Using Implementation Science to Support the Introduction and Scale-up of Multiple Micronutrient Supplementation

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HEALTHY MOTHERS HEALTHY BABIES

Multiple Micronutrient Supplementation in Pregnancy
TECHNICAL ADVISORY GROUP

Micronutrient FORUM

ACRONYMS

ANC	antenatal care
BMGF	Bill & Melinda Gates Foundation
EML	essential medicines list
HCD	human-centered design
HMHB	Healthy Mothers Healthy Babies Consortium
IFA	iron and folic acid
IR	implementation research
IS	implementation science
MEL	monitoring, evaluation, and learning
MMS	multiple micronutrient supplements
MOH	Ministry of Health
PAR	participatory action research
QI	quality improvement
SBCC	social behavior change communication
SQ-LNS	small quantity lipid-based nutrient supplement
TAG	technical advisory group
TIPS	trials of improved practices
UNIMMAP	United Nations International Multiple Micronutrient Antenatal Preparation
UNRWA	United Nations Relief and Works Agency for Palestine Refugees in the Near East
WHO	World Health Organization

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FOREWORD

Multiple micronutrient supplements (MMS) are a daily nutritional supplement of vitamins and minerals specifically formulated for pregnant women to meet the increased micronutrient requirements to support growth and development during pregnancy. Research conducted over the past two decades has provided clear and consistent evidence that MMS are safe and provide additional benefits over iron and folic acid (IFA) supplements in reducing adverse pregnancy outcomes. MMS and IFA are equally effective in preventing anemia.[1–3]

In 2020, the World Health Organization (WHO) released a recommendation that countries adopt MMS during pregnancy within the context of rigorous research, including implementation research (IR) that examines the acceptability, feasibility, sustainability, equity, and cost-effectiveness of MMS implementation.[4] As of mid-2024, the Healthy Mothers Healthy Babies Consortium (HMHB) World Map of MMS Activities shows 23 countries and counting in different phases of MMS introduction and scale-up.

The MMS in Pregnancy Technical Advisory Group (MMS TAG), hosted by the Healthy Mothers Healthy Babies (HMHB) Consortium, is supporting related efforts of its members. The MMS TAG commissioned this document to meet stakeholder demand for more guidance on the use of implementation science (IS), including rigorous IR across the phases of MMS program introduction and scale-up.

This guidance document complements the Framework for Country MMS Scale-up (Framework) that was set forth by a collaboration of donors — Kirk Humanitarian, the Bill & Melinda Gates Foundation (BMGF), the Children's Investment Fund Foundation (CIFF), and the Eleanor Crook Foundation (ECF) — in their May 2024 publication, Healthier Pregnancies and Brighter Futures for Mothers and Babies: A global investment roadmap for multiple micronutrient supplementation. The Framework presents a generalized approach to MMS program introduction that can be adapted and applied by national governments and their partners. Additionally, it identifies key results and high-level actions and activities at each phase of MMS program introduction and scale-up, and champions using IS across the process.

This guidance document complements the Framework by explaining the rationale for using IS, the essential components of IS, and how IS can be applied across the pillars and phases defined in the Framework.

We envision the primary audience for this guidance document to be national-level stakeholders who want to understand more specifically how IS can support efforts to introduce and scale MMS programming. These may include national or subnational MMS TAGs or task force members, government partners, implementing partners, research and academic partners, and/or private sector partners. It may be helpful to work through this guidance as a group.

There is no assumption that every country starting the process and carrying out IS will ultimately decide to introduce and scale MMS programming. We believe, however, that an IS approach will contribute to improved outcomes for all maternal micronutrient supplementation interventions.

– Global MMS TAG, September 2024

INTRODUCTION:

WHY USE IMPLEMENTATION SCIENCE TO SUPPORT MMS INTRODUCTION AND SCALE-UP?

As of 2020, the World Health Organization (WHO) recommends countries adopt multiple micronutrient supplements (MMS) during pregnancy *within the context of rigorous research.*[4]

Both clinical research and implementation research (IR) can meet the WHO definition of "rigorous research" in that they:

- answer well-formulated research questions;
- are guided by a theory or framework; and
- use a study design appropriate to the questions.

Clinical efficacy and effectiveness research has demonstrated that MMS works. Studies across low- and middle-income countries among more than 100,000 pregnant women have shown that MMS, including the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) MMS, are associated with better pregnancy outcomes[1,2] and provide comparable protection against maternal anemia[5] when compared with iron and folic acid (IFA). Effects are even greater among pregnant women with anemia.[1] UNIMMAP MMS contain 15 vitamins and minerals, including iron and folic acid, in doses recommended for pregnant women.

While there is convincing evidence on the efficacy of MMS, there are many unanswered questions about how to secure access to and deliver MMS to pregnant women across different contexts, as well as how to transition from IFA to MMS as a standard of care.

National health systems have experienced similar challenges around implementation of IFA programs, impacting whether pregnant women receive an adequate supply of supplements and consume them daily throughout their pregnancy.

A multi-country analysis shows that across 22 countries, over 81% of pregnant women received IFA tablets — but only 25% and 8% consumed for at least 90 or 180 days, respectively.[5] Common implementation challenges include inconsistent attendance at antenatal care (ANC), breaks in supplement supply chain, poor quality of counseling, and/or low adherence to the supplement.[6]

For MMS programs to improve health outcomes among women and children, solutions to these types of implementation challenges must be identified and implemented. In addition to adapting and strengthening supplement delivery platforms, countries need to address other issues related to introducing a new product into their existing health system, including policy changes, financing, and product manufacturing and/or procurement.

The methods and tools of implementation science (IS) can help identify, address, and resolve many implementation challenges impacting the transition from IFA to MMS. IS is an evidence-based approach for strengthening the introduction and delivery of proven interventions in real world contexts. IS involves both synthesizing and applying existing knowledge about how to improve implementation (e.g., knowledge from IFA implementation) and generating new knowledge about how best to deliver MMS programs across different contexts. IS activities and findings can also support efforts to gain stakeholder consensus around key issues for successful MMS program introduction or scaling in a specific context.

Questions that can be answered by IS include[7]:

- What can be learned from the strategies and systems used for IFA programs?
- What are implementation strategies to improve the distribution and acceptance of MMS among different populations, including the hard-to-reach populations?
- How do contextual factors influence MMS program implementation success or failure? How can these contextual factors be modified to increase chances of success?
- How can implementation strategies that are not working be discontinued?
- What are the costs associated with different implementation strategies?

This guidance document will help national stakeholders identify how to use IS to support their MMS program introduction and scale-up process. The IS approach described in this guidance document can be applied to other nutrition interventions including ongoing IFA distribution, and new interventions such as balanced energy protein for pregnant women and small-quantity lipid-based nutrient supplements (SQ-LNS) for children.

Part 1 of the guidance document provides an overview of IS concepts. Part 2 focuses on how IS supports the different phases of MMS program introduction and scaling. Part 3 highlights IS methods relevant to MMS MMS program introduction and scaling. Throughout the document, we have included examples of how countries have used IS to guide their process.

The appendices include additional resources. Appendix A addresses research ethics approvals for IR studies. Appendix B presents in-depth country case studies that illustrate how IS approaches have been adapted to different settings. Appendix C includes a list of IS resources and tools, many of which are specific to MMS. The online versions of Appendices B and C will be updated by the Healthy Mothers Healthy Babies Consortium (HMHB) as new resources become available.

PART 1:

WHAT IS IMPLEMENTATION SCIENCE?

This guidance document is about taking an IS approach to introduce and scale an MMS program for pregnant women. IS aims to improve the uptake of evidence-based interventions in real world contexts. IS involves synthesizing and applying existing global and contextual knowledge to improve implementation and conducting implementation research (IR) to generate new knowledge. All three sources of knowledge — global, contextual, and IR — are important for MMS introduction and scale-up (Figure 1).

MMS introduction often begins by accessing and applying existing knowledge about how to deliver the intervention. This can be *global knowledge*, from other countries or delivery contexts, or *contextual knowledge*, the practical knowledge and experience of people in the place where the intervention is being considered or implemented. IR generates *new knowledge* about how to effectively deliver an intervention in a specific context.

FIGURE 1: SOURCES OF IMPLEMENTATION SCIENCE KNOWLEDGE

IMPLEMENTATION SCIENCE

GLOBAL KNOWLEDGE

Access and apply global guidelines, evidence-based findings, practical knowledge & experience **from other countries or contexts** facing similar implementation challenges.

EXAMPLES OF HOW THIS IS DONE

- Consult global guidance and frameworks
- Carry out literature or scoping review
- Attend conferences
- Host/participate in peer exchange visits

CONTEXTUAL KNOWLEDGE

Access and apply the practical knowledge & experience of policy makers, implementers, women, community, influencers and others **from within your context**.

EXAMPLES OF HOW THIS IS DONE

- Conduct a bottleneck assessment for IFA and/or ANC
- Map key stakeholders and host consultations
- Review existing relevant policy and program documents
- Analyze trends and equity of IFA coverage
- Use human-centered co-design processes to identify solutions to implementation challenges
- Gather local cost-effectiveness and budget impact analysis data to explore MMS supply scenarios and MMS affordability to government budgets

IMPLEMENTATION RESEARCH (IR)

Carry out a pilot study, demonstration project, or other type of research to generate new knowledge about MMS *implementation outcomes* in your context.

EXAMPLES OF HOW THIS IS DONE

- Carry out formative research about MMS acceptability to pregnant women and/or health providers
- Conduct an IR study to understand whether an MMS program implementation strategy affects implementation outcomes (e.g., coverage, adherence)
- Analyze national surveys to project trends in coverage of IFA vs. MMS across different scaling scenarios

What existing knowledge is relevant?

MMS is a relatively new intervention, but many countries have experience and research related to delivering iron-containing supplements (e.g., IFA). There is also relevant knowledge, experience, and research from health systems interventions with similar characteristics (e.g., adherence to daily HIV treatment, community outreach by community health workers [CHWs] for integrated community case management [iCCM], other interventions delivered during antenatal care [ANC]). This existing knowledge and evidence should be systematically identified and applied to MMS programs.

Existing knowledge about IFA and MMS has been carefully reviewed and synthesized as part of global guidance documents. The Interim Country-level Guidance for Introducing Multiple Micronutrient Supplementation for Pregnant Women can be utilized to start MMS transition and serve as a reference for National MMS distribution guidelines. This and other guidance documents can be found in Appendix C.

COUNTRY EXAMPLES: ACCESSING AND APPLYING MULTIPLE SOURCES OF KNOWLEDGE TO INFORM DECISIONS ABOUT MMS

GLOBAL KNOWLEDGE: HMHB REGIONAL MEETINGS

Cross-country sharing of experiences at regional meetings hosted by the HMHB Consortium in Asia (Jakarta 2022) and Africa (Addis Ababa 2023) has catalyzed interest in and momentum for MMS introduction in several countries. For example, the Kenyan Ministry of Health (MOH) expressed interest in exploring MMS introduction after hearing from peers at the Africa regional meeting. Kenya has launched a national MMS task force and is starting to assess their context. Additionally, Cambodia MOH delegates attending the Asia regional meeting renewed their commitment to conduct IR to improve MMS rollout in their country.

CONTEXTUAL KNOWLEDGE: DESK REVIEW OF LOCAL IMPLEMENTATION EXPERIENCES

MMS stakeholders conducted a thorough desk review of policy documents and peer-reviewed and gray literature about ANC in Indonesia, including barriers and enablers to ANC access, supplementation programs, and previous efforts to improve IFA uptake and adherence. The information was used to 1) identify and prioritize knowledge gaps around implementation that require more rigorous IR; and 2) produce a policy brief for advocacy to the national government.

GLOBAL + CONTEXTUAL KNOWLEDGE: NUTRITION INTERNATIONAL'S COST-BENEFIT TOOL

Nutrition International's MMS Cost-Benefit Tool uses global estimates of the health effects attributed with MMS, as well as cost of IFA and MMS and national population data, to develop country-specific cost benefit models for transitioning from IFA to MMS. Nutrition International has supported multiple countries with context-specific answers to the question 'is antenatal MMS better value for money than IFA?'.

IMPLEMENTATION RESEARCH: SUPPLEMENT DELIVERY STRATEGIES

In Mali, Jhpiego partnered with the Center for Vaccine Development and the Johns Hopkins Bloomberg School of Public Health to evaluate how adherence to and acceptability of antenatal supplements compared across three different delivery strategies: IFA given 30 tablets at a time, MMS given 30 tablets at a time, or MMS given 180 tablets at a time. The IR also evaluated the acceptability of a new MMS counseling package.[8-10]

As the number of countries using IS to guide IFA and MMS implementation increases, so does the potential to access and apply existing knowledge. This underscores the importance of sharing IS knowledge through national, regional, and global MMS networks.

