Experience from the Field
The Case for Reintroducing Multiple Micronutrient Supplements in South Africa’s Essential Medicines List

Creating an enabling environment for nutrition-specific interventions in antenatal care

Key messages

- For 6 years, between 2010 and 2016, most provinces in South Africa provided multiple micronutrient supplements (MMS) to all pregnant and lactating women, but removal from the national essential medicines list (EML) led to the discontinuation of provision in late 2016. *Sight and Life* documented South Africa’s MMS journey in 2018.
- Based on *Sight and Life*’s case study, transitioning from iron and folic acid (IFA) to MMS has been shown to be cost-effective for the South African context, and translates into substantial future social and public health benefits and economic savings for South Africa.
- Transitioning from IFA to MMS has been shown to be relatively straightforward, but investing in training and social and behavioral change communication is important because this strengthens uptake and adherence, which in turn will amplify the health impact.
- Given the strong scientific evidence, the South African national government and international bodies can help to restart the provision of MMS. A strategy for reintroduction and a four-step action plan are outlined in this article.
- We also present a suggested table of contents, for advocacy purposes, that was co-created with MMS champions in South Africa. This can be adapted to suit the local contexts of other low- and middle-income countries (LMICs) considering the inclusion of MMS in their EMLs.

The rise and fall of MMS in South Africa

Between 2010 and 2015, South Africa was the only LMIC that provided MMS through government channels. In 2016, the national government dropped MMS from the national EML because of the lack of knowledge about the strong evidence base for MMS and the lack of clear guidelines from WHO. This action prevented provinces from ordering it, and pregnant women from accessing it. In 2018, *Sight and Life* undertook a policy and programmatic analysis, conducting interviews with key informants in the country to fill the gaps in the knowledge required to build a strong consensus for MMS in South Africa’s policy landscape and advocate for MMS being reintroduced into the EML (Figure 1 and Box 1).

“In 2018, *Sight and Life* undertook a policy and programmatic analysis to build a strong consensus for MMS in South Africa’s policy landscape”

In the first section of this article, we provide an overview of the policy hurdles for MMS in South Africa to set the context. In
the next section, we address the knowledge gap around the evidence base by taking the birth outcomes and cost-effectiveness of MMS from two recent scientific reviews,\textsuperscript{1,2} and applying it to the South African context. In the third part of this article, we address the knowledge gap around programmatic aspects of MMS and synthesize learnings from provinces to establish a transition back to MMS. We close out the article by presenting recommendations and strategies for the reintroduction of MMS into the EML.

**BOX 1: What are the arguments for placing MMS in the EML?**

A substantial body of observational, experimental and programmatic data documents the efficacy and cost-effectiveness of MMS, as described elsewhere in this *Sight and Life* Special Report. There is precedent for countrywide MMS distribution in South Africa, and all the programmatic barriers and enabling factors are well known, which would facilitate a smooth reintroduction:

- Inclusion of MMS in the EML would lead to improved integration of nutrition within the health system.
- Inclusion of MMS in the EML would result in better management of newborn and maternal nutrition programs.
- Increased financial resources would be available for MMS, and this could decrease overall product costs. This is based on assumptions that this commitment and demand would stimulate local production of MMS and that harmonization of standards could lead to a larger scale of production for bigger producers, thus decreasing unit costs.
- Inclusion of MMS in the EML would assist in changing perceptions around MMS and contribute to raising awareness of prenatal supplementation, as well as of maternal and newborn undernutrition in general, thus motivating healthcare workers.

