Focusing on Multiple Micronutrient Supplements in Pregnancy

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Imprint

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Maternal Multiple Micronutrient Supplementation (MMS): There is no turning back

Klaus Kraemer
Sight and Life, Basel, Switzerland

Key messages

- Multiple micronutrient supplementation (MMS) has the potential to save the lives of women and children, in particular, and strengthen antenatal care (ANC) and health systems around the world.
- Over the past two decades, evidence has been generated showing the efficacy and cost-effectiveness of MMS; there has also been a cocomitant increase in the number of low- and middle-income countries (LMICs) seeking guidance on how to safely and affordably provide MMS during pregnancy.
- However, the lack of information due to data gaps and clear global and national guidance on micronutrient deficiencies is holding LMICs back.
- To address these issues and harness the potential of MMS, *Sight and Life* and other organizations are working across several fronts – from research to project implementation to joint advocacy – to ensure that MMS is available to the most vulnerable.
- The current COVID-19 pandemic will disrupt food systems in many parts of the world, reducing the general availability of nutritious, micronutrient-rich foods. Communicating the proven benefits of MMS for pregnant women is therefore more important than ever during this challenging time.

Improving maternal nutrition

Nutrition is fundamental to human health and development. Addressing malnutrition saves lives, reduces inequalities, and builds strong and resilient individuals, families, communities and populations.

Women are particularly vulnerable to malnutrition in all its forms and, during pregnancy, their children can be negatively impacted. Any form of malnutrition during a woman's pregnancy can have lasting repercussions on fetal and child development, as growth failure can be transmitted from mother to child. It is therefore vital to ensure adolescent and maternal nutrition to protect the health and wellbeing of women and their children, boosting gender equality and breaking the vicious cycle of poverty.

A component of poor nutrition is micronutrient deficiency, which can have devastating impacts on maternal health and pregnancy outcomes. Over half of adolescent girls and young women in low- and middle-income countries (LMICs) have inadequate micronutrient intake. Rates of anemia in women of reproductive age increased between 2000 and 2016 – from 31.6 percent to 32.8 percent globally – and little progress has been made in recent years. Because of this and other factors, more than 300,000 women currently die from pregnancy or childbirth-related complications. And each year, ~20.5 million babies are born with low birth weight (LBW), accounting for 14.6 percent of all births worldwide, with the majority in sub-Saharan Africa and South Asia.

> **"Micronutrient deficiencies are still poorly understood in most countries"**

The burden of micronutrient deficiencies is still poorly understood in most countries because of vast data gaps and a lack of clear global and national guidance. This applies equally to potential solutions. The good news is that the tide is turning. Catalytic commitments have been made to make multiple micronutrient supplementation (MMS) available to those who need it the most, and research from the past two decades has demonstrated a solid evidence base and

documented the widespread need for new approaches to combat deficiencies in key vitamins and minerals. New evidence and specific requests from individual countries have also inspired a sea change in the international community. There is no turning back.

MMS retrospective

My personal appreciation of vitamins and minerals dates back to my training as a nutrition scientist, during which I learned about the role these micronutrients play in metabolism and health. Throughout my early career, I admired *Sight and Life* for supporting vitamin A supplementation programs around the world in the 1980s and 1990s, and then expanding its focus to cover the full range of micronutrients towards the end of the 20th century. When, in 2005, I became the Director of *Sight and Life*, I found myself in the privileged position of being able to push these initiatives further.

For example, in early 2006, I had the opportunity to gain deep insights into JiVitA, a high-quality, community-based research program run by Johns Hopkins Bloomberg School of Public Health (JHBSPH). Operational since 2001 in northwest rural Bangladesh, JiVitA has examined – and continues to examine – the critical role of micronutrient deficiency prevention in reducing mortality and morbidity and improving child development during the first 1,000 days and beyond. Its goal is to inform and guide policies and programs through the conduct of large-scale, community-based nutrition studies.

In 2008, *Sight and Life* facilitated local MMS production in Bangladesh of 16 million tablets for a JiVitA study (JiVitA-3) of 45,000 pregnant women. The trial showed that daily MMS throughout pregnancy offered greater health benefits than an iron-folic acid (IFA) supplement alone, reducing the numbers of preterm birth, LBW and stillbirth by 10–15 percent. A subsequent trial (JiVitA-5) is currently being implemented. This trial is focused on prenatal supplementation of adolescent girls and women under 20 years of age, using MMS from the same local producer as in 2008. The dedication of the JHBSPH team over the years, under the leadership initially of Al Sommer and Keith West, has delivered findings that have transformed our understanding of the potential of MMS; however, that important work is not yet finished.

"JiVitA-3 showed that taking a daily MMS throughout pregnancy offered greater health benefits than an IFA supplement alone"

Despite numerous studies confirming the benefits of MMS over IFA, in 2016 the World Health Organization (WHO) released antenatal care (ANC) guidelines that recommend IFA, while simultane-

Together, the 'Power for Mothers' speakers present the importance of MMS during the Women Deliver conference in Vancouver, Canada. Left to right: Robert Black, Johns Hopkins University Bloomberg School of Public Health; Joanna Mikulski, CIFF; Spencer Kirk, Kirk Humanitarian; Kristen Hurley, Vitamin Angels; Klaus Kraemer, *Sight and Life*; Parul Christian, Bill & Melinda Gates Foundation; Emily Smith, Bill & Melinda Gates Foundation; Danielle Porfido, 1,000 Days; and Lenore Spies, KwaZulu-Natal Department of Health.

ously (and somewhat confusingly) stipulating that policymakers in populations with a high prevalence of nutritional deficiencies may, if they so wish, choose to give MMS.

In response to these guidelines, a task force, the Multiple Micronutrient Supplementation Technical Advisory Group (MMS TAG), was convened by the New York Academy of Sciences (with funding from the Bill & Melinda Gates Foundation) to evaluate new evidence not available at the time of the development of the WHO guidelines and help countries interpret the guidelines. The MMS TAG firmly concluded that MMS is safe and cost-effective and that it provides greater benefit than IFA for pregnancy outcomes. Gilles Bergeron and Megan Bourassa of the New York Academy of Sciences anatomize the relevant science in the contribution on page 17 entitled 'Reviewing the Evidence and Promoting the Adoption of MMS.'

As MMS, foods rich in micronutrients and/or adequate ANC are not readily available to many women in LMICs, women in these countries have a higher risk of poor pregnancy outcomes than women in high-income countries. Consequently, LMICs are eager for guidance on how to safely and affordably provide MMS during pregnancy.

"LMICs are eager for guidance on how to safely and affordably provide MMS during pregnancy"

Because of both the unclear global policies related to MMS and the clear evidence on its safety and impact, *Sight and Life* joined with others in the nutrition community to help ensure that relevant evidence be made available, and that opportunities to implement MMS be created. We came together to frame MMS in new ways, including positioning it as a women's rights and equity issue. As Spencer Kirk of Kirk Humanitarian said: *"In North America and much of Europe, pregnant women get 15 essential micronutrients [...] For the rest of the world and in LMICs, women get something less. They get two micronutrients – iron and folic acid. The inequity is unacceptable."*

Harnessing partnerships for MMS policy change

In June 2019, *Sight and Life*, along with partners (Vitamin Angels, Kirk Humanitarian, 1,000 Days, CIFF and the MMS TAG), brought together a unique group of like-minded organizations during a 'Power for Mothers' event at Women Deliver in 2019, the world's largest conference on gender equality. This was a tipping point: this group not only elevated the issue of MMS and maternal equity to a new level, but also agreed to build consensus on the need for greater effort, and established a collaborative approach to increase the momentum. This inspired many individual organizations to take action.

Following Women Deliver, at the Bill & Melinda Gates Foundation's Goalkeepers event in September 2019 during the United Nations General Assembly, the Healthy Mothers, Healthy Babies Accelerator was launched. This new partnership brought together nearly US$50 million in contributions to reach more than 17.5 million pregnant women and their newborns with MMS in countries including Myanmar, Indonesia and Bangladesh over the next three years. Since then, additional commitments to the Accelerator have started taking shape. Turn to page 08 and read 'Accelerating Maternal Nutrition through Multiple Micronutrient Supplementation in Pregnancy: The Healthy Mothers, Healthy Babies Accelerator' by Saskia Osendarp, Reed Atkin and Aynsley Morris to learn more about this initiative.

"The year 2020 is ripe with more opportunities to put MMS on global and national agendas"

2020 is ripe with opportunities to put MMS on global and national agendas. This effort kicked off with an MMS Stakeholder Consultation in early February in Washington, DC. At the time this *Sight and Life* Special Report is going to press, the COVID-19 pandemic has impacted conference and travel plans worldwide, making it necessary to temporarily replace physical meetings with online ones. The global nutrition community is adapting to the challenges of our current situation, however, and the path for advocacy, outreach and engagement remains clear.

The COVID-19 pandemic will also disrupt food systems in many parts of the world, reducing the general availability of nutritious, micronutrient-rich foods. This will make it harder for many pregnant to achieve a healthy diet containing the micronutrient levels necessary for maintaining general health and supporting the immune system. Communicating the proven benefits of MMS is therefore more important than ever during this challenging time.

Advancing the goal

To elevate and maintain the health of women and give more children a healthy start to life, we must ensure that women have access to the nutrients they need, at all stages of life. Now is the time to introduce MMS: countries with widespread micronutrient deficiencies have requested implementation research and donations of MMS to replace IFA in their health sectors. ANC, the main delivery platform for maternal nutrition interventions, covers less than half of pregnant women in LMICs, and only 34 percent of pregnant women are covered with IFA. Introducing MMS is an opportunity to strengthen ANC and the health system as a whole. As countries consider this transition, there are several tools available to support them. One example put forth by Nutrition International is explained in 'Multiple Micronutrient Supplement (MMS) Cost-

Benefit Tool to Guide Decision-Making' by Jennifer Busch-Hallen, Dylan Walters and Sarah Rowe on page 77.

This *Sight and Life* Special Report on MMS compiles and curates the latest evidence base, experience from the field, and resources for scale-up. It aims to serve as an important resource for decision-makers and implementers, thereby driving the introduction and adoption of MMS. We are deeply grateful to all who have contributed to this Special Report. A particular "thank you" goes to Kirk Humanitarian and Spencer Kirk for making this publication possible and to the Family Larsson Rosenquist Foundation and Katharina Lichtner for making copies of this Special Report available in print. We also owe a debt of gratitude to our friends from Vitamin Angels, Quinn Harvey, Kristen Hurley and Clayton Ajello, for their invaluable editorial support and their attentive reviewing of the articles in this Special Report.

"The time is now to adapt global and national guidelines to the overwhelming evidence"

There is no turning back. If the evidence from the past decade has taught us anything, it is that MMS is far superior to IFA, and that the global community is eager to ensure that it is available, affordable, scaled and effective. The time is now to adapt global and national guidelines to reflect the overwhelming evidence. Disparities in ANC, including the provision of MMS, are unacceptable, and it is up to us to work together to make the critical difference to people's future lives.

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Accelerating Maternal Nutrition through Multiple Micronutrient Supplementation in Pregnancy

The Healthy Mothers, Healthy Babies Accelerator

Saskia JM Osendarp, Reed Atkin, Aynsley Morris
Micronutrient Forum, Washington, DC, USA

Key messages

- Despite clear evidence of the safety and benefits, progress in delivering multiple micronutrient supplementation (MMS) at scale to pregnant women in low- and middle-income countries (LMICs) remains too slow.
- Led by the Micronutrient Forum, the Healthy Mothers, Healthy Babies Accelerator (a Bill & Melinda Gates Foundation Goalkeepers Accelerator project) aims to expedite the implementation and scale-up of MMS worldwide by reaching more than 17.5 million pregnant women and their newborns in multiple countries, including Myanmar, Indonesia, Bangladesh, Tanzania, Burkina Faso and Madagascar, over the next three years.
- With significant new funding and commitments from more than 10 partners across the private sector, academia, civil society and more, this Accelerator will make much-needed progress against Sustainable Development Goals (SDGs) 2 and 3, saving lives and improving the health of millions of women and newborns (see **Box 1**).
- As a follow-up to the launch of the Accelerator, the Micronutrient Forum convened 30 stakeholders from different organizations, including foundations, academia, implementers, the private sector, governments and NGOs, in early February 2020 to identify, inform, align and accelerate activity on MMS.

BOX 1: Accelerator partners

Micronutrient FORUM	The Micronutrient Forum
CHILDREN'S INVESTMENT FUND FOUNDATION	Children's Investment Fund Foundation (CIFF)
DSM BRIGHT SCIENCE. BRIGHTER LIVING.	DSM
Eleanor Crook Foundation	The Eleanor Crook Foundation
halodoc	Halodoc
KIRK HUMANITARIAN	Kirk Humanitarian
The New York Academy of Sciences	New York Academy of Sciences (NYAS)
NUTRITION INTERNATIONAL	Nutrition International
	The Republic of the Union of Myanmar
sightandlife	Sight and Life
unicef	UNICEF
vitamin angels	Vitamin Angels

Details on the partner commitments can be found on the Micronutrient Forum's Goalkeepers website at: **https://micronutrientforum.org/goalkeepers/**

The launch of the Healthy Mothers, Healthy Babies Accelerator

Background

While the evidence is clear that MMS for pregnant women significantly decreases the risk of low birth weight and very low birth weight, [1–3] MMS is still not readily available in LMICs. Only a few countries have switched from iron and folic acid (IFA) supplements to MMS as the standard antenatal care (ANC) for pregnant women.

"MMS is particularly important in LMICs because diets rich in micronutrients are often unavailable or unaffordable for women of childbearing age"

MMS is particularly important in LMICs because diets rich in micronutrients are often unavailable or unaffordable for women of childbearing age.[3] The result is that women in LMICs have a higher risk of poor pregnancy outcomes than women in high-income countries.

To address this inequity, the Bill & Melinda Gates Foundation (Foundation) asked the Micronutrient Forum to lead the Healthy Mothers, Healthy Babies Accelerator, in order to advance the introduction and implementation of MMS over the next 3 years. The Accelerator project was launched at the 2019 Goalkeepers event in New York City.

Accelerators

Goalkeepers Accelerators bring together organizations from different sectors – including governments, the private sector, civil society and philanthropy – around common agendas for action, seeking to catalyze investments, expertise and innovation to drive further progress towards the SDGs.

Each Accelerator makes a commitment that goes beyond 'business as usual.' The Foundation provides a platform and global stage to catalyze progress towards reaching the SDGs through the Accelerators.

The Healthy Mothers, Healthy Babies Accelerator

The Healthy Mothers, Healthy Babies Accelerator leverages new investments from the private sector, philanthropies, NGOs and country leadership to: save lives, improve the health of millions of women and newborns, correct inequitable access to MMS and make progress towards the SDGs. From the outset, the Accelerator was building on strong momentum for MMS among donors, implementing agencies and governments who were ready to act.

"The level of commitment and enthusiasm for Healthy Mothers, Healthy Babies was almost overwhelming"

Against this background, the Healthy Mothers, Healthy Babies Accelerator mobilized nearly US$50 million in financial and in-kind contributions, and will, over the next 3 years, reach more than 17.5 million pregnant women and their newborns in more than 60 countries, through a mix of introductory and large-scale programs. More than 10 partners from the private sector, academia, civil society and the United Nations have already committed to:

- **Increase demand** to help women, providers and governments understand the benefits of MMS, establish markets and provide technical assistance to those considering adoption.
- **Increase supply** to ensure that a reliable, high-quality, cost-efficient and effective source of MMS is available to those who wish to access them.
- **Increase the quality of service delivery** by integrating supply and demand via context-specific solutions to effectively deliver MMS to women globally.

Progress and next steps

The next important pieces of work for the Healthy Mothers, Healthy Babies Accelerator are to:

1) widen the reach and broaden the scope of the Accelerator with additional partners and commitments;

2) track partners' progress on commitments; and

3) advocate for MMS around the Accelerator themes of increasing demand, supply and service delivery quality during key global, regional and national events including the Micronutrient Forum Global Conference in November 2020, the Tokyo Nutrition for Growth (N4G) Summit 2020 and the 2020 Goalkeepers event.

What went well

The level of commitment and enthusiasm for Healthy Mothers, Healthy Babies was almost overwhelming. As a neutral, convening organization, the Micronutrient Forum was fortunate to work with all partners to bring this Accelerator together in a very short time. Four factors seem to have been instrumental to the Accelerator's success:

Firstly, the Accelerator was an overnight success years in the making. So many organizations have been involved in conducting research and advocating for MMS adoption for many years – and even successfully exploring the implementation of MMS use in ANC services – that a communal chorus of support had built to a crescendo. A critical tipping point in the acceptance of MMS as a superior intervention compared with IFA alone came with the publication of two definitive meta-analyses outlining the safety and efficacy of MMS.

Secondly, a handful of nimble organizations willing to act fast (and on a large scale) in support of the Accelerator gave other participants the confidence to support the Accelerator.

Thirdly, there were many linkages and a shared sense of respect among the donor organizations. Rather than competing, organizations acknowledged each other's strengths and focused on ensuring that the Accelerator benefited overall from each organization's complementary skills and focus areas.

Finally, there was a clear call to action with a deadline, creating a sense of urgency. The Bill & Melinda Gates Foundation

Stakeholders brought together by the Micronutrient Forum in Washington, DC, on 5–6 February 2020 to discuss the acceleration of the use of maternal micronutrient supplements

Goalkeepers event is a wonderful advocacy opportunity, and motivated Accelerator partners to prioritize and execute this important work.

It was fortuitous that these factors came together to enable the Healthy Mothers, Healthy Babies Accelerator; the Forum will continue to foster collaboration and seek complementarities in its work, and will strive to achieve this level of impact in other areas.

MMS Stakeholder Consultation: Summary findings

On 5–6 February 2020, the Micronutrient Forum, with funding from Kirk Humanitarian, convened 30 stakeholders from various organizations, including foundations, academia, implementers, the private sector, governments and NGOs to identify, inform, align and accelerate activity on MMS for pregnant women.

The objectives of the MMS Stakeholder Consultation were to:

1) achieve a greater understanding of current MMS evidence, advocacy, policy and program implementation experience;

2) identify factors that impede MMS implementation (including implementation research), viewed through the lenses of supply, demand and delivery;

3) develop an agenda that aligns donor interests and priorities with gaps in advocacy, policy and MMS implementation (including implementation research); and

4) achieve a greater shared understanding of the upcoming advocacy opportunities for MMS vis-à-vis the Micronutrient Forum 5th Global Conference and N4G 2020.

The consultation participants reviewed the evidence, supply, policies, program experiences and advocacy opportunities to scale up MMS for pregnant women.

"There is robust evidence of the benefits and cost-effectiveness of MMS for improving pregnancy outcomes"

Thanks in part to two recent meta-analyses outlining the safety and efficacy of MMS, there is robust evidence of the benefits and cost-effectiveness of MMS for improving pregnancy outcomes. Importantly, there is recent evidence that MMS can be produced at price parity compared with IFA. This evidence has not yet translated into strong normative guidance or broad adoption at the country level. However, the policy landscape is shifting as WHO ANC guidelines, including the recommendations on MMS, are currently under revision, and countries are increasingly exploring MMS as the standard of care. Because of this increasing demand, the global production of MMS will soon be insufficient. Efforts are underway to improve international and local supply and access to the UNIMMAP formula.

Experiences from case studies in Bangladesh, Haiti and Indonesia showed a range of context-specific approaches to scale up MMS in each country. These case studies also contained commonalities, including the importance of having clear and consistent safety evidence, cost-effectiveness and affordability, all of which are important for local advocacy. The success of MMS depends on the success of ANC services, and highlights the need to improve these programs. There is a growing effort to create awareness and demand on a global scale, but this can only be achieved at a country level when national stakeholders, institutes and policymakers are involved in these efforts, recognizing that there are many competing priorities.

Upcoming global advocacy efforts for MMS include the November Micronutrient Forum Global Conference in Bangkok, Thailand, and the December N4G Summit 2020 in Tokyo, Japan. Donors, including governments, foundations and the private sector, are expected to make significant commitments during the N4G event. MMS stakeholders must ensure that micronutrient nutrition generally and MMS specifically are on the agenda at the N4G Summit. Although global momentum for evidence-based, implementation-ready, nutrition interventions is growing, it is important to frame MMS within the context of maternal nutrition in general, focusing on the comprehensive package of interventions, not just a single product, and to link it to the need to improve ANC platforms in the context of 'universal health care.'

During the consultation, participants discussed a road map for the scale-up of MMS, and prioritized the following actions for the coming year:

1) Translating the compelling evidence for impact and cost–benefit ratio, as well as interpreting the evolving WHO ANC guidelines with a view to global, national and local advocacy.

2) Continuing the development of compelling advocacy and planning tools to demonstrate the low cost and high return associated with MMS investments.

3) Creating an implementation toolbox for scale-up, building on country experiences to help share lessons learned on improving adherence and delivery and increasing supply, while acknowledging the importance of context.

4) Developing financing mechanisms to increase supply from both the public and the private sectors. Ensuring registration in the essential medicines list has the potential to open up opportunities for different funding mechanisms.

5) Recruiting new partners with strong commitments to the Healthy Mothers, Healthy Babies Accelerator. Leveraging major global moments this year, including the Micronutrient Forum in Bangkok and the N4G Summit in Tokyo. Engaging country leadership.

To further facilitate dialogue and collective action on this agenda, the Micronutrient Forum, together with partners, committed to: further build, formalize and lead the MMS Stakeholder Group; add local and country representatives; monitor progress on the agreed actions; share learnings; and help to bring maternal nutrition and MMS to the global advocacy space.

The Micronutrient Forum prepared the following four concluding statements based on the dialogue during the MMS Stakeholder Consultation:

1) MMS is a superior product to IFA in terms of pregnancy outcomes, including low birth weight, small-for-gestational-age birth and preterm birth.

2) Maternal nutrition and ANC must be prioritized globally, and MMS programs present valuable opportunities to strengthen maternal care and ANC.

3) The nutrition community is committed to **partnering with national government entities and other relevant stakeholders** to develop effective and context-specific programs.

4) With key advocacy events occurring in 2020, all MMS stakeholders, with support from the Micronutrient Forum, will **continue and strengthen advocacy efforts to build on the current momentum for MMS.**

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References

1 Bourassa, MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444:6–21.

2 Smith ER, Shankar AH, Wu LS-F, 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 randomized trials in low-income and middle-income countries. Lancet Glob Health. 2017; 5(11):e1090–e1100.

3 Gernand AD, Schulze KJ, Stewart CP, West KP Jr, Christian P. Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. Nat Rev Endocrinol. 2016;12:274–89.

Glossary

Accredited third-party certification body
An accredited third-party certification body means a third-party certification body that meets the applicable requirements of ISO/IEC 17020:2012 and/or ISO/IEC 17065:2012 and is accredited to conduct audits or inspections according to the applicable standard or regulatory requirements.

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

Antiretroviral therapy
Antiretroviral therapy (ART) is the use of HIV medicines to treat HIV infection.

Article
Article includes substances (such as excipients, food/dietary/nutritional ingredients, in-process material), products (such as food/dietary/nutritional supplements) and materials (such as packaging containers and closures, and labels).

Batch
Batch is a specific quantity of a food/dietary/nutritional supplement or other article that is: intended to be uniform; intended to meet specifications for identity, purity, strength and composition; and produced during a specified time period according to a single manufacturing record during the same cycle of manufacture.

Capital goods
A capital good is a durable good that is used in the production of goods or services. Capital goods are one of the three types of producer goods, the other two being land and labor. Examples of capital goods include buildings, machines, equipment, furniture and fixtures.

Certificate of Analysis (CoA)
CoA is a document relating specifically to the results of testing a representative sample drawn from a batch of material. The CoA should list each test performed in accordance with compendial or manufacturer requirements, including reference to the test procedure, the acceptance limits and the results obtained.

Code of Federal Regulations (CFR)
The CFR annual edition is the codification of the general and permanent rules and regulations published in the Federal Register by the executive departments and agencies of the Federal Government of the United States. It is structured into 50 subject matter titles; title 21 applies to food and drugs. Titles are broken down into parts, subparts, sections and paragraph.

Commercial tax
A type of tax that is established with respect to the commercial provision of goods or services. Value added tax and excise tax are examples of different commercial taxes.

Common trade tariff
Tax or duty used to restrict imports by increasing the price of goods and services purchased from overseas to protect the local economy, thereby making them less attractive to consumers.

Competitive pricing
When producers set their prices at the same level as those of their competitors.

Cost of registration
A fee paid either to the drug regulation authority or the food regulation authority in order to register a product (i.e., a new supplement).

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

Country of destination
The country in which the product is intended to be marketed/used.

DALY
Disability-adjusted life years.

DHIS2
District Health Information Software 2.

Early neonatal mortality
The death of a live-born baby within the first seven days of life.

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.

Excipients
Excipients are substances other than food/dietary ingredients that have been appropriately evaluated for safety and are intentionally included in a food/dietary supplement to do one or more of the following: aid in the manufacture of a food/dietary supplement; protect, support or enhance stability, bioavailability or user acceptability; assist in product identification; and/or enhance any other attribute of the overall safety or delivery of the food/dietary supplement during storage or use. The term excipient is sometimes used synonymously with the term inactive ingredients and other ingredients.

Excise tax
A tax on manufactured goods levied at the time of manufacture rather than at sale. Excise tax is typically imposed on producers and manufacturers, and is ultimately passed on to the consumer.

Food/dietary/nutritional ingredient
Food/dietary/nutritional ingredients are ingredients with an established nutritional value, namely vitamins and minerals in their respective chemical entity.

Food/dietary/nutritional supplement
Food/dietary/nutritional supplement is a product intended to supplement the diet that: contains one or more food/dietary/nutritional ingredients; is intended for ingestion in a tablet, capsule or liquid form; is not represented for use as a conventional food or as the sole item of a meal or the diet; is labeled as a food/dietary/nutritional supplement; and is sometimes referred to as a multiple micronutrient supplement (MMS).

Food/dietary/nutritional supplement ingredient
Food/dietary/nutritional supplement ingredient includes food/dietary ingredients (i.e., vitamins and minerals) and excipients.

Gestational age
The period between conception and birth, ranging from 38 to 42 weeks.

GMP
Good manufacturing practices (GMP) are part of quality assurance and ensure that products are consistently produced and controlled to the quality standards appropriate for their intended use and as required by the market regulator. See WHO quality assurance guidelines.

HACCP
Hazard Analysis and Critical Control Points (HACCP) is a preventative food safety system in which every step in the manufacture, storage and distribution of a product is scientifically analyzed for microbiological, physical and chemical hazards. Potential hazards are identified and appropriate control measures are put in place before a problem can occur.

Import tax
A tax collected on imports or exports by a country's customs authorities. Also called customs duty.

In-kind contribution
A non-monetary contribution. Goods or services offered free of charge or at less than the usual charge constitute an in-kind contribution.

Installed capacity
The maximum a facility can produce using its machinery.

KII
Key informant interview.

Luxury tax
A tax placed on products or services that are deemed to be nonessential or unnecessary. A luxury tax is an indirect tax that increases the price of the good or service and is a price-inflationary burden that is incurred only by the end consumer who purchases or uses the product.

Micronutrient Forum (MNF)
The Micronutrient Forum serves as a global catalyst and convener for sharing expertise, insights and experience relevant to micronutrients in all aspects of health promotion and disease prevention, with special emphasis on the integration with relevant sectors.

Neonatal mortality
A death during the first 28 days of life (0–27 days).

Perinatal
The perinatal period commences at 22 completed weeks (154 days) following gestation and ends seven completed days after birth.

Pharmaceutical Inspection Co-operation Scheme (PIC/S)
PIC/S is a nonbinding, informal co-operative arrangement between regulatory authorities in the field of good manufacturing practice (GMP) of medicinal products for human or veterinary use. PIC/S currently consists of 52 participating authorities and aims at harmonizing inspection procedures.

Pharmacopeia Compendial Standard
1. British Pharmacopoeia (BP)
2. European Pharmacopoeia (Ph.Eur.)
3. International Pharmacopoeia (Ph.Int.)

4. Japanese Pharmacopoeia (JP)
5. United States Pharmacopeia (USP)

Policy coherence
An approach and policy tool for integrating the economic, social, environmental and governance dimensions of sustainable development at all stages of domestic and international policymaking.

Preterm birth
Baby born alive before 37 weeks of pregnancy are completed.

Price ceiling
A situation where a product is priced above or below the market equilibrium and a ceiling is established to limit how high the price of the product can be.

RDA
Recommended dietary allowance.

Sales tax
A tax that is levied on the sale of goods and services.

Small for gestational age
Foetuses or newborns that are small for gestational age (SGA) are smaller in size than normal for their gestational age; SGA is mostly defined as a weight below the 10th percentile for the gestational age.

Straight ingredients
Active ingredients (vitamin and minerals) and their forms for dry tableting.

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

Upstream policies
Manufacturer-friendly policies, i.e., policies that focus on improving fundamental social and economic structures in order to help people reach their full health potential.

Value added tax
VAT is a tax on the amount by which the value of an article has been increased at each stage of its production or distribution. It is levied on the added value that results from each exchange. It differs from a sales tax in that a sales tax is levied on the total value of the exchange.

Working capital
Money available to a company for day-to-day operations. Working capital measures a company's liquidity, efficiency and overall health. It gives an indication of whether local companies are able to produce a new product on their own.

Prepared by Pavithra Balasubramanian, Executive Assistant, *Sight and Life* with input from the editors

The Evidence Base

Reviewing the Evidence and Promoting the Adoption of Multiple Micronutrient Supplements

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Key messages

- Micronutrient deficiencies are common during pregnancies; they can have deleterious effects on multiple antenatal and perinatal outcomes.
- Evidence outlined in this paper shows that multiple micronutrient supplements (MMS) are a highly cost-effective way to prevent many adverse antenatal and perinatal outcomes.
- A Technical Advisory Group (TAG) has been created to further support the adoption and implementation of MMS, to advance knowledge and to serve as a communications hub to all MMS stakeholders.

The importance of micronutrients in pregnancy

Global pregnancy-related mortality and morbidity of both mothers and infants remain unacceptably high.[1,2] A key determinant of perinatal outcomes is maternal nutrition: a woman's diet during pregnancy should include an adequate intake of energy, protein, essential fatty acids and vitamins and minerals (micronutrients) to meet maternal and fetal needs. Micronutrients are essential for positive pregnancy outcomes because they play a critical role in the successive phases of fetal development, from the formation of the placenta, to the organ and neurological development, tissue deposition and body composition of the offspring.[3]

Programmatic responses to micronutrient deficiencies in pregnancy

Public health programs have long promoted dietary change and the use of dietary supplements – particularly iron and folic acid (IFA) – to prevent micronutrient deficiencies during pregnancy. However, those interventions alone are generally insufficient to fill the various micronutrient gaps that may exist. This prompted the United Nations Children's Fund (UNICEF), along with the World Health Organization (WHO) and the United Nations University, to develop the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) in 1999 to provide the Recommended Daily Allowance (RDA) of 15 micronutrients, including IFA, and offer a cost-effective strategy to address a broad spectrum of micronutrient deficiencies (**Box 1**). To date, more than 20 trials have used the UNIMMAP formulation or similar formulations in comparison with IFA alone. In 2016, WHO considered the 2016 Cochrane Review of 15 of these trials when developing its guidelines on antenatal care (ANC), but found that further evidence was needed on the benefits, risks and costs of MMS to universally recommend these supplements over IFA.[4,5] Subsequently, WHO reaffirmed its recommendation of IFA for routine use in pregnancy, with the caveat that countries with a high prevalence of nutritional deficiencies may want to consider MMS over IFA.

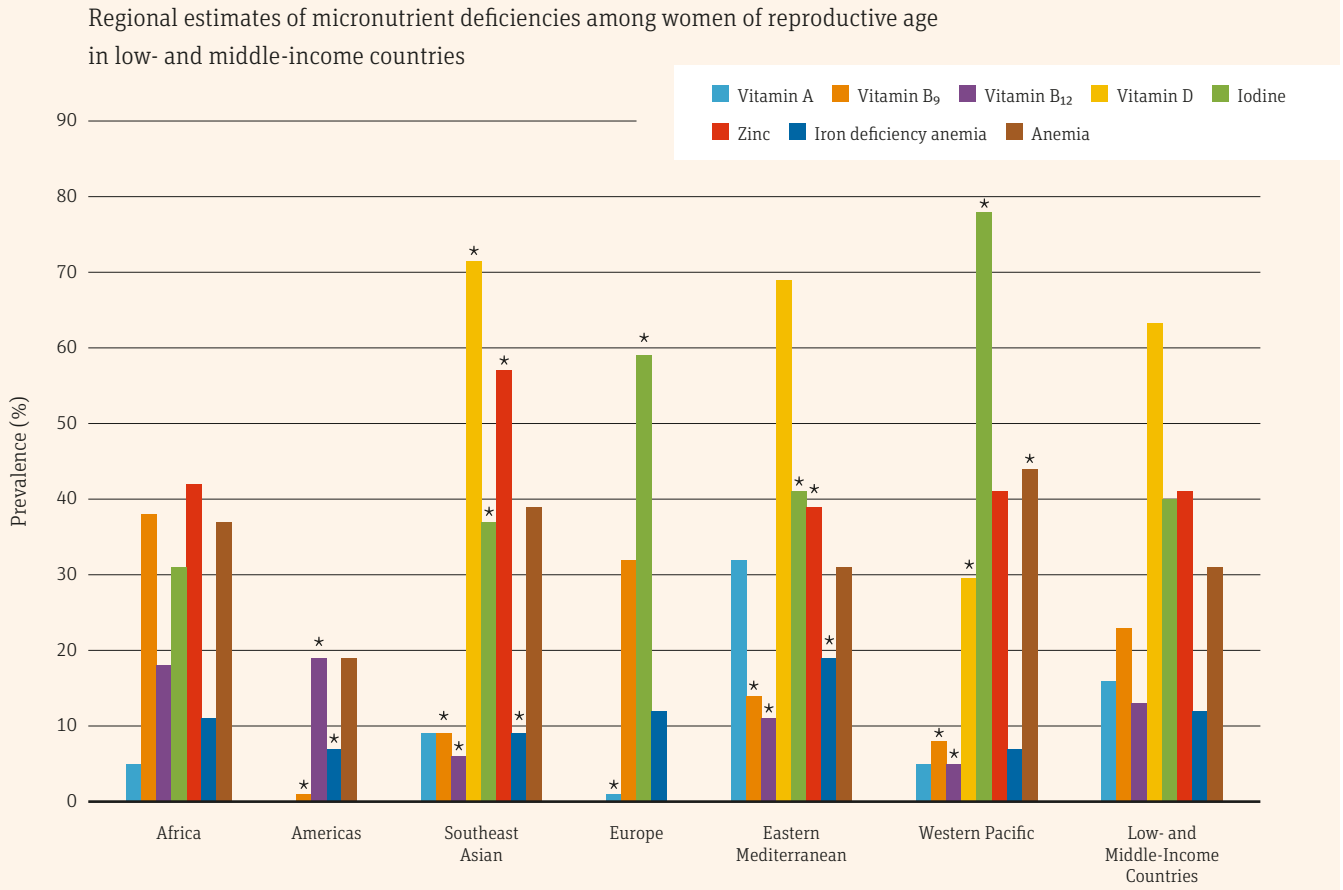
BOX 1: UNIMMAP Micronutrient formula

- Iron 30 mg
- Zinc 15 mg
- Copper 2 mg
- Selenium 65 µg
- Iodine 150 µg
- Vitamin A 800 µg retinol equivalent (RE)
- Vitamin B_1 1.4 mg
- Vitamin B_2 1.4 mg
- Vitamin B_3 (niacin) 18 mg
- Vitamin B_6 1.9 mg
- Vitamin B_9 (folic acid) 400 µg
- Vitamin B_{12} 2.6 µg
- Vitamin C 70 mg
- Vitamin D 200 IU
- Vitamin E 10 mg

MMS or IFA? Comparing the evidence

To help countries understand the WHO guidelines and assess emerging evidence around MMS during pregnancy, the New York Academy of Sciences (NYAS), with support from the Bill & Melinda Gates Foundation (BMGF), assembled a Task Force in 2017. In particular, the group aimed to assess: the prevalence of micronutrient deficiencies among women of reproductive age and pregnant

FIGURE 1: Global prevalence of micronutrient deficiencies among women of reproductive age



*Not representative (<3 countries) **Source:** Bourassa et al., 2019[7]

women; the prevalence of adverse birth outcomes; and the safety considerations, side effects, adherence and cost-effectiveness of MMS. To this end, the Task Force compiled the latest scientific evidence on the prevalence of micronutrient deficiencies from literature reviews of national and regional surveys. The Task Force used new meta-analyses published after the release of the 2016 WHO ANC Guidelines, inclusive of an individual person data (IPD) analysis.[6] This data reiterated the high prevalence of micronutrient deficiencies among pregnant women and women of reproductive age. For example, it reported that 63.2 percent of women of reproductive age in low- and middle-income countries (LMICs) are vitamin-D-deficient, 41.4 percent are zinc-deficient and 15.9 percent are vitamin-A-deficient (**Figure 1**).[7] These deficiencies put the mothers and their infants at increased risk of adverse birth outcomes. Indeed, the prevalence of adverse birth outcomes for both the infants and their mothers remains unacceptably high, as shown by evidence compiled by the Task Force: 34.2 percent of newborns in South Asia are small for gestational age, and maternal mortality is as high as 546 women per 100,000 live births in sub-Saharan Africa. Adequate nutrition, including the provision of micronutrients, is an important and well-documented way to mitigate these adverse effects.

"The prevalence of adverse birth outcomes for both the infants and their mothers remains unacceptably high"

The IPD meta-analysis reaffirmed the findings of the Cochrane Review that MMS during pregnancy can reduce the risk of low birth weight, small-for-gestational-age birth and preterm birth when compared with IFA. However, the IPD meta-analysis also deepened our understanding of the data by conducting several subgroup analyses based on individual data. This is in contrast to the Cochrane Review analysis, in which only the trial average (i.e., maternal body mass index or hemoglobin) is used in the subgroup analyses. As a result, the IPD meta-analysis was able to identify subgroups that could have greater benefit with MMS, including underweight women, anemic women and female infants whose mothers received MMS during pregnancy.

It was also important to the Task Force to examine the potential risk of the excess intake of micronutrients in order to address any potential safety concerns. An analysis performed by Gernand showed that there is relatively little risk associated with the excess intake of any of the micronutrients included in UNIMMAP.[8] Additionally, a 2019 analysis by Schulze et al.[9] shows that even with MMS, many women in Bangladesh remain micronutrient-deficient. Similarly, the Task Force examined the side effects and adherence that were reported by the trials comparing MMS with IFA because this would be an important consideration for the uptake of the intervention. While the trial data reported these outcomes in a variety of ways, there was no apparent change in the side effects or adherence rates between the two supplements across the trials.[7]

One of the concerns highlighted in the WHO ANC Guidelines was the increased cost of MMS compared with IFA. At the time of the WHO analysis, MMS was about three times the cost of IFA, using costs from UNICEF's supply catalogue. However, the costs have been dramatically reduced in recent years and will likely decline further as demand increases.[10] More importantly, MMS was shown to be a highly cost-effective intervention compared with IFA, even when allowing for the increased costs, as discussed in greater detail elsewhere in this *Sight and Life* special report.

"MMS was shown to be a highly cost-effective intervention compared with IFA"

Based on these findings, the Task Force concluded that countries having a high prevalence of maternal micronutrient deficiencies should consider using MMS instead of IFA to reduce the risk of micronutrient deficiencies and adverse birth outcomes. A more detailed account of the Task Force's conclusions was published in a special issue of the *Annals of the New York Academy of Sciences*. A number of articles in this *Sight and Life* Special Report introduce and expand upon these Task Force products.

The MMS Technical Advisory Group (TAG)

To consolidate the strong scientific basis established by the Task Force, UNICEF, with support from the BMGF, is currently

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The MMS Task Force, New York City, November 2017. From left to right, first row: Lindsay Allen, USDA; Katherine Dewey, UCD; Emorn Udomkesmalee, Mahidol University; Gilles Bergeron, NYAS; Alison Gernand, Penn State University; Kathleen Rasmussen, Cornell University. Second row: Chris Sudfeld, Harvard University; Megan Bourassa, NYAS; Lynnette Neufeld, GAIN; Robert Black, Johns Hopkins University; Saskia Osendarp, Micronutrient Forum; Saskia de Pee, WFP; Simon Cousens, LSHTM. Third row: Clayton Ajello, Vitamin Angels Alliance; Roland Kupka, UNICEF; Lars Ake Persson, LSHTM; Shams al Arafeen, ICDDR,B; Klaus Kramer, *Sight and Life*; Anuraj Shankar, Oxford University; Saima Ahmed, NYAS; Banda Ndiaye, Nutrition International.

implementing the MMS strategy in four country demonstration programs (Bangladesh, Burkina Faso, Tanzania and Madagascar). Separately, Vitamin Angels and Kirk Humanitarian, consistent with Task Force findings, are supporting a country demonstration program in collaboration with the Haitian Ministry of Population and Public Health. In conjunction with these efforts, NYAS is facilitating the global coordination of MMS actors via the creation of a TAG. Activities under the TAG include: the establishment of a communications hub to advise and document global program implementation; the production of generic technical reference materials that could be adapted to the context of adopting countries; and the provision of technical support when needed to address issues that emerge. The activities of the MMS TAG, since its creation in November 2018, are described below.

Technical reference materials and policy briefs for adopting countries

A series of technical reference materials was prepared to support countries aiming to adopt MMS in their ANC programs. The documents include generic pre- and in-service training materials for medical professionals and frontline health workers. In addition, FAQs and job aids are available. Further, country-specific policy briefs were prepared for Bangladesh and India, to explain in simple terms the potential benefits of MMS compared with IFA, taking into account the burden of maternal micronutrient deficiencies evident in these countries. These documents are available on the MMS TAG website (see below).

Identification of key implementation knowledge gaps

A research prioritization exercise using a methodology known as the Child Health and Nutrition Research Initiative identified key knowledge gaps in the implementation of MMS interventions. This approach involved bringing together a group of international experts to specify and rank which research questions most urgently need to be resolved in order for prenatal MMS interventions to be successfully implemented. Thirty-five consolidated research questions were identified and scored, yielding a ranking of 10 priority research topics. These range from strategies to increase antenatal care attendance and MMS adherence, to methods needed to identify populations more likely to benefit from MMS interventions, to issues such as the potential benefit of extending MMS through lactation.

Organization of an MMS product specification workshop

While the formulation of UNIMMAP is not currently being revisited, standard manufacturing specifications have not yet been proposed for the fabrication of MMS products. To address this, NYAS and the Micronutrient Forum co-hosted an expert technical consultation in November 2019 to generate an MMS product specification document that can be used by any manufacturer or buyer seeking to manufacture or procure an MMS product. This document described on page 102 of this Special Report is a broader quality manual on the production of MMS that includes variances in aspects such as packaging and unit count, which may vary between countries and manufacturers.

