that there was a need to progress efforts to introduce MMS in the DRC. To do this, a plan was developed to revise the *National Maternal Health and Nutrition Guidelines* to include MMS as part of standard ANC services and develop a plan to strengthen ANC delivery in order to ensure high MMS uptake and adherence.

The call to develop this plan triggered the formation of a working group of public health nutrition stakeholders including UNICEF, Helen Keller International, VA, development agencies, government agencies, academia, and more. This group met on 11–12 November 2021 to draft a *Plan de mise à l'échelle de la Supplémentation en micronutriments multiples chez les femmes enceintes, aux consultations prénatales* (or Plan for scaling up multiple micronutrient supplementation in pregnant women at antenatal clinics). Ultimately, the plan was developed and signed into effect by the General Secretary of the MoH on 14 January 2022.

Development of National Guidelines and Plan for the Introduction of Antenatal MMS

Based on the findings from the landscape analysis and corre-

FIGURE 1: Timeline of MMS program milestones in DRC



sponding awareness-raising and consensus-building activities, in 2021 the *National Maternal Health and Nutrition Guidelines* were revised to include antenatal MMS in place of IFA. At the same time, tools used within the ANC system, such as the ANC consultation register and the ANC client's clinical form and card, were updated to include MMS. These guidelines and tools were printed and distributed by local health authorities and provided to frontline workers to inform them of the new guidelines and to facilitate the ultimate introduction of MMS for pregnant women.

Conducting implementation research to optimize MMS uptake and adherence

As part of the continued plan for introduction and scale-up of MMS in the DRC, the MoH is also partnering with VA and other key stakeholders to conduct implementation research to address various questions raised by the MMS working group in November 2021. This includes developing social and behavior change strategies to optimize MMS demand and delivery, answering supply questions such as how to implement MMS in the context of a cash-driven healthcare system, determining strategies to increase MMS uptake and adherence, and addressing issues of achieving a sustainable supply of MMS in-country.

“The landscape analysis found that maternal anemia remains high”

Lessons learned from the MMS exploratory distribution efforts

Since the MMS exploratory distribution program was first introduced in 2018, the provision of MMS has grown despite challenges due to political insecurity, weak infrastructure and high logistical costs. The provision of MMS has increased from 50,000 pregnant women in 2018 to over 600,000 pregnant women in 2022, and demand for MMS continues to increase due to awareness-raising activities and by directly addressing common misunderstandings about MMS. For example, MMS nutrition information has reached even the most remote communities by using communication methods that are trusted sources of health information and news, such as radio shows and faith-based women's groups. Having local support from key community members has also helped to build trust and has led to higher care-seeking and use of MMS by pregnant women.

Another key learning from the exploratory MMS program has been the value of investing in capacity-building of service providers. In the exploratory program, providers were taught about MMS, how to provide it, and how to counsel patients on MMS and other critical nutrition practices. The creation of a strong training program and associated learning support tools is highly valued by service providers. Further, in 2022 VA sponsored an independent

household coverage study in three provinces, which found that most (88.8%) reported high adherence to MMS, with reasons for non-adherence including forgetfulness, fear of having a big baby, and an increased appetite after taking the supplements. Having trained service providers who can provide effective counselling along with the provision of MMS could help reduce these barriers to adherence.

“Demand for MMS continues to increase due to awareness-raising activities and by directly addressing common misunderstandings”

Conclusions

DRC's policy environment combined with landscaping and exploratory MMS distribution efforts have played a critical role in raising awareness, building consensus, creating new guidelines, and planning for MMS program introduction and scale-up in the DRC. As the MMS program in DRC grows into the future, the focus is to ensure the sustainability of the program and its integration into government health systems as part of ANC services. Several lessons from the existing MMS exploratory efforts have helped and will continue to inform this integration. For example, VA partners continue to raise awareness and act as influencers and champions in the national and subnational public health nutrition space, and MMS service providers continue to explore different delivery platforms and strategies to improve its overall coverage and adherence.

Acknowledgement

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Correspondence: Shannon E King, Implementation Science Manager, Vitamin Angel Alliance, 6500 Hollister Ave Suite 130, Goleta, CA, 93117, USA

Email: sking@vitaminangels.org

References

- 1 World Bank. Maternal Mortality Ratio. 2020. <https://data.worldbank.org/indicator/SH.STA.MMRT> Accessed 30 October 2022.
- 2 World Bank. Neonatal Mortality Ratio. 2020. <https://data.worldbank.org/indicator/SH.DYN.NMRT>. Accessed 30 October 2022.

- 3 World Bank. Under-five Mortality Ratio. 2020. <https://data.worldbank.org/indicator/SH.DYN.MORT>. Accessed 30 October 2022.
- 4 Chola Mwansa Joseph et al. Prevalence and associated factors of anemia during pregnancy in Lubumbashi, in the south of Democratic Republic of Congo: situation in 2020. *PAMJ – Clinical Medicine*. 2021; 7:19.
- 5 Fiston Ilunga Mbayo et al. The determinants of premature birth during the year 2018 at the General Reference Hospital of Malemba in the Democratic Republic of Congo. *Pan African Medical Journal*. 2020; 37:30. <http://dx.doi.org/10.11604/pamj.2020.37.30.25205>
- 6 World Bank. Low-birthweight rate. 2020. <https://data.worldbank.org/indicator/SH.STA.BRTW.ZS> Accessed 30 October 2022.
- 7 Republique Democratique du Congo Ministere de la Sante Publique. Plan National de Développement Sanitaire (PNDS) Volet Nutrition 2011 – 2015. December 2010. <https://www.medbox.org/document/drc-plan-national-de-developpement-sanitaire-pnds-volet-nutrition-2011-2015#GO>. Accessed 10 November 2018.

Enabling the United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) to Implement and Evaluate Antenatal Multiple Micronutrient Supplementation in Jordan

Masako Horino, Rami Habash, Lui Al-Khatib, Tamara Hani, Tareq Al-Jilani, Salam Ghanem, Akihiro Seita
United Nations Relief and Works Agency for Palestine Refugees in the Near East, Amman, Jordan

Klaus Kraemer

Sight and Life Foundation, Basel, Switzerland

Kristen M Hurley

Vitamin Angel Alliance, Goleta, CA, USA

Keith P West, Jr

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Introduction

Micronutrient deficiencies (MNDs) represent a global burden that affects an estimated 372 million preschool-aged children and 1.2 billion women of reproductive age.¹ Pregnant women are susceptible to MNDs due to increased nutritional demands.² Several trials have revealed the efficacy of multiple micronutrient supplementation (MMS) in improving nutrient status, reducing inflammation³ and lowering risks of low, preterm and small-for-gestational-age births.⁴ Maternal anemia, largely attributed to iron deficiency,⁵ can also be due to effects of deficiencies in hematinic nutrients such as vitamins A,⁶ B-complex,⁷ C,⁸ D,⁹ and E,¹⁰ zinc¹¹ or other nutrients that facilitate the absorption, storage, release and transport of iron, support erythropoiesis and strengthen host defenses against infections.^{12,13} Reports have repeatedly shown gestational deficiencies of vitamins A, D, E and B-complex, iron, zinc and iodine likely coexisting in Palestine refugee enclaves throughout the Middle East.^{14,15} Complementary to dietary counselling, MMS offers a safe, directed and effective approach to control this problem.

In 2020, the World Health Organization (WHO) updated its guideline on antenatal MMS, recommending its use in the context of rigorous research where programs are being considered¹⁶ and, in 2021, added a generic supplement composition to its Essential Medicines List, providing an approximate recommended dietary allowance for 15 micronutrients¹⁷ that aligns with the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS formulation. Among several qualifying remarks on use of MMS, is the advice that implementation research (IR) should be conducted to evaluate acceptability, feasibility, sustainability, equity and cost-effectiveness of MMS delivery.¹⁶ The current environment offers an actionable policy framework to support the goal of the United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) to replace iron-folic acid (IFA) with MMS through its antenatal care (ANC) system serving ~90,000 pregnant women annually in Palestine refugee enclaves in Jordan, Syria, Lebanon and Palestinian

Key messages:

- Antenatal micronutrient deficiencies and anemia represent a public health burden in Palestine refugee enclaves throughout the Middle East.
- UNRWA, providing care to 90,000 Palestine refugee pregnant women each year, started considering MMS intervention in early 2020, launching a three-year program gestation.
- Processes within the UNRWA health system were prospectively noted, assigning and retroactively adjusting (+/-) scores to events, reflecting perceived contributions toward enabling the Agency to implement this new program.
- Plotting assigned scores of events revealed that ~20% of the Agency's enablement was attained in the first two years of discussions, planning and resourcing while navigating external influences; 80% was achieved as processes coalesced to accelerate progress in the year before start-up.

Territories of the Gaza Strip and West Bank. This paper describes processes whereby UNRWA developed its capacity and readiness to replace IFA with MMS,¹⁸ with an IR agenda that complies with the current WHO guideline.¹⁶

Iron-Folic Acid Supplementation: existing standard of preventive care²²

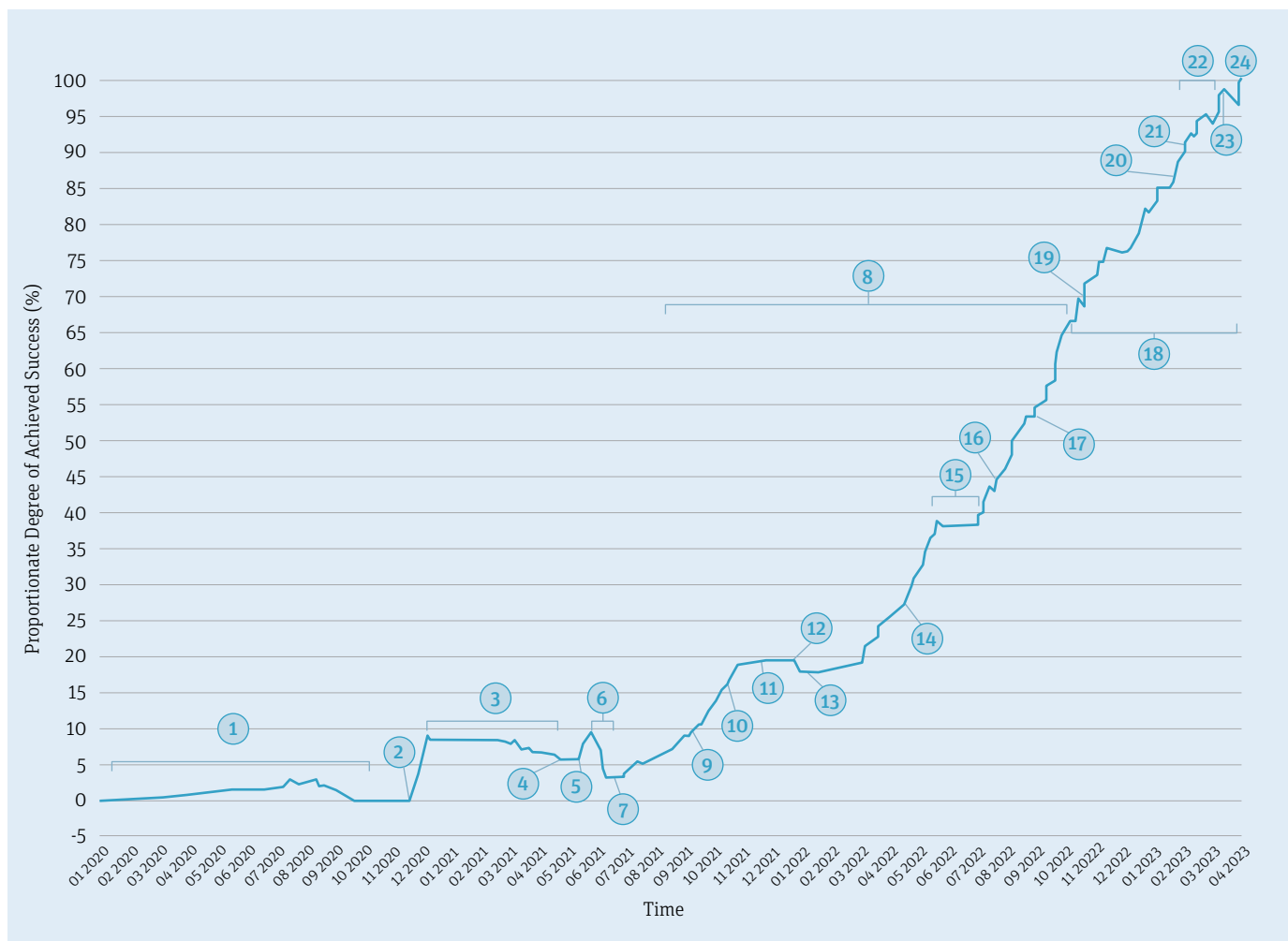
UNRWA has a 30-year history of addressing maternal anemia through the provision of antenatal IFA supplementation.¹⁹ Following publication of its Technical Instruction on Antenatal Supplementation in November 2001,²⁰ the Agency began providing tablets containing 60 mg of iron plus 400 µg folic acid daily as a standard of ANC care, starting late in the first trimester. In 2015, motivated to reduce complaints of early side-effects attributed to iron, UNRWA modified its protocol to prescribe only daily folic acid (400 µg) for prophylaxis at registration, followed ~1 month later (early 2nd trimester), with a combination of 100 mg of iron plus 400 µg folic acid, 2–3 times weekly, to be taken the remainder of pregnancy.²¹ Effectiveness of the revised protocol has, however, remained uncertain, reflected by a clinic prevalence of anemia (hemoglobin <110 g/L) in the 24th week of gestation of

22.5% in 2005 and 43% in 2019.²² Plausible explanations for a lack of effect include poor adherence due to gastrointestinal side effects (constipation, nausea, vomiting and diarrhea) possibly linked to the larger, if less frequent, prescribed dose of iron;²¹ difficulties adhering to a complex regimen of daily folic acid in first trimester replaced by twice-thrice weekly IFA in second and third trimesters; deficiencies of other hematinic micronutrients that could limit iron homeostasis and erythropoiesis;⁸ and inadequate maternal knowledge about IFA, which has been associated with lower adherence.²³

MMS: new UNRWA standard of preventive care

Concerned about the low effectiveness of its IFA protocol amidst evidence of micronutrient deficiencies among Palestine refugee pregnant women,¹⁴ and prompted by evidence of improved pregnancy outcomes in large trials,^{24–26} supported by meta-analyses,²⁷ UNRWA started considering introducing MMS into ANC services in 2020. Interest within the Agency grew through internal reviews of policy guidelines,¹⁶ clinic data on a persistent high rate of maternal anemia, standardized MMS product specifications²⁸ and external assurances of the intervention’s safety

FIGURE 2: MMS Enabling Environment Graph



Event	Date	Score		Description
		% +/-	Sum	
1	1-9/2020	0	0	Orientation, evidence reviews, system discussions, in-Agency constituency building.
2	10/2020	9	9	MMS supplies committed to UNRWA for health system program from Kirk Humanitarian.
3	10/2020	-3	6	Multiple agency staff meetings, debates on effectiveness of MMS vs IFA to prevent anemia, system changes to switch products, purpose of research, favoring maintaining IFA as standard of care.
4	3-4/2021	0	6	Gaza Strip identified for start-up due to high anemia rate. Constructive debate on impact, feasibility and pros/cons of MMS vs strengthening IFA standard of care procedures extends to Gaza Field Office.
5	4/2021	4	10	MMS Working Group formalized, MMS IR concept paper shared, gains support across UNWRA health leadership.
6	5/2021	-7	3	Israel-Palestine hostilities erupt in Gaza, severely affecting services and plans for MMS program and IR.
7	6/2021	6	9	Director of Health visits Gaza, defers launching MMS in Gaza and redirects efforts to Jordan.
8	7/2021-7/2022	*	*	MMS Working Group reorganizes, routinely meets with leadership, staff and technical advisors to build staff support, program procedures, and UNWRA clinical and IR-systems evaluation protocols to implement ANC MMS delivery in Jordan,
9	8/2021	8	17	Director of Health requests plan for ~3-month MMS pilot familiarization phase, to be conducted in 2 ANC clinics.
10	9/2021	2	19	UNWRA meets with Nutrition Dept, Jordanian Ministry of Health, receives concurrence to scale up MMS in 25 clinics with parallel IR plan; signals interest in learning IR findings to help guide MOH decisions on MMS use.
11	11/2021	1	20	MMS program and IR plan presented and receives support at retreat for nursing chiefs in all Fields of Operation.
12	11/2021	-2	18	MMS plan in Jordan presented at retreat for health chiefs in all Fields of Operation; met with concerns about MMS replacing IFA to prevent anemia, resources needed for other priorities, budget limitations and staff shortages.
13	2/2022	2	20	MMS IR proposal reviewed, deemed exempt, and given approval by UNRWA Research Review Board.
14	4/2022	13	40	Memorandum of Understanding signed by UNRWA and Vitamin Angel Alliance and on behalf of Johns Hopkins Program in Human Nutrition/Sight and Life faculty, formalizing support and technical assistance for Jordan MMS IR.
15	4/2022	-1	39	Process stalled, with further debates on integrating and documenting varied IFA treatment protocols for anemia with MMS prophylaxis, and approaches to harmonize data collection across planned MMS and IFA clinics.
16	6/2022	15	54	Following comprehensive review, Jordanian Food and Drug Administration approved MMS formulation, allowing UNWRA Central Pharma to import large supplies of MMS into Jordan.
17	7/2022	13	67	MMS orientation meetings with staff from all 25 clinics, discussing clinician (midwife and physician) guides, standard operating procedures, education materials for patients, data collection methods and timetable for program and IR
18	9/2022-1/2023	15**	82**	Planned ~3-month MMS pilot starts in three clinics (Amman New Camp and Marka) with observations, meetings to clarify procedures, data collection refinement, eHealth data entry programming, and IR protocol finalization and submission to Johns Hopkins Institutional Review Board (IRB); extends to ~5 months while program evaluation awaits start-up.
19	9/2022	4	86	UNWRA Director of Health and Chief of Maternal & Child Health present and receive support from attendees at a WHO MMS Consultation in Geneva for UNWRA program with IR plan in compliance with WHO guidelines.
20	11/2022	6	92	Training program (4 days) held for staff from all 25 clinics on MMS and IFA program and IR procedures, including patient flow, data collection, exit interviews for pregnant women, and monthly staff opinions.
21	12/2022	3	95	Johns Hopkins Institutional Review Board classifies IR protocol as system-focused "public health surveillance".
22	1/2023	4	99	eHealth programming to support MMS IR tested in four clinics, functioning well.
23	1/2023	-4	95	Diverse, minor procedural glitches detected, discussed and fixed as program and IR procedures undergo complete review and "fine tuning" leading to ~1 month delay in MMS program and IR start-up.
24	2/2023	5	100	Start of MMS vs IFA parallel program, in 13 and 12 UNWRA antenatal clinics, respectively, stocked with appropriate supplement, staff trained, and IR protocol approved.

and preventive potential. A commitment from Kirk Humanitarian (Salt Lake City, UT, USA) through the Vitamin Angel Alliance to make UNIMMAP-formulated, US Pharmacopeia-certified MMS supplies available to the Agency catalyzed UNRWA's resolve to replace IFA with MMS.

Envisioning the need for adequate time to plan the MMS program and evaluation, and guided by theoretical frameworks,^{29,30} UNRWA scheduled a series of meetings to: build constituent knowledge, support and capacity; consider in which country (Field of Operation) to start; revise internal policies; and secure supplies, funding and approvals for planned research. Anticipating the process to be a learning experience, our research team coordinator (MH) tracked processes, decisions and events along the way, assigning and additively plotting (+/-) scores representing perceived values of these processes toward reaching the goal of enabling the Agency to start this new program. Prior to the program starting in late February 2023, initially assigned scores were reexamined and, for some, adjusted retroactively to more closely reflect their impact on the process. Raw scores were transformed to proportions on a scale ranging from 0%, representing earliest discussions in January 2020, to 100%, representing the start date of the program. This exercise created a MMS Enabling Environment Graph (Figure 1), with appended annotations illustrating selected episodes.

Early stage of MMS planning and discussion

Following an initial nine months of discussions, the Gaza Strip, where widespread maternal MNDs have been documented,¹⁴ was identified as the health system in which to pilot MMS with an IR component.³¹ By April 2021, an MMS Working Group was organized by the Director of Health and was functioning within UNRWA Headquarters, comprising chiefs of health services (maternal and child health, nursing, midwifery and central pharmacy) and Agency experts in e-health programming, research, communications and biostatistics. The working group was charged to be familiar with the health consequences of maternal micronutrient deficiencies, effects of MMS from trials, international policy guidelines for MMS use, and the intervention's compatibility with Health Department anemia treatment guidelines. However, following the bombing of Gaza during an Israeli-Palestine conflict in May 2021, the UNRWA Director of Health (AS) visited the territory in June, which led to a decision to defer launching MMS in Gaza. The goal of deferring was to enable clinics in Gaza to focus on addressing widespread mental, physical and other public health burdens wrought by the conflict.

MMS program and evaluation in Jordan

In July 2021, the Director of Health instructed antenatal MMS to be launched in clinics serving Palestine refugees in Jordan, where stable conditions and proximity to Headquarters could favor an early success and generate IR findings to guide subsequent MMS

introduction across the UNRWA health system. The working group refocused on implementing MMS prophylaxis in Jordan to: (a) develop an ANC clinical guide on the use of antenatal MMS supplements for prevention while retaining IFA for anemia treatment, (b) coordinate the acquisition, importation, inventorying, issuance and tracking of MMS for clinic use, (c) develop manuals for program surveillance and data collection across the 25 UNRWA clinics in Jordan, and (d) serve as the Health Department headquarters' liaison on MMS with clinics and stakeholders, including the Jordan Ministry of Health and Food and Drug Administration (FDA), WHO Eastern Mediterranean Office (EMRO) and UNICEF Jordan Office. Looking ahead, as the program launches, the working group is expected to monitor MMS scaling-up in Jordan and, later, guide MMS implementation Agency-wide.

Building the enabling environment: Preparing an organization to develop, execute, evaluate and sustain a new program requires capacity-building across relevant levels the health system.³² From mid-2021 to mid-2022, UNRWA engaged its clinic staff in Jordan to discuss maternal anemia, other nutrient deficiencies, evidence supporting antenatal delivery of MMS, current prescribing practices for IFA, and system modifications needed to deliver MMS prophylactically without affecting treatment regimens for anemia. Meetings motivated widespread staff participation to identify concerns to address, procedures to modify, and training needed to accommodate replacing IFA with MMS.

IR procedures have been developed, with staff feedback, to (a) enter data on supplement prescriptions, tablet use, hemoglobin levels and maternal reports of side effects into the eHealth system, (b) capture clinic logs on supplement inventory management, (c) elicit monthly staff opinions online, (d) interview mothers, as end-users in the system, about supplement acceptability, adherence and other practices through anonymous clinic exit interviews, and (e) prepare training modules at various operational levels. At the Agency level, this period of enablement included signing of a memorandum of agreement with collaborating organizations, acquiring funding to support in-country implementation research, securing approval of the UNIMMAP-formulated supplement by the Jordan FDA, and organizing the importation and inventorying of MMS supplies.

“The pilot period also allowed positive staff experiences to be shared”

Pilot introductory phase: In September 2022, antenatal MMS was informally introduced to replace FA and IFA prescription protocols in two clinics, in Marka and Amman New Camps.

Initially planned for 2–3 months, this five-month period provided the opportunity for clinic staff to become familiar with, and



Market in the Amman New Camp, Jordan. Photo credit: Masako Horino

offer feedback on, MMS logistics, side-effects to monitor based on clinical experience, the process of weighing bottles of MMS brought back by mothers at follow-up visits to validate reported supplement use, planned research questions, and drafted education materials. During this informal pilot phase, eHealth system data entry programs were modified or written to support MMS use, and were tested. The pilot period also allowed positive staff experiences to be shared, heightening the interest of UNWRA clinic staff across Jordan and their commitment to participate in the planned MMS program and its evaluation.



A midwife providing MMS education to a pregnant woman at UNWRA clinic, Amman New Camp, Jordan. Photo credit: Masako Horino

Planned launch with implementation research

As of February 2023, the MMS program is planned to be scaled up in Jordan in two phases.

In phase 1, a planned 10-month comparative evaluation in which midwives in 13 clinics (two pilot plus eleven assigned by randomization) will replace blister packets of IFA with a 180-count bottle of MMS²⁸ to all registered pregnant women. Intakes will be monitored during pregnancy and, when the bottle is depleted, it will be replaced with a second 180-count bottle in the 3rd trimester, providing a sufficient supply to last at least through three months postpartum. During this evaluation phase the remaining 12 UNWRA clinics, randomized to current standard of care, will

continue issuing blister packs with folic acid at registration in the 1st trimester followed by the usual IFA regimen throughout the remainder of pregnancy. In both groups data will be evaluated reflecting supplement flow from inventory to issuance, prescription fidelity, patient population coverage, adherence and acceptability, reported side effects, mid-pregnancy hemoglobin, and other maternal supplement usage. Deidentified maternal data will be output from the Agency's eHealth system, exit interviews with mothers leaving a sample of 12 clinics (6 per group), monthly staff survey reports on system factors and operations records. Data analysis will occur periodically with oversight of an international advisory committee and will be reviewed for differences in systems performance indicators between groups. It is possible that, depending on interim analyses, the evaluation protocol and period could be modified.

Following the evaluation, a second phase will be launched in which MMS is planned to be scaled up to replace prophylactic IFA in all remaining UNWRA antenatal clinics in Jordan, anticipated to be completed in the first quarter of 2024.

“Tracking enablement may help identify catalysts and deterrents”

Conclusions

A process of enablement is described in which UNWRA, a United Nations agency charged with providing health care in Palestine refugee communities in the Middle East, has prepared its clinics to replace IFA with UNIMMAP-formulated MMS as a new standard of care for pregnant women. In the plan, MMS prophylaxis complements UNWRA's standard clinical regimens for treating anemia with iron supplements. In accordance with WHO guidelines, a detailed implementation research protocol has been developed, ethically approved, and integrated into launching MMS in Jordan. An Enablement Graph is presented as a learning tool to track and subjectively gauge effects that processes, events, and decisions have had on time to start-up and level of preparedness. Notably, in this experience, about 20% of the Agency's apparent enablement occurred during the first two years, when early discussions, constituency building, organizing processes and program resourcing were taking place. On the other hand, in our judgement, ~80% of Agency enablement to launch MMS occurred in the year prior to start-up, when numerous supportive factors converged to accelerate progress. We propose that tracking enablement may help identify catalysts and deterrents to achieving MMS program and implementation research readiness.