**Missed opportunity: the impact of national policy changes on provinces**

*Sight and Life*’s interviews with three provincial nutrition managers indicated that provincial nutrition departments championed MMS, but that the National Department of Health remained unconvinced. In the absence of clear guidelines from national government, the National Expert Medicine List Committee (NEMLC) deemed MMS nonessential and removed it from the national EML. After the MMS indication for pregnant and lactating women was removed from South Africa’s standard treatment guidelines and EML in 2016, the guidelines indicated MMS provision only for pregnant and lactating women at risk of malnutrition. More recently, in 2017, the standard treatment guidelines were changed to remove MMS altogether, and the 2018 standard treatment guidelines recommend IFA supplementation only (Figures 2A–C).\textsuperscript{3}

![FIGURE 2A: Province-level guidelines 2016: change to MMS provision only for pregnant and lactating women classified as at risk of malnutrition](image)

<table>
<thead>
<tr>
<th>Target Groups</th>
<th>Supplement</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0 to 59 months) at risk of Severe Acute Malnutrition/ TB/HIV</td>
<td>Zinc syrup</td>
<td>As per standard protocol</td>
</tr>
<tr>
<td>Children 0-59 months with diarrhea</td>
<td>Vitamin A – age appropriate dose as per standard protocol</td>
<td>Six – monthly intervals</td>
</tr>
<tr>
<td>Children 6-59 months</td>
<td>Complete multiple micronutrient supplements, calcium</td>
<td>Duration of pregnancy</td>
</tr>
<tr>
<td>Pregnant women at risk of malnutrition</td>
<td>Complete multiple micronutrient supplements</td>
<td>6 months of lactation</td>
</tr>
<tr>
<td>Lactating women at risk of malnutrition</td>
<td>Complete multiple micronutrient supplements</td>
<td>6 months</td>
</tr>
<tr>
<td>Adults – Underweight with TB, HIV, AIDS</td>
<td>Complete multiple micronutrient supplements</td>
<td>6 months</td>
</tr>
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</table>

**FIGURE 2B: Province-level guidelines 2017: MMS for pregnant and lactating women completely removed from the guidelines**

<table>
<thead>
<tr>
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</thead>
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<td>Zinc syrup</td>
<td>As per standard protocol – IMCI guidelines</td>
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</tr>
<tr>
<td>Pregnant women</td>
<td>IFA and calcium as per maternity guidelines</td>
<td>Duration of pregnancy</td>
</tr>
</tbody>
</table>

**Level of care**

At PHC level
- Complete multiple micronutrients will not be procured at hospital level
- In the event that the hospital requires complete multiple micronutrients to treat a specific case, motivation would have to be done at facility level with relevant stakeholders

Below is the revised schedule for micronutrient supplementation

<table>
<thead>
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<td>IFA and calcium as per maternity guidelines</td>
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</tr>
</tbody>
</table>

The change is effective from the 1st of April 2017. Facilities who still have stock on hand should continue supplementation as per previous recommendation until the stock is finished. The stock should not be replenished thereafter.
3 years is lower than the total amount of prenatal IFA in 2019 alone. These numbers are procured and distributed by provincial governments over the past 3 years since MMS was removed from the EML. These numbers are abysmally low, and it is striking that the cumulative quantity of MMS capsules/tablets procured and distributed over the past 3 years is lower than the total amount of prenatal IFA in 2019 alone (Table 1B). This highlights that, even with political will and budget availability at the provincial level for MMS, not having it on the EML created major programmatic challenges in ordering large volumes.

Provincial nutrition leaders remain committed to MMS because of its superioritv to IFA, and continue procuring it in very small quantities as a backup to IFA. Table 1A shows the number of MMS capsules procured and distributed by provincial governments over the past 3 years since MMS was removed from the EML. These numbers are abysmally low, and it is striking that the cumulative figure for number of MMS capsules/tablets procured and distributed over the past 3 years is lower than the total amount of prenatal IFA in 2019 alone (Table 1B). This highlights that, even with political will and budget availability at the provincial level for MMS, not having it on the EML created major programmatic challenges in ordering large volumes.

