



Multiple micronutrient supplementation cost–benefit tool for informing maternal nutrition policy and investment decisions

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Abstract

Antenatal multiple micronutrient supplementation (MMS) is an intervention that can help reach three of the six global nutrition targets, either directly or indirectly: a reduction in low birth weight, stunting, and anaemia in women of reproductive age. To support global guideline development and national decision-making on investments into maternal nutrition, Nutrition International developed a modelling tool called the MMS cost–benefit tool to help users understand whether antenatal MMS is better value for money than iron and folic acid supplementation (IFAS) during pregnancy. The MMS cost–benefit tool can generate estimates on the potential health impact, budget impact, economic value, cost-effectiveness and benefit–cost ratio of investing in MMS compared to IFAS in LMICs. In the 33 countries with data included in the tool, the MMS cost–benefit tool shows that transitioning is expected to generate substantial health benefits in terms of morbidity and mortality averted and can be very cost-effective in multiple scenarios for these countries. The cost per DALY averted averages at US\$ 23.61 and benefit–cost ratio ranges from US \$ 41–US\$ 1304: \$1.0, which suggest MMS is good value for money compared with IFAS. With its user-friendly design, open access availability, and online data-driven analytics, the MMS cost–benefit tool can be a powerful resource for governments and nutrition partners seeking timely and evidence-based analyses to inform policy-decision and investments towards the scale-up of MMS for pregnant women globally.

KEYWORDS

economic evaluation, maternal nutrition, multiple micronutrient supplementation, nutrition

1 | INTRODUCTION

Despite the World Health Organization (WHO) Member States commitment to achieving the World Health Assembly Global Nutrition Targets by 2025, millions of women and children remain undernourished (Heidkamp et al., 2021; Victora et al., 2021).

Multiple micronutrient supplementation (MMS) for pregnant women, a daily dose (i.e., a single daily tablet) containing 13–15 vitamins and minerals, including iron and folic acid (UNIMAP formulation), is a population-level health and nutrition intervention that can contribute to addressing micronutrient deficiencies where they are a public health problem and reaching three of the

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six global nutrition targets, either directly or indirectly: a reduction in low birth weight (LBW), stunting in children, and anaemia in women of reproductive age (World Health Organization, 2014). MMS, like IFAS, is a preventative intervention that complements but does not replace individualized care and treatment for women.

It is estimated that annually more than 20 million newborns (15.5%) are born with LBW (birth weight below 2500 g)—the highest prevalence being in South Asia and sub-Saharan Africa (UNICEF, 2004). Preterm birth (births before 37 weeks gestation) is the most common direct cause of neonatal mortality, and LBW is a major predictor of neonatal mortality and child morbidity, including stunting (World Health Organization, 2014). Anaemia affects 46.2% and 48.2% of pregnant women in Africa and South-East Asia, respectively (World Health Organization, 2021). In addition to maternal death, maternal anaemia is associated with an increased risk of infant mortality, preterm birth, LBW, lower infant iron stores, and compromised brain development in offspring (Gleason & Scrimshaw, 2007).

In 2016, the WHO guidelines for antenatal care stated that MMS was not recommended for routine use in antenatal care and that more evidence was required (World Health Organization, 2016). The guideline indicated, however, that policymakers in countries with a high prevalence of nutritional deficiencies may consider implementing MMS programmes for pregnant women. Shortly after that, two reviews concluded that MMS provides additional health benefits for newborns compared to IFAS and with no adverse health effects on newborns or mothers (Keats et al., 2019; Smith et al., 2017).

Moreover, recent cost-effectiveness studies showed that transitioning from IFAS to MMS for pregnancy was also cost-effective in saving lives and reducing life-long disability in Bangladesh, Pakistan and India (Kashi et al., 2019) as well as in Bangladesh and Burkina Faso (Engle-Stone et al., 2019). Despite this economic evidence in multiple countries, there remained caution from policymakers to invest in MMS during pregnancy until a clear WHO recommendation was released and more context-specific cost-effectiveness analyses were available.

To bridge this evidence gap, Nutrition International developed and launched a modelling tool called the MMS cost-benefit tool (referred to as “the MMS Tool”) in October 2019 to provide national and global policymakers with context-specific analyses that addresses the question: is antenatal MMS better value for money than IFAS? The MMS Tool was designed as an evidence-based, user-friendly and open-access online modelling tool that allows users to view results for health and economic analyses of 33 pre-loaded countries or conduct custom analysis for other LMICs (See user guide: <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>). The MMS Tool can be used by government policymakers or other users to generate estimates on the potential health impact, budget impact, economic value, cost-effectiveness and benefit-cost ratio (BCR) of investing in MMS compared to IFAS, which are important indicators to inform evidence-based decision-making on transitioning from IFAS to MMS programmes for pregnant women.