Key features of IS

IS has **five distinguishing features** compared to clinical research:

1. Focus on implementation strategies and implementation outcomes

Implementation strategies are how MMS programs are delivered in real world settings. They include everything from how the product is packaged and how the supply chain functions to the key messages delivered during counseling and how frontline workers are trained and supervised (Table 1).

Implementation outcomes are measures of whether these implementation strategies are successfully delivered. Table 2 defines a set of implementation outcomes that are commonly assessed and provides example questions as they relate to MMS program introduction and scale-up.

Implementation outcomes are not the same as health outcomes. Health outcomes, such as low birth weight, small for gestational age (SGA), preterm, micronutrient status, or maternal hemoglobin are best assessed in efficacy and effectiveness trials. These types of studies use controlled approaches to ensure the supplement is delivered to the participants. They must have an adequate sample size to detect differences between groups in health outcome (Figure 2).

2. Rooted in a specific context or system

IS addresses implementation in specific contexts. There may be multiple MMS implementation contexts in a single country (e.g., urban vs. rural settings, public vs. private delivery systems, higher-income vs. lower-income households, humanitarian/emergency vs. development contexts). Different geographic areas or sub-populations within an individual country may have unique barriers and facilitators to MMS implementation and in turn, require answering different IS questions in each setting.

FIGURE 2: IMPLEMENTATION SCIENCE DIFFERS FROM EFFICACY AND EFFECTIVENESS RESEARCH

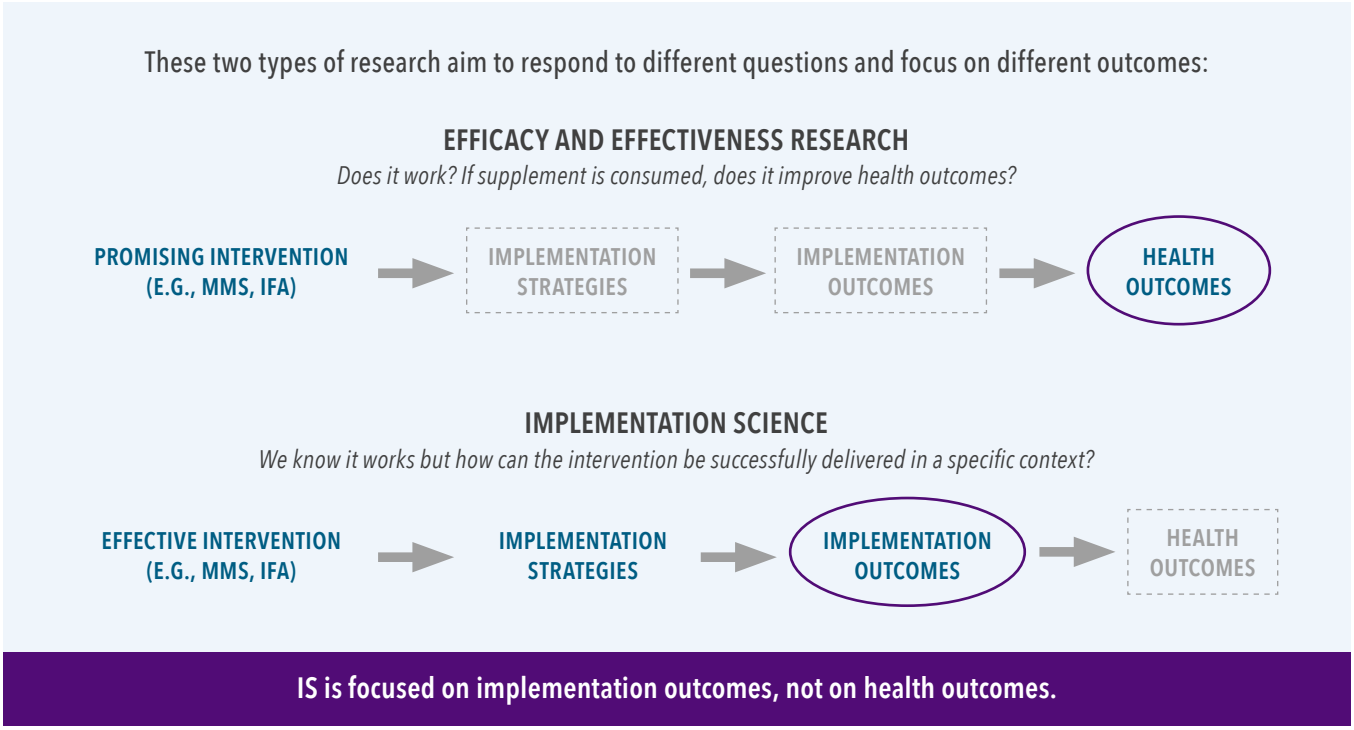

TABLE 1: EXAMPLES OF IMPLEMENTATION STRATEGIES AND IMPLEMENTATION OUTCOMES RELEVANT TO MMS

IMPLEMENTATION STRATEGY	DESCRIPTION
MODES OF TRAINING AND/OR SUPERVISION FOR FRONTLINE WORKERS	Compare different training mechanisms (e.g., full-day in-person training, hybrid training, train the trainer). Relevant implementation outcomes may include acceptability, feasibility, and cost.
QUALITY MONITORING SYSTEMS	Compare different approaches for monitoring quality of program implementation (e.g., comparing checklist, supervisor dialogue and beneficiary survey approaches for monitoring quality of adherence counseling provided by frontline workers). Relevant implementation outcomes may include acceptability and feasibility of the supervision mechanism from both the supervisee and supervisor perspective.
DISTRIBUTION POINTS	Compare different MMS program delivery platforms (e.g., health care facility, community health workers, market-based). Relevant implementation outcomes may include uptake, acceptability, feasibility, and equity.
PACKAGING	Compare different packaging options (e.g., blister packs, 30-count bottles, 180-count bottles). Relevant implementation outcomes may include acceptability of packaging to women and/or to the facility staff, MMS uptake and adherence by women, and cost.
SOCIAL BEHAVIOR CHANGE COMMUNICATION (SBCC) STRATEGY	Compare different SBCC strategies (e.g., community events, engaging family members through community groups, mass media) or contextualized messaging options. Relevant implementation outcomes may include acceptability of SBCC strategies to the women and/or the frontline workers and SBCC strategy reach.
FINANCING OPTIONS	Assess options for financing MMS program such as tax generation, charitable donations, and individual out-of-pocket expenses. Relevant implementation outcomes may include acceptability, feasibility, and sustainability of the financing options.
MONITORING & EVALUATION SYSTEM	Assess tools that support data use (e.g., quarterly review meetings, online dashboard with key performance indicators, etc.). Relevant implementation outcomes may include acceptability, fidelity, and feasibility of each approach.
PROCUREMENT CHANNELS	Compare options for MMS procurement (e.g., local manufacturing, bulk purchase with local repackaging, purchase final product). Relevant implementation outcomes may include feasibility, cost, and sustainability.

TABLE 2: IMPLEMENTATION OUTCOMES COMMONLY ASSESSED AS PART OF IS FOR MMS INTRODUCTION AND SCALE-UP

IMPLEMENTATION OUTCOME *(related terms)*	DEFINITION WITHIN CONTEXT OF MMS	EXAMPLES OF RELEVANT QUESTIONS
APPROPRIATENESS *(perceived fit, compatibility, suitability)*	The perception that the MMS program* is suitable for a given setting (precursor to feasibility)	What are the documented micronutrient deficiencies in a population and what is the prevalence of poor pregnancy outcomes? Would MMS address these nutrition problems better than IFA? Is there an established process for the MMS UNIMMAP formula to be approved by the government so that it can be used as a standard of care?
ACCEPTABILITY *(satisfaction, willingness)*	The perception that the MMS program* is agreeable	How do pregnant women perceive MMS in terms of its sensory attributes (e.g., taste) or its side effects? How do pregnant women, influential family members, and/or health care providers perceive the implementation strategies being utilized? What product packaging and/marketing strategies can be used to enhance uptake and acceptability among pregnant women from diverse socioeconomic contexts?

(Table 2 continues on the next page)

FEASIBILITY *(actual fit, practicability)*	The extent to which the MMS program* can be successfully implemented within a given agency or setting	What changes/ improvements are needed for existing IFA delivery platforms if they will be used for MMS moving forward? How can high-quality MMS counseling be delivered within the allotted time for a standard ANC visit? Are each of the commodities needed to deliver the MMS program available and do they all have potential for a sustained supply over time? (e.g., pills, counseling materials, etc.) What proportion of women are willing to pay for MMS through market-based distribution channels?
IMPLEMENTATION COST *(marginal cost, incremental cost)*	Specifying the financial and/or non-financial costs associated with executing the MMS program* (e.g., money, time, human resources)	Is switching from IFA to MMS affordable? How much will a transition from IFA to MMS impact the government budget? What new investments need to be made by the government to transition from IFA to MMS (e.g., training healthcare workers, developing new guidelines, new behavior change materials, etc.)?
COVERAGE *(reach, adoption)*	The extent to which the MMS program* is delivered to / received by all eligible women	What % of women in X district received at least 180 MMS tablets across the course of their most recent pregnancy? How does the rate of MMS scale-up vary by district? What % of the target population continues to receive IFA? What % of the target population is not receiving any iron-containing supplement?
FIDELITY	The extent to which the MMS program* is delivered as intended to eligible women	Do midwives or other frontline workers follow MMS implementation guidelines? Do midwives consistently distribute/prescribe MMS instead of IFA? Do health system staff follow supply chain guidelines for forecasting, ordering, and distributing MMS program commodities?
EQUITY	The extent to which the MMS program* is accessible to all segments of the target population (socioeconomic status, geography, ethnicity, emergency setting, etc.)	How does the quality of MMS counseling differ across women in public vs. private facilities? How does coverage of the MMS program differ across women in rural, urban poor, other urban, and hard-to-reach populations?
ADHERENCE *(uptake, compliance)*	The extent to which the MMS program* is taken up by eligible women as directed (e.g., one pill daily)	What proportion of women consume MMS at the recommended dosage across their pregnancy? What proportion of women initiate MMS prior to 20 weeks of gestation?
UNINTENDED CONSEQUENCES	The extent to which introduction of the MMS program* affects other aspects of ANC delivery systems	How can MMS be integrated within the context of ongoing health systems strengthening efforts for ANC services? How does switching from IFA to MMS impact the supply chain at national, regional, and facility levels? How do supply systems adapt to including two different iron-containing commodities: iron or IFA for anemia treatment and MMS for prevention?
PENETRATION *(systems integration)*	The integration of MMS program* within ANC or other delivery system	What % of facilities providing ANC have made the switch from IFA to MMS? What is the trend in overall attendance at ANC and/or number of ANC contact points before, during, and after the IFA to MMS transition?
SCALABILITY	The potential for expanding the reach of MMS program* within a certain geography or sub-population	Can the intervention be replicated across new areas in the country or region? What are the potential barriers or challenges in expanded areas?
SUSTAINABILITY *(maintenance, durability, institutionalization)*	The extent to which MMS program* is maintained or institutionalized within ANC or a community delivery system's ongoing, stable operation	After X years of MMS implementation, what % of women are receiving at least 180 days of MMS? After X years of MMS implementation, what is the quality of counseling provided by frontline workers? After X years of implementation, are government annual plans and budget allocations adequate to maintain MMS within ANC services?

*MMS program refers to the MMS product and/or any of the implementation strategies to support MMS delivery

3. Fit to the phase of program design and implementation

IS will answer different questions and use different methods depending on the phase of MMS introduction or scale-up. For example, formative research and other baseline assessments during early phases of the introduction process ensure that the intervention package design is appropriate and feasible for the context. Later phases focus on refining the implementation strategies to be scalable and sustainable. Part 2 of this guidance document presents more about the phases of MMS introduction and scale-up.

4. Actively engages stakeholders

Stakeholder ownership and engagement are critical components of IS. They should begin as early in the process as possible and continue throughout all phases of MMS introduction and scale-up. A national MMS Technical Advisory Group (MMS TAG) can help to shape the IS agenda and oversee a country's IS activities. A TAG can also disseminate and promote uptake of IS findings. It is also essential to involve subnational and community-level implementation stakeholders in the TAG.

5. Involves iteration

IS approaches are iterative. They involve repeated cycles of implementation, reflection about what is being learned, and refinement based on that learning. This requires flexibility, as new information may prompt the need to re-engage and align MMS stakeholders around proposed changes. Sufficient time and financial resources must be included in work plans and budgets to allow for iteration.