"Although the efficacy of MMS is now well established, the effectiveness of this intervention will only materialize if pregnant women adhere to the supplementation regimen"

Preparation of a systematic review on adherence to MMS

Although the efficacy of MMS is now well established, the effectiveness of this intervention to decrease adverse pregnancy and birth outcomes will only materialize if pregnant women adhere to the supplementation regimen. Adherence, defined as "the extent to which a patient's behavior matches the agreed recommendations from a healthcare provider,"appears to be poor.[11] Based on Demographic and Health Surveys data from 22 countries with IFA programs, coverage of IFA is often higher than 80 percent, but only 8 percent of the targeted recipients consume the recommended dose (180 tablets or more). The MMS TAG is currently carrying out a systematic review to assess the effectiveness of interventions designed to increase adherence to MMS in pregnant women. Results from this review will be available later in 2020.

Creation of an MMS website

A website platform (www.nyas.org/mms) was created to broadly represent MMS TAG activities to the public. The website is continually updated, and visitors can download key documents prepared by the expert group, consult a repository of information on the issue and request technical assistance in the implementation of MMS programs.

Conclusion

MMS offers a highly cost-effective intervention to improve a variety of antenatal outcomes. Promoted by actions such as the BMGF Goalkeepers Accelerator Initiative, the approach is rapidly gaining interest from national- and international-level stakeholders. Several technical issues remain to be answered, but this rapidly evolving field of knowledge is well served by the solid technical support provided by the MMS TAG and associated groups, as described in this *Sight and Life* Special Report.

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References

1 World Health Organization. Infant Mortality. Global Health Observatory (GHO) data. Internet: https://www.who.int/gho/child_health/mortality/neonatal_infant_text/en/ (accessed 7 January 2020).

2 Bongaarts J. WHO, UNICEF, UNFPA, World Bank Group, and United Nations Population Division Trends in Maternal Mortality: 1990 to 2015. Geneva: World Health Organization; 2015. Popul Dev Rev. 42(4):726. Internet: https://onlinelibrary.wiley.com/doi/full/10.1111/padr.12033 (accessed 9 January 2020).

3 Gernand AD, Schulze KJ, Stewart CP, West Jr KP, Christian P. Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. Nat Rev Endocrinol. 2016;12(5):274–89.

4 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016.

5 Haider B, Bhutta Z. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2017;4(4):CD004905.

6 Smith ER, Shankar AH, Wu LS-F, 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(11):e1090–e1100.

7 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019 May;1444(1):6–21.

8 Gernand AD. The upper level: examining the risk of excess micronutrient intake in pregnancy from antenatal supplements. Ann N Y Acad Sci. 2019; May 1;1444(1):22–34.

9 Schulze KJ, Mehra S, Shaikh S, Ali H, Shamim AA, Wu LSF, 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 Jul;149(7):1260–70.

10 Engle-Stone R, Kumordzie S, 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 May;1444(1):35–51.

11 Gomes F, Bourassa MW, Adu-Afarwuah S, Ajello C, Bhutta ZA, Black R, et al. Setting research priorities on multiple micronutrient supplementation in pregnancy. Ann NY Acad Sci. 2019. [Epub ahead of print; DOI: 10.1111/nyas.14267].

12 Sununtnasuk C, D'Agostino A, Fiedler JL. Iron+folic acid distribution and consumption through antenatal care: identifying barriers across countries. Public Health Nutr. 2016 Mar;19(4):732–42.

New Scientific Evidence on the Benefits of Maternal Multiple Micronutrient Supplements

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Key messages

- Maternal nutrition is critical for the health and wellbeing of mothers and babies. Inadequate nutrition in pregnancy, including micronutrient deficiencies, can lead to health problems for mothers, can cause babies to be born too soon or too small, and increases the babies' risk of death, poor health and suboptimal development.
- Multiple micronutrient supplements (MMS) – a combination of iron, folic acid and typically more than a dozen additional vitamins and minerals – addresses pregnant mothers' special nutritional needs.
- Global evidence from high-quality, randomized trials demonstrates that daily supplementation with MMS in pregnancy compared with supplementation with iron and folic acid (IFA) alone improves birth outcomes. Two systematic reviews and meta-analyses show that MMS reduces the risk of babies being born with a low birth weight by 12–14 percent, reduces the risk of small-for-gestational-age births by 3–8 percent and may reduce preterm birth by 5–7 percent.
- New analyses also show that MMS in pregnancy reduces the risk of mortality among female infants. All women and children were found to benefit, but the data suggests that MMS helps undernourished women especially.
- The evidence is clear: MMS is superior to IFA alone in supporting a positive pregnancy and a healthy infant. Policymakers and program developers should take swift action to implement MMS: it is safe, it is cost-effective, it helps mothers and it gives babies a healthy start to life.

Maternal nutrition is critical for a healthy pregnancy

Nutrition in pregnancy is important for mothers' health, as well as to support fetal growth and development. Inadequate diets – those without diversity of fruits and vegetables, animal-source foods and micronutrient-fortified foods – are common among pregnant women in low- and middle-income countries (LMICs). Such diets can lead to concurrent micronutrient deficiencies.[1] In pregnancy, micronutrient deficiencies tend to be more common and more severe because pregnant women and their developing babies have elevated nutrient requirements.[2] Studies estimate that roughly 38 percent of pregnant women in LMICs are anemic.[3] And a recent review of survey data found that – among women of reproductive age in LMICs – 63.2 percent were vitamin-D-deficient, 41.4 percent were zinc-deficient, 22.7 percent were folate-deficient and 15.9 percent were vitamin-A-deficient.[4]

> **"Micronutrient deficiencies in pregnancy can lead to health problems for mothers and cause babies to be born too small or too soon"**

Micronutrient deficiencies in pregnancy can lead to health problems for mothers and cause babies to be born too small or too soon.[5] In 2015, an estimated 20.5 million babies were born at low birth weight (< 2,500 g), and 91 percent of them were born in LMICs.[6] That same year, roughly 15 million babies were born preterm (before 37 weeks of gestation), of which 80 percent were born in Asia and sub-Saharan Africa.[7] Infants who are born low birth weight, preterm or small for gestational age (< 10th percentile of weight for their gestational age) are at increased risk of death.[8] And low birth weight infants face an elevated risk for a host of other concerns, including stunting and suboptimal cognitive and motor development, as well as cardiovascular disease and other noncommunicable diseases in adulthood.[9–11] Accordingly, supporting mothers' nutrition in pregnancy, including adequate micronutrient intake, is critical to addressing the large burden and consequences that flow from low birth weight, small-for-gestational-age birth and prematurity in LMICs.

Dr Fayaz Umrani, research associate at Aga Khan University, checking a young boy during his field visit in Hussain Bhambro village, Matiari district, Sindh province, Pakistan, on 1 December 2016. The Sindh province is participating in the SEEM project, a study of environmental enteropathy and malnutrition sponsored by the Gates Foundation and Aga Khan University. Through the project, field officers calculate the weight-for-height z-scores (WHZ) of newborns in the province and monitor their progress. Enrolled cases are tracked on a weekly basis and nutritional supplements are given to combat malnutrition.

MMS can help address the high micronutrient demands of pregnancy. A commonly used MMS formulation is the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP). UNIMMAP is a once-daily supplement that was developed at an expert consultation hosted by UNICEF in 1999 to give pregnant women their Recommended Daily Allowance (RDA) or Adequate Intake (AI) of 15 essential vitamins and minerals. The UNIMMAP supplement includes iron and folic acid, vitamin A, vitamin D, vitamin E, thiamin, riboflavin, niacin, vitamin B_{12}, vitamin B_6, vitamin C, zinc, iodine, copper and selenium.

Randomized trials and the 2016 WHO Antenatal Care Recommendations

Over the past two decades, more than 20 randomized trials have examined the effects of MMS (including UNIMMAP) on maternal and infant health outcomes as compared with IFA alone. These trials included a total of over 140,000 women, and were conducted across the globe.

In 2016, the World Health Organization (WHO) reviewed the evidence on MMS as part of the development process for the Recommendations on Antenatal Care for a Positive Pregnancy Experience.[12] At that time, the 2015 Cochrane Review – including 17 trials involving 137,791 women – was the primary source of summary evidence on the effects of MMS, showing that MMS reduced the risk of low birth weight, being born small for gestational age and stillbirth.[13] Despite these beneficial effects, WHO did not universally recommend MMS, citing gaps in the evidence and concerns about potential risks associated with MMS. But the recommendations noted that "policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMN [multiple micronutrient] supplements on maternal health to outweigh the disadvantages, and may choose to give MMN supplements that include iron and folic acid."[12]

Of note, the 2016 WHO Antenatal Care Guidelines did recommend other nutrition interventions including universal IFA supplementation, as well as calcium supplementation in contexts where calcium food intake is low.[12] They also recommended nutritious food supplementation (i.e., balanced energy and protein supplements) in places where more than 20 percent of women of reproductive age are underweight (body mass index < 20 kg/m²).[12]

New evidence demonstrates clear benefits of MMS

Since the 2016 WHO Guidelines were released, additional research has confirmed that MMS reduces the risk of being born low

Fozia Arbab (right), research assistant at Aga Khan University, measuring the weight of severely malnourished 6-month-old Ghayan Chand during the field work in Hussain Bhambro village, Matiari district, Sindh province, Pakistan, on 1 December 2016

Zayada Jemal, health extension worker at Germama Health Post, preparing to measure the weight of Zebiba Yusuf's 6-month-old baby, Moaz Behari, as Zebiba's other children look on excitedly in Silte, Gurage Zone, Ethiopia, on 26 July 2016

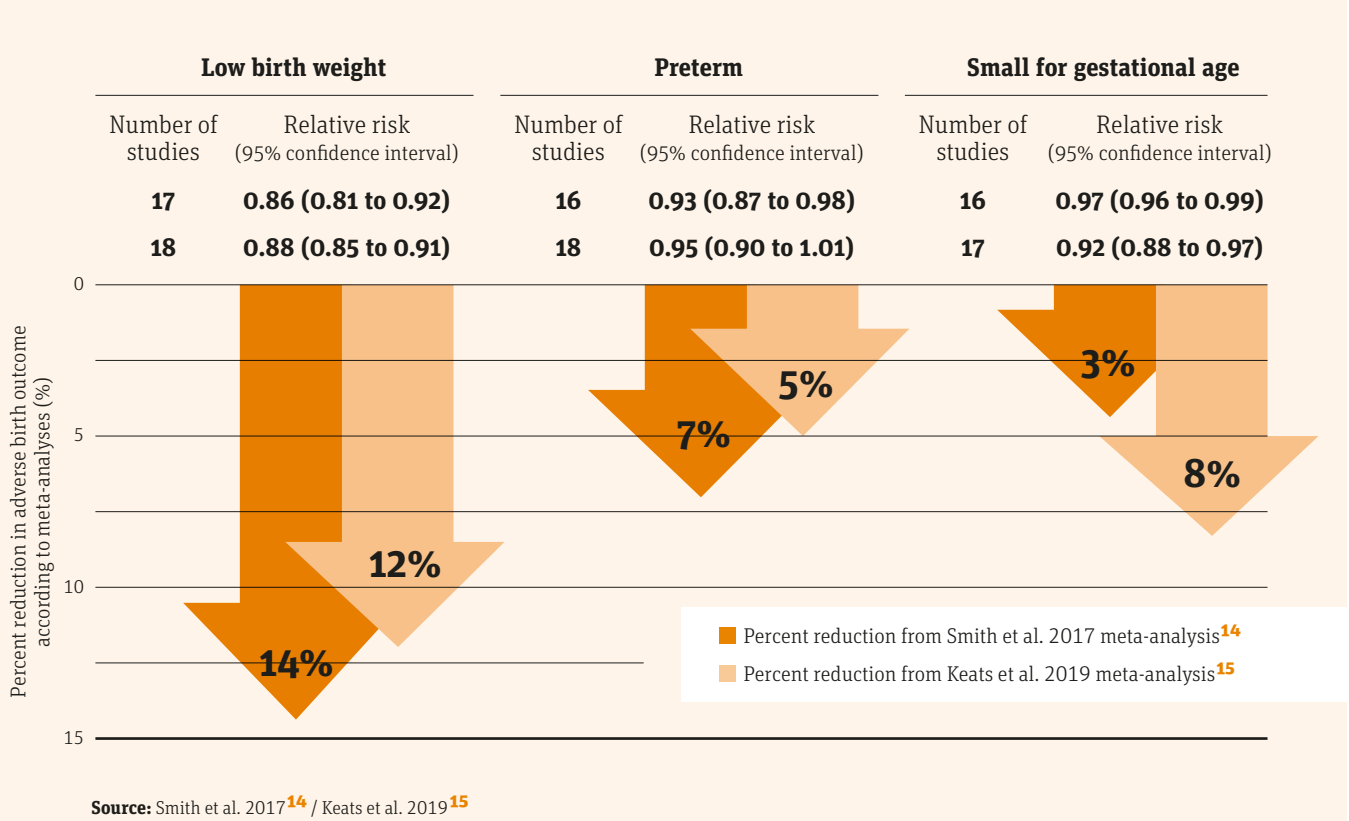
birth weight and small for gestational age, and also revealed additional benefits for subgroups of mothers and infants. This new evidence includes new randomized trials, an individual patient data meta-analysis and an updated Cochrane Review, which are summarized below.

In response to the 2016 WHO Guidelines, investigators who had conducted randomized trials of MMS came together to investigate more systematically the efficacy and safety of MMS. More than 30 scientists from around the world collaborated on an 'individual patient data meta-analysis,' a method that is considered to be the gold standard for summarizing scientific evidence. The analysis included data from 17 randomized trials that analyzed data from 112,000 pregnant women in 14 countries (Burkina Faso, Ghana, Guinea-Bissau, Malawi, Niger, Tanzania, Zimbabwe, Mexico, Bangladesh, China, India, Indonesia, Nepal and Pakistan). Overall, this meta-analysis was consistent with the 2015 Cochrane Review; it found that MMS – as compared with IFA alone – improves birth outcomes. On average, the studies showed that MMS reduced the risk of: low birth weight by 14 percent, preterm birth by 7 percent, being born small for gestational age by 3 percent and stillbirth by 8 percent (see **Figure 1**).[14] Furthermore, it found that MMS is especially beneficial for undernourished women. For example, women who were anemic or were too thin at the start of pregnancy saw even greater improvements in birth outcomes when taking MMS. The study also showed that the survival of baby girls improved when their mothers took MMS rather than IFA. Importantly, the meta-analysis did not find any evidence of increased risk of mortality or adverse birth outcomes related to MMS, and this was consistent across all subgroups of women (e.g., anemic versus non-anemic women, underweight versus non-underweight women). The meta-analysis therefore allayed the concerns offered by the 2016 WHO Guidelines regarding potential risks associated with MMS.

"The meta-analysis allayed the concerns offered by the 2016 WHO Guidelines regarding potential risks associated with MMS"

In March 2019, the Cochrane Review of MMS trials was revised.[15] The updated version included data from three new trials and corrected minor errors that had appeared in the previous versions. Specifically, the study reviewed 20 randomized trials that compared MMS with iron supplements or iron with folic acid, and the trials captured data from 141,849 pregnant women. MMS was found to provide a robust and consistent 12 percent reduction in

FIGURE 1: Two recent meta-analyses summarize data from high-quality randomized trials and show that MMS reduces the risk of babies being born too small (low birth weight or small for gestational age) or too soon (preterm)



Source: Smith et al. 2017[14] / Keats et al. 2019[15]

A group of *Agogos* (meaning 'grandparents') help a mother bring home her newborn baby from Ekwendeni Mission Hospital, in the Mzimba district, Malawi. *Agogos* are a community group that have been trained through Ekwendeni Mission Hospital to advise pregnant women on proper health practices during pregnancy. They encourage women to get early antenatal care and to arrange for delivery to take place at a health center or hospital.

the risk of having a baby with a low birth weight and an 8 percent reduction in the risk of having a small-for-gestational-age baby (see **Figure 1**). The authors also concluded that MMS probably reduced the risk of preterm birth by about 5 percent.

In order to synthesize and interpret the new evidence for policymakers and healthcare providers, the New York Academy of Sciences convened a Multiple Micronutrient Supplementation in Pregnancy Task Force. The Task Force consisted of nutrition and maternal health experts, scientists researching micronutrients in pregnancy, donors, key development partners and interested country-level decision makers. The Task Force took on four areas of work: (**a**) it conducted additional analyses to quantify the benefits of MMS and to check for any associated risks; (**b**) it characterized the contexts where adoption of MMS would be warranted based upon mothers' diets, prevalence of deficiencies, available healthcare services, costs and cost-effectiveness; (**c**) it explored the practical considerations of MMS introduction, such as procurement and promotion; and (**d**) it developed an information-sharing strategy regarding the introduction and use of MMS. The Task Force recently released its findings in a special issue on MMS in the Annals of the New York Academy of Sciences.[4, 16–18] This work concluded that the use of a daily MMS is overall beneficial, does not increase the risk of adverse effects or result in excess micronutrient intake, has a number of additional benefits for mortality reduction and birth outcomes compared with IFA,[4] and can be a cost-effective intervention for pregnant women in LMICs.[14]

"The use of a daily MMS is overall beneficial and does not increase the risk of adverse effects"

Ongoing evidence efforts

Following this first phase of work, a subgroup of the Task Force now serves as a Technical Advisory Group (TAG) to support the growing momentum and interest in the distribution of MMS by NGOs, funders and governments. The TAG will support efforts by providing information, coordination services and advice regarding the introduction of MMS in various contexts. Specifically, the TAG will: (**a**) be a coordinating body for groups seeking to promote or fund the distribution of MMS; (**b**) provide ongoing technical guidance regarding all things related to MMS; (**c**) provide partners with technical briefs, roadmaps for introduction in countries and other documents as needed; and (**d**) organize collaborative efforts to share work and information.

The TAG held its first meeting in February 2019, and it developed a website to serve as an up-to-date resource. In addition, the TAG conducted a Child Health and Nutrition Research Initiative

exercise to identify priority research questions related to MMS; that effort was recently published.[19] The TAG is currently conducting a systematic review of barriers to, and enablers of, adherence to an MMS regimen in pregnancy. The TAG, together with the Micronutrient Forum, has co-organized a workshop to develop a global MMS product specification for manufacturers; the meeting was held in Washington, DC, in November 2019.

A call to action

The scientific evidence is clear: MMS is superior to IFA to give women and their babies a positive pregnancy experience and healthy start to life. Making the switch from IFA alone to comprehensive MMS is a solution that is readily available to be delivered at scale through established delivery channels for supplements in pregnancy. The global community must move swiftly from evidence to action to support healthy mothers and babies.

"MMS is superior to IFA to give women and their babies a positive pregnancy experience and healthy start to life"

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References

1 Jiang T, Christian P, Khatry SK, Wu L, West KP, Jr. Micronutrient deficiencies in early pregnancy are common, concurrent, and vary by season among rural Nepali pregnant women. J Nutr. 2005;135(5):1106–12.

2 King JC. Physiology of pregnancy and nutrient metabolism. Am J Clin Nutr. 2000;71(5 Suppl):1218S–25S.

3 Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob Health. 2013;1(1):e16–25.

4 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6–21.

5 Black RE. Micronutrients in pregnancy. Br J Nutr. 2001;85 Suppl 2:S193–7.

6 Blencowe H, Krasevec J, de Onis M, Black RE, An X, Stevens GA, 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.

7 Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health. 2019;7(1):e37–e46.

8 Katz J, Lee AC, Kozuki N, Lawn JE, Cousens S, Blencowe H, et al. Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. Lancet. 2013;382(9890):417–25.

9 Christian P, Lee SE, Donahue Angel M, Adair LS, Arifeen SE, Ashorn P, et al. Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. Int J Epidemiol. 2013;42(5):1340–55.

10 Fall CH. Fetal malnutrition and long-term outcomes. Nestlé Nutr Inst Workshop Ser. 2013;74:11–25.

11 Sania A, Sudfeld CR, Danaei G, Fink G, McCoy DC, Zhu Z, et al. Early life risk factors of motor, cognitive and language development: a pooled analysis of studies from low/middle-income countries. BMJ Open. 2019;9(10):e026449.

12 World Health Organiziation. WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience. WHO Guidelines Approved by the Guidelines Review Committee. Geneva: WHO; 2016.

13 Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2015(11):CD004905.

14 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(11):e1090–e1100.

15 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;3:CD004905.

16 Black RE, Dewey KG. Benefits of supplementation with multiple micronutrients in pregnancy. Ann N Y Acad Sci. 2019;1444(1):3–5.

17 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.

18 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.

19 Gomes F, Bourassa MW, Adu-Afarwuah S, Ajello C, Bhutta ZA, Black R, et al. Setting research priorities on multiple micronutrient supplementation in pregnancy. Ann N Y Acad Sci. 2019. [Epub ahead of print; doi: 10.1111/nyas.14267].

Cost-Effectiveness of Replacing Iron-Folic Acid with Multiple Micronutrient Supplements

Assessing the costs, impacts, and cost-effectiveness in the context of pregnant women in Bangladesh

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Key messages

- The consumption of multiple micronutrient supplements (MMS) during pregnancy offers additional benefits compared with iron-folic acid (IFA) supplementation, but MMS tablets contain more ingredients and hence are likely to be more expensive.
- Replacing IFA with MMS in Bangladesh (assuming current rates of IFA coverage, 180 tablets per covered pregnancy and 100 percent adherence) could avert over 7,600 deaths and 16,000 cases of preterm birth annually.
- The estimated cost per death averted was ~US$183, and the estimated cost per disability-adjusted life year (DALY) averted ranged from ~US$3.50 to ~US$13.30, depending on whether the analysis accounted for subgroup effects.
- This policy change would cost-effectively save lives and reduce life-long disabilities.
- Improvements in program delivery and supplement adherence will increase the cost-effectiveness of shifting to MMS.

Introduction

Adequate nutrition during pregnancy is essential for the health of mothers and their infants.[1] WHO recommends the provision of iron-folic acid supplements (IFA) as part of routine antenatal care, and IFA distribution programs are almost universally in place.[2] Yet, deficiencies of other micronutrients are also prevalent in low- and middle-income countries, and affect maternal nutrition and fetal growth and development.[3] Currently, the choice to distribute multiple micronutrient supplements (MMS) instead of IFA is left to national decision-makers (**Box 1**).

> **"Currently, the choice to distribute multiple micronutrient supplements (MMS) instead of IFA is left to national decision-makers"**

BOX 1: Decoding MMS-IFA cost parity and what it means for policymakers

It is generally expected that MMS tablets are and will be more expensive than IFA tablets, primarily because of the larger number of ingredients that they contain. Indeed, this has been the case as recently as 3 years ago. Over the past few years, however, as a result of significant efforts by nongovernmental organizations and others to negotiate better prices for MMS tablets, the cost of IFA and MMS produced to similar standards of international quality has reached parity. When manufactured at a volume of 3–5 million bottles, and packaged in 180-count bottles, MMS is currently avai-lable at 1 US cent per tablet, which is roughly the same as the current market price for IFA tablets.

It is true that IFA has not benefited from the same rigorous international negotiations to lower its price, and there is no guarantee that today's relative price reality will continue into the future. IFA prices may well fall, due either to reduced demand or to increased efforts to negotiate lower prices, or both. Undeniably, the MMS tablets have higher ingredient costs, though some small trade-offs may be offered by including less iron in them than is included in IFA tablets. Countries may also choose local production of MMS at a volume

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Adequate nutrition during pregnancy is essential for the health of mothers and their infants

not providing the benefits of economy of scale, hence leading to a more expensive product. As a result, it is difficult to predict what the costs of MMS or IFA tablets will be in the future, and even small differences in per tablet prices will translate into large differences in total tablet costs at the country level. What we do know is that scale economies in production have very significant impacts on tablet prices, as do coordinated and sustained negotiations to secure lower prices.

However, the price of MMS might not always be the only factor that will determine the wisdom of this intervention. Overall cost-effectiveness of MMS reflects the positive health benefits of MMS beyond the expected effects of IFA. These benefits depend on the number of pregnant women who actually consume the recommended regimen of either tablet. Poor adherence is a factor impeding the cost-effectiveness of antenatal services and products generally, so switching from IFA to MMS offers countries an opportunity to rebrand their efforts and reinvest in distribution models so that the benefits of the MMS will accrue, even if prices change such that each MMS tablet costs slightly more than an IFA tablet.

The bottom line is that, while we are currently in a situation where MMS and IFA tablets have cost parity, the analysis presented in this article suggests that the shift from IFA to MMS is worth doing even if MMS tablets are considerably more expensive than IFA tablets.

To help guide these decisions, we estimated the impacts, costs and cost-effectiveness of hypothetically replacing IFA supplements with MMS for 1 year in the context of an ongoing program to deliver supplements to pregnant women in Bangladesh. We first modeled a scenario with current program coverage, and assuming 100 percent adherence and no tablet 'wastage' (i.e., all purchased tablets are consumed and 'count' toward health benefits). We then extended the analysis to introduce the costs of programmatic transitions and possible tablet distribution scenarios.

Methods

Calculations were conducted separately for four strata (urban, male child; urban, female child; rural, male child; rural, female child) and took into account different program coverage (60.7 percent for the urban strata and 47.4 percent for the rural strata).[4] The results for the expected benefits and costs for each stratum were then added up to produce national-level estimates of benefits, costs and cost-effectiveness. Calculated benefits included: cases of mortality and poor birth outcomes averted, years of life lost (YLL) and years lived with disability (YLD) averted, and disability-adjusted life years (DALYs) averted. DALYs provide an estimate of the burden associated with living with different illnesses, diseases, and other physical and mental impairments.

Demographic information regarding the size, age structure and urban/rural distribution of the population was taken from the Lives Saved Tool, a tool designed to estimate the impacts of healthcare investments on saving children's lives.[5] The Lives Saved Tool also provided estimates of the rates of stillbirths, neonatal and infant mortality, and birth outcomes (low birth weight [LBW], small for gestational age [SGA] and preterm).

We applied results from a meta-analysis of the additional impact of MMS compared with IFA to estimate overall effects and effects among specific subgroups.[6] For example, a reduction in infant mortality was observed among female, but not male, children. We calculated DALYs using a standard methodology,[7–9] as described previously.[4]

We calculated the cost of replacing IFA with MMS based on the differences in ingredient costs of MMS tablets compared with IFA tablets. We estimated that producing MMS tablets using the UNIMMAP (United Nations International Multiple Micronutrient

Antenatal Preparation) formula would cost ~US$0.004878 more per tablet than producing the currently available IFA tablets (30–60 mg iron and 400 µg of folic acid); this translates into a marginal increase in tablet costs of US$4,878 per million tablets.

The total number of tablets consumed was estimated by calculating the total number of annual births as the sum of live births and stillbirths and then multiplying this number by program coverage and the assumed number of tablets consumed per pregnancy (180 tablets). Current recommendations promote the consumption of IFA throughout pregnancy, and the exact dose–response relationship between the number of tablets consumed and the expected health impact is unknown for both MMS and IFA. Thus, for this analysis, 180 tablets/person was identified as a minimum threshold.

Programmatically, transitioning from IFA to MMS tablets may take several years and may require substantial financial and human resources. Based on consultations with country representatives, we report estimates of the expected costs of the planning, training and other activities that would be required for this shift, as well as the possible timing of region-specific rollout activities.

Finally, IFA programs face many challenges; coverage rates are generally well below 100 percent, and even among women who are covered, many do not consume at least 180 tablets per pregnancy. 'Oversupplying' of MMS (for example, because of low adherence or the purchase of tablets in excess of programmatic needs) is likely to be more expensive than the same program performance challenge for IFA. We address these issues by examining alternative models of tablet distribution.

Results

Population characteristics and baseline burden of natural outcomes

The baseline information required to estimate the effects of shifting from IFA to MMS, for urban and rural populations in Bangladesh, is presented in **Table 1**.

Estimated tablet costs

At current coverage levels (~50 percent, nationally), the marginal cost of shifting from IFA to MMS for 1 year would be US$1.4 million, assuming the purchase of 180 tablets per covered pregnancy (**Table 2**).

Predicted effects and cost-effectiveness for mortality and birth outcomes

The predicted additional benefits and cost-effectiveness of replacing IFA with MMS during pregnancy in Bangladesh are presented in **Table 3**. In 1 year, ~35,000 cases of LBW and over 7,500 deaths would be averted by the shift. The predicted cost per death averted under current coverage ranged from ~US$239 (infant mortality, accounting for subgroup effects) to ~US$785

TABLE 1: Population characteristics and baseline burden of natural outcomes for Bangladesh in 2018, assuming current coverage of IFA tablets in pregnancy

	Urban	Rural
Total population (*n*)	66,217,830	99,776,312
Population of age 0–4 years (*n*)	4,966,020	10,072,979
Total annual births (*n*)	1,101,038	1,898,474
Male births (%)	51.2	51.2
Maternal anemia (%)	31.4	43.2
Maternal underweight (%)	16	28
Presence of a skilled birth attendant (%)	75.7	32.4
Life expectancy at birth for males (years)	71.8	70.6
Life expectancy at birth for females (years)	75.1	74.1
Stillbirth rate (deaths per 1,000 live births)	4.78	21.17
Early neonatal mortality rate (deaths per 1,000 live births)	10.87	21.76
Neonatal mortality rate (deaths per 1,000 live births)	12.94	25.91
Infant mortality rate (deaths per 1,000 live births)	24.5	34.4
Low birth weight (%)	20.93	21.66
Very low birth weight (%)	0.42	0.43
Preterm and SGA births (%)	2.57	2.68
Preterm and AGA births (%)	10.85	10.85
Term and SGA births (%)	30.15	31.46
Term and AGA births (%)	56.43	55.01

For definitions, data sources and details, see Engle-Stone et al. 2019[4] **AGA:** appropriate for gestational age; **SGA:** small for gestational age

TABLE 2: Estimated costs of replacing IFA tablets with MMS tablets in Bangladesh, assuming current coverage

	Urban	Rural
Annual births: live births + stillbirths (*n*)	1,106,305	1,938,665
Proportion of births covered (%)	60.7	47.4
Number of tablets consumed per covered birth (*n*)	180	180
Total number of tablets distributed annually (*n*)	120,874,884	165,406,898
Total annual incremental tablet cost (US$)	589,668	806,910

For definitions, data sources and details, see Engle-Stone et al. 2019[4]

TABLE 3: Marginal benefits of replacing IFA tablets with MMS tablets for pregnant women in Bangladesh*

		Number of cases averted annually	Cost in US$ per case averted
Stillbirths	Overall effect	1,780	784.61
	Subgroups effects	n/a	n/a
Early Neonatal Mortality	Overall effect	0	n/a
	Subgroup effects (infant sex)	1,809	772.21
Neonatal Mortality	Overall effect	0	n/a
	Subgroup effects (infant sex)	2,307	605.41
Infant Mortality	Overall effect	0	n/a
	Subgroup effects (infant sex and presence of skilled birth attendant)	5,848	238.79
Low Birth Weight	Overall effect	35,452	39.39
	Subgroup effects (maternal anemia)	37,869	36.88
Very Low Birth Weight	Overall effect	1,300	1,074.37
	Subgroup effects	n/a	n/a
Very Preterm Birth	Overall effect	3,472	402.21
	Subgroup effects (maternal underweight)	1,804	774.33
Preterm Birth	Overall effect	16,437	84.97
	Subgroup effects (maternal underweight)	17,112	81.62
SGA Oken	Overall effect	13,465	103.72
	Subgroup effects (n/a)	13,710	101.87
SGA Intergrowth	Overall effect	22,441	62.23
	Subgroup effects	n/a	n/a
Total mortality (Stillbirths + infant mortality)	Varied (overall effect for stillbirth; subgroup effects for infant sex and skilled birth attendant for infant mortality)	7,628	183.08

*Estimates are based on applying the overall effects or subgroup effects reported by Smith et al. 2017[6] ('n/a' indicates that effects did not differ by subgroup); effects were applied to population data derived from the Lives Saved Tool[5] For definitions and details, see Engle-Stone et al. 2019[4] **SGA:** small for gestational age

(stillbirths, overall effect), or ~US$184 per death averted in total (stillbirths + infant mortality). For adverse birth outcomes, the cost per case averted ranged from ~US$37 per case of LBW averted (accounting for subgroup effects) to ~US$1,074 per case of very low birth weight averted (overall effect).

The predicted numbers of YLL, YLD and DALYs averted by shifting from IFA to MMS are presented in **Table 4**. Total predicted DALYs averted ranged from ~105,400 (DALYs estimated using YLL + preterm YLD, overall effect of MMS) to ~385,600 (DALYs estimated using YLL + LBW YLD, accounting for subgroup effects). The predicted cost per DALY averted was ~US$8–13 for overall effects and US$4–5 when accounting for subgroup effects. By comparison, Horton and Levin (2016) report cost per DALY averted for treatment of severe malaria as ~US$8 and for community-based management of severe malnutrition as ~US$40–50.

Addressing programmatic transitions and adherence

Results reported to this point focus on an instantaneous, waste-free, 1-year shift from IFA to MMS tablets. In reality, transitions

TABLE 4: Marginal benefits and cost-effectiveness of replacing IFA with MMS for pregnant women in Bangladesh

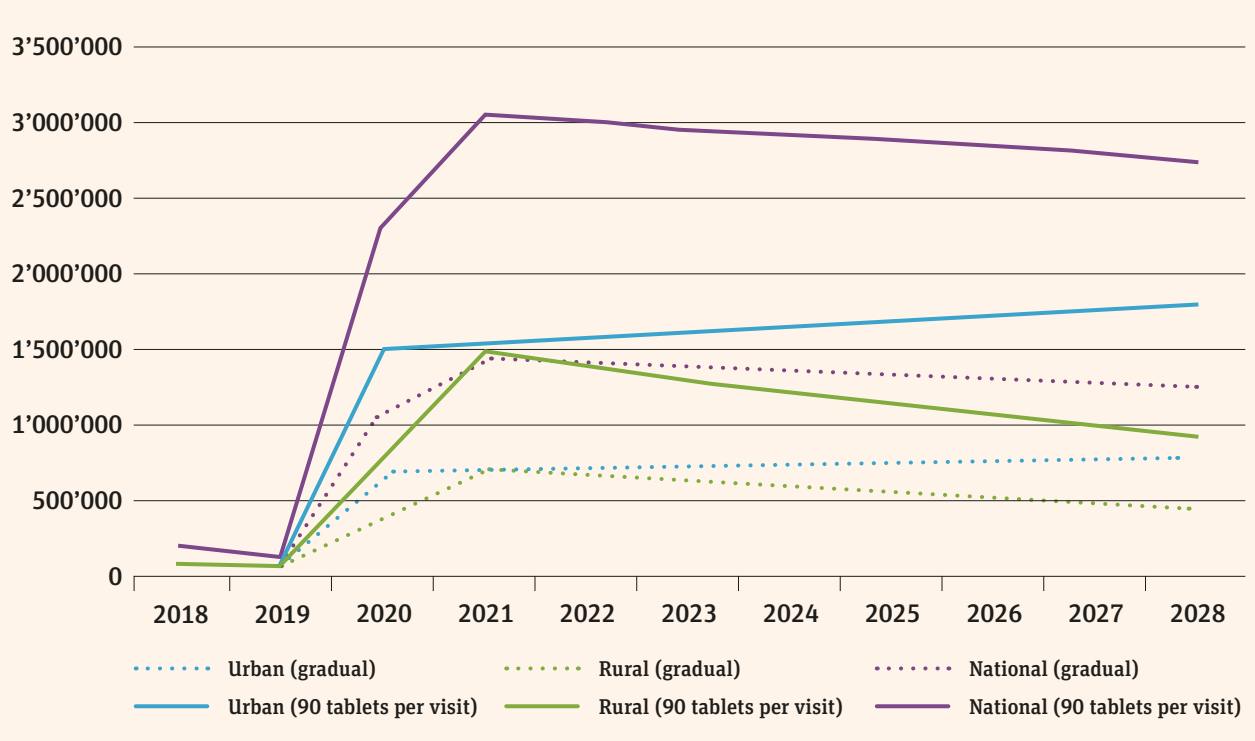
		Number of YLL, YLD or DALYs averted	Cost in US$ per YLL, YLD or DALY averted
YLL (mortality)	Overall effect	58,142	24.02
	Subgroup effects (multiple)	254,708	5.48
YLD (low birth weight)	Overall effect	122,486	11.40
	Subgroup effects (maternal anemia)	130,861	10.67
YLD (preterm birth)	Overall effect	47,250	29.56
	Subgroup effects (maternal underweight)	49,067	28.46
Total (mortality + low birth weight)	Overall effect	180,628	7.73
	Subgroup effects (multiple)	385,569	3.62
Total (mortality + preterm)	Overall effect	105,392	13
	Subgroup effects (multiple)	303,775	4.60

For definitions, data sources and details, see Engle-Stone et al. 2019[4] **DALY:** disability-adjusted life year; **YLD:** years lived with disability; **YLL:** years of life lost

will take several years and may be done sequentially across geographic areas. When the transitions are complete, tablet delivery models will not likely deliver exactly 180 MMS tablets to each pregnant woman. Finally, women may not consume all acquired tablets: adherence has been a long-standing challenge for IFA programs, and will likewise need attention for MMS programs. These transition costs and program management challenges will affect the cost-effectiveness of IFA to MMS shifts, even if the health benefits are similar for women receiving 180 tablets or *fewer* than 180 tablets.

We used 2014 Demographic and Health Survey (DHS) data to estimate the number of tablets that might actually be distributed, based on antenatal clinic attendance. In urban areas, 10.5 percent of women did not visit any antenatal clinic during their most recent pregnancy, 12.2 percent visited once, 31.5 percent visited two or three times, and 45.5 percent visited four times. For rural areas, the percentages per visit category were 25.0 percent, 19.9 percent, 28.6 percent and 26.1 percent, respectively. Women making at least two visits to clinics and receiving 90 tablets each visit would receive 180 tablets – the assumed minimum threshold for the dosage that underlies all estimates of the expected health and birth outcome impacts presented above. Women visiting antenatal clinics three or four times would receive 'surplus' tablets according to this threshold.

FIGURE 1: Marginal costs (US$) over time and under alternative tablet distribution scenarios



"Adherence has been a longstanding challenge for IFA programs and will likewise need attention for MMS programs"

Figure 1 depicts the costs of a hypothetical gradual rollout of the transition to MMS tablets over time. The scenario assumes that the replacement of IFA with MMS occurs in urban areas first and takes ~1 year; distribution in rural areas follows and is completed by 2021.

The lines represent the program costs over time, accounting for startup costs (faced in the first year, and before the distribution of any MMS tablets) and the gradual increase in tablet purchase costs as MMS tablets are phased in. Distribution costs fall over time in rural areas but increase in urban areas, reflecting an (assumed) urbanization rate of 5 percent per year.

The dashed lines (one each for rural and urban areas, and for the nation) reflect total costs assuming exactly 180 tablets are purchased and distributed per covered pregnancy, and the solid lines depict the estimated tablet costs using antenatal care attendance as a proxy for tablet purchase. Transition costs in 2019 are similar for both scenarios. However, once rollout begins, the marginal costs of shifting from IFA to MMS are significantly higher in the second scenario (solid lines), because more than half of all covered pregnant women are visiting antenatal clinics more than twice and hence receiving more than 180 tablets.

Conclusions

The expected benefits of the shift from IFA to MMS are substantial, in terms of reducing both mortality and undesirable birth outcomes. If all pregnant women consumed a regimen of 180 tablets during the course of their pregnancies, shifting from IFA to MMS would save over 15,000 young lives and ~30,000 cases of preterm birth in Bangladesh from a 1-year switch. Even at current coverage, we estimate that over 7,500 lives would be saved and more than 15,000 cases of preterm birth would be averted.

"The expected benefits of the shift from IFA to MMS are substantial, in terms of reducing both mortality and undesirable birth outcomes"

The costs associated with shifting from IFA to MMS will be significant if the MMS tablets are more expensive than IFA tablets (an estimated 35 percent more costly in this analysis, based on different ingredient costs) and, in the context of Bangladesh, hundreds of millions of tablets would be required each year. Under these assumptions, the complete and immediate shift from IFA to MMS for 1 year in Bangladesh, given current coverage levels, would cost ~US$1.4 million, which translates into between US$3.62 and US$13.25 per DALY averted and ~US$184 per death averted. This cost-effectiveness estimate of the IFA to MMS shift for averting child mortality is quite favorable when compared with other mortality-averting policy options: for example, providing pneumococcal vaccines to infants may cost less than US$10 per death averted, but most other investments are expected to be much less cost-effective (e.g., over US$1,000 per death averted for some maternal and child health interventions).[11] As illustrated in a scenario for which tablet distribution costs were estimated using data on antenatal care attendance (rather than assuming 180 tablets per pregnancy), cost-effectiveness will be impacted if adherence is low or when tablet distribution models undersupply or oversupply the MMS tablets. Shifting to MMS increases the potential impact of maternal supplementation during pregnancy. Strong performance of the delivery platform, including managing supplies and adherence, will increase both the impacts and the cost-effectiveness.

"This cost-effectiveness estimate of the IFA to MMS shift for averting child mortality is quite favorable when compared with other mortality-averting policy options"

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References

1 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016.

2 World Health Organization, United Nations Children's Fund (UNICEF), United Nations University. Iron deficiency anaemia – assessment, prevention, and control: A guide for programme managers. Geneva: World Health Organization; 2001.

3 Müller O, Krawinkel M. Malnutrition and health in developing countries. CMAJ. 2005;173(3):279–86.

4 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.

5 Walker N. The Lives Saved Tool in 2013: new capabilities and applications. BMC Public Health. 2013;13(Suppl. 3).

6 Smith E, Shankar A, Wu L, 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(11):e1090–e1100.

7 Fox-Rushby J, Hanson K. Calculating and presenting disability-adjusted life years (DALYs) in cost-effectiveness analysis. Health Policy Plan. 2001;16(3):326–31.

8 Murray C, Lopez A, World Health Organization, World Bank, Harvard School of Public Health. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary. Geneva: World Health Organization; 1996.

9 Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2016 (GBD 2016) Disability Weights. Seattle, USA: Institute for Health Metrics and Evaluation (IHME); 2017.

10 World Health Organization. Guideline: daily iron and folic acid supplementation in pregnant women. Geneva: WHO; 2012.

11 Horton S, Levin C. Cost-effectiveness in interventions for reproductive, maternal, neonatal, and child health. In: Black R, Laxminarayan R, Temmerman M, Walker N, editors. Reproductive, Maternal, Newborn, and Child Health Disease Control Priorities. Washington, DC: World Bank; 2016.

