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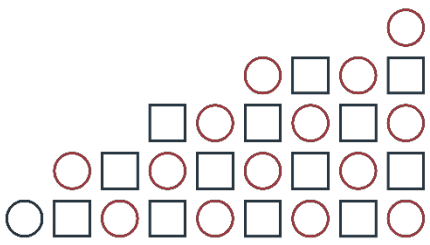
Cost-effectiveness analyses for the WHO review on multiple micronutrient supplements during pregnancy

Technical Report



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Preface

The World Health Organization (WHO) released the nutritional interventions update on multiple micronutrient supplementation (MMS) during pregnancy in July 2020, recommending MMS in the context of rigorous research. Upon request, this Nutrition International technical report was prepared in November 2019 to provide the WHO Guideline Development Group (GDG) with additional MMS cost-effectiveness analyses to support the guideline review process.

In 2016, the WHO released the "WHO recommendations on antenatal care for a positive pregnancy experience". Under nutritional interventions in the context of routine antenatal care (ANC), MMS was not recommended. At the time, the higher cost of MMS, concerns about feasibility and unclear effects on neonatal outcomes contributed to MMS not being recommended for all pregnant women as a part of routine ANC (WHO, 2016). In 2016, to fill the cost-effectiveness analysis gap, Nutrition International and Limestone Analytics undertook research in Pakistan, Bangladesh, and India to understand if MMS is more cost-effective than iron and folic acid supplementation (IFAS) − the results of which were published in the Journal of Nutrition in a study entitled "Multiple Micronutrient Supplements Are More Cost-Effective Than Iron and Folic Acid: Modeling Results from 3 High-Burden Asian Countries" (Kashi et al., 2019). The methodology for this research was used to create the *MMS Cost-Benefit Tool* to respond to countries' interest in exploring the costs, feasibility, and value-for-money of transitioning from IFAS to MMS for pregnancy. The tool was made publicly available in 2019 with 12 pre-set country analyses and has since expanded to over 30. The analyses in the *MMS Cost-Benefit Tool* are based on the most recent meta-analyses comparing the effectiveness of IFAS and MMS conducted by Keats et al. (2019) and Smith et al. (2017). In all scenarios modelled, the tool shows MMS to be very cost-effective compared with IFAS based on the statistically significant effects reported in these reviews.

In 2019, as part of the guideline review process, the WHO conducted a supplemental analysis based on data found in Keats et al. (2019) focused on comparing various formulations of IFAS to various formulations of MMS. Upon request, Nutrition International, with the support of Limestone Analytics, modelled the effect sizes from this "WHO Analysis" in an offline version of the *MMS Cost Benefit Tool* for a sample of twelve low- and middle-income countries (LMICs).This technical report is being published to ensure these custom cost-effectiveness analyses are publicly available and provide an additional resource for countries considering MMS in the context of implementation research. Apart from minor updates and an expanded discussion, the content of this and the technical report shared with the WHO in November 2019, remain the same.

Table of Contents

Executive Summary

Overview

Recent evidence has encouraged LMICs to consider transitioning from long-standing IFAS to MMS during pregnancy. To aid countries' decision-making, Nutrition International, in partnership with Limestone Analytics, developed the *MMS Cost-Benefit Tool*. The tool applies a rigorous methodology to calculate the incremental benefits and costs of transitioning from IFAS to MMS in various countries (Kashi et al., 2018). In this context, the term "transition" refers to substituting IFAS with MMS for pregnancy care in a government's antenatal service package.

The existing, publicly available analyses in the tool are based on the most recent meta-analyses comparing IFAS and MMS conducted by Keats et al. (2019) and Smith at al. (2017). Across the 12 countries in the tool representing Nutrition International's focal countries, transitioning to MMS has consistently been found to yield positive infant health outcomes and found to be very cost-effective.

The GDG-specified WHO analysis based on data found in Keats et al. (2019) herein referred to as the "WHO analysis" focused on comparing various formulations of IFAS to various formulations of MMS. The purpose of this technical report is to respond to a direct request from the WHO to model the cost-effectiveness of transitioning to MMS in 12 LMICs, using this "WHO analysis" estimates (see list below). Since the WHO analysis was not publicly available, all analyses are conducted using an offline version of *MMS Cost-Benefit Tool*, which applies the methodology from Kashi et al. (2019).

- **13/15 MMS vs. IFAS**: transitioning from any IFAS formulation to an MMS that contains 13-15 micronutrients including IFA.
- **UNIMMAP vs. IFAS**: transitioning from any IFAS formulation to the UNIMMAP MMS formulation.
- **13/15 MMS vs. IFAS (30 mg)**: transitioning from an IFAS that contains 30 mg of iron and 400 µg folic acid to an MMS that contains13-15 micronutrients including IFA.
- **13/15 MMS vs. IFAS (60 mg)**: transitioning from an IFAS that contains 60 mg of iron and 400 µg folic acid to an MMS that contains 13-15 micronutrients including IFA.
- **UNIMMAP vs. IFAS (30 mg)**: transitioning from an IFAS that contains 30 mg of iron and 400 µg folic acid to the UNIMMAP MMS formulation.
- **UNIMMAP vs. IFAS (60 mg)**: transitioning from an IFAS that contains 60 mg of iron and 400 µg folic acid to the UNIMMAP MMS formulation.

In this report, the primary analysis focused on the cost-effectiveness using statistically significant impacts on health. For robustness, a sensitivity analysis including the non-significant health outcomes was also included.[1] Overall, the evidence on health impact and cost-effectiveness of transitioning to

[1] The non-significant outcomes across meta-analyses were: male neonatal mortality and infant mortality (Smith et al.); stillbirth, neonatal mortality, preterm, maternal mortality, and maternal anaemia (Keats et al.); stillbirth, neonatal mortality, maternal mortality, and maternal anaemia (WHO).

MMS from IFAS suggests that MMS will likely be cost-effective in achieving a significant and positive health outcomes for newborns and children in many LMICs.

Cost-Effectiveness Analysis

Figure 1: 12 countries included in this analysis are Bangladesh, India, Pakistan, Philippines, Indonesia, Burkina Faso, Ethiopia, Madagascar, Nigeria, Kenya, Senegal, Tanzania

The key assumptions in the cost-effectiveness analysis include:

- **Coverage**: Assumed that thirty percent of pregnant women in each country scenario will receive the 180 supplements.

- **Timespan**: A 10-year timespan was used for the analysis. This is the length of the supplementation program over which costs and benefits are counted. The costs and benefits are calculated over the lifespan of each mother and child in each cohort year.

- **Unit Costs**: Supplement costs (assumes each woman receives 180 supplements) based on UNICEF UNIMMAP Supply Catalogue pricing (2016). Sensitivity analysis considers transition costs (cost for non-commodities expenses related to transition from an IFAS to MMS program).

- **Health Effects (health outcomes)**: The primary analysis uses statistically significant impacts on health outcomes. These are stillbirth, female neonatal mortality, preterm, low birth weight, and small for gestational age (Smith et al.); low birth weight and small for gestational age (Keats et al.); and preterm, low birth weight, and small for gestational age (WHO-Keats et al.).

Table 1. Summary from Primary Cost-Effectiveness Analysis Across 12 LMICs Using Statistically Significant Health Effects

Analyses	Additional DALYs Averted (Range across countries)	Confidence in Positive Health Outcomes	Additional $ per DALY Averted (US) (Range across countries)
Smith et al. - MMS vs. IFAS	181,893 - 9,509,245	100.0%	$4.83 - $11.56
Keats et al. - MMS vs. IFAS	47,187 - 3,922,329	100.0%	$15.82 - $49.50
WHO analysis - 13/15 MMS vs. IFAS	27,743 - 1,913,169	99.8%	$28.79 - $70.56
WHO analysis - UNIMMAP vs. IFAS	53,077 - 4,411,068	98.9%	$14.07 - $44.05
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	27,743 - 1,913,169	99.8%	$46.07 - $112.89
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	27,743 - 1,913,169	99.8%	$28.79 - $70.56
WHO analysis - UNIMMAP vs. IFAS (30 mg)	53,077 - 4,411,068	98.9%	$22.51 - $70.49

Analysis is conducted using statistically significant health effects of transitioning from IFAS to MMS.

Key Messages from Primary Cost-Effectiveness Analysis Using Statistically Significant Health Effects

- Across all meta-analyses used (Smith et al., Keats et al., WHO analysis.), transitioning from IFAS to MMS averts DALYs with almost 100% certainty, regardless of formulation and is considered cost-effective for all 12 countries.
- Some differences in cost-effectiveness between the 12 countries are attributed to the different epidemiological profiles of countries such as the prevalence of health outcomes, life expectancy, and age of first pregnancy.
- Transitioning to the UNIMMAP formulation averts more DALYs than transitioning to the 13/15 MMS formulation and is considered more cost-effective.

