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Title: A Cost-Effectiveness Model for Comparing Multiple Micronutrient Supplements to Iron and Folic Acid Supplements During Pregnancy: Applications in Pakistan, Bangladesh, and India

Article Type: Article (Original Research)

Keywords: Cost-effectiveness, iron and folic acid supplements, multiple micronutrient supplements, anaemia

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Abstract: Background - Recent evidence has encouraged low- and middle-income countries to consider transitioning from long-standing iron and folic acid supplementation (IFAS) to multiple micronutrient supplementation (MMS) during pregnancy. However, global guidance is limited. To help countries' decision-making, a cost-effectiveness model to compare the supplementation modalities was developed, and applied to: Pakistan, Bangladesh, and India.

Methods - The effectiveness of IFAS relative to MMS during pregnancy was compared using eight health outcomes reported in the literature: maternal anaemia, preterm delivery, small-for-gestational-age newborns, low birth weight, stillbirths, and maternal, neonatal, and infant mortality. Outcomes were aggregated using disability-adjusted life years (DALYs) to derive an overall effectiveness of IFAS and MMS. Costs included the supplements and their distribution through antenatal care. The incremental cost-effective ratio (ICER) for transitioning from IFAS to MMS was calculated for each country, and Monte Carlo simulations were applied to generate a measure of certainty around the results.

Findings - In Pakistan, Bangladesh, and India, MMS would avert 11,749, 12,462 and 9,332 more DALYs than IFAS per 100,000 pregnancies, respectively (80.0%, 91.0%, 87.0% certainty). The ICER of transitioning from IFAS to MMS was 15.53, 13.94, and 19.55 USD (2016) per DALY averted, respectively.

Interpretation - As per World Health Organization criteria, transitioning from IFAS to MMS is cost-effective. While the effectiveness of MMS is sensitive to the prevalence of various health outcomes, with high confidence 80.0%-91.0% MMS averts more DALYs than IFAS and should re-enter public health discussion in Pakistan, Bangladesh, and India.

Funding - Nutrition International with a grant from Global Affairs Canada and World Vision Canada.

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Research in Context

Evidence before this study

We searched PubMed with the terms “iron and folic acid supplementation” (IFAS) in combination with “multiple micronutrient supplementation” (MMS) and “pregnancy” to identify papers up until May 31, 2018. To identify cost-effectiveness studies, the searches included the terms ‘cost’ or ‘cost-effectiveness’ without time or language restrictions. One cost-effectiveness study comparing IFAS and MMS (published February 2018) was identified. In this study, pregnant women in rural Bangladesh were randomized to receive either IFAS or MMS. The supplements were compared based on their effect on under five-year mortality and stunting, expressed in disability-adjusted life years (DALYs) averted. It was found that the incremental cost of one DALY averted, by transitioning from IFAS to MMS in rural Bangladesh, is 24 USD. The study acknowledged that some potential benefits or harms of transitioning from IFAS to MMS were excluded.

To identify other potential benefits and harms of the supplement modalities on both infant and maternal and infant health, we conducted a literature review, limited to randomized control trials among pregnant women in low- and middle- income countries (LMICs). A systematic review comparing the effectiveness of IFAS and MMS was published in April 2017. The review contained 17 trials; 15 of these were in LMICs and so were included in this study. MMS was associated with a significant decrease in low birth weight infants and small-for-gestational age newborns. No significant differences were identified for other maternal or pregnancy outcomes including preterm births, stillbirth, maternal anaemia, maternal mortality, or neonatal mortality. Study quality ranged from moderate to high.

These findings were in line with past systematic reviews, providing evidence for considering the replacement of IFAS with MMS during pregnancy in LMICs. The uncertainty regarding some health outcomes has limited global guidance on MMS.

Added value of this study

This study is the most comprehensive cost-effectiveness analysis comparing IFAS and MMS. It is the first study to aggregate both maternal and infant health outcomes of IFAS and MMS, and account for their uncertainty through Monte Carlo Simulations.

This study demonstrated that MMS is highly cost-effective relative to IFAS in Pakistan, Bangladesh, and India (80.0%, 91.0%, 87.0% certainty). A sensitivity analysis demonstrated that even if a changeover cost is incurred by the country when switching from IFAS or MMS, MMS is still very cost-effective.