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Experience from the Field

Experiences Supporting the Introduction and Implementation of Multiple Micronutrient Supplementation for Pregnant Women Globally

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Key messages

- Given the clear evidence that antenatal multiple micronutrient supplementation (MMS) is superior to iron and folic acid supplementation (IFA) for improving pregnancy outcomes and preventing maternal anemia, Vitamin Angels (VA) and other stakeholders are exploring how to introduce and scale MMS for pregnant women effectively and efficiently in the context of the current World Health Organization (WHO) guidelines.
- VA's global MMS campaign has made meaningful progress towards the introduction and implementation of MMS programs globally.
- Different approaches have been used by VA to balance the need to reach more women, especially the most vulnerable, with the long-term goal of ensuring effective introduction and scaling of MMS as a sustainable component of existing nutrition services.

MMS landscape

Micronutrient deficiencies are a major public health problem, especially during pregnancy on account of the increase in nutrient requirements that occurs at this time.[1] MMS for pregnant women has been demonstrated to be superior to IFA supplementation as an effective, safe and cost-effective intervention that reduces maternal anemia and improves pregnancy outcomes.[2,3] While WHO continues to recommend IFA, it has stated that, where appropriate, governments could begin to explore the use of MMS in their national programs.[4] Given this guidance, and taking into account the reality that existing IFA programs struggle to reach women and achieve adherence to the prescribed regimen, VA initiated its global MMS campaign to: (**1**) raise awareness of the benefits of MMS use; (**2**) advocate for the use of MMS in place of IFA and support policy change within large healthcare systems; and (**3**) reach more pregnant women effectively and efficiently with MMS – especially those who are hardest to reach. VA has focused its efforts on conceptualizing and applying a variety of approaches to balance the urgent need to reach more women with the long-term goal of ensuring the effective and sustainable introduction and scaling of MMS within programs globally.

> **"VA's model is premised on the reality that national health services are unable to reach all eligible beneficiaries"**

Role of Vitamin Angels

VA aims to reduce health and economic disparities across the life span by effectively delivering evidence-based nutrition interventions to hard-to-reach populations globally. Specifically, VA delivers interventions that target the first 1,000 days of life (i.e., from conception to 24 months of age) and children up to 5 years of age.

A group of pregnant women gathers in Oyam District, Uganda, for a distribution of MMS provided by Vitamin Angels

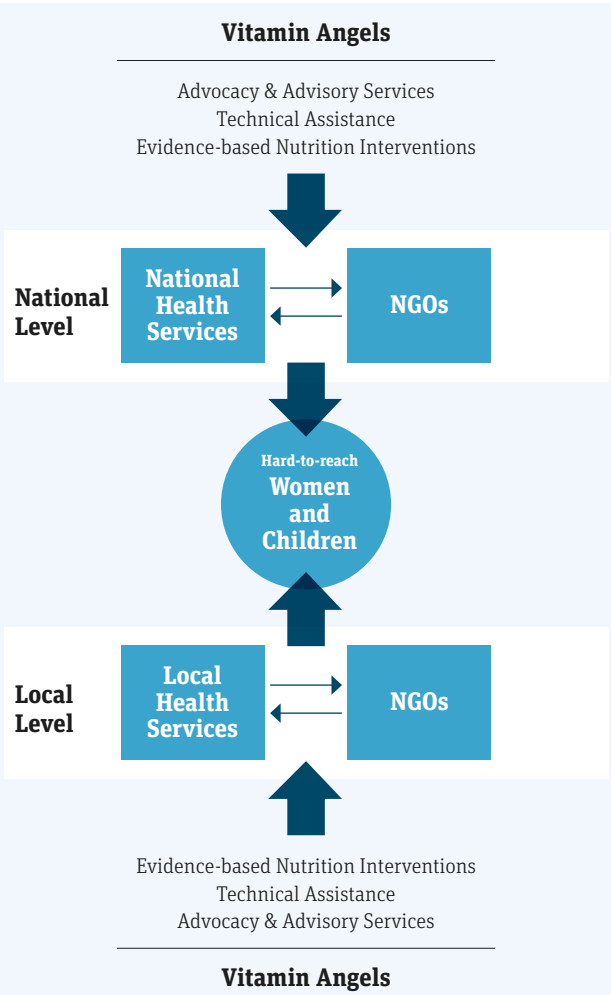
VA's model is premised on the reality that national health services are unable to reach all eligible beneficiaries, especially those who reside in marginalized or hard-to-reach communities. Through a range of strategies working with multiple stakeholders, VA coordinates with government and nongovernmental organizations (NGOs) to effectively and efficiently fill gaps in coverage. VA supports a range of nutrition-specific interventions, reaching over 70 million beneficiaries in 70 countries annually, through over 1,600 field partners. VA initiated its current model for programming (as applied to universal vitamin A supplementation) in 2007, and has since refined it to include an expanded range of evidence-based nutrition interventions, including MMS for pregnant women.

Vitamin Angels' approach

VA employs context-specific approaches by engaging in advocacy and advisory services, delivering technical assistance and providing evidence-based nutrition interventions to reach underserved pregnant women (**Figure 1**).

VA works at both the national and local level, through a blended approach, to identify governments and NGOs interested in exploring the introduction and implementation of MMS for pregnant women. At the national level, VA works with national health services to understand gaps in coverage and determine how best to address the gap – either using the national health system or in coordination with the health service delivery platforms of NGOs. At the local level, VA works with local health services and also identifies registered NGOs that operate existing programs, have knowledge of the populations they serve, coordinate with their local government health facilities and can absorb the incremental costs of adding nutrition services (such as MMS delivery) to their existing delivery platform. VA's blended approach is operationalized through its work with both national and local health services and NGOs, seeking to increase coordination at all levels.

FIGURE 1: Vitamin Angels' approach



Legend: Vitamin Angels engages in advocacy and advisory services to create an enabling environment for the introduction and implementation of evidence-based nutrition interventions, like MMS. VA provides technical assistance to ensure effective delivery through learning solutions, monitoring and evaluation, and implementation research. Where gaps in coverage persist, VA supports the delivery of evidence-based nutrition interventions to hard-to-reach women and children.

Vitamin Angels' global MMS campaign

With support from Kirk Humanitarian, VA initiated a global prenatal campaign in 2017 to accelerate access, availability and use of MMS by working to:

- **Ensure a global supply** of MMS by working with key partners to support efforts to develop an open-access MMS product specification that can result in an affordable MMS product of internationally accepted quality (as described elsewhere in this *Sight and Life* Special Report).
- **Create demand** for MMS by participating in and co-chairing internationally recognized meetings (e.g., the Women Deliver Conference and the Asian Congress of Nutrition) that raise awareness of MMS, advocate for the uptake of MMS and advance policies needed to support the implementation of MMS. In conjunction with these initiatives, VA participates in and convenes technical consultations to support policy formation and planning.
- **Deliver services** to over 2 million pregnant women in 2019 through a network of government and NGO field partners, by providing them with technical assistance to establish an MMS intervention within their antenatal care services and supplying them with a high-quality MMS product.
- **Influence policy and effective programming** by conducting implementation research to inform the introduction and scaling of MMS within national programs (as described on page 54 in this Special Report).
- **Act as a catalyst** to mobilize governments and other organizations into action to participate in the introduction and scaling of MMS.

> **"VA's global MMS campaign has made meaningful progress towards the introduction of MMS programs globally"**

Using the approaches described above, VA's global MMS campaign has made meaningful progress towards the introduction of MMS programs globally. In addition to the implementation research conducted in Haiti (as described elsewhere in this Special Report, see **Boxes 1–3** for country case studies that highlight additional work.

BOX 1: Indonesia case study

The Indonesian Ministry of Health is among those national health services interested in learning more about MMS as a potential replacement for IFA as part of routine antenatal care services. Several district health offices in Indonesia have successfully implemented MMS programs to replace IFA as part of ongoing research studies. For example, in Central Sulawesi, Vitamin Angels is providing a supply of MMS to support a joint partnership between Hasanuddin University and the district health office to integrate MMS into its antenatal platform as a replacement for IFA. Based on these successes, other districts have also indicated their interest in exploring MMS use.

VA conducted an initial assessment to understand how best to support the introduction and scaling of MMS in Indonesia and identified, together with the Ministry of Health, the need to review and disseminate recent evidence on MMS to catalyze the introduction of MMS product within its national health system, and to support the procurement and manufacturing of a high-quality, low-cost MMS product in Indonesia.

Using this national-level approach, VA partnered with two Indonesian universities (Hasanuddin University and Airlangga University) to co-sponsor a symposium at the Asian Congress of Nutrition in Bali, Indonesia, in August 2019 to update participants on global MMS policy and the most recent evidence of the benefits of MMS compared with IFA supplementation. Following the symposium, VA hosted a two-part technical consultation to provide participants with an opportunity to:

- seek guidance from international experts on maternal health and nutrition strategy to inform Ministry of Health strategy and policy pertaining to MMS use; and
- explore issues, challenges and opportunities related to immediate access to a standardized MMS product while local capacity is created to meet long-term demand.

To build on the momentum and progress generated following the Asian Congress of Nutrition and technical consultations, Institut Gizi Indonesia (IGI) / Indonesia Nutrition Institute, with support from VA, convened an expert meeting in Indonesia in January 2020 with participants from government, local universities, UNICEF and other key stakeholders. The primary objective of this meeting was to generate consensus regarding a recommendation pertaining to the adoption of an MMS policy. Key outputs included:

- consensus regarding current findings related to MMS use in Indonesia;
- consensus regarding a recommendation that will lead to the formation of MMS policy; and
- development of an Indonesian MMS Taskforce to support policy adoption.

BOX 2: Democratic Republic of the Congo case study

The Ministry of Health in the Democratic Republic of the Congo has had an existing national policy for MMS for 18 years. However, during an assessment launched in 2018, Vitamin Angels found that women were not receiving any antenatal supplementation (MMS or IFA) because of a lack of resources. VA's team of local advisors in the Democratic Republic of the Congo identified the immediate opportunity to leverage its network of local NGO field partners to reach an incremental number of pregnant women with MMS, both through local health facilities and through antenatal community outreach programs.

VA initiated the program in 2018 and has since expanded it to include over 100 NGO field partners, providing MMS to more than 200,000 pregnant women in 2019. The program is poised to reach 400,000 pregnant women with MMS in 2020. The reach of the program is due in part to the strong collaboration between the NGOs and the local Ministry of Health, which targets underserved areas of the country. This local-level approach has yielded immediate results in the short term for incremental beneficiary reach. However, VA's team is also working diligently to explore how best to advance MMS implementation with the national Ministry of Health through their health system by convening a workshop with key stakeholders to lay out a roadmap for scaling MMS in the country.

BOX 3: Dominican Republic case study

In December 2018, the Ministry of Public Health (MSP) in the Dominican Republic indicated their interest in exploring the introduction of MMS in place of IFA. Their existing antenatal care platform reaches around 96 percent of pregnant women; however, their IFA supplementation program coverage has remained around 57.1 percent.[5] During a series of technical consultations, MSP noted their interest in exploring MMS as part of their newly launched national strategy for reducing infant and maternal mortality.

In March 2019, Vitamin Angels provided a supply of MMS for approximately 1,000 women who will receive MMS as part of MSP's pilot 'companion program.' The program seeks to 'accompany' women throughout their entire pregnancy by having community health workers provide nutrition education, antenatal care, and delivery, breastfeeding and postpartum support. To help increase coverage and adherence, community health workers will provide pregnant women with MMS and then follow up with them weekly to give support and counseling. MSP plans to use the findings from the pilot to determine if they will adopt the companion program nationwide as their new MMS delivery system.

> **"Progress has been substantial, resulting in millions more women gaining access to MMS"**

Key learnings and call to action

VA's global MMS campaign has built upon existing national-level and local-level programs to catalyze efforts, with increasing momentum, to ensure that all women have access to MMS during pregnancy. Progress has been substantial, resulting in millions more women gaining access to MMS. Along with incremental reach, there has been a focused effort to ensure acceptance, coverage and adherence to MMS among pregnant women. To do this effectively, VA has recognized:

- **the importance and value of multisectoral partnerships** for leveraging expertise and collectively advancing an MMS agenda globally and within specific countries;
- **the need to strike a balance** between reaching more women with MMS in order to increase demand and reaching women *effectively* by conducting implementation research in key contexts to inform program design and increase adherence; and
- **that a blended approach** between (**1**) national-level and local-level program advocacy and implementation, and (**2**) context-specific collaboration between governments and NGOs can result in reaching more women, especially the hardest to reach.

Despite the evidence that MMS has been proven to be superior to IFA supplementation, millions of pregnant women do not have access to it. VA calls upon the global community to join the effort to ensure that pregnant women have access to a high-quality, low-cost MMS product, and that they receive it through delivery platforms that ensure they take MMS every day to improve birth outcomes and reduce health and economic disparities across the life span.

Edna holds her one-day-old newborn, Femia, in a hospital near Mlumbe, Malawi.

"VA calls upon the global community to join the effort to ensure that pregnant women have access to a high-quality, low-cost MMS product"

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References

1 King JC. Physiology of pregnancy and nutrient metabolism. Am J Clin Nutr. 2000;71(5 Suppl):1218S–25S.

2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient 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 World Health Organization. World Health Organization recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016.

5 Mora JO, Boy E, Lutter C, Grajeda R. Anemia in Latin America and the Caribbean, 2009. Situation analysis, trends, and implications for public health programming. Washington, DC: Pan American Health Organization; 2010.

The Introduction of Multiple Micronutrient Supplementation Requires a Comprehensive Systems Approach

UNICEF's support for high-burden countries in South Asia and sub-Saharan Africa

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Key messages

- Globally, maternal malnutrition and low birth weight trends show insufficient progress.
- Multiple micronutrient supplements (MMS) offer an important opportunity to improve the quality of pregnancy care and survival and development outcomes for women and children.
- Experiences across four countries show that MMS advocacy is facilitated by the use of global evidence, national data, cost-effectiveness analysis and alignment with national priorities.
- The introduction of MMS should be linked to the strengthening of relevant systems as well as to formative research so as to reach scale, quality and equity.
- Measuring and documenting success plays a critical role in informing adjustments to implementation approaches and guiding scale-up in other countries.

Introduction

Maternal nutrition is integral to the 1,000 days approach; yet global trends reveal insufficient progress in reducing the prevalence of maternal malnutrition and low birth weight.[1] While strong evidence exists to support iron and folic acid supplementation (IFA), only 34 percent of pregnant women are covered.[2] Antenatal care (ANC), the main delivery platform for maternal nutrition interventions, covers less than half of pregnant women in low- to middle-income countries as measured by the completion of at least four ANC visits (ANC4).[3] Moreover, there are significant gaps between ANC4 and IFA coverage (90+ days).[4]

The systems approach

Introducing MMS is an opportunity to accelerate progress towards global goals and targets, and is an important component of UNICEF's new Nutrition Strategy. Such an approach requires a well-functioning health system, in the absence of which, programs will face the same barriers currently impeding IFA coverage. To address this constraint, UNICEF is adopting a systems approach to MMS scale-up in four high-burden countries (Bangladesh, Burkina Faso, Madagascar and Tanzania). The aim is to build operational experiences in scaling up MMS using strengthened ANC and community systems.

UNICEF is supporting this approach to MMS transitions as follows:

A prenatal consultation at Ambanintsena Health Center (Analamanga Region, Madagascar)

TABLE 1: Selected maternal and child nutrition indicators from participating countries

Indicator	Percentage per country (year of survey)			
	Bangladesh	Burkina Faso	Madagascar	Tanzania
Women of reproductive age with a BMI < 18.5 kg/m²	18.6% (2014)	16% (2010)	27% (2009)	10% (2015)
Pregnant women with anemia (Hb < 11 g/dL)	49.6% (2011)	72.5% (2014)	38% (2009)	57% (2015)
Pregnant women who received any IFA	62.1% (2017)	93% (2010)	55% (2014)	58% (2015)
Pregnant women who received 90+ IFA tablets	5.3% (2017)	50% (2010)	7.1% (2014)	21% (2015)
Women who received 4+ ANC visits during pregnancy	47% (2017)	38% (2017)	50.6% (2018)	51% (2015)
Pregnancies resulting in low birth weight	38% (2014)	13.9% (2010)	12.6% (2018)	7% (2015)
Stunting among children < 5 years	36% (2014)	21.2% (2017)	42% (2018)	34% (2015)

Source: Demographic and Health Survey, Multiple Indicator Cluster Survey

1. A **robust situation analysis** drawing policymakers' attention to the poor state of women's diets and their poor nutritional status, and low birth weight. All four countries have high burdens of maternal and child undernutrition (**Table 1**).

2. Analyses of **health system building blocks** including delivery platforms, workforce, supply chains and commodities, and information systems as the basis of program strategies to introduce MMS. Analysis was undertaken of the adequacy of policies, regulations, coordination and financing. Studies of MMS production and procurement were undertaken to facilitate national ownership and sustainability. Commonly cited health system barriers include:

   a. **Weak ANC delivery platforms:** access (distance) to services, inadequate organization of ANC, weak integration and prioritization of nutrition interventions.

   b. **Weak health workforce:** inadequate numbers, high vacancies, high turnover, inadequate training and supervision, poor attitudes on the part of health workers.

   c. **Weak supply chains** and frequent rupture in commodity availability for IFA and adult scales, anemia measurement instruments.

   d. **Weak health information systems:** IFA coverage and counseling not routinely monitored, data not used to improve programs.

   e. **Social determinants:** women's knowledge, decision-making authority, perceptions and experiences of ANC, household and social barriers, such as beliefs about disclosing pregnancy and when to attend ANC, role of key influencers such as mother-in-law and husband.

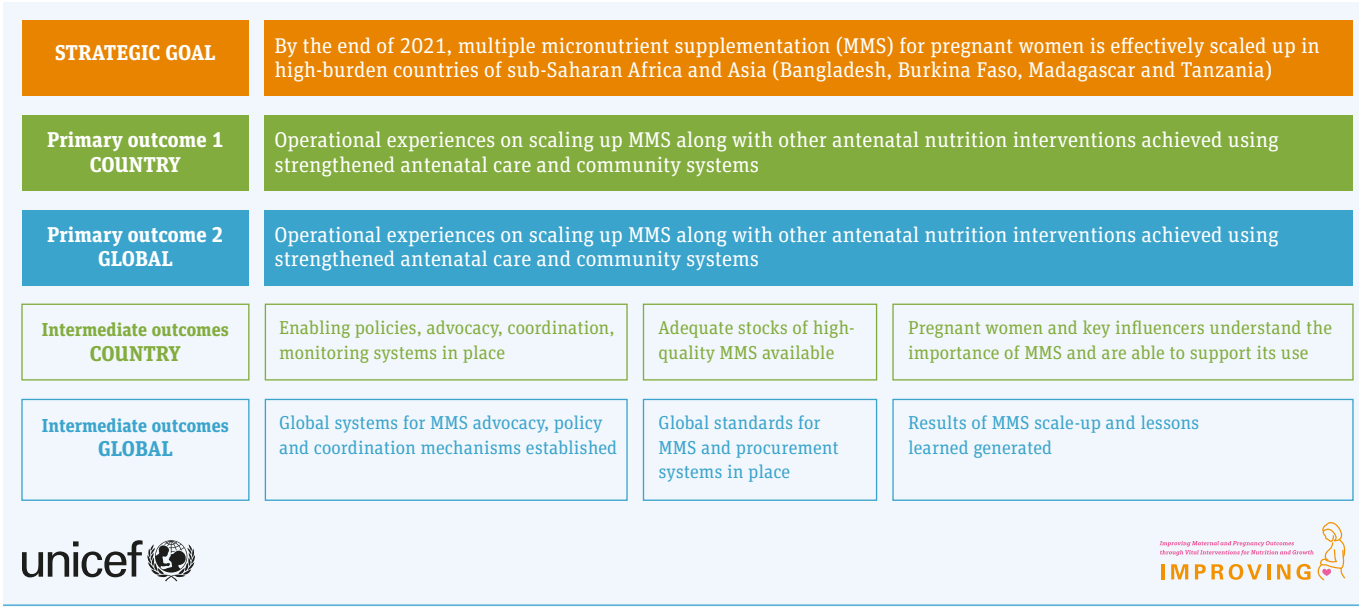
3. **Advocacy using global evidence** supported the transition from IFA to MMS. The availability of MMS clinical trials in Bangladesh, Burkina Faso and Tanzania was instrumental in generating awareness among policymakers of the potential impact of MMS in their specific context.[4–6] Cost-effectiveness analysis conducted by Nutrition International estimated the disability-adjusted life-years (DALYs) to be gained by switching to MMS.[7] In Tanzania, a national advocacy workshop with key stakeholders was influential in galvanizing government commitment for a comprehensive approach to maternal nutrition including MMS.

4. A **core implementation package** including MMS and enhanced nutrition counseling to improve nutritious diets, MMS adherence, appropriate gestational weight gain, and early and exclusive breastfeeding. Inclusion of other interventions follows national policies and local contexts.

5. **ANC is the main delivery platform for MMS** in all four countries and has strong links to community systems. In Burkina Faso, paid community health workers will counsel women on ANC attendance and MMS adherence, whereas ANC and community health workers will be responsible for MMS distribution and counseling in Madagascar.

6. Implementation design is guided by **country-specific theories of change**, addressing the enabling environment, and supply- and demand-side ANC and MMS barriers. Projects were designed with the goal of national-level scaling as opposed to research projects. For this reason, MMS has been integrated into ongoing maternal nutrition programs in all four countries. In Madagascar, MMS is embedded in a project funded by the World Bank that aims to improve the coverage of nutrition-specific interventions during the first 1,000 days. In Bangladesh, MMS will be distributed in the same districts where government and the World Bank are strengthening

FIGURE 1: UNICEF theory of change for high-burden countries in sub-Saharan Africa and South Asia



health systems and health workers' nutrition competencies. In Tanzania, MMS will be part of a continuum of services provided through community, school and health contacts to adolescents and pregnant women to strengthen the promotion of dietary diversity, food fortification and micronutrient supplementation. MMS packaging for the project was influenced by national preferences to use blister-packed MMS to match current practices and to facilitate MMS distribution and adherence. In-country partnerships and coordination mechanisms have been established. In Tanzania, a technical advisory group has been established, whereas in Bangladesh the Maternal Nutrition Task Force will coordinate MMS-related activities supported by partners. **Figure 1** illustrates a generic theory of change for the project.

A mother waits for a prenatal consultation at a health center in Madagascar

7. **Monitoring and knowledge generation.** Success across countries will be measured by demonstrated increases in MMS coverage and adherence, and documented learning on the scaling up of MMS. MMS will be integrated into routine health information systems using the District Health Information Software 2 (DHIS2) in all four countries. In Burkina Faso, MMS will be introduced in the same districts selected to strengthen nutrition in the national health information system (ENDOS). Tanzania's information system already generates semiannual data on IFA stock-outs, ANC and IFA coverage. In Bangladesh, individual-level pregnancy tracking will capture ANC and MMS coverage. Countries have also identified key implementation questions that will contribute to what constitutes successful MMS programming in other countries.

Country-level approaches are backed by global advocacy to support a systems approach, MMS market shaping and program evidence for future MMS scale-up. In partnership with *Sight and Life*, UNICEF is supporting situation analyses of MMS production and procurement in all four countries (on pages 49–53 of this Special Report). The partnership also covers formative research (on pages 54–57 of this Special Report) focused on identifying factors for demand generation and adherence. Links have been created with other global and regional initiatives to strengthen primary healthcare and community systems, pregnancy quality of care and regional platforms for economic cooperation.

Moving forward

UNICEF's systems approach to scaling up MMS in four high-burden countries can provide important learnings about what constitutes successful MMS programming and inform further scaling up in other countries.

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Disclaimer

The opinions and statements in this article are those of the authors and may not reflect official UNICEF policies.

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References

1 United Nations Children's Fund (UNICEF), World Health Organization (WHO). UNICEF-WHO Low birthweight estimates: Levels and trends 2000–2015. Geneva; 2019.

2 United Nations Children's Fund (UNICEF). NutriDash. 2019.

3 United Nations Children's Fund (UNICEF). Global Database. 2016.

4 Christian P, Kim J, Mehra S, Shaikh S, Ali H, Shamim AA, et al. Effects of prenatal multiple micronutrient supplementation on growth and cognition through 2 y of age in rural Bangladesh: the JiVitA-3 Trial. Am J Clin Nutr. 2016. 104(4):1175–82.

5 Roberfroid D, Huybregts L, Lanou H, Henry MC, Meda N, Menten J, 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):1330–40.

6 Kawai K, Kupka R, Mugusi F, Abous S, Okuma J, Villamor E, et al., A randomized trial to determine the optimal dosage of multivitamin supplements to reduce adverse pregnancy outcomes among HIV-infected women in Tanzania. Am J Clin Nutr. 2010. 91(2):391–7.

7 Kashi B, Godin CM, 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):1222–9.

Formative Research

Ensuring adequate demand and compliance of MMS in Bangladesh, Burkina Faso, Madagascar and Tanzania

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Key messages

- Multiple micronutrient supplements (MMS) will require careful introduction to ensure acceptability and appropriate utilization among pregnant women.
- *Sight and Life* is using a focused ethnographic study (FES) approach to support UNICEF's MMS demonstration pilots and inform context-specific design and implementation in Bangladesh, Burkina Faso, Madagascar and Tanzania.
- The approach will have three iterative phases, with an emergent design to allow for findings from each phase to be built into subsequent data collection efforts.
- Working with in-country partners has allowed us to tailor the generalized formative methodology to suit the unique needs of each program and context. Findings drawn from this approach across the four contexts will be synthesized to develop standardized formative research guidance to help programs to appropriately introduce MMS in other settings.

The social marketing mix

As with commercial marketing, the main focus of social marketing is on the consumer – that is, on understanding what people desire and need rather than trying to convince them to purchase what a firm is producing.[1] The planning process takes this consumer focus into account by addressing four elements that make up the 'marketing mix.' This refers to decisions about the conception of (**1**) Product, (**2**) Price, (**3**) Place and (**4**) Promotion. These are often called the 'four Ps' of marketing and are used as the pillars of the 'social marketing mix' (**Figure 1**).

MMS formative research

For multiple micronutrient supplements (MMS) to be a scalable antenatal intervention that effectively addresses maternal nutrition and pregnancy outcomes, both an adequate supply of and a commensurate demand for the supplement are necessary.

FIGURE 1: The 'four Ps' of social marketing

Source: *Sight and Life*

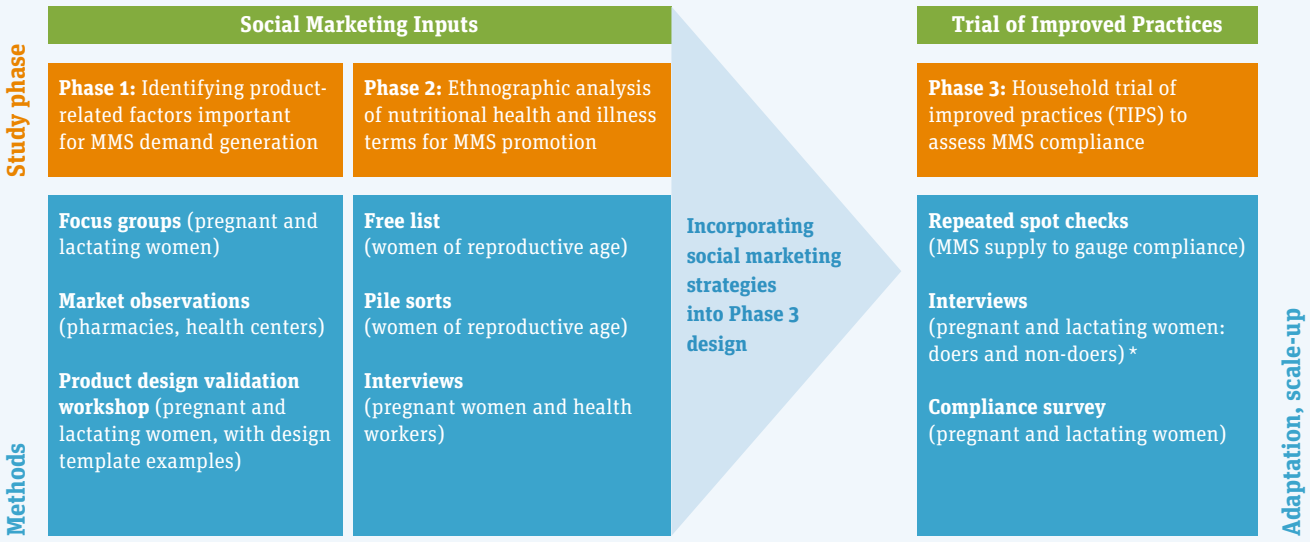
Lessons learned from the introduction of other specialized nutritional products, such as micronutrient powders (MNP) and iron–folic acid (IFA) tablets, underscore the challenges intrinsic to both the supply and the demand sides of program implementation.[2] MMS may thus require careful introduction to ensure acceptability and appropriate utilization among consumers (i.e., pregnant women). Using well-designed formative research as a first stage of program planning, we can understand the key social and behavioral elements (e.g., perception of the risk of malnutrition) important for the acceptance and utilization of MMS, as well as the requisite system-related factors (e.g., supply chain, health worker capacity and tools) necessary to ensure all population groups are reached.

> **"Using well-designed formative research, we can understand the key social and behavioral elements important for the acceptance and utilization of MMS"**

Research objectives

In support of the country governments and UNICEF, and to inform the context-specific design and implementation of MMS in Bang-

FIGURE 2: MMS formative research framework



* Doers and non-doers will be identified during the repeated spot checks in the course of Phase 3

ladesh, Burkina Faso, Madagascar and Tanzania, we prioritized formative research with the following aims:

1. Identify product- and placement-related factors important for generating demand for MMS.
2. Generate contextually appropriate and targeted promotional strategies.
3. Understand the multilevel factors (i.e., facilitators and barriers) influencing the acceptability and utilization of MMS.

Methodology

This formative study will have three iterative phases, with an emergent design to allow for findings from each phase to be built into subsequent data collection efforts (**Figure 2**).

Phase 1 includes focus groups, market observations and validation workshops that aim to identify the Product- and Placement-related factors (e.g., packaging, logo, language) important for ensuring adequate consumer demand. **Phase 2** builds on those findings by using ethnographic methods that will explore local nutritional terms, medical belief systems and perceptions of illness risk for informing MMS Promotions. Together, findings from **Phases 1** and **2** will inform uniquely tailored social marketing strategies in each context.

After interpretation and translation of raw data into useable program inputs, **Phase 3** will be conducted involving a trial of improved practices (TIPS). It will involve an assessment of tailored behavior change strategies intended to ensure adequate supply, optimal demand and continued utilization of MMS.[3] Repeated spot checks, interviews and compliance surveys[4–7] will be conducted among a subset of households to identify 'doers' versus 'non-doers.' Understanding the behavioral factors important for program success before or during scale-up may be achieved using this Phase 3 methodology.[8] This phase can also be incorporated into program implementation, and does not necessarily have to be undertaken before distribution of MMS begins.

Overall, this suite of methods follow a FES approach, which allows for high-quality data collection in a relatively short period of time – a design that is well suited for this type of public health programming.[9,10] Findings drawn from this approach across the four contexts will be synthesized to develop standardized formative research guidance to help program officers appropriately introduce MMS in other similar settings globally.

Operationalizing formative research – collaboration across contexts

Working with in-country partners has allowed us to operationalize the generalized formative methodology described above while tailoring the work to suit the needs of each program and context. In Bangladesh and Tanzania, *Sight and Life* is collaborating with local institutions to support formative research efforts specific to each context. These efforts not only include the methodology outlined in Phases 1–3 above, but also include additional analyses relevant to each context.

For instance, in Bangladesh, the MMS formative work will also evaluate current antenatal care (ANC) services through observations, interviews and coverage surveys to determine gaps in

maternal health and nutrition services. In doing so, individuals' knowledge, attitudes and practices will be assessed.

In Tanzania, in collaboration with a local nongovernmental organization, barrier analyses are being carried out to reveal the range of multilevel factors influencing ANC services in that setting. This work will also include a quantitative survey to assess the nutritional status of pregnant women and estimate IFA and ANC program coverage.

In Madagascar, *Sight and Life* is working with UNICEF and local partners to evaluate: existing policies and guidelines related to ANC services and IFA distribution; barriers and enablers associated with IFA consumption; and MMS supply chain and delivery platforms (health centers and/or community agents). The formative research being undertaken by *Sight and Life* will serve as a key building block for the situational analyses in all contexts.

"This multi-country MMS project has great potential to improve maternal nutrition and pregnancy outcomes"

Conclusion

This multi-country MMS project has great potential to improve maternal nutrition and pregnancy outcomes. Investing in collaborative and participatory formative work for the appropriate introduction of MMS in each setting will help ensure MMS does not face the same fate as IFA, with poor program coverage and compliance globally.[11] Furthermore, important lessons learned will be drawn from this work as part of increased efforts to enhance maternal health and nutrition services to the world's most vulnerable populations.

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References

1 Weinreich NK. What is social marketing? Weinreich Communications. Internet: http://www.social-marketing.com/Whatis.html (accessed 4 April 2020).
2 Tumilowicz A, Vossenaar M, Kjaer K, Vettersand J, Possolo E, Pelto GH, et al. Mixed methods evaluation explains bypassing of vouchers in micronutrient powder trial in Mozambique. Matern Child Nutr. 2019;15(Suppl 5):e12718.
3 Omotayo MO, Martin SL, Stoltzfus RJ, Ortolano SE, Mwanga E, Dickin KL. With adaptation, the WHO guidelines on calcium supplementation for prevention of pre-eclampsia are adopted by pregnant women. Matern Child Nutr. 2018;14(2):e12521.
4 Nguyen TM, La Caze A, Cottrell N. What are validated self-report adherence scales really measuring?: a systematic review. Br J Clin Pharmacol. 2014;77(3):427–45.
5 Lavsa SM, Holzworth A, Ansani NT. Selection of a validated scale for measuring medication adherence. J Am Pharm Assoc (2003). 2011;51(1):90–4.
6 Berti C, Gaffey MF, Bhutta ZA, Cetin I. Multiple-micronutrient supplementation: Evidence from large-scale prenatal programmes on coverage, compliance and impact. Matern Child Nutr. 2018;14 (Suppl 5):e12531.
7 Chikakuda AT, Shin D, Comstock SS, Song S, Song WO. Compliance to Prenatal Iron and Folic Acid Supplement Use in Relation to Low Birth Weight in Lilongwe, Malawi. Nutrients. 2018;10(9).
8 Davis TP. Barrier Analysis Facilitator's Guide: A Tool for Improving Behavior Change Communication in Child Survival and Community Development Programs. Washington, DC: Food for the Hungry: 2004.
9 Pelto GH, Armar-Klemesu M, Siekmann J, Schofield D. The focused ethnographic study 'assessing the behavioral and local market environment for improving the diets of infants and young children 6 to 23 months old' and its use in three countries. Matern Child Nutr. 2013;9(Suppl 1):35–46.
10 Nitcher M, Acuin CS, Vargas A. Introducing zinc in a diarrhoeal control programme: guide to conducting formative research. World Health Organization; 2008.
11 Sanghvi TG, Harvey PW, Wainwright E. Maternal iron-folic acid supplementation programs: evidence of impact and implementation. Food Nutr Bull. 2010;31(2 suppl):S100–S107.

Supply-Side Insights from Bangladesh, Madagascar and Tanzania

Key learnings and recommendations for the integration of MMS into health programs of low- and middle-income countries

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Key messages

- This situation analysis offers a framework on the market, manufacturing and policy enablers and barriers for the local procurement and production of multiple micronutrient supplements (MMS) in three high-burden countries in South Asia and sub-Saharan Africa (Bangladesh, Madagascar and Tanzania), and includes learnings for other countries interested in introducing MMS into health programs.
- **Market assessment:** prenatal MMS is available in all three countries, but none of the products conform to the United Nations Multiple Micronutrient Preparation (UNIMMAP) formulation.
- **Market assessment:** Bangladesh has a vibrant pharmaceutical industry and also has the capacity to manufacture affordable and high-quality MMS locally. In Madagascar, domestic production capabilities are limited and MMS is currently imported. Hence, the most feasible way to ensure access to MMS in the near future is through government-or-donor-subsidized free distribution to all pregnant women. Tanzania is well placed to become a regional pharmaceutical manufacturing powerhouse.
- **Production assessment:** in all three countries, quality assurance and quality control mechanisms throughout the supply chain would need to be improved to ensure high-quality procurement and production of MMS.
- **Regulatory and policy assessment:** MMS is included in the essential medicines list (EML) in Madagascar, but not in Bangladesh and Tanzania. Including MMS on the EML would subject it to price controls, thus making it affordable for all.

Background

In the contribution entitled 'The Introduction of Multiple Micronutrient Supplementation Requires a Comprehensive Systems Approach' by Nita Dalmiya and Roland Kupka in this Special Report (pp. 42–45), UNICEF outlines a systems approach, one component of which is the market shaping of MMS for future country-level and regional scale-up. In partnership with UNICEF, *Sight and Life* conducted a situation analysis of the procurement and production of MMS in Bangladesh, Madagascar and Tanzania in October 2019 and April 2020. Because our study is still ongoing, the present article will only provide key findings of analyses conducted till now, while comprehensive reports are being prepared for individual countries. We applied the *Sight and Life* MMS Supply Analytical Framework (**Figure 1**) for this project.

Notes:

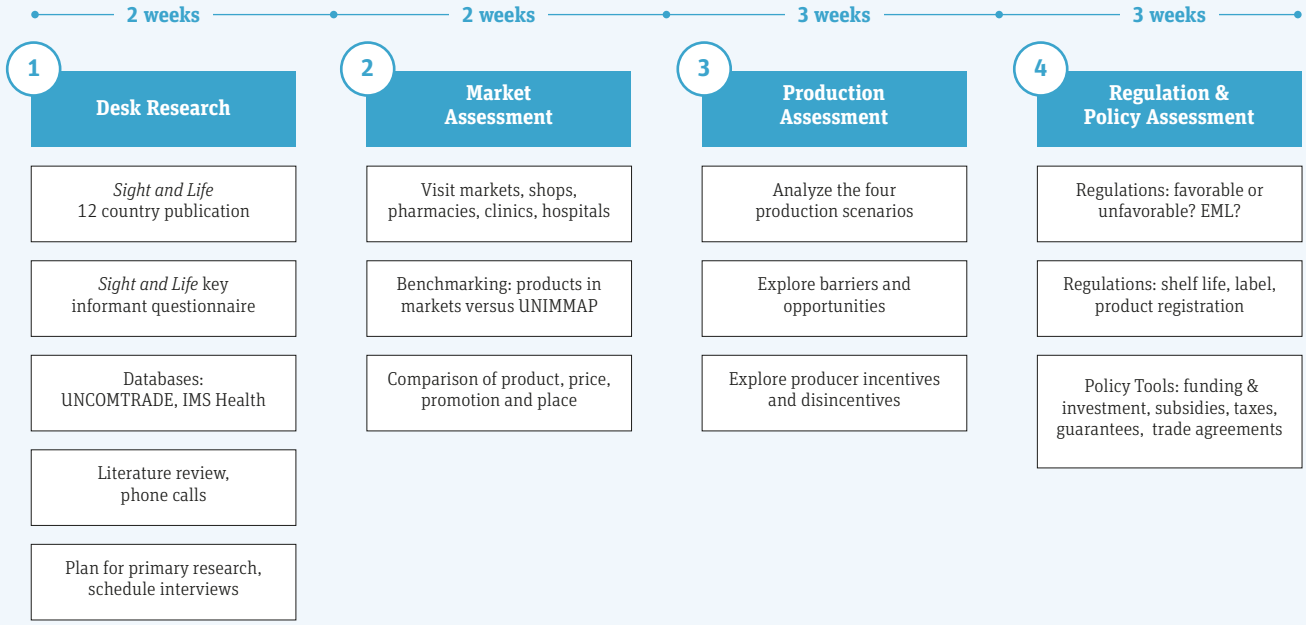
1. Analysis is underway in Burkina Faso and will be shared in a subsequent publication
2. Described in 'Procurement and Production of Multiple Micronutrient Supplements for Pregnant Women: A country assessment toolkit' by Kalpana Beesabathuni and Kesso Gabrielle van Zutphen on pp. 90–101 of this Special Report

1. Market assessment

Bangladesh has a vibrant pharmaceutical industry and several brands of prenatal multiple micronutrients are available in the market. However, none of them match the UNIMMAP formulation. Most of the prenatal supplements contain a lower number or dosage of critical micronutrients. For example, selenium, which has been shown to have a positive impact on preterm birth, is missing or virtually absent in all of them.[2] However, a small handful of local manufacturers have already developed, or are currently developing, the UNIMMAP formulation.

In Madagascar, private pharmacies sell imported prenatal MMS products that can only be bought by affluent women, who constitute 16 percent[3] of Madagascar's total population. These imported MMS have a retail price ranging between US$9.7 and US$29.0 per package of 30 tablets. There is no free distribution

FIGURE 1: The SAL-MMS Supply Analytical Framework[1]



of essential medicines in Madagascar despite it being one of the poorest countries in the world – 71 percent of the population lives below the international poverty line (existing on less than US$1.90 per day).[4] In the public distribution channel, there is only one supplement available. This supplement does not meet the nutritional requirements for pregnant women, as it lacks critical micronutrients such as iron, folic acid and selenium. Moreover, it is priced at US$1.10 for a pack of 30 tablets and is thus not affordable for the poor.

In Tanzania, pharmacies import over 85 percent of the drugs and supplements. We found more than 10 brands of prenatal MMS in these pharmacies, but none of them conform to the UNIMMAP formulation and their price ranges between US$7.0 and US$10.0 per 30-count pack. These price points will be affordable to only the 10 percent of the pregnant women in Tanzania who belong to the 'affluent' consumer segment (i.e., with a household income in excess of US$5.5 per day).

One supplement brand made by a local manufacturer, priced between US$1.40 and US$4.30 for a pack of 30 tablets, depending on the distribution channel, is more affordable than the imported products. This local brand is sold in both public and private pharmacies in Tanzania. In public facilities, the local brand is prescribed by practitioners. It is free for pregnant women who are anemic. However, it has fewer micronutrients than UNIMMAP and would need to be improved (see **Box 1**).

2. Production assessment

We found significant variability across the three countries for local and sustainable production of MMS, but quality assurance and quality control (QA and QC) remain a common bottleneck.

BOX 1: Market assessment: Key learnings and recommendations

The market assessment reveals a critical need for affordable MMS products that are UNIMMAP-compliant in low- and middle-income countries. Key considerations for facilitating this are noted below:

1. For countries like Bangladesh, which have multiple local brands of MMS in the market, there are several options to introduce MMS using local suppliers in programs. In Bangladesh, the options include two pharmaceutical companies that have both developed UNIMMAP-conformant products.

2. Despite varying levels of local brand availability in the three countries, the affordability of prenatal supplements is a key issue, especially for low-income women. Ensuring free access to MMS will be critical. Thereby, including UNIMMAP MMS in the EML will be an important price control lever. For example, in Bangladesh, once an item is on the EML, its price is monitored, fixed and cannot be exceeded even through commercial channels.