RELATED TERMS:

Adaptive, dynamic, responsive, non-linear, evolving, continuous course correction, continuous feedback, loopback response, progressive refinement, feedback-driven development, adaptive implementation, Plan-Do-Study-Act (PDSA), Assessment, Analysis, Action (Triple A)

COUNTRY EXAMPLE: ITERATION IN INDONESIA

In Indonesia, a consortium from Universitas Indonesia, Universitas Airlangga, Universitas Hasanuddin, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins Center for Communications Programs, and Vitamin Angel Alliance used a human-centered design (HCD) approach called "design thinking" to design and test an SBCC strategy to improve MMS adherence. Design thinking is a methodology that uses multiple iterative stages of prototype testing and refinement. The process started with several months of formative research to identify adherence challenges followed by a three-day co-design workshop with pregnant women, midwives, and district health officials. During the facilitated workshop, participants identified potential SBCC solutions for challenges identified in the formative research. The study team produced simple, "low-fidelity" prototypes of several of the strategies identified by the group. These prototypes were refined across multiple cycles of testing and subsequent adaptation with pregnant women and their families, midwives and community health workers, and district health officials. The final strategy strengthens provider interpersonal communication skills and leverages Indonesia's strong oral culture through storytelling and song-based messaging. Indonesia is now conducting a new round of IR to evaluate implementation of this SBCC component within the full ANC system.[11-13]

PART 2:

APPLYING IMPLEMENTATION SCIENCE TO SUPPORT MMS INTRODUCTION AND SCALE-UP

The Framework for Country MMS Scale-up (Framework) describes the process of MMS introduction and scale-up as it relates to four pillars — policy/regulatory, financing, quality product, and delivery channels. Each pillar has its own strategic objective, or output. More information on the Framework can be found in Healthier Pregnancies and Brighter Futures for Mothers and Babies: A global investment roadmap for multiple micronutrient supplementation. Key activities needed to achieve objectives differ by pillar and phase. Phase I focuses on building an enabling environment, Phase II on designing and testing implementation strategies, and Phase III on scaling and maintenance. Stakeholder coordination and monitoring, evaluation, and learning (MEL) activities cut across all three phases.

FIGURE 3: FRAMEWORK FOR COUNTRY MMS PROGRAM SCALE-UP

PILLARS	I. BUILDING AN ENABLING ENVIRONMENT »	II. DESIGN & TEST IMPLEMENTATION STRATEGIES »	III. SCALING & MAINTENANCE »	STRATEGIC OBJECTIVES »	OUTCOMES
POLICY/ REGULATORY	» Landscaping & analysis » Stakeholder mapping & engagement » Advocacy	» Advocacy » Policy & guideline development » Roadmap	» Policies & guidelines adoption » Operationalize Roadmap	**Product is included in relevant policies & instruments at all levels of government**	REACH COVERAGE
FINANCING	» Cost-effectiveness analysis	» Forecasting » Financing strategy	» Demand planning » Finance mechanisms » Market shaping	**Sufficient funding committed by governments & donors for procurement & delivery of product**	»
QUALITY PRODUCT	» Supply readiness assessment	» Manufacturing support » Supply chain strengthening	» Cost-effective procurement coordination » Monitor & address supply chain/ distribution/stock outs	**Sufficient volumes of quality product are manufactured, available & procured**	IMPROVED MATERNAL NUTRITION & BIRTH OUTCOMES
DELIVERY CHANNELS	» Delivery platform(s) assessment » Exploratory distribution of Product	» Demonstration projects » System strengthening	» National rollout » Expansion of delivery channels	**Product is available & accessible & pregnant women receive product during ANC & use as recommended**	
	COORDINATION AND MONITORING, EVALUATION, AND LEARNING				

Early on, it is important to start promoting awareness of MMS and the evidence of its health benefits relative to IFA among key decision-makers and policymakers. The stakeholders who will be involved in coordination and oversight of the process should be organized into an MMS TAG or similar structure. They should be sensitized and reach consensus around using an IS approach. High-level coordination by an MMS TAG can ensure that the most important IS questions and activities are prioritized for the national or subnational context and help avoid duplication of efforts across different partners. Relevant national and subnational stakeholders should be engaged at key moments to raise awareness, review evidence, build consensus, make decisions, and plan next steps.

Figure 4 summarizes the purpose of IS activities by phase and the relative contribution of the three different sources of IS knowledge in each phase.

FIGURE 4: PURPOSE OF IS ACTIVITIES ACROSS PHASES

	I. BUILDING AN ENABLING ENVIRONMENT	II. DESIGN & TEST IMPLEMENTATION STRATEGIES	III. SCALING & MAINTENANCE
POLICY/ REGULATORY FINANCING QUALITY PRODUCT DELIVERY CHANNELS	Take stock of what is known about the implementation context and provide opportunities for dialogue and consensus building among key stakeholders. Identify and prioritize questions about implementation strategies to test in the next phase.	Synthesize new and existing knowledge to inform design and testing of implementation strategies. Pilot test implementation strategies, adapting and improving as appropriate	Routinely monitor implementation and changes in context. Course correct implementation strategies, using existing knowledge and IR as required.
SOURCES OF IMPLEMENTATION SCIENCE KNOWLEDGE	Primary Source = ● ⬢ Secondary Source = ■	Primary Source = ⬢ ■ Secondary Source = ●	Primary Source = ⬢ ■ Secondary Source = ●

● GLOBAL KNOWLEDGE ⬢ CONTEXTUAL KNOWLEDGE ■ IMPLEMENTATION RESEARCH (IR)

A country will not necessarily need to complete every activity in the Framework or approach activities in the same way as other contexts. The amount of time and resources required to carry out activities will vary by context. For example, in the policy pillar, some countries have mature regulatory bodies with clear regulatory development processes, while other countries have limited existing regulatory infrastructure. Different timelines and resources will be needed to carry out an assessment, draft policy content, and design and implement a regulatory roadmap in each of these contexts. We highlight context-specific timelines in country examples featured in Appendix B.

Phase I assessments are particularly important to avoid ungrounded assumptions. For example, even if a country has local production of IFA, it does not necessarily mean that local manufacturing of MMS is feasible or cost-effective. A supply context assessment and cost estimates are needed to inform this decision.

Another important factor that varies by context is the level of consensus required among MMS stakeholders to advance through the three phases. In some countries, stakeholder engagement will extend timelines by a considerable amount. Still, this time investment is essential to the overall success of the process.

Below we briefly describe the focus and aims of each phase of the Framework and present a summary table with questions and issues that can be pursued with IS for each pillar (policy/regulatory, financing, quality product, delivery channels).

PHASE I: BUILDING AN ENABLING ENVIRONMENT

IS methods and tools can be used to take stock of the implementation context and identify barriers and opportunities to consider when designing the MMS program delivery strategies and advancing the policy/regulatory, financing, and quality product pillars. Tools such as desk reviews, landscape analyses, and consensus-building workshops help to harness existing global and contextual knowledge. Table 3 provides a sample of guiding questions and issues that can be explored as part of Phase I activities (Figure 3).

At the end of Phase I, stakeholders should reach consensus around whether to continue to explore MMS introduction and identify and prioritize IS research questions to answer in the next phase. Some countries may decide not to pursue MMS introduction but can continue to use IS to design and test ways to strengthen existing IFA implementation strategies.


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TABLE 3: GUIDING QUESTIONS FOR BUILDING AN ENABLING ENVIRONMENT

PILLARS	GUIDING QUESTIONS	SPECIFIC ISSUES TO EXPLORE
POLICY/ REGULATORY 	» What are the existing policies and regulations for micronutrient supplementation during pregnancy? » Who are key stakeholders who influence these policies and regulations? » What advocacy efforts are needed with key influencers to inform and support a policy change?	» Health and nutrition burden among pregnant women in the country » Current policy specifications regarding the type, quantity, timing, and mechanism for maternal nutrition service delivery » Existing regulations around procurement and distribution for nutritional supplements including their classification (e.g., medicine, supplement, or food) » Identify individuals and institutions who are key policy and regulatory influencers – understand their perspectives, questions, and concerns regarding MMS
FINANCING 	» What is the cost-effectiveness, cost-benefit, and affordability of replacing IFA for pregnant women with MMS? » What are the costs associated with transition/initial scaling of MMS? » What are potential financing mechanisms for MMS?	» Number of disability-adjusted life years (DALYs) & additional preventable child deaths that could be averted by transitioning from IFA to MMS » Additional costs to replace IFA with MMS within the existing platform (training, supply chain, demand generation, regulatory, change of guidelines, etc.) » Budget impact analysis » How IFA and other maternal nutrition interventions are currently being financed; alternative financing mechanisms used in the context
QUALITY PRODUCT 	» What is the supply system for the existing supplementation program for pregnant women and how well is it functioning? » What are the supply needs for MMS in terms of quantity and product specifications? » What are the options for obtaining MMS in the near term vs. the future (e.g., capacity for local manufacturing, importation, or a combination of both)? » What systems will need to be adjusted to accommodate a new MMS product (e.g., budgeting, regulatory, procurement, and distribution systems)?	» Established MMS standards and specification » Current supplement procurement processes » Sufficiency and quality of the current supplements for pregnant women » Number of pregnant women in the country that would need to receive MMS » Quality standards and current/potential systems for monitoring quality » Government packaging and labeling requirements » Identification of the universe of potential manufacturers or importers – local or global » Local manufacturing capacity to produce quality MMS at volumes needed to achieve manufacturing efficiency
DELIVERY CHANNELS 	» What are the existing delivery platforms for supplementation during pregnancy and how well are they functioning? » How might existing strategies be strengthened or enhanced? » What alternative implementation strategies could be explored in this context?	» Frequency, timing, cost, and quality of ANC services provided » Description of other platforms delivering supplements to pregnant women (e.g., markets) » Learning from other similar interventions that have been implemented well in the context » Resiliency and flexibility of delivery platforms in response to shocks (e.g., evidence from COVID, natural disasters, etc.) » Barriers and facilitators affecting uptake and adherence of supplements provided during pregnancy

COUNTRY EXAMPLES: USING CONTEXTUAL KNOWLEDGE TO BUILD THE ENABLING ENVIRONMENT IN CAMBODIA, VIETNAM, TANZANIA, AND INDONESIA

Stakeholders in Cambodia and Vietnam conducted comprehensive landscape analyses to better understand their respective contexts for introducing MMS and strengthening overall ANC services. Each country carried out 1) a comprehensive desk review of available information on nutritional status and current maternal nutrition and ANC policies and programs; 2) key informant interviews to supplement desk review findings; 3) consultative meetings with government and supply stakeholders; and 4) a consensus-building workshop with key MMS stakeholders. A landscape analysis report was shared in advance of the consensus-building workshop through which stakeholders agreed to advance MMS introduction and identified priority IR questions. To learn more, visit Sight and Life's MMS 2.0 report.[14]

In Tanzania, cost-benefit data for the transition from IFA to MMS were generated using the Nutrition International MMS Cost-Benefit Tool and shared with the Government of Tanzania to encourage them to explore MMS introduction. The data showed clearly that MMS was "good value for money" and this evidence was identified as a "tipping point" for the government's agreement to move forward with MMS. To learn more, visit Nutrition International's policy brief.

In Indonesia, national leadership called for development of local manufacturing of UNIMMAP MMS while procuring imported MMS until local production infrastructure was established. They conducted a detailed supply context assessment to identify gaps in local manufacturing capacity, shortlist local manufacturers for capacity-building, test whether local manufacturing could achieve pricing and quality standards and develop plans for production and future quality assurance. The findings are being used to develop a five-year roadmap for transitioning from donated products to locally manufactured products.

PHASE II: DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

The design and test phase is when implementation strategies (Table 1) are identified, created, tested, and refined in an iterative manner. Implementation strategies will be different for each of the four pillars (policy/regulatory, financing, quality product, delivery channels), but all should be grounded in context-specific evidence and contribute to their respective strategic objectives.

Phase II will often involve development of new knowledge using rigorous IR. However, not every MMS implementation strategy needs to be supported with IR; global and contextual knowledge can also guide design decisions. For example, policy changes may not require designing and testing prior to adoption; rather, they can benefit from applying global and contextual knowledge about similar policy changes.

In many contexts, MMS are being introduced into an existing ANC system, so it is important that the feasibility of integration into and strengthening of the existing services are prioritized as implementation outcomes during this phase.

It is important to identify and address the context-specific barriers that have historically affected low coverage and adherence to IFA supplementation (e.g., supply chain issues, healthcare system constraints, socio-cultural factors, individual-level challenges). In some contexts, there are well-performing IFA implementation strategies that can be transitioned to MMS with limited adaptation.

