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Introduction

Recent evidence has encouraged low- and middle-income countries (LMIC) to consider transitioning from long-standing iron and folic acid supplementation (IFAS) to multiple micronutrient supplementation (MMS) during pregnancy. However, global guidance to facilitate this transition is limited.

To aid countries' decision-making, the MMS Cost-Benefit Tool was developed. It uses a rigorous methodology to calculate the incremental benefits and costs of transitioning from IFAS to MMS in various countries (Kashi et al., 2019). In this context, the term “transition” refers to substituting IFAS with MMS for pregnancy care in a government’s antenatal service package.

With the MMS Cost-Benefit Tool, users can construct and test different scenarios by updating the assumptions within the tool. Up to eight health outcomes are included in the analysis, and these are aggregated using disability-adjusted life years (DALY). A DALY represents one lost year of perfect health. It is calculated by aggregating the effect of a health issue on mortality and morbidity. Interventions seek to avert DALYs.

The tool has been designed to balance simplicity of use with meaningful results. This user guide provides an overview of the functionality of each section of the tool. It also provides guidance on interpretation of the results.
Report Interface

Please note: screenshots are for information only. Numbers may not be accurate.
The first step to running an analysis is to choose between the Report interface and the Custom interface.

Key Parameters and Results for Bangladesh

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>Health Outcome Analysis</th>
<th>Cost-Effectiveness Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population: 2,960,026</td>
<td>Additional DALYs averted by MMS Compared to IF4S (Significant outcomes only)</td>
<td>$3,696,039,235 Value of DALYs averted</td>
</tr>
<tr>
<td>Time span: 10</td>
<td>Stillbirth</td>
<td>$7,589,729 Additional investment over 10 years</td>
</tr>
<tr>
<td>Coverage: 99%</td>
<td>Neonatal mortality (1)</td>
<td>487 Benefit Cost Ratio</td>
</tr>
<tr>
<td></td>
<td>Neonatal mortality (10)</td>
<td>$5.99 Additional cost per DALY averted</td>
</tr>
<tr>
<td></td>
<td>Infant mortality</td>
<td>Very Cost Effective</td>
</tr>
<tr>
<td></td>
<td>Prematurity</td>
<td>according to WHO guidelines</td>
</tr>
<tr>
<td></td>
<td>Low birth weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Small for gestational age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maternal mortality</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maternal anemia</td>
<td></td>
</tr>
<tr>
<td>Cost: $3.27</td>
<td>Significant</td>
<td>$1,268,067</td>
</tr>
<tr>
<td>Transition</td>
<td>Not significant</td>
<td>12,640</td>
</tr>
<tr>
<td></td>
<td>Not reported</td>
<td>100.0%</td>
</tr>
<tr>
<td>Source of health effects</td>
<td>Confidence in positive health outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deaths</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Progress</td>
<td></td>
</tr>
</tbody>
</table>

For more information contact MMS@nutritionsoft.org
Last updated: 2019-10-05

Dashboard developed by LimeStone
In the Report interface, select a country by either choosing it from the list in the upper-left of the tool, or by clicking on a dot on the map. Only one country may be selected at a time. When a country is selected, its dot on the map will become pink and the button beside its name in the list will be filled.
Hovering the cursor over a point on the map will reveal a tooltip with country-specific information.

Clicking the Home button in the top left corner of the map will restore the map to its default view.

Double-clicking the map will zoom the view of the map. Clicking and holding will pan the view of the map.
Key Parameters and Results

The bottom half of the report interface displays key assumptions and results for the selected country.

Key Parameters and Results for Bangladesh

Assumptions
- Population: 2,965,826
- Timespan: 10
- Coverage: 30% 889,748
- Costs per beneficiary
  - IFAS: $2.27
  - MMS: $3.27
- Transition Cost: $0
- Source of health effects
  - Keats et al. 2019 (Cotinine)
  - Smith et al. 2017 (Lancet)

Significant outcomes only

Health Outcome Analysis
- Additional DALYs averted by MMS Compared to IFAS (Significant outcomes only)
  - Stillbirth
  - Neonatal mortality (F)
  - Neonatal mortality (M)
  - Infant mortality
  - Pre-term
  - Low birth weight
  - Small for gestational age
  - Maternal mortality
  - Maternal anemia

- 1,268,067

Confidence in positive health outcomes

Cost-Effectiveness Analysis
- $3,696,039,235
  - Value of DALYs averted
- $7,589,729
  - Additional investment over 10 years
- 487
  - Benefit-Cost Ratio
- $5.99
  - Additional cost per DALY averted

Very Cost Effective according to WHO guidelines

For more information contact MoMS@nutritionintl.org
Last updated: 2019-10-05
Assumptions

The left hand pane groups together assumptions that the user can modify. Hovering over any of the parameter names will reveal a tooltip that provides more information about the parameter.