Key points

- With recent evidence and updated World Health Organization's guidance encouraging low- and middle-income countries (LMICs) to consider multiple micro-nutrient supplementation (MMS) for pregnant women, national governments are looking for additional analysis on the cost and cost-benefit of this nutrition intervention.
- Nutrition International's MMS cost-benefit tool is an evidence-based, open-access, and dynamic tool designed for governments and their partners to inform policy decisions and investments into MMS as part of maternal nutrition programming.
- The MMS cost-benefit tool uses a rigorous methodology to estimate the potential health impact, budget impact, economic value, cost-effectiveness, and benefit-cost ratio of investing in MMS compared to IFAS for 33 LMICs and has the capability to conduct custom analysis.
- The MMS cost-benefit tool's analysis demonstrates that investing in MMS compared to IFAS for antenatal care programming is consistently cost-effective in LMICs and the long-term economic value of health benefits generated by MMS far outweighs the costs.

At the request of the WHO Guideline Development Group in 2019, Nutrition International prepared a technical report with additional cost-effectiveness analyses to inform the guideline review process for the *nutritional interventions update on Multiple Micro-nutrient Supplements (MMS) during pregnancy* (World Health Organization, 2020). These updated guidelines recommend MMS as a population-level health and nutrition intervention to address micro-nutrient deficiencies where they are a public health problem to be delivered in the context of rigorous research, which means countries can initiate an antenatal MMS programme while conducting implementation research to better understand its impact and feasibility. The guidelines also recommended controlled clinical research to better understand the effects of MMS on preventing LBW (Tuncalp et al., 2020).

The aim of this paper is to describe the underlying methodology of the MMS Tool, present the results of a hypothetical MMS scale up scenario for four focus countries and 29 additional countries with pre-loaded data, and discuss the application of the MMS Tool for supporting the translation of evidence into action.

2 | METHODS

The MMS Tool applies a rigorous methodology (Kashi et al., 2019) to calculate the health impact, budget impact, economic value, cost-effectiveness, and cost-benefit of transitioning from IFAS to MMS

