# Who Benefits?

Differential effects of nutrition interventions for a positive pregnancy experience and improving infant survival

Emily R. Smith, ScD, MPH
October 7, 2019

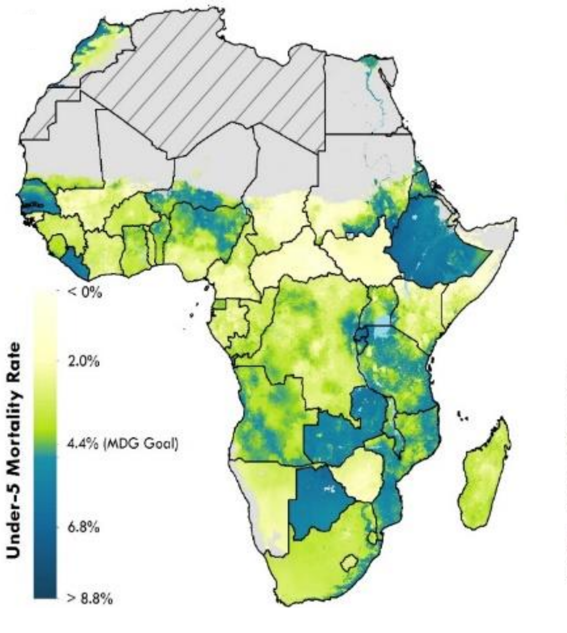
# Roadmap

PART I – The Case for MNCH
Born Too Small, Too Soon
Life Course Approach

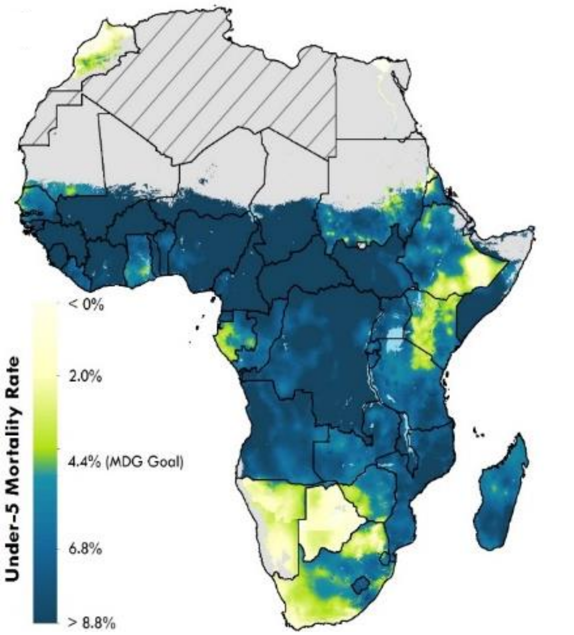
PART II – Maternal Nutrition
Multiple Micronutrients
Nutritious Food Supplements
Calcium Supplementation

# We need to make faster progress against an increasingly complex burden

## Historical & target annualized rates of U5MR reduction[1]

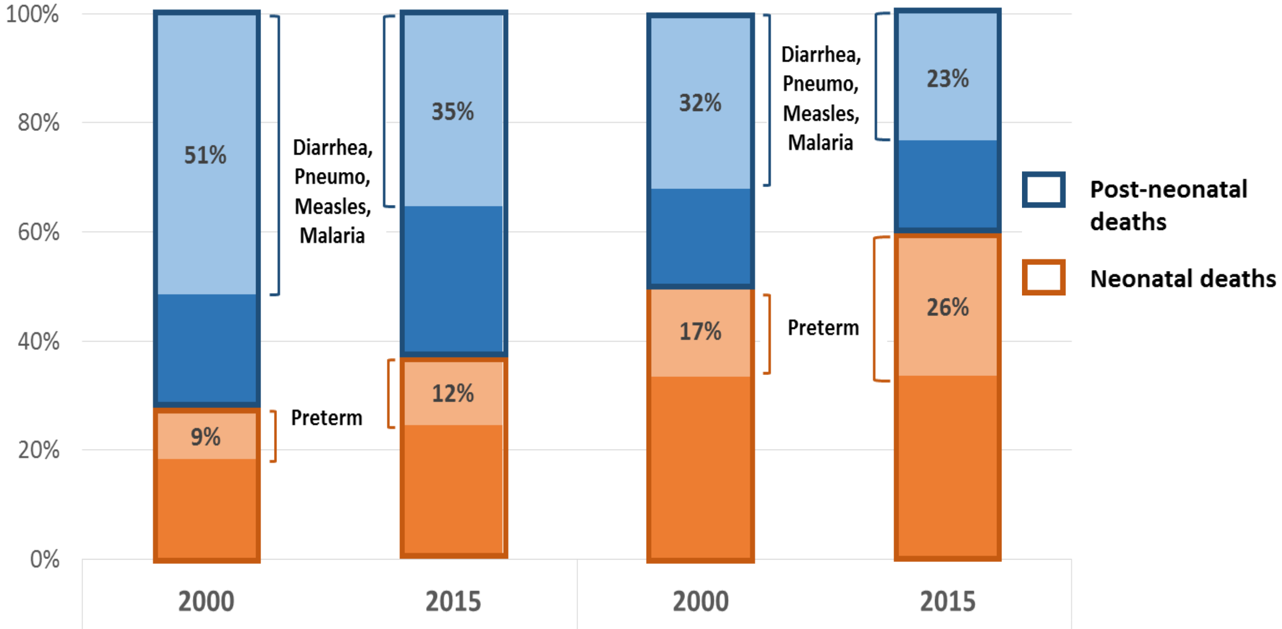



Annualized rate of U5MR reduction observed, 2000-2015




Annualized rate of reduction needed to reach SDG targets

## Composition of U5 deaths, 2000 vs. 2015 [2]




Sub-Saharan Africa

South/SE Asia

[1] Golding N et al. *The Lancet.* 2017

[2] Liu L et al. *The Lancet*. 2016

# Causes of Low Birthweight

- Short Stature
- Low Pre-Pregnancy BMI
- Low Weight Gain During Pregnancy
- Micronutrient Deficiency/Anemia
- Adolescent Pregnancy
- Infections (e.g. Malaria, UTI, BV)
- Lifestyle (e.g. Tobacco, others)

**BORN TOO SMALL**

**Small for Gestational Age (SGA)**

*< 10th percentile*

**BORN TOO SOON**

**Preterm Birth (PTB)**

*< 37 weeks gestation*

**Low Birth Weight**

*(<2500 g)*

**Newborn Morbidity & Mortality**

**Poor Postnatal Growth and Cognition**

**Table V. Risk of early neonatal and neonatal mortality stratified by birth weight, gestational age-size at gestational age category, preterm severity, and SGA severity (n = 31 988)**

| | Early neonatal mortality (0-7 d) | | | | Neonatal mortality (0-28 d) | | | | Infant mortality (0-12 mo) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Deaths n | Infants n | HR* (95% CI) | *P* value | Deaths | Infants | HR* (95% CI) | *P* value | Deaths | Infants | HR* (95% CI) | *P* value |
| All infants | 318 | 31 988 | | | 430 | 31 988 | | | 1240 | 31 988 | | |
| Birth weight | | | | | | | | | | | | |
| ≥2500 g | 224 | 29 639 | 1.00 | | 298 | 29 639 | 1.00 | | 999 | 29 639 | 1.00 | |
| <2500 g | 94 | 2349 | 5.41 (4.24, 6.90) | <.01 | 132 | 2349 | 5.70 (4.64, 7.01) | <.01 | 241 | 2349 | 3.23 (2.80, 3.72) | <.01 |
| GA-SGA category | | | | | | | | | | | | |
| Term-AGA | 149 | 21 854 | 1.00 | | 198 | 21 854 | 1.00 | | 668 | 21 854 | 1.00 | |
| Preterm-AGA | 79 | 4820 | 2.42 (1.84, 3.19) | <.01 | 104 | 4820 | 2.40 (1.89, 3.05) | <.01 | 266 | 4820 | 1.86 (1.61, 2.14) | <.01 |
| Term-SGA | 88 | 5231 | 2.56 (1.96, 3.34) | <.01 | 124 | 5231 | 2.68 (2.14, 3.37) | <.01 | 301 | 5231 | 1.93 (1.68, 2.21) | <.01 |
| Preterm-SGA | 2 | 83 | 3.61 (0.89, 14.61) | .07 | 4 | 83 | 5.43 (2.01, 14.63) | .001 | 5 | 83 | 2.02 (0.84, 4.88) | .12 |
| Preterm severity | | | | | | | | | | | | |
| Term | 237 | 27 085 | 1.00 | | 322 | 27 085 | 1.00 | | 969 | 27 085 | 1.00 | |
| Preterm | 46 | 3853 | 1.37 (1.00, 1.88) | .05 | 66 | 3853 | 1.45 (1.11, 1.88) | <.01 | 173 | 3853 | 1.27 (1.08, 1.49) | <.01 |
| Early preterm | 35 | 1050 | 3.72 (2.61, 5.32) | <.01 | 42 | 1050 | 3.31 (2.40, 4.57) | <.01 | 98 | 1050 | 2.75 (2.23, 3.38) | <.01 |
| SGA severity | | | | | | | | | | | | |
| AGA | 228 | 26 674 | 1.00 | | 302 | 26 674 | 1.00 | | 934 | 26 674 | 1.00 | |
| Moderate SGA | 43 | 2857 | 1.82 (1.31, 2.52) | <.01 | 55 | 2857 | 1.74 (1.30, 2.32) | <.01 | 152 | 2857 | 1.54 (1.30, 1.83) | <.01 |
| Severe SGA | 47 | 2457 | 2.30 (1.68, 3.16) | <.01 | 73 | 2457 | 2.67 (2.06, 3.45) | <.01 | 154 | 2457 | 1.82 (1.53, 2.16) | <.01 |

*Model adjusted for study cohort, household wealth, maternal education, parity, mode of delivery, and maternal age.