The values in input fields can be changed by clicking on the input field and typing in the new value.

An input can be reset to its default value by clicking on the circular arrow button to the right side of the input field.

All input values can be reset at once by clicking the Reset all inputs button.
The population of pregnant women in the intervention area is calculated based on the national population and crude birth rate. Sources for these values can be found in the Data Sources file which is available for download from Nutrition International's web page where the tool is embedded.

Length of the supplementation program over which costs and benefits are counted. Maximum allowable timespan for analysis is 20 years. Additional benefits provided by MMS begin in Year 1 of the MMS supplementation program. The costs and benefits are calculated for the over the lifespan of each mother and child in of each cohort year.

Proportion (%) and number of pregnant women in the intervention area who will receive 180 supplements.

Default supplement unit costs for IFA were reported from the current UNICEF supply catalogue. User can modify to different value. Transition cost is the cost for non-commodities expenses related to transition from a IFA 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. The calculations assume that transition costs are all incurred in Year 0 (i.e. the year during which the transition from IFAS to MMS begins). The transition cost should be input as the total present value of the transition cost. If transition costs are anticipated in more than one year, input the total anticipated transition cost across all years.
In the **assumptions pane**, a number of assumptions are required in order to undertake the analysis. Two recent meta-analyses that compared MMS and IFAS in LMICs were used as the **sources of health effects**. The user can select which meta-analysis to use for the analysis. One source was published in Cochrane (Keats et al., 2019) and the other in 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, and looked at additional health effects including very preterm birth and gender dis-aggregated values for neonatal mortality. Smith et al. found that when compared to IFA, MMS reduces the risk of stillbirth, very LBW, LBW, early preterm birth and SGA; Keats et al. reported only significant effects for the reduced risk of LBW and SGA.

Two meta-analyses comparing MMS and IFAS in LMICs were used as the sources of health effect sizes. A Cochrane Review was published by Keats et. al. in 2019 (1) and a meta-analysis of individual patient data (IPD) was published in the Lancet by Smith et. al., 2017 (2). While the inclusion criteria for these two meta-analyses were comparable, Keats et. al. included studies that compared MMS with IFAS or iron alone. Smith et. al. only included studies comparing MMS to IFAS, and looked at additional health effects including very preterm birth and gender dis-aggregated values for neonatal mortality. Smith et al. found that when compared to IFA, 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 while Keats et al. only found evidence of significant effects on LBW and SGA (Bourassa et al., 2019).

The **population** is the number of pregnant women in the intervention area where the supplementation program will take place. The default value assumes the intervention area is the whole country. It is calculated based on the national population and crude birth rate. Sources for these values can be found in the *Data Sources* file. To generate an analysis for a sub-national population the user will need to input the population of pregnant women for the area of interest (sub-national population X crude birth rate). The **timespan** is the length of the supplementation program over which the costs and benefits are counted. It must be a value between 1 and 20 years. The costs and benefits are calculated for the lifespan of both the mother and the child for each cohort year. **Coverage** is expressed as a percentage and a number. It represents the proportion or number of pregnant women in the intervention area who will receive 180 supplements. This is aligned with the trials included in the meta-analyses.

The **costs per beneficiary** refers to the cost of 180 supplements. The default values were taken from UNICEF’s supply catalogue which is in USD. The **transition cost** is the cost for non-commodities expenses related to transition from an IFA 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. The calculations assume that transition costs are all incurred in Year 0 (i.e. the year during which the transition from IFAS to MMS begins). The transition cost should be input as the total present value of the transition cost. If transition costs are anticipated in more than one year, input the total anticipated transition cost across all years.
Health Outcome Analysis

The middle pane reports several measures of the change in health outcomes from resulting from the transition from IFAS to MMS.

The results are calculated based on only those health outcomes that have been selected for inclusion in the analysis.

As with other elements in the tool, hovering over a bar in the chart reveals a tooltip with more information.
In the **Health Outcome Analysis pane**, the bar chart reports the number of **DALYs averted** by transitioning from IFAS to MMS for each health outcome. The calculation for the number of **DALYs averted** factors in a discount rate of 3% in line with the Bill and Melinda Gates Foundation (BMGF) Methods for Economic Evaluation Project Reference Case in Global Health (BMGF & NICE International, 2014). The tool can compare IFAS and MMS through all health outcomes, or only those that are reported in the selected meta-analyses to have an impact that is statistically significant from 0. By default, the tool includes only significant outcomes in the analysis. The colour of the bar indicates whether the result is significant, non-significant or not reported in the selected meta-analysis. Below the bar chart are three summary measures of the change in health outcomes resulting from the switch from IFAS to MMS. To the left, the **total number of DALYs averted** across all included health outcomes is reported. In the center, the number of **child deaths averted** is reported. This number is calculated by summing the DALYs averted from stillbirth, neonatal and infant mortality and dividing by life expectancy at
birth in the selected country. To the right, the *confidence in positive health outcomes*, which 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, and is reported as a percentage.