3. To increase product availability in an affordable manner, there is an opportunity for a cross-subsidy model in countries with low manufacturing capacity and rising disposable incomes, like Tanzania. In a cross-subsidy model, the same MMS would be available to

all pregnant women, with differential pricing based on income group or general ability to pay. An example of such a model can be found in Mexico: *Farmacias Similares*,[5] a pharmaceutical chain serving the base of the pyramid in the country, provides unbranded but high-quality generic drugs and supplements that are up to 75 percent cheaper than branded drugs.

4. Meanwhile, for a country like Madagascar, which has no local manufacturing and chronic poverty, the most feasible way to ensure access to MMS in the short to medium term is through free distribution to all pregnant women, given that MMS is already on the EML of the country.

"Quality assurance and quality control (QA and QC) remain a common bottleneck"

Many Bangladeshi manufacturers have tableting, capsuling and blending capabilities and procure straight ingredients. Several facilities in the country have WHO Good Manufacturing Practices (GMP) certification and the capacity to meet all local demand and increase production if required. Some of them have US Food and Drug Administration approval. When demand surges, Bangladeshi manufacturers would have to import equipment in order to increase production capacity or build new facilities.

Local manufacturers expressed minimal challenges along the QA/QC value chain. However, in our interviews with international agencies that procure locally, and through our own experience in conducting independent lab tests, we found that some of these local products do not meet the label claims and GMP requirements. In Bangladesh, it is common for pharmaceutical companies to manufacture products for local markets under less stringent conditions than those used for products destined for export markets.

In Madagascar, there is no local MMS manufacturing capacity, and all drugs are imported. The government imposes a high import duty as well as value added tax (VAT) on raw materials for drugs. These together add up to 40 percent. Furthermore, social and physical infrastructure is underdeveloped and insufficient to support local production.

In Tanzania, one local manufacturer has the capacity to produce UNIMMAP-conformant MMS and can start manufacturing right away. The entire local pharmaceutical sector in the country would benefit if the government supports procurement from local manufacturers. There are 13 pharmaceutical companies in Tanzania and almost all of them cannot compete with the low-priced imported drugs. They are all producing below their capacity and would need an increase in minimum order volumes to stay competitive. It is possible for these local companies to receive more orders as they have access to the markets of the countries in the Southern African Development Community (SADC), which together have nearly 9 million pregnancies every year (see **Box 2**).[6]

BOX 2: Production assessment: Key learnings and recommendations

Through our interviews and analysis, we identified a number of key actions for countries looking to build local production capacity in the short, medium and long term.

For countries that have the capacity to begin local production in the short term (e.g., Bangladesh and Tanzania), the most important action to consider is:

Partnering with an international premix manufacturer to bring MMS to market in a cost-effective manner.
In our QA/QC analyses of local companies, common issues that emerged were achieving blending consistency and maintaining the stability of the vitamins. High-quality UNIMMAP premix is already being manufactured by leading companies. Partnering with one of these companies will allow local manufacturers to obtain the technical expertise and experience to address challenges in mixing the micronutrient ingredients before tableting.

For countries such as Madagascar that have the capacity to begin production in the medium to long term, the most important actions to consider are:

- Build **human resource capacity** to meet the lack of trained industrial pharmacists who can assist with the development of pharmaceutical products.
- **Upgrade** the physical infrastructure (electricity, roads, etc.) to enable last-mile access.
- **Create an enabling environment** (single-window clearance, elimination of kickbacks) for foreign investments and technology transfer, which will allow local producers to upgrade to state-of-the-art facilities.
- A single window clearance body will help **promote and sustain ever-increasing investment flows and will create a competitive investment environment** that promotes the business environment in the country.
- **Lower import duty and VAT on raw materials** for drugs and supplements so that local producers can be competitive with imported products.
- **Lower import duty and VAT on QA/QC equipment,** which is the prerequisite for high-quality production.

3. Regulation and policy assessment

Across all three countries, greater regulatory and policy coherence could improve the affordability of MMS. Of the three countries, Bangladesh has the most effective regulatory environment for local companies to produce MMS affordably. The Drug Administration has set a price ceiling on finished supplements, a low import duty of 5 percent on the straight ingredients and a prohibitively high import duty on finished supplements from foreign companies. In Madagascar, the regulatory environment is also supportive, in that imported drugs are exempt from import duty and VAT. This facilitates the easy and relatively quick importation of MMS for pilots and programs. In Tanzania, the regulatory environment for local companies to produce MMS and other pharmaceutical products at affordable prices needs strengthening. Local manufacturers would need a tax subsidy, especially a reduction of VAT on raw materials, to lower the price of the product to the consumer. Various government ministries would need to work together to create an enabling environment for local pharmaceutical manufacturing.

Currently, UNIMMAP MMS is on the EML in one of the three countries (Madagascar). MMS is registered as a drug, which makes it easier to integrate the supply of MMS into the health system. MMS is not as yet part of the EML in Bangladesh and Tanzania, although with the establishment of Technical Advisory Groups for MMS in both these countries, these bodies may be in a position to advocate its inclusion.

However, the lack of QA/QC processes makes **high-quality procurement difficult**. Each batch of MMS would need to be sent out of the country for lab analysis, which is expensive and is not feasible for local manufacturers. Strong monitoring and enforcement by regulatory authorities is recommended to ensure adequate storage and warehousing conditions and to check the label claims of imported products (see **Box 3**).

BOX 3: Regulation and policy assessment: Key learnings and recommendations

Key recommendations for an enabling regulation and policy environment for a country that is interested in establishing high-quality local production of MMS:

- Develop a revenue structure that minimizes VAT and import duty on raw materials for drugs, including on packaging material.
- Consider imposing import duty on finished drugs and supplements and an import ban for any product that is adequately manufactured by local companies, to ensure local industry stays competitive.
- Harmonize QA/QC processes, standards and compliance across all the products being manufactured locally.

Key recommendations to strengthen the enabling environment for a country that is procuring MMS from abroad:

- Exempt import duty and VAT on finished drugs and supplements such as MMS.
- Establish a strong QA/QC protocol for the batch testing of imported products, along with strong enforcement of storage and warehousing conditions and checking the label claims of imported products.

It is important to note that, in both the local production and overseas procurement scenarios, including MMS in the EML will be a critical factor in enabling integration into maternal nutrition programs. For further details, please see 'The Case for Reintroducing Multiple Micronutrient Supplements in South Africa's Essential Medicines List: Creating an enabling environment for nutrition-specific interventions in antenatal care' by Madhavika Bajoria, Kalpana Beesabathuni and Klaus Kraemer on pp. 61–67 of this Special Report.

> **"Including MMS in the EML will be a critical factor in enabling integration into maternal nutrition programs"**

Conclusion

This situation analysis has described the key elements of the market, manufacturing and policies that are likely to influence the local procurement and production of MMS in three high-burden countries, and offers generalized lessons for other countries interested in introducing MMS into their health programs. We found significant variability across the three countries in terms of local and sustainable procurement and production of MMS. Adequate WHO-GMP-certified manufacturing capacity exists in Bangladesh, along with many local brands. Madagascar is not in a favorable position to produce locally. Meanwhile, in Tanzania, political will, access to SADC markets and technology transfer could be leveraged to support affordable local production of MMS. None of the three countries surveyed had products as per the UNIMMAP formulation, either through private retail or public distribution channels.

In all three countries, greater policy coherence could improve affordability through one or more competitive and sustainable price ceilings, import subsidies, commercial tax exemptions and company tax subsidies. A guiding dossier could help build capacity for QA and QC throughout the supply chain, which is a

prerequisite for ensuring high-quality procurement and production of MMS.

In conclusion, a potential scale-up of MMS will need to be viewed holistically, taking into account manufacturing, policy and human capacity/skill factors, as these will together influence the implementation, sustainability and affordability of MMS in the three countries discussed here and beyond.

Acknowledgements

We would like to extend our sincerest thanks to all of the key stakeholders from government, industry and NGOs who took time out to be interviewed for this analysis.

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References

1 Monterrosa EC, Beesabathuni K, van Zutphen KG, Steiger G, Kupka R, Fleet A, et al. Situation analysis of procurement and production of multiple micronutrient supplements in 12 lower and upper middle-income countries. Matern Child Nutr. 2018;14(Suppl 5):e12500.

2 Zhang G, Feenstra B, Bacelis J, Liu X, Muglia LM, Juodakis J, et al. Genetic Associations with Gestational Duration and Spontaneous Preterm Birth. N Engl J Med. 2017;377:1156–67.

3 World Bank data. www.worldbank.org/en/country/madagascar/overview (accessed 16 April 2020).

4 Ibid.

5 Harvard Business School Case 307-092. Internet: http://hbr.org/product/Farmacias-Similares--Priv/an/307092-PDF-ENG

6 United Nations, Department of Economic and Social Affairs, Population Division (2019). World Population Prospects 2019, Online Edition. Rev.1. Fertility: Crude Birth Rate by region, subregion and country, 1950–2100 (births per 1,000 population) (Selection: 2015–2020). Available from: https://population.un.org/wpp/Download/Standard/Fertility/ (accessed 3 August 2019).

Ensuring Effective Implementation of MMS for Pregnant Women in Haiti

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Key messages

- The Haitian Ministry of Public Health and Population (MSPP), Vitamin Angels, Johns Hopkins Bloomberg School of Public Health (JHSPH) and the Haitian Health Foundation (HHF) are conducting implementation research to inform the introduction and scale-up of a multiple micronutrient supplementation (MMS) program in Haiti.
- The implementation research includes the following aims:
  - Develop and field-test social and behavior change communication (SBCC) strategies and tools intended to support the uptake of and adherence to MMS among pregnant women.
  - Field-test the provision of MMS, including the distribution platform, supply chain and cost.
  - Identify and implement a methodology to evaluate MMS acceptance, coverage and adherence among pregnant women.

Introduction

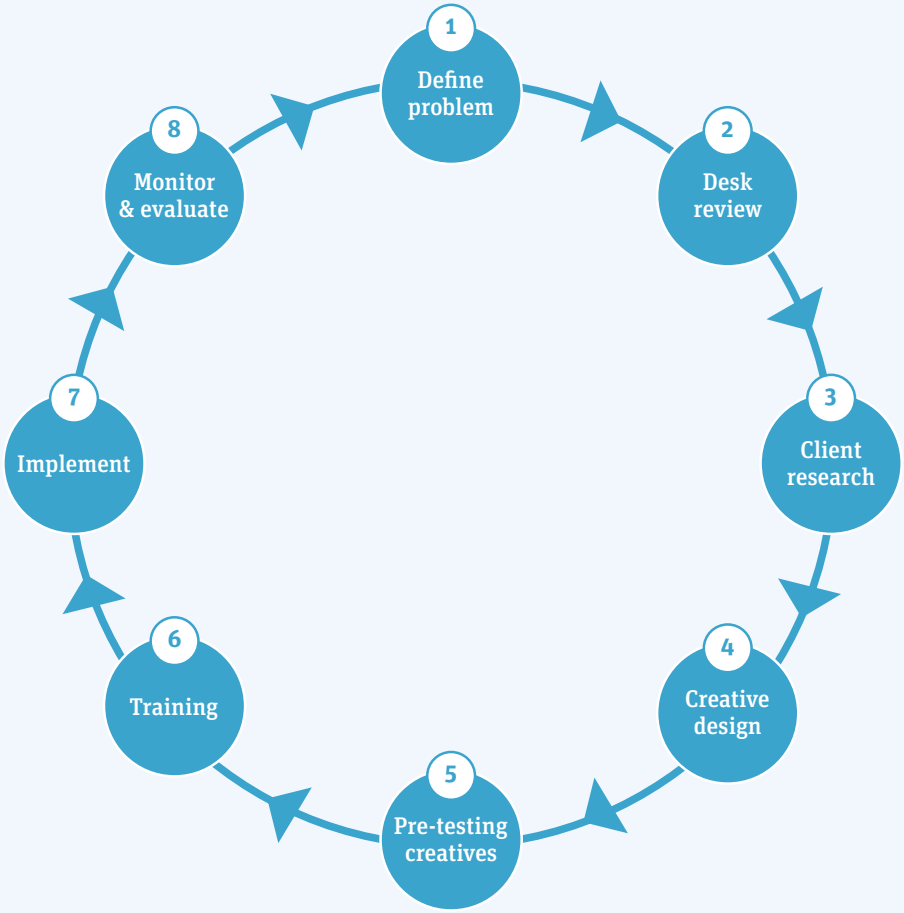
Micronutrient deficiencies during pregnancy remain a public health problem in low- and middle-income countries.[1] The current standard of care to address these deficiencies is the provision of iron and folic acid (IFA). However, evidence has found that a daily MMS (containing IFA, as well as 13 other micronutrients) during pregnancy improves women's health and pregnancy outcomes over and above the effects from IFA alone.[2,3]

While the World Health Organization (WHO) does not recommend MMS use in place of IFA in its 2016 Antenatal Care Guidelines, it states that where nutritional deficiencies are prevalent, governments might use their discretion to explore the use of MMS in their national programs.[4] Following issuance of WHO's 2016 Antenatal Care Guidelines, the New York Academy of Sciences (with sponsorship from the Bill & Melinda Gates Foundation) convened an MMS Task Force to address concerns about MMS use identified by WHO. To do this, the MMS Task Force was charged with conducting follow-on analyses of existing efficacy trial data that were not available at the time of the development of WHO's guidelines, and to develop operational guidance to assist national health officials to gauge when to explore the introduction of MMS.[5]

> **"Following issuance of WHO's Antenatal Care Guidelines, an MMS Task Force and its successor group, the MMS technical advisory group (MMS TAG), were convened by the New York Academy of Sciences to complete follow-on analyses of datasets from MMS efficacy trials and to provide operational guidance to help public health officials gauge when to begin to explore MMS use in public health nutrition programs"**

Based on this guidance, the Haitian MSPP, Vitamin Angels,[6] JHSPH and the HHF decided to begin exploring national MMS use and are conducting implementation research to inform MMS pro-

FIGURE 1: *Sight and Life's* 'Process that culminates in a strategy to change behaviors'



Credit: *Sight and Life*

gram introduction and scale-up (see **Box 1** for a description of each partner's roles). The aims are to:

1. Develop and field-test SBCC strategies and tools intended to support the uptake of and adherence to MMS among pregnant women.
2. Field-test the provision of MMS, including the distribution platform, supply chain and cost.
3. Identify and implement a methodology to evaluate MMS acceptance, coverage and adherence among pregnant women.

BOX 1: Role of partners

- **Haitian Ministry of Public Health and Population (MSPP):** study investigators, scientific oversight and implementation of MMS within the government's antenatal care platform
- **Vitamin Angels:** study investigators, technical assistance and provision of MMS
- **Haitian Health Foundation (HHF):** implementation of MMS within hard-to-reach areas
- **Johns Hopkins Bloomberg School of Public Health (JHSPH)**: study investigators, scientific oversight and ethical review

Aim 1: Develop and field-test SBCC strategies and tools

A key finding of the technical advisory group was that IFA supplementation programs for pregnant women have struggled to ensure high coverage and adherence to the daily supplementation regimen. Establishing and maintaining the daily use of the supplement can be challenging.

Based on this finding, we sought guidance from *Sight and Life* and utilized their Behavior Change Communication webinar series.[7] This webinar provided an eight-step process for developing, implementing and evaluating new behavior change strategies and tools (**Figure 1**).

Starting with **Step 1** of *Sight and Life's* process, Vitamin Angels and MSPP hosted a workshop in Haiti in September 2018

Participants from the 2018 stakeholders' workshop come together to develop program and SBCC goals and objectives to support MMS introduction and implementation

with key government stakeholders from all geographic departments in Haiti.

During **Step 2**, a desk review identified the constraints, barriers and enablers of the daily adherence to supplementation during pregnancy, and considered other SBCC programs that have been tried to instill these behaviors. This information provided a foundation for the development of our formative (client) research, including highlighting the respondent groups of interest, the themes and topics to explore, and the assumptions to test.

During **Step 3**, formative research was conducted to understand our audience, the barriers and enablers in relation to seeking antenatal care and to MMS uptake and adherence, and the channels through which SBCC could be delivered.[8] Ethical approval for this research was obtained from the JHSPH Institutional Review Board and the Haiti Ethics Board.

In October 2019, investigators held a 2-day workshop with project investigators to review formative research findings and discuss the subsequent processes and steps needed to develop and test an MMS intervention.

Aim 2: Field-test the provision of MMS

To field-test the provision of MMS, including the distribution platform, supply chain and cost, we selected five communes within the Grand'Anse department in Haiti. This department was identified as an underserved area that has high rates of anemia, an existing antenatal delivery platform and experience distributing IFA supplements. The department is located in the south of Haiti and has the second highest rates of anemia among women of reproductive age in the country (54.9 percent) despite the presence of high antenatal care coverage (90.3 percent).[9]

The MMS will be distributed to all pregnant women (n ≈ 6,000) in the five communes (third administrative level) through both MSPP and HHF. MSPP will be responsible for the distribution of MMS through existing health facilities, and HHF will be responsible for the distribution of MMS to hard-to-reach populations not served by the government. The implementation period covers June 2020 to December 2020.

Aim 3: Identify and implement a monitoring and evaluation methodology

The objective of this aim is to identify and evaluate a methodology to assess MMS acceptance, coverage and adherence (both before and after implementation of the project), and to measure fidelity (i.e., if the program is delivered as intended) during the implementation period. Based on monitoring results, implementation challenges will be identified and real-time course corrections will be made to improve program delivery.

Summary and next steps

In summary, the overall objectives of this project are to:

(1) develop and field-test SBCC strategies and tools intended to support the uptake of and adherence to MMS among pregnant women;
(2) field-test the provision of MMS, including the distribution platform, supply chain and cost; and
(3) identify and implement a methodology to evaluate acceptance, coverage and adherence of MMS among pregnant women.

To date, findings from the desk review and the formative research have provided actionable insights that are being used to develop the SBCC strategy, with the support of a creative design agency in Haiti. Next steps include field-testing the provision of MMS within the context of a comprehensive SBCC and monitoring and evaluation strategy. Both before and after the initiation of the project, a coverage survey will be conducted within the Grand'Anse department to assess changes in MMS acceptance, coverage and adherence among pregnant women.

"The project in Haiti has highlighted the importance and value of multisectoral partnerships to leverage expertise and collectively advance MMS"

The implementation research project in Haiti has highlighted the importance and value of multisectoral partnerships to leverage expertise and collectively advance MMS. These collaborations

have also allowed for increased coordination among government and NGO sectors (e.g., using a blended approach), read more about this on pages 37–41 of this Special Report, to expand coverage, ensure effective and efficient programs, and work towards ensuring long-term program sustainability.

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Disclosure Statement

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References

1 Bhutta ZA, Das JK, Rizvi A, Gaffey 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.

2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient 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 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 2 March 2020).

5 Bourassa, MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6–21.

6 Vitamin Angels. Internet: https://www.vitaminangels.org (accessed 4 November 2019).

7 *Sight and Life*. 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 Institut Haïtien de l'Enfance (IHE) and ICF. Enquête Mortalité, Morbidité et Utilisation des Services (EMMUS-VI 2016–2017). IHE, ICF; 2018. Internet: https://www.dhsprogram.com/pubs/pdf/FR326/FR326.pdf (accessed 2 March 2020).

Better Quality for Better Impact

Optimized packaging and appearance of maternal multiple micronutrient supplements for pregnant women in Indonesia

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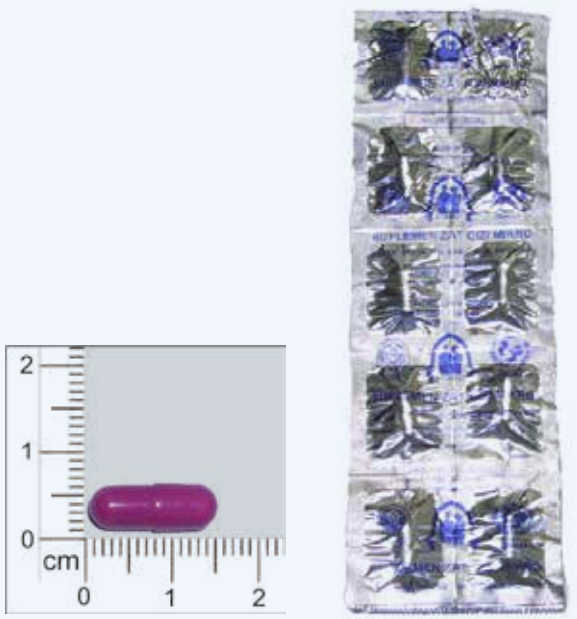
Micronutrient deficiencies in pregnant women are common in low- and middle-income countries, as these countries are often characterized by limited consumption of animal products, fruits, vegetables and fortified foods.[1] In Indonesia, maternal daily consumption of foods rich in micronutrients is insufficient to fulfill dietary requirements; the average consumption of fruits and vegetables is low in urban and rural areas alike.[2]

While many countries are considering transitioning to multiple micronutrient supplements (MMS), several challenges remain within iron and folic acid (IFA) programs that could affect the health impact of MMS, including – as seen in many programs – low adherence. Factors influencing this low adherence include perceptions concerning the benefits of supplements, their availability, the manner in which they are promoted, reminders to consume them, and their organoleptic properties, appearance and packaging.[3]

The SUMMIT study

The Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) conducted in Indonesia was the first large-scale randomized double-blind MMS trial in pregnant women designed to assess impact on mortality. Because the study was integrated into the existing government maternal care system, all factors that could enhance compliance in a programmatic setting were optimized to promote adherence. Therefore, before manufacturing of the supplements commenced, the investigators at the Summit Institute of Development (SID) conducted over 50 focus groups using interactive qualitative methods to assess the preferences of pregnant women regarding the appearance and packaging of supplements. This resulted in the GMP production of more than 30 million supplements as 1.5 cm pink capsules, individually wrapped in 10-count foil blister packs with Halal certification. In one of the first such examples of cus-

A selection of pregnancy supplement forms and types of packaging available in Indonesia



SUMMIT supplement in the form of a pink capsule (left) and SUMMIT supplements in strip packaging (right)

tomer-driven design of an intervention, the women in the study received supplements with the appearance and packaging they had specified. As a result, adherence to supplement consumption in SUMMIT was high, at more than 85 percent[4] – and well in excess of the previous consumption figures for IFA provided as round red tablets in 30-count sachets.

"Adherence to supplement consumption in SUMMIT was high, at more than 85 percent"

Based on this experience, and that of market research conducted by vitamin manufacturers, transitioning to MMS must take into account women's preferences regarding packaging. Their views should help manufacturers, both local and global, to deliver a product that appeals to women, thereby fostering adherence and impact (see **Box 1**).

BOX 1: Key features of the survey

In pursuit of this goal, and in order to develop a methodology, SID designed a survey and information platform comprising proctored web surveys, SMS and chatbots, and conducted a national survey of preferences concerning packaging type and supplement count per package.

Here we report the data from 407 respondents who articulated their preferences with Likert-scale ratings for either bottle or blister packs, and for a supplement count of either 30 or 180 per package. Ratings of 1 and 2 were interpreted as disliked, 3 as neutral, and 4 and 5 as liked; the reasons for the choices were also recorded and coded. Overall, 60.3 percent of the respondents were 20–29 years of age and 25.3 percent were 30–39, with 52.3 percent living in rural areas and the remainder in urban settings.

Results

The results of the survey showed that 48.4 percent of women liked bottle packaging, while 25.3 percent disliked it, with 26.3 percent being neutral about it. Positive comments for bottle packaging included "higher capacity," "recyclable container" and "safer." Drawbacks included "less practical to carry" and "higher contamination potential." For blister packs, 40.5 percent of respondents liked them, and 24.1 percent disliked them, while 35.4 percent were neutral. Advantages included "more hygienic," "seeing or feeling the product without opening the packaging" and "helps to prompt consumption," with one disadvantage being "easily damaged if carried around."

With regard to the number of supplements per package, a count of 30 was liked by 45.0 percent of women and disliked by 32.9 percent, with 22.1 percent being neutral. Advantages expressed included "more hygienic," "more practical to carry around," "helps to prompt consumption" and "as an incentive

An SID team member (left) asks a mother (right) about her preferred supplement packaging types using a digital platform on a smartphone

to continue consumption." By contrast, a count of 180 was liked by only 7.6 percent of women, and disliked by 75.4 percent, with 17.0 percent being neutral. Negative comments regarding the 180 count were "taking too much space" and "the mental burden of too many in one pack." Positive comments were "less waste" and "more economical."

The survey also inquired about the importance of the supplement being Halal, as the Indonesian population is predominantly Muslim. Overall, 67.4 percent agreed that it is important for supplements to be Halal, while 31.4 percent were neutral and only 1.2 percent disagreed. Clearly, to reach a broader target in Indonesia and potentially other Muslim populations, a Halal product is essential. It is important to note that with effect from 2019, the Halal law in Indonesia stipulates that all products such as foods, drinks and medicines, including nutritional supplements, must have Halal certification, which applies both to the ingredients and to their processing. All such products, whether manufactured in Indonesia itself or imported into the country, must be Halal.

> **"A product designed to optimize adherence, though costing more, may provide a more favorable cost–benefit ratio"**

Suggested recommendation

Based on the results so far, a suggested recommendation could be that either bottles or blister packs would be suitable, with a strong preference for 30 supplements per package, and for Halal supplements. Additional data from the ongoing survey specify color and shape, and other attributes, as well as cost preferences. Although the foregoing recommendation does not take account of the cost of production, it is noted that distribution of the lowest-cost packaging options may not be optimal. Rather, a product designed to optimize adherence, though costing more, may provide a more favorable cost–benefit ratio. Assessment of the direct impact of different packaging formats and measurement of consumption would be warranted. There is also a need for implementation research to determine the best context-specific balance of price, packaging, and social and behavioral change campaigns, with a view to increasing MMS acceptance and compliance. Moreover, further work on rolling out the survey to other populations in order to assess regional and global preferences would support the goal of attaining high-impact, cost-effective and sustainable maternal MMS programs.

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References

1 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6-21. doi: 10.1111/nyas.14121.

2 Hermina H, Prihatini S. Gambaran Konsumsi Sayur dan Buah Penduduk Indonesia dalam Konteks Gizi Seimbang: Analisis Lanjut Survei Konsumsi Makanan Individu (SKMI) 2014. Buletin Penelitian Kesehatan. 2016; 44(3):4–10. doi: 10.22435/bpk.v44i3.5505.205-218

3 Clermont A, Kodish SR, Seck AM, Salifou A, Rosen J, Grais RF, et al. Acceptability and utilization of three nutritional supplements during pregnancy: Findings from a longitudinal, mixed-methods study in Niger. Nutrients. 2018;10(8). doi: 10.3390/nu10081073

4 SUMMIT Study Group. Effect of maternal multiple micronutrient supplementations on fetal loss and infant death in Indonesia: A double-blind cluster-randomized trial. Lancet. 2008;371:215–27.

The Case for Reintroducing Multiple Micronutrient Supplements in South Africa's Essential Medicines List

Creating an enabling environment for nutrition-specific interventions in antenatal care

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Key messages

- For 6 years, between 2010 and 2016, most provinces in South Africa provided multiple micronutrient supplements (MMS) to all pregnant and lactating women, but removal from the national essential medicines list (EML) led to the discontinuation of provision in late 2016. *Sight and Life* documented South Africa's MMS journey in 2018.
- Based on *Sight and Life's* case study, transitioning from iron and folic acid (IFA) to MMS has been shown to be cost-effective for the South African context, and translates into substantial future social and public health benefits and economic savings for South Africa.
- Transitioning from IFA to MMS has been shown to be relatively straightforward, but investing in training and social and behavioral change communication is important because this strengthens uptake and adherence, which in turn will amplify the health impact.
- Given the strong scientific evidence, the South African national government and international bodies can help to restart the provision of MMS. A strategy for reintroduction and a four-step action plan are outlined in this article.
- We also present a suggested table of contents, for advocacy purposes, that was co-created with MMS champions in South Africa. This can be adapted to suit the local contexts of other low- and middle-income countries (LMICs) considering the inclusion of MMS in their EMLs.

The rise and fall of MMS in South Africa

Between 2010 and 2015, South Africa was the only LMIC that provided MMS through government channels. In 2016, the national government dropped MMS from the national EML because of the lack of knowledge about the strong evidence base for MMS and the lack of clear guidelines from WHO. This action prevented provinces from ordering it, and pregnant women from accessing it. In 2018, *Sight and Life* undertook a policy and programmatic analysis, conducting interviews with key informants in the country to fill the gaps in the knowledge required to build a strong consensus for MMS in South Africa's policy landscape and advocate for MMS being reintroduced into the EML (**Figure 1** and **Box 1**).

FIGURE 1: The three South African provincial nutrition departments interviewed by *Sight and Life*

> **"In 2018, *Sight and Life* undertook a policy and programmatic analysis to build a strong consensus for MMS in South Africa's policy landscape"**

In the first section of this article, we provide an overview of the policy hurdles for MMS in South Africa to set the context. In

the next section, we address the knowledge gap around the evidence base by taking the birth outcomes and cost-effectiveness of MMS from two recent scientific reviews,[1,2] and applying it to the South African context. In the third part of this article, we address the knowledge gap around programmatic aspects of MMS and synthesize learnings from provinces to establish a transition back to MMS. We close out the article by presenting recommendations and strategies for the reintroduction of MMS into the EML.

BOX 1: What are the arguments for placing MMS in the EML?

A substantial body of observational, experimental and programmatic data documents the efficacy and cost-effectiveness of MMS, as described elsewhere in this *Sight and Life* Special Report. There is precedent for countrywide MMS distribution in South Africa, and all the programmatic barriers and enabling factors are well known, which would facilitate a smooth reintroduction:

- Inclusion of MMS in the EML would lead to improved integration of nutrition within the health system.
- Inclusion of MMS in the EML would result in better management of newborn and maternal nutrition programs.
- Increased financial resources would be available for MMS, and this could decrease overall product costs. This is based on assumptions that this commitment and demand would stimulate local production of MMS and that harmonization of standards could lead to a larger scale of production for bigger producers, thus decreasing unit costs.
- Inclusion of MMS in the EML would assist in changing perceptions around MMS and contribute to raising awareness of prenatal supplementation, as well as of maternal and newborn undernutrition in general, thus motivating healthcare workers.

Missed opportunity: the impact of national policy changes on provinces

Sight and Life's interviews with three provincial nutrition managers indicated that provincial nutrition departments championed MMS, but that the National Department of Health remained unconvinced. In the absence of clear guidelines from national government, the National Expert Medicine List Committee (NEMLC) deemed MMS nonessential and removed it from the national EML. After the MMS indication for pregnant and lactating women was removed from South Africa's standard treatment guidelines and EML in 2016, the guidelines indicated MMS provision only for pregnant and lactating women at risk of malnutrition. More recently, in 2017, the standard treatment guidelines were changed to remove MMS altogether, and the 2018 standard treatment guidelines recommend IFA supplementation only (**Figures 2A–C**).[3]

FIGURE 2A: Province-level guidelines 2016: change to MMS provision only for pregnant and lactating women classified as at risk of malnutrition

11.1 Micronutrients schedule for adults and children

Target Groups	Supplement	Duration
Children (0 to 59 months) at risk of Severe Acute Malnutrition/TB/HIV	Multivitamin syrup	6 months
Children 0-59 months with diarrhea	Zinc syrup	As per standard protocol – IMCI guidelines
Children 6-59 months	Vitamin A – age appropriate dose as per standard protocol	Six – monthly intervals
Pregnant women at risk of malnutrition	Complete multiple micronutrient supplements, calcium	Duration of pregnancy
Lactating women at risk of malnutrition	Complete multiple micronutrient supplements	6 months of lactation
Adults – Underweight with TB, HIV, AIDS	Complete multiple micronutrient supplements	6 months

FIGURE 2B: Province-level guidelines 2017: MMS for pregnant and lactating women completely removed from the guidelines

Level of care

At PHC level

- Complete multiple micronutrients will not be procured at hospital level
- In the event that the hospital requires complete multiple micronutrients to treat a specific case, motivation would have to be done at facility level with relevant stakeholders

Below is the revised schedule for micronutrient supplementation

Target Groups	Supplement	Duration
Children 0-59 months with diarrhea	Zinc Syrup	As per standard protocol – IMCI guidelines
Children 6-59 months	Vitamin A – age appropriate dose as per standard protocol	Six – monthly intervals
Pregnant women	IFA and calcium as per maternity guidelines	Duration of pregnancy

The change is effective from the 1st of April 2017. Facilities who still have stock on hand should continue supplementation as per previous recommendation until the stock is finished. The stock should not be replenished thereafter.

FIGURE 2C: Province-level guidelines 2018: IFA for pregnant and lactating women

Description

Supplements before and during pregnancy and lactation can help to prevent, or lessen the effect of, a number of conditions or complications associated with pregnancy. Specifically:

- Folic acid, given for at least one month before conception and during pregnancy (particularly the first 12 weeks) can help prevent neural tube defects (abnormal development of spinal cord/brain).
- Iron can help to prevent anaemia.
- Calcium can help to prevent pre-eclampsia.

Note: Figures 2A, 2B and 2C are sourced from internal provincial memos and documents

Provincial nutrition leaders remain committed to MMS because of its superiority to IFA, and continue procuring it in very small quantities as a backup to IFA. **Table 1A** shows the number of MMS capsules procured and distributed by provincial governments over the past 3 years since MMS was removed from the EML. These numbers are abysmally low, and it is striking that the cumulative figure for number of MMS capsules/tablets procured and distributed over the past 3 years is lower than the total amount of prenatal IFA in 2019 alone (**Table 1B**). This highlights that, even with political will and budget availability at the provincial level for MMS, not having it on the EML created major programmatic challenges in ordering large volumes.

TABLE 1A: Number of prenatal MMS capsules or tablets supplemented during 2017–2019

	MMS capsules/tablets (in millions)
Eastern Cape	8.30
KwaZulu-Natal	1.30
Northern Cape	5.60
Gauteng	0.40
Mpumalanga	0.01
Western Cape	0.03
TOTAL MMS	**15.64**

TABLE 1B: Number of prenatal IFA capsules or tablets procured in 2019

	IFA capsules/tablets (in millions)
Total iron	256.10
Total folic acid	258.70

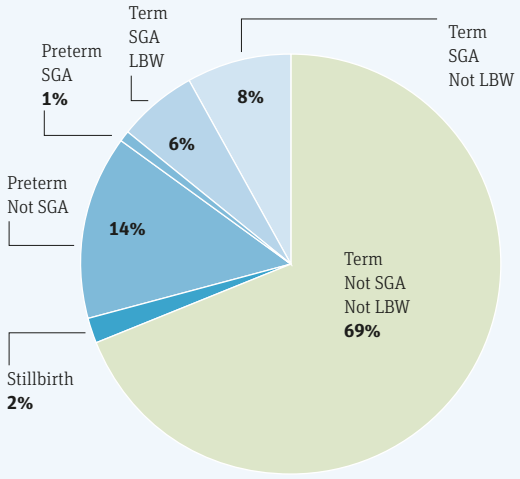
The evidence base: public health relevance of MMS in South Africa

a. Birth outcomes

As an LMIC, South Africa presents with high rates for preterm birth (< 37 weeks gestational age) and low birth weight (LBW; < 2,500 g); the rates can be as high as 14 percent, as opposed to 7 percent in high-income countries. The estimated rates for adverse birth outcomes in South Africa are shown in **Figure 2**. Apart from increased risk of increased maternal and child mortality, the risk for suboptimal child growth and development can be long term.[4] Severe developmental disabilities associated with LBW and/or preterm birth include cerebral palsy, sensory impairments of vision and hearing, mental disability and seizure disorder. In addition, neurodevelopmental functions, such as attention, cognition, executive functioning, emergent literacy, sensory processing, gross and fine motor skills, communication and language, as well as infant feeding and swallowing, may be affected in children with LBW and/or preterm birth.

In South Africa, the largest category of perinatal deaths is unexplained stillbirth, of which up to one-quarter are related to small for gestational age (SGA). High on the global health agenda is accelerating progress to end preventable stillbirths. In 2014, the Every Newborn Action Plan set a target of 12 or fewer stillbirths per 1,000 births in every country by 2030. MMS is a ready and cost-effective solution to help us meet these targets.[5]

FIGURE 3: Current birth outcomes in South Africa



SGA: small for gestational age
LBW: low birth weight

b. Potential impact of MMS on birth outcomes

Table 2 shows the average estimated costs of MMS and IFA in South Africa. The larger the number of capsules/tablets per unit supply, the smaller the cost difference between MMS and IFA, since packaging determines the largest portion of the total costs.

TABLE 2: Cost of MMS and IFA in South Africa

	Price of MMS*	Price of IFA
30 capsules/tablets	US$2.23	US$0.80
60 capsules/tablets	US$3.34	US$1.20

*Includes transportation costs; government bears no additional costs to get MMS to clinics because of streamlining through existing depots

TABLE 3: Impact of MMS over IFA at 25% (conservative) to 62% (optimistic) coverage on birth outcomes (there are ~1.1 million pregnancies per year in South Africa)[6,7]

Outcome	Rate	Cases	Reached at 25–62% MMS coverage	Reduced risk with MMS[6]	Prevented cases
Preterm	8%	~88,000	37,000-91,000	18%	4,000–9,800
Low birth weight	7.9%	~87,000	20,000-49,000	12%	2,600–6,500
Small for gestational age	6.7%	~74,000	23,000-58,000	3%	500–1,400
Stillbirth	2%	~20,000	5,000-13,000	8%	400–1,000

If the switch were to be made from IFA to MMS, the health impact on the South African population would be tremendous: 1,100–2,700 additional preterm births and 300–600 additional stillbirths could be prevented (**Table 3**). The impact of MMS on LBW and SGA would be even more significant: an additional 2,600–6,500 cases of LBW and an additional 1,500–3,600 cases of SGA could be averted. Thus, given the potential price differences between MMS and IFA supplementation in South Africa (**Table 2**), the additional benefits of MMS clearly outweigh the higher costs.

Recently, an MMS Cost-Benefit Tool was launched to allow governments to calculate the cost-benefit ratio of transitioning from IFA to MMS based on their country-specific demographics.[8] When assuming risk reduction rates in adverse birth outcomes as reported by Smith et al,[1] 212,120 additional disability adjusted life years (DALYs) and 2,505 additional child deaths could be averted in South Africa when transitioning from IFA to MMS at a cost-effectiveness of US$12.17 per DALY averted, making MMS a very cost-effective intervention (**Figure 4**).

Programmatic experiences: transitioning from current system in South Africa

Sight and Life's interviews revealed two key triggers that first led to the inclusion of MMS for pregnant and lactating women in South Africa in 2010.

1. The budget for MMS has always been in place in provinces because of highly prioritized HIV treatment:

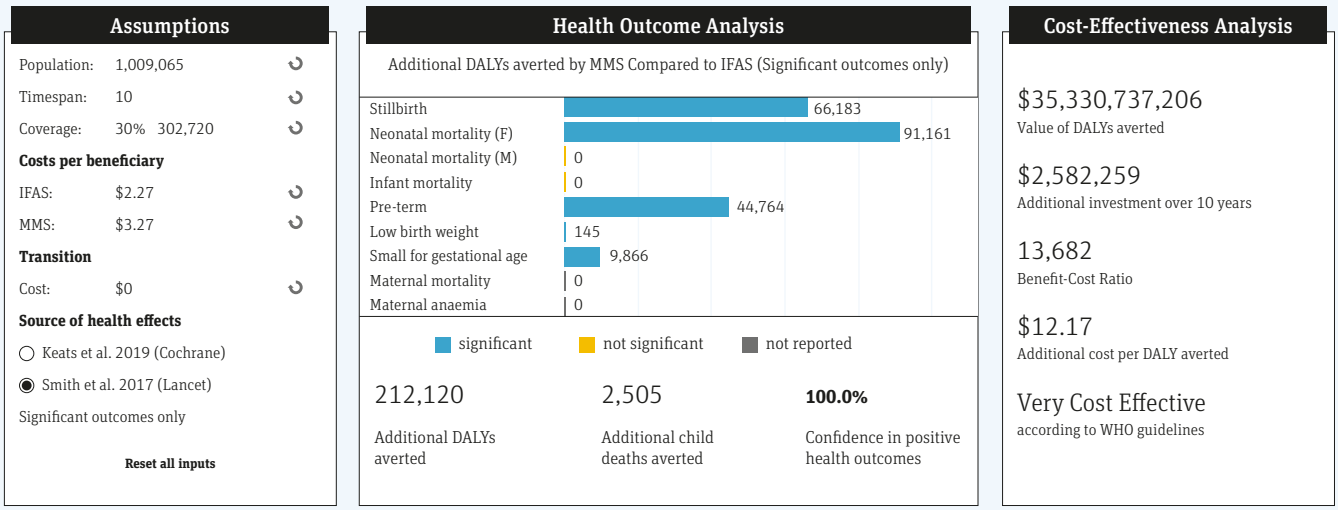
- Providing MMS as part of antiretroviral therapy for HIV was mandatory.

- With improving HIV rates over the years, provincial focus shifted to low birth outcomes and preventative maternal care.

- With the shifting priorities, provinces started using HIV conditional grants to procure MMS for all pregnant and lactating women to improve birth outcomes. However, no programmatic investments were made in training and behavior change communication to avoid any HIV-related stigma associated with MMS consumption.

2. MMS was considered a low-burden health intervention because it leveraged the IFA supply and distribution channels:

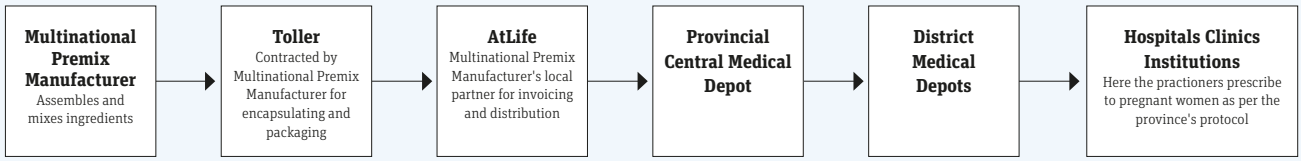
FIGURE 4: Cost-effectiveness of MMS in South Africa



* Currency in US$

Note: This analysis was conducted on Nutrition International's MMS Cost-Benefit Analysis Tool. An updated version of the analysis can be found on: https://www.nutritionintl.org/knowledge-centre/mms-cost-benefit-tool/

FIGURE 5: MMS production and distribution flow diagram



- The health system in South Africa is overburdened, and officials are reluctant to introduce any interventions that would further weigh down the system.
- Since the supply and distribution channels were already in place for IFA and calcium, MMS was easy to integrate into the health system.
- MMS was distributed through the existing medical depot system in provinces, which handles supply and distribution to clinics.