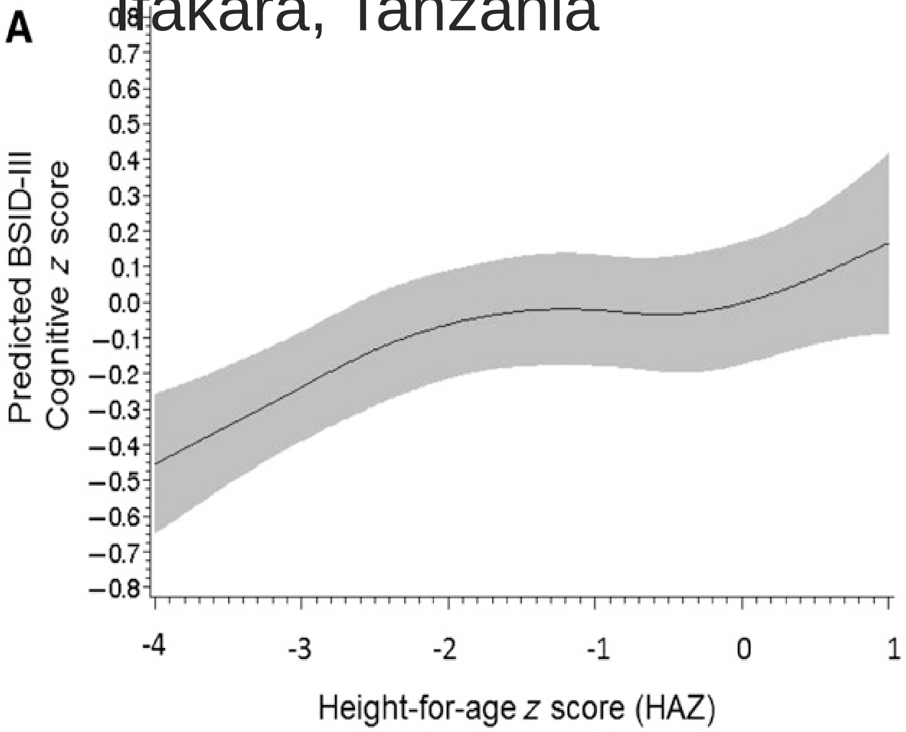
Sania, Smith, et al. *The Journal of pediatrics, 2018*

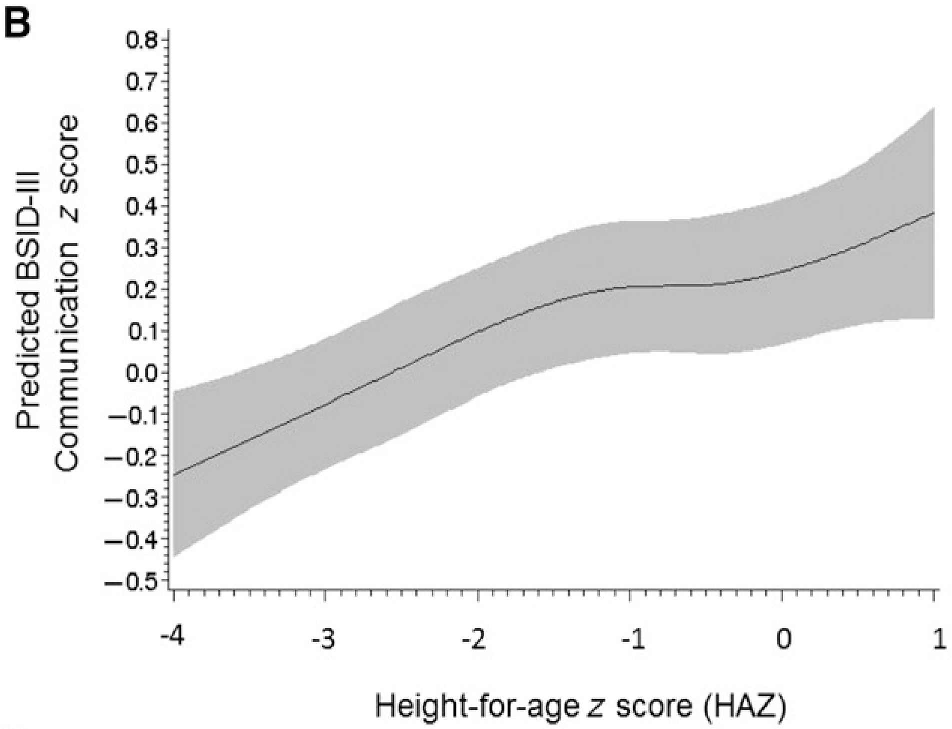
# Low birthweight, preterm birth, & IUGR contribute to poor growth throughout childhood

| | Children followed | Stunting | | | Wasting | | |
|---|---|---|---|---|---|---|---|
| | | Events ($n$) | Hazard ratio(95% CI)* | | Events ($n$) | Hazard ratio(95% CI)* | |
| | | | Crude | Adjusted† | | Crude | Adjusted† |
| GA-SGA category | | | | | | | |
| Term-AGA | 4335 | 1479 | 1.00 (Ref) | 1.00 (Ref) | 864 | 1.00 (Ref) | 1.00 (Ref) |
| Preterm-AGA | 919 | 513 | 2.27 (2.05–2.51) | 2.13 (1.93–2.36) | 216 | 1.27 (1.09–1.80) | 1.25 (1.07–1.47) |
| Term-SGA | 1369 | 824 | 2.43 (2.23–2.64) | 2.21 (2.02–2.41) | 398 | 1.53 (1.36–1.72) | 1.45 (1.28–1.65) |
| Preterm-SGA | 41 | 35 | 7.11 (5.08–9.94) | 7.58 (5.41–10.64) | 18 | 2.96 (1.85–4.72) | 3.05 (1.90–4.87) |
| Birthweight | | | | | | | |
| ≥2500 g | 6291 | 2554 | 1.00 (Ref) | 1.00 (Ref) | 1367 | 1.00 (Ref) | 1.00 (Ref) |
| <2500 g | 373 | 297 | 4.41 (3.90–4.97) | 4.28 (3.78–4.85) | 129 | 1.80 (1.50–2.15) | 1.76 (1.46–2.11) |

Sania et al. *Maternal & Child Nutrition*, *2015*

# Low Birthweight, Malnutrition, and their Determinants Are Associated with Suboptimal Cognitive, Communication, and Motor Development among Children 18-36 months of age in Ifakara, Tanzania

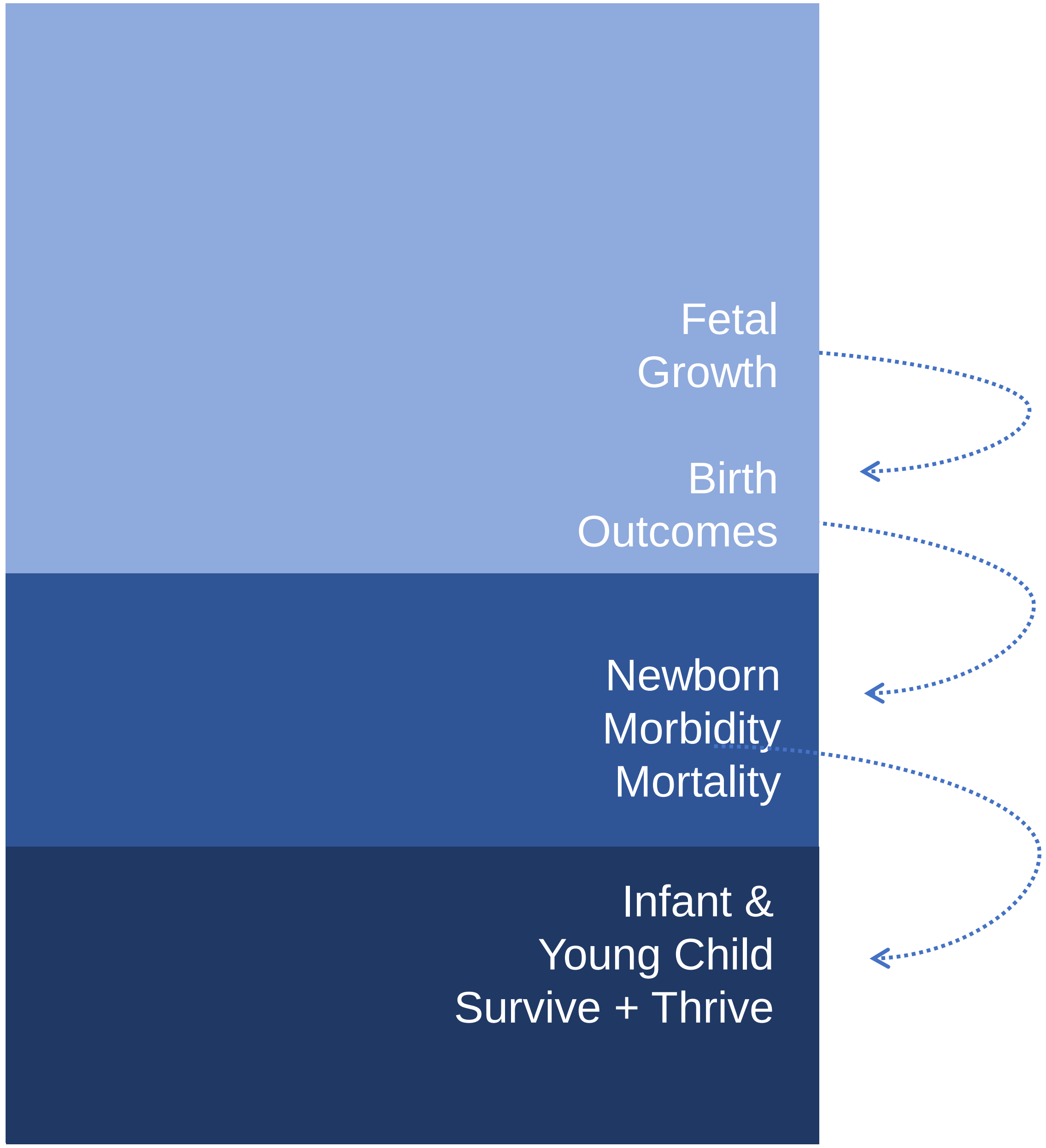



Adjusted for: infant sex, infant age, maternal education, wealth quintile, stimulation tertile, BSID-III assessor, randomized regimen, and wasting