- While the future pricing of MMS tablets is unknown, it is likely to decrease if production and distribution increases globally, which would result in an even greater cost-effectiveness in achieving positive health outcomes.
- Overall, the evidence on health impact and cost-effectiveness of transitioning to MMS from IFAS suggests that MMS will likely be cost-effective in achieving a significant and positive health outcome for newborns and children in many LMICs.

Key Messages from Sensitivity Cost-Effectiveness Analysis including Non-Significant Health Effects

- Most results remained unchanged upon including non-significant outcomes: transitioning to MMS from IFAS averts DALYs with high certainty and the UNIMMAP formulation remains more effective and cost-effective than the 13/15 MMS formulation.
- Transitioning from IFAS (30 mg) to any type of MMS formulation was found to be cost-effective and yield positive health outcomes with high certainty.
- Transitioning from IFAS (60 mg) to any type of MMS formulation was not found to be cost-effective and had a low chance of yielding positive health outcomes. This result is entirely driven by the relative risks for neonatal mortality which were non-significant but concentrated above 1.00.

Acronyms & Abbreviations

BCR	Benefit-Cost Ratio
DALY	Disability-adjusted life year
GDG	Guideline Development Group
IFAS	Iron and folic acid supplement
LBW	Low birth weight
LMIC	Low- and middle-income countries
MMS	Multiple micronutrient supplement
RR	Relative risk
SGA	Small for gestational age
UNIMMAP	UNICEF/WHO/UNU international multiple micronutrient preparation
WHO	World Health Organization
VLBW	Very low birth weight

Introduction

Recent evidence has encouraged LMICs to consider transitioning from long-standing IFAS to MMS during pregnancy. However, global guidance to facilitate this transition is limited.

To aid countries' decision-making, Nutrition International, in partnership with Limestone Analytics, developed the *MMS Cost-Benefit Tool*. The tool applies a rigorous methodology to calculate the incremental benefits and costs of transitioning from IFAS to MMS in LMICs (Kashi et al., 2018). In this context, the term "transition" refers to substituting IFAS with MMS for pregnancy care in a government's antenatal service package. Across the 12 countries in the tool, representing Nutrition International's focal countries, transitioning to MMS has consistently found to yield positive infant health outcomes and found to be very cost-effective.

The existing analyses in the current tool estimate the incremental benefits of transitioning from IFAS to MMS based on the most recent meta-analyses published by Cochrane (Keats et al., 2019) and The Lancet (Smith et al., 2017). While the inclusion criteria of these meta-analyses were comparable, the Cochrane (Keats et al., 2019) meta-analysis included studies that compared MMS with IFAS or iron alone. The Lancet (Smith et al., 2017) meta-analysis only included studies comparing MMS to IFAS, looked at additional health effects including very preterm birth, and explored effect modification by various variables such as sex of neonates. Both reviews found improved health outcomes among pregnant women receiving MMS and showed no statistically significant risk of increased harm to the mother or baby. Smith et al. (2017) found that compared to IFAS, MMS had a significant reduction on the risk of stillbirth (using the fixed effects analysis), low birth weight (LBW), very low birth weight (VLBW), early preterm birth, preterm birth and small for gestational age (SGA) and mortality outcomes such as female neonatal mortality and female infant mortality. Keats et al. (2019) conversely only found evidence of significant effects on LBW and SGA (Bourassa et al., 2019).

The WHO conducted a supplemental analysis ("WHO analysis") of the Keats et al. (2019) study focused on comparing various formulations of IFAS to various formulations of MMS. The purpose of this technical report is to respond to the direct request from the WHO to model the cost-effectiveness of transitioning to MMS in 12 LMICs, using these "WHO analysis" estimates. Since the WHO analysis were not publicly available, all analyses are conducted using an offline version of the *MMS Cost-Benefit Tool*, which applies the methodology from Kashi et al. (2019).

Model Scenarios

The effect of transitioning from IFAS to MMS on various health outcomes were compared. Each scenario is based on Relative Risks (RR) derived from a different meta-analysis (**Table 2**) using different formulations of IFAS and MMS (**Table 3**).

Table 2. Relative Risk Assumption Descriptions

Model Scenario	Source	Description
Smith et al. MMS vs. IFAS	Smith et al. (2017) meta-analysis	"MMS vs. IFAS" refers to the RRs of transitioning from any IFAS formulation to any MMS formulation.
Keats et al. MMS vs. IFAS	Keats et al. (2019) meta-analysis	"MMS vs. IFAS" refers to the RRs of transitioning from any IFAS formulation to any MMS formulation.
WHO analysis 13/15 MMS vs. IFAS	WHO analysis	"13/15 MMS vs. IFAS" refers to the RRs of transitioning from any IFAS formulation to an MMS contains 13-15 micronutrients including IFA.
WHO analysis UNIMMAP vs. IFAS	WHO analysis	"UNIMMAP vs. IFAS" refers to the RRs of transitioning from any IFAS formulation to the UNIMMAP MMS formulation.
WHO analysis 13/15 MMS vs. IFAS (30 mg)	WHO analysis	"13/15 MMS vs. IFAS (30 mg)" refers to the RRs of transitioning from an IFAS that contains 30 mg of iron and 400 µg folic acid to an MMS contains 13-15 micronutrients including IFA.
WHO analysis 13/15 MMS vs. IFAS (60 mg)	WHO analysis	"13/15 MMS vs. IFAS (60 mg)" refers to the RRs of transitioning from an IFAS that contains 60 mg of iron and 400 µg folic acid to an MMS contains 13-15 micronutrients including IFA.
WHO analysis UNIMMAP vs. IFAS (30 mg)	WHO analysis	"UNIMMAP vs. IFAS (30 mg)" refers to the RRs of transitioning from an IFAS that contains 30 mg of iron and 400 µg folic acid to the UNIMMAP MMS formulation.
WHO analysis UNIMMAP vs. IFAS (60 mg)	WHO analysis	"UNIMMAP vs. IFAS (60 mg)" refers to the RRs of transitioning from an IFAS that contains 60 mg of iron and 400 µg folic acid to the UNIMMAP MMS formulation.

Table 3. Formulation Descriptions

Type		Formulation
MMS	**UNIMMAP**	Iron (30 mg); Folic Acid (400 µg); Retinol (800 µg); Vitamin D (200 IU); Vitamin E (10 mg); Ascorbic acid (70 mg); Vitamin B1 (1.4 mg); Niacin (18 mg); Vitamin B2 (1.4 mg); Vitamin B6 (1.9 mg); Vitamin B12 (2.6 µg); Zinc (15 mg); Copper (2 mg); Selenium (65 µg); Iodine (150 µg)
	13/15 MMS	Containing 13-15 micronutrients including IFA
IFAS	**IFAS (30 mg)**	Iron (30 mg); Folic Acid (400 µg)
	IFAS (60 mg)	Iron (60 mg); Folic Acid (400 µg)

Methodology

This cost-effectiveness analysis is based on the methodology used in the *MMS Cost-Benefit Tool* (Kashi et al., 2019). The original analyses in the tool include health outcomes from Smith et al. (2017) and Keats et al. (2019). The "WHO analysis" includes the same health outcomes, except for infant mortality, and includes c-sections, congenital abnormalities and perinatal mortality (see **Table 4**).

In this cost-effective analysis the health outcomes reported in each respective meta-analysis were used, with the exception of c-sections, congenital abnormalities and perinatal mortality given low data quality and issues around double counting benefits.

Table 4. Health Outcomes Included in IFAS vs. MMS Meta-Analyses

Health Outcome	Definition	Smith et al.	Keats et al.	WHO Analysis
Stillbirth	Third trimester fetal deaths (≥ 1000 g or ≥28 weeks) (WHO).	✓	✓	✓
Perinatal mortality	Number of stillbirths and deaths in the first week of life (early neonatal mortality) (WHO).			✓
Neonatal mortality	Death in the first 28 days of life.	✓ †	✓	✓
Infant mortality	Death between birth and exactly 1 year of age (UNICEF). To observe the separate effects on neonatal and infant mortality, this model subtracts neonatal mortality from infant mortality in the calculation of DALYs averted.	✓		
Preterm	Baby born alive before 37 weeks of pregnancy are completed (WHO).	✓	✓	✓
Low birth weight	Birthweight that is below the 10th percentile for gestational age.	✓	✓	✓
Small for gestational age	Weight below the 10th percentile for gestational age.	✓	✓	✓
Congenital abnormalities	Congenital anomalies are also known as birth defects, congenital disorders or congenital malformations. They can be defined as structural or functional anomalies (e.g. metabolic disorders) that occur during intrauterine life and can be identified prenatally, at birth or later in life (WHO).			✓
Maternal mortality	Death among women who were pregnant or within 42 days of termination of pregnancy (irrespective of the duration and site of the pregnancy, from any cause related to, or aggravated by, the pregnancy or its management but not from accidental or incidental causes).		✓	✓
Maternal anaemia	Third trimester haemoglobin < 110 g/L.		✓	✓
C-sections	Delivery by cesarean section.			✓

*Statistically significant outcomes are highlighted.