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References

- 1 Stevens GA, Beal T, Mbuya MNN, Luo H, Neufeld LM; Global Micronutrient Deficiencies Research Group. Micronutrient deficiencies among preschool-aged children and women of reproductive age worldwide: a pooled analysis of individual-level data from population-representative surveys. *Lancet Glob Health*. 2022;10(11):e1590-e1599. doi:10.1016/S2214-109X(22)00367-9
- 2 Gernand AD, Schulze KJ, Stewart CP et al. Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. *Nat. Rev. Endocrinol*. 2016;12:274-289.
- 3 Schulze KJ, Mehra S, Shaikh S, et al. Antenatal Multiple Micronutrient Supplementation Compared to Iron-Folic Acid Affects Micronutrient Status but Does Not Eliminate Deficiencies in a Randomized Controlled Trial Among Pregnant Women of Rural Bangladesh. *J Nutr*. 2019;149(7):1260-1270. doi:10.1093/jn/nxz046
- 4 Bourassa MW, Osendarp SJM, Adu-Afarwuah S, et al. Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Ann N Y Acad Sci*. 2019;1444(1):6-21. doi:10.1111/nyas.14121
- 5 Baldi A, Pasricha SR. Anaemia: Worldwide Prevalence and Progress in Reduction. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 3-17.
- 6 Gernand A, Xu X, West KP Jr. Vitamin A in nutritional anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 153-171.
- 7 McNulty H. The role of B-vitamins in nutritional anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 173-185.
- 8 Fishman SM, Christian P, West KP. The role of vitamins in the prevention and control of anaemia. *Public Health Nutr*. 2000 Jun;3(2):125-50. doi: 10.1017/s136898000000173. PMID: 10948381.
- 9 Netting MJ, Best KP, Green TJ. The role of vitamin D in anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 195-204.
- 10 Traber MG, Kamal-Eldin A. Oxidative stress and vitamin E in anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 205-219.
- 11 Killilea DW, Siekmann JH. The role of zinc in the etiology of anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 187-194.
- 12 Mitterstille AM, von Raffay L, Nairz M. Iron deficiency, anemia, and the immune system. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 235-248.
- 13 Hoffman A, Valente de Souza L, Nairz M. Iron deficiency and anemia associated with infectious and inflammatory diseases. In: Karakochuk CD, Zimmermann MB, Moretti D, Kraemer K, ed. *Nutritional Anemia*, 2nd edition. Springer Nature; 2022: 223-234.
- 14 Horino M, Bahar L, Al-Jadba G, Habash R, Akihiro S, West KP Jr. Dietary Inadequacy, Micronutrient Deficiencies, and Approaches to Preventing Poor Nutrition in the Gaza Strip. *Food Nutr Bull*. 2020;41(4):503-511. doi:10.1177/0379572120967819
- 15 Ministry of Health, UNICEF, WFP, Jordan Health Aid Society International. Department of Statistics, Biolab, GroundWork. Jordan National Micronutrient and Nutrition Survey 2019. Amman Jordan; 2021. https://groundworkhealth.org/wp-content/uploads/2022/02/JNMNS19_report_220207_printable.pdf (accessed March 27, 2022).
- 16 WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: Multiple micronutrient supplements during pregnancy. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
- 17 WHO Model List of Essential Medicines – 22nd List, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.02). Licence: CC BY-NC-SA 3.0 IGO.
- 18 UNRWA Health Department Annual Report 2021. https://www.unrwa.org/sites/default/files/content/resources/annual_report_2021_final_version_update_18_august_2022_low_size.pdf. Accessed 27 November 2022.
- 19 Pappagallo S, Bull DL. Operational problems of an iron supplementation programme for pregnant women: an assessment of UNRWA experience. *Bull World Health Organ*. 1996;74(1):25-33.
- 20 UNRWA Technical Instruction Series, Prevention and Treatment of Iron-Deficiency Anaemia. Amman, Jordan: UNRWA. No. HD/HF/01/2000 Revision 02/November 2001.
- 21 UNRWA Technical Instruction Series, Prevention and Treatment Guidelines for Micronutrient Deficiencies. Amman, Jordan: UNRWA. No. HD/FH/03/2015.
- 22 United Nations Relief and Works Agency for Palestine Refugees in the Near East. Health Department Annual Report 2019. 2020. Internet: https://www.unrwa.org/sites/default/files/content/resources/health_department_annual_report_2019_final.pdf. Accessed 16

- November 2022.
- 23 Saragih ID, Dimog EF, Saragih IS, Lin CJ. Adherence to Iron and Folic Acid Supplementation (IFAS) intake among pregnant women: A systematic review meta-analysis. *Midwifery*. 2022;104:103185.
 - 24 Fawzi WW, Msamanga GI, Urassa W, Hertzmark E, Petraro P, Willett WC, et al. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. *New England Journal of Medicine* 2007;356(14):1423–31.
 - 25 Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) Study Group, Shankar AH, Jahari AB, et al. Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet* 2008; 371: 215–27.
 - 26 West, KP Jr, Shamim AA, Mehra S, et al. Effect of maternal multiple micronutrient vs iron-folic acid supplementation on infant mortality and adverse birth outcomes in rural Bangladesh: the JiVitA-3 randomized trial. *JAMA* 2014; 312: 2649–58.
 - 27 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews*. 2019: Issue 3. Art. No: CD004905. Available from: DOI:10.1002/14651858.CD004905.pub6
 - 28 Atwater J. Understanding product quality as applied to UNIM-MAP-MMS product donated by Kirk Humanitarian. Salt Lake City: Kirk Humanitarian. September 2020.
 - 29 Peters D H, Adam T, Alonge O, Agyepong I A, Tran N. Implementation research: what it is and how to do it *BMJ* 2013; 347:f6753.
 - 30 Tumilowicz A, Ruel MT, Pelto G, et al. Implementation Science in Nutrition: Concepts and Frameworks for an Emerging Field of Science and Practice. *Curr Dev Nutr*. 2018;3(3):nzy080. Published 2018 Oct 13.
 - 31 Horino M, Bahar L, Al-Jawaldeh A, Hurley KM, Kraiemer K, West KP Jr, Seita A. Antenatal multiple micronutrient supplementation in the State of Palestine: A proposed protocol for implementation and evaluation. *Nutrition 2021 LIVE ONLINE*, June 7-10, 2021.
 - 32 Frahsa A, Rutten A, Roeger U, Abu-Omar K, Schow D. Enabling the powerful? Participatory action research with local policymakers and professionals for physical activity promotion with women in difficult life situations. *Health Promotion Intl* 2012;29:171-184.

Eight Country Experiences Informing Development of a UNIMMAP MMS Supply Strategy to Meet Growing Demand

Clayton A Ajello

Kirk Humanitarian, Salt Lake City, UT, USA

Shannon E King, Otte Santika, Jarno de Lange,

Quinn Harvey

Vitamin Angel Alliance, Goleta, CA, USA

Auliya Suwantika, Holis A Holik

Universitas Padjadjaran (UNPAD), Raya Bandung Sumedang, West Java, Indonesia

Key messages:

- Momentum is growing to introduce or explore the introduction of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation for a Multiple Micronutrient Supplement (MMS). Currently at least 20 national health systems are in various stages of exploring or introducing UNIMMAP MMS consistent with the established global policy framework.
- Demand for MMS is projected to outpace supply beginning in 2024 and will continue to widen through 2030 based on current manufacturing capacity projections.
- Addressing the supply gap requires immediate planning and action to ensure that MMS suppliers are positioned to meet future demand. Urgency to act is driven by several important realities. Top among these is the prolonged period (i.e., 3–5 years) needed by a manufacturer producing MMS for the first time.
- Analysis of experiences from eight country settings reveals common questions and issues related to MMS supplies that fit into three broad categories: availability and accessibility, affordability, and building manufacturing capacity. Examination of the questions and issues raised by stakeholders brings into focus specific supply-related considerations of interest to national, regional, and global actors – and helps to inform urgent actions to secure necessary supplies to address long-term needs for MMS.

Introduction

The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation for a Multiple Micronutrient

Supplement (MMS) for pregnant women is being systematically introduced in major regions of the world. With 15 essential micronutrients, UNIMMAP MMS (hereinafter referred to as ‘MMS’) was developed by a panel of experts assembled by the World Health Organization (WHO), the United Nations Children’s Fund (UNICEF), and the United Nations University (UNU) in 1999 for the specific purpose of creating a supplement for pregnant women to use in clinical trials.¹ Since its creation, numerous randomized clinical trials have contributed to an extensive body of evidence showing that MMS is safe, improves maternal health and reduces adverse pregnancy outcomes as compared to iron and folic acid (IFA).² Cost-benefit of MMS has been demonstrated, and large-scale commercial transactions show MMS can be produced at an affordable price for public and non-profit health systems. The evidence accumulated to date has given rise to an initial global policy framework supporting MMS introduction that consists of:

- WHO’s Antenatal Care Recommendations for a Positive Pregnancy Experience,³ updated in 2020;
- UNICEF’s Interim Country-level Decision-making Guidance for Introducing MMS⁴ in the context of antenatal care services informed by implementation research;
- UNICEF’s Programming Guidance. Maternal Nutrition: Prevention of malnutrition in women before and during pregnancy and while breastfeeding⁵ issued in 2022;
- UNICEF’s policy recommendations contained in Undernourished and overlooked, a global nutrition crisis in adolescent girls and women,⁶ issued in March 2023; and
- WHO’s Model List of Essential Medicines,⁷ updated in 2021 to include MMS.

“Cost-benefit of MMS has been demonstrated, and large-scale commercial transactions show MMS can be produced at an affordable price for public and non-profit health systems”

This policy framework encourages national initiatives to explore the introduction of MMS in the context of antenatal care services (ANC) informed by rigorous research, including implementation science (IS), which includes implementation research. Currently, at least 20 nations are introducing MMS consistent with this policy framework.⁸ The focus has been on using IS to design and test strategies to deliver MMS effectively.⁹ As described elsewhere in this MMS Special Report 2.0 (Synchronizing Access to UNIMMAP MMS Product Supplies with Program Implementation), IS is also being applied by national stakeholders to understand enablers and barriers to product availability and access, and to identify and test strategies to secure a sustainable supply of MMS. As a result of these national experiences, lessons are being learned about securing MMS supplies that are beginning to inform development of an overall supply strategy – whether nations access MMS supplies locally, through importation, or some combination of both.

This paper summarizes the initial lessons learned and operational considerations important to developing a national strategy to secure MMS supplies. It is based on observations of eight countries in various stages of introducing or exploring introduction of MMS using an IS approach, and is reported in detail in the resource document: UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy.¹⁰

Global demand for MMS: immediate and growing

With evidence, supportive policy guidance, and increasing interest in MMS, global demand for MMS is growing, as reflected in the numbers of countries beginning to introduce or explore the introduction of MMS since 2019. There are at least two methods to measure de-

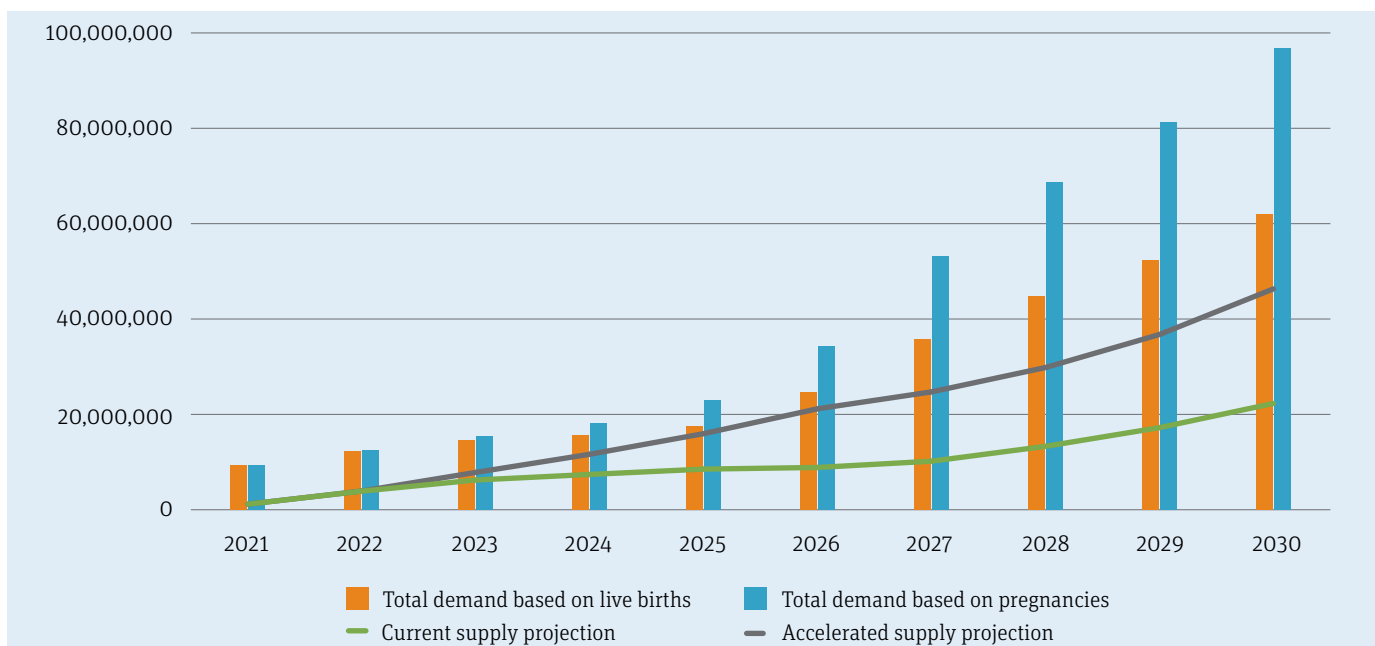
mand for MMS: examining total annual live births or total annual pregnancies. Irrespective of approach, demand is projected to outpace supply, as shown in **Figure 1**.¹¹

The orange bars in **Figure 1** show total demand by year based on live births; the blue bars show demand based on total pregnancies. The grey line across the ‘demand’ bars shows the volume of actual and projected MMS supplies produced by existing manufacturers assuming realistic expansion of their manufacturing capacity over 10 years. The green line shows the same but assumes a modest increase in the numbers of manufacturers.

“To balance MMS supply with projected demand, attention is needed now to build MMS manufacturing capacity”

Current progress to introduce MMS through application of IS suggests stakeholders are on a credible trajectory to reach 100 million pregnant women annually in LMICs by 2030. However, under both supply scenarios shown in **Figure 1**, MMS demand will outstrip supplies starting as soon as 2024, with the gap continuing (and widening) through 2030. Even under the ‘accelerated’ supply scenario, the volume of MMS produced in 2030 will support only ~50% of the 100 million pregnancies associated with projected MMS introduction initiatives. Without immediate action, the supply gap will become evident by 2024; and without more action, by 2030 there will be MMS supplies available for less

FIGURE 1: Projected demand in low- and middle-income countries (LMICs) for UNIMMAP MMS based alternatively on live births or pregnancies, and projected supply



than 25% of the 228 million pregnancies that occur annually now in LMICs. To balance MMS supply with projected demand (assuming momentum to introduce MMS continues), attention is needed now to build MMS manufacturing capacity. A detailed description of all assumptions underlying **Figure 1** can be found in the resource document: UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy.¹²

Accelerating global supply: critical realities

Addressing the supply gap requires planning and action to ensure MMS suppliers anywhere, including those situated in LMICs, are positioned to meet future demand. Urgency to act is driven by several realities:

- Manufacturing MMS for the first time requires a 3–5 year lead time to complete contracting, product development and test manufacturing (including product stability testing) and product registration for commercial use. An additional factor is the time to obtain ingredients to begin product development and commercial production. COVID-19's after-effects on supply chains linger. For example, staffing issues and time to acquire raw materials continue to affect production lead time significantly.
- Limited numbers of countries have the technical and industrial capacity to manufacture MMS. This means that regional high-volume manufacturers (who are best positioned to gear up quickly to export a high-quality, low-cost MMS product) must be identified and will be essential to help meet global demand – in addition to qualified local producers.
- Currently, only 13 manufacturers are able or close to being able to produce MMS for commercial sales; and the majority did not undertake product development without a contract signed by a qualified buyer.
- Adding MMS to a national government's procurement mechanism requires significant investment of time, expertise and financing to accomplish and synchronize with budget planning.

Developing a supply strategy

Observations derived from the experiences of the eight countries examined reveals questions, issues and operational considerations – described below – important to developing a national strategy for securing supplies of MMS using national, regional, and/or global suppliers.

Product supply questions and issues identified by stakeholders

As national governments explore the introduction of MMS into ANC services, decision-makers and stakeholders identify real or perceived supply-related questions and issues. In the absence of evidence-based adjudication by technical experts, many of these may initially cause stakeholders to consider deferring the introduction of MMS. These fall into three broad categories.

1. Availability and accessibility of MMS supplies. Product availability is defined as ensuring that an adequate quantity of quality product is produced for consumer use. Product accessibility is defined as ensuring that the product being produced can be secured in adequate quantities to meet demand through purchase or donation. The questions/issues most frequently mentioned by stakeholders include the following:

- Can health systems secure MMS supplies when worldwide production is so limited?
- How can supplies be accessed in the short- and long-term?
- How can access to MMS supplies be synchronized with each stage of program implementation, assuming application of IS approach to MMS introduction?

2. Affordability of MMS. The main issue expressed by stakeholders is whether MMS is affordable, and what it should cost. Affordability is generally assessed by governments based on the actual cost of MMS combined with a country-specific cost-benefit analysis and a budget impact assessment.

3. Building manufacturing capacity. The manufacturing questions and issues most frequently mentioned by stakeholders include:

- Should MMS be manufactured locally or be imported?
- How to predict which manufacturers can successfully produce a quality MMS product?
- How long does it take to deliver MMS if the manufacturer has never produced it before?
- How to assure product quality across manufacturers?
- Are there service delivery issues affecting how MMS is produced for the marketplace (e.g., identifying packaging of MMS that balances and satisfies consumer preferences, health care provider needs and government interests)?

Considerations for national, regional, and global stakeholders

These questions and issues bring into focus considerations that are of special (and sometimes overlapping) interest to national, regional, and global actors.

National actors' key considerations include:

- What are the local procurement options? Import finished MMS product in consumer packaging, import it in bulk and re-package locally, import a pre-mix, or manufacture from raw ingredients?
- Is the national government ready to adopt both the UNIMMAP formulation of MMS and relevant policies to incentivize its adoption?
- Is there a sound business case to support/justify MMS manufacturing by one or more manufacturers in the target country?
- Can and should production be supported by a single local

manufacturer to produce the entire national supply of MMS needed?

Each of these concerns comes with a complex set of issues as shown in **Box 1** – many of which overlap with, or underlie, concerns raised by regional and global actors.

Regional actors' key considerations include:

- Do manufacturers have a capacity to meet just local demand or can they also produce excess volumes of MMS for export?
- Whether/how to navigate selling MMS into the export marketplace?

Global actors' key considerations include:

- What does the manufacturing landscape look like?
- Where will investments have greatest impact, given the magnitude of the manufacturing challenge, to fulfill a meaningful level of coverage just in LMICs?
- How to ensure that manufacturers produce a standardized and interchangeable product that gives national health systems purchasing options free from quality concerns, irrespective of who produces it?
- How much technical assistance and/or technology transfer is needed by manufacturers?

“It is important for national, regional and global stakeholders to develop a shared vision for securing available and accessible supplies of MMS”

Five urgent actions needed to accelerate availability/accessibility of MMS supplies

The experiences of stakeholders begin to suggest elements of a supply strategy needed to accelerate the availability and accessibility of MMS. These reveal that relevant stakeholders should invest time and resources to:

1. **Gain consensus on MMS standards, its specification, and an approach to verification.** Effort is needed, starting with current donor agencies that procure MMS, to align on overall product standards and product specifications for MMS, regional standardization that benefits trade among regional partners, a common approach to building quality into product development and manufacturing that is verifiable, developing an approach to ongoing supply management,

BOX 1: Untangling the complexities of national actors' concerns

- **Procurement:** Importation of MMS is always an option, but local manufacturing has many potential starting-points, each with challenges and advantages that need to be assessed and which contribute to understanding the feasibility of local production.
- **Formulation:** Most governments have pre-existing nutritional requirements set by national agencies that may vary from those implied by the UNIMMAP formulation. Governments must navigate a decision-making process to decide whether to adopt UNIMMAP.
- **Business case:** While many reasons exist to encourage local MMS production, manufacturers need a business case for investment. National decision-makers also need to ascertain if the business case supports delivery of MMS at an affordable price acceptable to the national government where the price for MMS is heavily dependent upon volume.
- **Sole source procurement:** For nations with a small base of eligible users, the business case may support production by a single local manufacturer to produce the entire national supply. However, accepting sole source procurement may require closer monitoring of quality, and may also mean that the cost of MMS is at a considerably higher-than-average price point as compared to importation. National actors will need to form a consensus to accept sole source procurement.

and technical engagement with key high-volume manufacturers. Such actions could speed product availability and lower costs while optimizing benefits for manufacturers, purchasers, and consumers.

2. **Gain consensus on an approach for expanding manufacturing capacity to meet short- and long-term needs.** Most LMICs are without capacity (i.e., technical, industrial and/or manufacturing volume) for local manufacture of high-quality, low-cost MMS; and/or lack sufficient local MMS demand needed to optimize manufacturing cost-efficiency to deliver MMS at an affordable price point for the local government. Using donor-supplied product appears to be the most efficient way to manage and assure the short-term supply needed to accommodate an IS approach to introduction – during the application of which, national stakeholders (with global/regional stakeholder assistance) can identify, evaluate, and execute a strategy to secure product to meet long-term demand in specific country settings. In the long term, a consensus approach that delivers more MMS supplies will include expanding existing regional manufacturers' capacity while adding more manufacturers (regional and local) to close the supply/demand gap starting in 2024.

3. Build a product supply strategy to manufacture and deploy MMS commensurate with demand in 2024 and beyond.

Meeting future demand will require a combination of global/regional/national suppliers that can serve either or both domestic and export markets. Any MMS supply strategy developed by key donors (and other stakeholders directly involved) in purchasing product or growing manufacturing capacity should be informed by a systematic landscaping of MMS manufacturing capability viewed from a regional perspective. This will lead to enhanced supply/demand forecasting models.

4. Improve coordination of procurement and deployment of donated supplies.

Improved coordination among groups donating available product will accelerate opportunities to activate initiatives to explore, introduce, plan, and activate MMS introduction while making more efficient use of available MMS supplies.

5. Identify and activate financial pathways for existing donors to expand product availability and governments to fund regular MMS product purchases as they transition from iron and folic acid supplementation (IFAS) to MMS.

There will continue to be a need for donated product to support implementation research by countries introducing MMS using an IS approach, and once countries introduce MMS, some will require a continued level of MMS supplies to be donated, as national budgets may not be able to ensure MMS coverage consistent with national policy. Additionally, as governments scale their transition from IFA to MMS, individual nations will need financing and/or access to foreign exchange to make their initial purchases until their procurement systems transition to purchase MMS.

Conclusion

It is important for national, regional, and global stakeholders to develop a shared vision for securing available and accessible supplies of MMS. To realize a sustainable supply of MMS that is available and accessible to consumers that choose to use national health services, there is a need for collective action among stakeholders to:

- Understand the MMS supply landscape;
- Collaborate and partner to generate consensus on supply issues;
- Develop an actionable strategy and plan to assure (short- and long-term) availability and access to MMS supplies; and
- Act now to implement plans to expand existing supplier capacity and add new, qualified producers.

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Correspondence: Clayton A Ajello, Senior Strategic/ Technical Advisor, Kirk Humanitarian, 2755 E. Cottonwood Parkway, Suite 450, Salt Lake City, UT 84121, USA
Email: cajello@inlexo.com

References

- 1 World Health Organization, United Nations University & United Nations Children's Fund (UNICEF). (1999). Composition of a multi- micronutrient supplement to be used in pilot programmes among pregnant women in developing countries: report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO) and United Nations University workshop. UNICEF. Available for download at: <https://apps.who.int/iris/handle/10665/75358> Accessed 25 March 2023.
- 2 Bourassa, M.W., Osendarp, S.J.M., Adu-Afarwuah, S., Ahmed, S., Ajello, C., Bergeron G., et al. Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Annals of the New York Academy of Sciences*, 2019: 1444(1), 6–21. Available for download at: <https://doi.org/10.1111/nyas.14121> Accessed 25 March 2023.
- 3 World Health Organization (2020). WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy. Available for download at: <https://www.who.int/publications/i/item/9789240007789> Accessed 25 March 2023.
- 4 UNICEF, The Micronutrient Forum, Multiple Micronutrient Supplementation in Pregnancy – Technical Advisory Group, Nutrition International, and The Vitamin Angel Alliance (2020). Interim Country-Level Decision-making Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women. Available for download at: <https://www.unicef.org/media/96971/file/Interim-Country-level-Guidance-MMS-for-PW-2021.pdf> Accessed 25 March 2023.
- 5 UNICEF. (January 2022). UNICEF Programming Guidance. Maternal Nutrition: Prevention of malnutrition in women before and during pregnancy and while breastfeeding. Available for download at: <https://www.unicef.org/media/115361/file/Maternal%20Nutrition%20Programming%20Guidance.pdf> Accessed 25 March 2023.
- 6 UNICEF. (March 2023). Undernourished and overlooked, a global nutrition crisis in adolescent girls and women. Available for download at: https://data.unicef.org/resources/undernourished-and-overlooked/?utm_id=womens-nutrition-report Accessed 25 March 2023.
- 7 World Health Organization (2021). World Health Organization Model List of Essential Medicines, p. 53. Available for download at: <https://apps.who.int/iris/bitstream/handle/10665/345533/WHO-MHP-HPS-EML-2021.02-eng.pdf> Accessed 25 March 2023.
- 8 Healthy Mothers Healthy Babies Consortium. World Map of MMS Activities (as of March 2023): <https://hmbhconsortium.org/world->

map/ Accessed 25 March 2023.