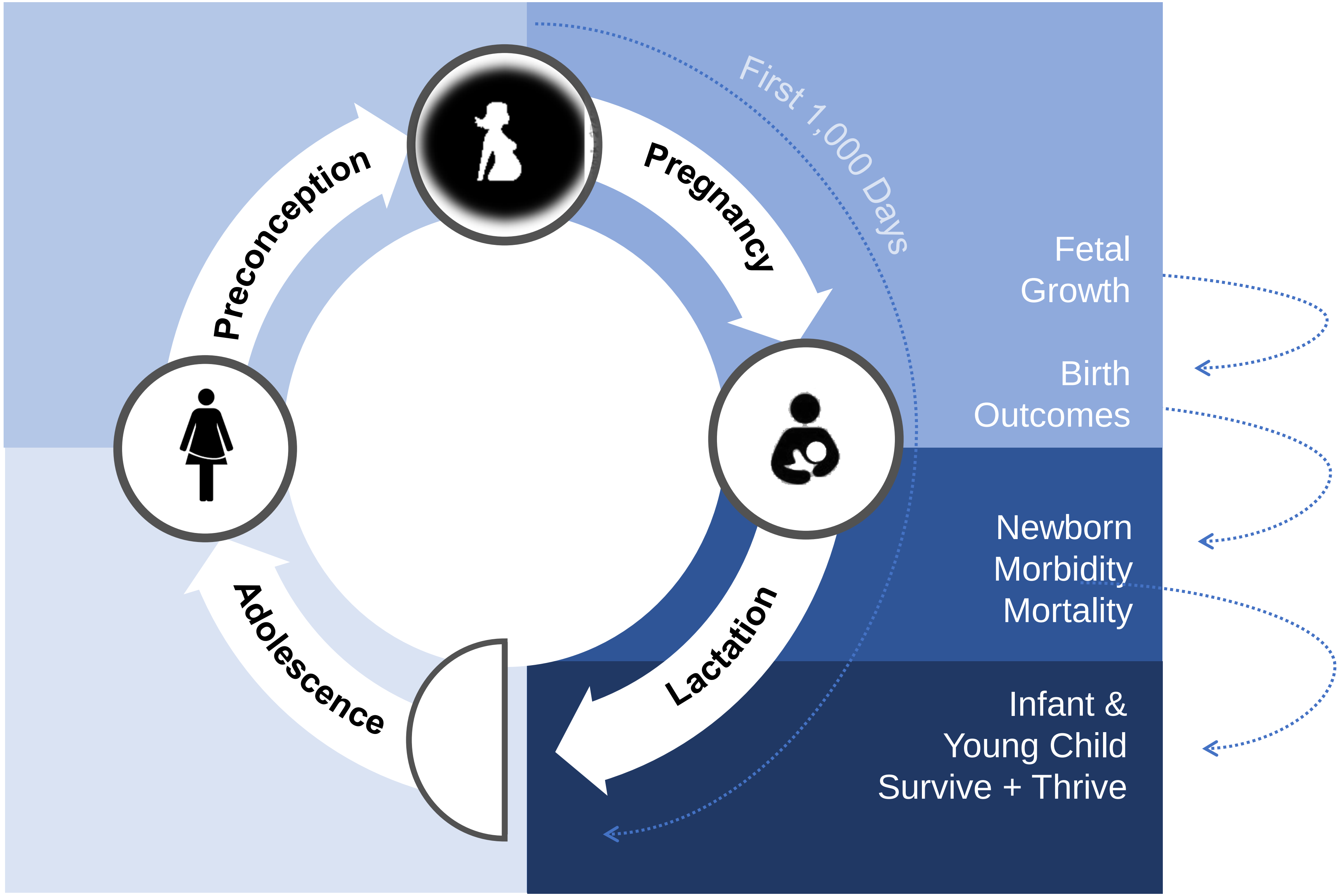
Sudfeld, et al. *The Journal of Nutrition*. 2015

# Nutrition Across the Life Course




Christian, Smith.
*Ann Nutr Metab*. 2018

# Nutrition Across the Life Course




Christian, Smith.
*Ann Nutr Metab*. 2018

# Maternal Nutrition

Building the Evidence Base

# WHO recommendations for supplementation in pregnancy

- Iron and Folic Acid
- Multiple Micronutrients
- Balanced Energy and Protein
- Calcium

## A.6: Multiple micronutrient (MMN) supplements

**RECOMMENDATION A.6: Multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes.** *(Not recommended)*

**Remarks**

- There is some evidence of additional benefit of MMN supplements containing 13–15 different micronutrients (including iron and folic acid) over iron and folic acid supplements alone, but there is also some evidence of risk, and some important gaps in the evidence. Although the GDG agreed that overall there was insufficient evidence to warrant a recommendation, the group agreed that policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMN supplements on maternal health to outweigh the disadvantages, and may choose to give MMN supplements that include iron and folic acid.

WHO Guidelines on Antenatal Care for a Positive Pregnancy Experience. 2016

## IFA

| Nutrient | Dose |
|---|---|
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| Folic acid | 400 g |
| Iron | 30 mg |
| | |
| | |
| | |
| | |

## MMS

| Nutrient | Dose |
|---|---|
| Vitamin A | 800 µg |
| Vitamin D | 5 µg |
| Vitamin E | 10 mg |
| Vitamin C | 70 mg |
| Vitamin B1 | 1.4 mg |
| Vitamin B2 | 1.4 mg |
| Niacin | 18 mg |
| Vitamin B6 | 1.9 mg |
| Vitamin B12 | 2.6 µg |
| Folic acid | 400 g |
| Iron | 30 mg |
| Zinc | 15 mg |
| Copper | 2 mg |
| Selenium | 65 µg |
| Iodine | 150 µg |

“This systematic review included 21 trials (involving 142,496 women), but only 20 trials (involving 141,849 women) contributed data. The included trials compared pregnant women who supplemented their diets with multiple micronutrients (including iron and folic acid) with pregnant women who received iron (with or without folic acid) or a placebo.”

Cochrane Library

Cochrane Database of Systematic Reviews

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

Keats EC, Haider BA, Tam E, Bhutta ZA

Published: 15 March 2019

THE LANCET
Global Health

# 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

Emily R Smith, ScD • Anuraj H Shankar, ScD • Lee S-F Wu, MHS • Said Aboud, PhD • Seth Adu-Afarwuah, PhD • Hasmot Ali, MPH • Rina Agustina, PhD • Shams Arifeen, DrPH • Per Ashorn, PhD • Zulfiqar A Bhutta, PhD • Parul Christian, DrPH • Delanjathan Devakumar, PhD • Kathryn G Dewey, PhD • Henrik Friis, PhD • Exnevia Gomo, PhD • Piyush Gupta, MD • Pernille Kæstel, PhD • Patrick Kolsteren, PhD • Hermann Lanou, MD • Kenneth Maleta, PhD • Aissa Mamadoultaibou, MS • Gernard Msamanga, ScD • David Osrin, PhD • Lars-Åke Persson, PhD • Usha Ramakrishnan, PhD • Juan A Rivera, PhD • Arjumand Rizvi, MSC • H P S Sachdev, FRCPCH • Willy Urassa, PhD • Keith P West Jr, DrPH • Noel Zagre, PhD • Lingxia Zeng, PhD • Zhonghai Zhu, MSc • Wafaie W Fawzi, DrPH • Dr Christopher R Sudfeld, ScD • Show less

Open Access • • Published: November, 2017 • DOI: https://doi.org/10.1016/S2214-109X(17)30371-6

# Who benefits from MMS?

Burkina Faso
Ghana
Guinea-Bissau
Malawi
Niger
Tanzania (2)
Zimbabwe

Mexico

Bangladesh (2)
China
India
Indonesia
Nepal (2)
Pakistan

35 Investigators

112,000 women

17 trials

14 outcomes

10 subgroups

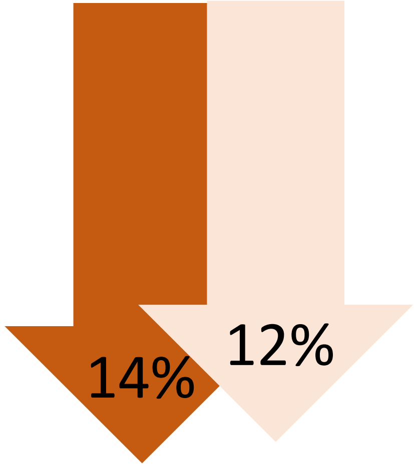
Stillbirth,
Infant Mortality,
Birthweight,
Gestational Age,
Size for Gestational Age

Infant Sex, Parity, Maternal Age, Maternal Anthropometry, Maternal Anemia, Gestational Age at Supplementation, Adherence

Overall, MMS reduces the risk of low birthweight, preterm birth, SGA. IPD results consistent with the 2019 Cochrane Review.