† Note only female neonatal mortality was statistically significant.

Cost

Two main categories of cost are included in this analysis: supplements and transition costs.

Supplement costs are based on the UNICEF supply catalogue (2016)[2]. It is assumed that each pregnant woman receives a course of 180 supplements. For this costing model, the assumed unit cost of 180 supplements are US $2.27 for IFAS and US $3.27 per pregnant woman. This unit cost of MMS is likely conservative, considering that it is based on the pricing of a 100-pac product. As of 2015, UNICEF has replaced 1,000-pac IFA containers with 100-pac containers, and therefore are not available at the previously cited price of US $0.91 for IFAS and US $2.98 for MMS used in the *One Health Tool Manual (2013)*. The future pricing of MMS is unknown; however, it is likely that the unit cost of MMS will decline relative to IFA as demand and production increases with scale-up over time.

Transition cost refers to the cost for non-commodity expenses related to transition from an IFAS to MMS program, which could include development of training materials and new policies/regulations, training of health workers, or behaviour change communications, etc. related to the startup of the new program. Since transition costs can vary widely by country, there is no standard input for transition costs. The primary analysis assumes a transition cost of US $0. An analysis of the sensitivity to transition costs is included in Annex B, which assumes a transition cost of ~US $1 /head, aligning with the Nutrition International MMS Country Policy Briefs. This translates to US $2 million for Burkina Faso, Senegal, Madagascar, Kenya, and Tanzania; US $5 million for Bangladesh, Ethiopia, Pakistan, Philippines, Indonesia; and US $10 million for India and Nigeria.

Effectiveness

The effect of transitioning from IFAS to MMS is summarized using disability-adjusted life years (DALY) averted. The magnitude of DALYs averted is based on the RRs reported across the meta-analyses. **Table 5** summarizes the RR estimates that are currently available in the tool (Smith et al. (2017) and Keats et al. (2019)) as well as the "WHO analysis" across the different formulations.

The primary analysis uses only the statistically significant health outcomes. A sensitivity analysis using all health outcomes (including non-significant health effects) is also included.

[2] Note that the live version of the *MMS Cost-Benefit Tool* is updated routinely, costs now reflect the current pricing in the UNICEF supply catalogue (2020).

Table 5. Relative Risk Estimates of Transitioning from IFAS to MMS From all Meta-Analyses

Health Outcome	Smith et al.	Keats et al.	WHO analysis					
	MMS vs.	MMS vs.	13/15 MMS vs.			UNIMMAP vs.		
	IFAS Overall	IFAS Overall	IFAS 60 mg	IFAS 30 mg	IFAS Overall	IFAS 60 mg	IFAS 30 mg	IFAS Overall
C-Sections	-	-	1.06 (0.75, 1.49)	-	1.04 (0.76, 1.43)	1.06 (0.75, 1.49)	-	1.06 (0.75, 1.49)
Maternal anaemia	-	1.04 (0.94, 1.15)	1.04 (0.90, 1.21)	1.01 (0.89, 1.14)	1.03 (0.92, 1.15)	0.90 (0.77, 1.05)	-	0.90 (0.77, 1.05)
Maternal mortality	-	1.06 (0.72, 1.54)	0.88 (0.41, 1.87)	1.12 (0.73, 1.74)	1.06 (0.72, 1.54)	0.77 (0.30, 1.97)	1.03 (0.64, 1.66)	0.97 (0.63, 1.48)
SGA	0.97 (0.96, 0.99)	0.92 (0.88, 0.97)	0.95 (0.89, 1.01)	0.98 (0.96, 1.00)	0.98 (0.96, 1.00)	0.89 (0.81, 0.97)	0.95 (0.85, 1.06)	0.91 (0.85, 0.98)
LBW	0.88 (0.85, 0.90)	0.88 (0.85, 0.91)	0.90 (0.82, 0.98)	0.88 (0.85, 0.91)	0.88 (0.86, 0.91)	0.84 (0.75, 0.94)	0.89 (0.81, 0.98)	0.87 (0.81, 0.94)
Preterm	0.92 (0.88, 0.95)	0.95 (0.90, 1.01)	0.99 (0.92, 1.07)	0.90 (0.80, 1.01)	0.94 (0.88, 1.00)	1.04 (0.96, 1.12)	0.93 (0.82, 1.05)	1.00 (0.96, 1.03)
Congenital Abnormalities	-	-	1.34 (0.25, 7.12)	-	1.34 (0.25, 7.12)	1.34 (0.25, 7.12)	-	0.99 (0.14, 7.04)
Neonatal† mortality	0.98‡ (0.90, 1.05)	1.00 (0.89, 1.12)	1.22 (0.94, 1.56)	0.95 (0.87, 1.04)	1.02 (0.90, 1.17)	1.25 (0.94, 1.67)	0.90 (0.78, 1.05)	-
Perinatal mortality	-	-	1.15 (0.93, 1.42)	0.92 (0.86, 0.98)	-	1.20 (0.95, 1.51)	0.90 (0.80, 1.01)	-
Infant mortality	0.97 (0.88, 1.06)	-	-	-	-	-	-	-
Stillbirth	0.92 (0.86, 0.99)	0.95 (0.86, 1.04)	1.11 (0.89, 1.37)	0.89 (0.82, 0.97)	0.98 (0.87, 1.10)	1.10 (0.86, 1.41)	0.91 (0.77, 1.07)	1.00 (0.86, 1.17)

* Statistically significant health outcomes are highlighted

† Effect modification was detected ($p<0.05$) by iron dosage in the "WHO analysis"

‡ Effect modification by sex of neonates was detected: Female 0.85 (0.75, 0.96) and Male 1.06 (0.95, 1.17)

Note that while the "WHO analysis" looked at effect modification by formulation, the only detectable differences for all health outcomes were between "13/15 MMS vs. IFAS", "UNIMMAP vs. IFAS". Only for neonatal mortality were there further differences detected based on the specific IFAS formulation (30 mg or 60 mg). Therefore, only for the neonatal mortality health outcomes are the specific RRs for the 30 mg or 60 mg formulation used. Otherwise the 'overall' RRs are used (see **Table 6**).

Table 6. Relative Risk Estimates of Transitioning from IFAS to MMS Used in Analysis

Meta-Analyses	Smith et al.	Keats et al.	WHO analysis					
Health Outcome	MMS vs.	MMS vs.	13/15 MMS vs.			UNIMMAP vs.		
	IFAS Overall	IFAS Overall	IFAS 60 mg	IFAS 30 mg	IFAS Overall	IFAS 60 mg	IFAS 30 mg	IFAS Overall
Maternal anaemia	-	1.04 (0.94, 1.15)		1.03 (0.92, 1.15)			0.90 (0.77, 1.05)	
Maternal mortality	-	1.06 (0.72, 1.54)		1.06 (0.72, 1.54)			0.97 (0.63, 1.48)	
SGA	0.97 (0.96, 0.99)	0.92 (0.88, 0.97)		0.98 (0.96, 1.00)			0.91 (0.85, 0.98)	
LBW	0.88 (0.85, 0.90)	0.88 (0.85, 0.91)		0.88 (0.86, 0.91)			0.87 (0.81, 0.94)	
Preterm	0.92 (0.88, 0.95)	0.95 (0.90, 1.01)		0.94 (0.88, 1.00)			1.00 (0.96, 1.03)	
Neonatal mortality	Female 0.85 (0.75, 0.96) Male 1.06 (0.95, 1.17)	1.00 (0.89, 1.12)	1.22 (0.94, 1.56)	0.95 (0.87, 1.04)	1.02 (0.90, 1.17)	1.25 (0.94, 1.67)	0.90 (0.78, 1.05)	1.00†
Infant mortality	0.97 (0.88, 1.06)	-	-	-	-	-	-	-
Stillbirth	0.92 (0.86, 0.99)	0.95 (0.86, 1.04)		0.98 (0.87, 1.10)			1.00 (0.86, 1.17)	

* Statistically significant health outcomes are highlighted.