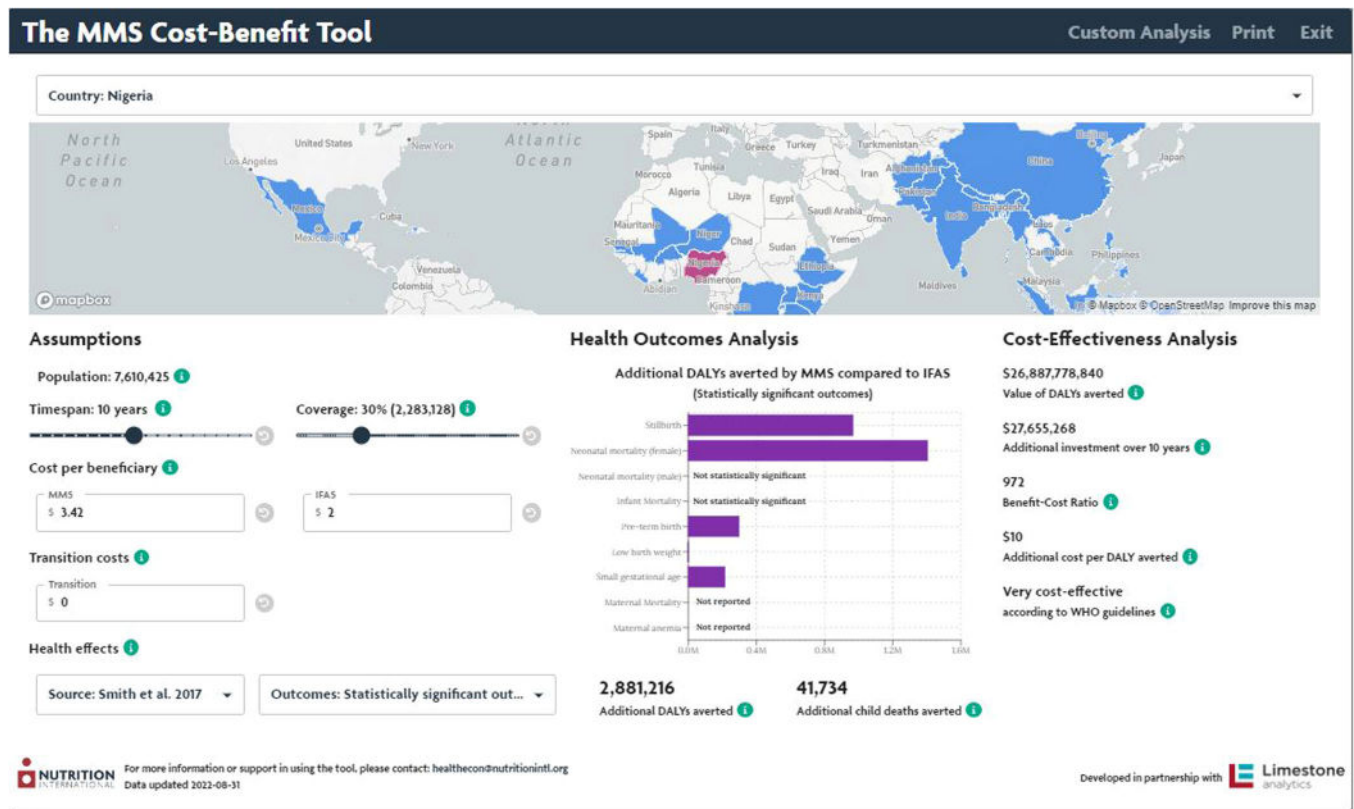


FIGURE 1 A screenshot example of the MMS cost-benefit tool. MMS, multiple micronutrient supplementation.

for pregnant women (Figure 1). At the time of this publication, there are 33 LMICs with quality-assured, pre-loaded data in the MMS Tool, whereby users can access results of analyses. There are also downloadable policy briefs for each of these countries to support advocacy and policy-oriented discussions (<https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/>).

2.1 | Default parameters and assumptions

The MMS Tool has an array of background data integrated into the underlying model, that were quality-assured (reviewed and validated by technical experts) to ensure accuracy, recency, and appropriateness. More detail on the standard data sources and definitions are found in the data source guide for the tool (Nutrition International, 2022). Several key default parameters can be modified by the user to align with the geographic or demographic context of interest. The population input is the number of pregnant women in the intervention area where the supplementation programme will take place and is calculated based on the national population (United Nations, 2019b) and crude birth rate (United Nations, 2019a). The default value assumes the intervention area is national. The hypothetical default intervention coverage percentage for MMS in the tool is that 30% of pregnant women in each country scenario will receive 180 tablets, to cover 6 months of pregnancy. This assumption is based on a conservative scenario informed by a review of Nutrition

International's programme data and Demographic Health Survey data on the receipt and consumption of at least 90 IFAS tablets in LMIC settings, but is mainly for illustrative purposes and can be changed in the tool by the user. The timespan of the supplementation programme over which the costs and health outcomes are calculated can be changed from a minimum of 1 year to a maximum of 20 years. The economic benefits are calculated for the lifespan (based on projections for each individual country) of both the mother and the child for each cohort year during that timespan. A 10-year programme timespan was used as a default in the tool.

Two main categories of cost are included in the MMS Tool: the unit cost of the supplements and programme transition costs. Supplement costs can vary by country, manufacturer, and over time. The published UNICEF supply catalogue prices were used as default values for the unit cost of IFAS and MMS (180 tablets) (UNICEF, 2018), however, users can modify the costs of the supplements to reflect their context. At the time of publication, the unit cost for 180 tablets is US\$ 2.00 for IFAS and US\$ 3.42 for MMS per pregnant woman. Transition cost refers to the cost of non-commodity expenses related to a transition from an IFAS to MMS programme. These could include the development of training materials and new policies and regulations, training of health workers, behaviour change communications, or other start-up programme costs. The calculations assume that transition costs are all incurred in the first year (i.e., the year during which the transition from IFAS to MMS begins). The MMS tool does not include a default value for transition costs,

instead, it is up to the user to input a value based on the country context. The transition costs can vary widely by country, and without systematically collected costing data on the transition it is difficult to accurately assign a default value.

2.2 | Health outcome analysis

The MMS Tool estimates a change in specific health outcomes from the transition of IFAS to MMS for pregnant women as well as total child deaths averted and disability-adjusted life years (DALYs) averted over a given programme scenario. Eight health outcomes of interest, based on findings from two published reviews (Keats et al., 2019; Smith et al., 2017), are included in the MMS Tool: maternal anaemia (third trimester haemoglobin <110 g per litre), preterm delivery, small for gestational age (SGA) newborns (defined by authors of trials), LBW, stillbirths, and maternal, neonatal (death in the first 28 days of life; disaggregated by sex), and infant mortality (death in the first year of life). When the MMS Tool calculates DALYs averted, the prevalence of LBW and infant mortality is adjusted to ensure that there is no double counting. Among LBW babies, most are preterm, SGA, or both. Therefore, reductions in preterm and SGA will result in fewer LBW babies. For this reason, LBW prevalence is adjusted to reflect only the change in term and adequate for gestational-age infants. The prevalence of SGA is adjusted to remove preterm SGA infants (Kozuki et al., 2017).