## Low Birthweight

| | N Studies | RR (95% CI) |
|---|---|---|
| Smith 2017 | 17 | 0.86 (0.81 to 0.92) |
| Keats 2019 | 18 | 0.88 (0.85 to 0.91) |



# Everyone Benefits

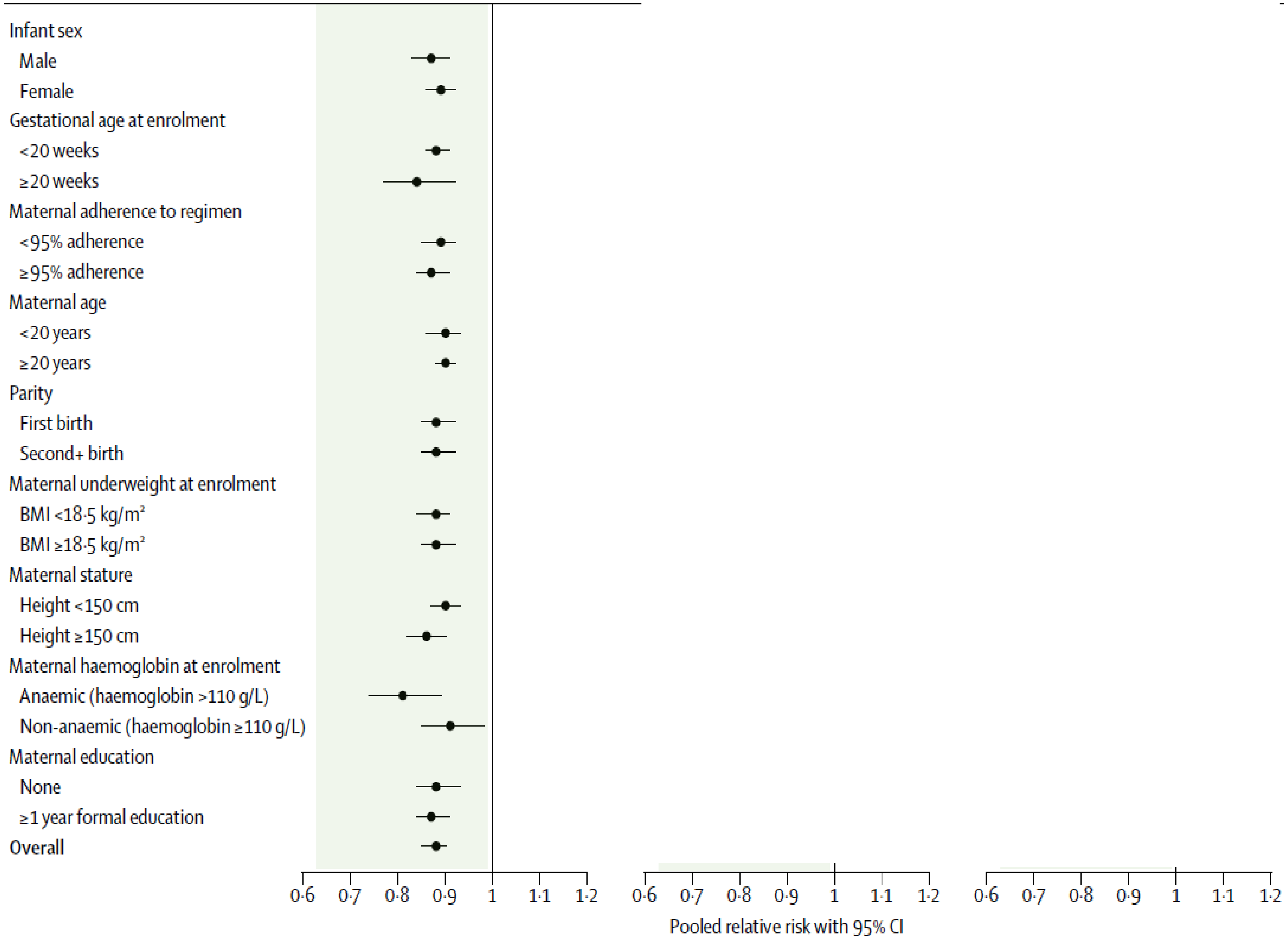
Benefit apparent in most subgroups

Larger gains for undernourished women

No harmful effects observed

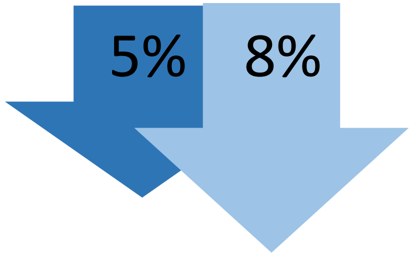
Smith et al. *Lancet Global Health.* 2017

## Low Birthweight



Overall, MMS probably slightly reduces the risk of stillbirth, but does not reduce mortality for the general population.
IPD results consistent with the 2019 Cochrane Review.

| | Stillbirth | | Neonatal Death | |
|---|---|---|---|---|
| | N Studies | RR (95% CI) | N Studies | RR (95% CI) |
| Smith 2017 | 16 | 0.92 (0.86 to 0.99) | 12 | 0.99 (0.89 to 1.09) |
| Keats 2019 | 17 | 0.95 (0.86 to 1.04) | 14 | 1.00, (0.89 to 1.12) |




**Overall Null Effect**

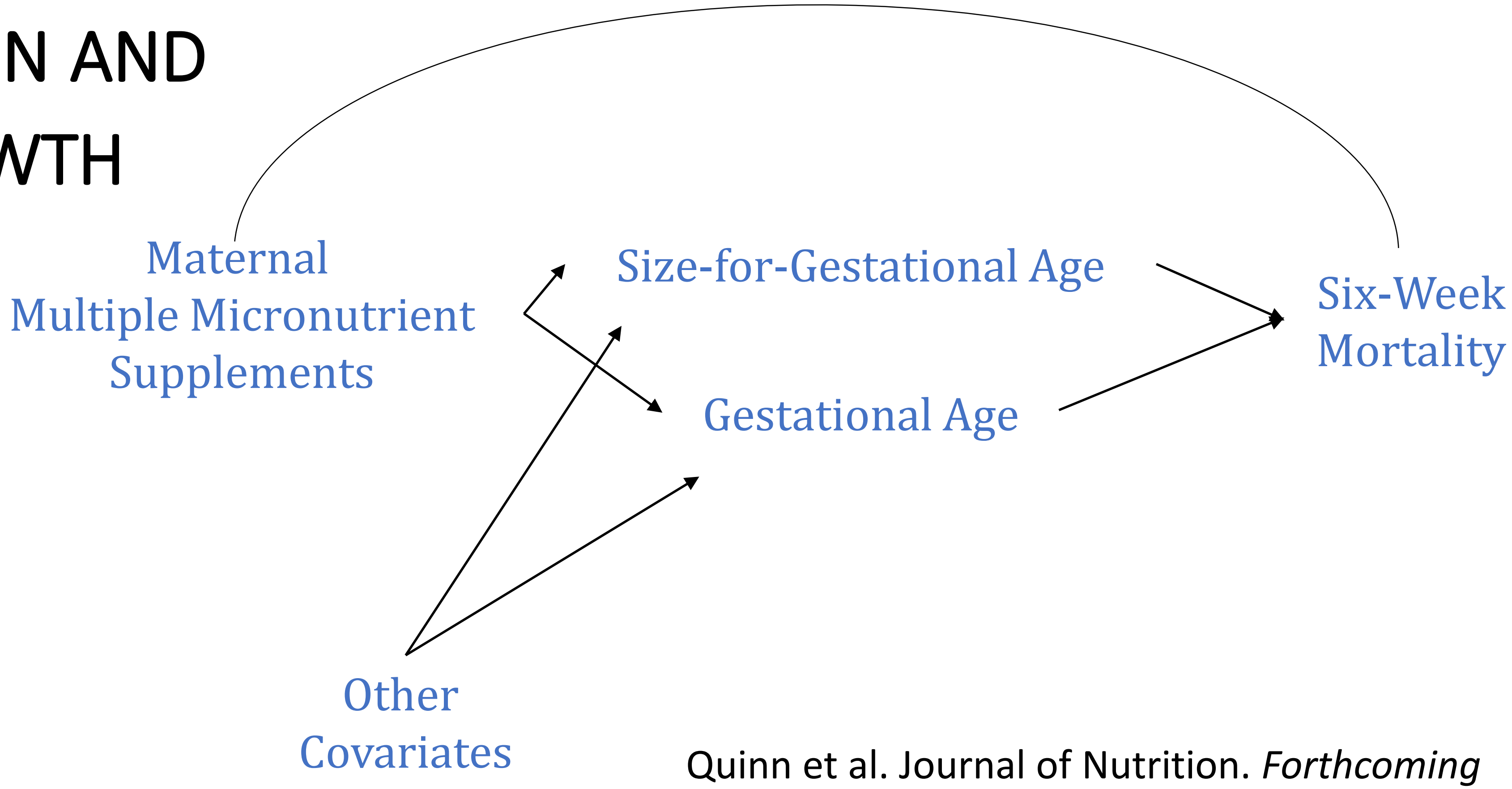
# MMS clearly & consistently reduces the risk of mortality for female infants through the first year of life.

| | | Neonatal Mortality | | 6 Month Mortality | | Infant Mortality | |
|---|---|---|---|---|---|---|---|
| Infant Sex | | | | | | | |
| | Male | 1.06 (0.95-1.17) | 0.007 | 0.98 (0.89-1.09) | 0.06 | 1.05 (0.93-1.18) | 0.04 |
| | Female | 0.85 (0.75-0.96) | | 0.85 (0.75-0.95) | | 0.87 (0.77-0.99) | |
| Regimen Adherence | | | | | | | |
| | <95% | 1.05 (0.94-1.17) | 0.05 | 0.98 (0.88-1.09) | 0.11 | 1.06 (0.94-1.20) | 0.02 |
| | ≥95% | 0.88 (0.77-1.01) | | 0.85 (0.74-0.97) | | 0.85 (0.74-0.91) | |

Smith et al. *Lancet Global Health*. 2017

# The effect of maternal multiple micronutrient supplementation on female early infant mortality is fully mediated by increased gestation duration and intrauterine growth

MK Quinn
Doctoral Candidate




Quinn et al. Journal of Nutrition. *Forthcoming*


# Translating Evidence for Impact

- NYAS Task Force
- Annals of the New York Academy of Sciences Supplement
- Re-Analysis of WHO Data (*J Nutr*)
- Gestational age & dose thresholds
- Demonstration & Policy Change (UNICEF)
- Goalkeepers 2019

*Annals*

# Special Issue: Multiple Micronutrient Supplementation in Pregnancy

Edited by
*Ann NY Acad Sci* editorial staff

Published: May 2019
*Volume 1444*



**The upper level: examining the risk of excess micronutrient intake in pregnancy from antenatal supplements**
AD Gernand

**Review of the evidence regarding the use of antenatal multiple micronutrient supplementation in low- and middle-income countries**
MW Bourassa et al

**Replacing iron-folic acid with multiple micronutrient supplements among pregnant women in Bangladesh and Burkina Faso: costs, impacts, and cost-effectiveness**
R Engle-Stone et al

*Annals*

**Special Issue: Multiple Micronutrient Supplementation in Pregnancy**

Edited by
*Ann NY Acad Sci* editorial staff

Published: May 2019
*Volume 1444*

Published since 1824, *Annals of the New York Academy of Sciences* is the Academy's premier scientific publication.