† The difference in the RRs were too substantive to allow for an overall estimate. Therefore, an RR of 1.00 was used.

The analysis includes three criteria pertaining to the effectiveness of transitioning from the various formulations of IFAS to the various formulations of MMS.

- **Additional DALYs Averted**: This is the sum of DALYs averted by transitioning from IFAS to MMS across all health outcomes.
- **Additional Child Deaths Averted:** This is the number of child deaths averted by transitioning from IFAS to MMS. This number accounts for stillbirth and neonatal mortality.
- **Confidence in Positive Health Outcomes**: This is a statistically calculated estimate of confidence that the transition from IFAS to MMS will result in overall positive health outcomes. It is calculated using probabilistic sensitivity analysis and the standard error of the health effect sizes.

"Additional DALYs Averted" and "Confidence in Positive Health Outcomes" are also reported separately for neonatal mortality and stillbirth. Note that for neonatal mortality, results are disaggregated by female (F) and male (M) neonates for consistency with the current tool.

Cost-Effectiveness

This analysis reported two criteria pertaining to the cost-effectiveness of transitioning from the various formulations of IFAS to the various formulations of MMS.

- **Additional Cost per DALY Averted**: This is the cost per DALY averted by transitioning from IFAS to MMS.
- **Benefit-Cost Ratio**: Reports how many times greater the benefits of transitioning from IFAS to MMS are relative to costs.

Other Assumptions

This analysis is consistent with the other assumptions in the *MMS Cost-Benefit tool*. These include:

- **Coverage**: It assumes that 30 percent of pregnant women in each country scenario will receive the 180 supplements.
- **Timespan**: A 10-year timespan was used for the analysis. This is the length of the supplementation program over which costs and benefits are counted. Additional benefits provided by MMS begin in Year 1 of the MMS supplementation program. The costs and benefits are calculated over the lifespan of each mother and child in each cohort year.
- **Discount Rate**: Benefits are discounted using a standard 3 percent discount rate.

For other details of the modelling, see the Nutrition International user guide for the *MMS Cost-Benefit Tool.*

Results

Overall Summary

Table 7 reports the ranges of results for select effectiveness and cost-effectiveness criteria across the 12 LMICs studied. Despite some expected country differences attributable to demographic differences, the results across countries show consistent results.

Table 7. Cost-Effectiveness Analysis: Range of Results Across 12 LMICs

Study	Additional DALYs Averted	Confidence in Positive Health Outcomes	Additional $ per DALY Averted (US))
Smith et al. - MMS vs. IFAS	181,893 - 9,509,245	100.0%	$4.83 - $11.56
Keats et al. - MMS vs. IFAS	47,187 - 3,922,329	100.0%	$15.82 - $49.50
WHO - 13/15 MMS vs. IFAS	27,743 - 1,913,169	99.8%	$28.79 - $70.56
WHO - UNIMMAP vs. IFAS	53,077 - 4,411,068	98.9%	$14.07 - $44.05
WHO - 13/15 MMS vs. IFAS (30 mg)	27,743 - 1,913,169	99.8%	$46.07 - $112.89
WHO - 13/15 MMS vs. IFAS (60 mg)	27,743 - 1,913,169	99.8%	$28.79 - $70.56
WHO - UNIMMAP vs. IFAS (30 mg)	53,077 - 4,411,068	98.9%	$22.51 - $70.49

Analysis is conducted using statistically significant health effects of transitioning from IFAS to MMS.

- Across meta-analyses, transitioning from IFAS to MMS averts DALYs with almost 100 percent certainty, regardless of formulation.
- Transitioning to the UNIMMAP formulation averts more DALYs than transitioning to the 13/15 MMS formulation.
- Across meta-analyses, transitioning from IFAS to MMS is considered cost-effective regardless of whether one applies demand side cost-effectiveness thresholds (such as the WHO GDP per capita) or supply side cost-effectiveness thresholds (Leech, Kim, Cohen & Neumann, 2018; Woods et al., 2016).
- The UNIMMAP formulation is more cost-effective than the 13/15 MMS formulation.[3]
- Differences in cost-effectiveness are attributed to the different epidemiological profiles of countries such as the prevalence of health outcomes, life expectancy and age of first pregnancy.

[3] It is important to note that we use the UNIMMAP unit cost for both the UNIMMAP and MMS 13/15 due to data availability. Therefore, while MMS 13/15 generates fewer health benefits, the cost-effectiveness of MMS 13/15 may be slightly underestimated if, on average, MMS 13/15 costs less than the UNIMMAP unit costs. This is unlikely to dramatically change results but is important to note.

Sensitivity Analysis: Using Statistically and Non-Statistically Significant Health Effects

The primary analysis evaluates the cost-effectiveness using statistically significant impacts on health. For robustness, a sensitivity analysis including the non-significant health outcomes was also incorporated. **Table 8** provides a comparison of the analysis with statistically significant health outcomes versus all health outcomes (significant and non-significant).

Table 8. Cost-Effectiveness Analysis Comparison of Statistically Significant Outcomes Versus all Health Outcomes (Significant and Non-Significant)

Study	Effect of Transitioning on Statistically Significant Health Outcomes			Effect of Transitioning on Statistically Significant and Non-Significant Health Outcomes		
	Additional DALYs Averted	Confidence in Positive Health Outcomes	Additional $ per DALY Averted (US))	Additional DALYs Averted	Confidence in Positive Health Outcomes	Additional $ per DALY Averted (US)
Smith et al.† MMS vs. IFAS	181,893 - 9,509,245	100.0%	$4.83 - $11.56	167,629 - 7,851,830	99.5% - 99.8%	$5.51 - $13.07
Keats et al. ‡ MMS vs. IFAS	47,187 - 3,922,329	100.0%	$15.82 - $49.50	97,196 - 6,592,582	85.0% - 97.5%	$7.67 - $18.42
WHO analysis ‡ 13/15 MMS vs. IFAS	27,743 - 1,913,169	99.8%	$28.79 - $70.56	18,319 - 1,479,997	52.4% - 67.5%	$34.07 - $192.51
WHO analysis UNIMMAP vs. IFAS	53,077 - 4,411,068	98.9%	$14.07 - $44.05	59,998 - 4,639,692	68.3% - 87.9%	$13.38 - $36.49
WHO analysis 13/15 MMS vs. IFAS (30 mg)	27,743 - 1,913,169	99.8%	$46.07 - $112.89	87,446 - 5,295,562	87.5% - 95.6%	$14.46 - $33.40
WHO analysis 13/15 MMS vs. IFAS (60 mg)	27,743 - 1,913,169	99.8%	$28.79 - $70.56	-179,187 - -9,421,620	2.7% - 8.6%	$-17.00 - $-4.34
WHO analysis UNIMMAP vs. IFAS (30 mg)	53,077 - 4,411,068	98.9%	$22.51 - $70.49	158,751 - 10,090,500	92.3% - 98.2%	$7.98 - $16.90
WHO analysis UNIMMAP vs. IFAS (60 mg)	53,077 - 4,411,068	98.9%	$14.07 - $44.05	-186,884 -8,987,329	3.0% - 10.2%	$-21.13 - $-4.13

*Highlighted column implies only statistically significant outcomes used.
† Included health outcomes (Smith et al.): small for gestational age, preterm, low birth weight, neonatal mortality, infant mortality, stillbirth.
‡ Included health outcomes (Keats et al. and WHO): maternal anaemia, maternal mortality, small for gestational age, preterm, low birth weight, neonatal mortality, stillbirth.

- Most results remained unchanged (in terms of direction and magnitude) upon including non-significant outcomes: transitioning to MMS from IFAS to MMS averts DALYs with high certainty and the UNIMMAP formulation remains more effective and cost-effective than the 13/15 MMS formulation.

- With respect to transitioning from IFAS (30 mg) versus IFAS (60 mg):
    - Transitioning from IFAS (30 mg) to any type of MMS formulation was found to be cost-effective and yields positive health outcomes with high certainty.
    - Transitioning from IFAS (60 mg) to any type of MMS formulation was not found to be cost-effective and had a low chance of yielding positive health outcomes. This result is entirely driven by the relative risks for neonatal mortality which were non-significant but concentrated above 1.00.

Individual Country Analyses

See Annex A for the results from the 12 individual country analyses.

Discussion

Overall, the analysis conducted using the MMS Cost-benefit Tool found that transitioning to MMS is a highly cost-effective nutrition intervention to improve maternal and newborn health. This Nutrition International analysis contributed to the WHO policy recommendation update released on July 30, 2020 as part of the "nutritional interventions update: multiple micronutrient supplements during pregnancy" where the recommendation on MMS during pregnancy changed from "not recommended" to "recommended in the context of rigorous research". With the new evidence on effectiveness and cost-effectiveness available as well as updated WHO Guidelines, governments in LMICs should strongly consider investment into implementation research on MMS.