While the most common Phase II IS questions relate to quality product and delivery channels, IS can also inform policy/regulatory and financing. Table 4 provides a sample of guiding questions and issues that can be explored to inform Phase II activities specified in the Framework (Figure 3).

By the end of Phase II, a set of implementation strategies that are supported by existing evidence and/or tested through IR are combined into an MMS program. At this point, the policy, financing, and product infrastructure identified in the Framework should be in place and ready to support scaling.

TABLE 4: GUIDING QUESTIONS FOR DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

PILLARS	GUIDING QUESTIONS	SPECIFIC ISSUES TO EXPLORE
POLICY/ REGULATORY 	» How might policies/regulations and their supporting infrastructure be changed to support implementation of MMS?	» Content revisions for existing national policies or guidance documents to support utilization of MMS » Identify relevant processes and timing of cycles/windows of opportunity to revise policy and guideline » Regulatory changes required to ensure MMS can be purchased using the national budget » Design and adoption of national specification and standard for MMS
FINANCING 	» Which steps need to be taken to ensure that MMS are included in the existing budget? » What financing is needed for the MMS program? » What financing mechanisms should be pursued?	» Cost of procuring MMS locally versus globally » Budget required for delivering MMS program » Process for securing budget for MMS program » Potential MMS program financing mechanisms for short- and long-term
QUALITY PRODUCT 	» Where will a stable supply of quality MMS be obtained in immediate vs. longer term?	» Actionable plans for transition from procuring IFA to MMS » Practical assessment of local manufacturing capacity in immediate vs longer term including whether and when local manufacturers could meet required quality and quantity; identify how to pre-qualify potential manufacturers » Process and timeline for importing MMS, including what is needed, who is responsible for getting MMS into the delivery system, and importation costs » Integration of MMS quality testing into existing or new systems
DELIVERY CHANNELS 	» What implementation strategies contribute to improved/high levels of ANC and MMS uptake, adherence, and acceptability? » What implementation strategies are cost-effective, feasible, and able to be delivered with high fidelity?	» Acceptability of implementation strategies and/or overall MMS program to pregnant women or other influential people (e.g., health care providers, family members, community leaders) » Appropriateness and feasibility of implementation strategies and/or overall MMS program for the existing delivery system (e.g., ANC, community-level distribution) » Integration of MMS into national information systems; quality improvement for routine data collection » Impact of implementation strategies and/or overall MMS program on initial uptake of MMS and daily MMS adherence » Unintended consequences of implementation strategies and/or overall MMS program for women and/or delivery systems » Fidelity of implementation strategy delivery to plan » How to make iterative improvements to the implementation strategies and/or overall MMS program

PHASE III: SCALING AND MAINTENANCE

The scale and maintain phase is when the refined MMS program is fully integrated into the delivery system and rolled out across target populations until it reaches scale. Sustaining implementation outcomes of fidelity, coverage, program quality, and equity over time can be a challenge, especially as the implementation context inevitably changes.

Monitoring data from national health management information systems (HMIS/DHIS-2), logistics monitoring systems, and other routinely collected sources including household surveys, can be used to identify geographic areas or sub-populations that are facing implementation bottlenecks. For example, disruptions in the MMS supply can be identified using supply chain data. The routine information systems may have data quality issues that should be accounted for when using data. IS can inform implementation strategies to improve routine data quality.

It is also important to monitor contextual factors such as acute shocks (e.g., conflict, natural disasters, climate events) and changes in the broader implementation environment (e.g., introduction of new programs such a large-scale food fortification that target the same health outcomes, health worker attrition due to migration) as these will influence implementation.

When implementation challenges or contextual changes are identified, IS methods and tools can be used for course correction. Contextual knowledge can be mobilized through a bottleneck assessment and applied to fix the systems and as required, IR can be used to test program adaptations.

During Phase III, countries have reached the pillar-specific strategic objectives. However, in practice, monitoring, reflection and course corrections will continue for as long as the intervention is being implemented. Table 5 provides a sample of guiding questions and issues that can be explored to inform Phase III activities specified in the Framework (Figure 3).

TABLE 5: GUIDING QUESTIONS FOR SCALING AND MAINTENANCE

PILLARS	GUIDING QUESTIONS	SPECIFIC ISSUES TO EXPLORE
POLICY/ REGULATORY 	» Are policies and regulations implemented to ensure effective implementation of MMS at scale?	» Inclusion of MMS in all necessary policies and regulations in a way that optimizes MMS implementation » Continuous review/adaptation of policies and regulations to further strengthen the platforms through which MMS are being implemented
FINANCING 	» Is the existing financing mechanism supporting effective implementation of MMS at scale?	» Sufficiency of funding for MMS procurement » Sufficiency of funding to support the platforms through which MMS program is being implemented » As funding landscape changes, new or existing funding is leveraged to support MMS program » Willingness of beneficiaries to pay for MMS
QUALITY PRODUCT 	» Is the existing procurement strategy supporting sufficient supply of MMS for scale?	» MMS being delivered to pregnant women meets all quality standards » MMS are available and accessible in a sufficient quantity to meet the demand » As MMS production options change, procurement options are continuously assessed to ensure optimal product availability » Monitoring system functioning continuously to identify disruptions in MMS supply and facilitate course corrections
DELIVERY CHANNELS 	» What other implementation strategies and/or adaptations to the existing implementation strategies need to be made to support high uptake and adherence to MMS at scale?	» Consistent and sufficient MMS availability at distribution points » Natural adaptations and intentional adjustments to strengthen the implementation strategies are identified, implemented, and documented » As the delivery platforms and existing systems change, opportunities to test new or better implementation strategies are identified » Monitoring of MMS implementation is embedded within the existing health information system; data quality challenges are being addressed

COUNTRY EXAMPLES: SCALE UP AND MAINTENANCE IN BANGLADESH AND INDONESIA

The **Bangladesh Ministry of Health in partnership with UNICEF and GAIN** successfully implemented and is engaged in scaling a cost-recovering market-based strategy for MMS delivery to 62 districts across the country. They worked primarily through the Social Marketing Company (SMC), which runs a network of pharmacies to reach rural and urban areas. The model was designed using a series of consumer insight and marketing studies. Pharmacies and community health workers sell Full Care, a UNIMMAP-recommended MMS formulation to pregnant women. The fee covers the cost to locally produce and distribute the MMS through a network of 40,000+ pharmacies. icddr,b uses monitoring data to continuously track adherence including adverse side effects, coverage, and acceptability of MMS among pregnant women. They are exploring how MMS can be integrated with other maternal and child nutrition services offered by social marketing companies.

In 2024, the **Indonesia Ministry of Health (MOH), with support from the Indonesian MMS TAG and Vitamin Angel Alliance**, plans to launch MMS as a national policy to replace IFA. The country will also initiate a product registration process for local manufacturers of MMS. The initial transition to MMS will encompass 11 provinces and 201 districts, with full implementation reaching 4.8 million pregnancies across all 38 provinces in 2025/2026, depending on the availability of locally produced MMS. While the initial MMS product for the first three years will be supported by donors such as Kirk Humanitarian, the government will begin procuring locally produced MMS from the second year onward. Key MOH-approved documents with scale-up plans include a Standard Formulation for UNIMMAP MMS, language for a national policy for MMS scale-up, an MMS transition plan, and Technical Guidelines for Implementing MMS.


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PART 3:

HOW TO DEVELOP A RIGOROUS IMPLEMENTATION SCIENCE PLAN

Revisiting the key sources of knowledge shown in Figure 1: In this document we refer to IS as the broader process and IR as one type of activity that falls under an IS approach. In some contexts, IR activities may be referred to as a pilot study or demonstration project.

There are many decisions to be made when designing an IS protocol or plan. This section takes key concepts from the WHO IR guidance documents (WHO/TDR Implementation Research Toolkit and IR Practical Guide) and provides more tailored explanations and examples relevant to the MMS introduction and scale-up process.

Depending on the backgrounds of the team members involved, it may also be necessary to consult experts from universities, research firms, or other technical assistance providers. Readers are encouraged to access and use other resources in Appendix C alongside this guidance document.

A rigorous IS plan should 1) answer well-formulated research questions; 2) be guided by a theory or framework; and 3) use a study design appropriate to the questions. It should also undergo ethical review, when appropriate. We discuss each of these concepts in more depth.

FRAME AND PRIORITIZE IMPLEMENTATION QUESTIONS

IS is grounded in questions about real-world implementation challenges. IS questions should identify 1) what is or is not working; 2) how and why implementation is going right or wrong; and/or 3) how to improve implementation.

Ideas for IS questions can come from many sources, including discussions with implementation stakeholders, findings from monitoring activities, and examples of studies carried out in other contexts. Part 2 of this guidance includes examples of questions that can be adapted to a specific implementation context (Refer to Tables 3-5).

When designing IS questions, it is important to consider[15]:

- Is the question relevant? *Is this something of interest to key stakeholders? Will the findings be both timely and actionable?*
- Is the question focused and precise? *Does it specify the target population and implementation outcome that will be investigated?*
- Is it arguable? *Does the question have more than one possible answer that the study can help determine?*
- Is it feasible? *Can the question reasonably be answered in the available timeframe?*

An example of a strong IR question is, 'What is the difference in MMS adherence between pregnant women who receive MMS with enhanced counseling at ANC and those who receive MMS with the standard counseling package at ANC?' This is strong question because it identifies the target population (pregnant women), the implementation strategy being tested (enhanced counseling

package) and what, if anything, it is being compared to (standard counseling package) as well as the implementation outcome (adherence).

There are multiple options for comparisons. For example, if there are two potential versions of a new MMS counseling curriculum (e.g., standard and enhanced) a study could compare the two versions to one another or they both could be compared to the current standard of care (e.g., IFA counseling). It is also possible to examine the performance of a single implementation strategy over time (e.g., whether intervention fidelity of the MMS counseling curriculum is maintained over time).

It is common for country stakeholders to generate more IS research questions about the IFA to MMS transition than are feasible to answer. Prioritization is necessary. IS research questions should be prioritized based on their relevance to the implementation decisions that need to be made at a particular time and how feasible it is to answer the questions in a rigorous but timely way.

New data collection is not needed if there is sufficient global or contextual knowledge to guide the decision. In some countries, however, influential stakeholders might demand new evidence be generated in their context. Ethical considerations related to data collection are also important to consider during prioritization. Several countries have effectively prioritized questions by having the MMS TAG or other stakeholder group rank proposed questions by pre-defined criteria.

COUNTRY EXAMPLE: PRIORITIZATION OF IMPLEMENTATION RESEARCH QUESTIONS IN PAKISTAN

At the beginning of their process, the Pakistan MMS TAG led a workshop to decide on research questions. Based on a situational analysis to understand ANC service delivery and a supply chain assessment, they identified 88 potential questions for IR. They scored and ranked questions based on pre-specified criteria (relevance, acceptability, maximizing impact, informing policy and practice, reducing inequity) and were able to identify two primary and secondary research questions. They then designed a formative research study to answer the questions about maternal nutrition practices. More details can be found in Appendix B.


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SELECT A THEORY OR FRAMEWORK

Implementation theories and frameworks help implementers and researchers develop a clear concept of how an implementation strategy or program was planned to happen in theory compared to how it happens in the real world. They help identify what to measure (i.e., key implementation outcomes and other factors), contextualize findings, and clearly communicate results. Using one of these common IS theories or frameworks can increase rigor of the work and contribute to local and global knowledge exchange by aligning the design with what has been done in other contexts using similar theories and frameworks.

There are multiple theories and frameworks that are commonly used to inform IS. The choice of which theory or framework depends on the purpose. It is possible to draw from more than one theory or framework to inform design of IS activities.

Table 6 presents some of the frameworks and theories that are commonly used to guide IS efforts. Appendix C includes additional resources to guide selection of an IS theory or framework.

TABLE 6: SELECTING AN IS THEORY OR FRAMEWORK

PURPOSE	DESCRIPTION IN THE CONTEXT OF MMS	EXAMPLES
IDENTIFYING FACTORS THAT INFLUENCE IMPLEMENTATION	These theories and frameworks are helpful in identifying the various factors that may be influencing MMS implementation. This information can help refine implementation strategies and explain outcomes.	Society for Implementation Science in Nutrition (SISN) Five Domains Framework Consolidated Framework for Implementation Science Theoretical Domains Framework Capability, Opportunity, Motivation and Behavior (COM-B) Theory
EVALUATING IMPLEMENTATION	These frameworks are helpful when trying to choose what to evaluate during IS and can be applied to assess MMS implementation outcomes.	RE-AIM (Reach, Efficacy, Adoption, Implementation, Maintenance) Implementation Outcomes Framework

COUNTRY EXAMPLE: ASSESSING MMS IMPLEMENTATION IN NIGERIA GUIDED BY THE SOCIETY FOR IMPLEMENTATION SCIENCE IN NUTRITION'S FRAMEWORK OF FIVE DOMAINS THAT AFFECT IMPLEMENTATION QUALITY

Work conducted in Nigeria by the Nutrition Agriculture and Health Initiative, Sight and Life, and UNICEF aimed to assess the implementation of the existing MMS programs in the country guided by the *Society for Implementation Science in Nutrition (SISN) Framework for "Five Domains that Affect Implementation Quality"*. These five domains include the intervention characteristics, implementing organizations and staff, enabling environment, characteristics of beneficiaries, and the processes of implementation.