Learn More ›

# 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 in 6 trials; 1 trial showed a few percent more vomiting in the MMS group compared to the IFA groups
- In trials there was no difference in adherence to IFA versus MMS

Engle-Stone R, et al. Ann N.Y. Acad. Sci, 2019

*Annals*

**Special Issue: Multiple Micronutrient Supplementation in Pregnancy**

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Published since 1824, *Annals of the New York Academy of Sciences* is the Academy's premier scientific publication.

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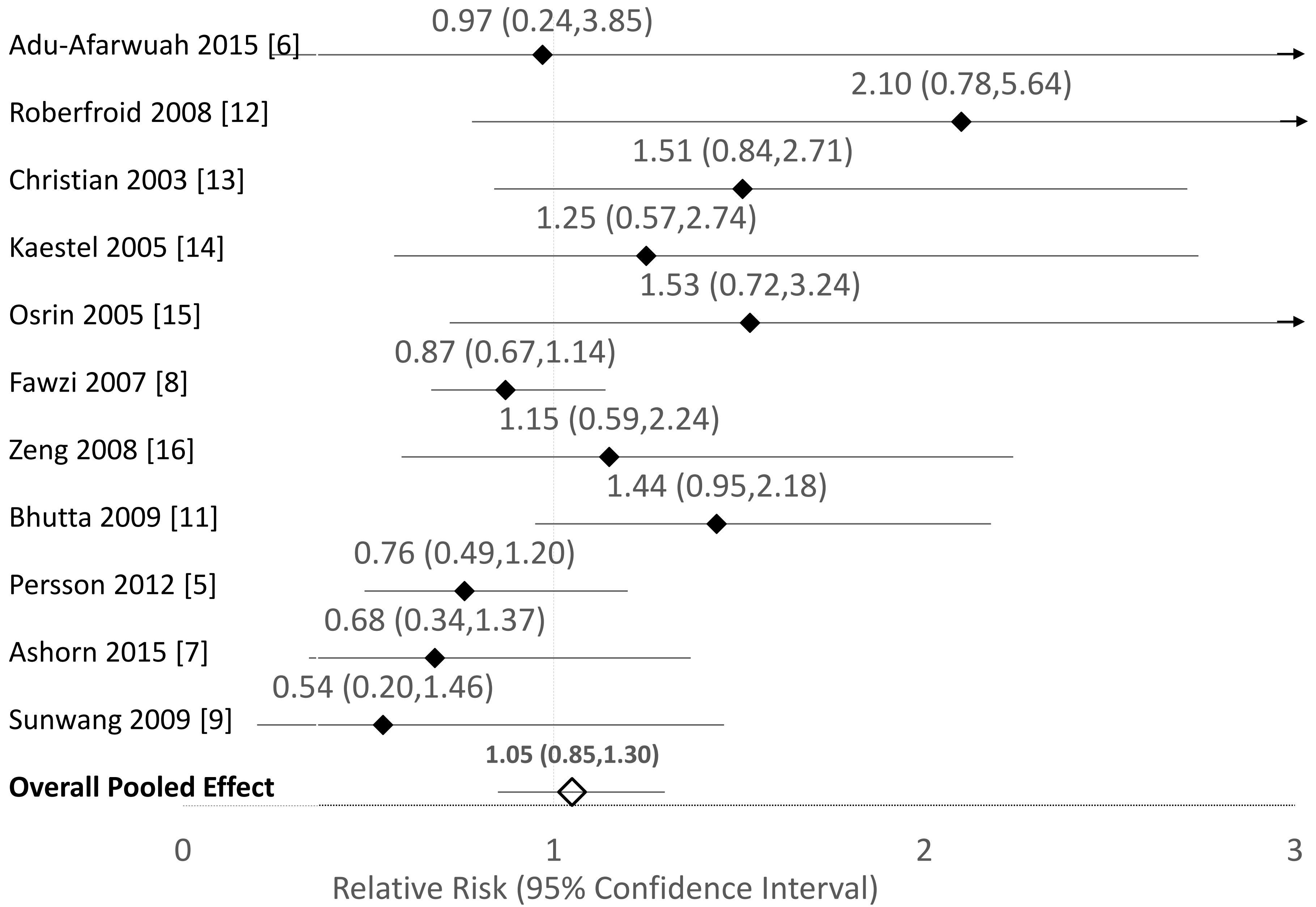
# Switching Antenatal Supplementation from IFA to MMS is Cost-Effective

- 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

Engle-Stone R, et al. Ann N.Y. Acad. Sci, 2019



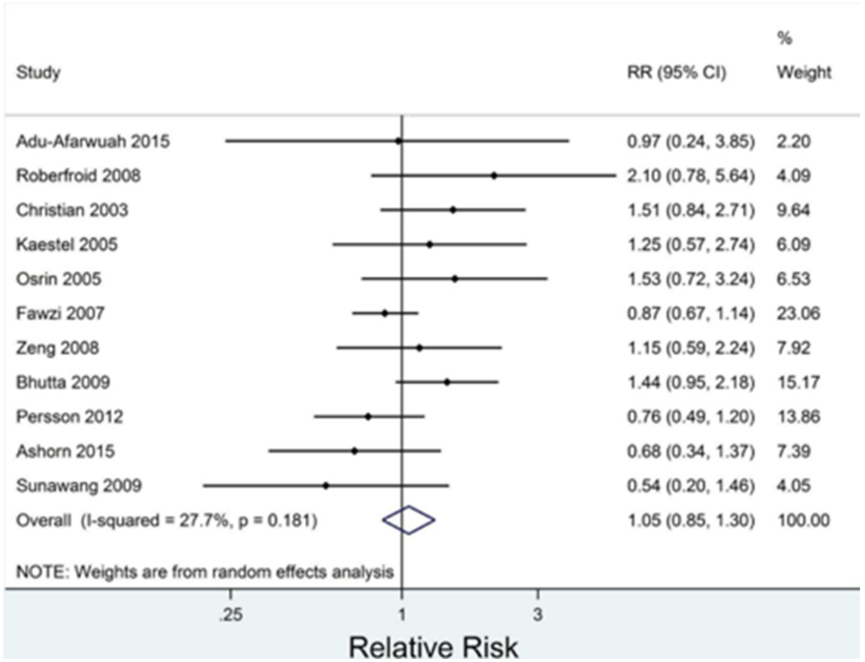

Sudfeld and Smith. New Evidence Should Inform WHO Guidelines on MMS in Pregnancy. J Nutr. 2019

# Revised WHO Subgroup Analysis Shows No Increase in Mortality Risk with Antenatal MMS

## Risk of Neonatal Mortality

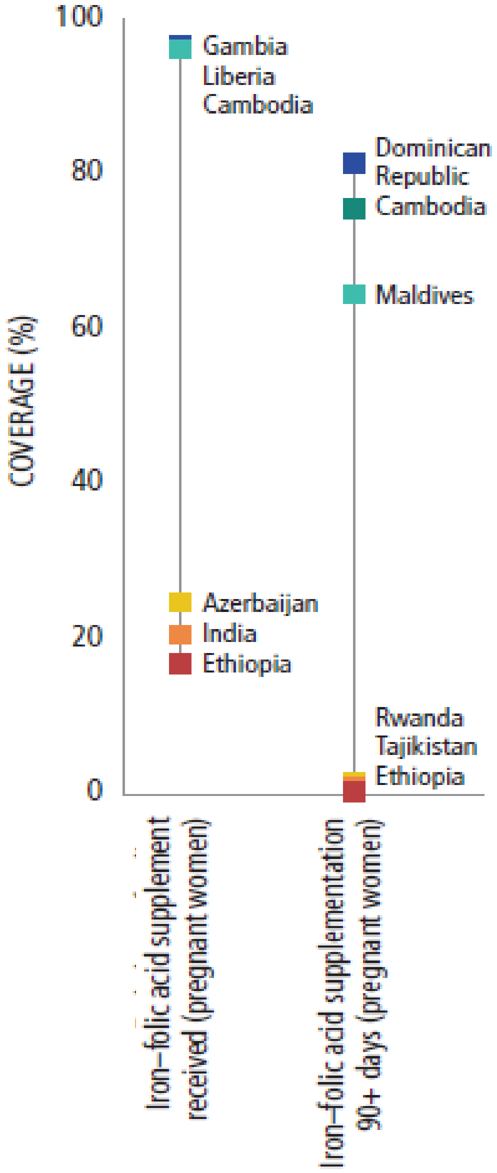
- The WHO ANC Guidelines (2016) raised concern about the potential risk of increased neonatal mortality in those receiving MMS with 30mg of iron, when compared to those receiving IFA containing 60 mg of iron (6 trials, RR: 1.22, 95% CI 0.95-1.57).
- A recent, updated analysis of these data plus five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

Sudfeld & Smith 2018 New evidence should inform WHO policy on multiple micronutrient supplementation in pregnancy. J. Nutr.