Since infant mortality (death in the first year of life) is inclusive of neonatal mortality (death in the first 28 days of life), the prevalence of infant mortality used in the calculation is net of neonatal mortality. The Smith et al. (2017) review only included analyses from studies comparing MMS to IFAS while the Keats et al. (2019) review also included comparisons of MMS to iron supplementation alone (without folic acid). Smith et al. found that MMS consumed during pregnancy reduced the risk of LBW by 12%, SGA births by 3%, preterm births by 8%, and stillbirth by 8%. Keats et al. (2019) found that MMS consumed during pregnancy also reduced the risk of LBW by 12%, and SGA births by 8% compared to IFAS. One main difference between these two studies is that Smith et al. (2017) found a difference in neonatal mortality for female neonates while Keats et al. (2019) did not examine sex-disaggregated mortality. Other health outcome differences between these meta-analyses can be found in Kashi et al. (2019). The user can select whether to use the Smith et al. (2017) meta-analysis or Keats et al. (2019) systematic review in the MMS Tool. The default view includes only the statistically significant health outcomes; however, the user can choose to view all health outcomes regardless of statistical significance. The number of child deaths averted is calculated by summing the stillbirth, neonatal and infant mortality averted (adjusted for double-counting).

DALYs averted were used to quantify the overall health impact of preventing these eight health outcomes by transitioning from IFAS to MMS for pregnant women. A DALY represents one lost year of perfect health. It aggregates years of life lost due to premature death and years lost due to disability. Since there is often a time lag between when the programme costs of an intervention are incurred and when some of the

health and economic benefits of the intervention are yielded over the coming decades, future benefits generated in the long run are devalued by a discount rate to be set into a present value. The total number of DALYs averted is calculated with a discount rate of 3% in accordance with guidelines on economic evaluation in global health (Robinson et al., 2019). The confidence in positive health outcomes is the statistically calculated estimate of confidence that the transition from IFAS to MMS will result in overall positive health outcomes. This estimate was calculated using probabilistic sensitivity analysis and the standard error of the health effect sizes.

2.3 | Cost-effectiveness analysis

The cost-effectiveness analysis section in the MMS Tool reports four indicators that may be informative for evaluating the value for money of investments into MMS programmes: the economic value of DALYs averted, the budget impact of transitioning to MMS from IFAS, the BCR and the additional cost per DALY averted.

The economic value of DALYs averted, which represents the total economic benefits estimated by transitioning to MMS, is estimated in the tool using a monetised DALY approach using the Value of Statistical Life (VSL) (Robinson et al., 2019). The VSL represents the amount of money that a person would be willing to pay to avoid injury or illness; VSLs vary by country. There are a number of different ways to calculate the VSL for a country. This MMS Tool uses the estimates of country-level VSLs in LMICs from Viscusi and Masterman (Viscusi & Masterman, 2017) and converts it into a Value of a Statistical Life Year (VSLY) by dividing the VSL by the expected life expectancy at birth. Then, the economic value of DALYs averted is calculated by taking the product of the estimated discounted DALYs averted in a particular scenario by the corresponding country's VSLY (Robinson et al., 2019). The calculation for the number of DALYs averted factors in a discount rate of 3% (Robinson et al., 2019).

The budget impact indicator in the MMS Tool reports the incremental cost of the MMS programme compared to the IFAS programme, or additional investment required, over the set timespan at the same coverage level in the scenario selected. The BCR is the ratio of the economic value of DALYs averted by transitioning to MMS compared to IFAS to the budget impact. If the BCR is greater than 1, then the additional economic value of the health benefits of transitioning to MMS exceeds the incremental costs. The second cost-effectiveness indicator reported is the additional cost per DALY averted, which is the amount of additional investment required to avert one DALY. The guideline from WHO (Leech et al., 2018) suggests that if the incremental cost per DALY averted is less than the country's Gross Domestic Product (GDP) per capita, then the transition can be considered "Very Cost Effective." If the cost of transition per DALY averted is less than three times the country's GDP per capita, then the transition can be considered "Cost Effective." Otherwise, the transition is considered "Not Cost Effective." However, cost per DALY estimates should also be compared to estimated supply-side cost-effectiveness

thresholds using local data or estimates of national health opportunity cost thresholds derived from cross-country data if available (Chi et al., 2020).

Given potential changes in key variables related to demographics, scale of coverage, unit costs, or source of effect sizes of MMS compared to IFAS over time, the MMS Tool was designed to make conducting analyses in multiple scenarios and sensitivity analysis available to users. Users can modify input variables to instantly view the effect each change has on the health outcome or cost-effectiveness analysis indicators.