This study also identified that stillbirths, neonatal and infant mortality are the health outcomes that generate the most uncertainty when comparing the overall effectiveness of MMS to IFAS.

Implications of all the available evidence

Evidence indicates that transitioning from IFAS to MMS is cost-effective in Pakistan, Bangladesh, and India. In India, MMS averted more DALYs than IFAS with higher certainty. The cost-effectiveness in other countries will depend on the prevalence of the health outcomes. More research on the effect of MMS relative to IFAS on stillbirths, neonatal and infant mortality will generate greater confidence when comparing the supplementation modalities.

Introduction

Improving birth outcomes and neonatal survival continues to be a public health priority for many low- and middle-income countries (LMICs). Maternal nutritional deficiencies, in particular iron deficiency anaemia can increase the risk of low birth weight (LBW), preterm birth, impaired cognitive and motor development, and maternal mortality, among other complications [1]. In 2016, the World Health Organization (WHO) estimated the prevalence of anaemia among pregnant women was 45% in LMICs; it was estimated that 50% of these cases could be eliminated through iron supplementation [2].

To reduce the risk of some of these complications, the WHO has recommended supplementing women with iron and folic acid (IFAS) as part of antenatal care (ANC) since 1968 [3]. The current recommended dose of the iron ranges from 30-60 mg, plus 400 ug of folic acid. Where the prevalence of anaemia is considered severe (>40% of the population), the WHO recommends 60 mg of iron [4].

Although the provision of IFAS has been part of ANC programming in LMICs for decades, success has been limited. Possible reasons include lack of compliance attributable to commonly reported side-effects (nausea, constipation, diarrhoea) [5, 6], concerns about the safety of this intervention among women with an adequate iron intake, and variable availability of the supplements at community level [7].

Women in LMICs often have poor diets, resulting in nutrient and micronutrient deficiencies [8]. As this is exacerbated during pregnancy and has implications for maternal and infant health [8], a multiple micronutrient supplementation (MMS) formulation was proposed by the United Nations Children's Fund (UNICEF), United Nations University (UNU), and the WHO in 1999 [9]. MMS comprises iron, folic acid, retinol, vitamins D, E, B1, B2, B6, and B12, ascorbic acid, niacin, zinc, copper, selenium, and iodine [9]; the exact formulation can vary.

A 2017 meta-analysis comparing the supplement modalities in LMICs found that MMS consumed during pregnancy reduced the risk of low birth weight by 12%, and small-for-gestational age births by 8% compared to IFAS [10]. No statistically significant differences were identified for other maternal or infant outcomes, including preterm births, stillbirth, maternal anaemia, maternal or neonatal mortality.

Currently, the WHO ANC guidelines do not recommend MMS for pregnant women, noting there are still gaps in the evidence and risk to newborns [3, 11]. The current guidelines may reflect a lag in translational research or residual hesitation regarding the risk of neonatal mortality despite the recent evidence. A 2005 study reported MMS was associated with increased risk of perinatal and neonatal mortality through increased birth asphyxia in heavier babies [12]. Later it was found, this was only significant where births were primarily home-based (rather than facility-based) [11].

The WHO ANC guidelines in their current form do however state that in populations with high prevalence of micronutrient deficiencies, the benefits on maternal and newborn health may outweigh any potential risk, and should be considered within a specific country and population context [3].

Due to limited global and national policy on MMS, countries have few tools to inform whether the benefits of transitioning from IFAS to MMS outweigh the risks (and costs). In 2018, one study evaluated the incremental cost-effectiveness of transitioning from IFAS to MMS in rural Bangladesh. While only two health outcomes were considered (five-year mortality and stunting), it found transitioning to MMS was very cost-effective [13]. Given that other health outcomes, including impact on maternal health are important for policy makers, this study developed the first comprehensive and generalizable model for calculating the incremental cost-effectiveness of transitioning from IFAS to MMS.

While pooled estimates of the effect of MMS relative to IFAS are available for a range of maternal and infant health outcomes, these do not capture the probability of these epidemiological averages, nor the overall effect on maternal and newborn health. The cost-effectiveness model developed in this study factors in for this uncertainty.