- 9 Tumilowicz A, Ruel MT, Gretel P, Pelletier D, Monterrosa EC, Lapping K, et al. Implementation Science in Nutrition: Concepts and Frameworks for an Emerging Field of Science and Practice. *Current Developments in Nutrition*. March 2019; Volume 3, Issue 3. Available for download at <https://academic.oup.com/cdn/article/3/3/nzy080/5129139> Accessed 25 March 2023.
- 10 Ajello, CA, Suwantika A, Santika O, King S, and De Lange J. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. *Kirk Humanitarian Resource Paper*. November 2022. Available for download at: https://kirkhumanitarian.org/wp-content/uploads/2022/11/UNIMMAP-MMS-Supply-Paper_Digital-Version-1-FINAL-1-1.pdf Accessed 25 March 2023.
- 11 *ibid*, note 10.
- 12 *ibid*, note 10.

Synchronizing Access to UNIMMAP MMS Product Supplies with Program Implementation

Clayton A Ajello, Shannon E King, Otte Santika,
Jarno de Lange

Vitamin Angel Alliance, Goleta, CA, USA

Auliya Suwantika, Holis A Holik

Universitas Padjadjaran, Kabupaten Sumedang, Jawa Barat,
Indonesia

Key messages:

- United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS) is being introduced in more than 20 national health systems as recommended by the World Health Organization (WHO) and United Nations Children’s Fund (UNICEF).
- Limited availability and access to UNIMMAP MMS supplies and affordability are perceived as the key barriers to introduction and scaling of MMS in all settings.
- Implementation science (IS) provides a systematic, evidence-based approach to identify the enablers and barriers to securing a sustainable supply of MMS, to design and test effective manufacturing/sourcing options for MMS, and to plan and implement actions to assure regularized product supplies are accessible for scaling and ongoing maintenance of MMS delivery in antenatal care (ANC) services.
- National health systems should focus on how to access product supplies needed in the long term, while accessing product supplies needed for short-term introduction activities from donor agencies. This approach would provide the required time and space for national health systems to identify supplier options most appropriate for national needs and the time to establish/integrate a long-term product supply strategy into existing procurement systems.
- Given that initial procurement of MMS by national governments is a key bottleneck in securing long-term MMS supplies, national health systems should not wait until scale-up begins to start thinking about securing long-term supplies.

Introduction

The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS) – referred to throughout this paper as “MMS” – is in various

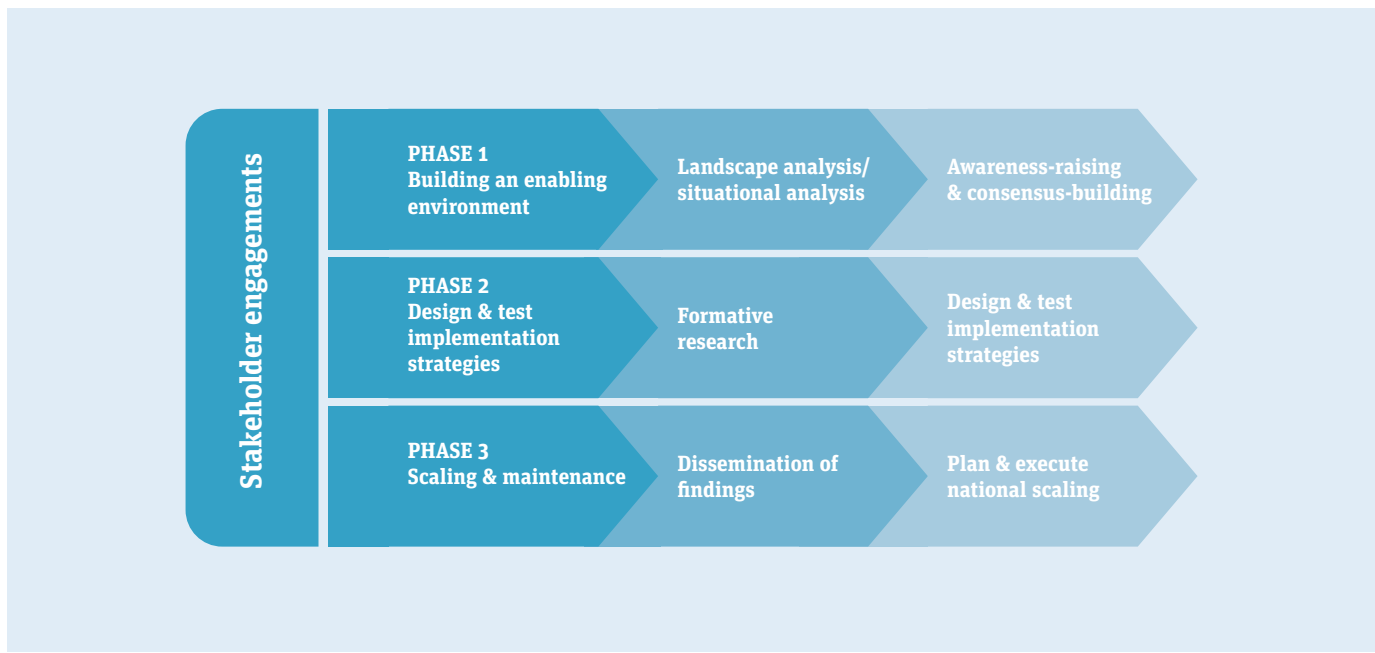
stages of introduction in more than 20 countries.¹ Consistent with the guidance provided by the World Health Organization (WHO) and the United Nations Children’s Fund (UNICEF), MMS is being introduced into antenatal care (ANC) services, informed by rigorous research, including implementation research.^{2,3} Examination of national environments into which MMS is being introduced has identified limited availability of, and access to, MMS as important barriers to introduction.⁴ **Product availability** is defined as an adequate quantity of quality product produced for commercial sale. **Product accessibility** is defined as the product being produced in adequate quantities to meet demand through purchase or donation. This paper describes how implementation science (IS) can be applied to ensure long-term availability and access to sufficient MMS supplies.

Applying IS to secure MMS product supplies in order to meet long-term needs

IS – defined as a systematic, evidence-based approach used to generate information to plan and implement an effective strategy to introduce an intervention⁵ – is key to informing MMS programming. **Figure 1** is a generic representation of the IS approach currently being applied to support introduction and scaling of MMS in at least 20 countries. It is being applied primarily to identify effective strategies to *deliver* MMS within ANC services. This includes using IS to identify and gain consensus regarding what are the enablers and barriers to the successful delivery of MMS (e.g., adherence, acceptability, feasibility, etc.), and to design and test strategies to distribute MMS.

“Through application of the IS approach to address the issue of securing MMS supplies on the long term, combined with the short-term accessibility of MMS from donation programs, governments can synchronize product availability with program implementation”

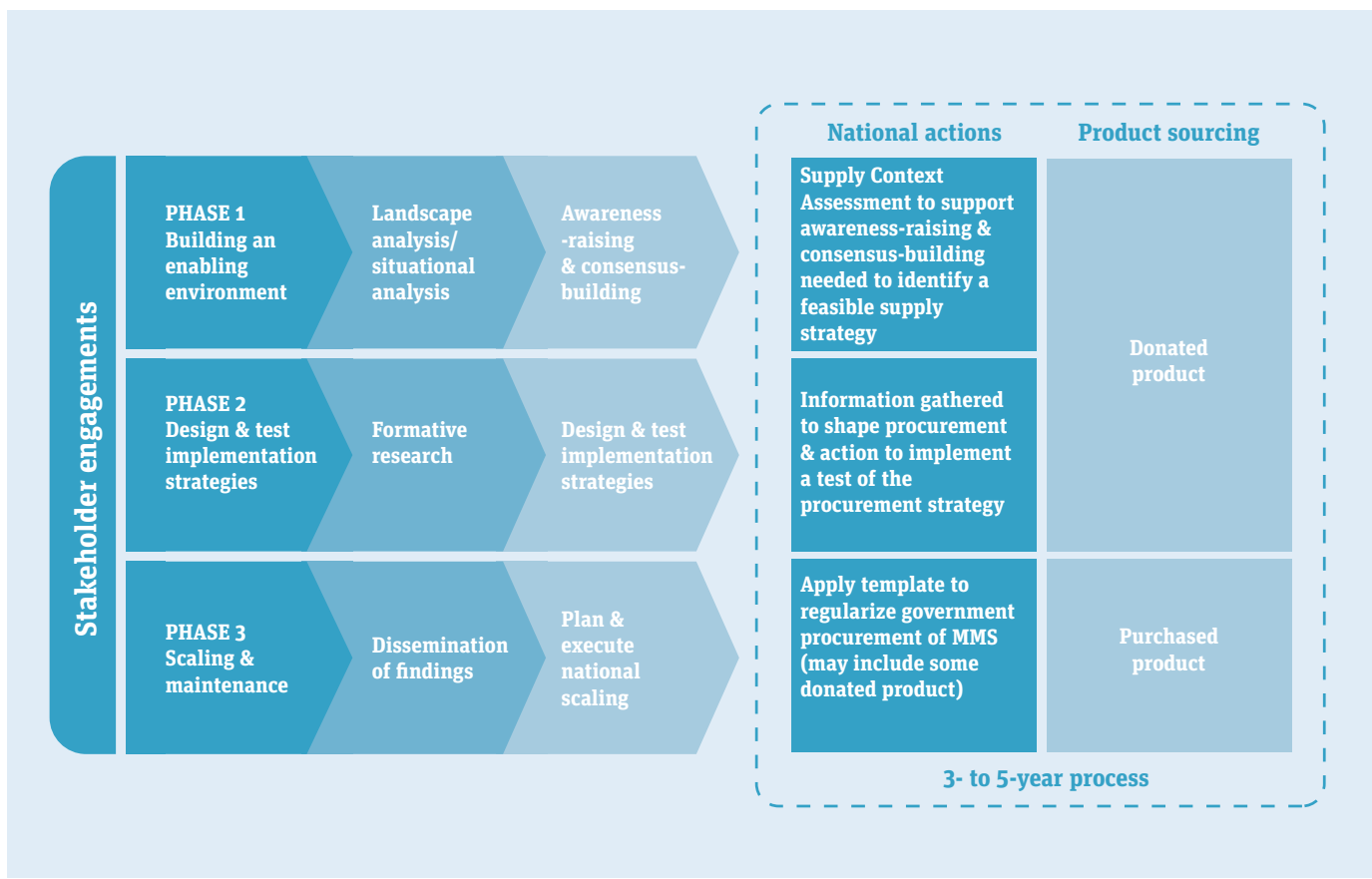
FIGURE 1: A generic implementation science (IS) approach



While the IS approach has been used mainly to examine ways to *deliver* MMS effectively, it can also be applied to determine an effective strategy for securing a sufficient amount of MMS *supplies*. **Figure 2** shows the key actions needed to: i) understand enablers and barriers to secure product supplies, promote awareness, and

build consensus around feasible options for securing MMS, and ii) design and test (and eventually plan and implement) options for securing the sustainable availability of, and access to, MMS necessary for meeting long-term needs.

FIGURE 2: Application of IS to support decision-making pertaining to securing MMS product supplies



Applying an IS approach to the issue of securing MMS product supplies gives decision-makers confidence to select one or a combination of approaches to secure those supplies. It also helps ensure that product supplies are synchronized with different phases of program implementation.

Exploring the specific activities to secure MMS product supplies

Consistent with the IS approach shown in **Figure 2**, the actions and activities needed to secure sustainable availability of, and access to, MMS supplies unfolds in three phases over a multi-year timeline. In general, application of IS to the issue of securing MMS supplies is recommended to be done in parallel with other implementation research to identify and test options for effective delivery of MMS services. Each IS phase is described below, along with its associated activities.

- **Phase 1: Building an enabling environment.** Product availability/accessibility is universally viewed as a rate-limiting factor, impeding adoption of an MMS policy and its implementation. A central issue for national stakeholders is determining how MMS can be secured to sustain services over the long-term, including whether local manufacturing is feasible or whether importation of product supplies is required. This decision is not straightforward. Manufacturing MMS of an acceptable quality is complex. While local manufacturing may be preferred by national stakeholders, this may be difficult to achieve in practice, given the specialized skills and experience required. Additionally, there may not be a credible business case for local manufacturing depending on the number of pregnancies each year within the target country, local manufacturers' production capacity, and costs to import raw materials. By contrast, importation of MMS may be difficult to achieve as a result of legal and regulatory requirements, as well as the high cost of import duties if applied, which can

adversely impact the importation of MMS for national programs.

Collectively, IS phase 1 actions and activities include:

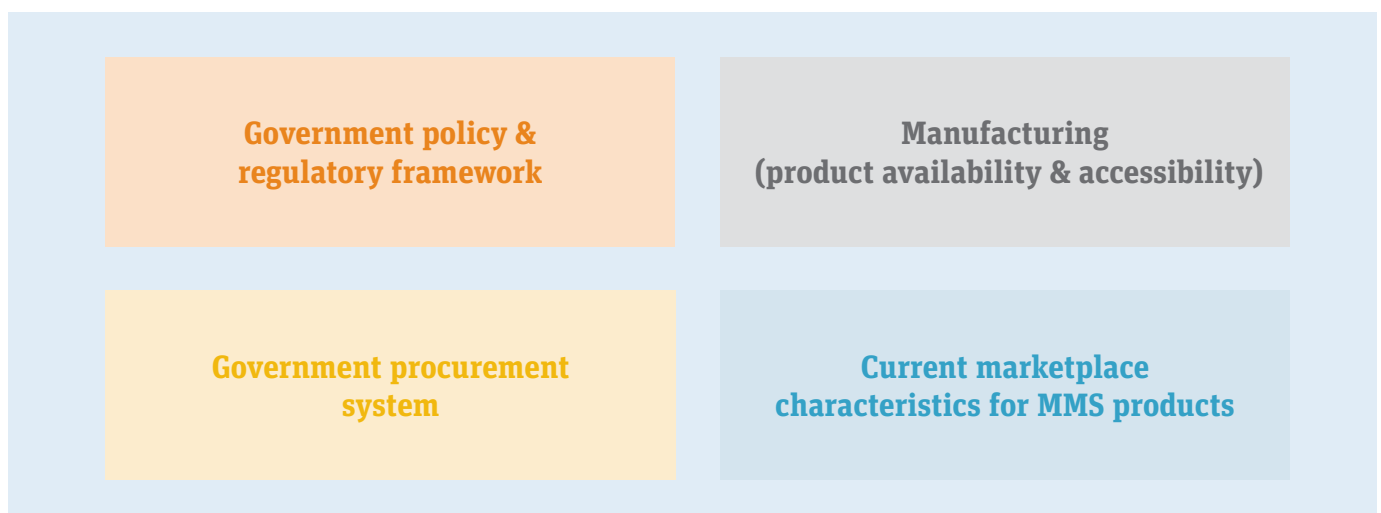
- **Implementing a Supply Context Assessment (SCA).** The SCA toolkit, described elsewhere in this MMS 2.0 Special Report in *Supply Context Assessment (SCA) Tool for National Governments*, was originally conceptualized as a Supply Readiness Assessment (SRA) by *Sight and Life* Foundation, but has been further adapted by Kirk Humanitarian in collaboration with the Vitamin Angel Alliance to focus on helping national health systems to secure a sustainable supply of MMS. Deciding on the feasibility of any supply strategy requires an understanding of the enablers and barriers to both local manufacturing and importation of MMS. Undertaking an SCA can help decision-makers fully understand the manufacturing and sourcing landscape. The SCA focuses on examining four elements relevant to securing and financing product supply, as shown in **Figure 3**.

The results of the SCA are intended to provide evidence to inform and shape subsequent awareness-raising and consensus-building actions and activities among decision-makers (e.g., individuals within academia, government, and the NGO sector).

- **Raising awareness** to various supply realities, advantages and challenges, as derived from landscaping activities (including the SCA) and their implications for local product manufacturing, product importation, and/or application of some combination of strategies.
- **Building consensus** around one or more potential strategies for investment that can result in securing long-term product supplies.

The outputs of the SCA, combined with awareness-raising and consensus-building activities, are designed to support an

FIGURE 3: Key areas for assessment and analysis of national supply context



evidence-based consensus on the enablers, barriers and possible options to secure product availability and access, leading to a consensus on feasible manufacturing and sourcing options to be explored further and tested in Phase 2.

Phase 2: Design and test manufacturing/sourcing strategies. Actions and activities in this phase aim to help decision-makers understand which strategies (e.g., a range of local manufacturing options vs importation options) are supported by a sound business case that can secure long-term MMS supplies for national health services, including:

- **Formative research on manufacturing and sourcing.** Information is gathered by conducting a ‘pre-qualification’ process to identify the universe of local manufacturers, engage to assess their capabilities, and compare the results to sourcing from international suppliers. This investigation examines options for local manufacturing (e.g., local repackaging only; use of pre-mixed ingredients that local contract manufacturers can press into finished product; or full manufacturing including blending of ingredients by the manufacturer, tablet pressing and coating, and finished packaging), and assesses whether the technical capacity exists among a segment of the universe of local manufacturers to undertake local manufacturing. Through pre-qualification, it is also generally possible to begin to understand the level of technical assistance specific manufacturers may need to activate manufacturing; and importantly, whether a given manufacturer is willing to sell to the government sector. Pre-qualification can also determine whether local manufacturing capacity alone can realistically suffice to fill national demand or whether a combination of national production plus importation may be required. For purposes of comparison between a local manufacturing options and importation, the investigation should examine in granular detail how the government ordinarily procures a new product (if not completed during implementation of the SCA) – including any challenges or impediments to international sourcing.
- **Identify and test supplier models.** In this activity, investigators develop a comparative business case analysis for local manufacturing vs importation. As part of the business case development or separately, investigators should examine the feasibility of generating sufficient local investment capital to develop and produce a new product to defined quality standards (e.g., the Expert Consensus on an Open-Access Product Specification for MMS for Pregnant Women).⁶ There are important actions needed to help generate information for the comparative business case and to test the identified supplier model(s), including:
 - First, if formative research suggests some form of local manufacturing is deemed feasible, a trial procurement action is recommended – funded by the national govern-

ment (or in limited instances, by a donor if the procurement targets a supplier with potential to serve both domestic and export markets with MMS). A trial procurement engages one or more manufacturers (via an **RFP** and **trial contracting**) to develop, test-manufacture, and register a commercial product – a multi-year process. In instances where local procurement is deemed not feasible or where international procurement is required as a permanent measure or as an interim measure until local manufacturing is accomplished, national health systems will still need to undertake a trial procurement from an already qualified international MMS producer. Irrespective of the preferred strategy for accessing a product (i.e., local manufacturing or importation), the process of a trial procurement must result in timely product delivery to activate scaling in Phase 3.

Apart from ensuring a local manufacturer can produce a high-quality, low-cost MMS product to specification, undertaking a trial procurement (either for locally manufactured or imported MMS) is critical to i) ensure that a mechanism for regularized procurement of MMS is in place before Phase 3 begins, and ii) address any constraints to initiating procurement of a new medicine. For example, government procurement systems are generally set up to purchase established medicines (i.e., listed on the national essential medicines list and readily available in the marketplace), so when government procurement systems need to procure a new medicine from a local manufacturer making the product for the first time (or from international vendors), traditional government procurement templates may not easily accommodate such transactions. Undertaking a trial procurement is especially important if the product is just being included in health policy, and is still in the process of being added to the essential medicines list (EML). Undertaking procurement of these types of products likely requires identification of special procurement mechanisms or processes, particularly because manufacturers will have little incentive to produce a product that is not yet officially recognized for inclusion in the national health services. Additionally, depending upon the constraints or barriers to procurement, the national government (or to the extent of a ministry of health’s authority) may need to take legislative or regulatory rule changes to fix procurement constraints.

While a trial procurement can take a substantial amount of time to organize (e.g., up to two or more years) and receive delivery (e.g., two or more years for a local producer manufacturing MMS for the first time, or six months or more from a qualified international producer), it can substantially shorten the time to product availability and create a template for future procurement actions with one or more established suppliers of MMS. The template for procurement to fill long-term needs for MMS can then be integrated into the government’s procurement system during Phase 3, when large quantities of

MMS supplies will be needed to support scaling and ongoing maintenance of MMS as a part of regular ANC services.

- Second, it may be important to draw upon information from other IS activities already underway or completed as part of an MMS introduction strategy to identify and test strategies that may affect product manufacturing decisions prior to its purchase. For example, it is important to understand whether and which consumer and health care provider preferences (e.g., packaging type, tablets per package, etc.) influence manufacturing decision-making; or whether the ability of the national health services to instruct health care providers in social behavior change communications mitigates the need for specialized packaging.

Phase 3: Plan and execute scaling and maintenance of the intervention. This phase is used to disseminate the findings from earlier phases, plan for national scaling, and activate efforts to scale the intervention and ensure access to product supplies needed to maintain ongoing deployment of MMS within ANC services. Finished product from the trial procurement started in Phase 2 should be delivered no later than the beginning of Phase 3; and Phase 3 should focus on regularizing/scaling product purchases using whichever supply strategy (or combination of strategies) is proven effective during Phase 2 by:

- Issuing routine procurement/purchase orders for MMS; and
- Scaling purchase orders to ensure procurement is synchronized with program expansion and program maintenance.

“Implementation science is key to inform MMS programming”

Synchronizing product supplies with program implementation

The IS approach described here focuses on assisting governments to address the issue of securing availability and access to MMS supplies for the long term. Yet many will note that governments are using IS to identify and test effective strategies for delivering MMS in the context of ANC services to pregnant women. Such testing requires immediate or short-term access to MMS product supplies. The model in **Figure 2** assumes:

- Governments will take advantage of the ample supplies of MMS that are available through donation programs offered by organizations such as Kirk Humanitarian, UNICEF, and the Vitamin Angel Alliance. Each of these donation programs provides high-quality MMS product that is available to governments introducing MMS informed by implementation research – itself a component of the IS approach illustrated and described earlier in **Figure 1**.
- National health systems will begin to procure their own sup-

plies of MMS as scaling its use begins. Most national health services now exploring the use of MMS are already purchasing iron and folic acid supplements (IFAS). It is assumed that as the transition to MMS progresses, national health systems already purchasing IFAS should be able to afford to purchase MMS (which is available at a price that is highly competitive with IFAS) to cover all or a substantial portion of national need, even if some continuing level of donation is needed.

- While IS is being undertaken, it is assumed that global stakeholders are continuing to take steps to catalyze increased manufacturing of MMS by global and regional suppliers to ensure that national governments have suppliers from whom they can purchase MMS if national manufacturing is not feasible.

Through application of the IS approach to address the issue of securing MMS supplies on the *long term*, combined with the *short-term* accessibility of MMS from donation programs, governments can synchronize product availability with program implementation.

Conclusion

Application of an IS approach illustrates how national stakeholders can achieve three key objectives pertaining to securing sustainable availability and access to MMS product supplies, including:

1. Identify the enablers and barriers that influence the ability of a health system to secure access to a sustainable supply of MMS product,
2. Identify and test sourcing options, and
3. Achieve synchronization of MMS product supplies with both program introduction and subsequent national scaling.

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Correspondence: Clayton A Ajello, Senior Technical Advisor, Vitamin Angel Alliance, 6500 Hollister Ave Suite 130, Goleta, CA 93117, USA
Email: cajello@vitaminangels.org

References

- 1 Healthy Mothers Healthy Babies Consortium. World Map of MMS Activities: <https://hmhbconsortium.org/world-map/> Accessed 25 March 2023.
- 2 World Health Organization (2020). WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy. Available for download at: <https://www.who.int/publications/i/item/9789240007789> Accessed 25 March 2023.
- 3 UNICEF, Micronutrient Forum, Multiple Micronutrient Supplemen-

- tation in Pregnancy – Technical Advisory Group, Nutrition International, and the Vitamin Angel Alliance (2020). Interim Country-Level Decision-making Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women. Available for download at: <https://www.nyas.org/media/23298/012721-mms-guidance-v11.pdf> Accessed 25 March 2023.
- 4 Ajello, CA, Suwantika A, Santika O, King S, and De Lange J. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. Kirk Humanitarian Resource Paper. November 2022. Available for download at: https://kirkhumanitarian.org/wp-content/uploads/2022/11/UNIMMAP-MMS-Supply-Paper_Digital-Version-1-FINAL-1-1.pdf Accessed 25 March 2023.
 - 5 Tumilowicz A, Ruel MT, Gretel P, Pelletier D, Monterrosa EC, Lapping K, et al. Implementation Science in Nutrition: Concepts and Frameworks for an Emerging Field of Science and Practice. *Current Developments in Nutrition*. March 2019; Volume 3, Issue 3. Available for download at <https://academic.oup.com/cdn/article/3/3/nzy080/5129139> Accessed 25 March 2023.
 - 6 The Multiple Micronutrient Supplement Technical Advisory Group (MMS-TAG) & The Micronutrient Forum (MNF). (2020). Expert consensus on an open access United Nations International Multiple Micronutrient Antenatal Preparation–multiple micronutrient supplement product specification. *Annals of the New York Academy of Sciences*, 1470(1), 3–13. Available for download at: <https://doi.org/10.1111/nyas.14322>

Product Standardization and Verification: Critical to UNIMMAP MMS availability and accessibility

Clayton A Ajello

Kirk Humanitarian, Salt Lake City, UT, USA

John B Atwater

Ataqua Regulatory Services, Paris, VA, USA

Jarno de Lange

Vitamin Angel Alliance, Goleta, CA, USA

Key messages:

- Evidence is compelling to support use of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS) formulation as the standard supplement for pregnant women.
- MMS is being introduced in more than 20 national health systems, consistent with the initial global policy framework established by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF).
- MMS is recommended to conform with key standards, including: use of the UNIMMAP formulation, conformance with internationally recognized quality (cGMP and pharmacopeial) standards, halal-certified product for Muslim populations, 180 tablets per pregnancy (until further clinical research or additional analysis of existing clinical trial data sets suggests otherwise), at least a 30-month shelf-life for product intended for export, and commitment to ex-factory pricing that compares favorably to known benchmark pricing of about US\$ 0.01–0.02 per dose.
- An open-access expert consensus product specification is available and intended for inclusion in contractual agreements between buyers and sellers to provide detailed information about the product to be manufactured.
- Use of a standardized product specification, use of independent verification services, and establishment of harmonized national regulatory standards are key elements of a UNIMMAP MMS supply strategy that can expand manufacturing capacity for a high-quality, low-cost product that is interchangeable among buyers irrespective of the manufacturer – a critical requirement for scaling up UNIMMAP MMS within antenatal care services globally.