2.4 | Programme scenario for demonstration

This paper demonstrates the use of the MMS Tool and discusses the results of the analysis for a specified MMS scale-up programme scenario. For this paper, four focus countries—Indonesia, Nigeria, Pakistan, and Tanzania—were selected to show the results in settings with different geography, population size, demographics, and disease burden. In addition to these four focus countries, the analyses for all 33 countries are available in the Web Appendix Table S1. For all analyses, we have used the default input values described above: the supplementation programme timespan is set at 10 years; the coverage of pregnant women in the intervention areas who will receive 180 tablets is set at 30%, and; the population of pregnant women in each focus country per year is calculated based on the national population (United Nations, 2019b) and crude birth rate (United Nations, 2019a) (Indonesia: 4.6 M; Nigeria: 7.6 M; Pakistan: 5.4 M, and; Tanzania: 1.9 M). The assumed unit costs of IFAS and MMS are based on the UNICEF supply catalogue, which are 2.00 for IFAS and 3.42 (2021 US\$) for MMS for each beneficiary per year. With respect to the transition costs, countries were grouped by population size then assigned a transition cost equal to US\$ 1 M, 2 M, 5 M or 10 M, which equates to approximately US\$ 1 per pregnant woman (Indonesia: US\$5 M; Nigeria: US\$ 10 M, Pakistan: US\$ 5 M; Tanzania: US\$ 2 M). The Smith et al., 2017 meta-analysis is the source of effect sizes of MMS compared with IFAS for the health outcomes presented in this scenario, and only significant health outcomes are factored into the analysis. In addition to the primary programme scenario for demonstration, two sensitivity analyses are

also included to show the impact of modifying the source of health effect sizes and the supplement unit costs.

3 | RESULTS

3.1 | Health outcome analysis

The analysis of transitioning to MMS from IFAS for pregnant women demonstrates substantial additional positive effects with respect to averted child morbidity, as indicated by LBW and SGA and preterm birth, and mortality, as shown by stillbirth and neonatal mortality, in all the four focus countries over 10 years (see Table 1). Stillbirths accounted for nearly half of the estimated DALYs averted in Nigeria and Pakistan while female newborn mortality accounted for the majority of additional DALYs averted in Tanzania. In these four countries alone, even at a conservative 30% coverage level, MMS could potentially avert nearly 100,000 child deaths and over 7 million DALYs over 10 years.

3.2 | Cost-effectiveness analysis

The analysis also suggests that transitioning to MMS is good value for money in all four focus countries analysed (Table 2). The total budget

TABLE 2 Estimated Incremental economic value of DALYs averted, additional budget impact, benefit-cost ratio, and incremental cost per DALY averted by MMS compared with IFAS for pregnant women in Indonesia, Nigeria, Pakistan, and Tanzania.

Country	Value of DALYs averted (US\$)	Additional budget impact over 10 years (US\$)	Benefit cost ratio (US\$:1)	Incremental cost per DALY averted (US\$)
Indonesia	\$8.3 B	\$21,871,599	\$380	\$23.55
Nigeria	\$27.0 B	\$37,655,268	\$717	\$13.00
Pakistan	\$10.8 B	\$24,638,928	\$441	\$9.00
Tanzania	\$1.6 B	\$9,072,747	\$173	\$15.00

Abbreviations: DALYs, disability-adjusted life years; IFAS, iron and folic acid supplementation; MMS, multiple micronutrient supplementation.

TABLE 1 Estimated additional health outcomes of transitioning to MMS compared with IFAS for pregnant women at 30% coverage of MMS over 10 years.

Country	Additional DALYs averted by MMS compared with IFAS for pregnant women					Averted DALYs	Additional child deaths averted
	Stillbirth	Female neonatal mortality	Preterm birth	LBW	SGA		
Indonesia	273,465	329,238	179,624	2591	143,974	928,892	8336
Nigeria	965,652	1,419,116	297,525	1268	214,092	2,897,653	41,985
Pakistan	1,005,684	1,213,969	165,445	9465	324,614	2,719,178	32,738
Tanzania	221,172	220,467	119,228	444	43,466	604,777	6651

Abbreviations: DALYs, disability-adjusted life years; IFAS, iron and folic acid supplementation; MMS, multiple micronutrient supplementation.

impact across the four countries ranges from US\$ 9–38 million over 10 years, however, generates billions of US dollars of value over 10 years in each of these countries. The BCR ranges from US \$173–\$717: \$1.0, with Tanzania having the lowest BCR and Nigeria having the highest. Note that since this analysis uses VSLs to value the benefits, and VSLs are country-specific, BCRs should not be directly compared across countries. Therefore, while the BCRs generated through this analysis can be used to compare interventions in the same country, they cannot be used to prioritise investment in one country versus another country.

The incremental cost per DALY averted ranges from US\$9.00 in Pakistan to US\$23.55 in Indonesia. In the four countries, the cost per DALY averted is considerably less than the GDP per capita of each country and therefore, the transition from IFAS to MMS is considered “very cost effective” according to the WHO guideline (Leech et al., 2018). Furthermore, this is considered favourable compared with many other common maternal, neonatal and child health interventions (Horton & Levin, 2016).