The figure on the next page presents the factors assessed and the data sources used in Nigeria for each domain. More information on this work is captured in a SISN Webinar.

FIGURE 5: DOMAINS OF THE SISN FRAMEWORK

SISN FRAMEWORK DOMAIN	FACTORS ASSESSED	SOURCE OF DATA
INTERVENTION CHARACTERISTICS (OBJECTS OF IMPLEMENTATION)	» Ability of policies, strategies, and guidelines to direct MMS implementation » Extent to which guidance is provided for each of the five domains of implementation	» Desk review of policies, strategies, and guidelines relevant to implementation of MMS
IMPLEMENTING ORGANIZATION(S) AND STAFF	» Interest and influence of stakeholders (e.g., State Nutrition Officers, traditional birth attendants, Civil Society Scaling Up Nutrition Network, World Health Organization, Vitamin Angel Alliance) » Linkages among stakeholders	» Desk review » Key informant interviews with policymakers, local government officers, and service providers » Focus group discussion for bottleneck analysis
ENABLING ENVIRONMENT	» Evidence generation and use (e.g., extent to which research is conducted and used to guide various aspects of implementation strategies) » Multisectoral and vertical coordination of interventions (e.g., fidelity in transfer of training and technical assistance from central administrators to frontline workers, supply chain and logistics management) » Advocacy (e.g., existence of MMS advocacy briefs, frequency of engagement with policymakers at various levels about MMS scale-up such as high-level events promoting MMS) » Funding (e.g., amount of government funding for MMS, percent of budget released, consistency and sufficiency of government MMS funding, financing of logistics for MMS distribution)	» Desk review » Key informant interviews with policymakers, local government officers, and supply chain actors » Frontline worker survey » Focus group discussion for bottleneck analysis
CHARACTERISTICS OF BENEFICIARIES (INDIVIDUALS, HOUSEHOLDS, AND COMMUNITIES)	» Demand for interventions (e.g., knowledge about, acceptability of, and adherence to MMS) » Barriers to intervention demand (e.g., factors that limit physical access to service providers)	» Secondary analysis of survey data » Beneficiaries' survey » Key informant interviews with direct and indirect intervention recipients (target beneficiaries and other household members including husbands and grandmothers) and community leaders
DELIVERY MECHANISMS AND IMPLEMENTATION PROCESSES	» Strategic, delivery, and operational capacity (e.g., ability of existing systems to adequately plan and deliver MMS to intended beneficiaries at required frequency and coverage, adequacy of personnel numbers and/or skills, availability of BCC materials, availability of MMS monitoring forms in facility, ability to deliver supplements in hard-to-reach areas) » Fidelity of intervention delivery (e.g., extent to which the components of the interventions including MMS formulation, dosage, duration, and behavior change communication, are delivered according to national protocol) » Barriers to intervention delivery (e.g., organizational challenges at facility/provider level, factors related to household behavior, and social norms)	» Frontline worker survey » Frontline worker direct observation » Key informant interviews with frontline service providers » Focus group discussion for bottleneck analysis

IDENTIFY METHODOLOGIES AND STUDY DESIGN

Researchers can use a range of IS methods to access and apply existing global and contextual knowledge or conduct IR. Methods will vary based on the context, implementation question, guiding theory or framework, and other factors including timeline and available resources.

This section provides an overview of methods for accessing global and contextual knowledge as well as IR methods and study designs; it does not capture all possibilities. Decisions about methods and study design often require advice from someone with relevant research expertise.

Global and Contextual Knowledge Methods

Table 7 summarizes methods for accessing and applying global and contextual knowledge.

TABLE 7: METHODS FOR ACCESSING AND APPLYING GLOBAL AND CONTEXTUAL KNOWLEDGE

● GLOBAL KNOWLEDGE ⬢ CONTEXTUAL KNOWLEDGE

● ⬢	**Literature review** presents, analyzes, and discusses published information about a particular topic or implementation question. Even if the scope needs to be narrow to allow for rapid turnaround (e.g., not covering all knowledge on topic) it should still use a systematic approach with a clearly defined protocol. For guidance on compiling a literature review refer to the SISN literature review **RELATED TERMS:** *scoping review, integrative review, mixed methods review, introductory review, mapping review, descriptive review, narrative review, rapid review, realist review*
● ⬢	**Landscape analysis** systematically documents relevant global and/or contextual information available in reports, articles, or other literature. A landscape analysis should have specific objectives and a protocol/process that defines the scope of the information being gathered and how it will be gathered. **RELATED TERMS:** *situational analysis, policy review, context analysis, environmental scanning*
⬢	**Stakeholder analysis** systematically identifies key stakeholders who may influence introduction and scaling of MMS and helps to strategize how to engage with and manage stakeholder relationships effectively. This includes understanding their priorities, power, positioning, and interests related to MMS including how they are connected to one another. **RELATED TERMS:** *power-interest matrix, influence-analysis grid, stakeholder mapping*
⬢	**Bottleneck assessment** identifies constraints or inefficiencies in delivery of the intervention and the wider system. **RELATED TERMS:** *root cause analysis, program assessment, barriers and enablers, SWOT (Strengths, Weaknesses, Opportunities, Threats), problem tree analysis, barrier analysis*
⬢	**Readiness assessment** focuses on evaluating how prepared the system is for implementing MMS, considering factors like resources, capacities, willingness, operational readiness, and organizational capacity. **RELATED TERMS:** *capacity assessment, operational assessment, readiness checklists, implementation readiness, innovation attributes assessment*
● ⬢	**Economic assessments** identify the broad range of economic considerations from specific cost studies that include financial and non-financial costs of adopting MMS into health policy to economic impact analysis. These tools can guide prioritization among multiple options. **RELATED TERMS:** *costing study, cost effectiveness, cost benefit, budget impacts, willingness to pay, financial analysis, cost-utility analysis*
● ⬢	**Relationship-based approaches** include interpersonal sharing of information about MMS implementation. They offer valuable opportunities for asking questions and developing learning partnerships and networks that can continue to be accessed across time. **RELATED TERMS:** *exchange visits, conferences, global or regional meetings, technical assistance*

IR Methods

IR is a broad category that includes or overlaps with other research and program evaluation methodologies. Table 8 lists some of the methodologies that are most relevant to the introduction and scale-up of MMS programming. Many of these methodologies have complementary goals and methods but may use different terminology. It is possible to apply more than one methodology to an IR activity. For example, a team may carry out formative research to inform an HCD co-design workshop.

IR Study Design

The key difference between IR and efficacy or effectiveness research is not in study design; for example, both IR and clinical research can use a randomized controlled trial design. The key difference is the outcomes being studied (see Figure 2). IR is focused on implementation outcomes, not health or clinical outcomes. Refer to Table 2 for a list of implementation outcomes and their definitions in the context of MMS introduction, and scale-up.

Regardless of the overarching methodology (Table 8), most IR studies use mixed methods, meaning they collect both qualitative and quantitative data on previous page. Quantitative data is data that can be counted or expressed as numbers; it is often used to assess whether implementation outcomes are achieved. Qualitative data describes qualities or characteristics and is typically presented in narrative form; it will help answer how or why questions. There are different ways to collect qualitative and quantitative data in an IR study (Table 9).

TABLE 8: METHODS USED TO GENERATE NEW KNOWLEDGE USING IMPLEMENTATION RESEARCH (IR)

Formative Research: Formative research is carried out during intervention or program design or as part of a process evaluation to better understand context and specify the target audience, understand factors that influence their behavior and identify insights to shape or improve intervention design. UNICEF, Sight and Life Foundation, and The Pennsylvania State University published a formative research guide for improved MMS acceptability and utilization amongst pregnant women based on their experiences in Bangladesh, Burkina Faso, Madagascar, and Tanzania. To access this formative research guide on UNICEF's website.
Participatory Action Research (PAR): Participatory action research is a research paradigm that emphasizes participation by members of affected communities as "co-researchers" and collaborative action towards social change. Like IS, PAR emphasizes iteration and utilizes very diverse methods. Within MMS IR, this could take several forms, including working directly with community members to understand their experiences obtaining supplements through ANC and developing strategies to support them in accessing and using MMS.
Human-centered design (HCD): Human-centered design is an approach to design of interventions, products, processes, etc. that places people and their needs at the center of the process. There are a range of HCD methods and tools to foster empathy with target users. HCD processes include iterative testing and refinement of prototypes among a target group. Some HCD approaches involve active co-design with users.
Trial of Improved Practice (TIPS): Trial of Improved Practice is a specific formative research methodology that involves intensively and iteratively pretesting practices the intervention seeks to promote among specific target populations. TIPs can be used to test new technologies or behaviors and develop strategies for social and behavior change.
Quality improvement (QI): Quality improvement is an approach to course correction that helps implementers decide on changes to make to ongoing implementation of an intervention package in a specific context. It involves interactive Plan-Do-Study-Act or similar iterative reflection and action cycles to make small refinements.
Process Evaluation: Process evaluation assesses whether and how the intervention package/implementation strategy is being implemented per plan or protocol and how/why.
Impact Evaluation: Impact evaluation assesses whether specific outcome(s) were or were not achieved by the intervention package/ implementation strategy. In the context of IR, the outcome is an implementation outcome. (see Table 2).

TABLE 9: EXAMPLES OF QUALITATIVE AND QUANTITATIVE DATA COLLECTION METHODS COMMONLY USED IN IR

QUALITATIVE METHODS	QUANTITATIVE METHODS
» individual key informant interviews » focus group discussions » focused ethnographic methods (e.g., free listing, pile sorting) » diaries or annotated logs based on observations, activities, and periodic reflection activities	» individual-level participant questionnaires » structured surveys (e.g., household, facility) » observation with checklist » administrative data/record review » budget/cost data extraction » modeling: agent-based modeling; simulation and forecasting modeling

Study design also includes whether and how you will assign participants into different study arms and at which time points you will collect data. IR studies can use a wide variety of study designs including observational (e.g., case report, case-control), experimental (e.g., cluster-randomized controlled trials, stepped wedge) and quasi-experimental (e.g., longitudinal or interrupted time series).

The timing of data collection should depend on how often you need to get information from participants to answer the research question. Cross-sectional studies collect data from a respondent at a single time point, while longitudinal studies collect data from the same respondents at multiple points in time.

A study design decision tree can help identify the designs that fit your questions and context. Refer to AcademyHealth's research design decision tree. For more information on study design selection, refer to WHO/TDR's IR toolkit and Academy Health's study design guide.

Selecting IR Measures

Measures are the data collected during IR studies; they are how we estimate or assess the extent, quality, value, or effect of the implementation outcome.

Some implementation outcomes related to MMS have commonly used measures. For example, coverage of IFA is typically measured using a set of standard household survey questions and defined as consuming IFA at least 90 days during the most recent pregnancy in last two to three years. Not all common measures have been validated for accuracy, however. The pros and cons of specific measures should be considered as part of the IR study design.

Flexible tools have emerged to measure other types of implementation outcomes. For instance, the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) are all pragmatic and adaptable four-item measures for their respective implementation outcomes. They can be administered to a wide range of stakeholders to assess whether an intervention package (e.g., MMS) or an implementation strategy (e.g., training, counseling, packaging) is acceptable, appropriate, and feasible.[16] These more generic assessment tools have limitations that need to be considered before they are used in a specific context, as in the example from Mali.

Process Documentation

Process documentation is essential in IR. Process documentation should capture meaningful events, decisions, and milestones as they happen during implementation. It should capture more nuanced factors that may impact implementation, such as motivations, attitudes, and decision-making.

COUNTRY EXAMPLE: DEVELOPING A CONTEXTUALIZED MEASURE OF MMS ACCEPTABILITY IN MALI

In Mali, Jhpiego partnered with the Center for Vaccine Development to evaluate the acceptability of a product packaging strategy and innovative counseling curriculum that were developed as part of a co-design process with pregnant women and healthcare providers. Researchers were interested in understanding acceptability of both the intervention (MMS) and the implementation strategy (counseling training and materials). The standard Acceptability of Intervention Measure (AIM) was not considered sufficiently contextualized to their questions. So, the team used a theory-based approach to develop a more detailed and context-specific set of indicators related to different domains of MMS acceptability (e.g., affective attitude, burden, ethicality, intervention coherence, opportunity cost, perceived effectiveness, and self-efficacy).[17]

Process documentation tools include timelines, diaries, meeting notes, interviews, observations, dialogue, and videos. USAID has developed Implementation Research Tips that includes guidance on planning for and conducting process documentation.