Introduction

The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation for a Multiple Micronutrient Supplement (MMS) for pregnant women (hereinafter referred to as MMS) is being systematically introduced and scaled up. At least 20 nations are introducing MMS, consistent with global recommendations for its introduction into antenatal care (ANC) services informed by rigorous research.¹ These initiatives access MMS primarily from three donor agencies that procure MMS from a limited number of qualified regional/global manufacturers. However, as national health systems scale up introduction of MMS, more commercially available supplies will be needed to accommodate the spending shift from iron and folic acid (IFA) to MMS. **Figure 1** shows a projected supply/demand forecast for the number of live births in a given year needing the recommended 180 doses of MMS, suggesting that MMS demand could outstrip supply by as early as 2024.²

To meet the ongoing demand for MMS from donors and the anticipated increasing future demand for MMS from national health systems, manufacturing capacity will need to be scaled up. This paper describes the importance of product standardization/verification and national regulatory requirements as primary considerations underlying a sustainable MMS supply strategy to secure long-term availability and accessibility to MMS.

“As national health systems scale up introduction of MMS, more commercially available supplies will be needed”

UNIMMAP MMS formulation: the standard

UNIMMAP MMS contains 15 vitamins and minerals, as shown in **Figure 2**.³ It was created in 1999 by a panel of experts assembled by WHO, UNICEF, and the United Nations University for the specific purpose of creating a standardized MMS formulation for pregnant women that could be used in clinical trials.⁴ Two decades of research in multiple country settings have demonstrated

FIGURE 1: Projected MMS supply and demand forecast from 2021 to 2030

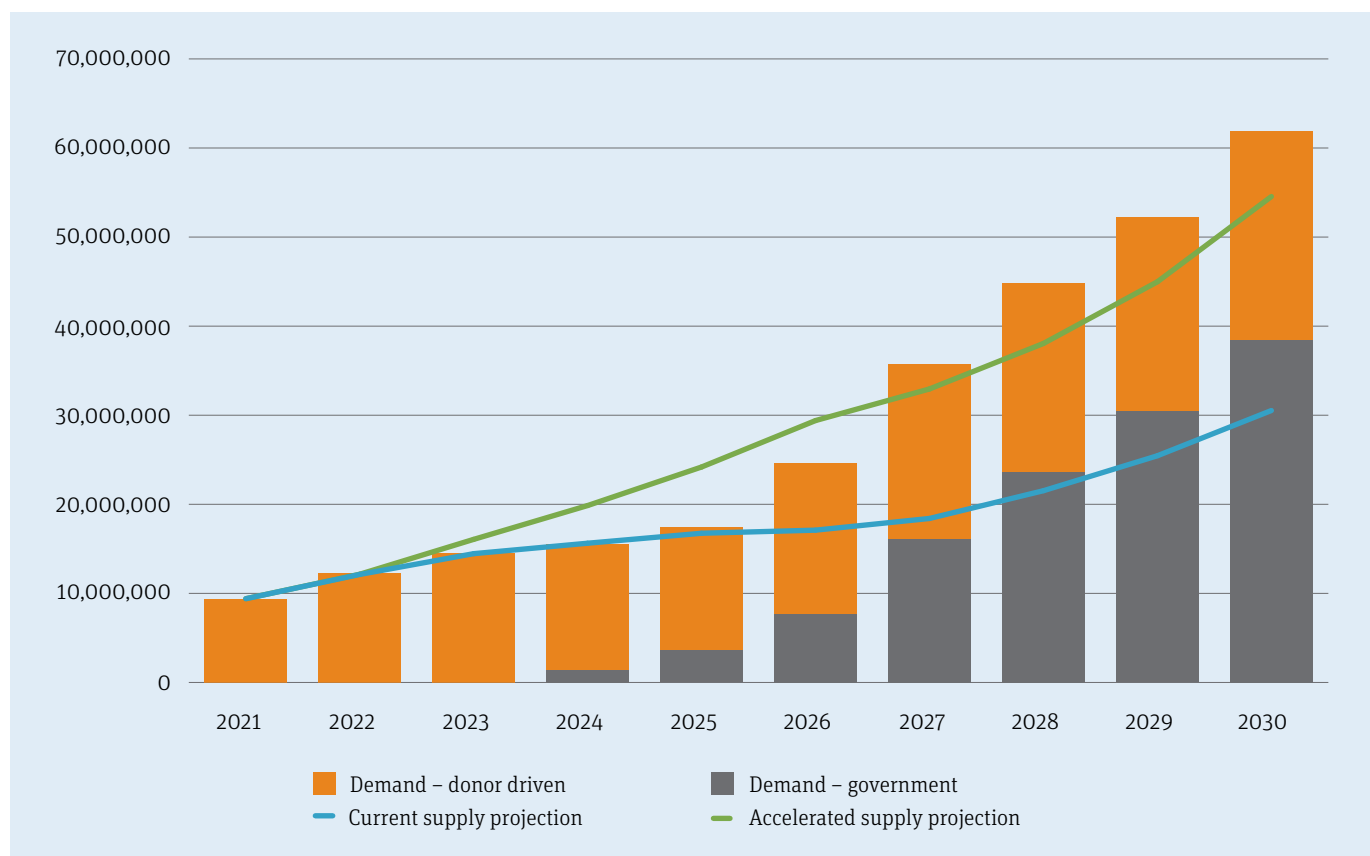


FIGURE 2: UNIMMAP composition

Vitamin A	800 µg
Vitamin D	200 IU
Vitamin E	10 mg
Vitamin C	70 mg
Thiamine	1.4 mg
Riboflavin	1.4 mg
Niacin	18 mg
Vitamin B ₆	1.9 mg
Folic Acid	400 µg
Vitamin B ₁₂	2.6 µg
Copper	2 mg
Iodine	150 µg
Iron	30 mg
Selenium	65 µg
Zinc	15 mg

its efficacy, safety, and cost-effectiveness,⁵ and several secondary analyses⁶ have demonstrated the many benefits that accrue to pregnant women, the fetus, and the infant once born as compared to women using IFA alone. The benefits include improved maternal health and reduced risk of adverse pregnancy outcomes, including stillbirth, mortality in infants at 6 months of age, low birth weight, preterm birth, and small for gestational age. The reduction in risks for adverse pregnancy outcomes are even greater among pregnant women who are anemic or underweight.

UNIMMAP MMS is accepted as the standard for supplementation of pregnant women as reflected in three key documents: WHO’s policy guidance *Recommendations on Antenatal Care for a Positive Pregnancy Experience (2020)*;⁷ UNICEF’s (et al.) *Interim Country-Level Decision-making Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women (2021)*;⁸ and WHO’s updated *Model List of Essential Medicines (2021)*.⁹ Collectively, these documents also provide critical policy guidance pertaining to introduction of MMS, and embed UNIMMAP MMS as the standard choice of MMS for pregnant women. Nonetheless, UNIMMAP MMS is not a ‘magic bullet’. MMS is accepted as an additional and highly effective tool among other public health nutrition interventions – including, most importantly, improved diet and optimal breastfeeding practices – that can result in better health and wellbeing for pregnant women and their infants.

Transforming the UNIMMAP MMS formula into a sustainable, available, and accessible finished product

Given growing acceptance of UNIMMAP MMS as an intervention and increasing demand that is projected to outstrip supply by as early as 2024 (see forecast description and assumptions in *UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy*¹⁰), a strategy is advised to ensure that an adequate, sustainable supply of MMS is both available and accessible. The urgency for a supply strategy is discussed elsewhere in this MMS Special Report 2.0 (*Eight Country Experiences that Inform Development of a UNIMMAP MMS Supply Strategy to Meet Growing Demand*). At the center of a supply strategy for MMS is gaining general agreement on an approach to ensure sufficient capacity to manufacture MMS to defined quality standards.

Regarding product requirements, consensus is emerging that MMS manufactured for national health systems and national insurance schemes should:

1. Follow the WHO UNIMMAP formulation;
2. Conform with internationally recognized quality (cGMP and pharmacopeial) standards;
3. Be halal-certified for Muslim populations;
4. Promote a dosing regimen of 180 tablets per pregnancy for planning purposes (until further clinical research or additional analysis of existing clinical trial data sets suggests otherwise);
5. Meet at least a 30-month shelf-life for product to be exported; and
6. Be purchased at an ex-factory price that is justifiable relative to the known benchmark price – recognizing that certain local conditions may prevent national producers from having the most efficient operations needed to achieve the most favorable pricing.*

*[NB. Benchmark pricing for MMS finished product (i.e., the price beyond which any incremental volume will not reduce the price in any meaningful way) is US\$ 0.0116–0.0125 per dose at current pricing through 2023 and consistent with UNICEF estimates of pricing.^{11,12} However, limited manufacturer production capacity, procurements at low volume, local tax treatment of imported ingredients and other local factors can make it difficult to achieve this pricing for producers manufacturing for a single domestic market where manufacturing occurs.]

“At the center of a supply strategy for MMS is gaining general agreement on an approach to ensure sufficient capacity to manufacture MMS to defined quality standards”

Role of a product specification and a system of product verification

To manufacture an MMS of a defined quality, a product specification is essential. A product specification is a technical document that provides a detailed description of the product and becomes part of a business agreement memorializing terms and conditions between a buyer and seller. The product specification can be either provided by the buyer or created by the manufacturer and is typically proprietary.

To support implementation of an MMS supply strategy, key stakeholders convened in 2020, under the joint leadership of the New York Academy of Sciences and the Micronutrient Forum, to explore ways to avoid the costly and time-consuming effort that would be incurred if every manufacturer created their own MMS product specification. The result of this initiative was the creation of the *Expert Consensus on an Open-Access Product Specification for MMS for Pregnant Women*.¹³ The contents of the open-access specification are summarized in **Figure 3**. Experience in implementing the open-access specification shows it is beginning to benefit manufacturers, purchasers, and consumers – as demonstrated by convergence among major MMS donors on use of a standardized product specification for procurement. An in-depth discussion of the rationale for creation of the open-access MMS consensus specification, its use and benefits are described and discussed elsewhere.¹⁴

FIGURE 3: What is in the open-access MMS product specification?

- Product composition (i.e., UNIMMAP) including the amount and recommended chemical form of each nutrient
- Pharmacopeial quality standards for all ingredients
- Dosage form (e.g., tablet or hard gelatin capsule)
- Packaging container closure system (e.g., bottle or blister pack)
- Tests, test methods and acceptance criteria
- Stability study requirements
- Recommended third-party certifications

“Through combined use of the open-access consensus specification and independent verification services, both buyers and sellers of MMS benefit”

Providing manufacturers with the open-access MMS product specification alone, however, is not sufficient in itself to ensure that a product manufactured conforms with the product specification and quantitative label claims. Regulatory oversight of manufacturing practices aims to ensure quality but varies around the world by country and manufacturer. To ensure that a product meets the open-access MMS product specification, it is recommended that purchasers take the additional step of verifying that manufacturing processes and the finished product conform with the product specification. An effective way to ensure quality standards are met is to have an independent verification organization (e.g., USP) audit the manufacturing process. Their services include the use of audits and product testing to verify that the processes and facilities used to manufacture the finished product conform to the product specification, and that the finished product itself conforms to the product specification. Independent verification services are designed to help manufacturers build quality into the manufacture of a product by continually auditing and testing product, but also by providing technical oversight to help manufacturers improve their manufacturing processes.

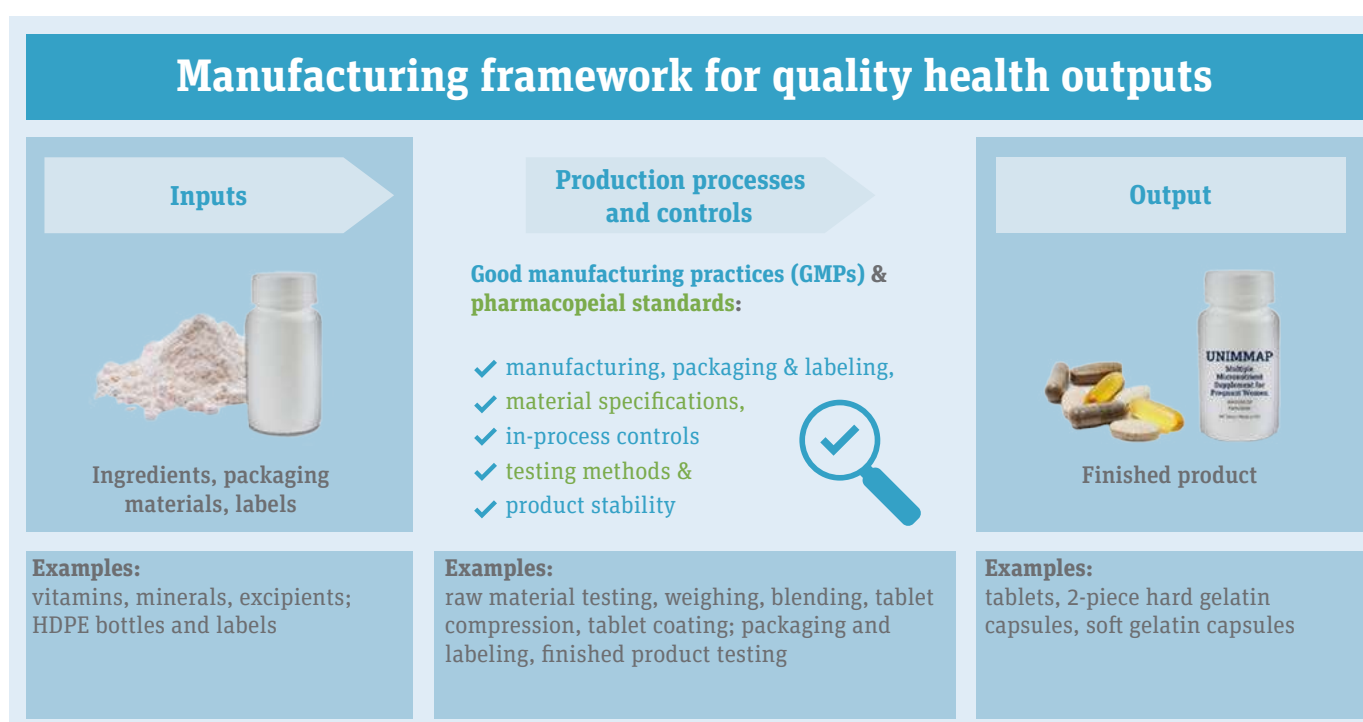
Through combined use of the open-access consensus specification and independent verification services, both buyers and sellers of MMS benefit. Their use achieves transparency towards (and accountability by) both parties to an agreement, facilitates interchangeability of product irrespective of the manufacturer, builds quality into the manufacture of MMS (which supports consumer confidence), and helps to optimize cost-efficiency of manufacturing while fostering pricing efficiency – all of which are essential for long-term success to scale MMS use.

The regulatory framework for MMS

Successfully securing a supply of quality MMS product is not solely dependent upon a manufacturer conforming to the terms and conditions of a contract inclusive of a product specification and utilizing independent verification services. MMS product must also comply with the regulatory framework of the country or countries in which MMS is manufactured and registered for use. National governments regulate MMS either as a drug or as a nutritional/dietary/food supplement. This difference can complicate regional manufacturing of MMS to a common standardized product specification that meets approval of all national regulatory authorities of concern. How an MMS is classified for regulatory purposes affects its quality, availability and accessibility and cost.

Figure 4 illustrates that product quality is a function of good manufacturing practices (GMPs) and pharmacopeial and/or compendial standards. GMP regulations and pharmacopeial/compendial standards are important because they promote the principal that quality needs to be built into the product, not tested into the product after manufacture. GMPs have basic requirements for methods, facilities, and controls used in manufacturing a health product (i.e., drug products and nutritional supplements). Drug product and nutritional supplement quality standards are addressed by pharmacopeial standards (e.g., United States Pharmacopeia – USP; British Pharmacopoeia – BP; European Pharmacopoeia – Ph. Eur.; and the International Pharmacopoeia – Ph. Int.); and food quality standards, by compendial standards (e.g., Codex Alimentarius and Food Chemical Codex). GMP and product quality standards are more rigorous for drugs and nutritional supplements than for foods, whereas those for drugs and nutritional supplements are similar.

FIGURE 4: Product quality explained



There is global consensus on the classification of drug products and how they should be manufactured, but that is not the case for nutritional/dietary/food supplements. Fortunately, most countries permit registration of a product when it is produced to equivalent or higher quality standards than those established by the national regulatory authority. Countries such as the USA that regulate MMS as a nutritional/dietary/food supplement, do so because they consider the product to be more like a food *from a safety standpoint*, and not like a drug that can be inherently unsafe. (There is little consensus on the terminology, definition, and requirements by which UNIMMAP MMS is classified by different countries. In the United States, the product is referred to as a “dietary supplement” according to the Dietary Supplement Health and Education Act [DSHEA]. UNIMMAP MMS is referred to as a “dietary supplement” in this paper.)

From a *product quality perspective*, official standards established by the United States Pharmacopeia (USP) treat dietary supplements with “drug-like” quality standards that assure quality similar to that of a drug product. No matter whether a product is sold as a drug or a nutritional/dietary supplement, a product complying with USP quality standards will comply with the same USP monograph requirements for the ingredients and finished product. The USP monograph for Oil- and Water-Soluble Vitamins with Minerals Tablets provides the quality specification for the MMS product. Also, USP general chapter <2750> *Manufacturing Practices for Dietary Supplements*¹⁵ tend to be drug-like GMPs. The key difference between USP dietary supplement GMPs and drug GMPs^{16,17} is the degree to which the GMP activities are monitored and documented. Ideally, with appropriate dialogue, most low- and middle-income countries (LMICs) can embrace USP “drug-like” standards for dietary supplement quality and manufacturing practices that are specified in the open-access MMS specification.

To support a supply strategy in which regional transactions are anticipated to occur among multiple buyers and manufacturers in which both parties seek an MMS product that is interchangeable irrespective of the country of manufacture or registration and use, there is a need for broad agreement among national regulatory authorities with respect to the applicable requirements and regulations supporting their country's registration of MMS. Currently, there is no consensus among national regulatory authorities on the type of GMPs that should apply to a high-quality, low-cost MMS product. However, consensus is beginning to emerge based on actual practices by major donors and purchasers of MMS to procure MMS that conforms to GMP and pharmacopeial standards established by USP or other internationally recognized quality standards. MMS classification by USP as a nutritional/dietary supplement provides a proper balance of GMP regulation and quality standards to achieve a high, drug-like quality product without the added cost associated with treating MMS as a drug product. The extra cost of product evaluation and documentation associated with drug products (as compared to a “drug-like” nutritional/dietary supplement)

does not provide a significant additional level of product quality for MMS. To raise awareness and build consensus around using “drug-like” nutritional/dietary supplement quality standards more widely, there is a need for national regulatory authorities to harmonize opinions to achieve a broadly accepted consensus specification for MMS. Harmonization could be based on the current procurement practices of donor organizations that purchase MMS for distribution to national governments based on adherence to the GMPs and pharmacopeial standards described in the *Expert Consensus on an Open-Access Product Specification for MMS for Pregnant Women*, which is further explained elsewhere.¹⁸

“Application of quality standards established in the open-access product specification represents the right balance of quality and cost”

Conclusion

Securing long-term availability and access to a sustainable supply of MMS that meets anticipated future demand requires an internationally harmonized MMS supply strategy. A workable strategy to secure MMS supplies that meets LMICs needs can be achieved by developing consensus product requirements with a standardized product specification; requiring use of independent verification services for assuring the quality of MMS that is manufactured for both local and export use; and establishing a consensus regulatory framework that allows the latitude for governments to regulate MMS without creating unnecessary costs that do not advance quality. This approach to national regulatory standards and registration should be applied irrespective of where the MMS product is manufactured and whether the MMS product is to be used locally or for export. The authors believe that application of quality standards established in the open-access product specification represents the right balance of quality and cost.

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Correspondence: Clayton Ajello, Senior Strategic and Technical Advisor, Kirk Humanitarian, 2755 E. Cottonwood Parkway, Suite 450, Salt Lake City, UT 84121, USA
Email: cajello@inlexo.com

References

- 1 Healthy Mothers Healthy Babies. World Map of MMS Activities (March 2023): <https://hnhbconsortium.org/world-map/> Accessed 25 March 2023.
- 2 Ajello, CA, Suwantika A, Santika O, King S, and De Lange J. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. Kirk Humanitarian Resource Paper. November 2022. Available for download at: https://kirkhumanitarian.org/wp-content/uploads/2022/11/FINAL-Kirk_UNIMMAP_MMS_SupplyPaper_Digital.pdf Accessed 25 March 2023.
- 3 World Health Organization, United Nations University & United Nations Children's Fund (UNICEF). (1999). Composition of a multi- micronutrient supplement to be used in pilot programmes among pregnant women in developing countries: report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO) and United Nations University workshop. UNICEF. Available for download at: <https://apps.who.int/iris/handle/10665/75358> Accessed 25 March 2023.
- 4 Ibid, note 3
- 5 Keats, E. C., Haider, B. A., Tam, E., & Bhutta, Z. A. (2019). Multiple-micronutrient supplementation for women during pregnancy. *The Cochrane database of systematic reviews*, 3(3), CD004905. <https://doi.org/10.1002/14651858.CD004905.pub6> Accessed 25 March 2023.
- 6 Bourassa, M.W., Osendarp, S.J.M., Adu-Afarwuah, S., Ahmed, S., Ajello, C., Bergeron G., et al. (2019). Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries. *Annals of the New York Academy of Sciences*, 1444(1), 6–21. Available for download at: <https://doi.org/10.1111/nyas.14121> Accessed 25 March 2023.
- 7 World Health Organization (2020). WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy. Available for download at: <https://www.who.int/publications/i/item/9789240007789> Accessed 25 March 2023.
- 8 UNICEF, Micronutrient Forum, Multiple Micronutrient Supplementation in Pregnancy – Technical Advisory Group, Nutrition International, and The Vitamin Angel Alliance (2020). Interim Country-Level Decision-making Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women. Available for download at: <https://www.unicef.org/media/96971/file/Interim-Country-level-Guidance-MMS-for-PW-2021.pdf> Accessed 25 March 2023.
- 9 World Health Organization (2021). World Health Organization Model List of Essential Medicines, p. 53. <https://apps.who.int/iris/bitstream/handle/10665/345533/WHO-MHP-HPS-EML-2021.02-eng.pdf> Accessed 25 March 2023.
- 10 Ibid, note 2.
- 11 Ibid, note 2.
- 12 UNICEF (2022). Multiple Micronutrient Supplementation, An Approach to Improving the Quality of Nutrition Care for Mothers and Preventing Low Birthweight. Available for download at: <https://www.unicef.org/media/123271/file> Accessed 25 March 2023.
- 13 The Multiple Micronutrient Supplement Technical Advisory Group (MMS-TAG) & The Micronutrient Forum (MNF). (2020). Expert consensus on an open-access United Nations International Multiple Micronutrient Antenatal Preparation–multiple micronutrient supplement product specification. *Annals of the New York Academy of Sciences*, 1470(1), 3–13. Available for download at: <https://doi.org/10.1111/nyas.14322> Accessed 25 March 2023.
- 14 *Sight and Life* Foundation. (2020). Expert Consensus on an Open-Access UNIMMAP-MMS Product Specification, 2020(3), 102–108. Available for download at: <https://kirkhumanitarian.org/wp-content/uploads/2020/04/Expert-Consensus-on-an-Open-Access-UNIMMAP-MMS-Product-Specification.pdf> Accessed 25 March 2023.
- 15 United States Pharmacopeia. Manufacturing Practices for Dietary Supplements <2750>. In USP-NF. Rockville, MD: USP; Aug 1, 2021. DOI: https://doi.org/10.31003/USPNF_M99987_02_01. Accessed 25 March 2023.
- 16 US FDA Code of Federal Regulations (CFR): Title 21 CFR Part 210: Current Good Manufacturing Practice (cGMP) in Manufacturing, Processing, Packing, or Holding of Drugs; General. <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-210> Accessed 25 March 2023.
- 17 Title 21 CFR Part 211: cGMP for Finished Pharmaceuticals. <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211>. Accessed 25 March 2023.
- 18 Atwater, J. B. (2020). Understanding Product Quality as Applied to UNIMMAP–MMS Product Donated by Kirk Humanitarian. https://kirkhumanitarian.org/wp-content/uploads/2020/10/KirkHumanitarian_ProductQualityWhitePaper_9.28.pdf Accessed 25 March 2023.

Introducing Multiple Micronutrient Supplements (MMS) to Improve Maternal Nutrition and Birth Outcomes in Ethiopia

Demonstrating sustainable scale-up of MMS in a resource-limited setting

Ramadhani Noor, Tesfaye Chuko, Hiwot Kelemu, Yemisrach Hussien, Abiy Tefera, Stanley Chitekwe

United Nations Children's Fund (UNICEF), Addis Ababa, Ethiopia

Kidist Woldesenbet, Hiwot Darsene

Ministry of Health (MoH), Addis Ababa, Ethiopia

Masresha Tessema

Ethiopia Public Health Institute (EPHI), Addis Ababa, Ethiopia

Key messages:

- Improving nutrition among women of reproductive age, especially during pregnancy, is vital to a healthy pregnancy, birth outcomes, and early child survival.
- Based on existing global evidence, the use of multiple micronutrient supplements (MMS) in pregnancy has been included into the revised National Adolescent, Maternal, Infant, and Young Child Nutrition (AMIYCN), Antenatal Care (ANC) and the National Micronutrient Prevention and Control guidelines in Ethiopia, but there is still a need to demonstrate sustainable scale-up of MMS in the country.
- The scope and size of the demonstration program incorporates an accelerated roll-out of MMS in selected *woredas* in Ethiopia and closely mirrors the implementation of MMS at scale in a resource-limited setting, and the learning agenda will be tailored to inform the science of delivery for impact, equity and sustainability.
- The introduction of MMS is an opportunity to generate sustained demand for antenatal care, improve quality and uptake of maternal nutrition services in Ethiopia, and improve service quality and existing programmatic bottlenecks through a learning-by-doing approach.
- Cost (who will be paying) is a key question informing sustainable scale-up of MMS in Ethiopia. Parallel efforts in developing market-based approaches and promoting local production of MMS will be catalytic and game-changing in the switch from IFA to MMS.