**Cost-Effectiveness Analysis**

![Cost-Effectiveness Analysis Image]

The results are calculated based on only those health outcomes that have been selected for inclusion in the analysis.

As with other elements in the tool, hovering over a result reveals a tooltip with more information.
The economic value of the benefits of the transition. It is estimated based on the number of DALYs averted and a measure of the Value of Statistical Life (VSL) for the country under analysis. The VSL can be thought of as the amount of money that a person would be willing to pay to avoid injury or illness. There are a number of different ways to calculate the VSL for a country. Viscusi and Masterman report the most recent estimates of the VSL in all low- and middle-income countries (Viscusi and Masterman, 2017). A country’s VSL is converted into a Value of a Statistical Life Year (VSLY) by dividing the VSL by the expected life expectancy at birth. Then, a monetized DALY approach is taken by multiplying the number of DALYs averted by the VSLY.

Additional investment required over timespan indicator reports how much more the MMS program will cost than the IFAS program in total over the timespan being
considered. This amount is based on the difference in IFAS and MMS supplement costs and the *Transition cost* input from the *Assumptions* pane.

The *Value of DALYs averted* (the benefits) is compared with the *Investment required* (the costs) to produce the *Benefit-Cost Ratio (BCR)*. If the BCR is greater than 1, then the value of the benefits of transitioning to MMS exceeds the costs.

The bottom two measures provide a different estimate of cost-effectiveness based on a guideline from the World Health Organization (Leech et al., 2018). This guideline suggests that if the *Incremental cost per DALY averted* (i.e. the amount of additional investment required to prevent one DALY) 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.*"
Custom Interface

Clicking on the Custom Analysis button beneath the tool title will open a new interface that allows the user to manually input parameter values to create a custom report. This is useful when there is a need to explore outcomes of transitioning from IFAS to MMS at sub-national levels, or when there is a need to simulate outcomes in a country that is not included in the pre-loaded options in the Report interface.
The custom analysis inputs are similar to the inputs in the *Assumptions* pane, with tooltips that open when hovered over and reset buttons. The *Reset all inputs* button in the *Custom Analysis* pane will only reset the inputs in the *Custom Analysis* pane, but will not reset the inputs in the *Assumptions* pane. The bottom half of the *Custom Analysis* interface is identical to the bottom half of the *Report* interface.

The *Data Sources* file serves as a guideline on the sources of information for the parameters. Recommended data sources for prevalence values include: World Bank Open Data, UNICEF and Demographic and Health Surveys.
A common method of quantifying the economic value of improved health outcomes is using a measure called the Value of Statistical Life (VSL). The VSL can be thought of as the amount of money that a person would be willing to pay to avoid injury or illness. There are a number of different ways to calculate the VSL for a country. Viscusi and Masterman report the most recent estimates of the VSL in all low- and middle-income countries (Viscusi and Masterman, 2017).

Life expectancy at birth: Average number of years that a newborn could expect to live if he or she were to pass through life exposed to the sex- and age-specific death rates prevailing at the time of his or her birth, for a specific year, in a given country, territory or geographical area. (WHO)

Life expectancy at median age at first birth among women aged 25-49 years (World Bank).
Number of stillbirths per 1000 total births. Stillbirths can occur antepartum or intrapartum. For purposes of international comparison, stillbirths are defined as third trimester fetal deaths (≥ 1000 g or ≥ 28 weeks). (WHO)

Number of deaths during the first 28 days of life, expressed per 1,000 live births (UNICEF).

Number of deaths 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) (WHO) expressed per 100,000 live births.

Number of deaths between birth and exactly 1 year of age, expressed per 1,000 live births (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.
When the tool calculates DALYs averted, the prevalence of LBW and infant mortality is adjusted for 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 (AGA) infants. The prevalence of SGA is adjusted to remove preterm SGA infants (Kozuki N, Katz J, Clermont A & Walker N, 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 results of the analysis can be downloaded as a PDF by clicking the *Export to PDF* button below the tool on Nutrition International’s webpage. By default, the tool downloads both the *Report* and *Custom* interfaces. To export only one of the interfaces to PDF, click the drop-down arrow under *Include* in the PDF Export dialog box. Click the option *Specific sheets from this workbook*.

Select the interfaces that you would like to include in the PDF report, set the Scaling, Paper Size and Orientation options and click the *Create PDF* button.
The tool will time out if left idle for more than five minutes. Click the refresh symbol in the web-browser to reset. However, please be aware the tool will return to default and you will lose any new data. If using the Custom Interface, it is recommended that you compile your data in advance.

For assistance, please email MoMS@NutritionIntl.org.

Thanks to Limestone Analytics for their support and technical leadership in developing the underlying model, tool and this supporting documentation.
References