A quote by one of the provincial nutrition managers who was interviewed sums up the ease of transitioning from IFA to MMS. She said, "The programmatic aspect of MMS is the least of the problems. The policy framework is the problem because of lack of evidence and because it is no longer on the EML. MMS is extremely easy to integrate into the healthcare system."

The lessons from the 5 years of MMS distribution indicate that in mature pharmaceutical markets such as South Africa, MMS is easy to manufacture and deliver (**Figure 4**); however, motivating practitioners through training is challenging when policy guidelines are inconsistent and equivocal. While the MMS supply chains were programmatically efficient, no resources were spent on training, demand creation and compliance. At the hospital/clinic level, nurses and practitioners were trained on the general supplementation policy of the province but never received explicit training on MMS and its benefits. MMS was just one of the many supplements that practitioners were trained to prescribe. Investing in training and social and behavioral change communication is important because it strengthens uptake and adherence, which in turn will amplify the health impact of MMS among women and children in South Africa.

Moreover, South African provinces are extremely autonomous and varied: in low-capacity provinces, budgetary allocations to prenatal care (such as MMS) are not always acknowledged and/or prioritized. Strong national policy guidelines, accompanied by a reintroduction of MMS into the EML, would make it easier for provinces to transition back to MMS and allocate budgets for procurement and training.

"For South Africa, thousands of preterm births and stillbirths and tens of thousands of LBW and SGA infants could be averted by transitioning from IFA to MMS"

MMS is one of the most cost-effective investments among the different potential antenatal care interventions. For South Africa, thousands of preterm births and stillbirths and tens of thousands of LBW and SGA infants could be averted by transitioning from IFA to MMS. Transitioning from IFA to MMS has been shown to be cost-effective for the South African context. This could translate into substantial future social and public health benefits and economic savings for South Africa. Transitioning from IFA to MMS has been shown to be relatively straightforward, but investment in training and social and behavioral change communication is required to strengthen uptake and adherence, and in turn increase the health impact in South Africa. Therefore, prioritizing financial resources towards nutrition-specific interventions in antenatal care would provide a significant return on investment and could ultimately decrease overall societal costs.

The path forward: strategies for reintroduction

With the scientific evidence in place and ease of transitioning established, four immediate actions would be needed to build consensus for MMS in South Africa's policy landscape:

1. **Sensitize the NEMLC.** This committee is made up of clinicians and academics whose decisions guide medicine procurement in the public sector. They are responsible for reviewing and updating the EML every 2–3 years. Sensitizing them to the latest evidence is paramount, and special attention needs to be paid to highlighting the medical outcomes (reduction of LBW, SGA and preterm births) of a simple and cost-effective micronutrient supplement.
2. **Provide technical support to provinces with pharmacy and therapeutics committees (PTCs).** PTCs can determine

province-level medicine needs, independent of the NEMLC. Typically, provincial nutrition departments do not advocate with PTCs given the process-heavy nature of engagement, which is why NGOs are well suited to support provinces and could provide technical support around the evidence base and programmatic aspects of MMS.

3. Build an advocacy plan for National Pediatric, Prenatal and Malnutrition Working Groups.

These multistakeholder groups are convened at the highest levels of national government and have not been engaged in a strategic manner to champion MMS, even given the advocacy effort of several prominent NGOs. There is an opportunity to create a strategic plan focused on the advocacy of MMS for pregnant women.

4. Convene provincial nutrition departments.

Knowledge sharing and capacity building among provinces are essential to create a joint advocacy plan for MMS. Currently, provincial advocacy efforts for MMS are fragmented and few opportunities exist for low-capacity provinces – such as Eastern Cape and Northern Cape – to learn from well-resourced provinces – such as KwaZulu-Natal – about programmatic aspects of MMS. By convening provincial departments, information could be shared more effectively and a joint advocacy plan for MMS could take shape.

Based on these recommendations, which emerged from *Sight and Life's* analysis in 2018, a group of experts has been convened to provide guidance to a national technical advisor. The expert group has co-created a memo with the aim of providing concise, easy-to-read, scientific and health-economic evidence-based guidance for the reintroduction of prenatal MMS into the EML and making it accessible by the end of 2020 (**Box 2**).

BOX 2: How can the global nutrition community support LMICs in advocating for the inclusion of MMS in national EMLs?

Through this exercise in South Africa, we were able to gather valuable insights into the key pieces of information that decision-makers in LMICs look for when deliberating on the inclusion of MMS in national EMLs, in the absence of a WHO recommendation. The global nutrition community has the opportunity to play the role of catalysts by helping LMICs compile this information. Below, we present a suggested table of contents that was co-created with MMS champions in South Africa, which can be adapted to suit the local contexts of other LMICs considering the inclusion of MMS in their EMLs.

All of the information below can be compiled through a combination of desk research and structured/semi-structured interviews with key informants, which include officials in government departments, industry and local NGOs.

Document outline

Objective
Executive summary
Background
1. Preventing poor birth outcomes
2. Scientific evidence:MMS versus IFA
3. Role of MMS in pregnant women
4. Cost-benefit of MMS versus IFA
5. Current WHO guidelines and possible evolution
6. Current product standard: UNIMMAP MMS implementation in country of interest
7. Public health relevance in country of interest
   - 7.1 Nutritional gaps in pregnant women in country of interest
   - 7.2 Birth outcomes in country of interest
8. Potential impact of MMS on birth outcomes in country of interest
9. Current policy and regulation in country of interest
10. Guidelines for maternal care in country of interest
11. Prenatal supplementation indication for pregnant women in country of interest
12. Ease of transitioning from current system in country of interest
13. Current government tender specifications in country of interest
14. Recommendations

Conclusion
References

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References

1 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(11):e1090–e1100.

2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;3i:CD004905.

3 Department of Health, Republic of South Africa. Standard Treatment Guidelines and Essential Medicines List for South Africa. Primary Healthcare Level. 2018. Internet: http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list (accessed 20 February 2020).

4 Fouche LC, Kritzinger A, Le Roux T. Gestational age and birth weight variations in young children with language impairment at an early communication intervention clinic. S Afr J Commun Disord. 2018;65(1):e1–e9.

5 Lavin T, Preen DB, Pattinson R. Timing and cause of perinatal mortality for small-for-gestational-age babies in South Africa: critical periods and challenges with detection. Matern Health Neonatol Perinatol. 2016;2:11.

6 BMJ. Estimates of burden and consequences of infants born small for gestational age in low and middle income countries with INTERGROWTH-21st standard: analysis of CHERG datasets. BMJ. 2017;358:j3677

7 Statistics South Africa. Perinatal Deaths in South Africa 2015. July 2017. Internet: https://www.gov.za/speeches/perinatal-deaths-south-africa-2015-report-31-jul-2017-0000 (accessed 20 February 2020).

8 Nutrition International. The MMS Cost-Benefit Tool. 2019. Internet: https://www.nutritionintl.org/knowledge-centre/mms-cost-benefit-tool/ (accessed 20 February 2020).

One MMS a Day and a Healthy Baby is on the Way

Building a market-based approach in Bangladesh

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Key messages

- In Bangladesh, the use of key maternal and newborn health services remains critically low: only 37 percent of all pregnant women attend four antenatal care visits. On the other hand, compared with many other low- and middle-income countries, 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.
- This article documents the transformative proposition of a market-based model to get high-quality multiple micronutrient supplements (product) to pregnant women in Bangladesh at the right price, with effective promotion and the correct place or channel of distribution, while creating the right policy environment.
- The goal of a market-based model is to develop pathways to sustainability; from the very beginning, the program is structured to ensure that the local implementing partner, Social Marketing Company, will be able to run the business model without any grant assistance.
- With a sustainable, locally owned and operated, market-based model, it is estimated that nearly 77,000 Bangladeshi children will be born healthy every year and will have the opportunity to reach their full potential.

Building the 'One MMS a Day and a Healthy Baby is on the Way' consortium in Bangladesh

There is enough evidence to switch from iron and folic acid (IFA) to multiple micronutrient supplements (MMS) based on improved pregnancy outcomes. In addition, recent studies show that ~1,268,067 disability-adjusted life years (DALYs) would be averted from the switch in Bangladesh over a 10-year period, and that the incremental cost per DALY averted would be US$9.93 (**Figure 1**).[1]

The Children's Investment Fund Foundation (CIFF) is the world's largest philanthropic organization that focuses specifically on improving children's lives. CIFF has assembled a consortium of stakeholders to sustainably shape the market for affordable and accessible MMS in Bangladesh. This consortium includes: a social enterprise partner, Social Marketing Company (SMC), which has a vast nationwide network of franchisee pharmacies; *Sight and Life*, a global nutrition knowledge organization with expertise in building social business models; and the Global Alliance for Improved Nutrition (GAIN), an international NGO that will lead a national-level task force to work collaboratively with the government to harmonize standards and facilitate the inclusion of MMS in Bangladesh's essential medicines list (EML) and national standard treatment guidelines.

Why a market-based model?

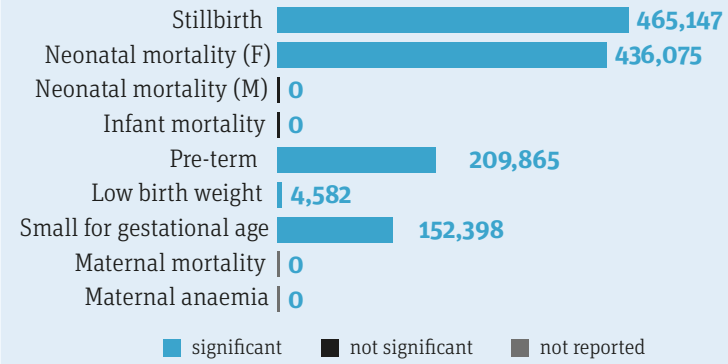
In Bangladesh, the use of key maternal and newborn health services remains critically low, with only 37 percent of all pregnant women attending four antenatal care visits.[2] On the other hand, compared with many other low- and middle-income countries, Bangladesh has a dense network of retail pharmacies 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. Furthermore, at the base of the pyramid, specifically those from the poor and aspirant segments together account for a staggering 75 percent of all pregnant women in Bangladesh. With a per capita daily household income between US$0.5 and US$2.5, these women purchase from neighborhood pharmacies. It is therefore important to ensure that MMS is available in these stores. SMC was selected for its commitment to public health, extensive coverage of pharmacies across Bangladesh and, most importantly, its large customer base of poor and aspirant socioeconomic groups (**Table 1**).

The market-based model is designed to complement the government's antenatal-care-based model, which is being piloted to reach ultra-poor women.

This article documents the transformative proposition of a market-based model to get high-quality MMS (product) to pregnant women in Bangladesh at the right price, with effective promotion and the correct place or channel of distribution, while creating the right policy environment.

FIGURE 1: Cost-effectiveness of transitioning from IFA to MMS in Bangladesh

HEALTH OUTCOMES ANALYSIS*



*Prospective health outcomes over a 10 year period

1,268,067 DALYs averted

12,640 child deaths averted

100% confidence in positive health outcomes

COST EFFECTIVENESS ANALYSIS

Value of DALYs averted (over 10 years)	$3,696,039,235
Additional investment over 10 years	$12,589,729
Benefit Cost Ratio	294
Incremental cost per DALY averted	$9.93
According to WHO guidelines	very cost effective

TABLE 1: Customer segmentation in Bangladesh

			2019	2025	2019
		Income/Capita/Day	All Pregnant Women in Bangladesh		SMC Pharmacies
			3 million		
	Affluent	> $4.5	1%	2%	2%
	Established	$2.5 – $4.5	10%	15%	12%
BOP	Aspirant	$1 – $2.5	48%	59%	34%
BOP	Poor	$0.5 – $1	25%	16%	47%
BOP	Ultra Poor	< $0.5	16%	8%	5%

Source: *Sight and Life* team analysis based on Bangladesh Demographic and Health Survey, BCG Bangladesh Surging Consumer Market, UN database (2017); telesurvey of supplements in 130 SMC pharmacies (May 2019)

Transformative proposition: building a market-based model

We will analyze the transformative proposition of the market-based model from the lens of product, price, place, promotion and policy.

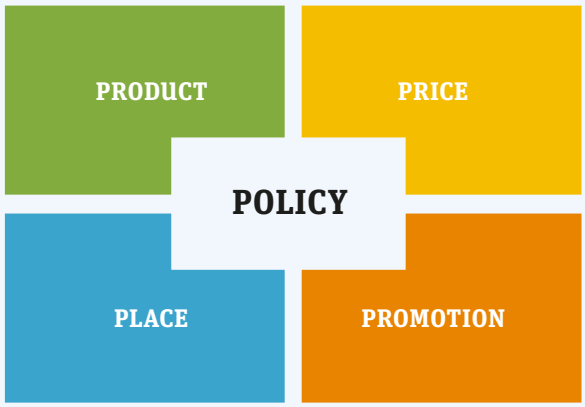
Neil Borden, of Harvard Business School, used the term 'marketing mix' in 1991 to describe the set of activities making up a firm's marketing program. He noted how firms blend elements of this 'mix' into a program, and how firms competing in one and the same product category may have dramatically different 'mixes' at work. As shown in **Figure 2**, the 4Ps of product, price, promotion and place are often used to set out the marketing mix in an easy-to-recall way.[3] Since this market-based model is in the service of a

TABLE 2: Product benchmarking analysis of non-UNIMMAP MMS in the Bangladeshi market

PRODUCT	Momvit	Aristo Mom	Nutrum PN	Precare
COMPANY	Beximco	Aristopharma	Acme	Incepta
	Local	Local	Local	Local
No. of Caps	Blister packs of 60	Blister packs of 10	Bottles of 30	Bottles of 30
Galenical form	Tablets	Tablets	Tablets	Tablets
Pack Shot				
Shelf Life	23 months	24 months	24 months	23 months
Nutrition Information per daily dose	2 tablets daily with meal	2 tablets daily	1 tablet daily	2 tablets daily with food
Vitamin A (µg RE)	1800	1800	2700	2700
Vitamin B_1 (mg)	0.5	0.5	3.4	3.4
Vitamin B_2 (mg)	0.75	0.75	3.4	3.4
Niacin (B_3) (mg)	7.5	7.5	40	40
Vitamin B_6 (mg)	0.75	0.75	10	10
Vitamin B_{12} (µg)	1.5	1.5		
Vitamin C (mg)	15	15	120	120
Vitamin D_3 (IU)	250	250		
Vitamin E (mg)	4.68	4.68	27	27
Vitamin K (µg)			65	65
Pantothenic acid (mg)			20	20
Calcium (mg)	59	59		
Chromium (µg)			25	25
Copper (mg)	0	0	2	2
Folic acid (µg)	250	250	800	800
Iodine (µg)	125	125	175	175
Inositol (mg)			50	50
Iron (mg)	5	5	30	30
Magnesium (mg)	15	15		
Manganese (µg)			1.2	1.2
Molybdenum (µg)			25	25
Phosphorous (mg)	45.6	45.6		
Selenium (µg)	0	0	12.5	12.5
Zinc (mg)	8	8	25	25
Quercetin (µg)			54	54

MultiVit Plus	Natal-16	UNIMAP
Square	Opsonin	UNU / UNICEF / WHO
Local	Local	
Bottles of 30	Bottles of 30	
Tablets	Tablets	
		
23 months	24 months	
1 tablet daily	2 tablets daily	
1500	1800	800
1.5	0.5	1.4
1.7	0.75	1.4
20	7.5	18
2	0.75	1.9
6	1.5	2.6
60	15	70
400	250	200
13.5	4.68	10
10.92		
	59	
2	0	2
400	250	400
196	125	150
50	5	30
	15	
1		
	45.6	
0	0	65
37.03	8	15

FIGURE 2: The 5Ps of a social business model



Source: *Sight and Life*

public health outcome, we have added 'policy' as a fifth P, which will help to create an enabling environment for the 4Ps.

Product

Bangladesh has a vibrant pharmaceutical market, and several brands of prenatal multiple micronutrients are already available in the market. However, none of them match the UNIMMAP formulation, which has been used in the majority of trials and has been shown to have significant positive effects on birth outcomes. Most of the prenatal micronutrients in the Bangladeshi market have a lower number or lower dosage of critical micronutrients. For example, selenium, which has been shown to affect preterm birth, is missing or negligible in all of them.[4] The consortium successfully negotiated with a pharmaceutical company to develop the UNIMMAP formulation of MMS; a first batch has been manufactured and verified by lab tests, and is currently undergoing stability tests.

> **"Bangladesh has a vibrant pharmaceutical market"**

Price

Based on the market analysis and product benchmarking conducted by *Sight and Life*, the price of current MMS brands in Bangladesh ranges from US$1.8 to US$2.1 for a pack of 30–50 tablets. An eight-point framework (**Table 3**) was developed for selecting the right pharmaceutical company to manufacture MMS. The consortium has successfully negotiated the price to be lower than what is currently available in the market for the same pack size, while adhering to the UNIMMAP formulation and ensuring that no actor in the value chain will make a loss. Focus group discussions with pregnant women at the base of the pyramid revealed that, at the negotiated price, MMS has been affordably priced.

TABLE 3: Selection of pharmaceutical company

Criteria (definition)
1. Only produce as per UNIMMAP formulation
(strong scientific evidence established)
2. Willingness to co-brand product with SMC
3. Price
(supply to SMC at lower negotiated price per 30-tablet pack)
4. Meet the minimum order volumes for the market-based model
(200,000 bottles/packs for the pilot; 1.2 million bottles/packs for scale-up)
5. Quality standards
(evaluated by an independent committee)
6. Commitment to social programs
(strong proven track record of manufacturing products for social programs)
7. Previous experience with UNICEF/WFP
8. Reasonable prep time
(must produce MMS in < 1 year)

> **"Bangladesh has a favorable regulatory environment for local companies to produce MMS affordably"**

Moreover, Bangladesh has a favorable regulatory environment for local companies to produce MMS affordably. The Drug Administration has set a price ceiling on finished supplements, a low import duty of 5 percent on the straight ingredients and a prohibitively high import duty on finished supplements from foreign companies. More than 20 million MMS doses have already been produced locally for clinical trials, and the pharmaceutical sector is well poised to bring a high-quality MMS directly to consumers.

Place

Bangladesh has a dense and extensive pharmaceutical distribution network. There are more than 200,000 pharmacies in Bangladesh, of which 81 percent are in rural areas. They are so ubiquitous that one or two pharmacies can be found in every village market, and more than seven, and sometimes even 14, in urban markets.

SMC operates a 12,000-strong social franchising network of community-level private medical practitioners and pharmacists who offer affordable public health products and services including medicines. Based on different characteristics described in **Box 1**, these pharmacies are classified as Blue Star, Green Star and Pink Star. During phase one (2020–2021) of the market-based model, MMS will be available in all of these 12,000 pharmacies. All of them serve base-of-the-pyramid (ultra-poor, poor and aspirants <US$2.5/capita/day) consumers. MMS clients are mostly pregnant women and their relatives who visit these pharmacies.

BOX 1: Profiles of SMC's pharmacies

Profiles of Blue Star, Green Star and Pink Star Pharmacies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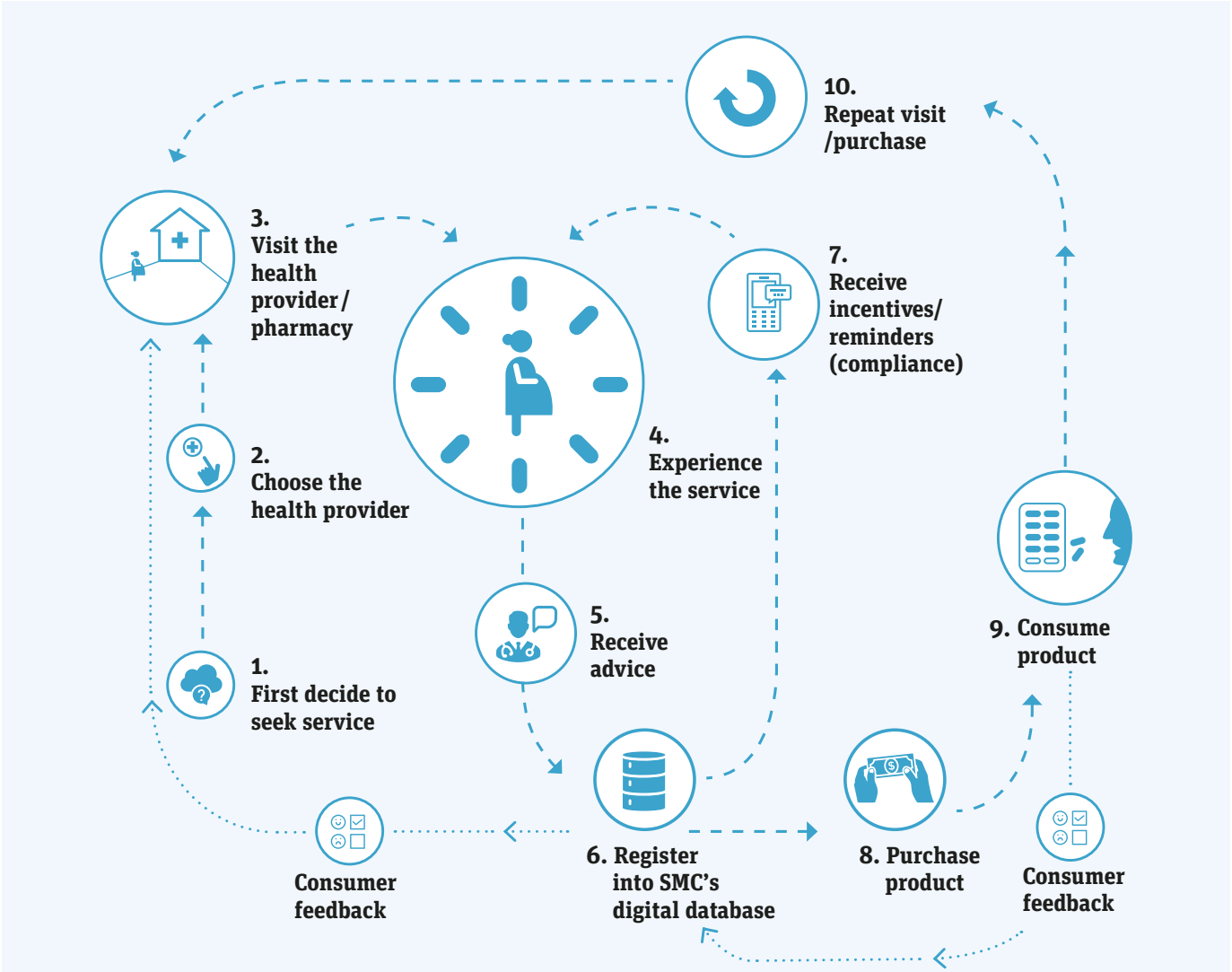
Blue Star Pharmacy	Green Star Pharmacy	Pink Star Pharmacy
7,500 outlets (> 75 percent in rural settings)	4,500 outlets (> 75 percent in rural settings)	650 (all urban settings)
Nongraduate medical practitioners; offer medical advice in chambers attached to pharmacies	Pharmacists provide over-the-counter health and family planning services	Obstetricians and gynecologists provide long-acting reversible contraceptives, antenatal care, postnatal care and other medical services to pregnant women

FIGURE 3: MMS customer journey in Bangladesh



Source: *Sight and Life*, created by Anne Milan, Design Specialist, *Sight and Life*

During phase two (2022–2025), the distribution will be expanded to cover the entire 200,000-strong pharmacy network in the country.

Promotion

To create awareness and aspiration for MMS, an intensive and integrated social marketing campaign will be implemented, targeting consumers, their key influencers and health pharmacies.

Demand creation for consumers and their key influencers

Activities will focus on: (1) creating a social norm for prenatal MMS supplementation, (2) generating a 'buzz' for the product, (3) creating value in the minds of consumers (lack of perceived need for supplementation during pregnancy), and (4) supporting the formation of a daily supplementation habit. The demand creation activities will be strategically integrated and based on human-centered-design research with pharmacies and consumers. A complete customer journey (Figure 3), including opportunities for customer segmentation and value creation, will be further refined through research.

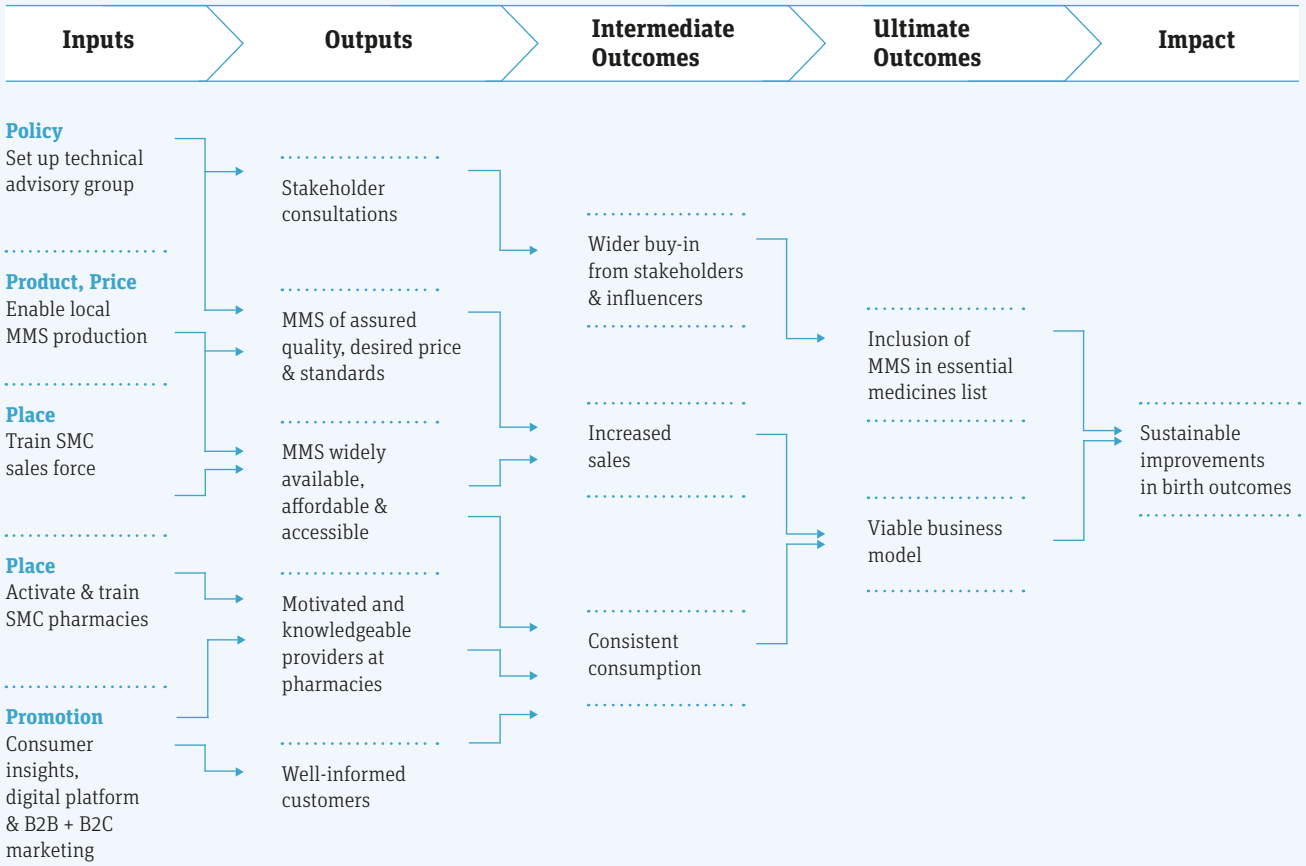
Demand creation with health providers

Focus group discussions revealed that pregnant women place their greatest trust in healthcare professionals, which means their buy-in is key for the successful uptake of MMS. Based on successful supplement marketing tactics, strategic engagement with health pharmacies at the start of the product launch involves sales pitches by SMC's medical and sales officers, product activation events and branded merchandising.

Digital interface with consumers

Mobile phone ownership, especially ownership of smartphones, is increasing rapidly in Bangladesh, which had 85 million unique subscribers in 2017.[5] This offers an opportunity to engage with consumers regularly and increase uptake of, and compliance with, MMS. To ensure compliance, SMC's existing consumer-facing dig-

FIGURE 4: Theory of change towards positive birth impacts



Source: *Sight and Life*, created by Anne Milan, Design Specialist, *Sight and Life*

ital interface will be leveraged to send relevant information on pregnancy, transmit MMS-related voice and text messages, and collect feedback from consumers.

Policy

In addition to the traditional 4Ps of a market-based undertaking, this consortium will help set up a technical advisory group to work collaboratively with government to create an enabling policy environment for MMS in the country. This group will provide assistance in setting standards, ensuring high-quality local production, and furnishing the science and evidence required to facilitate the inclusion of MMS in Bangladesh's EML and national standard treatment guidelines. In addition to key government officials and technical experts, this group will include international expert agencies such as GAIN and UNICEF. The theory of change of the proposed market-based model is outlined in **Figure 4**.

Conclusion

The 'One MMS a Day and a Healthy Baby is on the Way' model will be fully operational in 2020, and it is envisioned that by 2025 a total of 3.5 million pregnant women in Bangladesh will have accessed an affordable and high-quality MMS product. The goal of a market-based model is to develop pathways to sustainability from the very beginning, and the program is structured to ensure that by the end of year seven SMC will be able to operate the business model without any grant assistance. With a sustainable, locally owned and operated, market-based model nearly 77,000 Bangladeshi children will be born healthy every year and have the opportunity to reach their full potential.

> **"It is envisioned that by 2025 a total of 3.5 million pregnant women in Bangladesh will have accessed an affordable and high-quality MMS product"**

Acknowledgements

This article builds on research findings and diagnosis conducted in Bangladesh by our partner *Sight and Life*. The research consisted of business plan development, market assessment through secondary research, stakeholder and consumer interviews, mystery

shopping and market observations. We would like to acknowledge our partners Social Marketing Company, GAIN and the government of Bangladesh for their support and advice.

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References

1 Nutrition International. Policy Brief – Bangladesh: Cost-Effectiveness of Transitioning from Iron and Folic Acid to Multiple Micronutrient Supplementation for Pregnancy. October 2019. Internet: www.nutritionintl.org/content/user_files/2019/10/MMS-policy-brief-bangladesh-2019-10-18-web.pdf (accessed 19 February 2020).

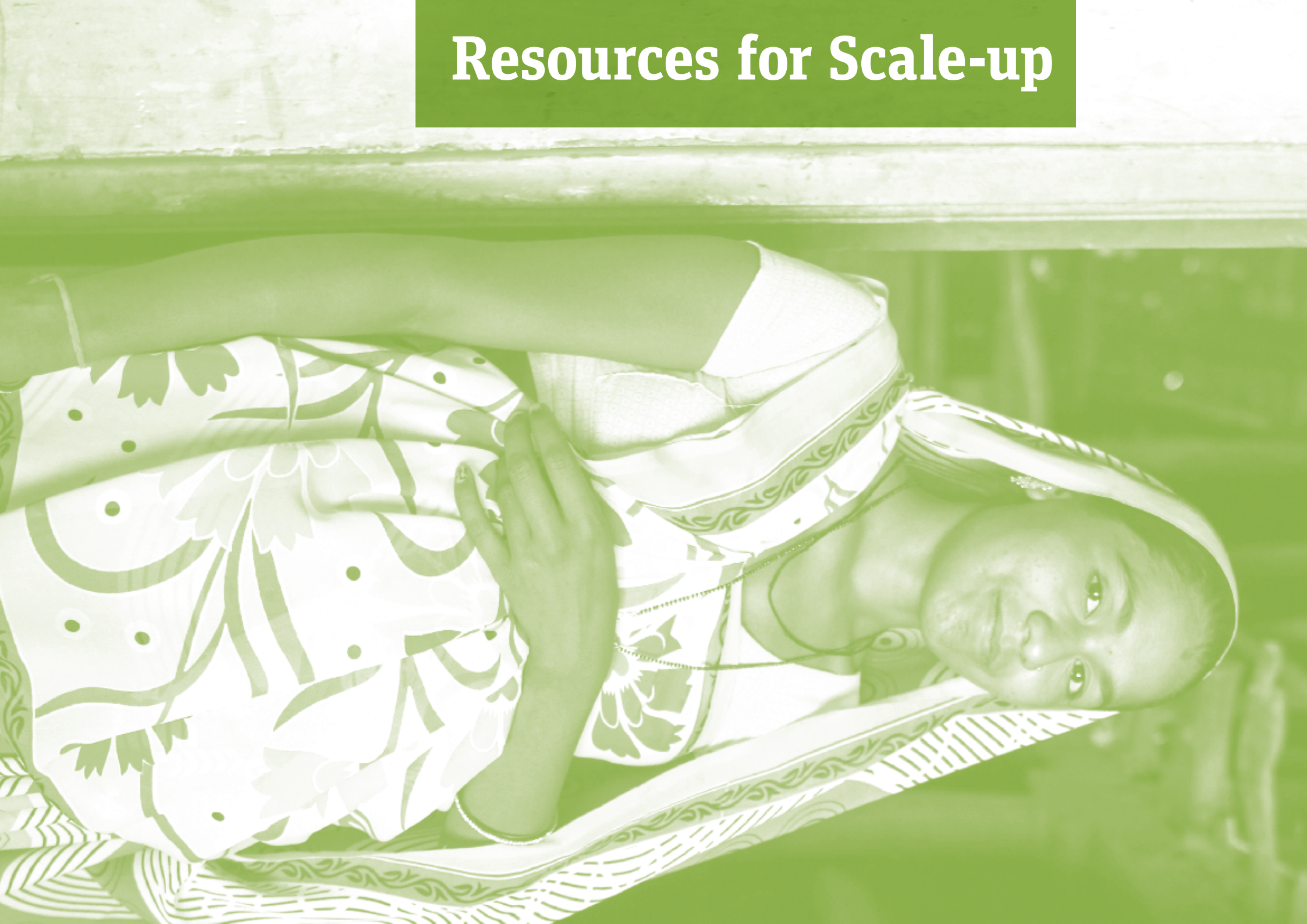
2 National Institute of Population Research and Training (NIPORT), International Centre for Diarrhoeal Disease Research, Bangladesh, MEASURE Evaluation. Bangladesh maternal mortality and health care survey (BMMS) 2016: Preliminary Report. Dhaka, Bangladesh, and Chapel Hill, NC, USA; 2017.

3 Borden NH. The Concept of the Marketing Mix. In: Dolan RJ. Strategic marketing management. Boston, MA, USA: Harvard Business School Press; 1991.

4 Zhang G, Feenstra B, Bacelis J, Liu X, Muglia LM, Juodakis J, et al. Genetic Associations with Gestational Duration and Spontaneous Preterm Birth. N Engl J Med. 2017;377:1156–67.

5 GSMA Intelligence. Country Overview – Bangladesh: Mobile industry driving growth and enabling digital inclusion. 2018. Internet: www.gsmaintelligence.com/research/?file=a163eddca009553979bcdfb8fd5f2ef0&download (accessed 19 February 2020).

Resources for Scale-up



Multiple Micronutrient Supplementation Cost-Benefit Tool to Guide Decision-Making

Jennifer Busch-Hallen, Dylan Walters, Sarah Rowe
Nutrition International, Ottawa, Canada

Key messages

- Launched in October 2019, the Nutrition International Multiple Micronutrient Supplementation (MMS) Cost-Benefit Tool is a free, online tool to help governments determine whether antenatal MMS is better value for money than iron and folic acid (IFA) for their maternal nutrition programs.
- The tool has been used to conduct cost-effectiveness analyses for 12 countries in Africa and Asia. In all cases, the findings showed with high certainty that MMS is very cost-effective, has a high return on investment and leads to additional significant positive health outcomes for newborns compared with IFA.
- Countries can input their data to generate a customized analysis and adjust parameters such as population of pregnant women, coverage and supplement cost to build context-specific investment cases.
- The tool is designed to be deployed widely as a public resource to facilitate the strategic use of data for policy decisions and investments concerning the introduction of MMS.
- The transition to, and scale-up of, MMS is an opportunity not only to accelerate progress toward the World Health Assembly Global Nutrition Targets 2025 but also to prioritize women's nutrition and empowerment as part of national nutrition and health programs, and to strengthen maternal nutrition globally.

Background

The World Health Organization 2016 antenatal care (ANC) guidelines[1] state that: "Policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMN [multiple micronutrient] supplements on maternal health to outweigh the disadvantages, and may choose to give MMN supplements that include iron and folic acid." Yet there is no global guidance on when and how to introduce MMS. Given the more recent evidence indicating that MMS provides additional health benefits for newborns compared to IFA supplementation, and with no adverse health effects,[2–5] many countries are now exploring the costs, feasibility and value-for-money of transitioning from IFA to MMS for pregnant women.

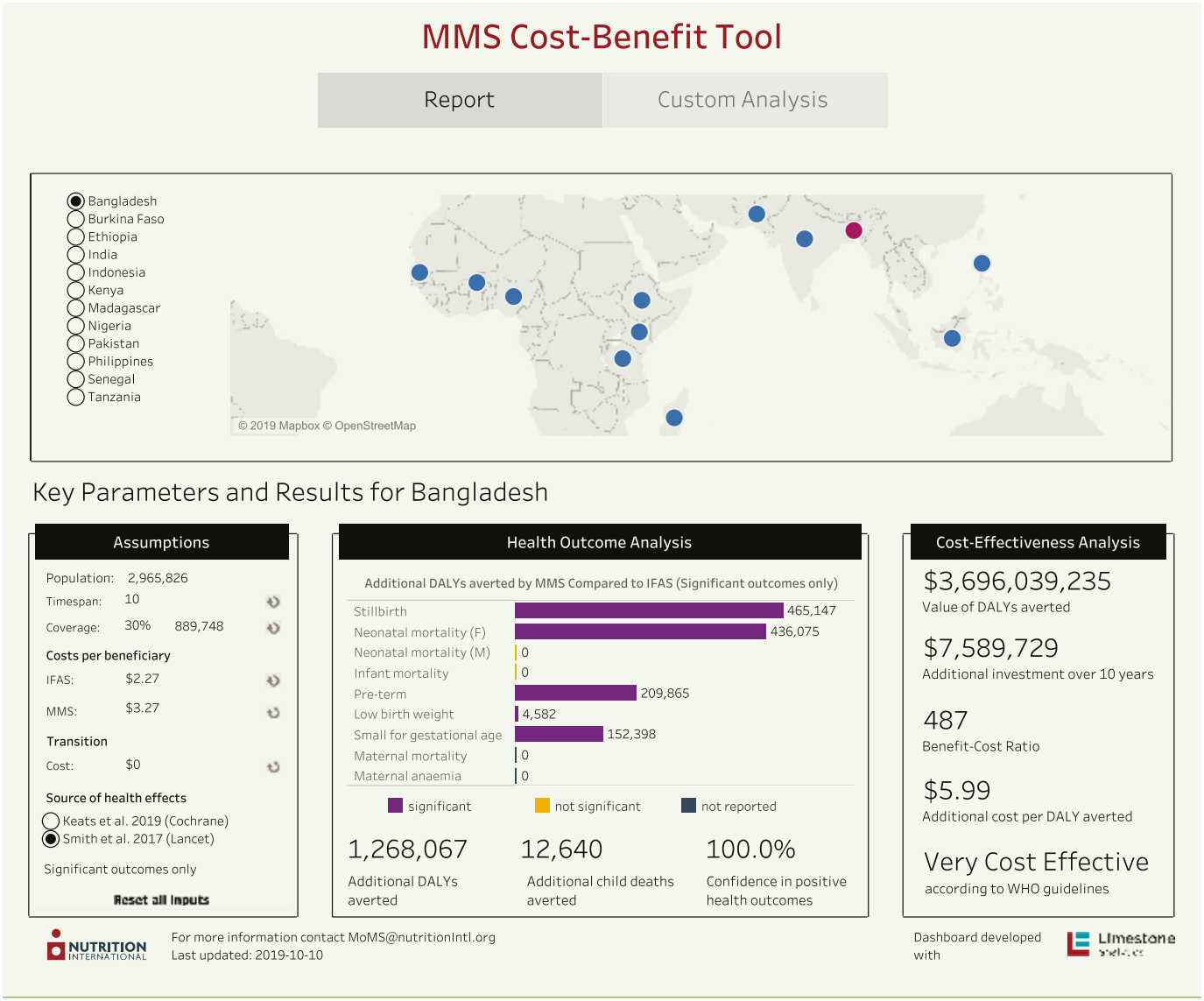
Mother in Touba Toul, Senegal

Over the past decade, Nutrition International has worked in partnership with governments in Africa and Asia to strengthen IFA programming and maternal nutrition services. This work has provided an opportunity to better understand what is needed to overcome barriers affecting IFA coverage and adherence, and to foster sustainable scale-up of maternal health programs.[6] Building on this experience and responding to requests from countries for more MMS guidance particularly around the cost-effectiveness of transitioning to MMS, Nutrition International, with the support of Limestone Analytics, developed the MMS Cost-Benefit Tool.[7]

What is the MMS Cost-Benefit Tool?

Launched in October 2019, the MMS Cost-Benefit Tool is an open-access, user-friendly, online analytical tool that supports governments' use of country-specific data in their decision-making on whether investing in antenatal MMS rather than IFA is better value for money. The tool is available on the Nutrition International

FIGURE 1: Report interface of the MMS Cost-Benefit Tool, featuring 12 preset country reports



website, alongside preset analyses for 12 countries (**Figure 1**) and a User Interface and Interpretation Guide.[7]

A recent study by Nutrition International and Limestone Analytics showed MMS is more cost-effective than IFA in three high-burden Asian countries that informed the model for the tool.[3]

> **"The tool estimates the health impact and cost-effectiveness of transitioning from IFA to MMS"**

The tool estimates the impact of MMS compared with IFA on maternal and newborn health outcomes for a defined coverage rate of the population of pregnant women in each country using health effect sizes from the most recent systematic reviews.[2,3] In addition, it computes the budget impact of switching to MMS, and the cost-effectiveness and cost-benefit ratio, which is critical information to inform government investment. It offers the user flexibility to modify population, supplement costs (to reflect price declines) and coverage for preset country reports. The tool also has a 'custom interface' to allow countries to input their data or modify existing data and generate a customized report (**Figure 2**). The hope is to expand the number of quality-assured preset reports for low- and middle-income countries (LMICs).

The tool calculates:

- **Effectiveness:** An aggregate of the number of additional disability-adjusted life years (DALY) and child deaths averted by transitioning from IFA to MMS across significant health outcomes.
- **Cost:** The additional costs or budget impact (in US$) of providing MMS if there is an existing IFA program or ANC platform in the country (considers supplement and program transition costs).

- **Cost-effectiveness:** The incremental cost-effectiveness ratio. The ratio of the difference in cost and the difference in effectiveness, estimated as the 'cost per additional DALY averted' by transitioning to MMS.

- **Benefit-cost ratio:** A comparison of the value of the health benefits in monetary terms relative to the costs of transitioning to MMS.