Developing an IR Analysis Plan

An analysis plan should be included in the IR protocol. The analysis plan should define key measures and how they will be assessed/analyzed, roles and responsibilities of specific actors in data analysis, proposed data presentation formats (e.g., table shells, data visualizations), and timelines for analysis milestones.

Ethical review of protocol

There are ethical considerations when taking on any form of research, including IR. Key principles include maximizing the benefits to both participants and society at large, as well as ensuring that participation is truly voluntary. Whether a protocol needs to be submitted to one or more accredited institutions for formal ethical review depends on the study design and local guidelines governing these processes. See Appendix A for additional guidance on ethics and submitting IR protocols to local institutional review boards (IRBs).

KNOWLEDGE SHARING

Global and contextual knowledge and IR summarized or generated through IS should be shared with key stakeholders, including those who participated in the research, MMS TAG members, and other decisionmakers in the context. It is also important to share with audiences in other countries as part of global knowledge transfer.

Journal publications and other IR outputs are frequently criticized for being unclear. They do not give readers seeking to use the findings sufficient information about the context and implementation strategies, including how implementation strategies were adapted across iterative cycles of IR. To help researchers present IR more clearly, the Standards for Reporting Implementation Studies (StaRI) is a 27-item checklist that helps the author ensure there is adequate description of the interventions, implementation strategies, and research methodology applied. More information on the StaRI tool can be found here.

COUNTRY EXAMPLE: KNOWLEDGE SHARING IN CAMBODIA

In Cambodia, Helen Keller Intl, UNICEF, University of British Columbia, and the Vitamin Angel Alliance held a dissemination workshop to share results from their IR study reporting the significant benefits of MMS compared to IFA in terms of adherence, reduced negative side effects of MMS in comparison to IFA, and positive overall experience with MMS from pregnant women. From this dissemination workshop, government and workshop stakeholders committed to develop national MMS guidelines, include MMS in the essential medicines list, integrate MMS indicators into the national health information system, and conduct a cost analysis for full transition to MMS.

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APPENDIX A:

GUIDANCE FOR OBTAINING ETHICAL APPROVAL FOR IMPLEMENTATION RESEARCH

It is essential that all implementation research (IR) activities are carried out in accordance with global and national ethical standards. It can be challenging to determine whether an IR study qualifies as **human subjects research** and therefore requires review by one or more ethical review boards, often called institutional review boards (IRBs).

General concepts: human subjects research

A **human subjects research** activity that meets formal criteria for both 1) **research** and 2) **involving human subjects** requires review by an IRB:

1) Research is a systematic investigation (e.g., research development, pilot testing, evaluation) designed to develop or contribute to generalizable knowledge. IR generally does not meet the definition of research if the purpose of the data collection activity is to inform internal management of a public health program. Examples of internal management-focused activities may include 1) project documentation; 2) quality assurance (e.g., self-evaluation to determine whether implementation in a specific context meets established standards of quality; and 3) public health surveillance (e.g., collection and testing of information or biospecimens by a public health authority).

2) Involving human subjects means that data are obtained through intervention or interaction with an individual and include identifiable private information about a subject. Some research activities that involve interactions with individuals may not be considered **involving human subjects**, such as 1) secondary analysis of publicly available deidentified datasets; or 2) collection of information solely about policies, practices, or procedures.

Context-specific ethical review requirements

IRB rules and regulations and submission processes vary across contexts. For any IR activity, you should contact local authorities early in the planning process to confirm rules and submission requirements.

In your inquiry or application to the IRB, be clear about:

- the primary objective of the IR and how the information will be utilized
- the primary research outcomes (e.g., health outcomes vs. implementation outcomes)
- how data are being collected (e.g., primary vs. secondary)

Where to obtain ethical review clearance required for MMS IR also varies by context — some countries require IRB approval, others a separate research license from a national research entity, and others approval by a drug regulatory board. It is imperative that any MMS IR follows all local research regulations.

Depending on local context and procedures, an IR study may 1) not need to be submitted at all (i.e., not be considered human subjects research); 2) be submitted using a shorter or expedited application process to determine whether it is **exempt**, or 3) undergo a **full review**. Options two or three should be pursued if there are plans to publish IR findings in a peer-reviewed research journal. Specific journals may require documentation of submission to an accredited IRB regardless of their final determination.

If there are individuals from multiple countries involved in the study as funders or co-investigators, it may be necessary to submit to IRBs in more than one country. Submission to one or more IRBs can be time consuming; in some contexts, there are required fees. These factors must be accounted for in IR workplans and budgets.

APPENDIX B:

IN-DEPTH COUNTRY CASE STUDIES

In this section we present a series of case studies that provide greater detail about how IS has been used to support introduction and scale-up of MMS programs across different country contexts.

We highlight which stakeholders are engaged in the process, share how the process has progressed, and provide more details about IS/IR activities.

These projects are ongoing and updated frequently. The materials listed under "references" helped to inform these active projects. New case studies will be added, when available, on the Healthy Mothers Healthy Babies Consortium Knowledge Hub.

COUNTRY CASE STUDY:

MADAGASCAR

BACKGROUND

Until 2017, provision of IFA supplements for pregnant women through ANC was the national policy in Madagascar. Available data suggest, however, that women in Madagascar experienced challenges accessing ANC and receiving adequate supplies of IFA. According to the 2021 Demographic and Health Survey, 90% of women accessed ANC services at least once during pregnancy. Only 27%, however, started ANC in the first trimester and only 60% attended at least four ANC appointments. Any IFA coverage was low, at only 55%, and only 8% of women reported receiving at least 90 days of IFA supplements.

KEY STAKEHOLDERS

Government:

- Ministry of Public Health (MSANP) Directorate of Family Health: Nutrition Service (SNUT) and Safe Motherhood Service
- Prime Minister's Office National Nutrition Office (ONN): National Community Nutrition Programme UNIT (U-PNNC)

UN Agencies:

- UNICEF
- WHO
- World Bank

Development Partner:

- GRET (Groupe de Recherche et d'Etude Technologique)

OVERVIEW OF THE PROCESS

PHASE I: BUILDING AN ENABLING ENVIRONMENT

Timeline: 2018-2022

The National Nutrition Action Plan for 2017-2021 included MMS alongside IFA supplementation in the ANC service package. The process for MMS introduction and scale-up, however, did not begin until 2018 when the government established the MMS National Technical Committee led by the MSANP SNUT to convene and coordinate the key stakeholders listed above.

In 2020, Madagascar was included in a multi-country MMS pilot project supported by UNICEF and funded by the Bill & Melinda Gates Foundation. The overall aims of the project were to identify effective implementation strategies for introducing MMS to achieve high coverage, acceptability, and adherence; and to develop programmatic evidence to support national scale-up. Two districts in Madagascar were originally selected for pilot activities (Soavinandriana and Ifanadiana).

Between December 2020 and January 2021, the working group carried out a situational analysis to understand the maternal health and nutrition status and implementation environment. The group conducted an assessment in the health facilities of the two pilot districts to identify bottlenecks and facilitating factors related to 1) timely ANC; 2) the IFA supply chain at health center and community level; and 3) IFA adherence by women.

In 2021-2022, MMS supplementation continued to be added to national policies, including:

- Supplementation Protocol for Major Micronutrient Deficiencies for Health, Nutrition, and Food Security Interveners in Madagascar (2021)
- Reference Manual on Infant and Young Child Feeding, Women's Nutrition, and Early Childhood Development (2021)
- Revised National Multisectoral Nutrition Action Plan (PNAMN) 2022-2026 (2022)
- National list of medicines and health inputs (2021)

PHASE II: DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

Timeline: 2021-ongoing

Phase II of the pilot project (2021-2022) included development of the implementation strategies and supporting tools as well as design of an IR study to evaluate their implementation.

In 2021, formative research was carried out to better understand the target group of pregnant women. This included understanding current diets and factors influencing optimal nutrition practices and health-seeking behaviors. To support design of MMS social marketing, investigators also engaged community members and examined price and promotion-related recommendations.

The government led on the design of the two MMS distribution models that started in September 2021. For the IR, strategies were implemented in one or both pilot districts as described in the table below.

IMPLEMENTATION STRATEGY	DESCRIPTION	WHERE?
Delivery through ANC	MMS and counseling delivered at health facility level by facility staff	Soavinandriana district
Delivery through ANC and community-based platforms	MMS and counseling by both facility staff and Community Health Worker	Ifanadiana district
Comprehensive cascade training for health care providers, community health workers, and traditional birth attendants	Training on maternal nutrition, including MMS and Interpersonal Communication (IPC)	Both districts
Social behavior change communication strategy (SBCC) to support acceptability and adherence to MMS	Social mobilization and media address cultural and social norms and educate influential community members to support MMS and maternal diet quality	Social mobilization (both districts); media (Soavinandriana only)

IR STUDY DESIGN AND METHODS

Questions:

1. What is the acceptability of MMS among pregnant women and health care providers at facility and community-levels?
2. What is the difference in adherence of pregnant women to MMS at 90 days and at 180 days in the district with delivery through ANC only compared to the district with ANC and community-based delivery?

Adherence is assessed using data from the routine monitoring data system (DHIS-2). New nutrition indicators were incorporated into Madagascar's DHIS-2 as summarized below.

SERVICE DELIVERY	SUPPLY CHAIN
» Pregnant women having taken at least 90 IFA/MMS tablets during ANC » Pregnant women seen in 1st trimester having received IFA/MMS » Number of pregnant women advised to take IFA/MMS » Pregnant women received at least [30/60/90/120/150/180] quantity of MMS » Pregnant women received at least [30/60/90/120/150/180] quantity of IFA	» Quantity distributed » Quantity received during the month » Lost Quantity: expired-broken-damaged » Stock at the beginning of the month SDSP level » Stock available and usable in inventory (SDU) » Stock available and usable in inventory (SDU) with expiration date [<3 months/3-6 months/>6 months] » Number of days stock out

Other study-specific outcomes including acceptability were collected as part of cross-sectional midline (2023) and endline (2024) evaluations using data from other sources.

Key findings:

- Adherence for at least 90 days of MMS was 70% in Soavinandriana and 61% in Ifanadiana; adherence for at least 180 days was only 10% in Soavinandriana and 4% in Ifanadiana. The team concluded that community distribution does not improve MMS adherence.
- At endline, all women surveyed found the taste and smell of MMS more acceptable than IFA. 40% reported side effects such as nausea and stomach aches, but many noted that they decreased over time. 71% of the pregnant women surveyed believe that MMS protect them from the consequences of postpartum hemorrhage. Other named benefits of MMS included a healthy pregnancy, prevention of anemia, and fewer instances of low birth weight were cited as advantages.

STATUS OF ACTIVITIES (MAY 2024)

The MMS National Technical Committee is conducting bi-annual reviews of the IR findings. In 2023, IR was expanded to include three more districts, and seven additional districts were expected in 2024. The IR is ongoing, with endline expected in June 2024.

Simultaneously, the MMS National Technical Committee has begun to explore obtaining MMS in Madagascar for national scale-up. Efforts to obtain market authorization for MMS products are currently underway. The Directorate of Pharmacy, Laboratories, and Traditional Medicine supported a quantification exercise for MMS product. UNICEF has facilitated the acquisition of essential documents, including the product summary, the good manufacturing practice certificate, and the certificate of analysis. At district level, UNICEF has supported the integration of nutritional inputs into the SALAMA central procurement office for storage and distribution; it will also be incorporated into this national supply system.

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COUNTRY CASE STUDY:

CAMBODIA

BACKGROUND

MMS has been a topic of discussion in Cambodia since 2017, when global evidence of the benefits of MMS in comparison to IFA was raised within government. Cambodia had an existing policy for the provision of IFA to pregnant women and a strong ANC system to support delivery. According to the 2021-2022 Demographic and Health Survey (DHS), 99% of women ages 15-49 who had a live birth in the two years preceding the survey received ANC from a skilled provider during their most recent birth. Eighty-six percent had at least four ANC visits. Near all (98%) women took iron tablets or syrup. Nearly nine in 10 women (88%) took iron supplements for 90-179 days during pregnancy.