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The evidence base: public health relevance of MMS in South Africa

a. Birth outcomes

As an LMIC, South Africa presents with high rates for preterm birth (< 37 weeks gestational age) and low birth weight (LBW; < 2,500 g); the rates can be as high as 14 percent, as opposed to 7 percent in high-income countries. The estimated rates for adverse birth outcomes in South Africa are shown in Figure 2. Apart from increased risk of increased maternal and child mortality, the risk for suboptimal child growth and development can be long term.⁴ Severe developmental disabilities associated with LBW and/or preterm birth include cerebral palsy, sensory impairments of vision and hearing, mental disability and seizure disorder. In addition, neurodevelopmental functions, such as attention, cognition, executive functioning, emergent literacy, sensory processing, gross and fine motor skills, communication and language, as well as infant feeding and swallowing, may be affected in children with LBW and/or preterm birth.

In South Africa, the largest category of perinatal deaths is unexplained stillbirth, of which up to one-quarter are related to small for gestational age (SGA). High on the global health agenda is accelerating progress to end preventable stillbirths. In 2014, the Every Newborn Action Plan set a target of 12 or fewer stillbirths per 1,000 births in every country by 2030. MMS is a ready and cost-effective solution to help us meet these targets.⁵

b. Potential impact of MMS on birth outcomes

Table 2 shows the average estimated costs of MMS and IFA in South Africa. The larger the number of capsules/tablets per unit supply, the smaller the cost difference between MMS and IFA, since packaging determines the largest portion of the total costs.

<table>
<thead>
<tr>
<th>Table 2: Cost of MMS and IFA in South Africa</th>
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</thead>
<tbody>
<tr>
<td><strong>Price of MMS</strong></td>
</tr>
<tr>
<td>30 capsules/tablets</td>
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<tr>
<td>60 capsules/tablets</td>
</tr>
</tbody>
</table>

*Includes transportation costs; government bears no additional costs to get MMS to clinics because of streamlining through existing depots.
When assuming risk reduction rates in adverse birth outcomes as 6,500 cases of LBW and an additional 1,500–3,600 cases of SGA would be prevented (Table 3). The impact of MMS on LBW and SGA would be even more significant: an additional 2,600–6,500 cases of LBW and an additional 1,500–3,600 cases of SGA could be averted. Thus, given the potential price differences between MMS and IFA supplementation in South Africa (Table 2), the additional benefits of MMS clearly outweigh the higher costs.

If the switch were to be made from IFA to MMS, the health impact on the South African population would be tremendous: 1,100–2,700 additional preterm births and 300–600 additional stillbirths could be prevented (Table 3). The impact of MMS on LBW and SGA would be even more significant: an additional 2,600–6,500 cases of LBW and an additional 1,500–3,600 cases of SGA could be averted. Thus, given the potential price differences between MMS and IFA supplementation in South Africa (Table 2), the additional benefits of MMS clearly outweigh the higher costs.

Recently, an MMS Cost-Benefit Tool was launched to allow governments to calculate the cost-benefit ratio of transitioning from IFA to MMS based on their country-specific demographics. When assuming risk reduction rates in adverse birth outcomes as reported by Smith et al., 212,120 additional disability adjusted life years (DALYs) and 2,505 additional child deaths could be averted in South Africa when transitioning from IFA to MMS at a cost-effectiveness of US$12.17 per DALY averted, making MMS a very cost-effective intervention (Figure 4).

### Programmatic experiences: transitioning from current system in South Africa

**Sight and Life’s** interviews revealed two key triggers that first led to the inclusion of MMS for pregnant and lactating women in South Africa in 2010.

1. The budget for MMS has always been in place in provinces because of highly prioritized HIV treatment:
   - Providing MMS as part of antiretroviral therapy for HIV was mandatory.
   - With improving HIV rates over the years, provincial focus shifted to low birth outcomes and preventative maternal care.
   - With the shifting priorities, provinces started using HIV conditional grants to procure MMS for all pregnant and lactating women to improve birth outcomes. However, no programmatic investments were made in training and behavior change communication to avoid any HIV-related stigma associated with MMS consumption.