To demonstrate the capacity of the model, a cost-effectiveness analysis comparing IFAS and MMS was developed, and applied to three countries in South Asia: Pakistan, Bangladesh, and India.

Despite steady improvements in nutrition and maternal and infant mortality in South Asia over the past decade, health disparities persist [14]. Thirty-seven percent of the stillbirths that occur globally are in South Asia [14]. Pakistan, for example, has one of the highest estimated prevalence of low birth weight (32%) [15]. In addition, all three countries have anaemia prevalence among pregnant women classified as severe public health problem: 51%, 46%, and 50%, respectively [16].

Studies have consistently found nutrition interventions to be highly cost-effective at improving the health of populations [17]. The outcome of this study offers policymakers in South Asia guidance regarding whether transitioning from IFAS to MMS can meet this goal. While this study focuses on Pakistan, Bangladesh, and India, the methodological approach can be applied to other contexts.

Methods

Hypothetical Intervention

IFAS was defined as an oral dose of elemental iron (60 mg) and folic acid (400 µg), in line with 2016 WHO guidelines [3]. MMS was defined according to the United Nations International Multiple Micronutrient Preparation (UNIMAP) formulation containing 30 mg of iron and 400 µg of folic acid along with 800 µg of retinol, 200 IU of vitamin D, 10 mg of vitamin E, 70 mg of ascorbic acid, 1.4 mg of vitamin B1, 18 mg of niacin, 1.4 mg of vitamin B2, 1.9 mg of vitamin B6, 2.6 µg of vitamin B12, 15 mg of zinc, 2 mg of copper, 65 µg of selenium, and 150 µg of iodine [18].

Aligned with each countries' policies regarding maternal supplementation, it was assumed pregnant women consumed at least 180 supplements, to cover six months of pregnancy, and that these were distributed through antenatal care at a health facility.

The model developed was based on hypothetical population coverage (95%) of supplements for the duration of a pregnancy. This does not reflect current nor attainable coverage, however, is a standardized coverage level used in WHO studies to enable comparison with other cost-effectiveness studies [19].

Effectiveness

The model compared the supplements based on their effectiveness on a range of health outcomes (including negative effects). The eight health outcomes informed by the literature were: maternal anaemia (third trimester haemoglobin < 110 g/L), preterm delivery (births before 37 weeks gestation), small-for-gestational-age (SGA) newborns (defined by authors of trials), LBW (birth weight below 2500g), stillbirths, and maternal, neonatal (death in the first 28 days of life), and infant mortality (death in the first year of life) [10].

The overall health burden of these eight health outcomes was derived by calculating disability-adjusted life years (DALYs). A DALY represents one lost year of perfect health, and aggregates morbidity and mortality into a single unit. A deterministic model was built to estimate the DALYs for each health outcome, in each country, using the standard DALY calculation approach by the WHO [20].

DALYs comprise Years of Life Lost (YLL) due to premature mortality, and Years Lost due to Disability (YLD) due to a particular morbidity. The parameters required to estimate YLL include prevalence and life expectancy at the time of death (Table 1). The parameters required to estimate YLD include prevalence, disability weights, and length of the disease. These values were obtained through the World Bank Data Base, UNICEF, WHO Burden of Disease, and the Demographic and Health Survey.

The length (years) of benefits attributed to averted mortality was assumed to be the life expectancy at mean age of first pregnancy in each country. The benefits of averted maternal morbidity were assumed to last one year since women can become anaemic once ceasing supplementation. The benefits of averted infant mortality and mortality were assumed to last for their entire life.

In countries where the prevalence of LBW is high (>10%), 30% of LBW cases are attributable to SGA and 7% of LBW cases are attributable to preterm birth [11]. To avoid double counting, the prevalence of LBW was adjusted for each country (Table 1). 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. This way, the effect on neonatal and infant mortality could be observed separately in the model (Table 1).

The effectiveness of transitioning from MMS to IFAS, or the *additional DALYs averted*, was estimated using relative risks (RRs) extracted from a 2017 systematic review comparing IFAS and MMS in LMICs [10] (Table 1). DALYs averted were reported per 100,000 pregnancies.