Background

Malnutrition among women and children is a significant public health problem in Ethiopia. More than one-third (39%) of children under five are stunted, 22% are underweight, and 11% are wasted.¹ Only 7% of women of reproductive age (WRA) meet the recommended dietary diversity.¹ Two in three WRA are deficient in one or more micronutrients.¹ Folate deficiency is the most prevalent micronutrient deficiency in Ethiopia, affecting almost half of the WRA.¹ One in four women of reproductive age (22.6%) is undernourished and one in three pregnant women (29.1%) is anemic.² More than 10% of all babies born in Ethiopia are born with low birth weight (<2,500 grams at term), increasing their risk of death and impaired growth and development.² Poor food security and low quality of diets negatively affect the nutrition of women of reproductive age, especially during pregnancy. Low-quality diets are the norm due to limited intake of animal products, fruits, vegetables and fortified foods, mainly due to limited access, deep-rooted social norms, taboos and long fasting periods.² Despite the high coverage of antenatal care (ANC) services in Ethiopia (74% of women attend at least one ANC visit and 43% attend the recommended four or more ANC visits), coverage of iron and folic acid (IFA) supplementation remains low: only around 17% of pregnant women in Ethiopia consume IFA supplements for 90 days or more.¹ The most common barriers to women consuming the recommended dose of IFA supplements during pregnancy include adverse side-effects, misconceptions that IFA is for the ill or that it is a form of contraceptive, and overall suboptimal demand for ANC services, poor quality of ANC services, IFA stock-outs, and poor counselling.^{3,4} Improving nutrition among women of reproductive age, and especially during pregnancy, is vital to a healthy pregnancy, birth outcomes, and early child survival. In line with the existing global evidence, sustainable scale-up of multiple micronutrient supplementation (MMS) as part of maternal nutrition programming is an opportunity to improve the delivery and quality of maternal nutrition services in Ethiopia.

The demonstration program

As part of the Healthy Mums Healthy Babies consortium, and with funding from the Children's Investment Fund Foundation (CIFF),

UNICEF Ethiopia is supporting the Ministry of Health (MOH) and the Regional Health Bureau (RHB) in introducing the use of MMS among pregnant women attending ANC services in 21 *woredas* (districts of Ethiopia) across five selected demonstration regions including Oromia, Gambela, SNNP, Sidama, and Somali (see **Figure 1**, map of intervention areas).

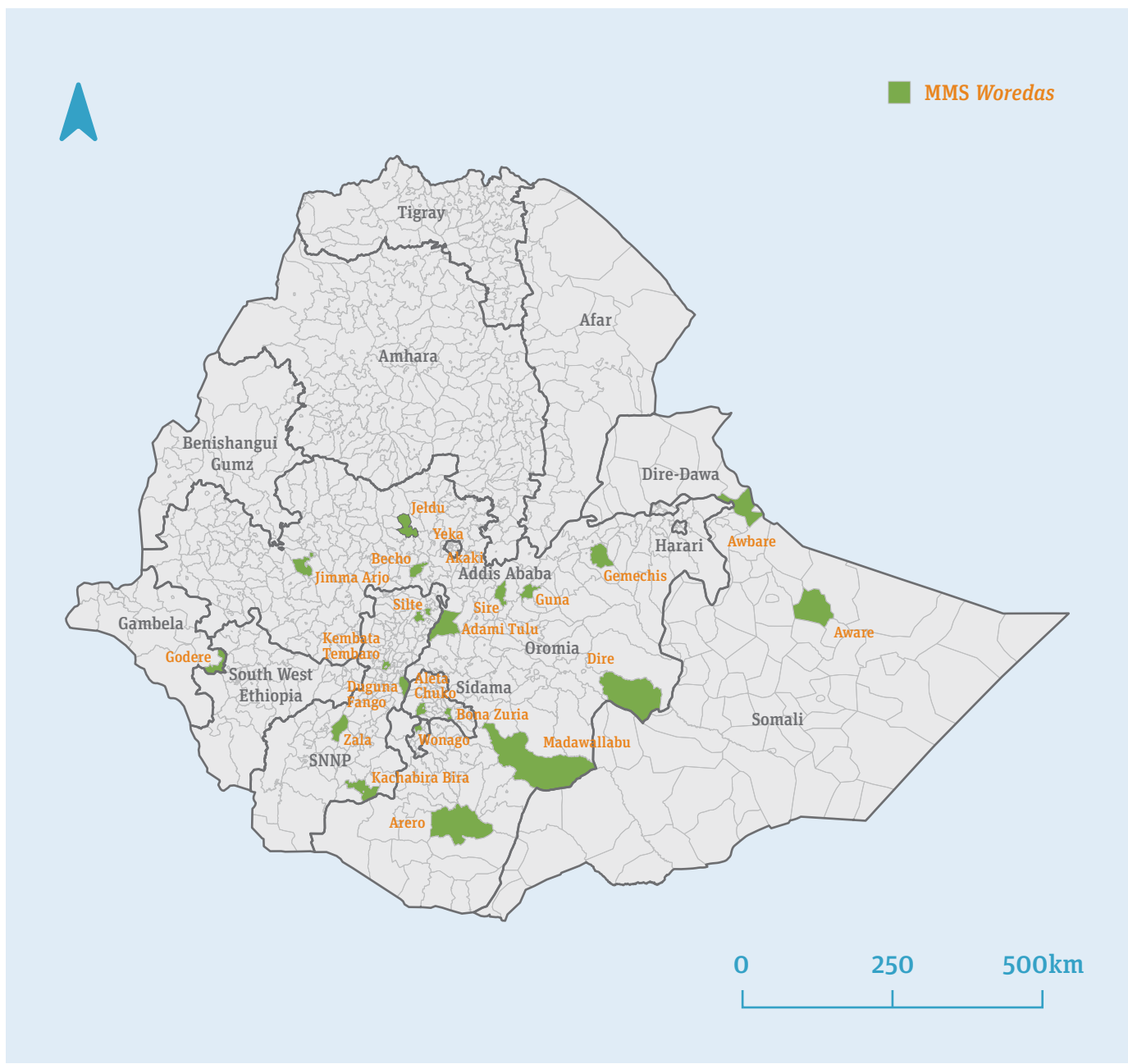
The demonstration program aims to reach 400,000 pregnant women by the end of 2025. Its primary objective is to set up a country model whereby MMS of assured quality is available and desirable to pregnant women in Ethiopia. Specifically, the program aims at generating sustained demand for ANC services, improving the quality of services based on recommended ANC interventions, especially nutrition counselling, and increasing coverage of, uptake of, and compliance with ANC services/interventions

including MMS. Secondly, the demonstration program aims at developing market-based approaches (social marketing), and social behavior change (SBC) strategies for maternal nutrition services, as well as promoting local production of MMS in Ethiopia. This demonstration program will inform sustainable scale-up of MMS, replacing IFA as part of the ANC services package while ensuring equitable access on the part of all pregnant women in Ethiopia.

Strategic design of the program

This demonstration program is strategically designed to set up a country model for translating the impact of MMS on improving pregnancy and birth outcomes in Ethiopia. The program is organized under four key results areas, outlined below in **Figure 2**, Theory of Change.

FIGURE 5: Map of intervention areas for the 21 *woredas* participating in the demonstration program



Overview of progress

In collaboration with the MOH and RHB, the accelerated roll-out plan for MMS was launched in November 2022. By the end of February 2023, a total of 30,000 pregnant women had already been enrolled in the program. The target is to reach **129,416** pregnant women in year one, and **133,543** and **137,041** in years 2 and 3 respectively.

“There is a need to identify and tailor friendly services for young mothers”

Challenges and opportunities

Based on experience of implementation to date, the following have been identified as key challenges and opportunities for the demonstration program:

- 7. Provision of quality ANC services:** Ensuring the delivery of a comprehensive ANC package remains a challenge, with suboptimal coverage and systems that in turn disincentive women from coming for ANC services early and frequently. Parallel efforts to improve the quality of services through the MoH and the RHBs remain necessary but should not limit efforts to scale up MMS.
- 8. Supply of MMS:** A challenging global supply chain for MMS has resulted in long delays in receiving the required stock, while importation procedures for the UNIMMAP formula-

FIGURE 6: Theory of Change for the MMS demonstration program in Ethiopia

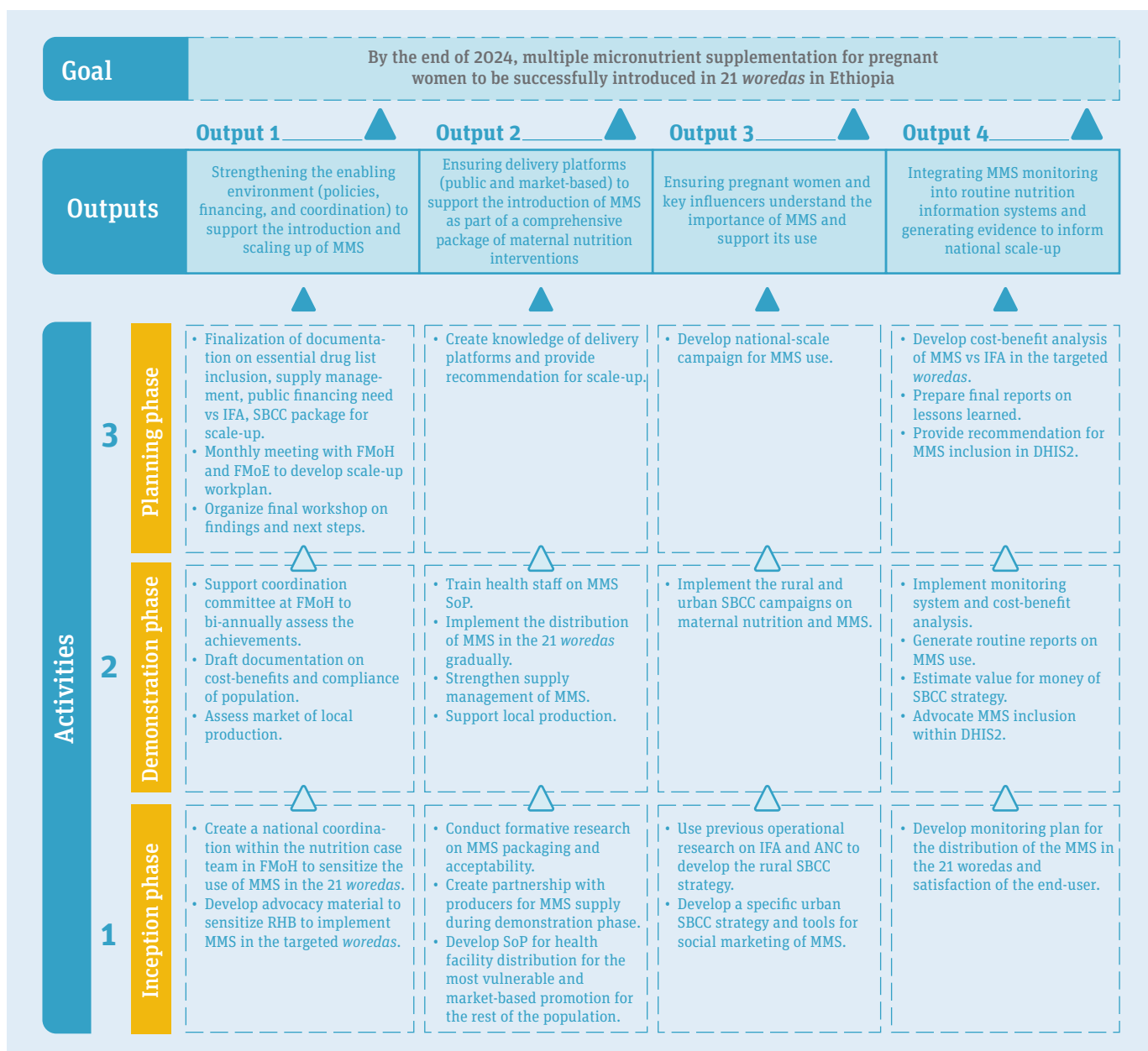


TABLE 2: Results framework and progress**OUTPUT 1: Reinforcing the enabling environment (policies, financing and coordination) to support the demonstration of MMS****1.1 Establishment of the national coordination mechanism:**

FMoH has engaged the existing Adolescent, Maternal, Infant, and Young Children Nutrition Technical Working Group (AMIYCN TWG) to provide efficient and regular oversight, and strategic direction.

1.2 A government-owned and -led partnership for MMS:

Establishment of an office of nutrition within FMoH, with a dedicated Chief Executive Officer (CEO) reporting to the FMoH and a Desk Head of Developmental Nutrition, including delivery of maternal nutrition services.

1.3 Incorporation of MMS into national guidelines:

MMS is indicated in the guidelines as a key strategy to prevent and control micronutrient deficiencies among pregnant women. These include the National Adolescent, Maternal, Infant, and Young Child Nutrition (AMIYCN), Antenatal Care (ANC) and the National Micronutrient Prevention and Control guidelines.

OUTPUT 2: Strengthening existing and expanding delivery platforms (public and market-based) and supply chains to support the introduction of MMS as part of a comprehensive package of maternal nutrition interventions**2.1 Procurement, certification, and distribution of MMS:**

Completed procurement and successful importation of MMS in line with the certification process of the Ethiopia Food and Drugs Authority (EFDA).

2.2 MMS demonstration program co-designed:

Lessons from other countries implementing similar programs, including Tanzania, Burkina Faso, Madagascar and Bangladesh. Uniquely, the demonstration program currently implemented in Ethiopia is the largest in the region in terms of geographical coverage and number of pregnant women targeted (400,000).

2.3 Intervention woredas selected, regional health bureaus engaged, and health care workers trained:

This investment builds on UNICEF's existing program of cooperation with the Government of Ethiopia in eight regions.

2.4 Accelerated roll-out of the demonstration program:

Following consultations with the FMoH and the RHBs, a roll-out plan for the 21 intervention woredas (**the rural/public model**) was developed.

2.5 Feasibility of local production of MMS in Ethiopia:

In collaboration with *Sight and Life* Foundation, a market assessment for local production of MMS in Ethiopia was completed, and a report has been submitted to the Government (FMoH and Ministry of Industries).

OUTPUT 3: Implementation of the rural and urban SBC campaigns on maternal nutrition and MMS (demand generation)**3.1 Integrating social and behavior change (SBC):**

Designed SBC package aiming at generating demand for ANC services, improving quality of counselling on maternal nutrition and increasing uptake of essential services, including MMS.

3.2 Applying behavioral insight approach to improve MMS adherence & ANC visit:

A Behavioural Health Insight Research and Design LAB (BIRD LAB) has been established at Addis Ababa University School of Public Health to support this work and become the center of excellence in behavioral insight in Ethiopia.

OUTPUT 4: Integrating MMS monitoring into routine nutrition information systems and generating evidence to inform national scale-up**4.1 Monitoring plan for the distribution of MMS in the 21 woredas:**

Developed a joint learning agenda based on the approved theory of change for this demonstration program. A light version of end-user monitoring system which complements the DHIS2 is being implemented to monitor progress of the program implementation using select key indicators reported monthly against targets by the participating woredas.

4.2 Program evaluation:

A five-step process is being implemented: (1) Defining: understanding the problem and deciding which specific behaviors to address; (2) Exploring and diagnosing socio-cultural, environmental and psychological factors; (3) Prototyping: using human-centered design to co-create tentative solutions directly with the people who will use them; (4) Testing proposed solutions using implementation research and experimental methods; and (5) Scaling up the recommended intervention.

CIFF has commissioned the London School of Hygiene and Tropical Medicine (UK) and the Ethiopia Public Health Institute (Ethiopia) to undertake an evaluation of the demonstration program.

tion of MMS in Ethiopia still require a third-party laboratory testing, given the lack of capacity to undertake required assays to test MMS nutrient contents in the country.

9. Lack of investments and a strategy at country level to support local production of MMS:

Beyond the market assessment, there remains a need to support the encouragement of local businesses to take ownership and leadership in establishing local production of MMS in Ethiopia. This includes facilitating an assessment of the enabling environment to support and stimulate local business appetite to invest in the local production and the development of an investment case and business plans to enhance advocacy efforts promoting local production.

10. Need to develop a scale-up plan for MMS in Ethiopia:

One barrier that inhibits scale-up is the cost of MMS, and the financing modalities to support sustainable scale-up in particular. While developing market-based approaches and promoting local production will be catalytic and game-changing in the replacement of IFA with MMS, currently there is a need to implement evidence-based advocacy around the level of waste incurred in terms of IFA that women receive but do not consume. Despite the Government of Ethiopia's investments in ensuring high coverage of the IFA program, the proportion of pregnant women taking iron/folic acid (IFA) tablets for 90+ days has remained consistently low. The government funds spent on procuring wasted IFA can

be used to procure MMS and to develop partners' resources to meet the gap as the country gradually increases equitable access to MMS for every pregnant woman.

11. Young mothers present a significant proportion of clientele visiting ANC services.

In Ethiopia, the burden of teenage pregnancy (young mothers) remains high, currently estimated at 24%.⁶ This specific group is vulnerable to additional challenges when it comes to demand, uptake, and compliance with maternal nutrition services including MMS, and may be at higher risk of poor pregnancy and birth outcomes. There is a need to identify and tailor friendly services for young mothers. Furthermore, advocacy efforts to scale up the use of MMS should also be aligned with micronutrient supplementation programs targeting the pre-pregnancy period, especially the weekly supplementation programs among adolescent girls. One in two adolescent girls is deficient in one or more micronutrients, and the prevalence of anemia among adolescent girls is 9%, with regions having prevalence rates as high as 20%.¹

“The introduction of MMS is an opportunity to generate demand for and to improve the quality of ANC”



Kokobe Ashebir, 20, has a two-month-old baby. She's attending a routine check-up with Workitu Abera, a health worker at Kolabe Bale Health Post in Sire, Oromia Region, Ethiopia.

Conclusion

The MMS demonstration program is aligned with the Government of Ethiopia's commitment to improve the nutrition of pregnant women and birth outcomes of their babies. The program is designed to demonstrate: (1) sustainable scale-up of MMS nationally; (2) the development of a market-based approach in a setting where supplementation programs are to a great extent based on public for-free delivery approaches; and (3) the promotion of local manufacturing of MMS to ensure affordable and equitable access to MMS on the part of all women in Ethiopia. The introduction of MMS is an opportunity to generate demand for and to improve the quality of ANC, to strengthen the health systems, and to improve the delivery of maternal health and nutrition services in Ethiopia. The joint learning agenda and the mobilization of integrated knowledge will leverage existing evidence to inform the sustainable scale-up of MMS in Ethiopia.

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Correspondence: **Ramadhani Noor**, Nutrition Specialist, UNICEF Ethiopia, United Nations Children's Fund, UNECA Compound, Zambezi Building 2nd, 3rd & 4th floors, Box 1169 Addis Ababa, Ethiopia

Email: rnoor@unicef.org

References

- 1 National Food and Nutrition Strategy, Baseline Survey, Key Findings Preliminary Report, MoH Ethiopia, March 2023.
- 2 Ethiopia Demographic Health Survey, 2019.
- 3 T. A. Zerfu, M. Umeta, and K. Baye, "Dietary habits, food taboos, and perceptions towards weight gain during pregnancy in Arsi, rural central Ethiopia: a qualitative cross-sectional study," *J. Health. Popul. Nutr.*, 2016, doi: 10.1186/s41043-016-0059-8 & Ethiopian Public Health Institute (EPHI), "National Micronutrient Survey Report," 2016.
- 4 Formative research key nutrition interventions in Ethiopia, May 2021.
- 5 Siekmans K, Roche M, Kung'u JK, Desrochers RE, De-Regil LM. Barriers and enablers for iron folic acid (IFA) supplementation in pregnant women. *Matern Child Nutr.* 2018;14(S5).
- 6 Mathewos S, Mekuria A. Teenage Pregnancy and Its Associated Factors among School Adolescents of Arba Minch Town, Southern Ethiopia. *Ethiop J Health Sci.* 2018 May;28(3):287-298. doi: 10.4314/ejhs.v28i3.6. PMID: 29983528; PMCID: PMC6016359.

Resources for Scale-up



Formative Research Guidance: Introducing Multiple Micronutrient Supplements (MMS)

Stephen R Kodish, Raphia Ngoutane

Pennsylvania State University, PA, USA

Rebecca Olson

Sight and Life Foundation, Basel, Switzerland

Key messages:

- Formative research is the process by which researchers or public health practitioners aim to understand the characteristics (e.g., current behaviors, perceptions, needs) of target populations that influence their decisions and actions.
- The process of programming where multiple micronutrient supplements (MMS) should be delivered would benefit from formative research, given the global surveillance and monitoring data that have forecasted both upstream and downstream challenges to delivering and scaling up MMS at the country level such as weak supply chains, low access to ANC services, and low-quality behavior change interventions.
- Formative Research Guidance was developed jointly by UNICEF, *Sight and Life* Foundation and Pennsylvania State University to assist countries to introduce MMS for pregnant women.
- This guidance provides an overview of the steps and methods used to conduct formative research for improved acceptability and utilization of MMS on the part of pregnant women. The guidance manual contents were developed, in part, based on formative research conducted in Bangladesh, Burkina Faso, Madagascar and Tanzania.

Introduction

The Formative Research Guidance, developed jointly by UNICEF, *Sight and Life* Foundation and Pennsylvania State University, contains simplified guidance to assist countries in introducing multiple micronutrient supplement (MMS) for pregnant women. It provides an overview of the steps and methods used to conduct formative research for improved acceptability and utilization of MMS on the part of pregnant women. The guidance manual contents were developed, in part, based on formative research conducted in Bangladesh, Burkina Faso, Madagascar and Tanzania; and lessons learned from conducting those formative studies were

synthesized using a combination of stakeholder feedback and evidence-based research methods. The guidance provides specific information to help support the development and design of a formative research process for introducing MMS or other nutrition interventions and may be used by implementing agencies and field practitioners when introducing MMS in country programs. The following is a snapshot of the contents of the guidance, with a link to access the full document.

“The guidance provides information to help support the development and design of a formative research process”

What is formative research and why is it important?

Formative research is the process by which researchers or public health practitioners aim to understand the characteristics (e.g., current behaviors, perceptions, needs) of target populations that influence their decisions and actions. Formative research may be conducted prior to the design of a behavioral intervention but also during implementation, as a type of process evaluation, for improving delivery or correcting course as needed.^{1,2} Typically, formative research approaches utilize multiple mixed methods (quantitative and qualitative) to triangulate findings across different participant types and data sources.³

Formative research is particularly important for enabling researchers and public health practitioners to identify potential obstacles to future programming, such as participation barriers, and to develop solutions to minimize or eliminate these obstacles. The process of programming where MMS should be delivered would benefit from formative research, given the global surveillance and monitoring data that have forecasted both upstream and downstream challenges to delivering and scaling up MMS at the country level. These factors include weak supply chains, low access to ANC services, and low quality behavior change interventions to support and motivate pregnant women. Formative research is important in the context of MMS to address evidence gaps and develop key insights on how to deliver MMS effectively across different contexts to ensure that MMS does not face the same fate as

IFA of low program coverage globally.⁴ Well-designed formative research may yield sociocultural and context-specific findings as a first stage of program planning to improve understanding of those social, behavioral and systems-level elements important for the acceptance and utilization of MMS.

“Formative research is particularly important for enabling researchers and public health practitioners to identify potential obstacles to future programming”

Proposed steps in conducting formative research for MMS

The following steps are a simplified process that practitioners may consider following before and during formative research.

Step 1: Understanding the context. Prior to implementing formative research, understanding what is *already* known about a specific context is important. This includes documenting the existing information available in each country/area using a literature review of ethnographic analyses, peer-reviewed and grey literature. Multiple sources of country-level information are available for gathering this information such as: sociocultural assessments, anthropological studies; Semi-Quantitative Evaluation of Access and Coverage (SQUEAC) and Standardized Monitoring and Assessment of Relief and Transitions (SMART) surveys; Knowledge, Attitudes and Practices (KAP) surveys; Demographic and Health Surveys (DHS); Multiple Indicator Cluster Surveys (MICS); and health facility surveys. These materials can provide rich information on context-specific causes of undernutrition, organization of stakeholders, health services coverage, and determinants of key behaviors of interest.

TABLE 1: Examples of methods for conducting formative research

Formative research method	Description
Free listing and pile sorting	Methods that help generate data to understand how community members conceptualize foods and illnesses common to pregnancy. These methods are implemented with the help of an interview guide.
Semi-structured interviews	Interviews are useful to gain a general understanding of the reported practices, individual perspectives, personal experiences, and perceptions of pregnant women in the community. They are best conducted using open-ended questions covering a specific list of topics and are implemented with the help of an interview guide.
Focus group discussion	Focused discussions with a small group (usually 6 to 12 people) of participants are key for better understanding the attitudes, perceptions, and beliefs pertinent to the issues being examined. These discussions will provide multiple perspectives and build consensus around topics, and pick up on social norms, group dynamics, and concrete experiences linked to a particular behavior. Essential tools for eliciting informative perspectives in focus groups include open-ended questions and participatory activities and are facilitated by a moderator using a prepared interview guide.
Participatory workshops	Participatory workshops with diverse groups of community members allow them to brainstorm ideas and identify common barriers that mothers experience in the context of seeking care and using prenatal supplements; these workshops also provide the opportunity to brainstorm and rank preferred strategies for overcoming those identified barriers. A guide should be developed containing specific questions that can generate one-word or one-phrase responses.
Direct observations	Direct observations are useful for gathering quantitative data that can be used to corroborate or expand on qualitative findings. For example, direct observations may help to inform MMS marketing materials by providing information about locally available supplements. They can also be used for collecting qualitative data in the form of textual field notes that describe meal preparation and feeding behaviors. An observational tool that should be developed to assist with direct observations can be paper-and-pencil-based or adapted for use on a tablet.