3.3 | Sensitivity analysis: Source of health effects

A sensitivity analysis was conducted to see the differences in results based on the different sources of health effects (Smith et al., 2017 compared with Keats et al., 2019). Table 3 presents estimates of DALYs averted (disaggregated by health outcome), and child deaths averted based on each source of health effects. In general, the Smith et al. (2017) analysis results in a two to three-times higher estimate of the total number of DALYs averted than using the Keats et al. (2019) effect sizes. This is largely driven by the inclusion of the effect of MMS on averting stillbirth and neonatal mortality in females in the Smith et al. (2017) study.

The cost-effectiveness analysis results from the MMS Tool using the different sources of health effects are presented in Table 4. Using data from Keats et al. (2019) is more conservative, compared with using data from Smith et al. (2017), in every country but it is still considered very cost-effective.

3.4 | Sensitivity analysis: Cost variations

Given there are few examples of MMS scale-up internationally at the present time, there is uncertainty as to the long-term incremental unit cost of MMS as it is produced by different suppliers and achieves economies of scale. Intuitively, as the differential between the unit cost of supplement manufacturing, packaging, and shipping compared to IFAS decreases as it is scaled, the value for money for MMS would increase even further. For demonstration purposes, the sensitivity analysis results are provided to compare the effect of a hypothetical scenario whereby cost parity between MMS and IFAS is eventually achieved so that the unit cost of MMS is reduced from US \$ 3.42 to US\$ 2.00 per pregnancy to equal the unit cost of IFAS, but that transition costs are still needed. This does not affect the

TABLE 3 Sensitivity analysis on the source of health effects of MMS compared with IFAS on health outcomes in Indonesia, Nigeria, Pakistan, and Tanzania over 10 years at 30% coverage of MMS.

Country	Additional DALYs Averted by MMS compared with IFAS				SGA				DALYs averted				Additional child deaths averted						
	Stillbirth		Neonatal mortality (F)		Preterm birth		LBW		Smith (2017)		Keats (2019)		Smith (2017)		Keats (2019)		Smith (2017)		Keats (2019)
Indonesia	273,465	N/A	329,238	N/A	179,624	N/A	2591	2591	143,974	383,931	928,892	386,522	8336	0					
Nigeria	965,652	N/A	1,419,116	N/A	297,525	N/A	1268	1268	214,092	570,911	2,897,653	572,180	41,985	0					
Pakistan	1,005,684	N/A	1,213,969	N/A	165,445	N/A	9465	9465	324,614	865,638	2,719,178	875,103	32,738	0					
Tanzania	221,172	N/A	220,467	N/A	119,228	N/A	444	444	43,466	115,908	604,777	116,353	6651	0					

Abbreviations: DALYs, disability-adjusted life years; IFAS, iron and folic acid supplementation; MMS, multiple micronutrient supplementation.

TABLE 4 Sensitivity analysis on the source of health effects of MMS compared with IFAS and on varying input data for the cost of MMS on cost-effectiveness in Indonesia, Nigeria, Pakistan, and Tanzania over ten years at 30% coverage of MMS.

Country	Sensitivity analysis: Source of health effects						Sensitivity analysis: Varying input data for the cost of MMS					
	Value of DALYs averted (US\$)		Benefit-cost ratio (US\$:\$1)		Incremental cost per DALY averted (US\$)		Additional investment over 10 years (US\$)		Benefit cost ratio (US\$:\$1)		Incremental cost per DALY averted (US\$)	
	Smith (2017)	Keats (2019)	Smith (2017)	Keats (2019)	Smith (2017)	Keats (2019)	Baseline scenario ^a	Unit cost parity scenario ^b	Baseline scenario	Unit cost parity scenario	Baseline scenario	Unit cost parity scenario
Indonesia	\$8.3 B	\$3.5 B	\$380	\$158	\$23.55	\$56.59	\$21.9 M	\$5 M	\$380	\$1,661	\$23.55	\$5.38
Nigeria	\$27.0 B	\$5.3 B	\$717	\$142	\$13.00	\$65.81	\$37.7 M	\$10 M	\$717	\$2,702	\$13.00	\$3.45
Pakistan	\$10.8 B	\$3.5 B	\$441	\$142	\$9.00	\$28.16	\$24.6 M	\$5 M	\$441	\$2,172	\$9.00	\$1.84
Tanzania	\$1.6 B	\$0.3 B	\$173	\$33	\$15.00	\$77.98	\$9.1 M	\$2 M	\$173	\$786	\$15.00	\$3.31

Abbreviations: DALYs, disability-adjusted life years; IFAS, iron and folic acid supplementation; MMS, multiple micronutrient supplementation.