Rather than calculating the effect of IFAS and MMS relative to placebo and then calculating the difference in effectiveness, we directly estimated the change in effectiveness (*additional DALYs averted*) using the RRs from the systematic review (Table 1). The rationale for this approach was that the studies comparing IFAS with MMS were more comprehensive and robust relative to the studies comparing IFAS or MMS with placebo. Under comparable study conditions, this would yield the same result.

Infant mortality was not included in the systematic review, but was deemed salient and so the RR was estimated separately. Within the trials in the systematic review, two studies reported on infant mortality [21, 22] and a random-effect meta-analysis was conducted on these two studies to obtain an average measure for this outcome (Table 1).

Costs

The model included four types of costs: supplement, patient, program, and changeover costs (Table 2). All costs were converted to USD (2016 PPP).

Supplement costs were identified through the UNCIEF Supply Catalogue. IFAS and MMS were priced at 0.86 USD and 1.82 USD, respectively, per 100 supplements. These costs were adjusted to reflect the six month coverage (Table 2). Patient and program costs were derived using the WHO-CHOICE system [19]. The WHO-CHOICE system estimates the cost of coverage of iron supplementation interventions for various regions worldwide.

Patient costs included the provision of supplements through ANC visits at a primary care facility and the health facility unit costs [19]. While the WHO 2016 ANC guidelines recommend a minimum of 8 ANC contacts, 4 ANC visits were used in the costs derived using the WHO-CHOICE system. Facility costs were derived from a separate study [23].

Program costs are those that go beyond the patient/provider, including administration at the national level, training, nutrition education programs, and supervision. The methodology to calculate the program costs, and exhaustive breakdown, is described in Johns et al. [24].

Lastly, a ‘changeover’ cost that would be incurred by countries switching from IFAS to MMS was considered. This could include, but is not limited to, re-training health staff, re-designing behaviour change intervention materials, and updating national guidelines. Although there are no available data on a changeover cost, we calculated the threshold at which transitioning from IFAS to MMS is no longer ‘very cost-effective’, defined as being more than GDP per/capita in the respective country. No longer ‘cost-effective’ is defined as being more than three times GDP per/capita. This threshold was selected in line with WHO cost-effectiveness guidelines that state if the cost/DALY averted is less than the national GDP/capita, the intervention is very cost-effective [25], and less than three times GDP/capita it is cost-effective. This study acknowledges that these guidelines are in the process of being revised and are imperfect estimates of a countries’ willingness-to-pay, however, provided some threshold upon which to compare the cost-effectiveness of health interventions in various countries.

Cost-effectiveness

The incremental cost-effectiveness of MMS compared to IFAS was calculated using the incremental benefits, measured through averted DALYs, and the incremental cost. The results were calculated for 100,000 pregnancies. Discount rates of 0%, 3% and 5% were applied to test for sensitivities in the choice of discount rate.

The average RRs used in the deterministic model widely diverged in significance level. To account for this, a probabilistic analysis was conducted on the deterministic model using Monte Carlo simulations. This approach allows the analysis to account for the fact that uncertainty in model inputs leads to uncertainty in model outputs. The Monte Carlo simulations generated the expected value and the standard error for the total averted DALYs. The Monte Carlo was conducted with 200,000 simulation runs.

These analyses were conducted in R version 3.3.2, Microsoft Excel 2016, and Oracle Crystal Ball Version 11.1.2.3.

Role of the funding source

The funder of the study consulted on the selection of parameters, interpretation of results, and writing of the manuscript, however was not responsible for conducting the analysis.

Results

Effectiveness

In the deterministic model, MMS would avert 11,749, 12,462, and 9,332 more DALYs than IFAS per 100,000 pregnancies in Pakistan, Bangladesh, and India, respectively. The most benefit was attributed to DALYs averted through the reduction in SGA. Neonatal mortality conversely gained the most DALYs (Table 3) and contributes to the most uncertainty in the expected DALYs averted (Figure 1).

Costs

The total cost for IFAS was estimated to be 15.04 USD (2016 PPP) and 16.86 USD (2016 PPP) for MMS, per pregnant woman (Table 2).