Step 2: Define formative research objectives, methods, and tools. Start with developing clear research objectives to focus the study on the most critical information needed to inform decisions and program design. Good research objectives include a general objective and specific objectives; use action verbs such as “to determine,” “to compare,” “to verify,” “to describe,” and “to assess.” Avoiding vague terms such as “to study” will help your objectives be more precise. Next, formulate research questions using the information gathered in Step 1. These questions should be designed to facilitate identification of knowledge gaps and match the research objectives. Narrow the list of questions to the ones that are most relevant and important for the research. Finally, identify the appropriate combination of data collection methods that will most effectively generate data to answer the established research questions. **Table 1** provides an overview of common formative research methods.

Step 3: Planning logistics of formative research. This step includes developing work plans, budgets, personnel, and sample size, to name a few factors, along with planning for and obtaining ethical approvals.

Step 4: Data collection and analysis. Once the data collection methods and tools have been identified, the process of collection can begin. Formative research is an iterative process, such that the data collection and analysis guide the program development rather than answering specific research questions. Data analysis is important for answering the guiding research questions and informing MMS programming. As with the literature review phase, it is useful to summarize the information collected in a document by theme, as well as to compare it to the literature review.

Step 5: Using formative research to inform the design of an MMS program/intervention and revise based on pilot testing. This step is focused on testing intervention strategies developed using findings from Steps 1 and 2 in an iterative design. Ethnographic findings from Step 1 may be used to generate local terms and phrases for tailored messaging promoting MMS, while participatory findings from Step 2 may be used to inform choice of intervention strategies that may assist pregnant women in overcoming key barriers to antenatal care and MMS usage.

“Formative research may help to improve the likelihood that MMS will be accepted and utilized”

Conclusion

Given the potential of MMS for improving pregnancy-related health and birth outcomes, investing time and resources in well-designed, systematic formative research may help to improve the likelihood that MMS will be accepted and utilized by pregnant women across cultural contexts. What is provided in the foregoing is only a snapshot of the full Formative Research Guidance for MMS developed by UNICEF, *Sight and Life* Foundation, and Pennsylvania State University, available here: <https://sightandlife.org/get-involved/news-announcements/new-formative-research-guide-multiple-micronutrient-supplements-mms>

Correspondence: Stephen R Kodish, Assistant Professor of Nutritional Sciences and Biobehavioral Health, Pennsylvania State University, Nutritional Sciences, 110 Chandlee Lab, Room 104, University Park, PA 16802, USA
Email: stephen.kodish@psu.edu

References

- 1 Evans R, Scourfield J and Murphy S. Pragmatic, formative process evaluations of complex interventions and why we need more of them. *J Epidemiol Community Health* 2015; 69(10): 925-926.
- 2 Kodish SR, Aburto N, Hambayi MN, Kennedy C and Gittelsohn J. Identifying the sociocultural barriers and facilitating factors to nutrition-related behavior change: formative research for a stunting prevention program in Ntchisi, Malawi. *Food Nutr Bull.* 2015; 36(2): 138-153.
- 3 Bentley ME, Johnson SL, Wasser H, Creed-Kanashiro H, Shroff M, Fernandez Rao S and Cunningham M. Formative research methods for designing culturally appropriate, integrated child nutrition and development interventions: an overview. *Annals of the New York Academy of Sciences*, 2014; 1308(1): 54-67.
- 4 Bert C, Gaffey MF, Bhutta ZA and Cetin I. Multiple-micronutrient supplementation: Evidence from large-scale prenatal programmes on coverage, compliance, and impact. *Mat Child Nutr* 2018; 14: e12531.

Using Participatory Formative Research to Inform Pregnant Women's Preferences on Multiple Micronutrient Supplements (MMS)

Stephen R Kodish, Raphia Ngoutane

Pennsylvania State University, PA, USA

Rebecca Olson, Klaus Kraemer

Sight and Life Foundation, Basel, Switzerland

Key messages:

- As more countries consider implementing multiple micronutrient supplements (MMS) policies and programs within country-level health systems, barriers to acceptability and uptake need to be systematically identified and addressed in order to enhance service delivery.
- UNICEF, in partnership with *Sight and Life* Foundation and Pennsylvania State University, used a mixed-method approach to conduct formative research whose results informed the context-specific design and implementation of MMS in four countries (Bangladesh, Burkina Faso, Madagascar, and Tanzania).
- The formative research study was designed using a social marketing framework and employed Rapid Assessment Procedures (RAP) conducted over two iterative phases.
- The formative research identified multi-level barriers and facilitators that may be considered when designing, implementing, and evaluating health services delivery where MMS is being offered within antenatal care (ANC).
- The work of implementation research conducted across the four countries will help to build the evidence base for further in-country scaling and policy adoption of MMS, as well as contributing to global evidence.
- Study findings and lessons learned from the formative methodology across the four contexts will be synthesized to develop a formative research guidance that may support programs to appropriately introduce MMS in other settings globally.
- Well-designed formative research may yield socio-cultural and context-specific findings as a first stage of program planning to improve understanding of social, behavioral, and systems-level elements important for the acceptance and utilization of MMS.

Background

Improving Maternal and Pregnancy Outcomes through Vital Nutrition and Growth (IMPROVING) is a multi-country project funded by the Bill & Melinda Gates Foundation. Using existing government delivery systems, it aims to implement demonstration projects and to advocate for, and scale up, the provision of MMS for use among pregnant women in four priority countries with high burdens of maternal and child undernutrition in sub-Saharan Africa and Asia (Bangladesh, Burkina Faso, Madagascar, and Tanzania). In addition, the project aims to strengthen global support systems on MMS supply chains and programmatic delivery approaches, which will support the availability of MMS supplies. In these countries, MMS is being delivered as part of antenatal care (ANC) with nutrition counselling and weight gain monitoring, which provides an opportunity to improve the quality of pregnancy care for all women.

Despite its potential for optimizing health and nutrition, MMS is a novel nutrition product in these countries and thus careful introduction is needed for improving the likelihood of acceptability and compliance during the pregnancy life-stage. Between October 2020 and May 2021, UNICEF, in partnership with *Sight and Life* Foundation and Pennsylvania State University, conducted a multi-phased, formative research study in four countries (Bangladesh, Burkina Faso, Madagascar and Tanzania) to inform the context-specific design and implementation of nutrition programs introducing MMS. These research efforts were carried out in support of national and subnational governments and in the context of strengthening their ANC services.

“IMPROVING aims to implement demonstration projects and to advocate for, and scale up, the provision of MMS”

Formative research design and purpose

The formative research used a mixed-method, participatory approach that was designed using an iterative research framework with the following overarching aims:

1. To understand the ethnomedical perspectives regarding maternal health and nutrition.
2. To generate demand for MMS through tailored social marketing approaches.
3. To determine important barriers and facilitators to appropriate MMS utilization using a Trial of Improved Practices (TIPS) approach.

Figure 1 provides a study design overview, whereby a combination of qualitative, participatory, and ethnographic methods were conducted across three iterative phases.

Design

The methodological approach drew from Rapid Assessment Procedure (RAP) for ensuring rigorous and systematic data collection in a programmatic context⁴. Phase 1 included free lists, pile sorts, and semi-structured interviews among pregnant women and health workers for an ethnographic understanding of pregnan-

cy-related practices in this setting. Phase 2 utilized community workshops, focus groups, and market observations to generate community inputs on product- and placement-related factors (e.g., packaging, logo, language) important for ensuring adequate consumer demand and to develop culturally appropriate and tailored MMS programming.

Phase 3 was designed as a TIPS to be conducted during the early phases of implementation to assess the behavioral factors of acceptability and compliance of MMS among pregnant women, allowing for feedback loops and course corrections as needed.

“The dataset yielded broad, cross-sector findings related to the experiences of women during pregnancy”

FIGURE 1: Examples of methods for conducting formative research



Analysis

This formative research approach utilized different analytic procedures per type of data generated. Textual data from focus groups and semi-structured interviews were thematically analyzed using Dedoose software, a mixed-methods research software program, to manage transcripts, code text, and retrieve text segments for interpretation. Numerical data from market observations and community workshops were summarized using simple descriptive statistics. Free list and pile data were statistically analyzed using cultural domain analysis procedures. Findings were grounded in a social marketing framework and triangulated across methods and participant types to enhance data credibility.²

Sample findings

The formative research provided information on three strategic areas of the demonstration project: (i) Strengthening of the demand creation for antenatal care and MMS through communication on social and behavioral change; (ii) Improving the consumer-facing packaging and labeling; and (iii) Capacity-building of Health Workers and Community Health Workers.

The resulting quantitative and qualitative dataset yielded broad, cross-sector findings related to the experiences of women during pregnancy, as well as those specific to micronutrient supplementation and antenatal care services. A few **sample findings** across the four countries are as follows (all of the findings can be found in the four country reports listed at the end of this paper):

Aim 1: To understand the ethnomedical perspectives regarding maternal health and nutrition

Understanding how local communities conceptualize health, illness, and diets is important in determining how they will receive and use a nutritional supplement. In Tanzania, researchers found differential levels of knowledge and perceptions regarding disease causation during pregnancy, optimal diets across trimesters, and long-standing social norms that influence dietary choices. While most pregnant women knew that prenatal supplements were crucial 'to increase blood' during pregnancy, few knew about their potential for preventing birth defects, for instance. Practical concerns also emerged during interviews: many participants cited challenges and complaints associated with the use of the available IFA (vomiting, nausea, dizziness, sweating, unappealing odor, and flavor and taste).

Cultural data reflecting food prescriptions (remedies – foods that should be eaten during pregnancy) and proscriptions (taboos – foods that should be avoided during pregnancy) were also identified during this formative work. **Table 1** summarizes examples of culturally prescribed foods from the Burkina Faso study site.

Aim 2: To generate demand for MMS through tailored social marketing approaches

Findings from the formative research also highlighted important insights obtained on the '4 Ps' – product, price, placement, and promotion – of MMS. They also offered an opportunity to introduce innovations. Regarding product design, pregnant and lactating women were purposely sampled in the four countries using community workshops, focus group discussions, and a survey (Burkina Faso only) to gain inputs regarding preferred MMS packaging characteristics (color, logo, slogan). Mock MMS box designs, with design options based on local contexts, were used to prompt discussion, and voting on preferred MMS design elements was conducted. Based on the participatory data collected on MMS packaging, UNICEF used the women's feedback and worked with suppliers to tailor the packaging with the goal of enhancing acceptability and uptake. The packaging is available in four languages (English, French, Arabic, and Spanish) as a standard product (**Figure 2**).

Aim 3: To determine important barriers to, and facilitators of, appropriate MMS utilization

Understanding possible barriers to MMS consumption is important for improving acceptability and adherence. Data from community workshops, focus group discussions, interviews, and market observations were synthesized to understand the range of factors influencing maternal health and nutrition during pregnancy. Results from the four countries revealed weak service delivery platforms. This is reflected in the way that ANC services are organized, as well as distance and financial barriers – such as transportation and cost of supplements – all of which prevent women from accessing routine ANC services and prenatal supplements. In addition, health workers are not adequately trained to counsel women on nutritious diets and supplements. Further, women face a range of cultural norms around food and misconceptions around iron supplements. Their capacity to access nutritious diets and antenatal care is greatly influenced by close family members and gendered norms. **Table 2** presents reported barriers from Bangladesh.

TABLE 1: Burkina Faso food prescriptions and proscriptions

Name and description of food	Cultural explanation for why it should be consumed during pregnancy
Nagouri (peanut)	It is a substitute for meat or fat.
Tando (clay)	Consumed to avoid nausea.
Babenda (mixed-leaf sauce with sour taste, available the year round)	Digestible, helps combat constipation and also contains a lot of vitamins because made of several leaves.

FIGURE 2: Customized MMS box design based on women's preferences in four countries o

“Findings are being utilized to develop tailored social marketing strategies for introducing MMS and increasing the coverage of ANC services”

Conclusions and next steps

Formative research in the four countries led to a better understanding of the multi-level barriers and facilitators to ANC use and MMS acceptability and compliance prior to design and implementation. Together, findings from Phases 1 and 2 are being utilized to develop tailored social marketing strategies for introducing MMS and increasing the coverage of ANC services. Several strategies have already been identified to support the introduction of MMS. By way of illustration, one of the strategies identified in Burkina Faso is to expand the number of days when ANC is offered to women – from 1 to 3 days per week. In Bangladesh, UNICEF is exploring a strategy to bring ANC services closer to where women are working in garment factories. Another tailored strategy is to strengthen the links between facilities and communities, as all four countries are planning to transfer responsibilities to community health workers to promote early ANC attendance and MMS adherence rather than relying on facility-based approaches only. Madagascar is also exploring whether community health workers can be effective in distributing MMS, and Tanzania is looking into whether switching to free MMS distribution might remove financial barriers to uptake.

Formative research reports

All four formative research reports can be found at the following links:

Bangladesh

https://hmhbconsortium.org/content/user_files/2021/12/Bangladesh_FormativeReport_MMS_09.13.2021-fieldwork-cover.pdf

TABLE 2: Reported barriers to prenatal supplementation in Bangladesh

Reported barriers to supplementation during pregnancy	Supporting quotations
High cost of supplements	“Of course, vitamins are required but we can't afford the vitamins.” <i>Bhola, interview, pregnant woman</i>
Supplement odor/smell	“Many people do not like the vitamins that are available in the clinic; the medicine has a mild odor, which is why many people do not want to eat [them].” <i>Bhola, interview, pregnant woman</i> “Yes, it's smelly [iron]. Iron and calcium cannot be taken due to their smell.” <i>Bhola, focus group with pregnant and lactating women</i>
Physiological side-effects of supplements	“Many [women] say that they cannot take iron because it causes constipation. Though their body needs vitamins, they [pregnant women] cannot take such vitamins due to these problems.” <i>Bhola, interview, health worker</i>
Perception that supplements can cause delivery complications	“Vitamin supplements make the baby large, for which babies cannot be delivered normally and require a C-section.” <i>Bhola, focus group with pregnant and lactating women</i>
Limited access to supplements due to poor road conditions and stock-outs	“The road to the clinic is not good and gets flooded during high tide.” <i>Bhola, focus group with pregnant and lactating women</i> “Medicines are not available in the clinics most of the time.” <i>Kurigram, focus group with pregnant and lactating women</i>

Burkina Faso

https://hmhbconsortium.org/content/user_files/2021/12/MMS_FormativeReport_BurkinaFaso_06.30.2021-English.pdf

Madagascar

https://hmhbconsortium.org/content/user_files/2021/12/Madagascar_FormativeReport_MMS_06.30.2021-Final.pdf

Tanzania

https://hmhbconsortium.org/content/user_files/2021/12/Tanzania_FormativeReport_MMS_06.29.2021_Final.pdf

References

- 1 Scrimshaw, SC. Adaptation of anthropological methodologies to rapid assessment of nutrition and primary health care. Rapid assessment procedures: Qualitative methodologies for planning and evaluation of health-related programmes, 1992: 25-38.
- 2 Bentley ME, Johnson SL, Wasser H, Creed-Kanashiro H, Shroff M, Fernandez Rao S et al. Formative research methods for designing culturally appropriate, integrated child nutrition and development interventions: an overview. Annals of the New York Academy of Sciences; 2014: 1308(1): pp.54-67.

Correspondence: **Stephen R Kodish**, Assistant Professor of Nutritional Sciences and Biobehavioral Health, Pennsylvania State University, Nutritional Sciences, 110 Chandlee Lab, Room 104, University Park, PA 16802, USA
Email: stephen.kodish@psu.edu

Accelerating Advocacy Actions and Building Policy-enabling Environments for Multiple Micronutrient Supplementation

Martin N Mwangi, Tanuja Rastogi, Marti van Liere
Micronutrient Forum, Washington, DC, USA

Introduction

Multiple micronutrient supplementation (MMS) is one of the most cost-effective, impactful investments available to improve maternal nutrition and birth outcomes. It is recommended by the World Health Organization (WHO) in the context of rigorous research.¹

Despite the breadth of evidence spanning over 20 years² on the impact of MMS on maternal nutrition and the WHO's inclusion of MMS onto its Essential Medicines List (EML) in 2021,³ many countries have not prioritized MMS or introduced it into their national health programs and platforms. Many countries grapple with difficult decisions, including whether to transition from iron and folic acid (IFA), the standard protocol for decades, to MMS. For policymakers to recommend the switch from IFA to MMS, systematic and targeted advocacy for MMS and a strong enabling environment are necessary.

The Healthy Mothers Healthy Babies (HMHB) Consortium's advocacy agenda

Advocacy can have far-reaching positive impacts on public health by providing policymakers with the information they need to make decisions and influence legislation. Effective public health advocacy encompasses various activities and requires research, public education, organizing, mobilizing, and lobbying.

The HMHB Consortium, hosted by the Micronutrient Forum, has over 100 organizational and individual members and is driving the advocacy agenda for MMS worldwide. HMHB aims to increase maternal nutrition and MMS awareness within the larger context of women's health and equity and to promote MMS implementation, adoption, and adherence. HMHB's advocacy efforts are directed towards increasing investments and triggering policy change to adopt and scale up MMS by providing critical evidence-based resources and amplifying women's voices.

Barriers to the introduction of MMS in policy and programming

Numerous barriers, some exclusive to MMS and some related to

“For policymakers to recommend the switch from IFA to MMS, systematic and targeted advocacy for MMS and a strong enabling environment are necessary”

general healthcare practices, are encountered by maternal nutrition actors in most countries. **Table 1** below lists a few of these barriers, but to overcome them national health and nutrition policies, strategies, and EMLs must include MMS.

Positive progress

Countries need comprehensive national maternal health and nutrition policies that are equitable, efficient, and effective in delivering service and which recognize MMS as an essential intervention for mothers. Advocacy efforts for MMS and technical consultations involving key normative agencies such as the WHO and UNICEF gained momentum in 2015–2018. The publication of the revised WHO Antenatal Care Guidelines on MMS in 2020 accelerated these efforts.¹ In 2021, following a joint evidence-based submission by the Micronutrient Forum and the New York Academy of Sciences, WHO updated its Model EML (22nd list) and included MMS,³ and the HMHB consortium was launched to spearhead MMS advocacy efforts globally. Momentum has also been built over the past years and can be leveraged in 2023 to accelerate the introduction and scale-up of MMS in other countries.

Advocacy for MMS: HMHB's approach

HMHB's strategic advocacy objective is to initiate, accelerate and amplify efforts that raise awareness about the scope and consequences of maternal malnutrition and the evidence base in support of high-impact maternal nutrition interventions, such as MMS, as well as build consensus for the introduction of MMS and advocate for maternal nutrition policy and program adoption within the larger context of women's nutrition and equity.

TABLE 1: Key barriers to progress on implementing MMS in LMICs**Individual and community levels**

- *Safety and effectiveness concerns:* Safety, e.g., of co-interventions in the same individual or population; dosage (30 mg versus 60 mg) of iron in MMS; poor adherence to supplementation regimens among target populations; women's empowerment – lack of female financial and health decision-making; cultural and religious beliefs.

Country level

- *Unclear guidance and regulatory environment:* Country governments hesitate to adopt MMS due to context-specific WHO recommendations; MMS is not yet included in the national essential medicines lists of many LMICs; misinformation or difficulty in interpreting MMS-related data leading to hesitation by national governments.
- *Funding:* Inadequate funding from government budgets, international donors, and private-sector partners; limited political commitment to invest in nutrition interventions, particularly in countries with competing health and development priorities; insufficient advocacy efforts to raise awareness of the benefits of MMS among policymakers and donors.

Institutional level

- *Effectiveness:* Insufficient monitoring and evaluation systems to track the impact of supplementation programs on nutritional status to inform program and policy review.
- *Cost and supply issues:* Unclear cost implications of switching from IFA to MMS; high cost of procuring and distributing MMS, particularly in low-income countries with weak health systems; lack of clear MMS product specifications or guidance for manufacturers and suppliers leading to few manufacturers investing in MMS production; limited availability of quality-assured supplements from reliable manufacturers; challenges in ensuring a steady supply of supplements, particularly during times of crisis or emergency.
- *Lack of prioritization in maternal health policies and by maternal health experts:* In many LMICs, MMS is not yet a mainstream priority in maternal health policies and nutrition policies; insufficient advocacy for high-impact maternal nutrition interventions during policy and guidelines review processes; competing health priorities, e.g., HIV, malaria, COVID-19.

“Knowledge without action is insufficient: policy-relevant evidence and expertise are critical to driving evidence-based policies and impactful activities”

Expected outcomes

1. **Global and regional advocacy** for maternal nutrition and MMS will result in aligning key stakeholders and normative agencies and adopting a comprehensive approach to maternal nutrition programming. Women's nutrition, health and wellbeing will be recognized as central to maternal nutrition, leading to increased investments by donors and governments.
2. **Policy** changes at regional and national levels, especially in low- and middle-income countries (LMICs), will create an enabling environment for maternal nutrition programming. These changes will include the inclusion of MMS into the national EMLs and the integration of MMS and other evidence-based interventions into national maternal nutrition and health policies and strategies. Additionally, advocacy for MMS policies and frameworks in regional level normative bodies such as the African Union Commission will pave

the way for improved maternal nutrition and health outcomes in LMIC.

3. **Supply improvements** that align product specifications and investments to increase manufacturing capacity and product supply to reach an additional 23.0 million pregnancies by 2024.⁴
4. **Implementation science** related to MMS scale-up will be better understood and coordinated by implementing agencies. Finally, national decision-makers, implementers, maternal health experts, and maternal nutrition stakeholders will be informed of, and will have, a common understanding of the scientific evidence regarding the impact, safety, and cost-effectiveness of essential maternal nutrition interventions.

The HMHB MMS Advocacy Toolkits

Regarding MMS, knowledge without action is insufficient: policy-relevant evidence and expertise are critical to driving evidence-based policies and impactful activities. HMHB has developed an Advocacy Resources Center to equip national actors with the necessary tools to scale up MMS in their countries and facilitate in-country dialogues that will support policy alignment and consensus.

To be an effective advocate, one needs the opportunity to tell one's story. The key advocacy resources in **Table 2** have been translated into four languages (English, French, Spanish and Ar-

TABLE 2: HMHB MMS advocacy tools and resources

Advocacy tool and link	Description
<u>MMS Advocacy Slide Deck</u>	These adaptable PowerPoint slides are divided into five core modules:
	<u>Module A</u> Pregnancy and Nutrition
	<u>Module B</u> Global Scope of Maternal Malnutrition
	<u>Module C</u> Evidence on MMS
	<u>Module D</u> National Impact and Investment Case
	<u>Module E</u> Introducing and Scaling MMS and Case Study on Indonesia.
<u>The MMS advocacy brief</u>	Meant to equip champions and decision-makers to advocate for safe, affordable and cost-effective MMS to improve maternal health.
<u>The FAQ brief on MMS</u>	Addresses questions on MMS such as the need, benefits, composition, and guidance on MMS; provides updated, evidence-based answers to questions from stakeholders.
<u>The Advocacy Brief and FAQ on Inclusion of MMS in WHO's EML</u>	Answers questions related to the inclusion of MMS in WHO's Essential Medicines List.
<u>The HMHB's world map of MMS activities</u>	Documents all MMS-related activities worldwide.
<u>The women's voices short films</u>	The 'women's voices' short films spotlight women in various global contexts and highlight the challenges and opportunities to improve micronutrient intake and the nutritional wellbeing of mothers.
<u>Blogs, expert/coffee and chai chats, knowledge bytes, newsletters</u>	Published on various technical topics, including periodic newsletters showcasing current news and events.
<u>HMHB Knowledge Hub including the Advocacy toolkit</u>	More advocacy resources and further evidence on the benefits of MMS, recent data, guidance and relevant tools.
<u>The HMHB Consortium website</u>	HMHB's main communication portal.

abic) for public health professionals, national health officials and partners in NGOs, research, academia, program implementors, and local MMS providers and distributors.

Organizations and individuals active in maternal health and nutrition are invited to join the HMHB Consortium as a member and subscribe to the HMHB newsletter. To learn more: HMHB@micronutrientforum.org. Follow us on Twitter, LinkedIn, Facebook, and Instagram.

Correspondence: **Martin N Mwangi PhD**, Micronutrient Forum, 10th Floor, 1201 Eye St, NW Washington, DC 20005-3915, USA

Email: martin.mwangi@micronutrientforum.org

References

- 1 World Health Organization. WHO antenatal care recommendations for a positive pregnancy experience. Nutritional interventions update: Multiple micronutrient supplements during pregnancy. Geneva: WHO, 2020.
- 2 Healthy Mothers Healthy Babies (HMHB). The HMHB knowledge hub Washington DC2022 [cited 2023 16-01-2023]. Available from: <https://hmhbconsortium.org/knowledge-hub/>. Accessed 16 January 2023.
- 3 World Health Organization. World Health Organization Model List of Essential Medicines – 22nd List, 2021 (WHO/MHP/HPS/EML/2021.02). Geneva: WHO, 2021.
- 4 Clayton A. Ajello (DRPH/MPH), Auliya Suwantika (PHD), Otte Santika, et al. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. Washington DC: KIRK Humanitarian, 2022.

MMS Supply Context Assessment (SCA) Tool for National Governments

Shannon E King, Clayton A Ajello, Quinn Harvey, Jarno de Lange
 Vitamin Angel Alliance, USA

Key messages:

- The Supply Context Assessment (SCA) guides a consolidation of information to be used to inform stakeholders and decision-makers about long-term United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplements (MMS) supply options and facilitates consensus-building of selected option(s) for further exploration.
- The SCA utilizes a comprehensive desk review and in-depth interviews to answer questions around four key modules: (1) Government Policy and Regulatory Framework, (2) Manufacturing (Product Availability and Accessibility), (3) Government Procurement Systems, and (4) Current Marketplace Characteristics for MMS Products.
- Researchers implementing the SCA should have a baseline understanding of procurement and associated regulations pertaining to medicines and nutritional supplements that needs to be synthesized from the information gathered and clearly present them as findings.