The analysis conducted using the *MMS Cost-benefit Tool* found that transitioning to MMS is highly cost-effective, across the sample of the twelve countries analyzed (representing Nutrition International's focal countries). These results were robust to the inclusion of non-statistically significant health outcomes. The only exception is the scenario of transitioning from IFAS (60 mg) to either type of MMS formulation when non-statistically significant health outcomes were included in the analysis, which should be interpreted with caution.

The *MMS Cost-Benefit Tool* has been expanded to include over 30 pre-set country analyses and remains available for running custom analyses for additional countries. The *MMS Cost-Benefit Tool*, with its outputs and country-level knowledge briefs available, can be used by governments and the nutrition community to inform evidence-based policy decisions and investments into maternal nutrition.

Recent research has filled essential evidence gaps related to MMS needed to produce an updated WHO recommendation. The new WHO recommendation, however, highlighted the need for rigorous research to be conducted to further inform the introduction of MMS in interested countries. Research areas included better understanding the impact and program effectiveness of switching from IFAS to MMS on

important health outcomes, equity, acceptability, feasibility, sustainability, cost-effectiveness and healthcare resources in different country settings. At this time, the meta-analyses used as the basis for the MMS effect sizes on health outcomes, including Keats et al. (2019) and Smith et al. (2017), are the best available evidence of the effectiveness of MMS. Moving forward, the WHO recommends establishing higher quality estimates on select infant and neonatal outcomes by conducting "controlled clinical trials in which early pregnancy ultrasound is used to establish gestational age with certainty." It would also be helpful to explore the real cost of 'transitioning' (rather than the supplement and delivery cost) from IFAS to MMS, such as re-training staff on MMS, updating and developing behaviour change communication materials on supplementation, updating guidelines and administration. In addition, it will be important to monitor the future of MMS pricing, particularly if MMS production were to scale greatly, and study the unit cost of quality MMS production and delivery across manufacturers based in LMICs over time. Future evaluation and research in these areas may improve the precision of the cost-effectiveness estimates on MMS versus IFAS.

We recommend countries invest in better understanding inputs for their context. The *MMS Cost-Benefit Tool* remains openly available for users to run custom scenarios in the cost-effectiveness analyses to inform their policy decisions, investments and implementation research.

Annex A

Bangladesh

Bangladesh: Key Messages

- Bangladesh is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $16.42) than transitioning to an MMS with 13/15 micronutrients (US $28.79) in the context of Bangladesh.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 9. Bangladesh: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	1,268,067	12,640	100.0%	$5.99	487
Keats et al. - MMS vs. IFAS	410,978	0	100.0%	$18.47	158
WHO analysis - 13/15MMS vs. IFAS	263,580	0	99.8%	$28.79	101
WHO analysis - UNIMMAP vs. IFAS	462,159	0	98.9%	$16.42	177
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	263,580	0	99.8%	$46.07	63
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	263,580	0	99.8%	$28.79	101
WHO analysis - UNIMMAP vs. IFAS (30 mg)	462,159	0	98.9%	$26.28	111
WHO analysis - UNIMMAP vs. IFAS (60 mg)	462,159	0	98.9%	$16.42	177

Table 10. Bangladesh: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	1,114,239	10,482	99.9%	$6.81	428
Keats et al. - MMS vs. IFAS	804,990	4,077	96.8%	$9.40	309
WHO analysis - 13/15 MMS vs. IFAS	222,794	-205.5	67.5%	$34.07	86
WHO analysis - UNIMMAP vs. IFAS	489,968	0	82.9%	$15.49	188
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	681,073	6,222	95.1%	$17.83	163
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-1,086,575	-18,570	6.2%	$-6.99	-417
WHO analysis - UNIMMAP vs. IFAS (30 mg)	1,144,653	9,182	97.0%	$10.61	275
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-1,146,743	-22,955	8.4%	$-6.62	-440

Table 11. Bangladesh: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	436,075 (F) -218,381 (M)	99.2% (F) 12.6% (M)	465,147	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	290,717	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-58,143 (F) -72,794 (M)	38.8%	116,287	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	145,358 (F) 181,984 (M)	89.4%	116,287	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-639,576 (F) -800,730 (M)	4.5%	116,287	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	290,717 (F) 363,968 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-726,791 (F) -909,920 (M)	3.0%	0	50.0%

Burkina Faso

Burkina Faso: Key Messages

- Burkina Faso is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $34.43) than transitioning to an MMS with 13/15 micronutrients (US $53.88) in the context of Burkina Faso.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 12. Burkina Faso: Statistically Significant Health Outcomes

Meta-Analyses	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	254,162	3,635	100.0%	$7.34	268
Keats et al. - MMS vs. IFAS	48,143	0	99.9%	$38.72	51
WHO analysis - 13/15 MMS vs. IFAS	34,604	0	99.7%	$53.88	37
WHO analysis - UNIMMAP vs. IFAS	54,153	0	98.8%	$34.43	57
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	34,604	0	99.7%	$86.20	23
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	34,604	0	99.7%	$53.88	37
WHO analysis - UNIMMAP vs. IFAS (30 mg)	54,153	0	98.8%	$55.08	36
WHO analysis - UNIMMAP vs. IFAS (60 mg)	54,153	0	98.8%	$34.43	57

Table 13. Burkina Faso: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	205,899	2,784	99.2%	$9.00	217
Keats et al. - MMS vs. IFAS	110,467	972.7	86.5%	$16.88	117
WHO analysis - 13/15 MMS vs. IFAS	9,684	-245.9	53.5%	$192.51	10
WHO analysis - UNIMMAP vs. IFAS	64,197	0	74.4%	$29.00	68
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	135,701	1,977	93.5%	$21.98	89
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-350,364	-6,596	2.7%	$-5.32	-370
WHO analysis - UNIMMAP vs. IFAS (30 mg)	244,220	3,175	96.7%	$12.21	161
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-385,863	-7,938	3.0%	$-4.83	-407

Table 14. Burkina Faso: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	117,848 (F) -60,875 (M)	99.2% (F) 12.6% (M)	88,243	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	55,152	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-15,713 (F) -20,292 (M)	38.8%	22,061	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0 (F) 0 (M)	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	39,283 (F) 50,729 (M)	89.4%	22,061	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-172,844 (F) -223,209 (M)	4.5%	22,061	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	78,565 (F) 101,459 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-196,413 (F) -253,646 (M)	3.0%	0	50.0%

Ethiopia

Ethiopia: Key Messages

- Ethiopia is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $21.50) than transitioning to an MMS with 13/15 micronutrients (US $43.58) in the context of Ethiopia.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 15. Ethiopia: Statistically Significant Health Outcomes

Meta-Analyses	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	1,561,983	19,677	100.0%	$6.39	257
Keats et al. - MMS vs. IFAS	412,906	0	99.9%	$24.18	68
WHO analysis - 13/15 MMS vs. IFAS	229,136	0	99.8%	$43.58	38
WHO analysis - UNIMMAP vs. IFAS	464,474	0	98.8%	$21.50	76
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	229,136	0	99.8%	$69.70	24
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	229,136	0	99.8%	$43.58	38
WHO analysis - UNIMMAP vs. IFAS (30 mg)	464,474	0	98.8%	$34.40	48
WHO analysis - UNIMMAP vs. IFAS (60 mg)	464,474	0	98.8%	$21.50	76

Table 16. Ethiopia: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	1,217,099	14,203	98.5%	$8.20	200
Keats et al. - MMS vs. IFAS	875,133	6,826	89.6%	$11.41	144
WHO analysis - 13/15 MMS vs. IFAS	111,979	-735.4	55.6%	$89.1	18
WHO analysis - UNIMMAP vs. IFAS	510,198	0	74.9%	$19.50	84
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	876,168	11,395	91.1%	$18.23	90
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-2071,416	-35,392	4.2%	$-4.82	-340
WHO analysis - UNIMMAP vs. IFAS (30 mg)	1,601,896	17,329	95.4%	$9.97	165
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-2,219,045	-43,321	5.2%	$-4.50	-365

Table 17. Ethiopia: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	551,640 (F) -434,362 (M)	99.2% (F) 12.6% (M)	688,030	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	430,019	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-73,552 (F) -144,787 (M)	38.8%	172,008	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	0.0%	0	50.0%
WHO analysis - 13/15 MS vs. IFAS (30 mg)	183,880 (F) 361,969 (M)	89.4%	172, 008	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-809,072 (F) -1,592,662 (M)	4.5%	172,008	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	367,760 (F) 723,937 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-919,400 (F) -1,809,843 (M)	3.7%	0	50.0%