KEY STAKEHOLDERS

Government:

- National Nutrition Program (NNP) of the National Maternal and Child Health Center (NMCHC)

UN Agency:

- UNICEF

Development Partners:

- Helen Keller Intl
- Vitamin Angel Alliance (VA)
- Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ)
- World Bank
- World Vision International
- Alive & Thrive

OVERVIEW OF THE PROCESS

PHASE I: BUILDING AN ENABLING ENVIRONMENT

Timeline: 2021-2022

The idea of transitioning from IFA to MMS was met with initial resistance from some national stakeholders in Cambodia because of the more than 20-year history of successful IFA implementation.

Across 2021, Helen Keller Intl and VA conducted a landscape analysis to 1) review the existing evidence on maternal nutrition status, national policies and programs, and monitoring systems in Cambodia; 2) document the context and readiness for MMS implementation through ANC; and 3) make recommendations for introducing and scaling MMS in country, including priorities for IR.

In September 2021, these partners supported the government in hosting a workshop to share the global evidence around MMS, discuss the results of a landscape analysis, and identify the next steps when considering the introduction and scaling of MMS. Participants agreed to establish an MMS steering committee to oversee this work, develop an MMS policy plan, and conduct IR.

Questions prioritized by government for further exploration included:

- What is the acceptability and adherence of MMS by pregnant women, including factors such as packaging, color, ease of consumption, and taste?
- What are the projected additional costs to provide MMS vs. the currently recommended dosing for IFA supplementation? Is local production feasible?
- What are the key product and supply chain issues with the domestic suppliers to ensure affordable and quality supply of MMS?
- Does MMS require substantial investment in the current ANC platform? In behavior change? Would adherence be impacted? What can be learned from other countries that have initiated MMS rollout and scale-up?

Phase I findings were disseminated to national stakeholders in March 2024 and were used during discussions of the roadmap for the introduction of MMS throughout Cambodia.

PHASE II: DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

Timeline: 2020-ongoing

IR STUDY DESIGN AND METHODS

IR is being conducted in Cambodia in multiple stages. The first stage answered the question related to acceptability and adherence using a mixed-methods cluster-randomized non-inferiority control trial. The three study arms included

- Arm 1 IFA-90: Current standard of care: women receive 60 tablets of IFA at ANC1 and 30 tablets at ANC2
- Arm 2: MMS-90: women receive 90 tablets of MMS at ANC1 and 90 tablets at ANC2 (180 total)
- Arm 3: MMS-180: women receive 180 tablets of MMS at ANC1

In Kampong Thom Province, 1,545 women were enrolled across 48 health centers. Primary implementation outcomes were adherence (i.e., % of tablets received that were consumed) and MMS acceptability to women (perceptions of supplement characteristics, side effects) as well as barriers to implementation. Following enrollment, study teams conducted 30, 90, and 180-day home visits and administered an acceptability questionnaire and counted tablets.

STATUS OF ACTIVITIES (MAY 2024)

The initial IR was recently disseminated to national stakeholders. Partners are discussing which further IS activities will be conducted to answer the remaining questions related to implementation strategies that integrated MMS into the existing ANC platform.

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COUNTRY CASE STUDY:

INDONESIA

BACKGROUND

Since 1975, MOH has implemented IFA supplementation for pregnant women as part of the ANC system in Indonesia, with guidelines recommending that every pregnant woman receive at least 90 tablets of IFA during pregnancy beginning at the first ANC contact. IFA is mainly delivered through primary health centers and a network of health outposts and outreach workers.

Despite the four decades-long IFA program, a 2018 national survey revealed that prevalence of anemia among pregnant women increased from 37% in 2013 to 49% in 2018. First ANC contact coverage was 96.1%, but only 87.6% of pregnant women received any IFA, 51% received 90+ IFA tablets, and 38% consumed 90+ IFA tablets (Riskesdas 2022).

In 2008, the Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) study group published the results of a double-blind cluster-randomized trial carried out in Lombok, Indonesia that followed 31,290 pregnant women receiving MMS or IFA during routine prenatal care between from 2001-2004. The study concluded that MMS could reduce early infant mortality as compared to IFA, especially in undernourished and anemic women (Shankar et al 2008). Research on the efficacy of MMS on birth outcomes continued to be conducted by Indonesian universities, including the University of Indonesia (Sunawang et al 2008), Airlangga University (Sumarmi et al 2015, 2018, 2018), and Hasanuddin University (Rahayu 2021).

KEY STAKEHOLDERS

Government:

- Ministry of Health Indonesia
- The National Agency of Drug and Food Control (NA-DFC)

Universities and Research Institutions:

- Universitas Indonesia
- Universitas Airlangga
- Universitas Hasanuddin
- Universitas Padjadjaran
- Indonesian Institute of Nutrition (IGI)
- Johns Hopkins Bloomberg School of Public Health (BSPH)

Development Partners:

- Vitamin Angel Alliance (VA)
- Johns Hopkins Center for Communication Programs (CCP)
- Kirk Humanitarian

OVERVIEW OF THE PROCESS

PHASE I: BUILDING AN ENABLING ENVIRONMENT

Timeline: 2019-2022

In 2019, during the Asian Congress of Nutrition (ACN) conference, VA, with University of Hasanuddin and University of Airlangga, hosted a symposium on the evidence, policy, and practice related to MMS for pregnant women, followed by a series of stakeholder meetings and consensus-building workshops.

In 2020, as a follow-up to the ACN, VA, in partnership with the Indonesian Institute of Nutrition, and with support from the Johns Hopkins Bloomberg School of Public Health (BSPH) and Kirk Humanitarian, conducted an expert meeting on MMS in Jakarta. The meeting resulted in consensus on the following points: the need for MMS in Indonesia, the need to conduct MMS IR to increase adherence, the need to ensure a local MMS supply, and the need to create a national MMS Task Force (later renamed to MMS TAG) as a mechanism for achieving policy adoption.

The Indonesian MMS Technical Advisory Group (MMS TAG) was formed in 2020, comprising members from various fields of expertise and hosted by the Indonesian Institute of Nutrition. The Indonesian MMS-TAG has produced three policy brief papers on MMS and has been intensively involved in MMS-related activities. During the COVID-19 pandemic (2020-2022), a series of stakeholder meetings and consensus-building workshops were conducted. These included a workshop to discuss the WHO 2020 recommendations for MMS and a stakeholders' meeting to respond to the WHO inclusion of MMS in the 2021 List of Essential Medicines.

At the same time (2021-2022), efforts to identify and facilitate a long-term local supply of UNIMMAP MMS began. The key activities in this effort included conducting a supply context assessment that included cost-benefit and budget impact analyses as well as in-depth interviews with key supply stakeholders. Key issues and barriers identified included need for national policy and regulations, manufacturing and marketplace, and procurement. The next step was to gather information to support a local sourcing strategy for long-term supply needs by identifying and prequalifying manufacturers and connecting them with international donors and national government for capacity strengthening.

PHASE II: DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

Timeline: 2021-present

From 2019-2023, several small-scale implementation studies of MMS as replacement of IFA were initiated by University of Hasanuddin and University of Airlangga (Thaha 2022; Sumarmi 2022). In 2021, additional IS activities were initiated in response to Phase I discussions. The process began with a formative research component that sought to understand barriers and enablers to coverage and adherence. This included a desk review of all relevant policies, regulations, and known factors associated with adherence to prenatal supplements; a content analysis of existing prenatal supplement communication materials; a quantitative electronic survey on IFA supply and delivery; and a qualitative study through in-depth interviews and focus group discussions with key stakeholders from the community to understand the barriers to and enablers of IFA delivery, uptake, and adherence.

Results from the formative research were used to facilitate a three-day HCD workshop to co-design solutions to address the key challenges identified through the formative research. Solutions informed the development of "low-fidelity" prototypes that were pre-tested and refined.

Building from HCD, an enhanced behavior change communication (BCC) implementation strategy and multiple packaging strategies were developed and pretested, and are now being evaluated through an IR study with the following research questions:

1. What is the difference in MMS adherence between pregnant women who receive 90-count bottles delivered at two time points (MMS-90) compared to pregnant women who receive 180-count bottle at one time (MMS-180)?

2. What is the difference in MMS adherence between pregnant women who receive a) BCC without interpersonal counseling; b) expanded BCC with interpersonal counseling; and c) standard of care (MMS orientation only)?

The IR is being conducted as a multi-arm randomized control trial across 25 districts in Indonesia (n=~150,000). Three sub-districts in each district are randomly assigned across study arms (Figure 6). Primary implementation outcomes are MMS uptake and adherence by pregnant women. Secondary outcomes include acceptability, feasibility, and fidelity of MMS program implementation within ANC services.

FIGURE 6: THREE ARMS OF THE IMPLEMENTATION RESEARCH

ARM 1	ARM 2	ARM 3
Antenatal MMS + enhanced BCC delivery (90 count x 2)	Antenatal MMS + enhanced BCC delivery (180 count)	Antenatal MMS + standard BCC (90 count package x 2)

PHASE III: SCALING AND MAINTENANCE

Timeline: 2024-ongoing

The Ministry of Health has a plan to scale MMS nationally over a three-year period starting in September 2024; it addresses program implementation and supply chain issues. The first period aims to reach 30% of pregnancies. The initial three-year MMS supply requires procuring 1.3 million MMS bottle donations. Starting in 2025, the national government will make a budgetary commitment to support local MMS procurement that will increase across a five-year period.

STATUS OF ACTIVITIES (JUNE 2024)

IR data collection will be completed by the end of 2024, but the MOH is using initial findings to guide MMS program design and launch. IS is also informing planning and implementation of a roadmap for a sustainable MMS sourcing within ANC structures. In June 2024, the MOH released an official Decree on MMS UNIMMAP as the Standard of Micronutrient Supplement for Pregnant Women. Packaging design is nearly finalized (Figure 7).

FIGURE 7: PACKAGING DESIGN

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COUNTRY CASE STUDY:

PAKISTAN

BACKGROUND

According to the 2017-2018 Demographic and Health Survey (DHS), 59% of women with a child born in the last five years took iron tablets during their most recent pregnancy, and only 29% took iron tablets for 90 days or more during their most recent pregnancy. In 2018, an estimated 14.4% of women of reproductive age were underweight, 41.7% suffered from anemia, 22.4% were vitamin A deficient, and 79.7% were vitamin D deficient.

KEY STAKEHOLDERS FOR THE IMPLEMENTATION RESEARCH

MMS Technical Working Group:

Government:

- Chaired by Director of Nutrition, Ministry of National Health Services Regulations & Coordination (MoNHSR&C), with representation from all provinces and regions*
- Local support from the Integrated Health Program of Khyber Pakhtunkhwa
- District Health Office of Swabi

Lead Research and Implementing Partner:

- Nutrition International (NI)

UN Agencies:

- WHO
- UNICEF
- WFP

Local Agencies:

- Shifa Foundation
- International Research Force
- Precision Health Consultants (PHC) Global
- Institute of Social and Policy Sciences (I-SAPS)

* Members Project Director/Representative: IRMNCH & Nutrition Program, DoH, Punjab Lahore LHW Program Director, Dy. Director IRMNCH&N, DoH, Punjab Lahore PC-Health, Accelerated Action Plan, Nutrition Program Manager (DoH) Sindh, Karachi LHW Program Manager, Director, DoH, Sindh, Hyderabad Director Nutrition, IHP, Khyber Pakhtunkhwa, DoH, KP Peshawar LHW program Director, Manager, DoH, KP Peshawar Director Nutrition, Nutrition Directorate, DoH, Balochistan, Quetta LHW Program Manager, DoH, Balochistan, Quetta Nutrition Program Manager, DoH, AJ&K, Muzaffarabad Provincial Coordinator LHW Program, DoH, AJ&K, Muzaffarabad Nutrition Program Manager, DoH, Gilgit Baltistan, Gilgit Provincial Coordinator LHW Program, DoH, Gilgit Baltistan, Gilgit District Health Officer, Swabi, Khyber Pakhtunkhwa

OVERVIEW OF THE PROCESS

PHASE I: BUILDING AN ENABLING ENVIRONMENT

Timeline: 2021-2022

In 2021, an evidence translation workshop was conducted by the MoNHSR&C Nutrition Wing and NI. It aimed to build consensus around the WHO 2020 updated MMS recommendation, the latest global effectiveness evidence, and findings from an NI-led cost-effectiveness analysis for transitioning from IFA to MMS. The workshop led to the formation of a Pakistan Technical Working Group (TWG) for MMS chaired by the Director of Nutrition, MoNHSRC&C to advise and oversee the research project on antenatal MMS.