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

# Ongoing Multisectoral & Multinational Efforts to Improve Maternal Nutrition through Effective Scale Up of MMS




To inform the implementation and scale-up of effective multiple micronutrient supplementation (MMS) and maternal nutrition programs

To gain operational experience on effectively scaling up MMS along with other antenatal nutrition interventions

To strengthen global systems that support MMS delivery among pregnant women

POWER FOR MOTHERS

BILL & MELINDA GATES foundation

# GOALKEEPERS

3 Years
10 Partners
$50 Million Committed
17.5 Million Pregnant Women

BILL & MELINDA GATES foundation

GOALKEEPERS

## HEALTHY MOTHERS, HEALTHY BABIES

### WHAT'S THE CHALLENGE?

Maternal and child undernutrition in low- and middle-income countries (LMICs) is the underlying cause of nearly half of all child deaths under the age of five. And babies who do survive are at a much greater risk of stunted growth, resulting in poor cognitive function, which limits education and economic opportunities later in life.

2 ZERO HUNGER

# Nutritious Food Supplementation in Pregnancy

# Types of Nutritious Food Supplements for Pregnant and Lactating Women

High Protein Supplements

✗ Not Recommended

Balanced Energy and Protein Supplements

✓ WHO Recommended

# Framework and Specifications for the Nutritional Composition of a Food Supplement for Pregnant and Lactating Women (PLW) in Undernourished and Low-Income Settings

**Report of an Expert Consultation held at the**

**Bill & Melinda Gates Foundation**

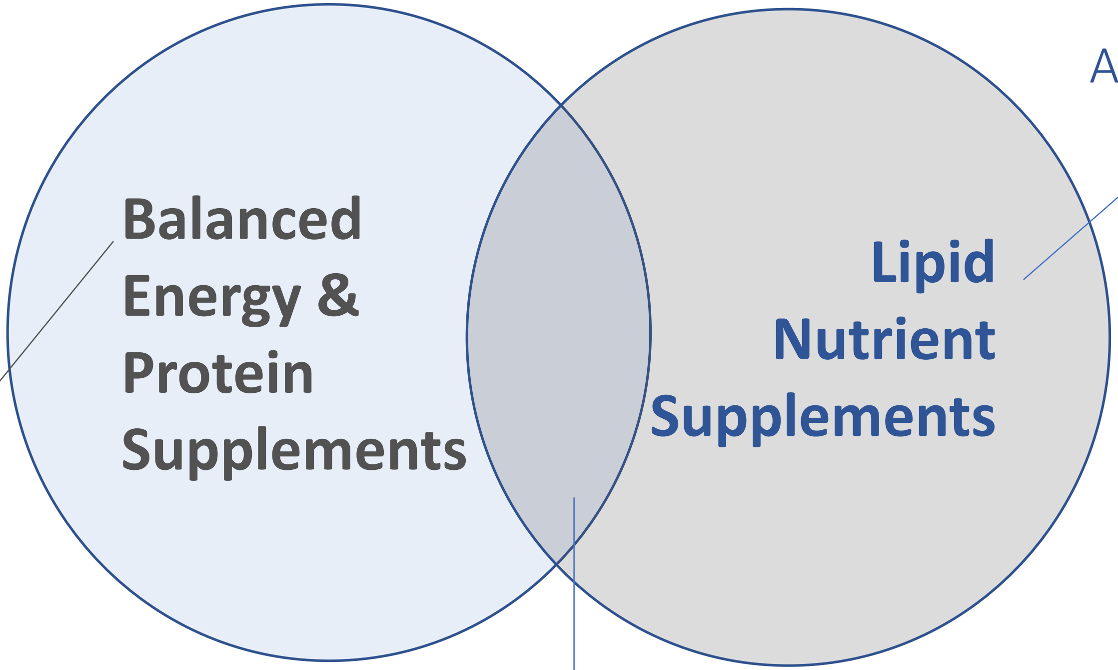
**September 19 & 20, 2016**
**Seattle, WA**


| Study | Description of Food Supplement | Calories (kcal) | Protein (g) |
|---|---|---|---|
| Atton et al 1990 | Flavored milk product packaged in a 200-ml Tetrabrick carton (with choice of flavors) | 407 | 14.6 |
| Blackwell et al 1973 | Protein-calorie liquid supplement (milk-based) taken daily plus vitamins and minerals | 800 | 40 |
| Campbell et al 1983 | Three different supplement options were offered based on subjects' preference:<br>• 0.5 pint of flavored milk drink<br>• 1 pint of fresh milk<br>• 75 g cheddar cheese | 300 | 14.6 |
| Ceesay et al 1997 | High energy groundnut biscuits (2) containing roasted groundnuts, rice flour, sugar and groundnut oil | 1017 | 22 |
| Elwood et al 1981 | Free tokens to purchase milk for their families | | |
| Girija et al 1984 | 50 g of sesame cake, 40 g jaggery and 10 g oil | 417 | 30 |
| Huybregts et al 2009 | 72 g of a prenatal MMN-fortified spread consisting of 33% peanut butter, 32% soy flour, 15% vegetable oil, 20% sugar and an MMN at 1x RDA | 372.6 | 14.7 |
| Mardones-Santander et al 1988 | There were two intervention groups, PUR and V-N<br>• PUR group received powdered milk (an isocaloric supplement)<br>• V-N group received a fortified formula milk (a balanced protein-energy supplement); In addition, through the same program all women received 2 kg of rice monthly | PUR: 498<br>V-N: 470 | PUR: 27.9<br>V-N: 14.5 |
| Metcoff et al 1985 | Monthly WIC vouchers for supplements of milk, egg and cheese | 900 – 1000* | 40 - 50* |
| Mora et al 1978 | Supplement provided 60 g of dry skim milk, 150 g of enriched bread and 20 g of vegetable cooking oil; plus, a vitamin mineral supplement | 856 | 38 |
| Rush et al 1980 | • Supplement: A 16-oz beverage (high protein-energy)<br>• Complement: A 16-oz drink (balanced energy and protein) | Supp: 470<br>Comp: 322 | Supp: 40<br>Comp: 6 |
| Viegas et al 1982 | Flavored carbonated dietary protein energy supplement (PrEnVit): containing 1/3 liquid glucose drink, chocolate flavored skim milk powder (26 g provided daily) along with vitamins | 273 | 30 |

# Evidence for nutritious food supplements for pregnant & lactating women

Blackwell 1973 (Taiwan)
Ceesay 1997 (Gambia)
Elwood 1981 (Wales)
Girija 1984 (India)
Kardjati 1988 (Indonesia)
Mora 1978 (Columbia)
Oaks 2014 (Ghana)
Ross 1985 (South Africa)
Rush 1980 (USA)
Viegas 1982a (USA)
Viegas 1982b (USA)

**300-1000 kcal/day**




Adu-Afarwupah 2015 (Ghana)
Ashorn 2015 (Malawi)
Mridha 2016 (Bangladesh)

**118 kcal/day**

Huybregts 2009 (Burkina Faso)

**372 kcal/day**

# Evidence for futritious food supplement for Pregnant & Lactating women

| | **Stillbirth** | **Birthweight** | **SGA** | **Preterm** | **Neonatal Death** |
|---|---|---|---|---|---|
| Balanced Energy & Protein Supplementation[1]<br><br>12 trials,<br>6705 women | RR = 0.60,<br>95%CI 0.39,0.94<br><br>n = 3408,<br>5 RCTs | MD 41g,<br>95%CI 4.66,77.3<br><br>n=5385,<br>11 trials | RR 0.79,<br>95%CI 0.69,0.9<br><br>n = 4408,<br>7 trials | RR 0.96,<br>95%CI 0.80,1.16<br><br>n=3384, women<br>5 trials | RR 0.68,<br>95%CI 0.43,1.07<br><br>n=3381,<br>5 trials |

[1]Ota, E., Hori, H., Mori, R., Tobe-Gai, R., & Farrar, D. (2015). Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane Database of Systematic Reviews.

# Evidence for nutritious food supplement for pregnant & lactating women

| | Stillbirth | Low Birthweight | SGA | Preterm | Survival | |
|---|---|---|---|---|---|---|
| LNS vs. IFA[2] | RR 1.14 [0.52, 2.48]<br><br>N=5575<br>3 studies | RR 0.87 (0.72 to 1.05)<br><br>N=4826<br>3 studies | RR 0.94 (0.89 to 0.99)<br><br>N=4823<br>3 studies | RR 0.94 (0.80 to 1.11)<br><br>N=5924<br>3 studies | Early neonatal RR 0.70 (0.45, 1.09)<br><br>N=5555<br>3 studies | Late neonatal RR 0.96 (0.14, 6.51<br><br>N=1617<br>2 studies |
| LNS vs. MMN[2] | Unavailable | RR 0.92 (0.74 to 1.14)<br><br>N=2404<br>3 studies | RR 0.95 (0.84 to 1.07)<br><br>N=2393<br>3 studies | RR 1.15 (0.93 to 1.42)<br><br>N=2393<br>3 studies | Unavailable | Unavailable |

[2]Das JK, Hoodbhoy Z, Salam RA, Bhutta AZ, Valenzuela-Rubio NG, Weise Prinzo Z, Bhutta ZA (2018). Lipid-based nutrient supplements for maternal, birth, and infant development outcomes. Cochrane Database of Systematic Reviews.

# Who Benefits?
# Use Case & Implementation Considerations for Nutritious Food Supplements for PLW

Eligible Population

Prevention

Nutritious Food Supplements for All Women (where low BMI >20%) ✓ WHO Recommended | 30 Million

Treatment

## A.3: Calcium supplements

**RECOMMENDATION A.3: In populations with low dietary calcium intake, daily calcium supplementation (1.5–2.0 g oral elemental calcium) is recommended for pregnant women to reduce the risk of pre-eclampsia.** *(Context-specific recommendation)*

**Remarks**

- This recommendation is consistent with the 2011 *WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia (57)* (strong recommendation, moderate-quality evidence) and supersedes the WHO recommendation found in the 2013 *Guideline: calcium supplementation in pregnant women (38)*.
- Dietary counselling of pregnant women should promote adequate calcium intake through locally available, calcium-rich foods.
- Dividing the dose of calcium may improve acceptability. The suggested scheme for calcium supplementation is 1.5–2 g daily, with the total dose divided into three doses, preferably taken at mealtimes.
- Negative interactions between iron and calcium supplements may occur. Therefore, the two nutrients should preferably be administered several hours apart rather than concomitantly *(38)*.
- As there is no clear evidence on the timing of initiation of calcium supplementation, stakeholders may wish to commence supplementation at the first ANC visit, given the possibility of compliance issues.
- To reach the most vulnerable populations and ensure a timely and continuous supply of supplements, stakeholders may wish to consider task shifting the provision of calcium supplementation in community settings with poor access to health-care professionals (see Recommendation E.6.1, in section E: Health systems interventions to improve the utilization and quality of ANC).