India

India: Key Messages

- India is transitioning from IFAS (100 mg) to using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $14.07) than transitioning to an MMS with 13/15 micronutrients (US $32.44) in the context of India.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 18. India: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	9,509,245	99,691	100.0%	$6.53	625
Keats et al. - MMS vs. IFAS	3,922,329	0	100.0%	$15.82	258
WHO analysis - 13/15 MMS vs. IFAS	1,913,169	0	99.8%	$32.44	126
WHO analysis - UNIMMAP vs. IFAS	4,411,068	0	98.9%	$14.07	290
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	1,913,169	0	99.8%	$51.90	79
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	1,913,169	0	99.8%	$32.44	126
WHO analysis - UNIMMAP vs. IFAS (30 mg)	4,411,068	0	98.9%	$22.51	181
WHO analysis - UNIMMAP vs. IFAS (60 mg)	4,411,068	0	98.9%	$14.07	290

Table 19. India: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	7,851,830	75,424	99.8%	$7.90	516
Keats et al. - MMS vs. IFAS	6,592,582	31,111	97.5%	$9.40	434
WHO analysis - 13/15 MMS vs. IFAS	1,479,997	-3,517	65.1%	$41.93	97
WHO analysis - UNIMMAP vs. IFAS	4,639,692	0	87.9%	$13.38	305
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	5,295,562	53,348	95.6%	$18.75	218
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-9,421,620	-163,131	5.0%	$-6.59	-620
WHO analysis - UNIMMAP vs. IFAS (30 mg)	10,090,500	79,807	98.2%	$9.84	415
WHO analysis - UNIMMAP vs. IFAS (60 mg	-8,987,329	-199,517	9.2%	$-6.91	-591

Table 20. India: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	3,409,065 (F) -1,906,859 (M)	99.2% (F) 12.6% (M)	3,999,826	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	2,124,891	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-454,542 (F) -635,620 (M)	38.8%	849,957	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	1,136,355 (F) 1,589,049 (M)	89.4%	849,957	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-4,999,962 (F) -6,991,816 (M)	4.5%	849,957	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	2,272,710 (F) 3,178,098 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-5,681,775 (F) -7,945,246 (M)	3.7%	0	50.0%

Indonesia

Indonesia: Key Messages

- Indonesia is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $27.24) than transitioning to an MMS with 13/15 micronutrients (US $50.76) in the context of Indonesia.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 21. Indonesia: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	925,250	8,616	100.0%	$11.56	709
Keats et al. - MMS vs. IFAS	349,041	0	100.0%	$30.63	268
WHO analysis - 13/15 MMS vs. IFAS	210,669	0	99.8%	$50.76	162
WHO analysis - UNIMMAP vs. IFAS	392,574	0	98.8%	$27.24	301
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	210,669	0	99.8%	$81.21	101
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	210,669	0	99.8%	$50.76	162
WHO analysis - UNIMMAP vs. IFAS (30 mg)	392,574	0	98.8%	$43.58	188
WHO analysis - UNIMMAP vs. IFAS (60 mg)	392,574	0	98.8%	$27.24	301

Table 22. Indonesia: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	818,022	7,151	99.8%	$13.07	627
Keats et al. - MMS vs. IFAS	624,877	2,930	95.7%	$17.11	479
WHO analysis - 13/15 MMS vs. IFAS	157,321	-213.1	65.9%	$67.97	121
WHO analysis - UNIMMAP vs. IFAS	430,536	0	85.7%	$24.84	330
WHO - 13/15 MMS vs. IFAS (30 mg)	512,146	4,634	94.5%	$33.40	245
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-856,464	-14,063	6.2%	$-12.48	-657
WHO analysis - UNIMMAP vs. IFAS (30 mg)	937,429	6,925	97.5%	$18.25	449
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-836,695	-17,312	10.1%	$-12.72	-642

Table 23. Indonesia: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	287,564 (F) -189,110 (M)	99.2% (F) 12.6% (M)	343,127	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	214,455	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-38,342 (F) -63,037 (M)	38.8%	85,782	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	95,855 (F) 157,592 (M)	89.4%	85,782	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-421,761 (F) -693,403 (M)	4.5%	85,782	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	191,709 (F) 315,183 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-479,273 (F) -787,958 (M)	3.7%	0	50.0%

Kenya

Kenya: Key Messages

- Kenya is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $44.05) than transitioning to an MMS with 13/15 micronutrients (US $70.56) in the context of Kenya.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 24. Kenya: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	353,537	4,619	100.0%	$7.92	458
Keats et al. - MMS vs. IFAS	56,488	0	99.9%	$49.50	73
WHO analysis - 13/15 MMS vs. IFAS	39,670	0	99.7%	$70.56	51
WHO analysis - UNIMMAP vs. IFAS	63,537	0	98.8%	$44.05	82
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	39,670	0	99.7%	$112.89	32
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	39,670	0	99.7%	$70.56	51
WHO analysis - UNIMMAP vs. IFAS (30 mg)	63,537	0	98.8%	$70.49	51
WHO analysis - UNIMMAP vs. IFAS (60 mg)	63,537	0	98.8%	$44.05	82

Table 25. Kenya: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	340,275	4,414	99.8%	$8.23	441
Keats et al. - MMS vs. IFAS	151,926	1,426	85.0%	$18.42	197
WHO analysis - 13/15 MMS vs. IFAS	21,608	-12.67	55.6%	$129.50	28
WHO analysis - UNIMMAP vs. IFAS	76,703	0	68.3%	$36.49	99
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	153,408	2,028	87.5%	$29.10	124
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-354,963	-5,842	4.7%	$-7.89	-460
WHO analysis - UNIMMAP vs. IFAS (30 mg)	264,989	2,915	92.3%	$16.90	214
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-394010	-7,287	5.5%	$-7.10	-510

Table 26. Kenya: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	151,038 (F) -52,556 (M)	99.2% (F) 12.6% (M)	147,354	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	92,096	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-20,138 (F) -17,519 (M)	38.8%	36,838	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	50,346 (F) 43,797 (M)	89.4%	36,838	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-221,522 (F) -192,706 (M)	4.5%	36,838	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	100,692 (F) 87,594 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-251,729 (F) -218,984 (M)	3.7%	0	50.0%

Madagascar

Madagascar: Key Messages

- Madagascar is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $26.52) than transitioning to an MMS with 13/15 micronutrients (US $34.72) in the context of Madagascar.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 27. Madagascar: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	250,754	2,549	100.0%	$8.13	135
Keats et al. - MMS vs. IFAS	68,291	0	99.9%	$29.80	37
WHO analysis - 13/15MMS vs. IFAS	58,678	0	99.6%	$34.72	32
WHO analysis - UNIMMAP vs. IFAS	76,815	0	98.8%	$26.52	41
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	58,678	0	99.6%	$55.56	20
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	58,678	0	99.6%	$34.72	32
WHO analysis - UNIMMAP vs. IFAS (30 mg)	76,815	0	98.8%	$42.44	26
WHO analysis - UNIMMAP vs. IFAS (60 mg)	76,815	0	98.8%	$26.52	41

Table 28. Madagascar: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	259,782	2,685	99.8%	$7.84	140
Keats et al. - MMS vs. IFAS	145,075	822.4	90.3%	$14.04	78
WHO analysis - 13/15 MMS vs. IFAS	46,330	-3.615	68.7%	$43.98	25
WHO analysis - UNIMMAP vs. IFAS	85,951	0	79.7%	$23.71	46
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	123,848	1,160	93.0%	$26.32	42
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-175,152	-3,329	8.6%	$-11.63	-94
WHO analysis - UNIMMAP vs. IFAS (30 mg)	196,692	1,663	95.4%	$16.57	66
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-190,901	-4,157	10.2%	$-10.67	-103

Table 29. Madagascar: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	82,153 (F) -33,583 (M)	99.2% (F) 12.6% (M)	87,630	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	54,769	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-10,954 (F) -11,194 (M)	38.8%	21,907	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	27,384 (F) 27,986 (M)	89.4%	21,907	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-120,491 (F) -123,139 (M)	4.5%	21,907	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	54,769 (F) 55,972 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-136,921 (F) -139,931 (M)	3.7%	0	50.0%