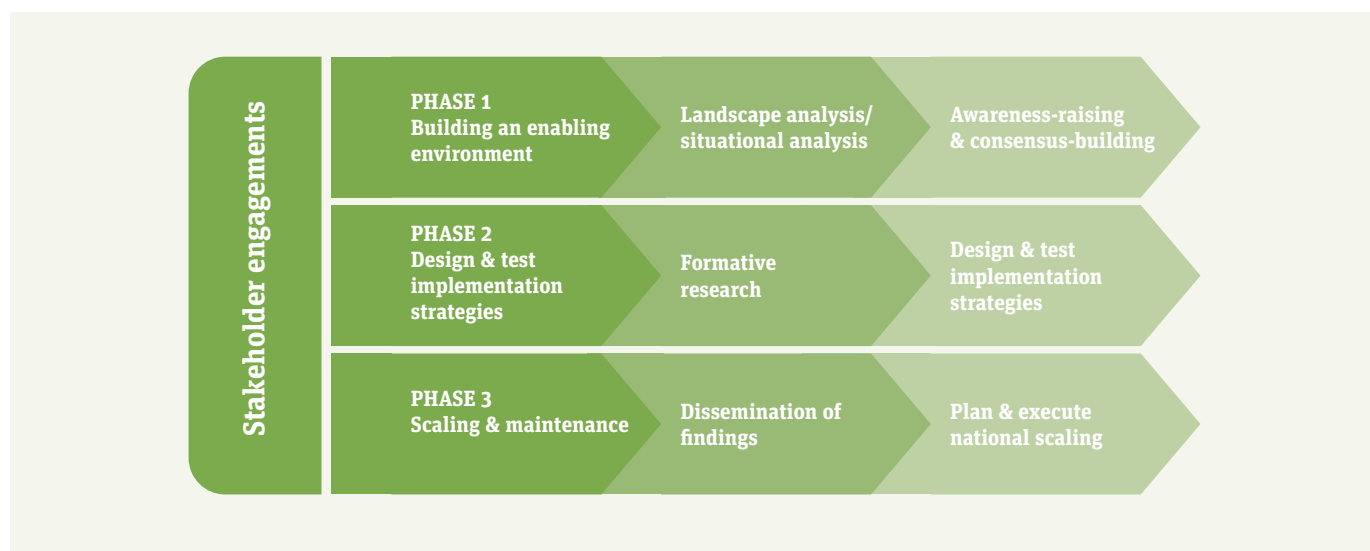
- The SCA findings are used to support evidence-based awareness-raising and consensus-generating activities to understand MMS supply options, build consensus on what the findings mean, identify any remaining questions, and gain consensus on the strategy or strategies national decision-makers should test to secure long-term access to MMS product supplies.

Introduction

Establishing and securing sustainable availability of, and access to, supplies of the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) Multiple Micronutrient Supplement (MMS) is a key requirement for national health services seeking to integrate MMS into national health systems. Most countries introducing MMS are keen to learn how they can access MMS supplies – whether through local manufacturing or importation.¹ Implementation science (IS) is being used by national health services to design and test effective strategies for securing access to MMS supplies.²

The generic IS model is shown below in **Figure 1**. A full description of its application to secure an available and accessible supply of MMS is presented elsewhere in this MMS Special Report in the paper entitled: *Synchronizing Access to UNIMMAP MMS Product Supplies with Program Implementation* (p. 132).

FIGURE 1: A generic implementation science (IS) approach



The initial step in the IS approach to MMS supply issues is to create an enabling environment for exploring and testing feasible options for securing MMS supplies. This paper presents a tool to facilitate a landscape or situational analysis of the supply environment: the Supply Context Assessment (SCA). The SCA helps national decision-makers to make an initial, evidence-based determination about the feasibility of potential options for securing MMS supplies: local manufacturing, importation, or some combination of the two.

“It is counterproductive for a nation to decide to manufacture locally or to import product before there is some evidence of the feasibility of either option”

FIGURE 2: Key areas for assessment and analysis

Government policy & regulatory framework	Manufacturing (product availability & accessibility)	Government procurement systems	Current marketplace characteristics for MMS products
<ul style="list-style-type: none"> • Current awareness about UNIMMAP MMS • How nutritional supplements for pregnant women are classified • Applicable regulatory requirements for medicines that are nutritional supplements • Good manufacturing practices (GMP and pharmacopeial) standards that are applicable to the production and distribution of medicines that are considered nutritional supplements • Regulatory audits (factory audit, required certifications, independent verification programs, etc.) • Product registration requirements • Existing provisions for taxation and regulatory enforcement of domestic/imported products • Halal certification requirements • Labeling requirements • The role of the national essential medicines list (NEML) vis-à-vis whether or not a national health system can incorporate/use a new medicine that is a nutritional supplement • Whether and how imported, donated medicines must meet local regulatory requirements • Sequence of actions required to establish an MMS policy and achieve regulatory approval for an MMS product 	<ul style="list-style-type: none"> • Availability and modes of accessing imported medicine products that are nutritional supplements • Information about the feasibility of creating a domestically manufactured medicine product consisting of nutritional ingredients • Whether there is a manufacturers' association; or whether the regulatory authorities maintain a list of all manufacturers who might be capable of producing MMS 	<ul style="list-style-type: none"> • Overall procurement operations – how the national government procures medicines, including how new medicines and nutritional supplements are added and integrated into the procurement system – with a focus on medicines that are new and not available off the shelf in the country • Decision-making about affordability • Procurement practices and the steps of procuring a medicine or nutrition supplement product for the first time, including any existing practices on procurement of medicines from international suppliers • Distribution, warehousing and other supply chain related practices at all levels of the health care system 	<ul style="list-style-type: none"> • Current MMS products available in the national marketplace (i.e., any product in the national marketplace intended for pregnant women) • Comparison of product formulations in the marketplace with UNIMMAP MMS • Comparison of price, promotion, sale/use of nutritional products nationally available • Whether available nutritional supplement products conform to label claims upon independent verification (assessed through independent product testing in an approved lab)

Why use this toolkit

The SCA generates and organizes information that can be used to raise the awareness of stakeholders and decision-makers regarding possible long-term supply options for accessing MMS, and to facilitate consensus-building around the selected option(s) for further exploration (i.e., in phase 2 of the IS approach). A full SCA toolkit is available from the Vitamin Angel Alliance upon request.

The SCA builds on *Sight and Life* Foundation's Supply Readiness Assessment (SRA) (Box 1) and aims to deliver a comprehensive assessment of the supply landscape in four areas – each of which is examined using a separate assessment 'module' (Figure 2). Conducting the SCA, raising evidence-based awareness about feasible supply options, and building consensus to focus national efforts on an identified strategy to test for securing access to MMS are critical steps for decision-makers. Without these efforts, national decision-makers may opt to undertake local MMS manufacturing without really knowing whether existing national technical capacity matches capacity required; alternatively, challenges of importing MMS may be underestimated. It is counterproductive for a nation to decide to manufacture locally or to import product before there is some evidence of the feasibility of either option.

BOX 1: Building on *Sight and Life* Foundation's Supply Readiness Assessment (SRA)

The SCA is modeled after the Supply Readiness Assessment (SRA) toolkit published by *Sight and Life* Foundation.³ The SRA has been modified here to focus only on the needs of national health systems, rather than a general market assessment. Specifically, the SCA includes a new module on government procurement and expands upon data collected in other modules in the SRA. While the SRA was originally designed to be implemented remotely and derive information through key-informant interviews, the SCA is achieved primarily through significant in-person interviewing by national experts and requires several weeks of in-country activities to complete.

Skills needed to conduct the SCA

Conducting the SCA requires a broad understanding of the in-country processes for obtaining and using medicines (including nutritional supplements) in national health systems. A baseline understanding of procurement and associated regulations pertaining to medicines is needed, and the ability to synthesize that information and present it clearly. Expertise in cost-benefit analysis, business case development, and budget impact analysis will be needed when these analyses are conducted.

Methods

Data collection includes a comprehensive desk review and in-depth interviews. Implementing the SCA requires an iterative and cyclical approach, shifting between reviewing existing materials and conducting interviews. Answers to questions will frequently

reveal subsequent questions that require more information. Depending upon the context, it may be appropriate to begin with a desk review of available information or it may be necessary to conduct initial interviews to better understand the supply context and know where to identify relevant materials for review.

1. Comprehensive desk review

An initial review of literature and policies will begin to help answer questions about the supply landscape.

To do:

- Conduct review of peer-reviewed literature, grey literature, and government policies and documents relevant to understand the maternal nutrition and supplement situation.
- Conduct an MMS cost-benefit analysis. We suggest using the existing Nutrition International cost-benefit calculator to facilitate this analysis available at: <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>.⁴
- Conduct a market assessment. Details on how to conduct the market assessment can be found in the *Sight and Life* Foundation SRA.³ In addition, samples of products should be purchased in sufficient quantities to allow for independent laboratory testing to assess how well a product's contents conform to product label claims on ingredients.

Outcome: A report that i) describes existing government policies and the regulatory framework applicable to MMS, MMS manufacturing landscape and factors that affect importation or local manufacturing of MMS, government procurement systems for new products, and the current availability of similar products in the marketplace); and ii) describes what critical information is not available from a desk review that requires further data gathering via interviews with local experts.

2. In-depth interviews (IDIs) with key stakeholders organized by each specialized module

Using the desk review findings, key informants will need to be identified who can provide more information that supports practical understanding of information generated during the desk review. The number and type of key-informant interviews will depend upon the findings of the desk review, the scope of expertise needed to clarify information generated, and the nature of additional questions raised while conducting the desk review. Tips for conducting in-depth interviews are included in Box 2.

To do:

- Identify areas within the review that require further inquiry.
- Identify key informants within the national context (including government officials or other informed national stakeholders inside or outside the government) who can

speak authoritatively about the process by which the government procures and distributes medicines and nutritional supplements.

- Conduct the key-informant interviews.
- Integrate findings into the comprehensive desk review report and continue conducting interviews as needed until identified questions are answered.

Outcomes: Information from IDIs should be integrated into the draft SCA report to identify new data, alignment, or discrepancies in the findings, and further areas of inquiry needed.

BOX 2: Tips for implementing in-depth interviews

- It is important to gather information that informs an understanding of how policy change is achieved; what are the steps for changing policy; and what are the specific steps, if applicable, for changing policy to include MMS use in the national health services; and how policy (and the timing of its formation) intersect with actions needed to incorporate MMS into the procurement system, including any requirements that need to be fulfilled.
- An important aspect of the SCA is gaining an understanding of how the totality of the government (i.e., not just the ministry of health, but also other relevant ministries such as the ministry of finance/planning) assesses the value of new interventions being considered for adoption. This may require further budget impact analysis if requested by government officials.
- Interviewers are encouraged to exert a healthy skepticism regarding key informants from the manufacturing sector about their stated capabilities, as these have a vested interest in the outcome of a discussion regarding whether a government should explore local manufacturing of MMS. Further verification of manufacturer abilities is essential.
- Prior to beginning the SCA, especially where a university is assisting with implementing the SCA, the need for *ethical review* should be discussed and confirmed with the research team. This work is generally considered ‘non-human subjects research’, since primary data collection is from key informants providing objective information about their work, and not about their own personal or subjective knowledge, opinions, attitudes and practices. However, each ethical review board has their own processes for making this determination that need to be followed to ensure the appropriate protection of study informants.

How to use SCA findings to give momentum to IS Phase 2 activities

The findings of the SCA, if robust, should support awareness-raising activities to the most probable strategies available in a national context for securing MMS access (while identifying any remaining issues, or eliminating certain strategies for securing access to MMS), and should lead to consensus around the strategy or strategies national decision-makers decide to test for gaining access to MMS product over the medium to long term. Actual testing of the strategies selected for securing MMS product is the objective of activities undertaken in phase 2 of the IS approach. Tools to facilitate phase 2 activities are being tested and will soon be made available by the Vitamin Angel Alliance.

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Correspondence: Shannon E King, Implementation Science Manager, Vitamin Angel Alliance, 6500 Hollister Ave Suite 130, Goleta, CA 93117, USA
Email: sking@vitaminangels.org

References

- 1 Ajello CA, Suwantika A, Santika O, King S, and De Lange J. UNIMMAP MMS for National Health Systems: Considerations for Developing a Supply Strategy. Kirk Humanitarian Resource Paper. November 2022. Available for download at: https://kirkhumanitarian.org/wp-content/uploads/2022/11/FINAL-Kirk_UNIMMAP_MMS_SupplyPaper_Digital.pdf
- 2 Tumilowicz A, Ruel MT, Gretel P, Pelletier D, Monterrosa EC, Lapping K, et al. Implementation Science in Nutrition: Concepts and Frameworks for an Emerging Field of Science and Practice. *Current Developments in Nutrition*. March 2019; Volume 3, Issue 3. Available for download at <https://academic.oup.com/cdn/article/3/3/nzy080/5129139>
- 3 Beesabathuni K, van Zutphen KG. Procurement and Production of Multiple Micronutrient Supplements for Pregnant Women. Focusing on *Multiple Micronutrient Supplements in Pregnancy*. 2020. <https://doi.org/10.52439/IZGR8541>
- 4 NI cost-benefit calculator tool can be located at: <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>

Asset Tracker: Identifying MMS progress toward reaching effective coverage

Evaluating barriers and enablers to reach coverage of key maternal and newborn interventions

Kimberly Mansen, Megan Parker, Elan Ebeling, Patricia S Coffey, Katharine D Shelley, Kiersten Israel-Ballard, Zoe Escalona, Sadaf Khan
PATH, Seattle, WA, USA

Key messages:

- Originally launched in 2020, PATH's Asset Tracker database is an open-access, online tool to equip advocates, donors, government decision-makers, and implementers with national coverage data for evidence-based interventions or 'assets' across 81 of the 'Countdown to 2030' countries.¹ In-depth data for MMS is included from six focus countries (Burkina Faso, Ethiopia, India, Kenya, Nigeria and Pakistan), with subnational data from all focus countries, excluding Pakistan.
- The Asset Tracker database tracks 26 milestones for scale-up, from global guidelines and market availability, national policy adoption, and system integration and readiness to implementation and service delivery, availability, and coverage of maternal, newborn, child health and nutrition (MNCHN) assets, including multiple micronutrient supplements (MMS) and iron and folic acid (IFA) during pregnancy.
- Global, national, and subnational stakeholder interviews and literature reviews revealed key barriers and enablers toward reaching effective coverage, key strategies supporting successful implementation, and priority next steps for overcoming barriers to reach successful scale for each asset.
- MMS still requires early milestone adoption in most countries. The **Stages of Achieving Effective Coverage framework** provides a guide to where efforts need focus to achieve effective and equitable coverage.
- Confusion between MMS, IFA, and micronutrient powders at the country and subnational levels must be resolved to help healthcare workers correctly identify the new product and implement associated policies.

Background

Accelerating progress of evidence-based interventions is key to improving maternal, newborn, child health and nutrition (MNCHN). Tracking successful implementation at scale across geographies is challenging, however.² To address this, PATH developed a framework to map the current progress of 14 MNCHN 'assets,' or interventions, and identify key barriers and enablers to reaching effective coverage. This interactive, open-access Tableau data visualization tool is available online for users to explore existing data (compilation of data from document review, surveys and routine sources), including the mapping of data on availability, access, implementation, and coverage of multiple micronutrient supplements (MMS) and iron and folic acid (IFA) 'assets.' By bringing multiple data sources together in one place, the Asset Tracker tool offers a quick and efficient comparison of different indicators or countries to help inform prioritization and decision-making strategies.

Methodology and introduction of the framework, *Stages of Achieving Effective Coverage*, across 'assets'

Building on the existing implementation literature,³ a six-stage framework, **Stages of Achieving Effective Coverage**, was created to assess the components of scale-up toward effective coverage of MNCHN, which included:

1. global guidelines and market availability;
2. national policy adoption;
3. system integration and readiness;
4. implementation and service delivery;
5. availability; and
6. coverage.

These categories represent primary components of successful scale and were further delineated into 26 milestones. For each 'asset,' indicators were assigned to relevant milestones. Key informants were interviewed, and global, national, and local data sources were reviewed to determine if assigned indicators and milestones had been achieved. Global datasets included DHS, SPA, SARA, HMIS, ENAP, and the WHO SRMNAH Policy Survey.

Interviews with global (n=74) and national (n=126) key informants across the six focus countries (Burkina Faso, Ethiopia, Kenya, India, Nigeria, and Pakistan) helped to complete a description of the local context and explore thematic barriers, enablers, and strategies utilized toward scale.

Across all 14 MNCHN assets, we reviewed more than 275 policy documents, budgets, guidelines, and training curriculums and collected subnational data within the five countries (Centre Ouest and Sud Ouest regions, Burkina Faso; Oromia region, Ethiopia; Uttar Pradesh and Bihar states, India; Kakamega and Kisumu counties, Kenya; and Niger and Sokoto states, Nigeria) via inventory spot checks, semi-structured interviews with 275 providers and 94 district health management team (DHMT) members, and focus group discussions with 391 community health workers.

Interactive data dashboards available for further exploration

To aid interpretation and presentation, our findings were synthesized into open-access Asset Tracker Tableau Visualizations for national and subnational findings.⁴⁻⁶ The national dashboards include:

1. scale-up maps indicating the countries where each milestone has been achieved;
2. summaries of national progress on MMS milestones achieved;
3. cascades of direct and indirect indicators involved in reaching effective coverage; and
4. availability data by information source.

In addition, the subnational facility assessments and qualitative findings help pinpoint gaps in programming to support fo-

cused planning for continued introduction and scale efforts. Data in these dashboards were not, in all cases, derived from randomized and/or representational samples and are thus not generalizable across country settings.

The following dashboard examples illustrate the milestones that need to be achieved, which milestones are not currently met, and why.

“The Asset Tracker tool serves as a key conversation-starter toward improved implementation and scale”

National-level Tableau visualizations

Figures 1 and 2 display examples of national-level visualizations, including the Asset scale-up map, which displays asset-specific indicators across countries, and the Countries’ progress on achieving milestones toward coverage, highlighting key milestones met on the Stages of Achieving Effective Coverage framework. Only two focus countries (Burkina Faso and Pakistan) have published national MMS policies; limited direct indicators exist to confirm Burkina Faso’s achievement of further milestones beyond national policy adoption.

Figure 3 displays Asset Cascade examples from Burkina Faso and India. This country comparison helps visualize the barriers and enablers to scale-up and offers critical insights to influence policy and implementation decisions at the global and country levels.

FIGURE 1: Asset scale-up maps – National policy on MMS

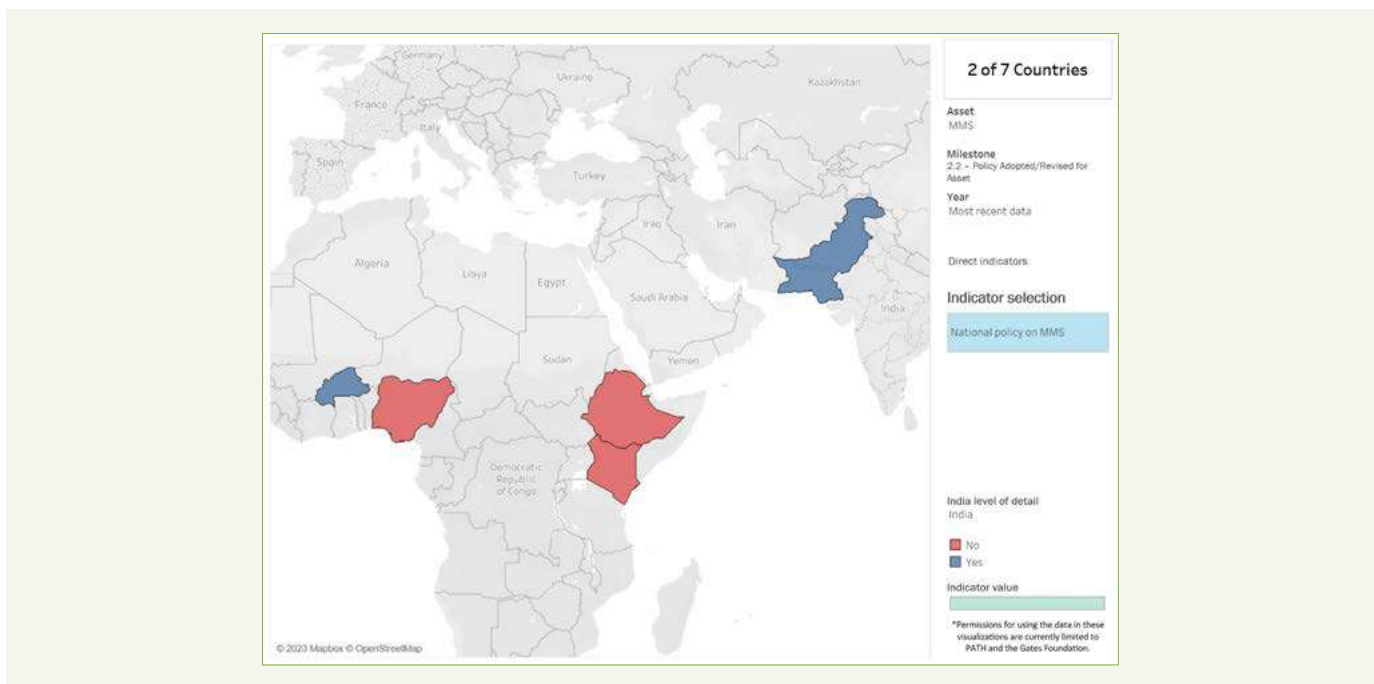


FIGURE 2: Countries' progress on achieving milestones toward coverage

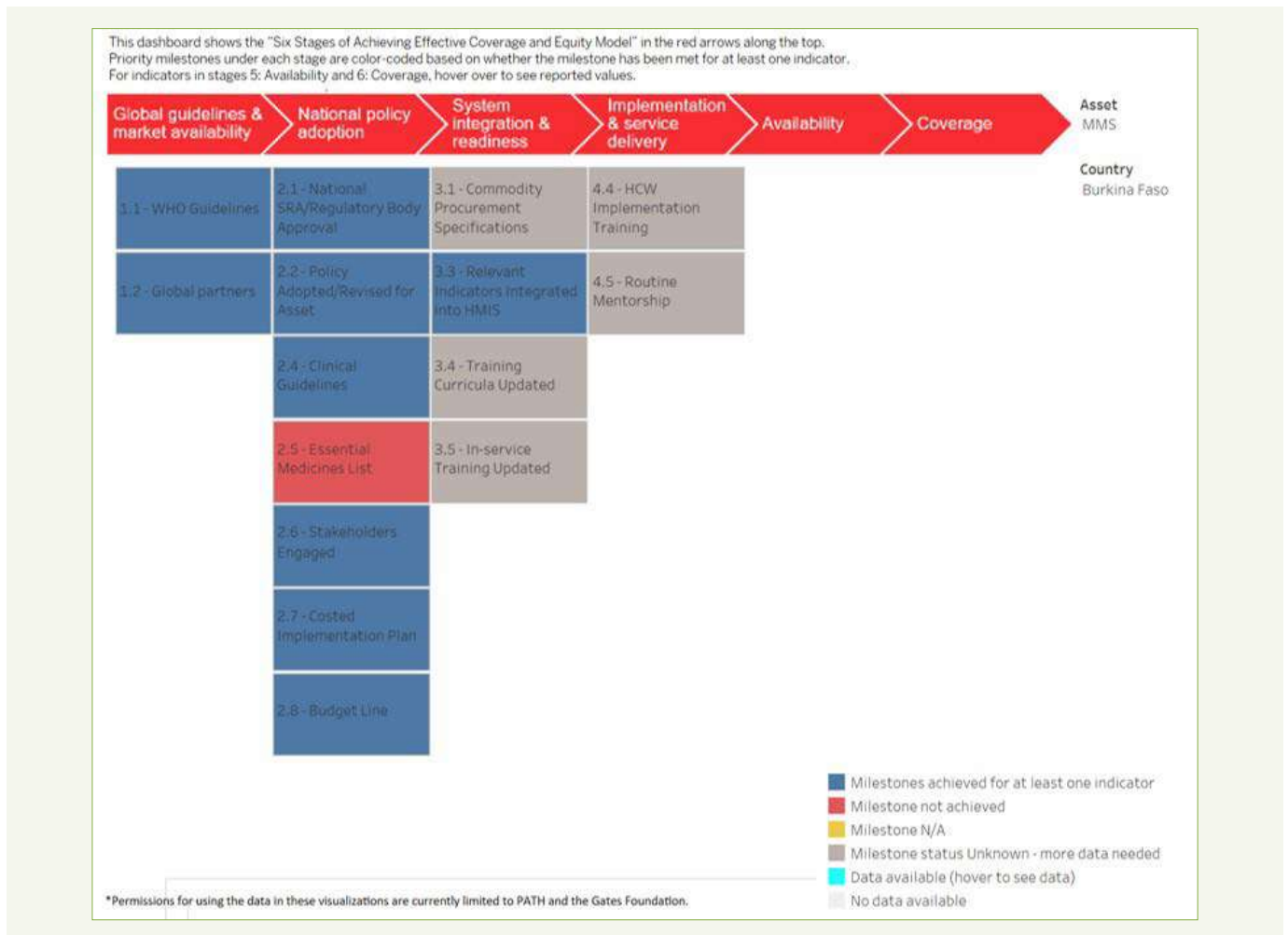
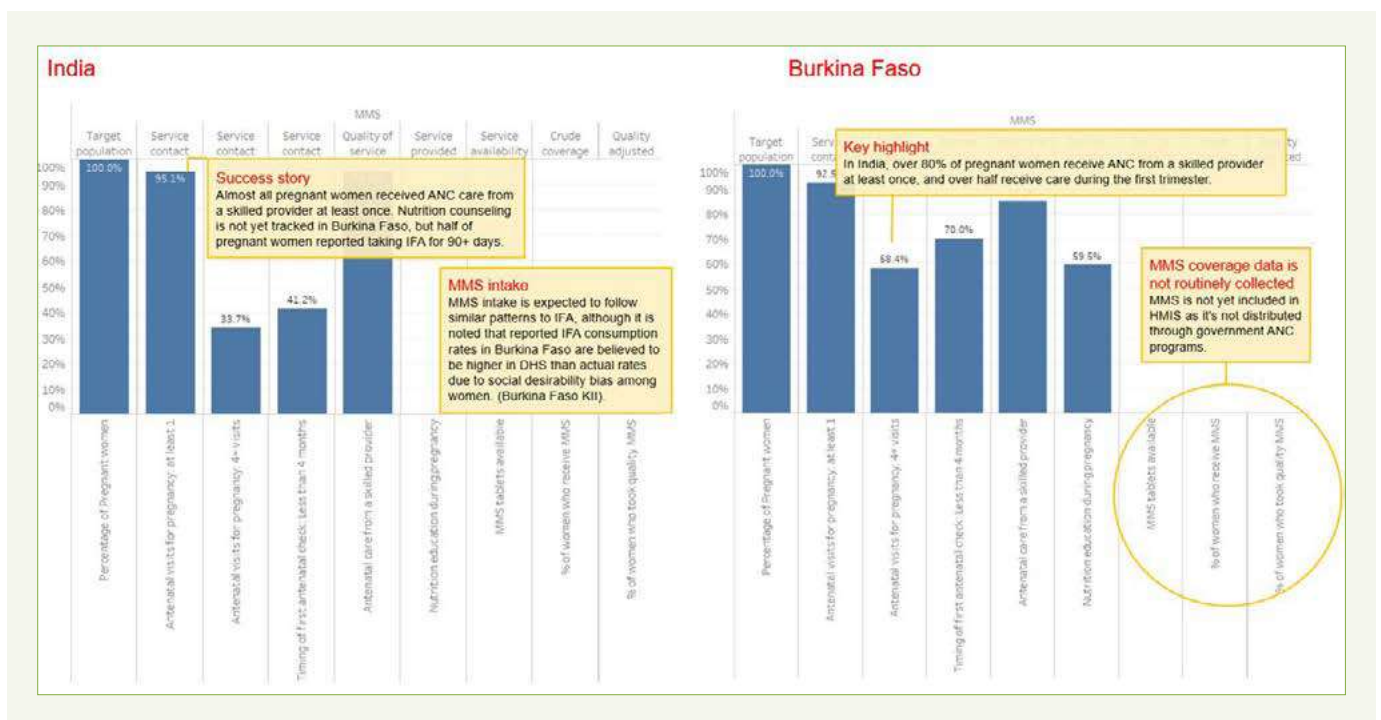


FIGURE 3: Asset Cascades provide a picture of opportunities and barriers at each stage of the continuum



Subnational Tableau visualizations

Further exploration of subnational findings is available for a subset of focus countries, including visualizations with both quantitative and qualitative data. **Figure 4** displays quantitative subnational findings from interviews and facility spot checks.