A prioritization process was undertaken to determine the implementation research questions most relevant to understanding the introduction of MMS into ANC in Pakistan. Working from an existing national IFA bottleneck analysis was TWG members participated in a national workshop to identify potential MMS program challenges and opportunities. These were consolidated into a list of 28 potential IR questions covering seven thematic areas. Using a modified version of the Child Health and Nutrition Research Institute (CHNRI) prioritization method, IR questions were scored by TWG members based on pre-specified criteria: relevance, acceptability, maximizing impact, informing policy and practice, reducing inequity. Five of the top ten scoring questions were discussed further to prioritize two IR questions.

A situational analysis was carried out to enhance understanding of the existing public ANC program and delivery platforms, stakeholders, IFA supply chain, and the feasibility of implementing MMS in Pakistan. Formative research was then conducted in the selected research site to better understand the beliefs, experiences, and practices of pregnant women, their family members and healthcare providers regarding ANC, IFA, and their perceptions of MMS.

The Government of Pakistan's strong commitment to address micronutrient deficiencies is reflected in the most recent National Maternal Nutrition Strategy (2022-2027). Thie strategy includes a recommendation to include MMS as part of ANC services for pregnant women with a 2027 national target of 50% pregnant women consuming 180+ MMS tablets.

PHASE II: DESIGN AND TEST IMPLEMENTATION STRATEGIES

Timeline: 2021-present

The *Advancing Maternal Health through MMS Implementation Research in Pakistan (AMMI)* project addresses the questions prioritized by the MMS TWG. Primary IR questions are:

1. What implementation approaches could be used to enhance the delivery of ANC nutrition services and introduce antenatal MMS in place of IFA in Pakistan?
2. Does implementation of these 'enhanced approaches' increase pregnant women's adherence to MMS compared to a standard implementation package? If so, how?

Secondary IR questions focus on ANC utilization and MMS adherence practices, why (or why not) the enhanced approaches increase adherence, acceptability, fidelity, feasibility, and cost-effectiveness of the enhanced approaches and the transition to MMS, effects of the enhanced approaches on quality of care, and enablers and barriers to successful implementation.

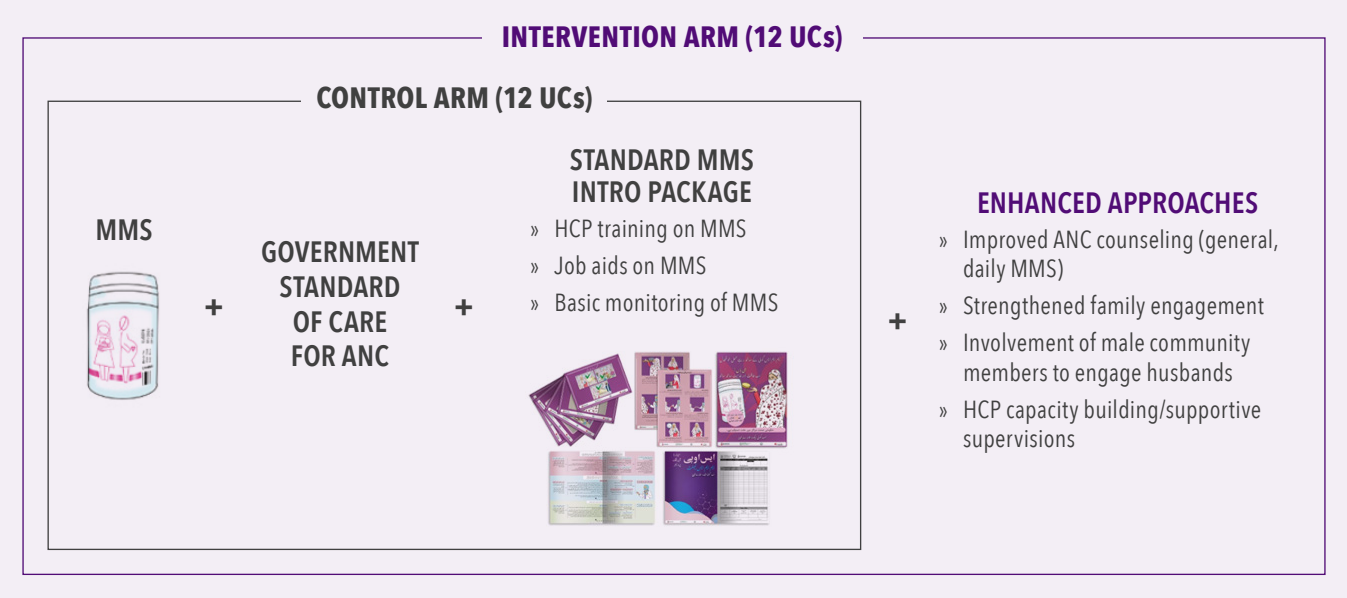
Swabi district, located in Khyber Pakhtunkhwa province was selected for this implementation research. In April 2022 MMS alongside a standard MMS implementation package was introduced into the public ANC platform across this district. All non-anaemic pregnant women were given up to two 100-count bottles of MMS, one upon ANC enrollment and second bottle at a subsequent visit after completion of the first bottle. The standard package included training for HCPs on MMS and the new standard operating procedures, tools for ANC counseling with MMS and other nutrition content, strengthened MMS supply chain, and improved program monitoring.

A mixed methods design is being used to answer the research questions. First, several 'enhanced' implementation approaches for delivering MMS and other ANC nutrition services were developed, tested, and refined using modified Trials of Improved Practices (TIPs) with health care workers, pregnant women, influential

family members, and community leaders to answer primary research question 1. Enhanced implementation strategies refined through TIPs include 1) capacity-building and supportive supervision of healthcare providers, with emphasis on MMS and nutrition counselling, 2) improved nutrition content and nutrition counselling tools and techniques integrated into ANC delivery, and 3) engagement of pregnant women's family members in ANC.

The enhanced approaches were then implemented and compared to the standard package to answer primary research question 2.i. An outcome evaluation with a two-arm cluster randomized control trial was set up with union councils as clusters. (Figure 8) MMS adherence, the primary outcome, and a series of secondary outcomes were evaluated using repeated cross-sectional surveys with pregnant and post-partum women, healthcare providers, and influential family members. A process evaluation was also conducted to answer primary research question 2.ii and the secondary research questions. The process evaluation gathered data on MMS and the enhanced approaches through in-depth interviews and focus group discussions with health care workers, pregnant women, community leaders, family members; and during observations and exit interviews at ANC visits. A costing study was also conducted to capture costs of transitioning from IFA to MMS for each implementation model.

FIGURE 8: MMS IMPLEMENTATION INTERVENTION DELIVERED IN 2-ARM CLUSTER RANDOMIZED CONTROL STUDY



STATUS OF ACTIVITIES (JUNE 2024)

There have been two years of rich implementation experience of delivering MMS through facility and community based public ANC platforms in Swabi district. The midline cross-sectional survey and the process evaluation for AMMI have been completed; the endline will be initiated later in 2024. The study will continue to observe the integration of MMS through the health system over time.

The GoP is committed to scaling MMS across the country. NI is translating the findings from AMMI to support the scale-up, providing technical support for health worker training and job aids, undertaking assessments in focal districts across the country and supporting the development of costed provincial and national roadmaps to sustain the transition and build on this opportunity to advance maternal nutrition.

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COUNTRY CASE STUDY:

PALESTINE REFUGEE COMMUNITIES IN JORDAN

BACKGROUND

Over the past 30 years, United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) has provided IFA supplementation as part of ANC services delivered through clinics serving Palestinian refugee communities in Jordan, Syria, Lebanon, West Bank, and the Gaza Strip. In 2016, the antenatal regimen was modified to reduce occurrence of side effects by providing folic acid (FA) in the first trimester and switching to iron-folic acid 2-3 times per week in the second trimester. Clinicians can modify the supplement type and frequency based on clinical judgement.

KEY STAKEHOLDERS

UN Agency

- UNRWA

Research and Development Partners:

- Johns Hopkins Bloomberg School of Public Health Center for Human Nutrition
- Vitamin Angel Alliance (VA)
- Kirk Humanitarian
- Sight and Life Foundation

OVERVIEW OF THE PROCESS

PHASE I: BUILDING AN ENABLING ENVIRONMENT

Timeline: 2020-2022

The process of introducing MMS as a potential replacement for IFA in the UNRWA ANC system started in early 2020 with discussions motivated by the lack of decline in maternal anemia and evidence of micronutrient deficiencies in pregnant Palestine refugee women. There was growing evidence that MMS could improve pregnancy outcomes compared to IFA, and an affordable high-quality UNIMMAP MMS supplement was available. Discussions within the Agency and with partners continued for a year.

In March 2021, an MMS Work Group composed of Agency officers and global partners was established at UNRWA Health Department Headquarters under the leadership of the Director of Health. The group's mandate was to:

- Become familiar with the epidemiology of maternal anemia and micronutrient deficiencies in the Middle East and trial evidence on MMS impact
- Track WHO policy guidance and other recommendations for MMS
- Identify donated product supply channels
- Draft an Agency program and implementation plan
- Formalize partnerships to pursue this strategy

Over the next 18 months, UNRWA secured a sufficient UNIMMAP MMS supply from Kirk Humanitarian to meet Palestine refugee needs. The Agency negotiated an MOU for IR funding and technical assistance in collaboration with the Vitamin Angel Alliance, Johns Hopkins University, and the Sight and Life Foundation.

PHASE II: DESIGNING AND TESTING IMPLEMENTATION STRATEGIES

Timeline: 2022-2024

Due to armed conflict in Gaza, the Agency's system of 25 clinics in Jordan was selected and approved by the Jordanian government as the IR site in mid-2022. In addition to the systems trial protocol design and IRB approvals, study preparations included resolving MMS supply chain issues like importation, clearance, storage, and inventory distribution procedures.

In September 2022, the Agency and its partners launched a six-month pilot program in two large UNWRA clinics. All pregnant women registering for ANC in the pilot clinics were given UNIMMAP MMS in 180-count bottles, instead of IFA. The pilot program allowed staff to become familiar with the MMS product, test its flow through the system, and provide feedback. At the same time, the study team refined IR questions, designed quantifiable indices of implementation outcomes (i.e., coverage, adherence, acceptability), validation tools, exit interview procedures, and advocacy materials (e.g., posters, booklets). The clinics refined procedures for monitoring MMS and IFA use, staff training, data entry, quality assurance, and database management.

By March 2023, the two-arm systems trial was launched in all 25 UNRWA ANC clinics in Jordan. Twelve clinics were randomly assigned to continue delivering the FA/IFA standard of care using 10-count blister packs. Eleven clinics were assigned to replace the FA/IFA regimen with MMS in 180-count bottles. These MMS bottles were given once at registration and, as possible, at a second visit later in pregnancy.

Implementation outcomes measured by trial included: 1) coverage and adequacy of coverage, 2) adherence by women, 3) side effects reported via midwives and independent exit interviews, 4) acceptability among women, 5) acceptability among staff, 6) fidelity to policy guidelines, and 7) cost savings to the Agency and women. Routine clinical data on hemoglobin were also collected. Data have been collected across all clinics through midwife entries into the eHealth system, sampling anonymous exit interviews, monthly online staff surveys, and other internal operational records.

STATUS OF ACTIVITIES (JUNE 2024)

The systems trial in Jordan was completed in February 2024. Database cleaning and initial analyses are underway, with early findings being disseminated amongst key stakeholders and in scientific meetings. The UNRWA collaborative MMS Work Group continues to be engaged in identifying lessons learned to inform plans to scale MMS in Jordan and other Agency Fields of Operation. There are discussions about how to evaluate sustainability of the MMS program after a minimal duration of full program operation.

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APPENDIX C:

RESOURCE LIST

A list of resources on case studies, implementation science/research resources, and tools can be found **here**. Appendix C will be updated by the Healthy Mothers Healthy Babies Consortium (HMHB) as new resources become available.

ABOUT THE HEALTHY MOTHERS HEALTHY BABIES CONSORTIUM

There is an ongoing global movement to improve maternal and newborn health. The Healthy Mothers Healthy Babies Consortium (HMHB), hosted by the Micronutrient Forum, is a growing collective of more than 250 organizations and individuals dedicated to improving maternal nutrition. HMHB supports collective action, advocacy, and information sharing on MMS activities in low- and middle-income countries and connects directly with stakeholders who have experience and are active in MMS. HMHB also hosts the Global MMS TAG (Technical Advisory Group), an interdisciplinary group of experts in nutrition, maternal health, and public health.

For additional resources and support, please visit the Healthy Mothers Healthy Babies Consortium (HMHB) website, which hosts the latest knowledge, evidence, guidance, and tools on maternal nutrition. Explore the World Map of MMS Activities, Knowledge Hub, Advocacy Resource Center, Women's Voices short films, and Knowledge Byte videos. Join us and become a member.

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HEALTHY MOTHERS
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Supplementation in Pregnancy
TECHNICAL ADVISORY GROUP

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