Nigeria

Nigeria: Key Messages

- Nigeria is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $29.70) than transitioning to an MMS with 13/15 micronutrients (US $52.18) in the context of Nigeria.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 30. Nigeria: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	3,602,446	52,475	100.0%	$5.09	1,630
Keats et al. - MMS vs. IFAS	547,413	0	99.9%	$33.48	248
WHO analysis - 13/15MMS vs. IFAS	351,248	0	99.7%	$52.18	159
WHO analysis - UNIMMAP vs. IFAS	615,789	0	98.8%	$29.70	279
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	351,248	0	99.7%	$83.48	99
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	351,248	0	99.7%	$52.18	159
WHO analysis - UNIMMAP vs. IFAS (30 mg)	615,789	0	98.8%	$47.62	174
WHO analysis - UNIMMAP vs. IFAS (60 mg)	615,789	0	98.8%	$29.70	279

Table 31. Nigeria: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	3,327,787	47,843	99.3%	$5.51	1,506
Keats et al. - MMS vs. IFAS	1,567,752	18,816	80.9%	$11.69	709
WHO analysis - 13/15 MMS vs. IFAS	111,268	473.7	52.4%	$164.71	50
WHO analysis - UNIMMAP vs. IFAS	794,844	0	65.2%	$23.06	360
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	1,575,076	25,158	82.7%	$18.62	445
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-4,071,039	-70,054	5.1%	$-4.50	-1,842
WHO analysis - UNIMMAP vs. IFAS (30 mg)	2,885,997	35,264	89.7%	$10.16	816
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-4,433,040	-88,160	6.4%	$-4.13	-2,006

Table 32. Nigeria: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	1,326,478 (F) -724,101 (M)	99.2% (F) 12.6% (M)	1,785,283	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	1,115,802	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-176,864 (F) -241,367 (M)	38.8%	446,321	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	442,159 (F) 603,417 (M)	89.4%	446,321	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-1,945,501 (F) -2,655,037 (M)	4.5%	446,321	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	884,319 (F) 1,206,835 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-2,210,797 (F) -3,017,087 (M)	3.7%	0	50.0%

Pakistan

Pakistan: Key Messages

- Pakistan is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $14.18) than transitioning to an MMS with 13/15 micronutrients (US $39.80) in the context of Pakistan.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 33. Pakistan: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	2,379,157	29,862	100.0%	$4.83	790
Keats et al. - MMS vs. IFAS	720,501	0	100.0%	$15.95	239
WHO analysis - 13/15 MMS vs. IFAS	288,132	0	99.8%	$39.80	96
WHO analysis - UNIMMAP vs. IFAS	810,238	0	98.9%	$14.18	269
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	288,132	0	99.8%	$63.80	60
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	288,132	0	99.8%	$39.80	96
WHO analysis - UNIMMAP vs. IFAS (30 mg)	810,238	0	98.9%	$22.69	168
WHO analysis - UNIMMAP vs. IFAS (60 mg)	810,238	0	98.9%	$14.18	269

Table 34. Pakistan: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	2,022,990	24,457	99.2%	$5.68	672
Keats et al. - MMS vs. IFAS	1,497,543	11,061	92.9%	$7.67	497
WHO analysis - 13/15 MMS vs. IFAS	255,432	20.53	58.8%	$44.98	85
WHO analysis - UNIMMAP vs. IFAS	852,315	0	75.7%	$13.48	283
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	1,271,168	15,434	90.3%	$14.46	264
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-2,646,670	-44,017	5.3%	$-4.34	-879
WHO analysis - UNIMMAP vs. IFAS (30 mg)	2,303,366	22,019	94.6%	$7.98	478
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-2,775,312	-55,047	7.5%	$-4.14	-922

Table 35. Pakistan: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	801,630 (F) -549,979 (M)	99.2% (F) 12.6% (M)	1,166,253	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	728,908	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-106,884 (F) -183,326 (M)	38.8%	291,563	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	267,210 (F) 458,316 (M)	89.4%	291,563	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-1,175,723 (F) -2,016,589	4.5%	291,563	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	534,420 (F) 916,631 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-1,1336,049 (F) -2,291,578 (M)	3.7%	0	50.0%

Philippines

Philippines: Key Messages

- Philippines is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $19.50) than transitioning to an MMS with 13/15 micronutrients (US $38.39) in the context of the Philippines.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 36. Philippines: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	590,505	5,162	100.0%	$10.74	829
Keats et al. - MMS vs. IFAS	288,787	0	100.0%	$21.96	405
WHO analysis - 13/15 MMS vs. IFAS	165,176	0	99.8%	$38.39	232
WHO analysis - UNIMMAP vs. IFAS	324,771	0	98.9%	$19.50	456
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	165,176	0	99.8%	$61.42	145
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	165,176	0	99.8%	$38.39	232
WHO analysis - UNIMMAP vs. IFAS (30 mg)	324,771	0	98.9%	$31.24	285
WHO analysis - UNIMMAP vs. IFAS (60 mg)	324,771	0	98.9%	$19.50	456

Table 37. Philippines: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	556,895	4,679	100.0%	$11.39	782
Keats et al. - MMS vs. IFAS	451,493	1,487	99.0%	$14.04	634
WHO analysis - 13/15 MMS vs. IFAS	139,715	-141.9	76.8%	$45.39	196
WHO analysis - UNIMMAP vs. IFAS	340,730	0	93.4%	$18.61	478
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	319,159	2,426	97.7%	$31.79	280
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-372,983	-7,508	8.8%	$-17.00	-523
WHO analysis - UNIMMAP vs. IFAS (30 mg)	597,079	3,683	99.0%	$16.99	524
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-300,142	-9,208	18.8%	$-21.13	-421

Table 38. Philippines: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	193,686 (F) -76,335 (M)	99.2% (F) 12.6% (M)	165,582	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	103,489	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-25,825 (F) -25,445 (M)	38.8%	41,396	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	64,562 (F) 63,612 (M)	89.4%	41,396	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-284,072 (F) -279,895 (M)	4.5%	41,396	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	129,124 (F) 127,225 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-322,810 (F) -318,062 (M)	3.7%	0	50.0%

Senegal

Senegal: Key Messages

- Senegal is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $23.83) than transitioning to an MMS with 13/15 micronutrients (US $45.58) in the context of Senegal.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 39. Senegal: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	181,893	2,288	100.0%	$6.95	394
Keats et al. - MMS vs. IFAS	47,187	0	99.9%	$26.80	102
WHO analysis - 13/15 MMS vs. IFAS	27,743	0	99.8%	$45.58	60
WHO analysis - UNIMMAP vs. IFAS	53,077	0	98.8%	$23.83	115
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	27,743	0	99.8%	$72.93	38
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	27,743	0	99.8%	$45.58	60
WHO analysis - UNIMMAP vs. IFAS (30 mg)	53,077	0	98.8%	$38.12	72
WHO analysis - UNIMMAP vs. IFAS (60 mg)	53,077	0	98.8%	$23.83	115

Table 40. Senegal: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	167,629	2,060	99.8%	$7.54	363
Keats et al. - MMS vs. IFAS	97,196	716.9	91.5%	$13.01	211
WHO analysis - 13/15 MMS vs. IFAS	18,319	-29.26	59.5%	$69.0	40
WHO analysis - UNIMMAP vs. IFAS	59,998	0	77.5%	$21.08	130
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	87,446	1,077	91.2%	$23.14	118
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-179,187	-3,189	4.8%	$-7.06	-388
WHO analysis - UNIMMAP vs. IFAS (30 mg)	158,751	1,580	95.6%	$12.75	215
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-186,884	-3,950	6.9%	$-6.77	-405

Table 41. Senegal: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	71,322 (F) -30,723 (M)	99.2% (F) 12.6% (M)	71,687	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	44,805	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-9,510 (F) -10,241 (M)	38.8%	17,922	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	23,774 (F) 25,603 (M)	89.4%	17,922	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-105,605 (M) -112,651 (F)	4.5%	17,922	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	47,548 (F) 51,205 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-118,869 (F) -128,013 (M)	3.7%	0	50.0%

Tanzania

Tanzania: Key Messages

- Tanzania is currently using IFAS (60 mg).
- Transitioning to UNIMMAP is more cost-effective per DALY averted (US $38.70) than transitioning to an MMS with 13/15 micronutrients (US $42.62) in the context of Tanzania.
- If the analysis is conducted using all health outcomes (statistically significant and non-statistically significant), the impact of transitioning from IFAS (30 mg) to any type of MMS is positive. However, the impact of transitioning from IFAS (60 mg) to any type of MMS is negative. This is entirely driven by the RRs for neonatal mortality which have a negative expected value.
- The effect of MMS on neonatal mortality is only positive for female neonates (Smith analysis) and for transitioning from IFAS (30 mg) to MMS. The effect of MMS on stillbirth is positive across all studies.