MMS key findings

Across Asset Tracker findings, MMS stood out as a new intervention, still reliant on donor funding to reach scale. Global guidelines exist for MMS use within the context of implementation research⁷ along with interim guidance for country-level decision-makers aiming to introduce MMS within antenatal care programs.⁸ Despite the existence of these key tools, MMS is far from reaching universal national level policy adoption. Only Burkina Faso and Pakistan out of our six focus countries have adopted a national policy for MMS implementation. Subnational data collection confirmed that the primary barriers to introduction and scale-up included a lack of policy adoption and a general lack of MMS product.

Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP)-MMS product specification was published in 2020 to support manufacturing and distribution.⁹

Burkina Faso has made significant strides toward MMS implementation by establishing market authorization, clinical guidelines, a costed implementation plan, and inclusion of a line item specific to MMS in national budgets. Still, further achievements

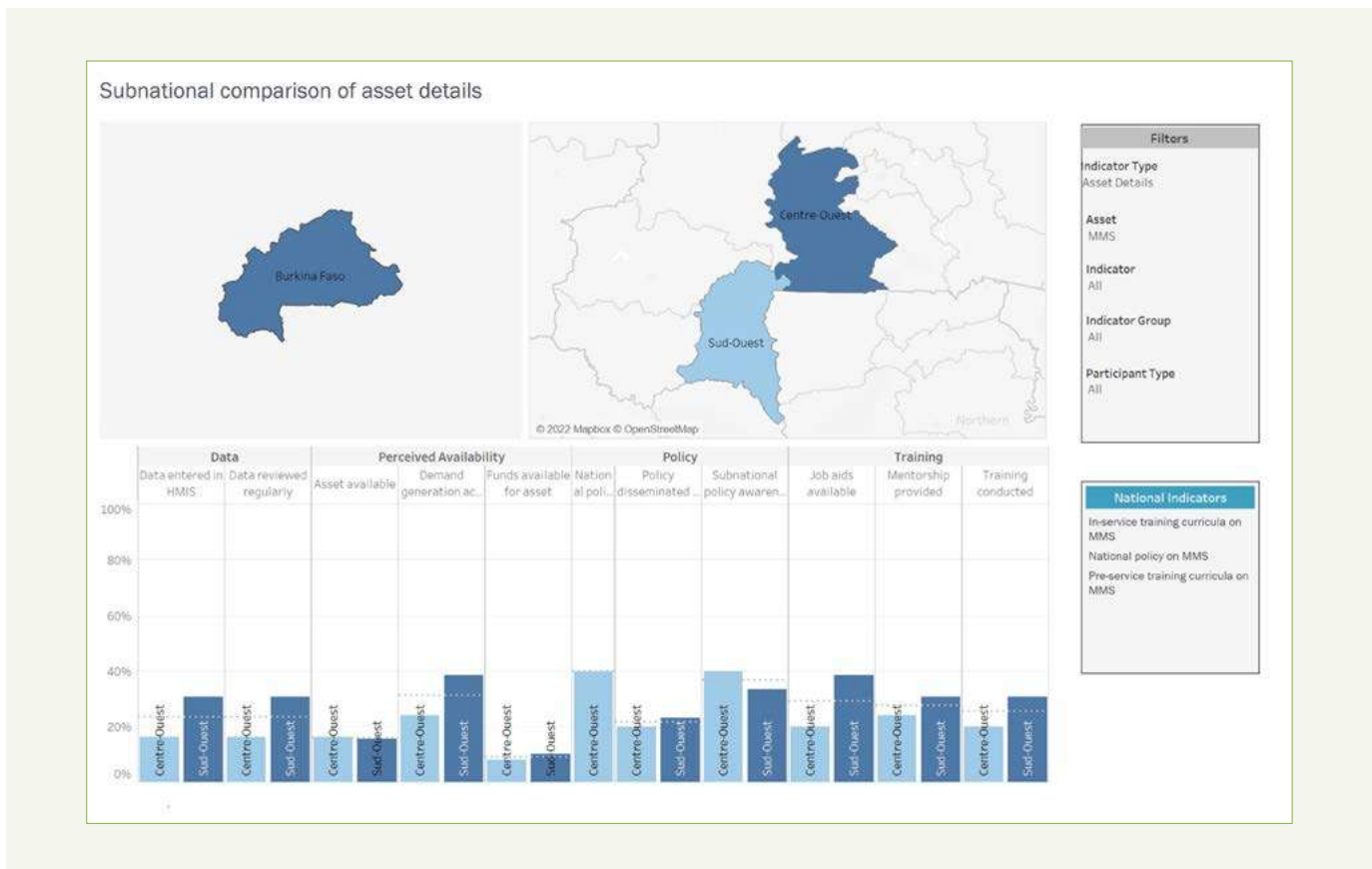
“The biggest barrier to MMS for pregnant women is availability. We only have iron.”

*Health care provider,
Sud-Ouest, Burkina Faso*

To accelerate the availability of MMS, an open-access United could be made by adding MMS to the national essential medicines list (EML) and fulfilling further system integration and readiness milestones from the Framework (see **Figure 3**). Pakistan similarly has several national milestones met, including clinical guidelines, and inclusion of MMS as a national budget line item, but market authorization, costed implementation plan, and EML inclusion are still needed.

Across the seven national milestones tracked, MMS Technical Working Groups were identified in Burkina Faso, Kenya, Nigeria, and Pakistan. One additional national milestone was met for MMS in India and Pakistan, where MMS job aids were developed. Almost no systems integration or implementation milestone indicators could be identified across the focus countries, apart from commodity procurement specifications and in-service training curricula on MMS in Pakistan. Availability and coverage data is

FIGURE 4: Subnational Tableau visualization of quantitative findings



not yet applicable and thus not tracked, and subnational interviews indicated little to no experience with MMS. A district health management team (DHMT) member in Burkina Faso stated: “I have heard a lot about it [MMS], especially with NGOs, but no experience.”

Lastly, country-level and subnational interviews indicated there was clear confusion between MMS, IFA, and micronutrient powders. This issue must be resolved via curriculums, trainings, mentorship, and improved branding to help healthcare workers identify the new product and associated policy.

“I have heard a lot about it [MMS], especially with NGOs, but no experience”

DHMT, Sud-Ouest, Burkina Faso

Key recommendations

Advocacy efforts made by the MMS Technical Advisory Group and the Micronutrient Forum have helped facilitate milestone achievements and must continue to be supported. In most countries, national policies (and subnational clinical care guidelines) for MMS distribution to pregnant women are not yet available. The 26 milestones from the *Stages of Achieving Effective Coverage* Framework guide need enhanced efforts to make strides toward MMS scale. Of particular importance are regional, uninterrupted supplies of MMS to support supply chain issues and drive down product cost for parity with IFA; national curriculums and job aids to assist health workers in their delivery of MMS counseling and support to pregnant women; preferred patient packaging options; and the addition of MMS coverage indicators into routine monitoring systems (e.g., HMIS).⁷

For advocates, donors, government decision-makers, and implementers, the Asset Tracker tool serves as a key conversation-starter toward improved implementation and scale. For optimal adoption, implementation, and coverage at scale, meeting key milestones will contribute to ensuring effective and equitable coverage for the most marginalized.

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Correspondence: **Kimberly Mansen**, MSPH, RDN, Senior Program Officer–Nutrition Technical Lead Maternal, Newborn, Child Health and Nutrition, PATH, 2201 Westlake Ave Suite 200, Seattle, WA 98121, USA
Email: kamundson@path.org

References

- 1 PATH. Tracking the journey to scale for lifesaving maternal, newborn, and child health and nutrition interventions. Accessed March 30, 2023. <https://www.path.org/programs/primary-health-care/tracking-the-journey-to-scale/>
- 2 Bryce J, Arnold F, Blanc A, et al. Measuring coverage in MNCH: new findings, new strategies, and recommendations for action. *PLoS Med.* 2013;10(5):e1001423. doi:10.1371/journal.pmed.1001423
- 3 Bitton A, Ratcliffe HL, Veillard JH, et al. Primary Health Care as a Foundation for Strengthening Health Systems in Low- and Middle-Income Countries. *J Gen Intern Med.* 2017;32(5):566-571. doi:10.1007/s11606-016-3898-5
- 4 PATH. Asset Tracker Phase 1 Dashboards. Accessed November 14, 2022. <https://tableau.path.org/t/BMGF/views/MNCHNutritionAssetTracker/Coverpage>
- 5 PATH. Asset Tracker Phase 2 Qualitative Dashboards. PATH Tableau. Accessed November 14, 2022. <https://tableau.path.org/t/BMGF/views/PATHSubnationalSurveyExploration-QualitativeDashboard/Home>
- 6 PATH. Asset Tracker Phase 2 Quantitative Dashboards. PATH Tableau. Accessed November 14, 2022. <https://tableau.path.org/t/BMGF/views/PATHSubNationalSurveyExploration/MostLeastSuccessfulAssetScale>
- 7 Guidelines Review Committee, Maternal, Newborn, Child & Adolescent Health & Ageing, Nutrition and Food Safety, Sexual and Reproductive Health and Research. WHO Antenatal Care Recommendations for a Positive Pregnancy Experience. Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy. World Health Organization; 2020:55. Accessed November 14, 2022. <https://www.who.int/publications/i/item/9789240007789>
- 8 Multiple Micronutrient Supplementation in Pregnancy Technical Advisory Group, UNICEF, Micronutrient Forum, Nutrition International, Vitamin Angels. Interim Country-Level Decision-Making Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women. WHO; 2021:1-8. Accessed November 14, 2022. <https://www.unicef.org/media/96971/file/Interim-Country-level-Guidance-MMS-for-PW-2021.pdf>
- 9 Group (MMS-TAG) TMMSTA, Forum (MNF) TM. Expert consensus on an open-access United Nations International Multiple Micronutrient Antenatal Preparation–multiple micronutrient supplement product specification. *Ann N Y Acad Sci.* 2020;1470(1):3-13. doi:10.1111/nyas.14322

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Afterword



A Call to Action to Switch to Multiple Micronutrient Supplements (MMS)

Klaus Kraemer

Sight and Life Foundation, Basel, Switzerland

William Moore

Eleanor Crook Foundation, Washington, DC, USA

Spencer Kirk

Kirk Humanitarian, Salt Lake City, USA

Improving women's nutrition, including during pregnancy and breastfeeding, should be a global priority. But progress is too slow. An estimated 40% of pregnant women globally suffer from anemia; two-thirds of non-pregnant women suffer from deficiencies in vitamins and other essential micronutrients; and in some countries, 9 out of 10 women are deficient in at least one essential micronutrient at the outset of pregnancy, putting their health and nutrition and that of their children at risk. We can change this.

This Special Report demonstrates that there are proven, cost-effective solutions to maternal malnutrition just waiting for the necessary attention and resources to be scaled. Doing so will save and transform the lives of women, their children, and their families. For years, iron and folic acid (IFA) supplements have been the standard of care for pregnant women in low-and-middle-income countries (LMIC), but women need more than just IFA to address multiple nutrient deficiencies. The United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) multiple micronutrient supplements (MMS) containing 15 vitamins and minerals are a safe and effective solution to address the low micronutrient intake found among pregnant women in LMIC with poor maternal health and adverse birth outcomes. There is consensus among the scientific community that UNIMMAP MMS reduces anemia in women, delivering the same impact as iron and folic acid (IFA) supplements. There is also consensus that UNIMMAP MMS performs better than IFA in preventing babies from being born too early and too small. UNIMMAP MMS is a superior product to IFA and yet few women are reaping its benefits.

MMS can also play a critical role in improving maternal nutrition and care as a whole: MMS can be used as a catalyst to update national antenatal care (ANC) guidelines, improve training of community-based health and nutrition workers, and strengthen overall ANC service delivery. However, too many opportunities

“There are proven, cost-effective solutions to maternal malnutrition just waiting for the necessary attention and resources to be scaled”

are being missed to ensure that all women have access to quality health and nutrition services during pregnancy and to overcome the challenges that have plagued IFA supplementation programs for many years.

Our call to action is simple: after more than 20 years of evidence-generation on the benefits of MMS, it's time to act. It's time to set out a global agenda to focus on maternal nutrition and ensure that women everywhere have the nutrition and health care that they need during pregnancy.

We call for the following:

1. **The World Health Organization (WHO) must transparently and expeditiously conduct a guideline review of MMS based on the updated evidence.** WHO's Antenatal Care (ANC) Guidelines, last updated in 2020, fell short of issuing a full recommendation for MMS, recommending implementation only in the context of “rigorous research.” As a result, no LMIC has fully made the switch from IFA to MMS. Since 2020, WHO's concerns regarding effectiveness, safety and cost-effectiveness have been addressed by the MMS Technical Advisory Group (MMS-TAG), and related research has been published in peer-reviewed journals. Our informed opinion, which is corroborated by many experts, is that there is evidence now to inform an updated WHO guideline review to recommend UNIMMAP MMS over IFA in ANC. Updated guidance will support national policymakers and program implementers to update their own policies for national MMS introduction and scale-up. Meanwhile, governments can already take steps to add the UNIMMAP MMS formulation to national Essential Medicine Lists (EML), in line with WHO's EML.

2. Country governments, donor governments and private funders need to come together to fund the scale-up of MMS.

This includes increased uptake of MMS in emergency settings, where MMS has been long recommended by UNICEF, WHO and the World Food Programme but is not widely used. At the same time, more than 20 countries have expressed interest in MMS adoption and are currently engaged in implementation research activities and should be prioritized for donor support in scaling UNIMMAP MMS. We must lay the foundation to scale MMS as quickly as possible once the WHO guidelines are updated, which will require coordination from all stakeholders to increase investments to procure UNIMMAP MMS and ensure a high-quality and sustainable supply at country level. As other articles in this report discuss, MMS supply chains will look different in different countries, but in all cases, switching to MMS will require a concerted funding effort. Country and community-level leadership will be key to introducing UNIMMAP MMS into the health system and as part of a comprehensive approach to meeting the specific nutritional needs of women in their country.

3. The global community must also prioritize improving ANC for women. It is no secret that IFA for pregnant women has faced many barriers to scale, including poor ANC in many

countries. Making the switch to MMS has the potential to transform the coverage of nutrition and health care for pregnant women by catalyzing improved integration and delivery of essential nutrition services through the health system. But success depends on governments and development partners agreeing that the current status quo of care for pregnant women is insufficient and requires innovative, community-led initiatives to reach those who are most difficult to reach. The full benefits of MMS will only be realized when pregnant women finally receive the care they need for a healthy pregnancy.

“After more than 20 years of evidence-generation on the benefits of UNIMMAP MMS, it’s time to act”

Every woman deserves a healthy pregnancy and the chance to guarantee a healthy start to life for her children. Switching to and scaling up MMS is an opportunity to ensure equity in access to key nutrition services and strengthen the ANC platform. We have the tools. We have the will. We have the evidence. Now it is time to make the switch and finally bring the power of MMS to scale.



Klaus Kraemer
Sight and Life Foundation,
Basel, Switzerland



William Moore
Eleanor Crook Foundation,
Washington, DC, USA



Spencer Kirk
Kirk Humanitarian,
Salt Lake City, UT, USA

Frequently Asked Questions

1. What are the specific health benefits of taking MMS compared to IFA during pregnancy for the baby?

Scientific evidence consistently shows the risk reductions associated with multiple micronutrient supplements (MMS) for low birth weight (LBW), small for gestational age (SGA), and other adverse birth outcomes, over and above the benefits provided by iron and folic acid (IFA) alone. Multiple new meta-analyses reveal a consistent relative risk (RR) reduction for LBW (ranging from 12% to 14% RR), SGA births (ranging from 2% to 9% RR), preterm births (ranging from 6% to 8% RR), very preterm births (ranging from 13% to 19% RR), and stillbirths (8% RR).

For LBW alone, a 12% risk reduction in LBW translates to an estimated 2.2 million infants in low- and middle-income countries (LMICs) annually, based on global estimates of 20.5 million live births with a birth weight of < 2,500 g, of which 91% occur in LMICs.

Specific to adolescent pregnant women (<20 years of age), a recent meta-analysis of this population showed that adolescents who received MMS had a significantly reduced risk of low birth weight, preterm births, and small-for-gestational-age births.

See articles: *Update On MMS Evidence Infographic* (p. 24) and *Prenatal Supplements and Maternal Anemia: Is more iron better?* (p. 32.)

2. What are the specific maternal health benefits of taking MMS compared to IFA during pregnancy?

Prenatal MMS provides 15 vitamins and minerals that are critical for a healthy pregnancy and to fill the gap between the higher nutrient requirements imposed by pregnancy and the typical low-micronutrient intakes often found in LMICs. For pregnant women, MMS has been shown to improve maternal nutrition status, in comparison to IFA, and plays an important role in reducing maternal micronutrient deficiencies (such as in vitamins A, B₂, B₆, B₁₂, D, folate and zinc).

Recent subgroup analyses demonstrate “the benefits of MMS (when compared to IFA) are even greater among anemic and underweight pregnant women, those who initiate supplementation earlier (before 20 weeks of gestation vs after 20 weeks), and those with higher adherence (95%+ adherence).”

Regarding gestational weight gain, another meta-analysis of studies conducted in LMICs revealed that MMS resulted in greater percentage adequacy of gestational weight gain, higher gestational weight gain at delivery, and reduced risk of severely inadequate gestational weight gain compared to IFA. Finally, MMS did not increase the risk of excessive gestational weight gain.

Specific to adolescent pregnant women (<20 years of age), a recent meta-analysis of existing data pertaining to this popu-

lation shows that adolescents who received MMS had a significantly reduced risk of low birth weight (LBW), preterm births, and small-for-gestational-age births (SGA).

See article: *Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements* (p. 15) and *Update On MMS Evidence Infographic* (p. 24).

3. Is switching from IFA to MMS cost-effective?

MMS is a cost-effective intervention that brings additional benefits to the health of the mother, from improved micronutrient status to adequate gestational weight gain. Four studies spanning 16 countries have demonstrated the cost-effectiveness of MMS compared to IFA. The results are consistent across all the modeled scenarios, demonstrating that even with a small incremental cost for MMS compared with IFA because of the additional micronutrients, MMS is highly cost-effective, with positive health outcomes for both pregnant women and infants.

Cost-benefit analyses in Bangladesh, India and Pakistan show that MMS can avert 2–3 times more disability-adjusted life years than IFA alone and that they have a higher return on investment, ranging from a few hundred to a few thousand dollars.

See articles: *Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements* (p. 15) and *Cost-effectiveness of Antenatal Multiple Micronutrient Supplementation Compared to Iron and Folic Acid Supplementation in India, Pakistan, Mali and Tanzania: Results of a microsimulation study* (p. 109).

4. Does scaling up MMS have potential human capital gains?

Overall, the potential human capital gains associated with scaling up MMS globally will likely be substantial. The ‘Thrive Model’ was developed to answer this question, estimating the potential human capital gains of scaling up MMS and other nutritional interventions in 132 LMICs. This model estimates that scaling up maternal MMS to 90% coverage globally may result in substantial gains (5 million additional years) in schooling, with the largest absolute gains in schooling attainment estimated to be for countries in South Asia and sub-Saharan Africa.

This information on additional years of schooling is then translated into increases in annual wages. Estimates show that scaling up MMS to 90% coverage in all 132 countries would result in US\$ 18.1 billion in lifetime wages gained every five years, with the largest absolute expected economic returns to lifetime income in India, Brazil and Mexico.

To conceptualize these numbers in terms of magnitude, the authors compared the MMS estimates to those for scaling up IFA and calcium supplementation to 90% coverage in the same 132 LMICs. Compared to scaling up MMS, scaling up IFA was estimated to result in roughly half of the estimated school years and lifetime earnings. Therefore, decision-makers considering expanding MMS coverage should consider these significant potential human capital returns in addition to direct maternal and child health benefits.

See article: *Potential Impact of Scaling Up Prenatal MMS on Human Capital Outcomes* (p. 38).

5. Is MMS included in the World Health Organization's (WHO's) Essential Medicines List (EML)?

MMS are now included on the WHO List of Essential Medicines (EML). In 2021, the UNIMMAP MMS formulation for pregnant women was added to the WHO 22nd EML. UNIMMAP is the United Nations International Multiple Micronutrient Preparation formulation of MMS. The WHO EML is updated every two years and is used by more than 130 countries as the basis for their national EMLs or drug formularies and to guide purchasing decisions. Currently, 479 medications, including MMS, are in the EML, based on efficacy, safety and cost-effectiveness data, because they are considered essential from a public health perspective.

See article: *Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements* (p. 15).

6. Does the UNIMMAP MMS formulation with 30 mg of iron have the same impact on maternal anemia as IFA with 60 mg?

Updated analyses provide evidence that MMS with 30 mg of iron during pregnancy is comparable to IFA with 60 mg of iron in terms of preventing maternal anemia and deaths during the neonatal period, as confirmed by analyses carried out by the MMS in Pregnancy Technical Advisory Group (MMS-TAG). The rationale for why a comparable effect is seen for 30 mg of iron in MMS vs 60 mg of iron in IFA supplements in preventing maternal anemia is threefold:

1. **The presence of other micronutrients (especially vitamins A, B₂ and C) can improve iron absorption and/or utilization compared with iron (and folic acid) alone.**
2. **MMS can help prevent other nutritional causes of anemia (anemia caused by deficiency of vitamins A, B₉ and B₁₂)**
3. **Iron doses greater than 60 mg have been shown to**

trigger a pathway that inhibits iron absorption, yet this phenomenon has not been seen with iron doses less than 40 mg.

Further, the MMS-TAG determined that a re-analysis of the neonatal deaths data stratified by iron dose in each supplement would be useful. The re-analysis showed no difference between 30 mg and 60 mg in the supplements on deaths during the neonatal period.

See article: *Prenatal Supplements and Maternal Anemia: Is more iron better?* (p. 32).

7. What is the ideal number of MMS tablets to consume during pregnancy, and when should it be initiated?

MMS should be initiated as soon as the pregnancy is identified, and efforts should be taken to maximize supplement adherence, as early initiation in pregnancy and high adherence to MMS have been associated with greater benefits in recent trials.

The minimum number of MMS tablets pregnant women should take to receive full benefits with a view to reducing adverse birth outcomes has not yet been determined. The contribution of the timing of initiation, adherence, and total number of tablets on the impact of MMS on birth and infant outcomes is currently being investigated in an ongoing meta-analysis. For practical program planning and implementation research to identify strategies to improve adherence, 180 UNIMMAP-formulated MMS tablets per pregnancy is generally used as the default number of tablets. This number serves as a baseline for comparison to actual adherence rates (until further clinical research or analysis of existing clinical trial data suggests otherwise). It is also useful for program supply planning.

A related topic is when to begin MMS use to achieve optimal results. To date, the evidence base has focused on assessing the effect of MMS vs IFA during pregnancy, with women included in those trials initiating supplementation after the first trimester. Less is known about the potential benefits of starting MMS before or just after conception or continuing during lactation. One trial in Bangladesh assessed the effect of starting MMS prior to conception through the first trimester of pregnancy on birth and pregnancy outcomes and demonstrated a reduction of early pregnancy loss. These early findings suggest potential benefits of pre-conception supplementation, but more research is needed.

See article: *Update on the Scientific Evidence on the Benefits of Prenatal Multiple Micronutrient Supplements* (p. 15).

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