

# **Impact of Antenatal Multiple Micronutrients on Women's Health and Pregnancy Outcomes**

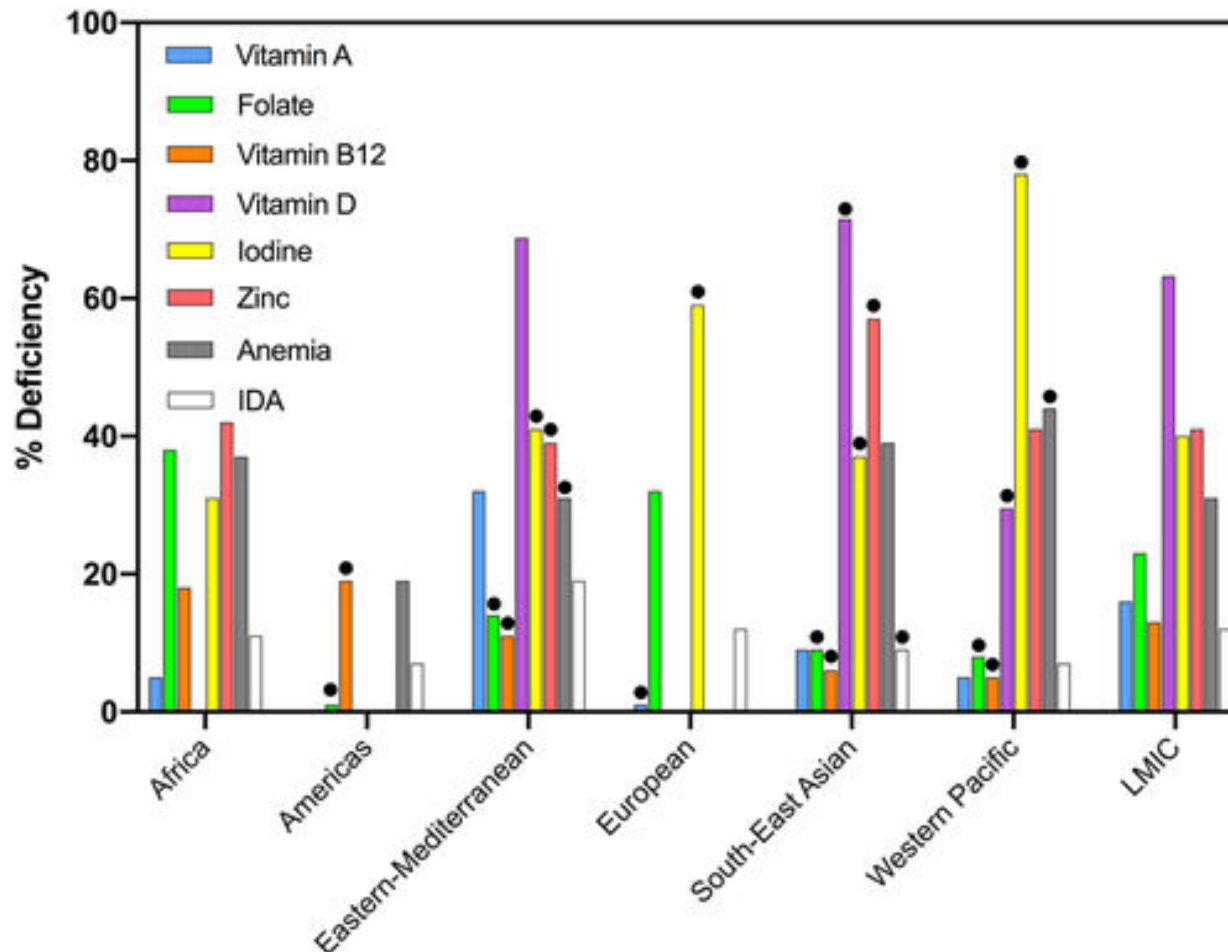
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# High Prevalence of Micronutrient Deficiency Among Women of Reproductive Age



# Evidence Supports the Switch from IFA to MMS in Pregnancy

**Cochrane Review**  
2019 update



**Multiple-micronutrient supplementation for women during pregnancy (Review)**

Keats EC, Haider BA, Tam E, Bhutta ZA

**Individual Patient Data (IPD)  
Meta-analysis (2017)**

**Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries**

Lancet Glob Health 2017;  
5: e1090-100

Emily R Smith, Anuraj H Shankar, Lee S-F Wu, Said Aboud, Seth Adu-Afaruwah, Hasmat Ali, Rina Agustina, Shams Arifeen, Per Ashorn, Zulfiqar A Bhutta, Panil Christian, Delanjathan Devakumar, Kathryn G Dewey, Henrik Friis, Exnevia Gomo, Piyush Gupta, Pernille Kästel, Patrick Kolsteren, Hermann Lanou, Kenneth Maleta, Aïssa Mamadou Itaïbou, Gernard Msamanga, David Osrin, Lars-Åke Persson, Usha Ramakrishnan, Juan A Rivera, Arjumand Rizvi, H P S Sachdev, Willy Urassa, Keith P West Jr, Noel Zagre, Lingxia Zeng, Zhonghai Zhu, Wafaie W Fauzi, Christopher R Sudfeld