Cost-effectiveness

The incremental cost-effectiveness ratio of transitioning from IFAS to MMS for Pakistan, Bangladesh, and India was 15.53, 13.94, and 19.55, per additional DALY averted, respectively (Table 3). This was considerably less than the GDP per capita of each country (Table 3). It was also found that even with a changeover cost, per pregnant women, of up to 614.78 (2016 PPP), 466.45 USD (2016 PPP), and 611.02 USD (2016 PPP) in Pakistan, Bangladesh and India respectively, MMS remains cost-effective. 4

Probabilistic and sensitivity analysis

The probabilistic analysis found that MMS would avert more DALYs than IFAS with 80.0%, 91.0%, 87.0 certainty in Pakistan, Bangladesh, and India, respectively. Furthermore, the probabilistic analysis found that stillbirths, infant mortality, and neonatal mortality are the main source of uncertainty in the overall model. The most precise estimates of the effectiveness of MMS relative to IFAS were on the potential reduction in SGA and LBW. The expected averted DALYs were not sensitive to the discount rates assumed by the analysis (Table 3).

Discussion

To our knowledge, this study is the most comprehensive cost-effectiveness analysis of IFAS to MMS during pregnancy. Our finding was that transitioning from IFAS to MMS would cost 15.53, 13.94, and 19.55 USD (2016 PPP) per additional DALY averted in the context of Pakistan, Bangladesh, and India, respectively. Given that this study included more health outcomes, resulting in more DALYs averted, the cost per DALY averted was lower in Bangladesh than a previous cost-effectiveness [13].

Applying the WHO threshold for cost-effectiveness [25], the study countries' GDP per capita widely exceeds the cost per additional DALY averted. This method is not meant to be an exclusive decision rule, but as a relative indication of an interventions' cost-effectiveness.

One of the primary contributions of this study was the aggregation of health outcomes and their uncertainty through DALYs and Monte Carlo simulations. This enabled a comparison of the overall effect of the supplements on both maternal and infant health, which was not available before.

The health outcomes that introduced the most uncertainty into the analysis were stillbirths, infant mortality, and neonatal mortality. Neonatal mortality was responsible for the biggest increase in DALYs when transitioning from IFAS to MMS. Nevertheless, upon aggregating all health outcomes, there is still sufficient evidence that MMS, overall, averts more DALYs than IFAS. It is likely that as the prevalence of these three health outcomes decreases, the more certainty there will be that MMS averts more DALYs than IFAS.

It was also found that even with a hypothetical changeover cost ranging from 46.65-61.45 million USD (2016 PPP) per 100,000 pregnancies, transitioning to MMS remains cost-effective in the study countries. The robustness of this finding provides compelling evidence to policy makers concerned about the resource implications of transitioning.

Studies have consistently found nutrition interventions to be cost-effective, with high returns. For example, investing 1 USD in reducing anaemia in women yields a return of 12 USD [17]. IFAS and MMS are not only cost-effective but are one of the few interventions with effects on multiple 2025 Global Nutrition Targets including reducing global prevalence of anaemia in women of reproductive age by 50%, and newborns with low birth weight by 30% [17].

Advocates at the 2017 Global Nutrition Summit urged policymakers to prioritize nutrition as part of anti-poverty and development efforts [26]. To maintain momentum in a volatile funding climate, and stay on track with 2025 Global Nutrition Targets, identifying highly cost-effective interventions is imperative.

It should be noted that for country advisors and policymakers of LMICs, evidence and resource implications are two of many factors considered when developing policies. Likely uptake by the target population, including the consideration of their values and preferences regarding their health care practices should be considered. For example, one perceivable challenge in improving maternal and infant nutrition is adherence, possibly rooted in concern over delivering large babies, particularly in the absence of skilled birth attendants [7, 27].

This study has the following limitations. First, the analysis did not consider whether program effectiveness differs by sex of the infant or severity of maternal anaemia. A recent study found that MMS had a differential effect on female and male neonates, as well as on maternal outcomes depending on the severity of anaemia [28]. A future iteration of the model could consider this. Second, the model did not explicitly account for correlation between health outcomes. While this does not affect the expected values, it could reduce/increase the variation around the expected values. Third, some potential health benefits were excluded. While not included in this study, the supplement modalities could also be compared based on their effect on cognitive development or future health care utilization. Data are currently limited on the long-term implications of either supplement when taken during the second and third trimester on cognitive development, however, as evidence amasses this can be integrated in the model. It is likely that these considerations would have generated additional support for transitioning to MMS, as micronutrients included in MMS (e.g. zinc, B vitamins, iodine) have been associated with improved cognitive development [29]. Health care utilization in the study countries is low, and so changes to future health care

utilization (either through reduced morbidity or increased survival) are negligible in this context. In higher income countries, this benefit would be salient and should be considered on a case-by-case basis. Lastly, the model makes no explicit assumptions about adherence; rather, it assumes the adherence of the women in the trials included in the systematic reviews.