^aIn the baseline scenario, the cost of MMS is US\$ 3.42, and the cost of IFAS is US\$ 2.00 per pregnancy.

^bIn the unit cost parity scenario, the cost of MMS and IFAS is US\$ 2.00 per pregnancy.

incremental health outcomes nor the economic value of health benefits, however, the BCR is 3.8–4.9 times higher in unit cost parity compared to the baseline, while the incremental cost per DALY averted is about a quarter of the cost in unit cost parity compared to the baseline in all countries as seen in Table 4.

3.5 | Health outcome and cost-effectiveness analysis of the 33 pre-loaded countries

The analysis of transitioning to MMS from IFAS for pregnant women reveals a substantial additional positive effects of MMS compared to IFAS on several health outcomes in all 33 countries. In all 33 countries, MMS could potentially avert over 250,000 child deaths and avert nearly 25 million DALYs over 10 years, even with a conservative 30% coverage of pregnant women.

The analysis also suggests that transitioning to MMS is good value for money in all 33 countries. The economic value of the health benefits generated from switching from IFAS to MMS for pregnant women ranges from as low as US\$ 56,608,215 in Timor-Leste to as high as US\$ 30,398,915,178 in China over 10 years. The total budget impact averages at just over US\$ 120 million for the countries, which is sizeable but would remain a low-cost intervention for each of these countries compared with other interventions (Shekar et al., 2017). The BCR ranges from US\$ 41:\$1 in Malawi to US\$ 1,304:\$1 in Afghanistan.

The incremental cost per DALY averted averages at US\$ 23.61 for the 33 countries and ranges from US\$ 8.92 in Pakistan to US\$ 21.72 in Indonesia. As Timor-Leste has such a small population, the incremental cost per DALY averted is US\$ 117.08 while the next greatest incremental cost per DALY averted is US\$ 42.50 in Sri Lanka. In all 33 countries, the transition from IFAS to MMS is considered “very cost-effective” according to the WHO guideline (Leech et al., 2018). Results for the health outcome and cost-effectiveness analysis using the MMS Tool for all 33 LMICs analysed can be found in Web Appendix Table 1.

4 | DISCUSSION

The MMS Tool is the first freely available online modelling tool that quickly generates estimates on the maternal and newborn health outcomes and cost-effectiveness of MMS compared with IFAS for pregnant women. This evidence-based modelling tool was created to provide national and international policy-makers with access to data to help determine if transitioning from IFAS to MMS for their pregnant women is good value for money. This is important data for decision-making given that the scale-up of MMS across LMICs could require US\$ 2–3 billion over the next 10 years (Shekar et al., 2017). This MMS Tool helps fill an evidence gap around the cost-effectiveness of MMS for pregnant women in many countries.

In general, the analyses completed by Nutrition International for the 33 LMICs using the MMS tool show that transitioning to MMS programmes can be very cost-effective in multiple scenarios for these countries, which aligns with previous cost-effectiveness research on MMS (Engle-Stone et al., 2019; Kashi et al., 2019). While there is minor variation in the results of countries analyzed due to difference in underlying data such as demographics and disease burden, the unit cost and/or the health effect size would have to have been greatly under or over-estimated for MMS to be considered not cost-effective. While the results suggest that the long-term economic value of health benefits generated by MMS far outweighs the costs, the recommendations should be considered by governments in the context of all forms of malnutrition and other nutrition interventions as well the potential budget impact.

The MMS Tool also provides an important resource for countries to conduct more in-depth, subnational and/or ongoing analyses as part of implementation research on MMS. Within 2 years of it being publicly accessible, the MMS Tool and its analyses have been shown to fill a critical gap in informing and influencing advocacy, policy development, and investment decision-making at the global and national levels by a variety of users. At the national level, Nutrition International has used the analysis of the MMS Tool as part of its role

as an ally to government in the provision of direct technical assistance and/or through partner support on maternal nutrition in Kenya, Ethiopia, Nigeria, Pakistan, Tanzania, Indonesia, South Africa, Mali, Bangladesh, Burkina Faso, Madagascar, and Philippines. At the global level, Nutrition International used the MMS Tool and its analysis on cost-effectiveness to provide direct technical assistance to the WHO Guideline Review Group in 2019 to inform the revision to the MMS recommendation in The WHO guidelines on antenatal care (World Health Organization, 2020). The MMS Tool has also been featured or adopted as part of other global/multi-organisational initiatives such as the Bill and Melinda Gates Foundation Goalkeepers Accelerator initiative, New York Academy of Sciences MMS Technical Advisory Group, and the Nutrition Modelers Consortium. These early examples have shown that the MMS Tool can be instrumental in supporting governments policy-making and implementation research on MMS. This tool is also helpful for global or international organisations in their technical decision-making, advocacy and planning for potential future investments. Nutrition International's experience with the MMS Tool—in approximately 2 years—has demonstrated great potential for future modelling tools to be created to help inform and influence national and global policies and investment decisions in other areas of nutrition.