# Effects of MMS vs. IFA: Birth and Infant Outcomes

| Outcomes   | Cochrane Review (15 RCTs)<br>Relative Risks (RR (95% CI)) | IPD Meta-Analysis (17 RCTs)<br>Relative Risks (RR (95% CI)) |
|--|---|---|
| Small for Gestational Age (<10 <sup>th</sup> percentile)             | <b>0.92 (0.88-0.97)<sup>a</sup></b>                       | <b>0.97 (0.96-0.99)<sup>b</sup></b>                         |
| Low Birth Weight (<2500g)  | <b>0.88 (0.85-0.91)</b>                                   | <b>0.88 (0.85-0.90)</b>                                     |
| Very Low Birth Weight (<2000g)                                       | Not Reported  | <b>0.78 (0.72-0.85)</b>                                     |
| Preterm Birth (<37 weeks)  | 0.95 (0.90-1.01)  | <b>0.92 (0.88-0.95)</b>                                     |
| Very Preterm Birth (<34 weeks)                                       | Not Tested  | <b>0.87 (0.79-0.95)</b>                                     |
| Large for Gestational Age (>90 <sup>th</sup> percentile Oken)        | Not Tested  | 1.05 (0.95-1.15)  |
| Large for Gestational Age (>90 <sup>th</sup> percentile INTERGROWTH) | Not Tested  | 1.11 (1.04-1.19)  |
| Stillbirth   | 0.95 (0.86-1.04)  | <b>0.92 (0.86-0.99)</b>                                     |
| Neonatal Mortality (≤28 days)  | 1.00 (0.89-1.12)  | 0.98 (0.90-1.05)  |
| Infant Mortality   | Not Reported  | 0.97 (0.88-1.06)  |

<sup>a</sup>SGA defined by authors of trials; <sup>b</sup>SGA defined by the INTERGROWTH-21 standard

MMS, multiple micronutrient supplementation; IFA iron with or without folic acid; IPD, individual participant data; RCTs, randomized controlled trials. RR in green show a significant decrease in RR.

# The 2017 Individual Participant Data (IPD) Meta-Analysis

Percent reduction in selected birth outcomes with MMS compared to IFA alone based on the IPD meta-analysis

| <b>Birth Outcomes</b>     | <b>Pregnant Women</b><br>(Overall) | <b>Anemic Pregnant Women</b><br>(Hb <110 g/L at enrollment) | <b>Underweight Pregnant Women</b><br>(<18.5 kg/m <sup>2</sup> ) |
|---------------------------|------------------------------------|---|---|
| Stillbirth                | 8%                                 | 21%   | NS  |
| Infant 6-Month Mortality  | NS                                 | 29%   | NS  |
| Low Birth Weight          | 12%                                | 19%   | 12%   |
| Preterm Birth             | 8%                                 | NS  | 16%   |
| Small for Gestational Age | 3%                                 | 8%  | NS  |

# Side Effects and Adherence Data

- Both side effects and adherence to supplementation can influence the effectiveness of the intervention, but these are not consistently reported in many trials comparing MMS and IFA
- Available data show no significant differences in side effects between IFA and MMS
- No subgroup had an increased risk of stillbirth, neonatal, 6 month or infant mortality
- In trials there was no difference in adherence to IFA versus MMS

# Switching Antenatal Supplementation from IFA to MMS is Cost-Effective

- Additional product cost assumed to be 30% (probably will be less)
- Analysis done for Bangladesh and Burkina Faso (180 tablets)
- Very cost-effective
  - \$3-15 per DALY averted (BEP supplementation \$500 per DALY averted)
  - \$125-184 per death averted (midwife and obstetric services \$1000-3000 per death averted)
  - \$37-44 per case of LBW prevented

# Conclusions on the Superiority of Antenatal MMN Supplementation vs IFA

- Strong evidence for reduction in LBW, SGA, preterm births and stillbirths
- Populations that would especially benefit are those with a high prevalence of anemia or underweight in women of reproductive age
- Babies of anemic women receiving MMS vs. IFA had reduction of deaths in the first 6 months
- No evidence of serious adverse effects
- Highly cost-effective compared to antenatal IFA and other interventions affecting birth outcomes or neonatal deaths



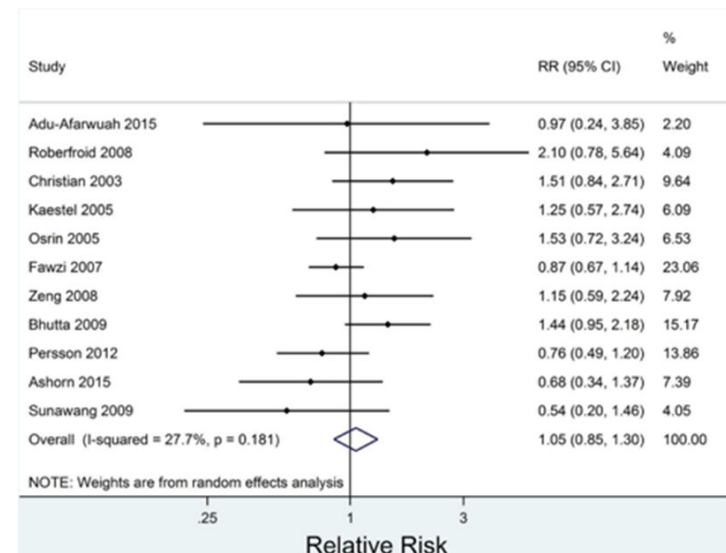
# Extra Slide

# No Increase in Mortality Risk with Antenatal MMS

## Risk of Neonatal Mortality

The WHO ANC Guidelines (2016) raised concern about the potential risk of increased neonatal mortality in those receiving MMS with 30mg of iron, when compared to those receiving IFA containing 60 mg of iron (6 trials, RR: 1.22, 95% CI 0.95-1.57).

A recent, updated analysis of these data plus five more studies found **no increased risk of neonatal mortality** associated with MMS (11 trials, RR: 1.05, 95% CI 0.85-1.30) – figure on the right.



Forest plot for the effect of MMS vs. IFA (with 60 mg of iron and any dose of folic acid) in the control group on neonatal mortality