Conclusion

This study determined that the incremental cost of transitioning from IFAS to MMS would be 15.53, 13.94, and 19.55 per additional DALY averted USD (2016 PPP) in the context of Pakistan, Bangladesh, and India, respectively. Applying WHO cost-effectiveness guidelines, initiating a transition from IFAS to MMS is very cost-effective, and should re-enter the public health discussion in the study countries. While the transition may not be appropriate in all settings, as it is dependent on the prevalence of the eight health outcomes included in the study, it is likely that in similar LMICs, MMS would also be considered cost-effective. Recommendations should be tailored to the specific country context and population.

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Tables and Figures

Table 1. Inputs for DALY calculations for Pakistan, Bangladesh, and India for 100,000 pregnancies

Health Outcome	Prevalence			MMS vs. IFAS RR	Disability Weight	Length of Effect [‡]		
	Pakistan	Bangladesh	India	(SE)	0-1	Pakistan	Bangladesh	India
Maternal anaemia	51,000	42000	58000	1.03 (0.11)	0.05	1.00	1.00	1.00
Preterm birth	39,280	22000	13000	0.96 (0.04)	0.06	65.86	71.25	68.30
SGA	43,470	46100	46900	0.92 (0.03)	0.06	65.86	71.25	68.30
LBW	20,160 [†]	13860 [†]	11970 [†]	0.88 (0.02)	0.06	65.86	71.25	68.30
MM	178	170	174	0.97 (0.26)	N/A	48.36	50.34	52.70
Stillbirth	4,315	3,900	2,303	0.97 (0.06)	N/A	65.86	71.25	68.30
Neonatal mortality	4,550	2,000	2,500	1.06 (0.08)	N/A	65.86	71.25	68.30
Infant mortality	1,850 [†]	800 [†]	1,000 [†]	0.95 (0.06)	N/A	65.86	71.25	68.30

[†] Prevalence has been adjusted for double counting. The actual prevalence of LBW in Pakistan, Bangladesh, and India at the time of analysis was 32,000, 22,000, and 19,000 per 100,000 pregnancies, respectively. Similarly, infant mortality was adjusted to avoid double counting of neonatal mortality. The actual prevalence of infant mortality at the time of the analysis was 6,400, 2,800, and 3,500 per 100,000.

[‡] The length of effect is not discounted. Discounting of 3% applied in DALY calculation.

Table 2. Breakdown of costs for IFAS and MMS (2016 USD PPP)

	IFAS	MMS
Cost of supplements	1.63	3.46
Patient cost	12.98	12.98
Program cost	0.42	0.42
Changeover cost	N/A	Unavailable [†]
Cost per pregnant woman	15.04	16.86
Total cost per 100,000 women	1,503,795	1,686,195

[†] This cost is unavailable for each country. A threshold changeover cost at which it is no longer 'very cost-effective' was calculated instead.