How has the tool been applied?

To date, the MMS Cost-Benefit Tool has been used to conduct cost-effective analyses for: Bangladesh, Burkina Faso, Ethiopia, India, Indonesia, Kenya, Madagascar, Nigeria, Pakistan, the Philippines, Senegal and Tanzania. In all cases, the findings showed with high certainty that MMS is cost-effective and that it generates additional positive health outcomes for newborns compared with IFA. Policy briefs that translate the results for each country are available on the Nutrition International website (**Figure 3**).[7]

Nutrition International conducted cost-effectiveness analyses to complement the preliminary stages of the efforts to acquire operational experiences on MMS use in four countries: Bangladesh, Burkina Faso, Madagascar and Tanzania. The data from this analysis, which was supported by the Bill & Melinda Gates Foundation and UNICEF, was particularly instrumental in garnering the high-level political commitment from the Government of Tanzania to introduce MMS. "The results helped answer the question of whether transitioning from IFA to MMS was good value for money, and essentially served as the tipping point that moved decision makers towards the introduction of MMS in Tanzania," said Nita Dalmiya, UNICEF. Similarly, Klaus Kraemer of *Sight and Life* states: "We are confident that the convincing data we generated with the MMS Cost-Benefit Tool will support the re-introduction of prenatal MMS to the South African health system."

The following examples illustrate how this tool can facilitate the strategic use of data for influencing policy decisions at the global and country levels.

FIGURE 2: Custom interface of the MMS Cost-Benefit Tool

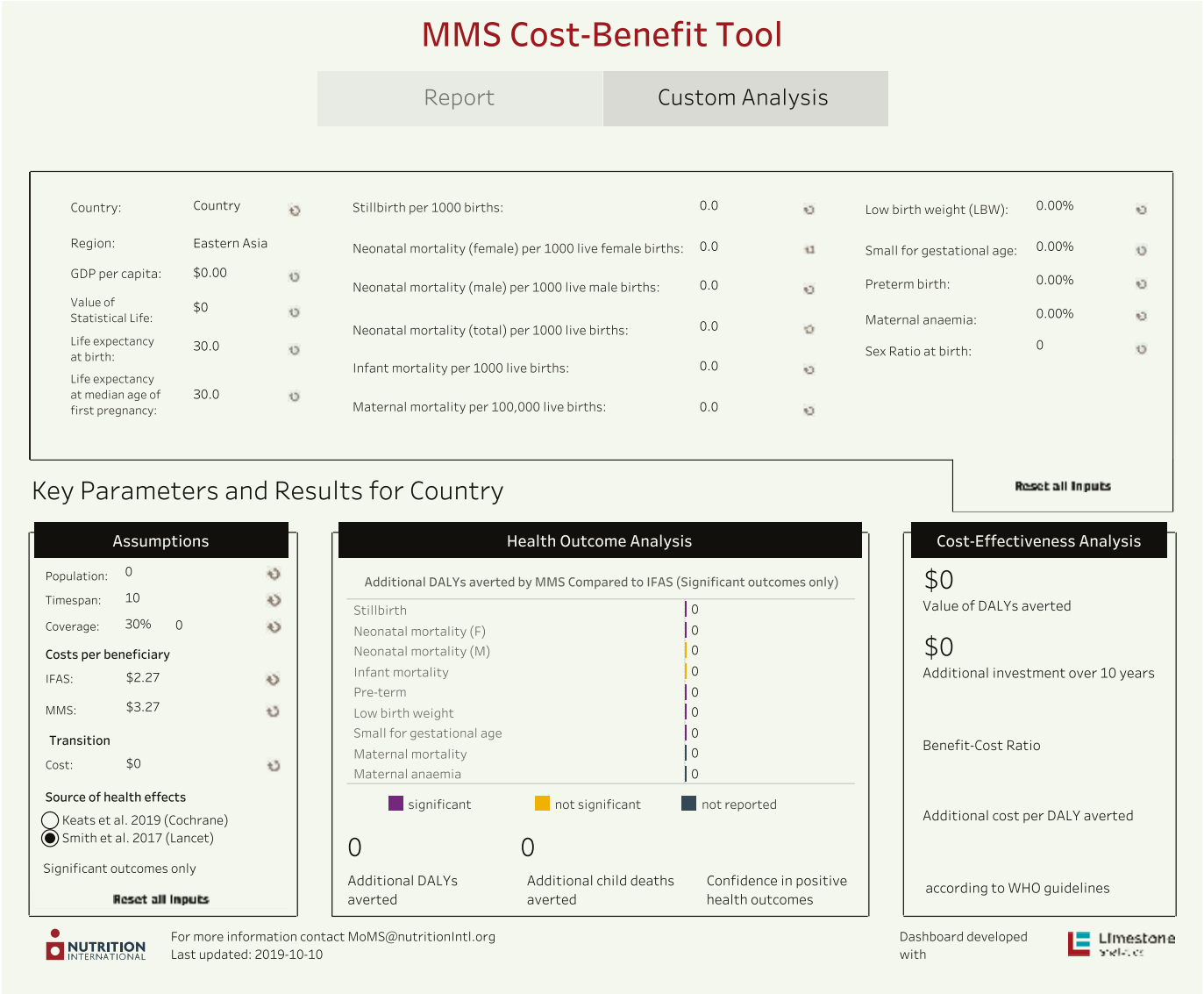


FIGURE 3: Policy briefs designed by Nutrition International accompany the tool to translate the cost-effectiveness results for policymakers

"The results served as the tipping point that moved decision makers towards the introduction of MMS in Tanzania"

At the request of WHO, the MMS Cost-Benefit tool was used to conduct additional analyses that were included in the evidence-to-decision framework for updating the WHO recommendation on the use of MMS in pregnancy.

Moving forward

The transition and scale-up of MMS presents an opportunity to increase progress toward the World Health Assembly Global Nutrition Targets 2025 on anemia, low birth weight and stunting – and also to prioritize women's nutrition as part of national nutrition and health programs and the universal healthcare agenda, and to broadly strengthen maternal nutrition. MMS was prioritized in the World Bank Group's Investment Framework for Nutrition. It was estimated that it would cost US$ 2.3 billion over 10 years to scale up MMS across LMICs.[8]

The MMS Cost-Benefit Tool was one of Nutrition International's commitments made as a Global Goalkeepers partner under the 2019 Gates Foundation Healthy Mothers, Healthy Babies Accelerator to help advance the global sustainable development goals. By supporting governments in making informed policy decisions about the introduction of MMS, the tool leads to more efficient use of resources, improvements in birth outcomes, and better overall health, survival and equality for women (**Figure 4**).

"This tool supports governments in steering MMS decision-making for their country"

FIGURE 4: Women's empowerment and gender equality are central to the discussions around maternal health and supplementation

Conclusion

The MMS Cost-Benefit Tool translates the new evidence on MMS and generates cost-effectiveness results for LMICs. It is designed to be deployed widely as a public resource for facilitating policy decisions and investments related to the introduction of MMS, and to support national governments in building evidence-informed, effective, affordable and sustainable maternal nutrition programs. "Government ownership and leadership is key to achieving scale-up and sustainability of MMS," said Jennifer Busch-Hallen, Senior Technical Advisor, Maternal and Neonatal Health and Nutrition, Nutrition International. "This tool supports governments in steering MMS decision-making for their country."

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References

1 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016.

2 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;(3):CD004905

3 Smith ER, Shankar AH, Wu LS-F, 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(11):e1090–e1100.

4 Kashi B, Godin CM, 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):1222–9.

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 Nutrition International. Iron-Folic Acid Supplementation in Pregnancy: Program Logic Model and Key Considerations for Program Success. Internet: www.nutritionintl.org/resources/iron-folic-acid-supplementation-in-pregnancy-program-logic-model/ (accessed 8 November 2019).

7 Nutrition International. The Multiple Micronutrient Supplementation Cost-Benefit Tool. Internet: www.nutritionintl.org/knowledge-centre/mms-cost-benefit-tool/ (accessed 31 October 2019).

8 Shekar M, Kakletek J, Eberwein JD, Walters D. An Investment Framework for Nutrition: Reaching the Global Targets for Stunting, Anemia, Breastfeeding and Wasting. Directions in Development. Washington, DC: World Bank Group; 2017.

Creating Demand for Multiple Micronutrient Supplements (MMS)

A mini guide

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Key messages

- Conduct formative research to understand how women perceive multiple micronutrient supplements (MMS). The results from such research will help you design a more effective promotion strategy.
- Focus on two priorities: making it easy for women to access MMS, and helping them remember to take MMS regularly.
- It is not enough to say that MMS are good for health. Promote this product in a way that women find attractive and relevant to what they really want.
- Whatever promotion activities and materials you prepare, pretest them first among the target audience. You will save resources and achieve better results.

Introduction

The influential economist Michael Rothschild once said that there are three classes of behavior change 'problems': education, regulation and marketing.[1] The public health sector has more often than not defaulted to education – telling people why they should practice the desired behaviors. However, the case of MMS, and other nutritional products, is also a 'marketing problem.' When we look at the usage of MMS, we can see that:

- MMS is a new product and is not widely accepted;
- the behavior necessary for adherence is not always easy, as people are required to take a tablet every day for a period of several months;
- as with all supplements, people need to be able to access MMS and know how to deal with potential side effects; and
- while there may be clear barriers to its use, MMS provides only a few immediate, visible benefits; therefore, perceived value for MMS needs to be created in the mind of the consumer.

As we can see, addressing such a 'marketing problem' requires more than just education. It requires marketing solutions that reduce the barriers to using the product and increase the benefits in the mind of the consumer.

This guide aims to help public health practitioners to effectively approach this marketing problem, and by doing so, achieve higher uptake of and adherence to MMS. We are aware that creating consumer demand is both an art and a science, and that it is impossible to cover this topic adequately in such short article. We therefore focus on three main phases of developing and implementing a demand creation strategy for MMS: getting started, project implementation, and monitoring and evaluation. Within each phase, we present tips that practitioners can apply to maximize the impact of their intervention. For a deeper dive on each of the tips and steps, we offer a further reading list with useful guidance. The key tips we provide are summarized in **Table 1**.

> **"While you yourself might be perfectly clear about the scientific benefits of MMS, their intended users might have different perceptions and experiences"**

Getting started

1. Seek to understand women's lives

While you yourself might be perfectly clear about the scientific benefits of MMS, their intended users – pregnant women – might have different perceptions and experiences. Since they are the intended users of MMS, it is their perceptions of benefits and barriers that matter the most. In the words of senior social marketer Dr William Smith: "Listen to consumers and what they really care about … and then find some way of tying that into what we care about … So begin with them, rather than beginning with us." It is important, therefore, to ensure that the development of any strategy for promoting MMS is based on a thorough understanding of:

(**a**) women's lives during pregnancy; and

TABLE 1: Summary of 14 key tips for creating demand for MMS

Top tips to keep in mind when creating demand for MMS	
1	Include conducting consumer research in your project proposal and budget.
2	When preparing consumer research, take advantage of the resources recommended in this mini guide.
3	Before producing and procuring the MMS product, consult consumers on product characteristics such as tablet size, color and packaging.
4	Before you start promoting MMS, ensure that a steady supply of MMS is in place, so that it is easy for women to access them.
5	Apply a marketing strategy that takes into account product, price, place and promotion elements.
6	Consider developing a brand for MMS to help consumers identify with your product.
7	Develop a communication strategy for the messages you want to convey to your consumers about your product.
8	Ensure that your intervention helps women understand the possible side effects of MMS and what they can do about them.
9	Use reminders to help your consumers take MMS on a daily basis.
10	Conduct a product trial, pretest your marketing mix and incorporate feedback before launching the product.
11	If involving health personnel in your intervention, plan to build their capacity in marketing MMS.
12	Use a marketing strategy that actively works with women who already use MMS (the 'Doers') and are willing to promote them among their peers.
13	Use a mix of communication channels that women trust and are frequently exposed to.
14	Explore or collect baseline data and data that helps you understand the extent to which pregnant women use MMS and the main reasons for not using MMS.

(**b**) women's perceptions of and experience of using MMS.

You can gain such an understanding through consumer research, which should help you answer the following **key questions**.

- How do women feel during their pregnancy, and how would they *like* to feel?
- What are women most concerned about during and after pregnancy?
- What are women's main wishes related to pregnancy and delivery?
- What activities do women enjoy doing and what motivations and aspirations do they have that may be linked to making MMS appealing?[2]
- What is the proportion of women who have heard of MMS?
- What do women perceive as the main positive and negative consequences of using MMS?
- What makes it difficult for women to use MMS? What could make it easier?
- Who approves and who disapproves of them using MMS?
- To what extent do women think that they (and their future babies) are at risk of the problems that MMS aim to address?
- In the opinion of women and other stakeholders (e.g., health workers), what would need to be done to enable women to overcome the main 'barriers'?
- What communication channels do women prefer for receiving health advice?

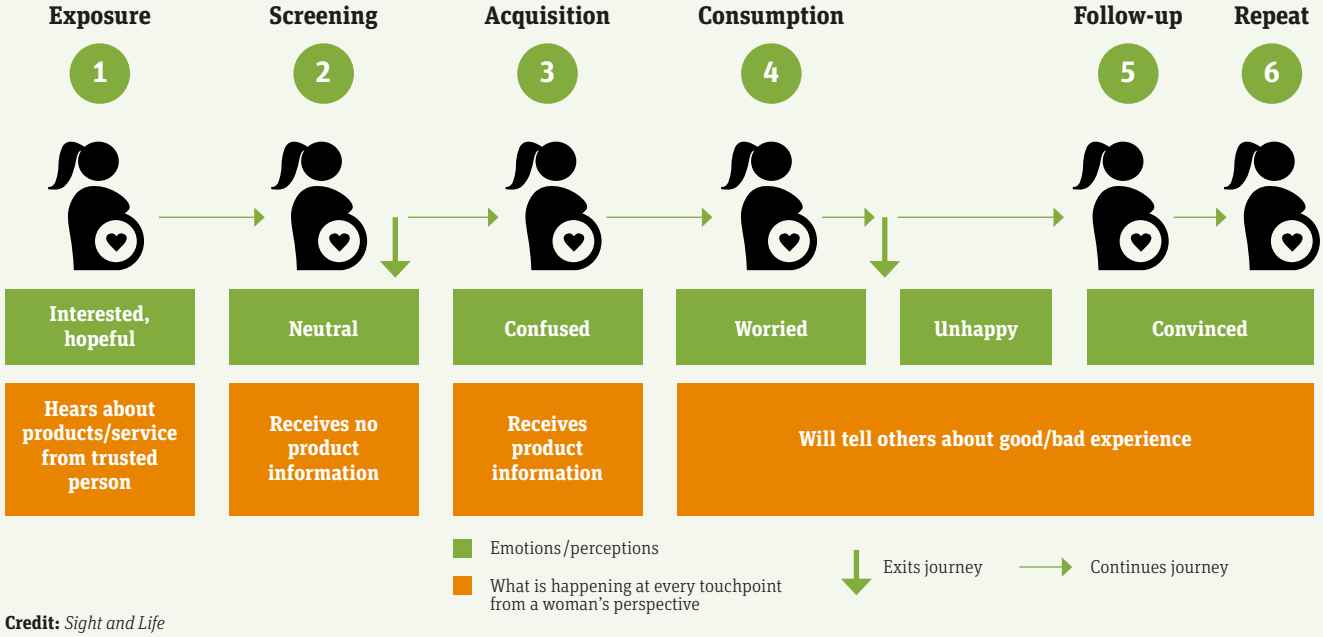
TABLE 2: Overview of commonly used research methods

Research method	What is it about?
Review of existing resources	• Avoid 'reinventing the wheel' by first looking at what research data already exists. Only then start thinking about doing primary research.
Semi-structured interviews[3]	• Interviews with 'key informants' who can provide useful information, such as health workers or women who already use MMS or iron and folic acid.
Focus group discussions[4]	• Informal, well-facilitated discussions about people's opinions and ideas. • Less suitable for exploring sensitive experiences if people are not willing to speak openly in front of others.
Barrier analysis[5,6]	• An approach that asks people who practice the behavior (the 'Doers') and those who do not (the 'Non-Doers') a series of questions aimed at identifying which barriers and motivators have the biggest influence on whether they (do not) practice the given behavior.
Customer journey mapping[7]	• Qualitative technique to understand the physical and emotional 'journey' a person goes through when practicing a behavior (such as using MMS). • Helps understand consumers' thoughts and feelings and find ways to make it easier and more attractive for them to adopt the behavior.
Trials of improved practices[7]	• A method whereby a small sample of women are asked to 'trial' practicing a behavior (such as using MMS) and their experience is then used to design (or improve) the promotion and marketing strategy.

TABLE 3: Example of interview questions used during barrier analysis

If the respondent is a Doer ⇣	If the respondent is a Non-Doer ⇣
• What are the **advantages** of using these micronutrient supplements?	• What would be the **advantages** of using these micronutrient supplements?
• What are the **disadvantages** of using the supplements?	• What would be the **disadvantages** of using the supplements?
• How easy or difficult is it to **access** the supplements?	• How easy or difficult would it be to **access** the supplements?
• How easy or difficult is it to **remember to take** the supplements every day?	• How easy or difficult would it be to remember to take the supplements every day?
• Are there any **cultural rules or taboos** against using such supplements?	• Are there any **cultural rules or taboos** against using such supplements?

FIGURE 1: Example of simplified consumer journey mapping (for micronutrient supplements) recording women's perceptions and emotions at every key 'touchpoint' with the service/product



Credit: *Sight and Life*

2. Take advantage of available research methods and guidance

Conducting research into the factors that influence the adoption of MMS might seem to be a daunting task. Questions such as: 'Where should I start?,' 'How should I collect the required data?' among others come to mind. The good news is that there are many proven, well-tested methods and much guidance to help you conduct the necessary research (for examples, see **Table 2**).

You can find a selection of useful guidance on using these methods at www.behaviourchange.net and also in the References section.

Table 3 and **Figure 1** provide more detailed examples of two selected methods – the barrier analysis and customer journey mapping – that you might want to use when conducting MMS consumer research.

3. Consult consumers on product characteristics

Ensure that the development of any new product is based on a thorough understanding of consumer preferences (for example, regarding MMS tablet size, color, packaging, price and promotion).[8] In the numerous studies of new product performance over the years, a consensus has developed that understanding consumer needs significantly contributes to the success of the product uptake.[9] Consulting consumers about product characteristics is also crucial to avoid ineffective investments.

4. Get the basics right

A multi-country study showed that one of the main barriers to a higher use of micronutrient supplements is their unavailability resulting from ineffective supply from the national to the local level.[10] For any demand creation strategy to work, the intended users must be able to access MMS. While this might seem logical, programs often fail by underestimating the role of supply. Therefore, get the 'basics' right: before you start implementing any demand-creating activities, make sure that a system ensuring a steady and consumer-friendly supply of MMS is in place and is actually working (see **Box 1** for key resources).

"Before you start implementing any demand-creating activities, make sure that a system ensuring a steady and consumer-friendly supply of MMS is in place"

BOX 1: Interested in learning more to help you get started?

The following resources might help you think through the process of creating demand for a new product and the importance of involving consumers in every step of this process, including research and development.

- Social Marketing Behavior: A Practical Resource for Social Change Professionals[11]
- The Role of Consumer Insight in New Product Development and Its Impact on Supply Chain Management: A Swedish Case Study[8]
- Consumer Research in the Early Stages of New Product Development: Issues and Applications in the Food Domain[9]
- Look up the supply-related checklist in the article entitled 'Procurement and Production of Multiple Micronutrient Supplements for Pregnant Women: A Country Assessment Toolkit' on page 90 of this *Sight and Life* Special Report
- Increasing Adherence to MMS among Pregnant Women in Haiti: Experiences using *Sight and Life's* process for designing behavior change programs[12]

Project implementation

5. Think beyond communication and develop a 'marketing mix'

Communicating the benefits of your product (MMS) is no doubt an important element of creating and maintaining demand. But it is not the only element that can be used to influence your consumers' decision to use the product. In fact, a mix of elements, often referred to as the 'marketing mix,' is needed. This includes product, price, place and promotion. **Table 4** describes each element of the marketing mix in more detail and provides examples relevant for MMS. More guidance is available in the publication Social Marketing Behavior: A Practical Resource for Social Change Professionals.[13]

6. Build a brand that consumers can identify with

According to consumer scientists, 95 percent of our purchasing decisions may be formed in the subconscious mind.[14] This is the part of the brain where logic takes a back seat and emotion grabs the wheel.[15] Branding is more than just a nice logo and packaging: it helps a consumer connect with your product on an emotional level and feel comfortable about consuming it. Your consumer research will help you define those characteristics of your brand that are most likely to resonate with your audience. When thinking about your MMS brand, keep in mind that you are branding for pregnant women's desires and aspirations, not for a topic (i.e., nutrition). Hiring a creative agency is a good idea when you want to build a brand for MMS (see example in **Figure 2**).

7. Develop a strategy for your communication content

Developing the content of your communication goes beyond drafting messages. It starts with asking yourself several questions about the things you want to communicate (see **Box 2**).

TABLE 4: What does 'marketing mix' mean?

Marketing mix element	Description	Example
Product	Any product or service that you are creating demand for (i.e., MMS and related health services).	MMS tablets should be designed considering consumers' preferences about their size, color, packaging, etc.
Price	The monetary cost, physical cost (time, effort) and emotional cost (fear of side effects) people incur in relation to the product.	Accessing and consuming MMS needs to reduce costs in the mind of the consumer, and provide to the user clear (and ideally immediate) benefits, such as feeling more relaxed about the baby's health or being more in control of the pregnancy outcomes.
Place	The channels through which the product is made available to women (i.e., pharmacies, health centers).	The easier it is for women to access MMS, the more likely they are to use it. Understand access from their point of view and make it as easy as possible.
Promotion	The communication channels and content used to promote the product.	Use different communication channels (see point 13 in this guide) and pretested messages and materials to ensure that women hear about MMS frequently and from different sources.

FIGURE 2: Example of a commercial supplement brand that appeals to mothers' emotions and desires

Credit: www.goop.com

BOX 2: Key elements of content strategy

Content strategy – key elements

Messages
What do you want your audience to do, know and believe?

Messengers
Who will be delievering the message?

The Creative
How will you say it and what will you show? (look and feel)

Communication Channels
Where and when your message will appear

Credit: *Sight and Life*

8. Communicate the benefits but also the side effects

Interventions promoting the use of MMS are often good at highlighting their health benefits. However, the existing research shows that it is equally important to prepare the consumer for potential side effects: when caregivers are prepared for the possible side effects of using micronutrient supplements, it is more likely that experiencing them will not deter their continued use – simply because they knew that this might happen.[16] It is also important that women have an opportunity to learn how they can deal with side effects.

"One of the main reasons for women not using MMS is very simple: they forget to take them"

9. Include reminders in your communication

One of the main reasons for women not using MMS is very simple: they forget to take them.[16] Tackling this barrier can help your intervention achieve much higher and longer adherence. In Nepal, for instance, caregivers who received a reminder card were two times more likely to meet the adherence criteria than those who did not receive the card (**Figure 3**).

10. Pretest your messages and materials

Imagine that you spent months of hard work on trying to design the best behavior change messages and materials. You might be keen to start using them. However, this is exactly the time when failure is most likely. While you might assume that the messages and materials are clear, attractive and useful, the target audience might not feel the same. As a result, your communication strategy will not deliver the desired effect.[18] Therefore, it is crucial that you invest a few days in pretesting the most important messages and materials among the target audience. When doing so, we can take advantage of the following questions.

- What was the first thing in this material that caught your attention?
- What do you think this material/picture is trying to say?
- To what extent do you believe that what the material says is true?

FIGURE 3:[17] Example of a reminder card

	Mo	Tu	We	Th	Fr	Sa	Su
Week 1	♥	♥	♥	♥	♥	♥	♥
Week 2	♥	♥	♥	♥	♥	♥	♥
Week 3	♥	♥	♥	♥	♥	♥	♥
Week 4	♥	♥	♥	♥	♥	♥	♥

- How does the material make you feel?
- In your opinion, what type of people should read it? For whom was it developed?
- To what extent do you think you could use the information in your own lives?
- What are your ideas on how the material could be improved?[19]

11. Strengthen the health workers' 'marketing' skills

Even the best-designed social and behavior change messages, materials and strategies can fail if the people who are supposed to use them lack the required motivation, attitudes or skills. A randomized control trial in Indonesia showed that better-performing health extension workers had a much higher impact on the use of micronutrient powders and their contribution to reducing early infant mortality.[20] The difference is not just about the workers' knowledge. Equally important are their 'marketing' skills – an ability to present MMS in a way that women find attractive and relevant to what they really want (e.g., a wish to have a safe delivery, a healthy baby or other 'desires' identified during consumer research).

12. Engage the 'Doers'

One of the strongest motivators for people to adopt a behavior is when they know other people who already follow it (the 'Doers') and gain clear benefits, such as feeling less tired or having greater peace of mind. The Doers are among the most effective 'agents of change,' as many people perceive them to be 'like us' and are more likely to follow their example. For example, in Peru, caregivers became less suspicious of micronutrient powders only when they received reassurance from neighbors who confirmed that 'they are vitamins.'[21]

"The more communication channels mothers are exposed to, the more likely they are to follow the desired behavior"

13. Use diverse communication channels

Research from Alive & Thrive showed that the more communication channels mothers are exposed to, the more likely they are to follow the desired behavior.[22] Therefore, it is important to ensure that pretested and consistent messages are communicated through multiple channels. While MMS is usually promoted during antenatal checks at the health facilities, you can also use many other channels. What matters most is that you choose those channels that pregnant women are most exposed to and which they trust regarding health advice. **Table 5** provides an overview prepared by the Compass website that presents various communication channels and summarizes their main strengths and limitations (also see **Box 3** for key resources).

BOX 3: Interested in learning more about project implementation?

- How to Develop a Channel Mix Plan[23]
- Recommended guidance on developing communication messages and materials[24]
- Recommended guidance on pretesting messages and materials[24]
- Public Health Branding: Applying marketing for social change[25]

Monitoring and evaluation (M&E)

14. Track the prevalence of different barriers and indicators

Implementing an intervention is like going on a journey. The better we know whether we are going in the right direction (and if not, why), the easier and faster it is to reach our destination. In the context of MMS, regular availability of useful and up-to-date data can help you steer the focus of your intervention and considerably increase its effectiveness. Therefore, consider collecting the following **data** as an integral part of your M&E system.

- The percentage of pregnant women who are aware of the main benefits of the promoted MMS.

TABLE 5: Examples of general strengths and limitations of different communication channels[23]

Channel	Strengths	Limitations
Interpersonal communication	• Tailored and personalized	• Lower reach
Community dialogue, peer-to-peer, health	• Interactive	• Relatively costly
provider-client, inter-spousal and parent-child	• Able to explain complex information	• Time-consuming
communication	• Can build behavioral skills	
	• Can increase intention to act	
	• Familiar context – enhances trust and influence	
Community/folk media	• Stimulates community dialogue	• Less personalized than interpersonal
Community drama, interactive storytelling,	• Motivates collective solutions	communication
music, community events, video group discussion,	• Provides social support for change	• Time-consuming to establish relationships
mobile video units, talks and workshops,	• Can increase intention to act	• Relatively costly
door-to-door visits, demonstrations and	• Reaches larger groups of people	• May have less control over content
community radio		
Mass media and mid-media	• Extensive reach	• Limited two-way interaction
Radio, TV, print, film, outdoor –	• Efficient and consistent repetition of message	• Available only at certain times
posters, billboards	• Capacity to model positive behaviors	• Relatively impersonal
	• Sets the agenda – what is important and how to	
	think about it	
	• Legitimizes norms and behaviors	
Digital and social media	• Fastest growing and evolving	• Program may have less control over content
Mobile phones, SMS, Facebook, internet,	• Potential to mobilize youth	• Requires literacy
Twitter, eToolkits, websites, eForums, blogs,	• Highly tailored	• Limited reach and accessibility
YouTube, chat rooms	• Interactive	• Can lack credibility
	• Quickly shares relevant information	
	in a personalized manner	
	• Flexibility to change and adapt as needed	

- The percentage of pregnant women who are aware of how to deal with the side effects of MMS.
- The percentage of pregnant women who report themselves as willing to use the promoted MMS.
- The percentage of pregnant women who know how to access the promoted MMS.
- The percentage of women in the fourth or higher month of pregnancy who were unable to access MMS.
- The average number of days that the providers did not have any MMS in stock.
- The percentage of women in the fourth or higher month of pregnancy reporting that it is easy to remember to take MMS regularly.
- The percentage of women in the fourth or higher month of pregnancy who use the promoted MMS.
- The percentage of women in the fourth or higher month of pregnancy who use the promoted MMS and adhere to the daily regimen.

It is also essential to collect reliable baseline data at the beginning of an intervention so that you know where you started and how far you have traveled (see **Box 4** for key resources).

BOX 4: Interested in learning more about monitoring and evaluation?

- Chapter 4 of Nutrition International's Behavior Change Intervention Toolkit[26]
- Chapter 3.5 of GIZ's Social and Behaviour Change: Insights and Practice[27]
- Guidance on social and behavior change communication indicators at www.indikit.net[28]

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References

1 Rothschild M. Separating Products and Behaviors. Soc Mar Q. 2009;15(1):107–10.
2 Schmied P. Social and Behaviour Change: Insights and Practice. Bonn: GIZ; 2019.
3 People in Need. Key Informant Interviews. Internet:

www.behaviourchange.net/key-informant-interviews (accessed 23 October 2019).

4 People in Need. Focus Group Discussions. Internet: www.behaviourchange.net/focus-group-discussions (accessed 23 October 2019).

5 People in Need. FAQs on Barrier Analysis. Internet: www.behaviourchange.net/faq/2-faqs-on-barrier-analysis (accessed 23 October 2019).

6 People in Need. Barrier Analysis (BA). Internet: www.behaviourchange.net/barrier-analysis-ba (accessed 23 October 2019).

7 People in Need. Other Methods. Internet: www.behaviorchange.net/other-methods (accessed 23 October 2019).

8 Eriksson D, Hilletofth P. The Role of Consumer Insight in New Product Development and Its Impact on Supply Chain Management: A Swedish Case Study. In: Blecker T, Kersten W, Lüthje C, eds. Innovative Process Optimization Methods in Logistics: Emerging trends, concepts and technologies. Berlin: Erich Schmidt Verlag; 2010:113–26.

9 Van Kleef E. Consumer Research in the Early Stages of New Product Development: Issues and Applications in the Food Domain. Wageningen: Wageningen Universiteit; 2006.

10 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(Suppl 5): e12532.

11 Smith WA, Strand J. Social Marketing Behavior: A Practical Resource for Social Change Professionals. Washington, DC: Academy for Educational Development; 2009.

12 King SE, Harvey Q, Ajello C, Dacius M, Marhone-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.

13 Smith WA, Strand J. Social Marketing Behavior: A Practical Resource for Social Change Professionals. Washington: Academy for Educational Development; 2009.

14 Zaltman G. How customers think: Essential insights into the mind of the market. Harvard Business Press; 2003.

15 Horan R. How Brands Get People to Care. And How Yours Can, Too. Entreptreneur. 3 April 2019. Internet: www.entrepreneur.com/article/331626 (accessed 23 October 2019).

16 Tumilowicz A, Schnefke CH, Neufeld LM, Pelto GH. Toward a Better Understanding of Adherence to Micronutrient Powders: Generating Theories to Guide Program Design and Evaluation Based on a Review of Published Results. Curr Dev Nutr. 2017;1(6):e001123.

17 Mirkovic KR, Perrine CG, Subedi GR, Mebrahtu S, Dahal P, Staatz C, et al. Predictors of micronutrient powder intake adherence in a pilot programme in Nepal. Public Health Nutr. 2016;19(10):1768–76.

18 Schmied, P. Behavior Change Toolkit. Prague: People in Need; 2017.

19 Schmied, P. Examples of Questions for Reviewing SBC Materials. Prague: People in Need; 2019. https://www.thecompassforsbc.org/how-to-guides/how-conduct-pretest (accessed 09 April 2020).

20 Shankar AV, Asrilla Z, Kadha JK, Sebayang S, Apriatni M, Sulastri A, et al. Programmatic effects of a large-scale multiple-micronutrient supplementation trial in Indonesia: using community facilitators as intermediaries for behavior change. Food Nutr Bull. 2009;30(2 Suppl):S207–14.

21 Creed-Kanashiro H, Bartolini R, Abad M, Arevalo V. Promoting multi-micronutrient powders (MNP) in Peru: acceptance by caregivers and role of health personnel. Matern Child Nutr. 2016;12(1):152–63.

22 Alive & Thrive. Understanding factors driving nutrition behavior change: the experience of Alive & Thrive. Washington, DC: Alive & Thrive; 2016. www.ifpri.org/publication/bangladesh-alive-thrive-end-line-survey-2014-households (accessed 09 April 2020).

23 Compass. How to Develop a Channel Mix Plan. Internet: www.thecompassforsbc.org/how-to-guides/how-develop-channel-mix-plan (accessed 24 October 2019).

24 People in Need. Communication Messages and Materials. Internet: www.behaviourchange.net/communication-messages-and-materials (accessed 24 October 2019).

25 Evans WD, Hastings G. Public Health Branding: Applying marketing for social change. Oxford: Oxford University Press; 2008.

26 Nutrition International. Behavior Change Intervention Toolkit. Nutrition International; 2019.

27 Schmied, P. Social and Behaviour Change: Insights and Practice. Bonn: GIZ; 2019.

28 People in Need. Behavior Change Indicators. Internet: www.indikit.net/sector/227-cross-cutting-topics (access

Procurement and Production of Multiple Micronutrient Supplements for Pregnant Women

A country assessment toolkit

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Sight and Life, Basel, Switzerland

Key messages

- The multiple micronutrient supplement (MMS) procurement and production toolkit serves as a guide to inform policymakers and donors about the range of key questions and topics associated with the inclusion of MMS in public health programs or market-based models.
- The *Sight and Life* MMS Supply toolkit has four main complementary domains to explore: (**1**) desk research, (**2**) market assessment, (**3**) production assessment, and (**4**) regulation and policy assessment.
- The skills required to implement the tools include: general research skills, good communication and interpersonal skills to conduct key informant interviews (KIIs), and analytical abilities to manage and analyze data. Basic statistical analyses, such as linear regression using either Excel or another software package, could be outsourced once the data has been collected.
- National governments need to consider downstream or consumer-friendly policies as well as upstream or manufacturer-friendly policies in order to achieve policy coherence.

"The MMS procurement and production toolkit is intended to be a publicly available resource"

The MMS procurement and production toolkit is intended to be a publicly available resource for governments, development practitioners, manufacturers and academia to perform country-level diagnostics. Furthermore, it serves as a guide to inform policymakers and donors about the range of key questions and topics associated with the inclusion of MMS in public health programs or market-based models. Commonly used terminology for such assessments is explained in **Table 1**. This toolkit has been tested and used in 12 countries (LATAM – Brazil, Colombia, Guatemala, Mexico and Peru; ASIA – Bangladesh, India and Vietnam; AFRICA – Ghana, Kenya, Nigeria and South Africa) and will be continually refined as we assess more countries (Indonesia, Tanzania, Burkina Faso and Madagascar). The experiences from these 12 country assessments have been instrumental in developing this toolkit and providing tips on how to use these tools (see **Box 1**).

After using this toolkit, you will be able to:

- determine whether MMS would need to be imported or produced in the country for use in public health programs;
- document in-country capacity to procure ingredients and produce an MMS product that can be delivered to the end consumer or institutional buyer (e.g., Ministry of Health);
- provide guidance on actions needed to ensure competitive and affordable sources of an MMS supply; and
- assess the impact of shifting from import to local production of MMS and vice versa on countries or regions.

How to use this toolkit

As a first step, review the analytical framework (**Figure 1**) and allocate resources to administer the toolkit. There are four main complementary domains to explore in the *Sight and Life* MMS Supply toolkit: (**1**) desk research, (**2**) market assessment, (**3**) production assessment, and (**4**) regulation and policy assessment. Typically, two full-time researchers would be able to complete the tasks listed in this toolkit. Desk research and KIIs are the recommended methods.

Skills needed

The skills required to implement the tools include general research skills, good communication and interpersonal skills to conduct KIIs, and analytical abilities to manage and analyze data.

TABLE 1: Glossary

Term / abbreviation	Definition / long form
Capital goods	A capital good is a durable good that is used in the production of goods or services. Capital goods are one of the three types of producer goods, the other two being land and labor. Examples of capital goods include buildings, machines, equipment, furniture and fixtures.
Commercial tax	A type of tax that is established with respect to the commercial provision of goods or services. Value added tax and excise tax are examples of different commercial taxes.
Common trade tariff	Tax or duty used to restrict imports by increasing the price of goods and services purchased from overseas to protect the local economy, thereby making them less attractive to consumers.
Competitive pricing	When producers set their prices at the same level as those of their competitors.
Cost of registration	A fee paid to either the drug regulator or the food regulator in order to register a product (i.e., a new supplement).
Downstream policies	Consumer-friendly policies, i.e., policies that focus on providing equitable access to care and services to all citizens.
Essential medicines list (EML)	A list of the minimum medicines needed for a basic healthcare system, listing the most efficacious, safe and cost-effective medicines for priority conditions.
Excise tax	A tax on manufactured goods levied at the time of manufacture rather than at sale. Excise tax is typically imposed on producers and manufacturers, and is ultimately passed on to the consumer.
WHO-GMP	Good Manufacturing Practices (GMP) are part of quality assurance and ensure that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing regulator. See World Health Organization quality assurance guidelines.[1]
Import tax	A tax collected on imports or exports by a country's customs authorities. Also called customs duty.
Installed capacity	The maximum a facility can produce from its machinery.
Luxury tax	A tax placed on products or services that are deemed to be nonessential or unnecessary. A luxury tax is an indirect tax that increases the price of the good or service, and is a price-inflationary burden that is incurred only by the end consumer who purchases or uses the product.
Policy coherence	An approach and policy tool for integrating the economic, social, environmental and governance dimensions of sustainable development at all stages of domestic and international policymaking.
Price ceiling	A situation whereby a product is priced above or below the market equilibrium and a ceiling is established to limit how high the price of the product can be.
Sales tax	A tax that is levied on the sale of goods and services.
Straight ingredients	Active ingredients (vitamin and minerals) and their forms for tableting.
UNIMMAP	UNICEF/WHO/United Nations University International Multiple Micronutrient Antenatal Preparation.
Upstream policies	Manufacturer-friendly policies, i.e., policies that focus on improving fundamental social and economic structures in order to decrease barriers and improve support that helps people reach their full health potential.
Value added tax	A tax on the amount by which the value of an article has been increased at each stage of its production or distribution. It is levied on the added value that results from each exchange. It differs from a sales tax in that a sales tax is levied on the total value of the exchange.
Working capital	Money available to a company for day-to-day operations. It measures a company's liquidity, efficiency and overall health. It gives an indication of whether local companies are able to produce a new product on their own.

Basic statistical analyses, such as linear regression using either Excel or another software package, could be outsourced after you have collected the data. Some exposure to market and manufacturing environments would be useful, but is not essential. If the tools provided here need further explanation, consider obtaining external expertise at any point during your study.

1. Desk research

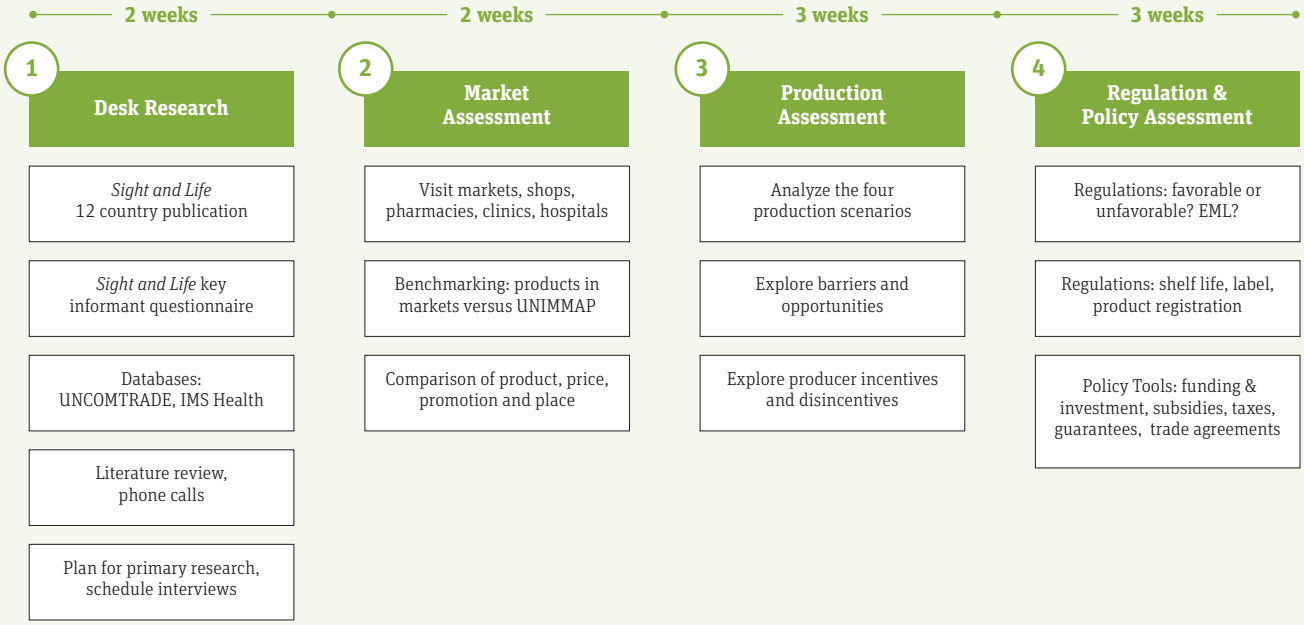
Conduct comprehensive desk research related to the production and procurement of iron and folic acid (IFA) supplements and MMS in your country.

Anticipated time required: 2 weeks

To do

- ☐ Review the following two sources as guiding questions, topics and analyses: (**1**) the KII questionnaire in **Box 5**; and (**2**) *Sight and Life's* article on procurement and production assessment in 12 low- and middle-income countries, published in the journal Maternal and Child Nutrition.[2]
- ☐ Contact government authorities or research institutes for

FIGURE 1: The analytical framework of the *Sight and Life* MMS Supply toolkit



BOX 1: Did you know?

In 2015, *Sight and Life* conducted a situation analysis on the procurement and production of MMS in 15 countries (12 lower and upper middle-income countries and three high-income countries). Globally, there are few vitamin and mineral ingredient manufacturers, and the paper aimed to better inform WHO's guidelines on prenatal supplements in its current transition from iron/folate tablets to multiple micronutrient tablets in pregnancy. Four years later, and in line with a relentless global effort by the scientific community to answer all WHO's concerns regarding risk and evidence, *Sight and Life* decided to expand its initial study to conduct a situation analysis for 32 countries worldwide (updated data for 15 countries and new data for 17 countries) to further and better inform the development of an enabling environment that can guarantee a stable, affordable and high-quality supply of MMS. Because our study is still ongoing, this article provides only some of the preliminary findings of our situation analysis for Bangladesh, India and Indonesia, which will be shared in **Boxes 2–4**.

incomplete documents that you find in the public realm but which are not published online.