Table 42. Tanzania: Statistically Significant Health Outcomes

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	689,955	8,378	100.0%	$7.26	350
Keats et al. - MMS vs. IFAS	115,062	0	99.9%	$43.53	58
WHO analysis - 13/15 MMS vs. IFAS	117,524	0	99.4%	$42.62	60
WHO analysis - UNIMMAP vs. IFAS	129,426	0	98.8%	$38.70	66
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	117,524	0	99.4%	$68.20	37
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	117,524	0	99.4%	$42.62	60
WHO analysis - UNIMMAP vs. IFAS (30 mg)	129,426	0	98.8%	$61.92	41
WHO analysis - UNIMMAP vs. IFAS (60 mg)	129,426	0	98.8%	$38.70	66

Table 43. Tanzania: Sensitivity Analysis Using all Health Outcomes (Significant and Non-Significant)

Study	Additional DALYs Averted	Additional Child Deaths Averted	Confidence in Positive Health Outcomes	Additional Cost per DALY Averted (US)	Benefit-Cost Ratio
Smith et al. - MMS vs. IFAS	607,544	7,072	99.6%	$8.24	308
Keats et al. - MMS vs. IFAS	304,672	2,580	84.7%	$16.44	154
WHO analysis - 13/15 MMS vs. IFAS	52,671	-304.1	56.5%	$95.10	27
WHO analysis - UNIMMAP vs. IFAS	162,479	0	70.0%	$30.83	82
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	347,725	4,372	90.2%	$23.05	110
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-790,342	-13,664	4.3%	$-6.34	-401
WHO analysis - UNIMMAP vs. IFAS (30 mg)	583,985	6,680	94.1%	$13.72	185
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-891,287	-16,700	4.4%	$-5.62	-452

Table 44. Tanzania: Deep Dive on Neonatal Mortality and Stillbirth

	Neonatal Mortality		Stillbirth	
Study	**Additional DALYs Averted**	**Confidence in Positive Health Outcomes**	**Additional DALYs Averted (US)**	**Confidence in Positive Health Outcomes**
Smith et al. - MMS vs. IFAS	268,165 (F) -145,638 (M)	99.2% (F) 12.6% (M)	260,462	98.8%
Keats et al. - MMS vs. IFAS	0 (F) 0 (M)	50.0%	162,789	85.2%
WHO analysis - 13/15 MMS vs. IFAS	-35,755 (F) -48,546 (M)	38.8%	65,115	63.1%
WHO analysis - UNIMMAP vs. IFAS	0 (F) 0 (M)	50.0%	0	50.0%
WHO analysis - 13/15 MMS vs. IFAS (30 mg)	89,388 (F) 121,365 (M)	89.4%	65,115	63.1%
WHO analysis - 13/15 MMS vs. IFAS (60 mg)	-393,306 (F) -534,005 (M)	4.5%	65,115	63.1%
WHO analysis - UNIMMAP vs. IFAS (30 mg)	178,777 (F) 242,729 (M)	92.4%	0	50.0%
WHO analysis - UNIMMAP vs. IFAS (60 mg)	-446,942 (F) -606,824 (M)	3.7%	0	50.0%

Annex B

Sensitivity to Transition Costs

The main analysis did not factor for transition costs. As mentioned above, transition cost is the cost for non-commodity expenses related to transition from an IFAS to MMS program. Transition costs could include development of training materials and new policies/regulations, training of health workers, or behaviour change communications, etc. related to the startup of the new program. Since transition costs can vary widely by country, there is no standard input for transition costs. In this sensitivity analysis we assume a transition cost of ~$1 US/head, aligning with the Nutrition International MMS Policy Briefs.

The following sensitivity analysis is for the "all health outcomes (significant and non-significant)" scenarios for robustness. Note the sensitivity for 13/15 MMS vs. IFAS (60 mg) and UNIMMAP vs. IFAS (60 mg) are not reported here since the cost-effectiveness criteria were already negative in all scenarios without the transition cost.

Across all countries and formulation scenarios, **the cost-effectiveness criteria (cost per DALY averted and Benefit-Cost Ratio) are not sensitive to transition costs** when evaluated against most cost-effectiveness thresholds. This said, in the case of transitioning from 13/15 MMS to any type of IFAS, it is less cost-effective relative to the other transitions and may be above the governments' ability to pay in some cases. For example, in Burkina Faso, factoring for the transition would result in going from a cost of US $192.51 per DALY averted to US $339.00 per DALY averted. This is much more expensive than in a comparable country (in terms of GDP) such as Madagascar, which would go from US $43.98 per DALY averted to US $87.15 per DALY averted.

Table 45. Sensitivity to Transition Costs: WHO 13/15 MMS vs. IFAS

	Without Transition Cost		With Transition Cost		
Country	**Additional Cost per DALY Averted**	**Benefit-Cost Ratio**	**Transition Cost (US)**	**Additional Cost per DALY Averted (US)**	**Benefit-Cost Ratio**
Bangladesh	$34.07	86	5 million	$56.51	52
Burkina Faso	$192.51	10	2 million	$399.00	5
Ethiopia	$89.10	18	5 million	$133.82	12
India	$41.93	97	10 million	$48.69	84
Indonesia	$67.97	121	5 million	$99.75	82
Kenya	$129.50	28	2 million	$222.10	16
Madagascar	$43.98	25	2 million	$87.15	13
Nigeria	$164.71	50	10 million	$254.58	33

	Without Transition Cost			With Transition Cost	
Pakistan	$44.98	85	5 million	$209.60	40
Philippines	$45.39	196	5 million	$81.17	110
Senegal	$69.00	40	2 million	$178.21	15
Tanzania	$95.10	27	2 million	$133.08	19

Table 46. Sensitivity to Transition Costs: UNIMMAP vs. IFAS

	Without Transition Cost			With Transition Cost	
Country	**Additional Cost per DALY Averted**	**Benefit-Cost Ratio**	**Transition Cost (US)**	**Additional Cost per DALY Averted (US)**	**Benefit-Cost Ratio**
Bangladesh	$15.49	188	5 million	$25.69	113
Burkina Faso	$29.00	68	2 million	$60.19	33
Ethiopia	$19.50	84	5 million	$29.30	56
India	$13.38	305	10 million	$15.53	263
Indonesia	$24.84	330	5 million	$36.45	225
Kenya	$36.49	99	2 million	$62.57	58
Madagascar	$23.71	46	2 million	$46.97	23
Nigeria	$23.06	360	10 million	$35.64	233
Pakistan	$13.48	283	5 million	$29.30	283
Philippines	$18.61	478	5 million	$33.28	267
Senegal	$21.08	130	2 million	$54.41	50
Tanzania	$30.83	82	2 million	$43.14	59

Table 47. Sensitivity to Transition Costs: 13/15 MMS vs. IFAS (30 mg)

	Without Transition Cost			With Transition Cost	
Country	**Additional Cost per DALY Averted**	**Benefit-Cost Ratio**	**Transition Cost (US)**	**Additional Cost per DALY Averted (US)**	**Benefit-Cost Ratio**
Bangladesh	$17.83	163	5 million	$25.17	116
Burkina Faso	$21.98	89	2 million	$36.72	54
Ethiopia	$18.23	90	5 million	$23.94	69
India	$18.75	218	10 million	$20.64	198
Indonesia	$33.40	245	5 million	$43.17	190
Kenya	$29.10	124	2 million	$42.23	86
Madagascar	$26.32	42	2 million	$42.47	26
Nigeria	$18.62	445	10 million	$24.97	332
Pakistan	$14.46	264	5 million	$21.79	380
Philippines	$31.79	280	5 million	$47.46	188
Senegal	$23.14	118	2 million	$46.01	60
Tanzania	$23.05	110	2 million	$28.80	88

Table 48. Sensitivity to Transition Costs: UNIMMAP vs. IFAS (30 mg)

	Without Transition Cost		With Transition Cost		
Country	**Additional Cost per DALY Averted**	**Benefit-Cost Ratio**	**Transition Cost (US)**	**Additional Cost per DALY Averted (US)**	**Benefit-Cost Ratio**
Bangladesh	$10.61	275	5 million	$14.98	195
Burkina Faso	$12.21	161	2 million	$20.40	96
Ethiopia	$9.97	165	5 million	$13.09	125
India	$9.84	415	10 million	$10.83	377
Indonesia	$18.25	449	5 million	$23.58	348
Kenya	$16.90	214	2 million	$24.48	148
Madagascar	$16.57	66	2 million	$26.74	41
Nigeria	$10.16	816	10 million	$13.64	609
Pakistan	$7.98	478	5 million	$11.89	697
Philippines	$16.99	524	5 million	$25.37	351
Senegal	$12.75	215	2 million	$25.34	108
Tanzania	$13.72	185	2 million	$17.15	148

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