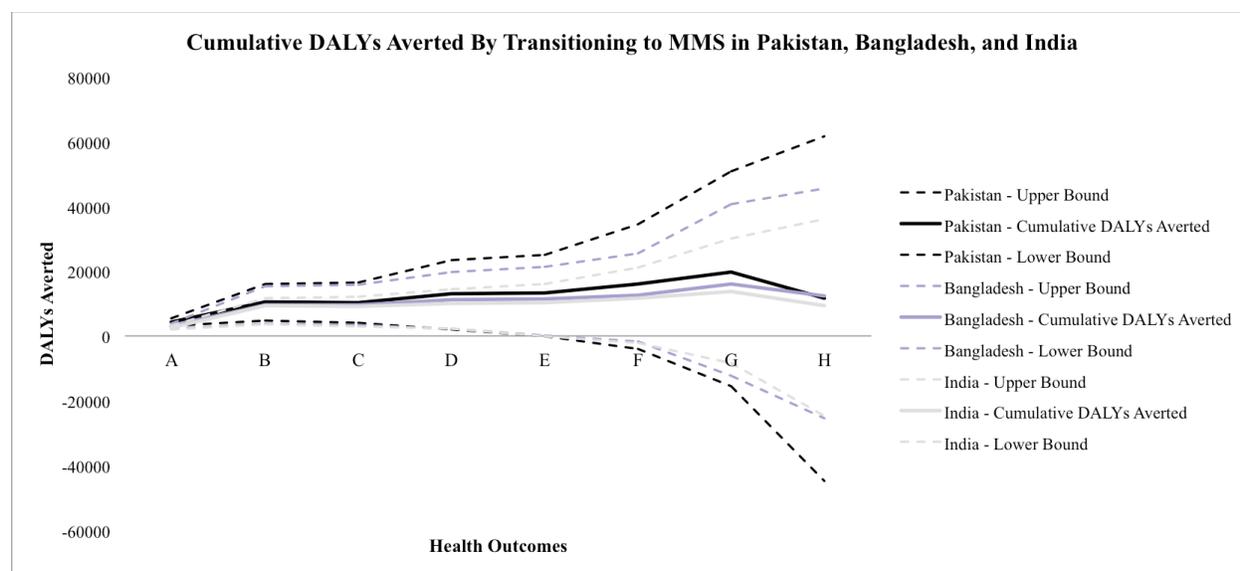
Table 3. Incremental DALYs averted, incremental costs, and incremental cost-effectiveness of MMS versus IFAS (3% discount rate) (2016 USD PPP)

	Pakistan	Bangladesh	India
Health outcome	Average incremental DALYS averted (95% CIs)		
Maternal anaemia	-77 (-612, 383)	-63 (-504, 315)	-87 (-696, 435)
Preterm birth	2,775 (-2081, 6937)	1,592 (-1194, 3980)	929 (-697, 2322)
SGA	6,141 (1535, 10747)	6,673 (1668, 11677)	6,703 (1675, 8378)
LBW	4,272 (3204, 5340)	3,009 (2257, 3761)	2,566 (1925, 3208)
Maternal mortality	139 (-2231, 1720)	136 (-2169, 1672)	141 (-2264, 1745)
Stillbirth	3,810 (3810, 16510)	3,528 (-10584, 15288)	2,057 (-6171, 8914)
Neonatal mortality	-8,035 (-29462, 10713)	-3,619 (-13268, 4825)	-4,646 (-16375, 5955)
Infant mortality	2,723 (-3812, 9257)	1,206 (-1689, 4101)	1,489 (-2084, 5062)
Incremental benefits [†] (DALYs averted)	11,749 (-44889, 61607)	12,462 (-25483, 45619)	9,332 (-24687, 36019)
Incremental costs [‡] (2016 USD PPP)	182,400	182,400	182,400
Incremental cost-effectiveness ratio (cost/DALY averted)	15.53	13.94	19.55
GDP per capita	5,429	3,580	6,570

[†]The incremental benefits are the additional DALYs averted by MMS.

[‡]The incremental costs are the additional costs of transitioning from IFAS to MMS.

Figure 1.



The graph demonstrates the effect on the overall DALYs averted as each health outcome is added, as well as the confidence intervals around the cumulative DALYs averted. The outcomes are added from A, only LBW, to H, having all the 8 outcomes. The biggest effect on the expected DALYs averted (and the confidence around it) occurs through the addition of neonatal mortality in H.

A - LBW;

B - LBW + SGA;

C - LBW+SGA+Anaemia;

D - LBW+SGA+Anaemia+Preterm;

E - LBW+SGA+Anaemia+Preterm+Maternal mortality;

F - LBW+SGA+Anaemia+Preterm+Maternal mortality+Infant mortality;

G - LBW+SGA+Anaemia+Preterm+Maternal mortality+Infant mortality+Stillbirth;

H - LBW+SGA+Anaemia+Preterm+Maternal mortality+Infant mortality+Stillbirth+Neonatal mortality