- ☐ Check the validity of sources and the reliability of any online publications.
- ☐ Identify gaps in information and list them as topics to explore in KIIs.
- ☐ Map out key stakeholders for interviews, or potential partnering opportunities.
- ☐ Access historical, current and forecasted sales data (value or volume) of local and imported vitamin and mineral supplements through online portals such as the United Nations International Trade Statistics Database and IMS Health Database (Danbury, CT, USA).

Outcome

- ✓ Identification of gaps in information on production and procurement of MMS in your country.
- ✓ Trends in sales data to denote the availability of MMS in markets as well as local manufacturing capacity.
- ✓ A KII questionnaire.
- ✓ Plan for primary research and data analyses.

2. Market assessment

A market analysis is helpful in determining the availability, accessibility and affordability of MMS, both now and in the future. Depending on the available budget, restrict purchase to supplements containing vitamins and minerals in tablets or capsules for adults and pregnant/lactating women. Exclude supplements for children (because of lower doses), formats such as syrups and powders (because of poor stability and palatability) and supplements that con-

TABLE 2: Required information to be collected during a market assessment

Product	Price	Promotion	Place
Product variety (e.g., gummies, tablets, capsules, powders)	Maximum retail price	Advertising (e.g., online, mass media, offline, health practitioners)	Channels of distribution (public private: clinics, hospitals, frontline health workers, e-commerce, multi-level marketing or direct sales, micro-franchisees, mom & pop stores)
Quality	Discounts	Sales promotion	Coverage
Packaging (e.g., blister/bottle, pack sizes, label claims)			Locations (e.g., rural, urban, peri-urban)

tain herbal ingredients (because of the lack of scientific evidence that they improve pregnancy outcomes). Key questions for this domain are explained in Section 1 of **Box 5**.

The UNIMMAP formulation (**Box 5**) is considered as the benchmark for ingredients and recommended daily dose because of the scientific evidence of its efficacy on pregnancy outcomes. Please review the MMS on page 102 of this *Sight and Life* Special Report; refer to it and recommend it during your discussions with manufacturers. Create four nonoverlapping **categories** between the product and the UNIMMAP formulation:

Category I: Less than 10 ingredients and dosage matches UNIMMAP.

Category II: At least 10 ingredients and dosage* consistent (80 percent or more of the recommended dosage) with UNIMMAP.

Category III: Ingredients and dosage consistent with UNIMMAP.*

Category IV: Ingredients and dosage consistent with UNIMMAP; could include other key nutrients such as docosahexaenoic acid (DHA). Category III is the benchmark.

Anticipated time required: 2 weeks

To do

- ☐ Visit pharmacies, clinics, stores and online platforms to collect supplements.
- ☐ Purchase supplements (follow the inclusion and exclusion criteria in **Box 5**).
- ☐ Compare and analyze the obtained supplements (branded or unbranded) by product features, packaging, price, promotion and place (explained in **Table 2**).
- ☐ Compare the collected products to the UNIMMAP formulation using the nutrient information on the label and classify into categories I, II, III and IV.
- ☐ Summarize nominal and qualitative response items into tables to allow for descriptive comparisons.
- ☐ Conduct simple descriptive statistics and reported mean and standard deviations for numeric response items.
- ☐ Consider linear regression to assess price differences by category type: local versus imported, packaging type, etc.
- ☐ Triangulate with findings from desk research.

Outcome

Through this assessment, you will be able to determine affordability and local manufacturing capabilities in your country. If you find local brands in category III or IV, you can be assured that local capacity exists and can start a development project for MMS procurement within 1–2 years. Manufacturers of local brands that are in category I or II would need to establish vendors for the procurement of the missing ingredients, conduct stability tests and register the new product. If budget allows, plan for a subsequent phase of laboratory analysis to determine the quality of the supplements, i.e., levels of micronutrients in the brands, microbial load and heavy metals load (see the MMS specification article in this Special Report, page 102). By doing so, you will be able to identify gaps in the quality of the supplements and recommend areas of improvement in the quality control processes for the manufacturers (see **Box 2**).

3. Production assessment

To support local in-country or regional procurement and production of MMS, four scenarios are possible:

*Supplement manufacturers confirmed that they would be able to match products in category II to the UNIMMAP formulation more easily than those in category I; hence, the cutoff for category II is 10 ingredients. Similarly, the manufacturers confirmed that at dosage greater than 80 percent of the required dosage, it is relatively easy for them to match the UNIMMAP formulation.

BOX 2: Market assessment

Local and imported MMS in blister or bottle packaging are found in Bangladesh, India and Indonesia. MMS are available only in pharmacies and are not available through government channels in the country. In India, MMS can be purchased through several channels – pharmacy, supermarket and 'mom & pop' stores – or directly sold to consumers through online portals or home delivery, and these channels have now extended to online portals such as Amazon and Flipkart when sold as food supplements.

We sampled 10 MMS brands from Bangladesh (2015 and 2019 study), all of which were locally manufactured. We then compared the collected products with the UNIMMAP formulation using the nutrient information on the label, and classified each product into categories I, II, III and IV. Our results showed that few brands were classified as category I (n = 2), most were classified as category II (n = 8) and none could be classified as category III (n = 0). We then used linear regression to assess price differences by category type and found that products were cheaper if they had fewer ingredients and lower dosage. A change from category I to II would lead on average to a US$1.49 increase in price (**Table 3**).

TABLE 3: Association between price (US$) and category (I or II) per package of 30 capsules or tablets of MMS in Bangladesh*

Variables	Coefficient (US$)	Average	Standard deviation
Category II versus category I	1.49	2.08	1.02

* *N* = 10 products

Scenario A: Import of liquid or dry forms of straight ingredients of vitamins and minerals that are mixed, tableted or encapsulated and packaged by a local manufacturer.

Scenario B: Import of a premix of vitamins and minerals that is tableted or encapsulated and packaged locally.

Scenario C: Import of a bulk, finished product (tablets or capsules) that is packaged and branded locally.

Scenario D: Import of a branded and packaged finished product.

Scenarios A and B are found in countries that have thriving branded supplements or pharmaceutical industries such as Bangladesh, Indonesia, Colombia and Peru. In most low-income countries, scenarios C and D are preferred, as production capacity and potential consumer demand are low. Section 5 in **Box 5** covers the key questions.

Anticipated time required: 3 weeks

To do

- ☐ Identify and interview small, medium and large local, regional or multinational companies.
- ☐ Interview employees in senior management, regulatory, research and development (R&D), and business development functions. Explore and examine from their perspective the barriers and opportunities, incentives and disincentives for each of the four scenarios.
- ☐ Triangulate with findings from desk research.

Outcome

Through this assessment, you will be able to determine affordability and local manufacturing capabilities, preferred production scenarios for your country in the short and long term, and opportunities and challenges for different types of producers (local, regional, multinational, small, medium and large enterprises).

4. Regulation and policy assessment

Policy guidelines and government oversight will be needed to switch from IFA to MMS. Local companies will find it difficult to compete with offshore producers in countries that have favorable policy environments. Policy coherence along the entire value chain for MMS can ensure the sustainability and affordability of local production of MMS. Consider having MMS on your country's essential medicines list (EML). As a result, MMS will be given public health importance and the government will prioritize resources for shaping markets, supply and demand. Having MMS on the EML will also lead to easier clearance of supplies at port, government storage at central medical stores, and government-led distribution and logistics.

Anticipated time required: 3 weeks

To do

- ☐ List the countries from which straights, premix and/or supplements are imported into your country. Then search for trade agreements your country has with those countries and see if any of the above imports are exempted. Validate your findings with KIIs.
- ☐ Interview regulatory functions in companies, government officials in finance and health ministries, and national regu-

latory bodies about each of the four production/procurement scenarios.

- ☐ Ask for policy and regulation documents on supplements.
- ☐ Triangulate with findings from desk research.
- ☐ Analyze your findings by the following policy tool categories: funding and investment, product registration, volume guarantees, shelf-life and labeling regulations, subsidies and price ceilings, taxes and trade agreements.

Key questions to understand the types of regulation and policy tools that would benefit your country are covered in Sections 2–4 in **Box 5**. National governments need to consider downstream or consumer-friendly policies as well as upstream or manufacturer-friendly policies in order to achieve policy coherence. Downstream policies include subsidies (through vouchers, for example) or free access through clinics. Upstream policies improve affordability through competitive and sustainable price ceilings, import subsidies, tax exemptions or soft funding (funding such as donations, subsidies and grants that have no direct requirement for a return on investment).

Outcome

You will be able to recommend relevant upstream regulations and policies at this stage:

- ✓ *Funding and investment:* Facilitate loans for companies towards facilities, R&D, systems and equipment. For example, the cost of debt in the procurement of capital goods and raw materials and the resulting working capital can be major constraints for local producers in scenarios A and B.
- ✓ *Product registration:* MMS for adults or pregnancy can be registered as a food or a drug. Drugs undergo stringent controls for quality, require more expensive and hard-to-access ingredients (without a corresponding increase in quality), and the cost of registration is high. Foods, on the other hand, are usually easier and less expensive to manufacture and register everywhere. Where there is a preference for drug registration over food registration, it might signal a greater degree of government oversight/monitoring from production to marketplace. While the registration costs have been low in many countries (i.e., less than US$2,000), they have been as high as US$10,000 in countries such as Nigeria. The costs of preparing for product registration, mainly stability tests, are usually high (see **Box 3**).
- ✓ *Volume guarantees:* Volume guarantees are agreements between a guarantor (government or donors) and an MMS producer to maintain agreed procurement volumes in exchange for price reductions. If the procurers do not reach the agreed volume, the guarantors undertake to finance complementary orders. This allows companies to plan long-term resources or supplies, and to lower the cost of MMS.
- ✓ *Shelf-life regulation:* Shelf-life requirements are needed for every stage of the production process to ensure that the active ingredients, intermediates and finished product are delivered to the full potency. A longer shelf life of 24–36 months allows products to be procured fewer times a year, and stored and transported in large volumes, and thus could be more cost-effective. In some countries including Ghana, India and Kenya, requirements for active ingredients, premix or finished product are both strict and mandatory.

BOX 3: Registered as a food or a drug?

We investigated whether MMS for adults or pregnancy were registered as a drug or a food in each country. While drugs undergo stringent controls for quality and the cost of registration is high, foods are generally easier and cheaper to register.

In India, MMS for adults can be registered as either a food or a drug, depending on the dosage of the ingredients. If the ingredient levels are less than one Recommended Dietary Allowance (RDA), the formulation will be registered as a food supplement. On the other hand, if the ingredient levels are more than one RDA, then the formulation will be considered as a drug. Therefore, in India, the UNIMMAP formulation would be considered as a drug, because it contains some vitamins at levels that are higher than one RDA for the Indian population.

In 2015, the cost of registration for MMS supplements in the country was US$6,293. However, MMS would be categorized under pharmaceutical regulations as a fixed-dose combination (FDC), which consists of the following cost structure: US$3,520 (import and marketing permission for 1 year) + US$1,408 (import and marketing permission after 1 year of grant approval) + US$211.20 for manufacturing and marketing permission (if all active ingredients are approved in India for more than 1 year) or US$704 for manufacturing and marketing permission (if any of the active ingredients are approved for less than 1 year).

This is not the case in Bangladesh, where MMS can be registered only as a drug; however, the registration cost has decreased by more than half (54 percent) since 2015 and now amounts to US$118.

BOX 4: What are the preferred import scenarios?

In Indonesia, the preferred import scenarios are the import of straight ingredients and/or the import of premix blends. In some cases, the import of finished products may be cheaper, in which case the product will be imported instead of manufactured locally. The standard import duty for the import of straight ingredients or premix blends is 5 percent, and there are no exemptions to import duties if the products are produced in the ASEAN region. The minimum shelf life required for import is 75 percent at the time of clearance.

In Bangladesh, the standard import duty for straight ingredients has increased by about 6.5 percent since 2015; the import shelf-life requirement of at least 75 percent is unchanged. The country's preferred import scenario is scenario A, because of low taxes and a 100 percent rebate upon tax payment.

- ✓ *Labeling regulation:* A product label is important for consumer awareness. It communicates what the product is, its contents and for whom it is intended. At the very minimum, a label should mention: date of manufacture, expiry date, a list of contents, and drug or nutrient facts. In some countries, health claims or structure/function claims are allowed.

- ✓ *Subsidies and price ceilings:* These are popular mechanisms to lower the cost of MMS to the consumer. For example, Indian producers who made MMS in excise-free zones were given price subsidies. In the USA, branded supplements can get rebates through state programs. In India and Brazil, a price ceiling is set by a national price agency.

- ✓ *Taxes:* Import and commercial taxes can potentially affect the affordability of MMS to low-income consumers. Taxes, along with taxation rules, are one of the most complex and confusing topics of any financial system. This complexity arises because of different types of taxes with different tax rates and continual amendments in the taxation rules, which are retrospective and prospective at times. Definitions of taxes are provided in **Table 1**. Typically, the highest taxes are paid for scenario D: imported branded supplements. Peru imposes zero tax on scenarios A and B, and a low tax on scenarios C and D. Commercial taxes in some countries can be as high as 40 percent for all four scenarios (see **Box 4**).

- ✓ *Trade agreements:* A trade agreement (also known as trade pact) is a wide-ranging tax, tariff and trade treaty that often includes investment guarantees. It exists when two or more countries agree on terms that help them trade with each other. For example, Mexico through the North American Free Trade Agreement offers waivers for ingredients or products from the USA and Canada.

Synthesis and recommendations

After completing the market, production and policy domain analyses, you will be able to assess for your country:

- ✓ Preferred production scenario (A, B, C or D) or recommend a mix of scenarios over time.
- ✓ Availability of MMS in the markets.
- ✓ Gaps and opportunities in the markets.
- ✓ Investment required for the supply of MMS.
- ✓ Capabilities of local manufacturers.
- ✓ Regulation and policy tools to support the shift from IFA to MMS.

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References

1 World Health Organization. Essential medicines and health products. WHO; 2019. Internet: https://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/ (accessed 24 March 2020).

2 Monterrosa EC, Beesabathuni K, van Zutphen KG, Steiger G, Kupka R, Fleet A, et al. Situation analysis of procurement and production of multiple micronutrient supplements in 12 lower and upper middle-income countries. Matern Child Nutr. 2018;14 (Suppl 5):e12500. doi:10.1111/mcn.12500.

BOX 5: Key informant interview questionnaire

Inclusion and exclusion criteria

Supplements	Include	Exclude
Type of consumer	Adults, pregnant women, lactating women	Children, +50 years
Multiple micronutrient	Products containing at least 10 vitamins & minerals	Products containing less than 10 vitamins & minerals
Delivery form	Pills, capsules and tablets	Syrups and powders
Ingredients	Minerals, vitamins, essential fatty acids, essential amino acids	Herbal ingredients, fusion blends of herbals and vitamins

Section 1. Product

1. *In your country, what type of manufacturing is available for MMS (for adults that meet the inclusion criteria in table A, page 1) for the consumer market?*
   - **a.** Local
   - **b.** Imported
   - **c.** Both

2. *Where can consumers purchase MMS for adults (circle all that apply)?*
   - **a.** Pharmacy
   - **b.** Supermarket
   - **c.** Mom & pop shop
   - **d.** Direct sales or home delivery
   - **e.** Other (please specify): _____

3. *How are these commercial products packaged?*
   - **a.** Bottles
   - **b.** Blister packages
   - **c.** Consumers will find both types of packages in the country

4. *Is MMS for pregnancy available through government institutions (e.g., public hospitals or clinics)?*
   - **a.** Yes, it is available at government institutions
   - **b.** No, MMS for pregnancy is not available through government institutions (skip to Q6)

5. *Is the product available to purchase at hospital or clinic pharmacies?*
   - **a.** Yes
   - **b.** No

6. *Where is the product available (circle all that apply)?*
   - **a.** Prenatal care with private doctor
   - **b.** Private pharmacy
   - **c.** Another institution or community program (please specify): _____
   - **d.** Don't know

7. *Provide pictures of labels of MMS brands from your country.*
   Note whether they are imported or local for each label. These MMS brands can be for adults and pregnant or lactating women, and must contain at least 10 vitamins and minerals.

Brand name (Include MRP)	Please specify if: **(a) Local or (b) Imported**	Front of package image	Back of package image (include the composition)

Section 2. Product registration

8. *Is MMS for adults registered as a food supplement or drug in your country?*

- **a.** Food supplement
- **b.** Drug
- **c.** The product is not registered (skip to Q10)

9. *What is the cost of registration for this product?*

_____ (please note the local currency cost)

10. *Is MMS for pregnancy registered as a food supplement or drug in your country?*

- **a.** Food supplement
- **b.** Drug
- **c.** The product is not registered (skip to Q 13)

11. *What is the cost of registration for this product?*

_____ (please note the local currency cost)

12. *Is there a price control (e.g., price ceiling) imposed by regulatory bodies for MMS for pregnancy?*

- **a.** Yes, please specify: _____
- **b.** No

13. *The UNIMMAP formulation (shown below) is considered a global standard for prenatal specification.*

Vitamins	Level	Minerals	Level
Vitamin A (µg RE)	800	Copper (mg)	2
Vitamin B_1 (mg)	1.4	Folic acid (µg)	400
Vitamin B_2 (mg)	1.4	Iodine (µg)	150
Niacin (B_3) (mg)	18	Iron (mg)	30
Vitamin B_6 (mg)	1.9	Selenium (µg)	65
Vitamin B_{12} (µg)	2.6	Zinc (mg)	15
Vitamin C (mg)	70		
Vitamin D_3 (IU)	200		
Vitamin E (mg)	10		

14. *Is the above UNIMMAP formulation considered a drug or a food supplement?*

- **a.** Food supplement
- **b.** Drug
- **c.** The product is not registered (skip to Q17)

15. *What is the cost of this product registration?*

_____ (please note the local currency cost)

16. *Is there a price control (e.g., price ceiling) imposed by regulatory bodies for manufacturers of the UNIMAP formulation?*

- **a.** Yes
- **b.** No

Section 3. Policies, taxes and tariffs

In the following table, please answer each question that is presented per row. Fill in the values as indicated for the question.
If a scenario does not apply to your country, please use NA (not applicable).

	A	B	C	D
	Straight ingredients	Premix blends	Bulk tablets/pills/capsules	Branded supplement
17. *What is the standard import duty?*				
(% tax on value of import)				
18. *Are there any exemptions*				
to import duties (e.g., free trade				
agreement)?				
(Yes, please specify, or No)				
19. *Are there any added import*				
duties (e.g., if imported from				
a specific country)?				
(Yes, please specify, or No)				
20. *What is the shelf-life requirement*				
for importing?				

21. *Of these four import scenarios, which is preferred in the country?*

- **a.** Straight ingredients
- **b.** Premix blends
- **c.** Bulk products
- **d.** Branded supplement

22. *Why is the import scenario preferred (circle all that apply)?*

- **a.** Low taxes
- **b.** Government subsidies
- **c.** Free trade agreements
- **d.** No manufacturing capacity
- **e.** Small consumer market for product
- **f.** Other (please specify): _____

23. *In your opinion what could be done to lower tariffs for each import scenario? Please add your response in the box corresponding to the scenario. If a scenario does not apply to your country, please use NA (not applicable).*

A	B	C	D
Straight ingredients	Premix blends	Bulk tablets/pills/capsules	Branded supplement

Describe the local commercial taxes and policies on the production of MMS for adults in your country.
If a scenario does not apply to your country, please use NA (not applicable).

	A	B	C	D
	Straight ingredients	Premix blends	Bulk tablets/pills/capsules	Branded supplement
24. *What are the commercial duties?*				
(% tax or amount in				
local currency)				

	A	B	C	D
	Straight ingredients	Premix blends	Bulk tablets/pills/capsules	Branded supplement
25. *Are there any price subsidies?*				
(Yes, please specify the value,				
or No)				
26. *Are there any price ceilings?*				
(Yes, please specify the max.				
value, or No)				
27. *Are there any tax exemptions?*				
(Yes, please specify, or No)				

28. *Are there any policies that enable regional or inter-country trade?*

a. Yes, please specify the policy: _____

b. No

Section 4. Label regulation

29. *Using the table below, note and describe the label regulations for MMS.*

Label item	Please specify if: (a) Required, (b) Not required or (c) Voluntary	Specification description, as appropriate
a. Dates (manufacture AND expiry/best before)		
b. Ingredient list		
c. Drug facts or nutrient facts		
d. Ingredient claims		
e. Health claims		
f. Dosage		
g. Storage conditions		
h. Government endorsement		
i. Other (please specify)		

Section 5. Local manufacturing capabilities

30. *Is local production of MMS for adults available in your country?*

a. Yes

b. No (skip to Q40)

Using the following table, please state the companies and their brands that are local production.
Also note the production scenario and whether the facility is certified.

31. *What is the name of the manufacturer?*	
32. *What is the brand name? What is the retail price (MRP)?*	
33. *Is this a leading brand in the country? (Yes or No)*	
34. *Is the company (a) multinational or (b) local?*	
35. *What is the production scenario? (A, B or C*)*	
36. *What is their (1) installed capacity and (2) actual/utilized capacity??*	
37. *Is the facility WHO-GMP certified? (Yes or No)*	

***** A: imports straights; B: imports premix; C: imports bulk

38. *What is the cost of local production of MMS? It is OK to provide a range.*

39. *Capital goods & working capital:*

- **a.** Can in-country manufacturers increase production capacity of MMS easily? Examples of capital goods include buildings, machines, equipment, furniture and fixtures. Consider whether equipment can be easily purchased locally or whether it needs to be imported.
- **b.** Do in-country (local) manufacturers have adequate access to working capital?
  1. Yes
  2. No. Will a debt/loan program be useful, and at what interest rates (cost of debt)? Please also mention the current lending interest rate in the country.

40. *In the table below, list major barriers for ensuring good quality control (QC) and quality assurance (QA) for the production and procurement of MMS along the value chain. Consider infrastructure, financial capacity and human skills or capacity. If there are no barriers, please state so.*

Value chain component	Barrier for QA/QC
Sourcing	
Blending	
Production of capsules/tablets	
Packaging	
Lab testing	
Transport	
Warehousing	
Point of purchase or disbursement	
Other	

Expert Consensus on an Open-Access Product Specification for MMS for Pregnant Women

A globally adaptable specification supplied to public health nutrition programs

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Key messages

- A complete product specification can serve as the basis of a quality agreement between a purchaser and a manufacturer. It provides a common and transparent technical understanding of the requirements for a product (and its packaging) to be manufactured and the means and methods by which both parties can verify that the product delivered for distribution is in fact the product that was ordered.
- The product specification is generally a proprietary document owned by either the purchaser or the manufacturer, and is often difficult for third parties to access. By contrast, an open-access product specification is freely available to any interested party and delivers benefits to both the purchaser and the manufacturer that help facilitate the initiation and scaling of important public health programs.
- A consensus open-access product specification for the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation of a multiple micronutrient supplement (MMS) for pregnant women has been developed and is made available in summary form in this contribution. The full version is available for download from *Sight and Life* (sightandlife.org/resources/#sal-magazine&id=6375&f=all) and the New York Academy of Sciences MMS Technical Advisory Group (MMS TAG), *www.nyas.org/media/21537/expert-consensus-on-an-open-access-unimmap-mms-prod-spec.pdf,* the Micronutrient Forum and Vitamin Angels; it provides an important contribution towards accelerating the availability of UNIMMAP-MMS for global public health nutrition programs.
- The open-access product specification for the UNIMMAP-MMS product is intended to be used globally by purchasers of UNIMMAP-MMS and by qualified manufacturers; it attempts to anticipate and address all of the MMS product/packaging specifications that most governments would include for a nutritional supplement to be placed on an essential medicines list, if and when they seek to transition from distributing iron and folic acid (IFA) supplements to MMS for pregnant women.
- Several insights that will be useful to both purchasers and manufacturers are offered at the conclusion of this article; these are the result of the decade-long journey it has taken to achieve a consensus on the UNIMMAP-MMS open-access product specification.

Introduction

Multiple micronutrient supplements (MMS) for pregnant women provide women and their babies with a positive pregnancy experience and healthy start to life beyond that which can be achieved with IFA supplements alone.[1,2,3] Clinical trials to date have compared IFA with MMS, most often using the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS formula. UNIMMAP-MMS was developed by experts during a workshop organized by WHO, UNICEF and the United Nations University in 1999, and convened to identify an MMS formula for efficacy/clinical trials.[4] Recently, UNIMMAP-MMS was recommended by the Task Force for MMS for Pregnant Women as the standard MMS formulation to be used in public health nutrition programs for pregnant women.[3]

"Recently, UNIMMAP-MMS was recommended as the standard MMS formulation to be used in public health nutrition programs for pregnant women"

With UNIMMAP-MMS proven to be efficacious, safe, cost-effective and affordable for public health nutrition programs, as reported elsewhere in this *Sight and Life* Special Report, the challenge turns to implementation and scaling the manufacture and distribution of MMS on a global scale. The nearly 200 million pregnancies occurring annually in low- and middle-income countries (LMICs) are most likely to benefit from the use of UNIMMAP-MMS. If most or all pregnant women in LMICs were to begin MMS use in early pregnancy and follow the recommended regimen of one tablet per day, equivalent to 180 tablets per pregnancy, there would be a total annual demand for more than 35 billion tablets for pregnant women in LMICs alone.[3] Producing 35 billion tablets per year is a significant manufacturing challenge that would require several manufacturers to fulfill it. Apart from the large volume required, an equally daunting task is to ensure consistency in the quality of an affordable MMS across various public health nutrition programs while allowing for variances in global manufacturing attributable to variations among internationally recognized regulatory and pharmacopoeia standards.

While the UNIMMAP-MMS formula is publicly available, alone, it is insufficient to characterize the quality aspects of an MMS product in a way that is useful for both manufacturers and purchasers. A product specification is customarily used by both purchasers and manufacturers to achieve a common understanding of the product that is to be manufactured and purchased.

What is a product specification?

A product specification is a technical document that provides a detailed description of the product to be manufactured. For UNIMMAP-MMS, it defines the specifications pertaining to the MMS product's formula (i.e., UNIMMAP formula) including: the amount and chemical form of each ingredient; the dosage form (e.g., tablet, capsule); the packaging container-closure system (e.g., bottle, blister pack); the tests, testing methods and reference standards, and acceptance criteria to be applied to the finished product to verify quantitative label claims; stability study requirements; and any third-party certifications expected of the manufacturer.

The primary function of a product specification is to support a procurement transaction. It serves as the basis for a 'quality agreement' between the purchaser and the manufacturer, providing both parties with a common and transparent technical understanding of the requirements for a product to be manufactured and the means and methods by which both parties can verify that the product delivered for distribution is in fact the product that was ordered.

"The primary function of a product specification is to support a procurement transaction"

Why is an open-access product specification needed?

A product specification is generally a proprietary document, owned by either the purchaser or the manufacturer, or else it might be accessed under a licensing arrangement with a third-party owner. An open-access product specification is freely available to any interested party, and is important for products used in public health programs requiring a product to be of high quality, available in high volume and procurable at a low cost. An open-access product specification – especially one that can be adapted for use everywhere – can play an important role in accelerating and maintaining the availability of UNIMMAP-MMS for global public health programs where multiple manufacturers are expected to play a role in meeting demand for product supply. The key benefits of an open-access product specification are described in **Box 1**.

BOX 1: Benefits of an open-access product specification for UNIMMAP-MMS

Purchaser-derived benefits:

- Gives users of donated or purchased product confidence that the product accessed is the clinically proven UNIMMAP-MMS product when introducing MMS into public health nutrition programs.
- Provides assurance – when verified by an independent verification process arranged by the purchaser for this purpose – that a product is made to the specification that conforms to international quality standards expected by large and responsible healthcare systems.
- Fosters confidence through the knowledge that it is the same product used most often in clinical trials and proven effective.
- Helps purchasers to focus negotiations with manufacturers on volume and price for a product of fixed or defined quality.

Manufacturer-derived benefits:

- Reduces time and investment needed to deliver a finished product to one or more purchasers by avoiding the need to recreate a product description.

- Provides direction pertaining to allowable variances in a product of defined quality that are attributable to different regulatory and pharmacopoeia requirements in different regions of the world.
- Defines other variances that might be sought by a purchaser and helps manufacturers assist purchasers to understand the impact of those variances on both cost and environmental impact.
- Helps attract interest from different potential purchasers that can result in multiple simultaneous orders, which in turn can lower manufacturing costs.

Who should use the open-access product specification?

The open-access product specification is intended for UNIMMAP-MMS purchasers, procurement agents (e.g., donor agencies, foundations, NGOs, governments, bilateral agencies and multilateral agencies) and manufacturers accessing or producing the MMS product for large-scale public health nutrition programs. It is intended as a resource for parties to the procurement process to: (**1**) inform discussions and help place purchasers and manufacturers on an equal footing; (**2**) foster transactions that result in procurement of a product of fixed, high quality at a price fair to both purchaser and manufacturer; and (**3**) enable production of a UNIMMAP–MMS product to globally recognized quality standards by many manufacturers.

> **"Purchasers and manufacturers should work collaboratively using the product specification"**

How should the open-access product specification be used?

Both purchasers and manufacturers should use the specification as the basis for a quality agreement and include it as an attachment to a purchase agreement. It is designed to be adaptable to conform to any globally recognized regulatory regime and pharmacopoeia as defined in the specification. Purchasers and manufacturers should work collaboratively using the product specification to agree on technical requirements acceptable to the purchaser with an understanding, provided by the manufacturer, of the cost implications of each decision. The specification can also be used to assess the capabilities of prospective manufacturers. The key criteria that should be met by manufacturers presenting themselves as qualified to bid on procurement contracts for UNIMMAP-MMS are shown in **Box 2**.

The open-access UNIMMAP-MMS product specification also serves as a reference standard underlying benchmark pricing. Currently, UNIMMAP-MMS can be produced in the USA to the UNIMMAP-MMS open-access product specification for about US$0.01 per tablet (with orders of 3–5 million, 180-count bottles) using the regulatory framework of the US Food and Drug Administration (US FDA) and the quality standards of the United States Pharmacopeia (USP). This pricing can serve as a benchmark for manufacturing in other parts of the world; however, it must be recognized that prices available from global manufacturers and those from manufacturers producing for a single domestic market will vary, depending upon a number of factors (e.g., volume capacity of the manufacturer, volume of product purchased, packaging option selected, local taxes, and the regulatory and pharmacopoeia framework selected).

BOX 2: Types of manufacturers intended to use and benefit from an open-access product specification for UNIMMAP–MMS

Manufacturers who:

- Possess current tablet and/or capsule manufacturing experience, expertise, and knowledge.
- Manufacture products according to current Good Manufacturing Practice (cGMP) regulations promulgated by an internationally recognized regulatory authority (e.g., US FDA), or by other Stringent Regulatory Authorities (e.g., WHO), by a PIC/S member, or by a globally recognized authority (e.g., USP), including but not limited to:
  - US FDA 21 CFR Part 111 Current Good Manufacturing Practice in Manufacturing, Packing, Labeling, or Holding Operations for Dietary Supplements; and
  - USP–NF general chapter (2750) Manufacturing Practices for Dietary Supplements.
- Regularly manufacture products consistent with globally recognized pharmacopoeias (i.e., United States Pharmacopoeia, British Pharmacopoeia, European Pharmacopoeia, International Pharmacopoeia and Japanese Pharmacopoeia).
- Have a verifiable capacity to manufacture to the consensus open-access UNIMMAP–MMS product specification (see **Box 3**).

The consensus open-access UNIMMAP–MMS product specification

An expert consensus on an open-access UNIMMAP-MMS product specification was recently achieved through a Technical Consultation jointly hosted by the New York Academy of Sciences Multiple Micronutrient Supplementation Technical Advisory Group (MMS TAG) and the Micronutrient Forum, with funding from the Bill & Melinda Gates Foundation. The key components of the specification are summarized in **Box 3**. The full version of the consensus open-access UNIMMAP-MMS product specification is available for download from *Sight and Life*, the New York Academy of Sciences MMS TAG, the Micronutrient Forum and Vitamin Angels.

BOX 3: Key technical components of the consensus open-access product specification for a UNIMMAP–MMS product

The complete specification is available for download from Sight and Life, the New York Academy of Science MMS Technical Advisory Group (MMS TAG), the Micronutrient Forum and Vitamin Angels: www.nyas.org/media/21537/expert-consensus-on-an-open-access-unimmap-mms-prod-spec.pdf,

1. **General product description and formula:** tablets conforming to UNIMMAP formula.
2. **Ingredients:** including food/dietary/nutritional ingredients, excipients and processing aids.
3. **Stability studies:** required to support key label claims (stated or implied).
4. **Packaging/labeling:** 180-count HDPE (high-density polyethylene), tamper-evident, child-resistant bottle (possible alternatives for specialized circumstances, although not recommended here for regular use, are: 30-count HDPE bottle and 30-count blister pack).
5. **Manufacturing standards and certificates:**
   - 5.1. **Pharmacopoeia standards:** globally recognized.
   - 5.2. **Certificate of Analysis (CoA):** verifies conformance to product specification.
   - 5.3. **Certificate of Origin:** verification of manufacturer's country of origin.
   - 5.4. **Certificate of Free Sale (CFS) (as required):** verification that product can be used in the country of manufacture.
   - 5.5. **Certificate of current Good Manufacturing Practices (cGMP):** verification product is manufactured in accordance with standards promulgated by an internationally recognized regulatory/scientific authority.
   - 5.6. **Halal Certification (as needed):** verifies conformance with IFANCA standards or a similar Islamic certifying body.
6. **Other documentation required:** includes documentation pertaining to change control notification.
7. **Finished product specifications for product identification, performance and purity:**
   - 7.1. Tablet characterization and purity, including tests, test methods and acceptance criteria.
   - 7.2. Potency assay requirements (per tablet), including form of each ingredient, test method, label claim and limit references.
8. **Analytical test methods:** validated or verified, as needed.
9. **Storage and transportation requirements.**
10. **Definitions.**

"The journey to reach the consensus open-access product specification started nearly a decade ago"

The journey to reach the consensus open-access product specification started nearly a decade ago. With emerging evidence on the benefits of MMS, Kirk Humanitarian and Vitamin Angels – each having worked separately at first – began a collaboration in 2016 to develop an MMS product that would be both of high quality and acceptable to grantees (including both governments and NGOs) already seeking a supply of MMS to explore its use.[6,7] Working with multiple manufacturers within and outside the USA, several independent consultants and the USP, an initial UNIMMAP-MMS product specification was developed. A key factor prompting its development was recognition that: (**1**) demand for MMS existed, but the supply was negligible; (**2**) the existing product cost seemed high and susceptible to significant reduction through contract manufacturing; and (**3**) the existing product specifications were proprietary and inaccessible. During a presentation of the specification (to present and explain its use and value) to about 35 people from a range of organizations (including manufacturers, purchasers, program implementers and funders) held in conjunction with the Women Deliver Conference in Vancouver, Canada (5 June 2019), participants recognized it as a credible interim open-access product specification, and recommended it be subjected to review by experts through an independent technical consultation. That expert review – the MMS Product Specification Technical Consultation – was subsequently co-hosted by the New York Academy of Sciences and the Micronutrient Forum on 11–12 November 2019 in Washington, DC.

Securing a UNIMMAP-MMS product supply for immediate and long-term needs: global manufacturers versus manufacturing for a single domestic market using the open-access UNIMMAP-MMS product specification

When large healthcare systems in a single domestic market contemplate the purchase of a locally manufactured UNIMMAP-MMS product (as compared with importation from a global manufacturer), a local manufacturer's product can conform with the open-access specification by applying any of the internationally recognized manufacturing standards generally used in their region of the world. Where large healthcare systems seek to activate a program quickly when domestic manufacturing is not yet available, there is a pathway for gaining immediate access to UNIMMAP-MMS (based on the open-access product specification) while building capacity for manufacturing in a single domestic market using the same open-access product specifications (see **Box 4**).

BOX 4: Proposed pathway to local manufacturing of UNIMMAP-MMS synchronized with MMS introduction

- **Step 1:** Initial dependence by a health system purchaser on donated finished MMS product (packaged for individual use) from reputable international donation programs during the introductory stages when local authorities are engaged in a large-scale implementation to understand how to effectively and efficiently introduce and scale UNIMMAP-MMS. For example, using a demonstration program to explore ways to strengthen existing antenatal care services, or by exploring ways to increase adherence to the MMS regimen of 180 tablets per pregnancy as compared with adherence achieved using IFA supplementation alone. Additionally, during this step, long-term procurement options and/or domestic manufacturing are explored.
- **Step 2:** Importation and redistribution by a local manufacturer (i.e., a *de facto* distributor in this case) of finished product packaged for individual use (for use in initial introduction activities), while stability studies are undertaken simultaneously to permit the importation of finished product in bulk that can be repackaged and redistributed for individual use by a local manufacturer (also for use in initial introduction activities). Involving qualified local manufacturers in the opportunity to be the importer and repackager of an imported product can be an important incentive and step for manufacturer(s) that seek to become a local manufacturer. This two-step process provides a useful role for local manufacturers while they are building out their capacity to manufacture the product locally to the defined open-access UNIMMAP-MMS product specification, working to add the product to the national essential medicines list and securing local registration of the product.
- **Step 3:** Local purchase of UNIMMAP-MMS when a local manufacturer (producing for a single domestic market) demonstrates the ability to manufacture to the open-access product specification – a goal that might be facilitated by using a premix of UNIMMAP ingredients. Where manufacturing for a single domestic market is desired, local officials should recognize that building capacity to deliver a product to the open-access product specification takes time – time that is uniformly underestimated by decision-makers. Depending upon the starting point of the manufacturer, it can often take 12–36 months or more to reach local manufacturing potential.

Note: in all cases, purchasers (or grantees receiving UNIMMAP-MMS) should seek to use product that meets the product specifications in the open-access product specification, recognizing that the specification provides regional options for regulatory and pharmacopoeia standards applied.

While the decision to manufacture in a single domestic market is affected by a range of factors, local manufacturing can remain highly cost-effective if the product is manufactured in moderate to high volume (e.g., the optimal volume for gaining economies of scale is achieved when producing product for at least 3–5 million pregnancies annually).

> **"With consensus around the UNIMMAP–MMS open-access product specification now achieved, purchasers and manufacturers everywhere can benefit from its immediate use"**

Insights derived during the development of a consensus open-access UNIMMAP-MMS product specification

With consensus around the UNIMMAP-MMS open-access product specification now achieved, purchasers and manufacturers everywhere can benefit from its immediate use. Apart from its use as described in this paper, large healthcare systems and manufacturers can benefit from the aggregated insights derived during the journey to achieve a consensus product specification – as summarized in **Box 5**.

BOX 5: Key insights derived during the journey to achieve a consensus open-access UNIMMAP-MMS product specification

- When large healthcare systems, especially national health services, have decided to begin to explore a transition from IFA for pregnant women to MMS, there should be vigorous discussion and early planning to consider how to gain access to an affordable, high-quality UNIMMAP-MMS product. A local MMS task force can provide an important forum to examine this issue (along with many others), which represents the first – and critical – rate-limiting step to any transition from IFA to MMS, even for the initial exploration and introduction of MMS. No program can effectively and

efficiently get underway without the UNIMMAP-MMS product or a plan to access the product.

- At the outset of 2020, there are only two or three existing manufacturers of UNIMMAP–MMS globally with the immediate or potential capacity to fulfill orders for UNIMMAP-MMS.
- Many more manufacturers will be required to fulfill the demand for UNIMMAP-MMS. Irrespective of how well qualified a prospective manufacturer is, or where they are based, it generally takes two or more years for a qualified manufacturer to achieve volume production of a product that meets the open-access UNIMMAP-MMS product specification.
- The benchmark price of about US$0.01 per tablet of UNIMMAP-MMS can be achieved when manufacturing capacity reaches 3–5 million, 180-count bottles of UNIMMAP-MMS product production per year. While some cost reduction occurs beyond this volume, an optimal economy of scale appears to be reached, and there is only limited incremental benefit in producing product for beyond 5 million pregnancies per year.
- Many nations may seek to develop or require local manufacturing of UNIMMAP-MMS for domestic needs for a variety of reasons. However, the benchmark price realized by global suppliers will be difficult to replicate by those manufacturing for a single, domestic market, because:
  - few countries actually have a demand for the volume of MMS product needed to achieve economies of scale;
  - most manufacturers do not have the capacity to produce the volume of MMS needed to achieve economies of scale; and
  - most LMIC manufacturers must import MMS ingredients, incurring significant import fees and excise taxes that significantly increase the price of the finished product.
- When any qualified manufacturer is making UNIMMAP-MMS for the first time, it is important for the purchaser to have an independently operated 'verification' program in place to verify manufacturing processes and the quality of the final product before the product is used; and it is prudent to keep the verification program in place over time.
- Where national governments seek to make a transition from IFA supplementation to MMS, and eventually use locally manufactured UNIMMAP-MMS product to satisfy local domestic demand, decision-makers can consider various options for accessing MMS product while developing and implementing a local procurement strategy. See **Box 4** for a road map of options to local manufacturing. The most important aspect of accessing UNIMMAP-MMS for large-scale programs (irrespective of whether the product is obtained through importation or local manufacturing) is for decision-makers to have a sustainable plan for accessing UNIMMAP-MMS. Such a plan is likely to include donated product during an introductory or transition period, but need not (and cannot) be based, exclusively, on long-term access to donated product. Financially sustainable access to UNIMMAP-MMS should not be problematic for most national health services since they already purchase IFA, and the current pricing of UNIMMAP-MMS is on par with that of IFA manufactured to similar international quality standards.
- Where local manufacturing for a domestic market is sought, it is especially important for local manufacturers to use open-access UNIMMAP–MMS Product specification if a national producer seeks to manufacture for export within their region.
- When planning a transition from IFA to MMS, it is important for local regulatory authorities to be involved with other stakeholders within a local MMS task force; and local regulatory bodies can benefit from reviewing the consensus open-access UNIMMAP-MMS product specification early as efforts are undertaken to include UNIMMAP-MMS in the local essential medicines list.
- Using the consensus open-access UNIMMAP-MMS product specification for a product that is to be used in a public health nutrition program provides significant benefits to purchasers and manufacturers irrespective of their location globally.

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References and notes

1 Keats EC, Haider BA, Tam E, Bhutta ZA, Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;3:CD004905.

2 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(11):e1090–e1100.