# Ongoing Research for Calcium Supplementation in Pregnancy

**The Problem**

- Despite WHO recommendation, it is not standard of care
- Barriers to effective coverage: cost, regimen complexity

**Study Design**

Parallel, individually randomized, double-blind, non-inferiority trials in Bangalore, India (n=11,000) and Dar es Salaam, Tanzania (n=11,000)

**Hypothesis**

A single dose (500mg) of calcium is as effective as higher dose (1500mg)calcium in preventing preeclampsia and preterm birth.

**Study Team**

Africa Academy of Public Health; Harvard School of Public Health; Ifakara Health Institute; St. John's Research Institute Bangalore

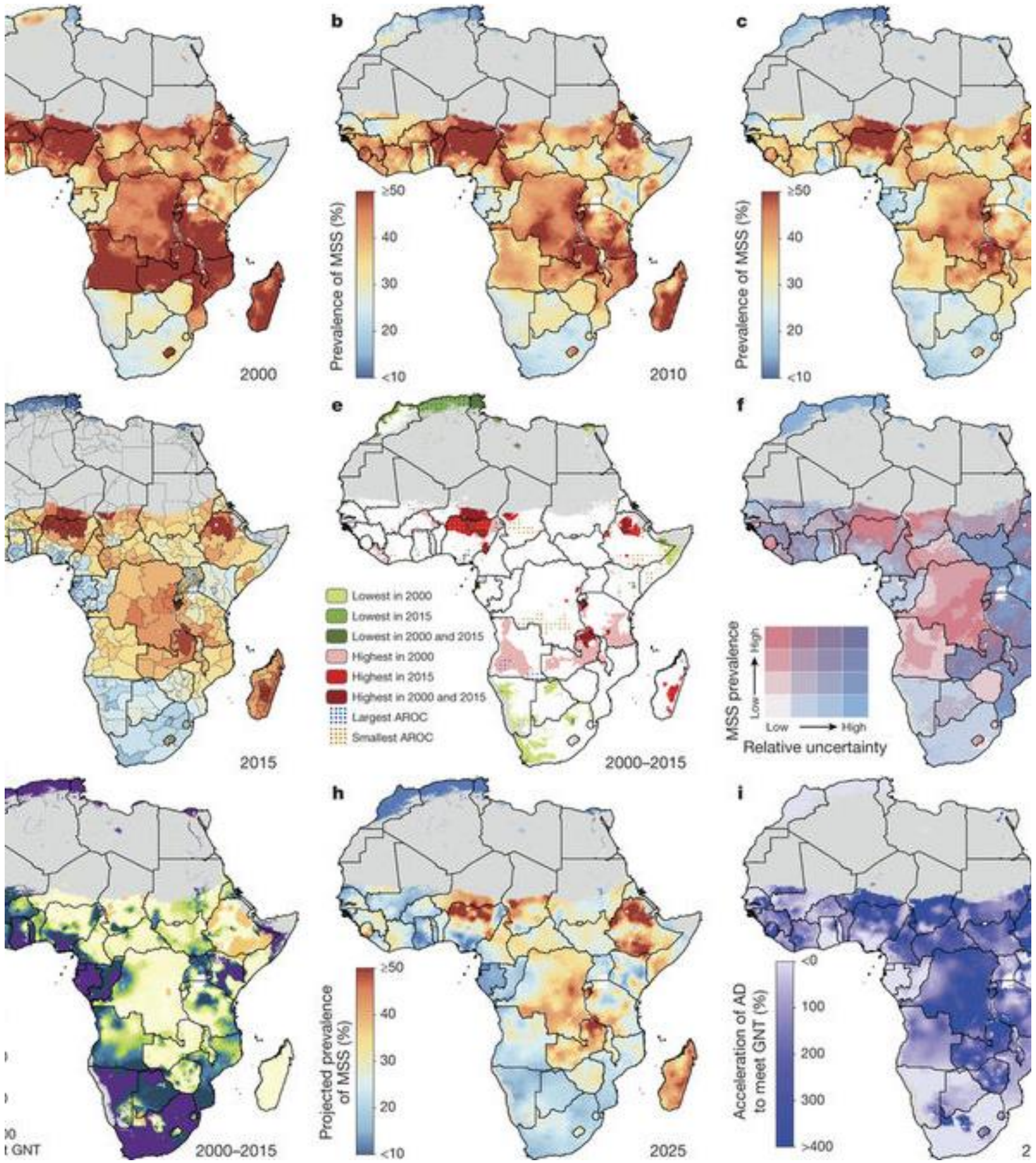
# Who Benefits?

Sometimes it depends.

Sometimes it doesn't.

How to translate to global policy?

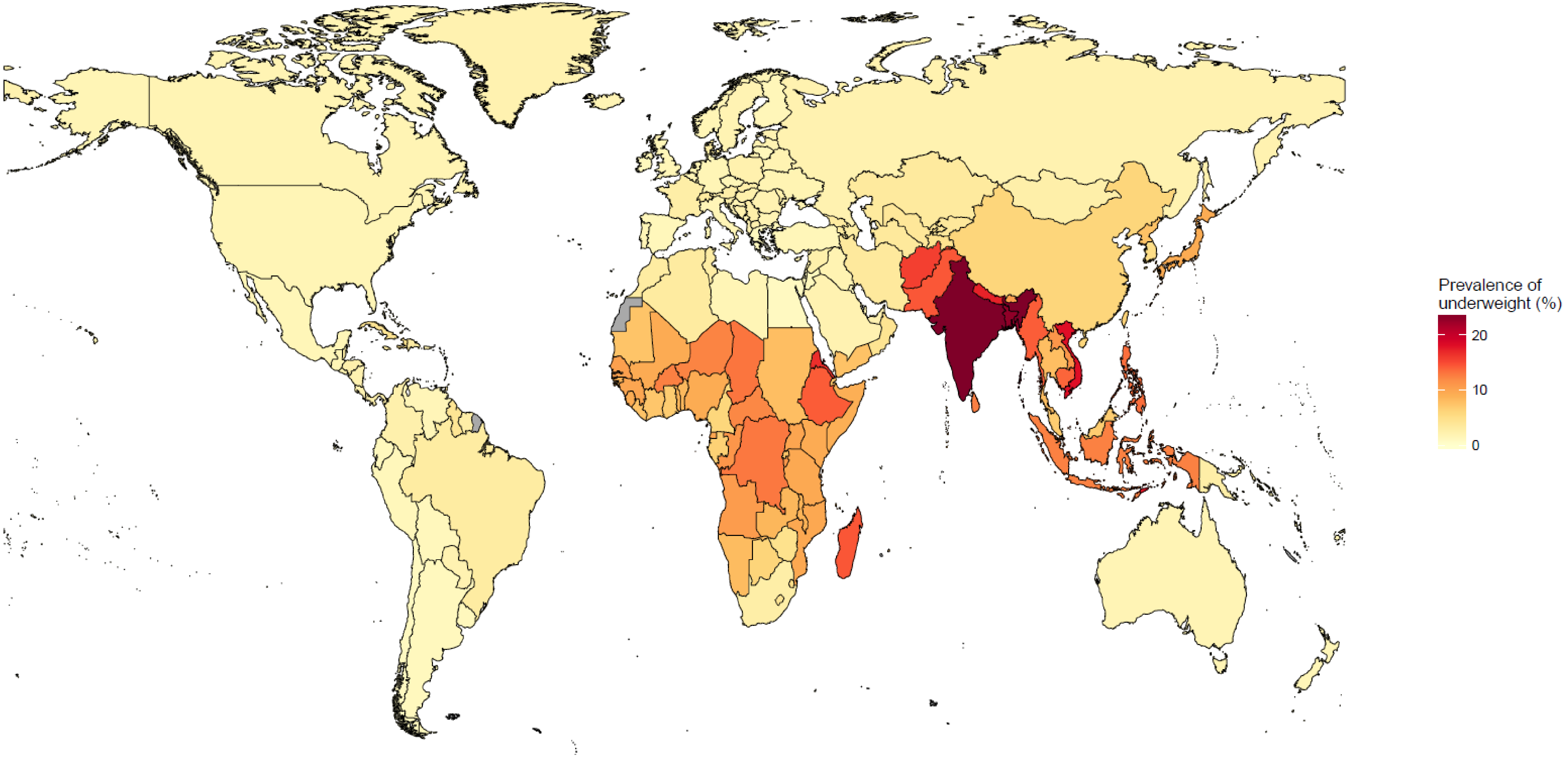
How to implement?