The MMS Tool has a unique advantage that it focuses on the comparison of MMS to IFAS for pregnant women for the purpose of transition decision-making, whereas other modelling tools such as the Lives Saved Tool (Heidkamp et al., 2017) and Optima Nutrition Model (Pearson et al., 2018) allow users to project the potential health impact and cost-effectiveness of MMS as part of a package of maternal and child health interventions. Depending on the needs of the analysis, these other tools may be useful for the analytics related to broader nutrition plans but require much more data gathering and entry and lack the detailed analysis on the single-policy question of whether MMS is good value for money.

Going forward, the MMS Tool may be beneficial for other countries to utilise as part of policy-decision making and implementation research on MMS initiatives. Implementation research can and should help to refine some of the underlying assumptions in this MMS tool, such as providing more robust information about the transition costs as well as feasibility, including supply and consumer demand factors such as acceptability. This is the case in Pakistan, where Nutrition International is working alongside the Government of Pakistan to conduct implementation research on the introduction of MMS and better understand feasibility, sustainability and costs of this transition. MMS should be implemented within the context of implementation research so that its initial introduction can be adequately evaluated.

The MMS Tool is the only model that can provide policymakers with rapid economic analyses for decision-making, however, there are some limitations. The inputs and assumptions are based on the most recent available evidence (reviewed and updated annually); however, all inputs are subject to change, which is why there are options for the user to generate custom analyses. An estimated transition cost figure has been suggested based on population size to

estimate context specific costs related to the start up of a new programme such as the development of training materials, new policies/regulations, training of health workers, behaviour change communications however the actual cost may vary. In the absence on better data on transition costs, implementers should conduct a costing exercise for transition activities in their context and make provisions in budgets for the transition in addition to the additional commodity cost to ensure implementation and adherence success. The MMS Tool includes a default value that suggests 30% of pregnant women receive 180 tablets. The 180 tablets per pregnancy are based on existing trial data where adherence can be closely monitored. However, in regular programming settings, adherence to antenatal supplementation remains a challenge (Siekman et al., 2018). In addition, the tool is based on the analytical methods of Kashi et al. (2019) that used a probabilistic approach in several countries, however to simplify the methods for this policy decision-making and advocacy tool it employed a modified deterministic analytical approach. To include some uncertainty in this approach, the tool has the capability to use effect sizes from both the Keats et al. (2019) and Smith et al. (2019) meta-analyses as well as adjust unit cost inputs and some other variables for sensitivity analysis. While best-quality referenced estimates were used that could be compared across the countries, these come with certain limitations and may not reflect the exact number for the countries. For these reasons, the custom analysis is available for decision-makers to input the data that best represents their population of interest. Therefore, we feel this analytical approach is justified given the existing evidence base, the purpose of the policy tool, and the supportive sensitivity analyses.

5 | CONCLUSION

With the current momentum for nutrition as demonstrated by the creation of the WHA Global Nutrition Targets, the International Conference on Nutrition 2 Rome Declaration on Nutrition, and the Sustainable Development Goals, modelling tools for nutrition can be helpful for policy and decision-makers. This MMS Tool was built to address the policy question on whether or not investing in MMS is good value for money compared to IFAS, and remains relevant with the update of the MMS guidelines (World Health Organization, 2020) and the latest recommendations in the Lancet Maternal and Child Undernutrition Series (Heidkamp et al., 2021). With its user-friendly design, open access availability, and online data-driven analytics, the MMS Tool can be a powerful resource for governments and nutrition partners to generate evidence-based analyses to inform national and global policy-decision and investments for the scale-up of MMS for pregnant women globally.

AUTHOR CONTRIBUTIONS

Allison M.J. Verney conceived of the manuscript, conducted and reviewed the analyses, and wrote significant sections of the manuscript. Jennifer F. Busch-Hallen conceived of the manuscript,

reviewed the analyses, and reviewed and revised the manuscript. Dylan D. Walters conceived of the manuscript, reviewed the analyses, and reviewed and revised the manuscript. Sarah N. Rowe conceived of the manuscript, reviewed the analyses, and reviewed and revised the manuscript. Zuzanna A. Kurzawa reviewed the analyses and reviewed and revised the manuscript. Mandana Arabi conceived of the manuscript, reviewed the analyses and reviewed and revised the manuscript. All authors read and approved the final submitted manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in <https://www.nutritionintl.org/learning-resources-home/mms-cost-benefit-tool/> and data sources for inputs can be found in the data guide on this site.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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