3 Bourassa, MW, Osendarp SJM, 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. Ann NY Acad Sci. 2019;1444(1):6–21.

4 United Nations Children's Fund, World Health Organization, United Nations University. Composition of a Multi-Micronutrient Supplement to be used in Pilot Programmes among Pregnant Women in Developing Countries. UNICEF, WHO, UNU Workshop Report. 1999. Internet: https://apps.who.int/iris/bitstream/handle/10665/75358/UNICEF-WHO-multi-micronutrients.pdf?sequence=1&isAllowed=y (accessed 3 March 2020).

5 The consensus open-access UNIMMAP–MMS product specification referenced here for download is based upon and adapted, with permission, from the open-access MMS product specification originally created by the Vitamin Angel Alliance and revised for global use by a Technical Consultation of experts convened in Washington, DC, on 11–12 November 2019, and hosted jointly by the New York Academy of Sciences Multiple Micronutrient Supplementation Technical Advisory Group (MMS TAG) and the Micronutrient Forum, with funding from the Bill & Melinda Gates Foundation. Technical Consultation participants included:

- Clayton A Ajello, Vitamin Angel Alliance
- Gisele Atkinson, Council for Responsible Nutrition
- John Atwater, United States Pharmacopeia
- Gilles Bergeron, The New York Academy of Sciences
- Megan Bourassa, The New York Academy of Sciences
- Nita Dalmiya, UNICEF (observer)*
- Jake Jenkins, Kirk Humanitarian (observer)
- Klaus Kraemer, *Sight and Life*
- Rajiv Kshirsagar, UNICEF (remote observer)*
- Jarno de Lange, Vitamin Angel Alliance
- Saskia Osendarp, Micronutrient Forum
- Anthony Palmieri, independent consultant
- Jeff Reingold, Contract Pharmacal Corporation
- Georg Steiger, DSM
- Alison Tumilowicz, Bill & Melinda Gates Foundation (observer)
- Ingrid Walther, Pharma Consulting Walther (Technical Consultation consultant)
- Keith West, Johns Hopkins Bloomberg School of Public Health
- Wolfgang Wiedey, Lomapharm

* Disclaimer: UNICEF's role in the Technical Consultation on the consensus open-access UNIMMAP–MMS product specification was solely as an observer and limited to sharing UNICEF's technical standards/specifications and its process for internal evaluation. Rajiv Kshirsagar participated as a remote observer only for the purpose of delivering a presentation on UNICEF's technical standards and its internal evaluation process. Nita Dalmiya participated in person as an observer. UNICEF does not endorse, or imply endorsement of the content in this publication, or outcomes of this Technical Consultation.

6 Kirk Humanitarian is a 501(c)(3) organization whose mission is to accelerate the availability, access, uptake and use of UNIMMAP–MMS among women at risk of undernutrition during pregnancy to create a healthier and more equitable world.

7 The Vitamin Angel Alliance (DBA Vitamin Angels) is a 501(c)(3) organization that aims to reduce health and economic disparities across the lifespan of individuals living in hard-to-reach populations through effective delivery of evidence-based nutrition interventions. Specifically, Vitamin Angels is a public health nutrition organization that delivers interventions that target the first 1,000 days of life (i.e., from conception to 24 months of age) and children up to five years of age. Vitamin Angels' model is premised on the reality that national health services are unable to reach all eligible beneficiaries, especially those who reside in marginalized or hard-to-reach communities. Through a range of strategies working with multiple stakeholders, Vitamin Angels coordinates with governments and NGOs to effectively and efficiently fill gaps in coverage.

The Role of Donors in Catalyzing Scale-up of Multiple Micronutrient Supplements

A perspective from the Eleanor Crook Foundation

Nicki Connell
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Key messages

- Given the high potential of multiple micronutrient supplements (MMS) to improve maternal and child health, the Eleanor Crook Foundation (ECF) has pledged US$1 million towards advocacy and implementation research activities to effectively implement and scale up MMS programs among pregnant women. This pledge was announced through the Healthy Mothers, Healthy Babies Accelerator as part of the Bill & Melinda Gates Foundation's 2019 Goalkeepers event.
- Three critical factors will determine the success of scaling MMS: a reliable supply of MMS, successful sustainable delivery platforms and demand generation among pregnant women in low- and middle-income country (LMIC) settings. Underpinning all of these factors is policy change at the global and national level, and prioritization of MMS by policymakers.
- ECF intends to strategically invest in three main areas to support MMS scaling: (**1**) research to improve the implementation of MMS delivery at scale in key East African countries with significant governmental interest; (**2**) research focused on generating demand for MMS through creative solutions; and (**3**) country-level advocacy to ensure prioritization of MMS delivery in national guidelines as the antenatal standard of care.

Mainstreaming MMS into ECF's long-range strategy

MMS for pregnant women, which contain 15 essential vitamins and minerals, have been shown to be safe and highly effective in reducing child mortality at 6 months of age by up to 29 percent, reducing low birth weight by up to 19 percent and reducing infants born small for gestational age by up to 8 percent, particularly for anemic mothers.[1,2] In high-income countries, doctors have long recommended that mothers take MMS during pregnancy. In LMICs, however, where the prevalence of maternal anemia and risk of child mortality is high, the World Health Organization (WHO) recommends that pregnant women be given a supplement containing only two nutrients, iron and folic acid (IFA). This double standard for expectant mothers in high-income versus low- and middle-income countries has troubling ethical implications but has long been justified by the significant additional cost of producing MMS in place of IFA. While challenges with delivery and demand remain, most experts agree it is time for LMICs to start shifting from IFA to MMS.[2,4]

> **"Most experts agree it is time for low- and middle-income countries to start shifting from IFA to MMS"**

Thanks to recent efforts by businessman-philanthropist Spencer Kirk of Kirk Humanitarian, working in collaboration with Vitamin Angels and Contract Pharmacal Corporation, MMS is now being produced at scale and at cost parity with IFA.[5] However, a key challenge remains: adherence to IFA supplementation by pregnant women in LMICs is low.[6] Without addressing how IFA is delivered, MMS is likely to suffer from low adherence as well. To tackle this low adherence, global nutrition donors and experts must engage with, and encourage creative thinking from, marketing professionals and those working in behavioral economics. Novel approaches, such as human-centered design focused on consumer insights, could help increase demand for, and adherence to, MMS.

As a US-based philanthropy working to scale up more cost-effective solutions to fight global malnutrition, ECF has committed a minimum of US$1 million in new funding for implementation research and advocacy through the Healthy Mothers, Healthy Babies Accelerator as part of the Bill & Melinda Gates Foundation Goalkeepers 2019.[7] This investment will help LMICs generate the additional evidence and solutions they need to make the switch from IFA to MMS, and to deliver it at scale.

Based on the deeply held conviction that we can, and should, end global malnutrition, the Foundation makes catalytic invest-

While challenges with delivery and demand remain, most experts agree it is time for LMICs to start shifting from IFA to MMS

ments in both on-the-ground research that shows how to end malnutrition and advocacy that can make the case for why. Over the past year, ECF has established its first long-range strategy, setting the Foundation's direction, including its investment strategy, through to 2025. Within this strategy, the Foundation has committed to fund implementation research to identify efficient and effective approaches to scaling promising nutrition interventions, filling what has been identified as a neglected gap in the funding landscape between demonstrating the efficacy of new approaches or interventions and scaling of effective interventions.[8]

"ECF has committed to fund implementation research to identify efficient and effective approaches to scaling promising nutrition interventions"

In addition, the Foundation's strategy is anchored in a commitment that all future ECF research investments will be made following two specific principles. First, funding will be directed towards promoting the adoption and implementation of evidence-based, cost-effective interventions that have a high likelihood of being scalable and sustainable. Second, ECF investments will capitalize on opportunities to bridge or connect larger initiatives, accelerate ongoing processes and partner with scale implementers. Through strategic analysis, it became apparent that a few key interventions not only had evidence behind their potential impact, but also had a great deal of momentum, facilitating an enabling environment for scaling. Given the high impact of intervening as early as possible (i.e., during pregnancy) on child outcomes, MMS was particularly primed for further investment at this critical time.

What does success look like?

Three key factors will determine the success of scaling MMS: a reliable supply of MMS, successful sustainable delivery platforms and generating demand for MMS among pregnant women living in LMIC settings. Underpinning all these factors is advocacy around policy change and prioritization of MMS by policymakers and budget holders. Given the work of Kirk Humanitarian and others in ensuring the supply of an affordable MMS product,[5] ECF intends to invest to improve the efficiency and effectiveness of MMS delivery at scale in key East African countries where there is significant governmental interest in scaling up MMS. This may take the form of implementation research or pilot activities to identify and test delivery platforms and mechanisms. It will also involve country-level advocacy activities to ensure prioritization

of MMS delivery in national guidelines as the antenatal standard of care, and may include global-level advocacy with WHO and other key stakeholders to update the relevant global guidelines on the use of MMS. ECF will also invest to generate demand for MMS among pregnant women once a delivery system and supply is established. This will include identifying the enablers and barriers in the countries of focus in support of increased uptake of MMS, and also researching the most successful ways to increase demand for MMS among pregnant women, through a strong focus on consumer insights, social marketing and social behavior change communication.

"ECF intends to invest to improve the efficiency and effectiveness of MMS delivery at scale in key East African countries"

ECF is one of several donors who are prioritizing the scale-up of MMS as part of the Healthy Mothers, Healthy Babies Accelerator, for which the Micronutrient Forum is a tentpole holder, and which has leveraged nearly US$50 million in financial and in-kind contributions.[7] This Accelerator will reach over 17.5 million pregnant women and their newborns over the next 3 years. This demonstrates a commitment by key stakeholders, including governments, to prioritize this urgently needed intervention to promote the health and wellbeing of both pregnant women and their newborns. Success will be measured by the level of MMS coverage and adherence achieved, and the impact, in terms of lives saved, of the effective use of MMS. Collectively, we have a singular opportunity to improve pregnancy outcomes now.

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References

1 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6–21.

2 Black R, Dewey K. Benefits of supplementation with multiple micronutrients in pregnancy. Ann N Y Acad Sci. 2019;1444(1):3–5.

3 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016.

4 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient

5 Kirk Humanitarian. Version current 31 October 2019. Internet: https://kirkhumanitarian.org/ (accessed 31 October 2019).

6 Garcia-Casal MN, Estevez D, De-Regil LM. Multiple micronutrient supplements in pregnancy: Implementation considerations for integration as part of quality services in routine antenatal care. Objectives, results, and conclusions of the meeting. Matern Child Nutr. 2018;14 (Suppl 5):e12704.

7 Micronutrient Forum Goalkeepers Accelerator. Version current 31 October 2019. Internet: https://micronutrientforum.org/goalkeepers/ (accessed 31 October 2019).

8 Eleanor Crook Foundation. Grantee Guidance Series: Theory of Sustainability and Theory of Scale. Washington DC. Internet: https://static1.squarespace.com/static/551db914e4b0998e40bbd10d/t/5bc518a971c10b9813d5c1e6/1539643577159/ecf-granteeguidance_Oct2018.pdf (accessed 31 October 2019).

Integrating MMS in the Wider Context of Improved Health and Human Capital

A perspective from the Family Larsson-Rosenquist Foundation

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Key messages

- Multiple micronutrient supplementation (MMS) is critical in promoting successful and healthy pregnancies.
- However, its importance does not end with pregnancy; it should be extended throughout the breastfeeding period to ensure the availability of micronutrients to children and mothers, and to maintain the mother's good nutritional status and health for subsequent pregnancies.
- Several critical elements must be integrated to achieve improved mother and child health by the end of the 1,000-day period, and to help develop human capital.
- To successfully support families to promote better mother and child health, it is important to view MMS as integral to the 1,000-day approach – in terms of both policy and the perspective of the ultimate recipient: the mother and family.

Setting the scene for an integrated approach

MMS is an established intervention for promoting successful and healthy pregnancies in women in low-resource settings where nutrition may be absent or of low quantity and quality. Healthy, successful pregnancies strongly influence the optimal development, later life health and intellectual potential of children, as well as the health of mothers.

"Pregnancy is only one segment of a crucial developmental period – the first 1,000 days"

While pregnancy is a crucial developmental window, it is only one segment of a longer developmental period – the first 1,000 days, which greatly determine a child's and the mother's later wellbeing and quality of life, especially if she experiences multiple cycles of pregnancy and breastfeeding, as is common in low- and middle-income countries (LMICs).

The formation of the Developmental Origins of Health and Disease (DOHaD) Society and the 1,000 Days movement are testament to the importance of this developmental window in ultimately determining the human capital that developing societies can draw from:

> *"Research in the field of Developmental Origins of Health and Disease (DOHaD) shows that the environment in which the embryo, fetus and young child grow and develop influences not only life course health and wellbeing but also the risk of later noncommunicable diseases (NCDs). Important aspects of the environment include maternal, fetal and infant malnutrition (including excess or insufficient macro- and micronutrients), toxins (e.g., maternal smoking or environmental chemical exposure), pregnancy in teenagers or older women and psychological or physiological stress."*[1]

> *"Research in the fields of neuroscience, biology and early childhood development provide powerful insights into how nutrition, relationships, and environments in the 1,000 days between a woman's pregnancy and a child's 2nd birthday shape future outcomes."*[2]

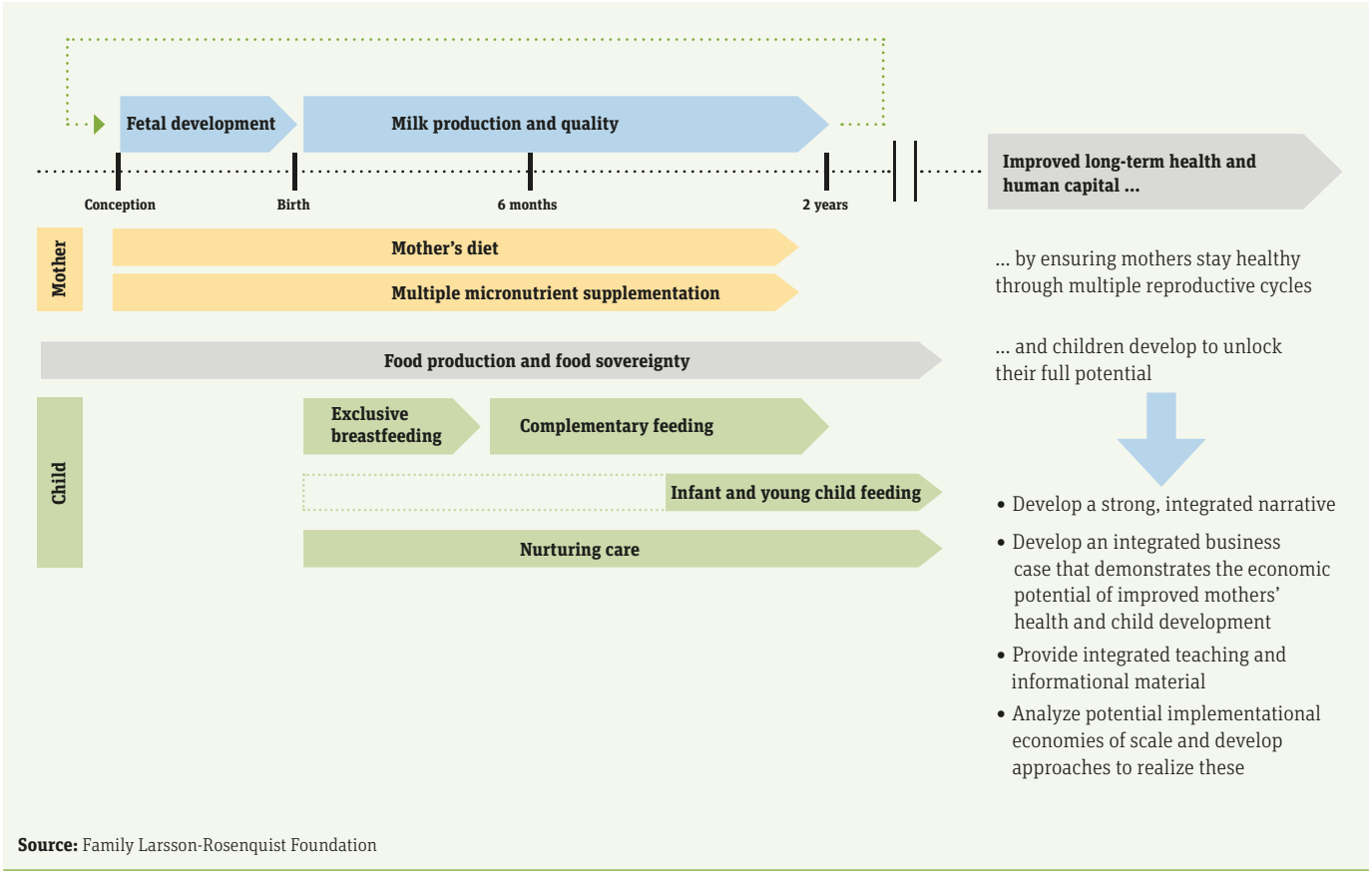
The role MMS plays in achieving improved pregnancy outcomes is further described in other articles in this *Sight and Life* Special Report.

Achieving optimal development in the first 1,000 days

Several critical elements must come together for children and mothers to achieve optimal development in the first 1,000 days (**Figure 1**):

- A mother's nutritional status throughout pregnancy *and* breastfeeding.

FIGURE 1: The first 1,000 days are critical for improving long-term health and the development of human capital



Source: Family Larsson-Rosenquist Foundation

- Exclusive breastfeeding for 6 months and continued breastfeeding until 24 months.
- Adequate and safe complementary feeding introduction when the child turns 6 months.
- Nurturing care of the infant and child.

Of these four elements, three are directly linked to nutrition. Until recently, much of the world's focus has centered on children. However, the health of mothers is also important, as mothers breastfeed their children. In most instances, mothers are the primary caregivers, responsible for complementary feeding and much of the nurturing care of children. Hence, it is necessary to look at a mother's health as well as the child's health.

To date, pregnancy and birth still pose high risks of morbidity and mortality for women. Approximately 99 percent (302,000) of global maternal deaths in 2015 were in developing regions, and roughly 66 percent (201,000) were in sub-Saharan Africa alone. At the country level, over one-third of all maternal deaths worldwide were in Nigeria (19 percent) and India (15 percent) in 2015.[3]

Of the five major complications responsible for 75 percent of this death burden,[4] three are directly linked to the nutritional/micronutrient status of the mother: severe bleeding after childbirth,[5] high blood pressure[6,7] and complications during delivery such as those stemming from premature labor.[8] Thus, MMS is vital to support better child development and also save mothers' lives.

> **"MMS is vital to support better child development and also save mothers' lives"**

When considering breastfeeding, and particularly the mother and child dyad, it is necessary to remember that the period *after* pregnancy and breastfeeding is also the period *before* the next pregnancy. In general, exclusive breastfeeding until 6 months and after that for a further 18 months together with adequate and safe complementary feeding is recommended for the child. In cases where nutritional supplementation is required, it is better given to the mother than the infant to avoid breastfeeding disruptions.[9] While not all micronutrients enrich the mother's breast milk, they still benefit the mother's health – and thus may indirectly affect the child's progress.[10, 11]

Unfortunately, very little research has been done on the impact of MMS on breastfeeding, despite its importance. However, a large study under the aegis of the Bill & Melinda Gates Foundation is

currently further exploring this topic, and landmark results are expected in 2–3 years.[12] Thus, the nutritional status of both mothers and children in the first 1,000 days is an essential foundation for health, neurocognitive development and, ultimately, human capital development.

The case for better integration

To unlock this potential, and given the magnitude of the challenge, we must consider effective, integrated 'delivery' of each element that is critical for success in the first 1,000 days – while also minimizing costs. To date, a nutritionally adequate diet, MMS, breastfeeding, complementary feeding and nurturing care are largely treated as separate at both the policy and intervention levels. FLRF would suggest this is likely not just to drive up costs, but also to generate suboptimal results:

- Policies focused only on single interventions run the risk of missing targeted outcomes, especially when factoring in the impact of the UN Sustainable Development Goals (SDGs), such as enrichment of human capital (Goals 4, 8).
- With respect to implementation, activities connected to each intervention affect women and families during the same period of time – thus, failure to integrate them will likely result in the duplication of effort and loss of potential 'distribution' synergies, which will drive up costs.
- Isolated delivery will most likely result in conflicting or missing information.

An integrated approach that includes education about the importance of this 1,000-day period, and consistent, straightforward guidance that is socioculturally adapted could substantially increase the effectiveness of each individual intervention.

FLRF's contribution to integration

FLRF, the only globally active foundation focused exclusively on breastfeeding and breast milk, has embraced those findings and is actively looking at touchpoints with other areas of the 1,000 days. In 2017, FLRF joined forces with others at the Global Nutrition Summit in Milan, pledging CHF75–100 million in donations over a 5-year period.

This commitment underpins Target 5 of the World Health Assembly (WHA) Global Targets 2025: "Increase the rate of exclusive breastfeeding in the first 6 months up to at least 50%."[13]

Breastfeeding has been designated as one of the interventions with the highest return on investment (World Bank 2017, Investment Framework for Nutrition[14]). As breastfeeding can also have a positive impact on nutrition and behavior, the FLRF commitment underpins additional WHA targets, through reductions in:

- Stunting in children under 5 (Target 1).
- Rates of childhood overweight (Target 4).
- Childhood wasting (Target 6).

In addition to endowing six research centers that are home to nine endowed professorships, FLRF is creating a global knowledge platform focused on breastfeeding and breast milk, with particular emphasis on the information requirements of LMICs (as defined by the World Bank[15]). Finally, FLRF is in the process of creating regional resources in LMICs, and is thus positioned to actively help stakeholders translate policy into execution plans.

It is at this level that the elements critical to success in the first 1,000 days should be integrated. Thus, FLRF sees a clear need to integrate its own work with the work of those in the fields of MMS, mother and infant nutrition, complementary feeding and nurturing care. Both MMS and breastfeeding have a substantial impact on early child development – hence, we advocate the importance for practitioners in those fields to start the conversation and work together more closely. Both MMS and breastfeeding are relevant for women around the time of conception, during pregnancy and in the months following birth. There are considerable synergies in developing a unified message to educate and guide mothers about their dietary needs, nutrition and supplementation, and those of their children, for the overall importance of the mother's health for child development. In time, this message could be broadened to integrate complementary feeding, community farming and nurturing care topics.

Furthermore, there are logistical synergies to be gained from delivering an integrated message about MMS and breastfeeding, as both topics could be covered during antenatal care and breastfeeding counseling sessions. Education material for mothers and train the trainer courses for practitioners could also be integrated to create tools that can be used in both fields.

> **"There are logistical synergies to be gained from delivering an integrated message about MMS and breastfeeding"**

Continuing the dialogue

Despite the huge impact that nutrition and related topics have on the quality of human life and the enrichment of human capital, the global focus on nutrition is diminishing, which is likely to have a negative impact on achieving the 2025 WHA Targets and the UN SDGs. Thus, FLRF believes this realization should provide the impetus to explore how MMS and breastfeeding can be better

integrated to increase their benefits and to create critical weight in the international discussion.

Several activities could support such integration:

- Exchanging insights to understand each field's aspirations, challenges and advantages, and then identifying critical touchpoints where synergies could be realized.
- Building convincing business cases at the country level to assess funding requirements, and demonstrating how closer collaboration among fields could improve the overall returns-to-cost ratio.
- Exploring how messages to mothers and families can be integrated and streamlined. It is imperative that informational and educational materials integrating messages about nutritionally adequate diets, MMS, breastfeeding, complementary feeding and nurturing care should be evidence-based, provide consistent messaging and be easy to digest.

In conclusion, we believe MMS and breastfeeding are complementary interventions, as both are critical to achieving improved mother and child health outcomes in the first 1,000 days. Let's work together to integrate them where possible and sensible, from policy and action planning all the way to delivery. Their integration could optimize their efficacy during the developmental window that is crucial to the lifelong health of the mother and her children, and the enrichment of human capital.

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References

1 International Society for Developmental Origins of Health and Disease. 2015. The Cape Town Manifesto – November 2015. A healthy start builds a bright future. Cape Town: International Society for Developmental Origins of Health and Disease. Internet: https://dohadsoc.org/wp-content/uploads/2015/11/DOHaD-Society-Manifesto-Nov-17-2015.pdf (accessed 28 February 2020).

2 1,000 Days. Why 1,000 Days? Internet: https://thousanddays.org/why-1000-days/ (accessed 28 February 2020).

3 World Health Organization. Trends in Maternal Mortality: 1990 to 2015: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: WHO; 2015. Internet: http://apps.who.int/iris/bitstream/10665/194254/1/9789241565141_eng.pdf?ua=1 (accessed 28 February 2020).

4 Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels JD, et al. Global Causes of Maternal Death: A WHO Systematic Analysis. Lancet Glob Health. 2014;2(6):e323–e333.

5 Khaskheli MN, Baloch S, Sheeba A, Baloch S, Khaskheli FK. Iron deficiency anaemia is still a major killer of pregnant women. Pak J Med Sci. 2016 May-Jun;32(3):630–4.

6 Omotayo MO, Dickin KL, O'Brien KO, Neufeld LM, De Regil LM, Stoltzfus RJ. Calcium Supplementation to Prevent Preeclampsia: Translating Guidelines into Practice in Low-Income Countries. Adv. Nutr. 2016 Mar 15; 7(2):275–8.

7 World Health Organization. WHO Recommendations: Calcium supplementation during pregnancy to reduce the risk of pre-eclampsia. WHO; 2018. Internet: https://www.who.int/elena/titles/calcium_pregnancy/en/ (accessed 28 February 2020).

8 Konje JC, Ladipo OA. Nutrition and obstructed labor. Am J. Clin Nutr. 2000 Jul;72(1 Suppl):291S–297S.

9 UNICEF. Related Maternal Nutrition. Internet: https://www.unicef.org/programme/breastfeeding/related.htm (accessed 28 February 2020).

10 Daniels L, Gibson RS, Diana A, Haszard JJ, Rahmannia S, Luftimas DE, et al.. Micronutrient intakes of lactating mothers and their association with breast milk concentrations and micronutrient adequacy of exclusively breastfed Indonesian infants. Am J Clin Nutr. 2019 Aug 1;110(2):391–400.

11 Corbitt M, Paredes Ruvalcaba N, Fujita M. Variation in breast milk macronutrient contents by maternal anemia and hemoglobin concentration in northern Kenya. Am J Hum Biol. 2019 May;31(3):e23238.

12 Bill & Melinda Gates Foundation. Nutrition: Strategy Overview. Internet: https://www.gatesfoundation.org/what-we-do/global-development/nutrition (accessed 28 February 2020).

13 World Health Organization. Global Nutrition Targets 2025: Policy brief series. WHO reference number: WHO/NMH/NHD/14.2; 2014. Internet: https://www.who.int/nutrition/publications/globaltargets2025_policybrief_overview/en/ (accessed 28 February 2020).

14 Shekar M, Kakietek J, Dayton Eberwein J, Walters D. An Investment Framework for Nutrition: Reaching the Global Targets for Stunting, Anemia, Breastfeeding and Wasting. Directions in Development. Washington, DC: The World Bank; 2017. Internet: https://www.worldbank.org/en/topic/nutrition/publication/an-investment-framework-for-nutrition-reaching-the-global-targets-for-stunting-anemia-breastfeeding-wasting (accessed 28 February 2020).

15 The World Bank. World Bank Country and Lending Groups. Internet: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups (accessed 28 February 2020).

Building Adoptability for Multiple Micronutrient Supplements through Affordability

Facilitating the introduction of MMS by creating an affordable product consistent with international quality standards

Spencer Kirk
Kirk Humanitarian, Salt Lake City, UT, USA

Key messages

- Multiple micronutrient supplements (MMS) have been proven to be more effective than iron and folic acid (IFA) alone for improving the health of pregnant women and pregnancy outcomes in low- and middle-income countries (LMICs).
- In the past two decades, enormous strides have been made to demonstrate that MMS is effective and safe.
- High-quality, USP-verified MMS is now also affordable and available at a price at par with IFA manufactured to a similar international quality. When manufactured at a volume of 3–5 million bottles, and packaged in 180-count bottles, MMS is available at a price of 1 US cent per tablet.
- Demand for MMS is increasing at unprecedented rates as interest in MMS grows. At present, however, manufacturing capacity is insufficient to meet existing – let alone future – demand.
- The time is now to ramp up production of a high-quality MMS product, while focusing on sustainability and the health of the market. Collective action is required to change the status quo and ensure that geography no longer determines accessibility.

Introduction

MMS are now widely known to be a product clinically superior to IFA that can help create a healthier, more equitable world. For this reason, Kirk Humanitarian has worked since 2002 to provide MMS to pregnant women in LMICs through governments and implementing partners, made efforts to drive down the manufacturing costs of MMS in order to create a healthy market, and also supported implementation research.

This is just the beginning, however. In order to increase the availability and adoption of MMS and ensure that MMS is a sustainable intervention, it is crucial to focus on the product pipeline. There are currently few MMS manufacturers: Kirk Humanitarian, via Contract Pharmacal Corp (CPC) USA, is currently the only large-scale producer manufacturing MMS for commercial transactions, and only a handful of other manufacturers are currently equipped to produce MMS.[1]

Over the past 15 years, Kirk Humanitarian has donated MMS product for more than 11 million pregnant women; starting in 2020, we have committed to provide MMS to an additional 15 million women over the next 3 years. We are proud of our reach, but we cannot reach all women alone.

> **"It is an injustice that tens of millions of women do not have access to the highest quality of care"**

It is an injustice that tens of millions of women do not have access to the highest quality of care. Given the evidence and cost parity, collective action is now required to accelerate the transition from IFA to MMS.

Highest quality, lowest cost

In the past two decades, enormous strides have been made to demonstrate that MMS is effective and safe. It is also essential to ensure that MMS can reach women who need it most by making it affordable for public health nutrition programs by reducing costs – without sacrificing efficacy, quality or safety. Kirk Humanitarian, in collaboration with CPC, has established benchmark price and quality standards for MMS – crucially, we have created a reference point, showing that high-quality MMS can be manufactured for the same price as IFA manufactured to the same international quality standard. Using the United Nations

MMS helps protect the health of mothers and babies before they are born

International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation for MMS, we found that, at large volumes, CPC can manufacture MMS at US$2.02 per 180-count bottle (approximately 1 US cent per tablet), while at large volumes, DSM can manufacture MMS at US$2.20 per 180-count bottle. This is the cost of manufacturing the tablet to internationally accepted product specifications, including the cost of United States Pharmacopeia (USP) verification and Halal certification.

"We were able to achieve an affordable, high-quality MMS product by negotiating on both price and volume until we found the optimal price point"

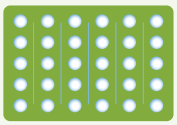
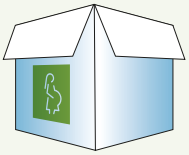
We were able to achieve an affordable, high-quality MMS product packaged in a manner that we believe will incur the lowest cost and environmental impact by negotiating on both price and volume until we found the optimal price point – parity with the price of IFA of a similar international quality – for a product that meets international quality standards. In consultation with experts, we chose to package the MMS product in a 180-count bottle, which is consistent with the recommended regimen for pregnant women.[2] While other options to the 180-count bottle exist that may satisfy the packaging preferences of selected large healthcare systems, these alternative packaging options are still in development and testing, have more significant environmental impact and will not be available for at least 2 years (see **Figure 1** for a comparison of MMS packaging options, costs and environmental impacts). Without findings from implementation research (which is currently being planned or conducted in multiple countries, including in Bangladesh and Indonesia by Johns Hopkins Bloomberg School of Public Health, and in Myanmar by Harvard University) showing that alternative packaging has a positive incremental effect on uptake, adherence and/or antenatal care visits, the most cost-efficient packaging with the smallest environmental impact should be viewed as the logical choice for MMS introduction programs.

"A significant spike in demand can be expected"

The pricing noted here can only be illustrative, as we cannot anticipate the impact of local/regional regulatory and pharmacopoeia differences that will apply as MMS manufacturing

FIGURE 1: Comparison of the features, costs, environmental impacts and availability of MMS by product packaging

UNIMMAP MULTIPLE MICRONUTRIENT SUPPLEMENTS (MMS) FOR PREGNANT WOMEN
PACKAGING OPTIONS, COSTS AND ENVIRONMENTAL IMPACTS

	 180 count	 30 count	 30 count	 Bulk[1]
Packaging features	Child-resistant and tamper-proof HDPE bottle	Child-resistant and tamper-proof HDPE bottle	Child-resistant and tamper-proof Aclar film with foil	No child-resistant or tamper-proof features
Product cost Per tablet [2,3]	1.1 cents Palletization costs an added 0.05 cents per bottle	2 cents Palletization costs an added 0.01 cents per bottle	1.7 cents Palletization costs an added 0.01 cent per card	0.9 cents Repackaging costs are variable
Environmental implication Per million women (180 doses each) [4]	Total waste: 22,900 kg	Total waste: 98,400 kg	Total waste:[5] 38,856 kg	Total waste:[6] variable
Availability	Available now Approved in the USA and commercially available now	Currently not available Each variation to the core UNIMMAP MMS product (180-count bottle) is considered a 'custom' product that will require new stability studies and significant manufacturing preparation to make, which will vary by country regulatory requirements. Variations from currently available units are estimated to take at least 18–24 months until obtainable for commercial use.		

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[1] MMS shipped in bulk requires repackaging before dissemination (business-to-business [B2B] option)
[2] Prices are based on high-volume production; product cost is higher for customers who buy the MOQ (minimum order quantity) of 100,000 bottles
[3] The current MMS Taskforce recommendation for MMS dosing is 180 tablets per pregnancy, beginning as early as possible
[4] Data provided by Contract Pharmacal Corporation (CPC), 2019
[5] It is more difficult and more costly to recycle Aclar film and foil than it is to recycle HDPE (high density polyethylene) bottles
[6] Waste amounts are variable, being contingent on both bulk configuration and required repackaging; excluding repackaging waste, bulk generates the least waste

UNIMMAP multiple micronutrient supplements (MMS) contain 15 vitamins and minerals consistent with antenatal micronutrient standards that women need to help ensure a healthy pregnancy and a healthy baby

capacity is built around the world. Nevertheless, what it illustrates is clear: it is possible to produce MMS – a clinically superior product as compared with IFA – at cost parity with IFA, and manufactured to the same international quality standards. This makes the choice to transition from IFA to MMS an easy one for governments, large healthcare systems, and implementing partners and advisors.

Demand ramps up; supply is needed

As awareness of and interest in MMS increases, we face growing demand from LMICs. MMS advocacy initiatives, including global and regional conferences and initiatives with major presentations devoted to updates on MMS use, raise awareness and lead to increased demand. As global guidelines are expected be updated to an unqualified recommendation of MMS, a significant spike in demand can be expected to ensue. Even in the absence of an unqualified global recommendation for MMS, demand is expected to at least double, and possibly even triple, in the next few years. In 2019, despite record MMS production, only about 5 million pregnant women in LMICs benefited from access to UNIMMAP-formulated MMS, including about 1 million women who received UNIMMAP-MMS originating from UNICEF. To meet the needs of the more than 195 million pregnancies each year in LMICs, at least 35 billion MMS tablets per year will be needed.

As MMS is expected to be part of public health nutrition programs around the world, substantial new manufacturing capacity will need to be added locally and globally. Currently, very few manufacturers have the capacity or know-how to manufacture and sell an MMS product that meets international quality standards. Adding this capacity globally is a complicated task, and assisting even existing qualified manufacturers to produce MMS will take years to accomplish.

The time is now: creating a vigorous market for MMS

To create a sustainable product pipeline for MMS, we must act now to ramp up global production while ensuring that manufacturers can produce high-quality MMS at an affordable price. Efforts are also needed to create a strong global market for MMS based on competition among high-quality manufacturers, and to monitor the supply chain to ensure that quality is maintained, environmental impact is minimized and supplies are readily available as MMS is scaled to national coverage. Finally, there is a need to continue and expand support for implementation and implementation research to improve access for women, inform manufacturing best practices and ensure effective and efficient approaches to scaling MMS use in large health systems.

Kirk Humanitarian is prepared to do its part to accelerate the availability, access, uptake and use of MMS among women at risk of undernutrition during pregnancy, furthering our mission to create a healthier and more equitable world.

Spencer Kirk has more than three decades of leadership experience in the private sector. Before founding Kirk Humanitarian in 2002, he co-founded Megahertz, a laptop modem manufacturing company. He was also CEO of Extra Space Storage until he stepped down in 2016. Spencer Kirk applies his experience in manufacturing, distribution and supply chain management to manufacturing and marketing MMS in LMICs, ensuring access to the highest-quality product at the lowest cost.

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References and notes

1 Manufacturers from which UNICEF has sourced MMS include Lomapharm, Lekapharm and Laboratoria Wolfs.

2 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6–21.

Afterword

Strong Evidence Supports Antenatal Multiple Micronutrient Supplementation

Implementation should be scaled up rapidly while addressing service delivery barriers

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Recognizing the complexity of decisions regarding the deployment of health interventions, many policy-setting bodies, including the World Health Organization (WHO), utilize GRADE (Grading of Recommendations Assessment, Development and Evaluation) frameworks.[1,2] Such systematic and transparent frameworks consider the priority of the health problem, the certainty of the evidence of benefits or harms, and the costs and feasibility of the intervention compared with alternatives. When the evidence regarding antenatal multiple micronutrient supplementation (MMS) in low- and middle-income country (LMIC) settings is considered using such criteria, it is compelling that MMS should be recommended instead of only iron and folic acid (IFA) for supplementation in pregnancy.[3]

Women in LMICs have deficiencies of multiple essential vitamins and minerals (micronutrients) that result in health consequences for pregnant women and their babies.[3] These range from maternal and perinatal mortality to complications throughout the life-course due to births that are premature or affected by fetal growth restriction or both. These are problems that must be accorded high priority and have been in global goals and targets.

As documented in 'The Evidence Base' section of this *Sight and Life* Special Report, the evidence supporting the use of MMS comes from randomized controlled trials in which MMS was compared with IFA.[4,5] It documents overall reductions in the rates of stillbirth and of newborns that are preterm, growth restricted and low birth weight. It also identifies populations that would benefit most from MMS, including those with a high prevalence of anemia, where there is a reduction in fetal and infant deaths.[5] No serious adverse effects were associated with MMS in these trials.[4,5]

This generally high-quality evidence is from Asia and sub-Saharan Africa. The 19 trials, involving more than 141,000 women, were considered to have low risk of bias in the latest systematic review.[4] The extent and quality of the data from multiple locations provide a high overall certainty that there would be substantial benefits in most LMICs today.

> **"Analyses have shown MMS to be very cost effective"**

Cost-effectiveness analyses have compared MMS with IFA supplementation, assuming either moderate or high incremental cost of the product.[6,7] Analyses have found MMS to be very cost-effective in comparison with both IFA supplementation and other interventions.[6–8] Recent data from large purchases of MMS indicate that the cost of the so-called UNIMMAP-MMS formulation of 15 vitamins and minerals has declined rapidly in the past 3 years, and is now virtually the same as that for IFA manufactured to a comparable international quality.[9]

IFA is usually provided during facility-based antenatal care (ANC) visits in LMICs, and provision of MMS instead should be straightforward. While switching the product is desirable, this alone is not enough to achieve the full benefits of MMS. Studies of barriers to the receipt of sufficient IFA supplementation in pregnancy have shown that inadequate ANC services, including limited and poor-quality supplies, and inadequate counseling work against consumption of IFA.[10] While the use of ANC at least once in pregnancy is moderately high in LMICs,[11] care-seeking late in pregnancy and missing some of the multiple visits at which IFA refills are provided contribute to the often-insufficient consumption of IFA before delivery. Reducing these health system barriers is important for improving receipt of MMS, as it would be for IFA supplementation. In addition, community-based platforms can be utilized to improve access, counseling and monitoring of use throughout pregnancy. Switching from IFA supplementation to MMS provides an opportunity in communities to discuss the enhanced health benefits and increase demand for ANC services, care early in pregnancy and MMS adherence. Learnings from early-adopter countries that have made this switch have been docu-

mented in the several case studies in the 'Experiences from the Field' section of this Special Report.

The evidence supporting the use of MMS is strong and applicable to women in most LMICs. Achieving high coverage and adherence in these settings would help achieve health equity, reducing adverse outcomes of pregnancy that have highest rates in disadvantaged populations. Evidence from trials of the benefits of MMS has been building for two decades and is now at the point at which additional trials cannot be scientifically or ethically justified. Implementation of MMS instead of IFA supplementation should begin immediately and be scaled up as rapidly as feasible. Concerns about challenges in service delivery in health-facility ANC and community contacts during pregnancy should not be a reason to delay the use of MMS, which has a significant comparative advantage over IFA supplementation at any level of coverage and adherence. Implementation research is needed to help policymakers understand how to improve uptake and adherence of MMS by pregnant women through behavior change communication strategies. These studies are underway and should help fine-tune training for healthcare providers in the months and years ahead.

Importantly, as health policy adapts to integrate use of MMS into health services, a critical impediment to operationalize MMS policy is the limited availability of a high-quality, low-cost supply of MMS product. An important step to advance the availability of MMS supplies is the creation of a standardized UNIMMAP-MMS product specification for manufacturers and purchasers worldwide. Such a specification is now available and described in the 'Resources for Scale-up' section of this Special Report. The availability of these specifications provides opportunities for national and regional manufacturers, as well as global suppliers.

"The next decade of the 21st century should be focused squarely on a global effort to scale up MMS"

Through the three sections, The Evidence Base, Experiences from the Field and Resources for Scale-Up, this special report leads to the conclusion that there has not been a time in recent decades when so many people agreed on what needs to be done. This consensus must lead to action by governments, donors, civil society and international agencies. The next decade of the 21st century should be focused squarely on a global effort to scale up MMS, while documenting how this is best done and sharing these findings with others. Implementing antenatal MMS would save lives and give babies the healthy start they deserve, no matter where they live.

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References

1 Alonso-Coello P, Schunemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016. doi:10.1136/bmj.i2016.

2 Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ. 2004;328:1490. doi:10.1136/bmj.328.7454.1490.

3 Bourassa MW, Osendarp SJM, 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. Ann N Y Acad Sci. 2019;1444(1):6–21.

4 Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;3:CD004905.

5 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(11):e1090–e1100. DOI:10.1016/S2214-109X(17)30371-6.

6 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.

7 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):1222–9.

8 Black RE, Dewey KG. Benefits of supplementation with multiple micronutrients in pregnancy. Ann N Y Acad Sci. 2019;1444(1):3–5.

9 Engle-Stone R, Kumordzie SK, Meinzen-Dick L, Vosti SA. Cost-Effectiveness of Replacing Iron-Folic Acid with Multiple Micronutrient Supplements: Assessing the costs, impacts and cost-effectiveness in the context of pregnant women in Bangladesh. Published in this *Sight and Life* Special Report, pp. 28–34.

10 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 Suppl 5:e12532.

11 Countdown to 2030 Collaboration. Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health. Lancet. 2018;391(10129):1538–48.

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