# Thank You!

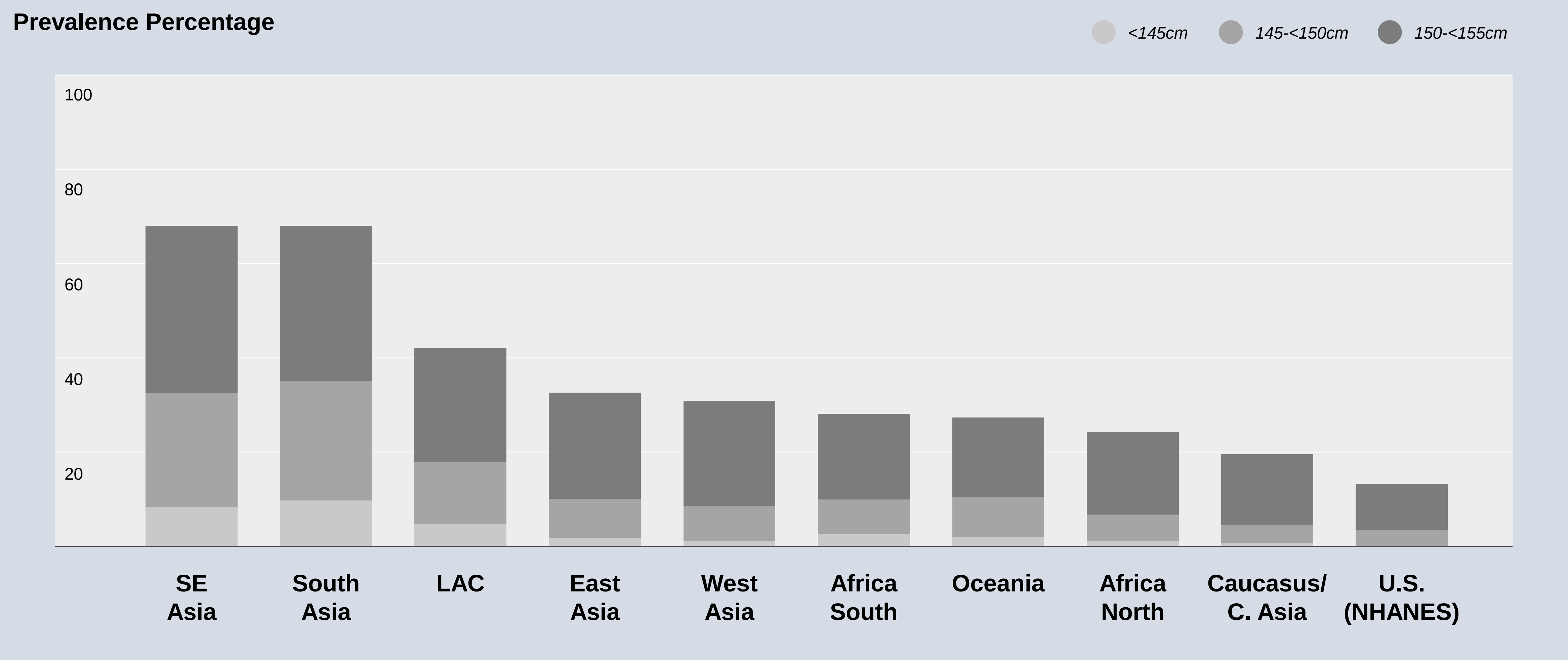
Twitter: @DrEmilyRSmith
Email: EmilySmith@GWU.edu

# Underweight (BMI<18.5): WOMEN AGES 15-45 Y




NCD Risk Factor Collaboration, *Lancet 2016*

# SHORT STATURE: WOMEN AGES 15-49 Y




*Kozuki et al; J Nutr 2015*

# Weight gain during pregnancy in LMICs

Global Data
Gap

# The problem

**Anemia Prevalence, 2011**
Among Women of Reproductive Age

Global Prevalence

- Women: 29%
  (496 mil)

- Pregnancy: 38%
  (32 million)

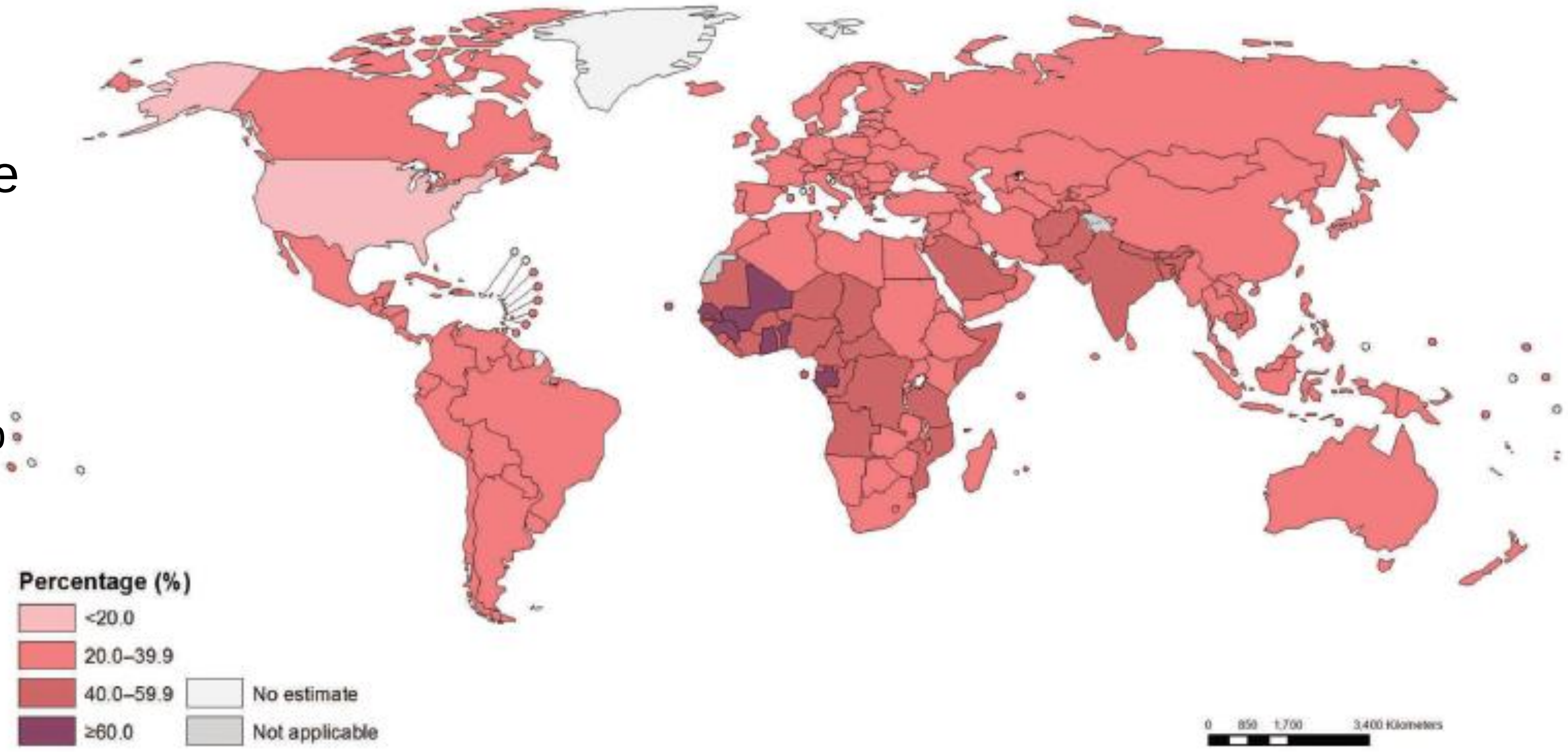
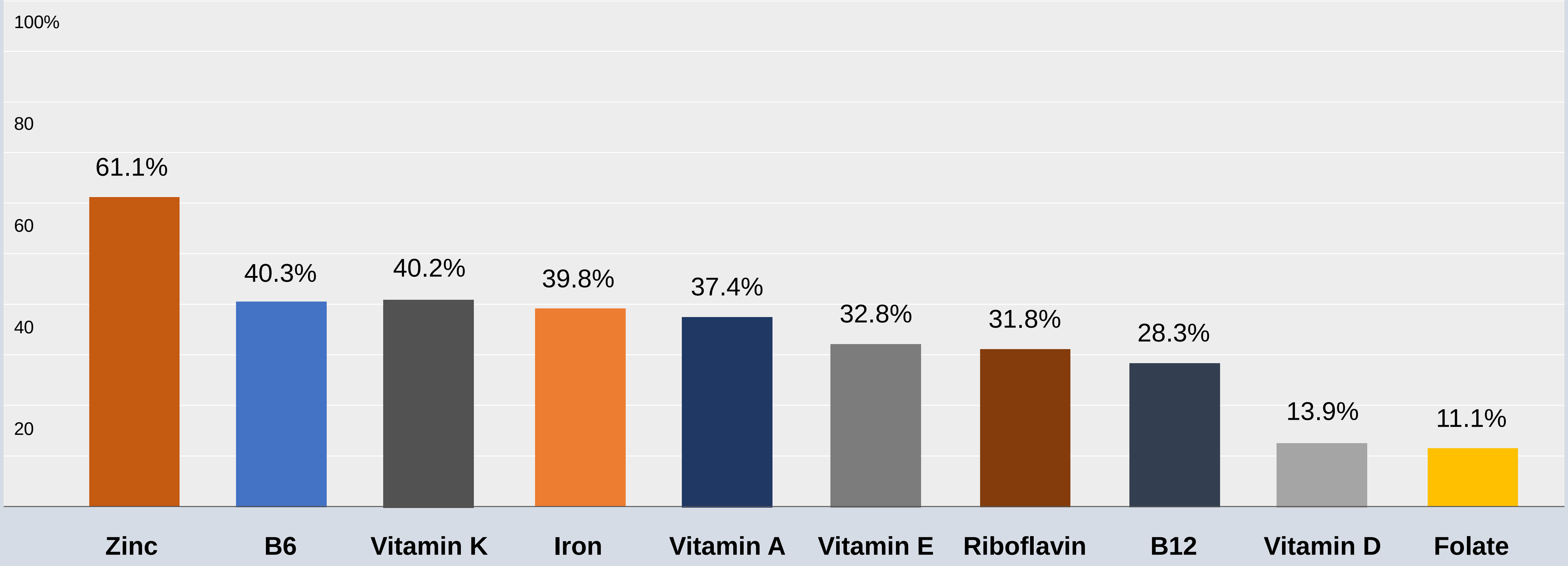



**Figure 9** Global estimates of the prevalence of anemia in pregnant women aged 15–49 years, 2011. Reprinted with permission from WHO [262]. Copyright WHO (2015).

# MULTIPLE MICRONUTRIENT DEFICIENCIES

**Percent of Women with Micronutrient Deficiency in Early Pregnancy**




*Source: (Jiang et al; J Nutr 2005). Nepal Data.*