2. MMS was considered a low-burden health intervention because it leveraged the IFA supply and distribution channels:

### TABLE 3: Impact of MMS over IFA at 25% (conservative) to 62% (optimistic) coverage on birth outcomes (there are ~1.1 million pregnancies per year in South Africa)*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate</th>
<th>Cases</th>
<th>Reached at 25–62% MMS coverage</th>
<th>Reduced risk with MMS*</th>
<th>Prevented cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>8%</td>
<td>-88,000</td>
<td>37,000–91,000</td>
<td>18%</td>
<td>4,000–9,800</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>7.9%</td>
<td>-87,000</td>
<td>20,000–49,000</td>
<td>12%</td>
<td>2,600–6,500</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>6.7%</td>
<td>-74,000</td>
<td>23,000–58,000</td>
<td>3%</td>
<td>500–1,400</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>2%</td>
<td>-20,000</td>
<td>5,000–13,000</td>
<td>8%</td>
<td>400–1,000</td>
</tr>
</tbody>
</table>

* Currency in US$

**Notes:** This analysis was conducted on Nutrition International’s MMS Cost-Benefit Analysis Tool. An updated version of the analysis can be found on: https://www.nutritionintl.org/knowledge-centre/mms-cost-benefit-tool/

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**FIGURE 4: Cost-effectiveness of MMS in South Africa**

### Assumptions
- Population: 1,099,065
- Time span: 10
- Coverage: 30% 302,720
- Costs per beneficiary
  - IFA: $2.27
  - MMS: $1.27
- Transition
  - Cost: $0
- Source of health effects
  - Keats et al. 2019 (Cochrane)
  - Smith et al. 2017 (Lancet)

**Health Outcome Analysis**

<table>
<thead>
<tr>
<th>Additional DALYs averted by MMS Compared to IFAS (Significant outcomes only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirth: $12,170</td>
</tr>
<tr>
<td>Neonatal mortality (N): Preterm: $0</td>
</tr>
<tr>
<td>Maternal mortality: $0</td>
</tr>
</tbody>
</table>

**Cost-Effectiveness Analysis**

- **Value of DALYs averted:** $35,330,737,206
- **Additional investment over 10 years:** $2,582,259
- **Benefit Cost Ratio:** 13,682
- **Additional cost per DALY averted:** $12.17

**Very Cost Effective**

According to WHO guidelines.
A quote by one of the provincial nutrition managers who was interviewed sums up the ease of transitioning from IFA to MMS. She said, “The programmatic aspect of MMS is the least of the problems. The policy framework is the problem because of lack of evidence and because it is no longer on the EML. MMS is extremely easy to integrate into the healthcare system.”

The lessons from the 5 years of MMS distribution indicate that in mature pharmaceutical markets such as South Africa, MMS is easy to manufacture and deliver (Figure 4); however, motivating practitioners through training is challenging when policy guidelines are inconsistent and equivocal. While the MMS supply chains were programatically efficient, no resources were spent on training, demand creation and compliance. At the hospital/clinic level, nurses and practitioners were trained on the general supplementation policy of the province but never received explicit training on MMS and its benefits. MMS was just one of the many supplements that practitioners were trained to prescribe. Investing in training and social and behavioral change communication is important because it strengthens uptake and adherence, which in turn will amplify the health impact of MMS among women and children in South Africa.

Moreover, South African provinces are extremely autonomous and varied: in low-capacity provinces, budgetary allocations to prenatal care (such as MMS) are not always acknowledged and/or prioritized. Strong national policy guidelines, accompanied by a reintroduction of MMS into the EML, would make it easier for provinces to transition back to MMS and allocate budgets for procurement and training.

MMS is one of the most cost-effective investments among the different potential antenatal care interventions. For South Africa, thousands of preterm births and stillbirths and tens of thousands of LBW and SGA infants could be averted by transitioning from IFA to MMS. Transitioning from IFA to MMS has been shown to be cost-effective for the South African context. This could translate into substantial future social and public health benefits and economic savings for South Africa. Transitioning from IFA to MMS has been shown to be relatively straightforward, but investment in training and social and behavioral change communication is required to strengthen uptake and adherence, and in turn increase the health impact in South Africa. Therefore, prioritizing financial resources towards nutrition-specific interventions in antenatal care would provide a significant return on investment and could ultimately decrease overall societal costs.

The path forward: strategies for reintroduction
With the scientific evidence in place and ease of transitioning established, four immediate actions would be needed to build consensus for MMS in South Africa’s policy landscape:

1. **Sensitize the NEMLC.** This committee is made up of clinicians and academics whose decisions guide medicine procurement in the public sector. They are responsible for reviewing and updating the EML every 2–3 years. Sensitizing them to the latest evidence is paramount, and special attention needs to be paid to highlighting the medical outcomes (reduction of LBW, SGA and preterm births) of a simple and cost-effective micronutrient supplement.

2. **Provide technical support to provinces with pharmacy and therapeutics committees (PTCs).** PTCs can determine...
province-level medicine needs, independent of the NEMLC. Typically, provincial nutrition departments do not advocate with PTCs given the process-heavy nature of engagement, which is why NGOs are well suited to support provinces and could provide technical support around the evidence base and programmatic aspects of MMS.

These multistakeholder groups are convened at the highest levels of national government and have not been engaged in a strategic manner to champion MMS, even given the advocacy effort of several prominent NGOs. There is an opportunity to create a strategic plan focused on the advocacy of MMS for pregnant women.

Knowledge sharing and capacity building among provinces are essential to create a joint advocacy plan for MMS. Currently, provincial advocacy efforts for MMS are fragmented and few opportunities exist for low-capacity provinces – such as Eastern Cape and Northern Cape – to learn from well-resourced provinces – such as KwaZulu-Natal – about programmatic aspects of MMS. By convening provincial departments, information could be shared more effectively and a joint advocacy plan for MMS could take shape.

Based on these recommendations, which emerged from Sight and Life’s analysis in 2018, a group of experts has been convened to provide guidance to a national technical advisor. The expert group has co-created a memo with the aim of providing concise, easy-to-read, scientific and health-economic evidence-based guidance for the reintroduction of prenatal MMS into the EML and making it accessible by the end of 2020 (Box 2).

BOX 2: How can the global nutrition community support LMICs in advocating for the inclusion of MMS in national EMLs?

Through this exercise in South Africa, we were able to gather valuable insights into the key pieces of information that decision-makers in LMICs look for when deliberating on the inclusion of MMS in national EMLs, in the absence of a WHO recommendation. The global nutrition community has the opportunity to play the role of catalysts by helping LMICs compile this information. Below, we present a suggested table of contents that was co-created with MMS champions in South Africa, which can be adapted to suit the local contexts of other LMICs considering the inclusion of MMS in their EMLs.

All of the information below can be compiled through a combination of desk research and structured/semi-structured interviews with key informants, which include officials in government departments, industry and local NGOs.

Document outline
Objective
Executive summary
Background
1. Preventing poor birth outcomes
2. Scientific evidence: MMS versus IFA
3. Role of MMS in pregnant women
4. Cost-benefit of MMS versus IFA
5. Current WHO guidelines and possible evolution
6. Current product standard: UNIMMAP MMS implementation in country of interest
7. Public health relevance in country of interest
   7.1 Nutritional gaps in pregnant women in country of interest
   7.2 Birth outcomes in country of interest
8. Potential impact of MMS on birth outcomes in country of interest
9. Current policy and regulation in country of interest
10. Guidelines for maternal care in country of interest
11. Prenatal supplementation indication for pregnant women in country of interest
12. Ease of transitioning from current system in country of interest
13. Current government tender specifications in country of interest
14. Recommendations
Conclusion
References

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We would like to extend our sincerest thanks to Maaike Bruins and Heidi-Lee Robertson for providing us with invaluable information and insights for this article. We would also like to thank all the other key stakeholders from government, industry and NGOs who took time out to be interviewed for this case study.

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References


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