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Antenatal MMS in Bangladesh: The JiVitA-3 Trial

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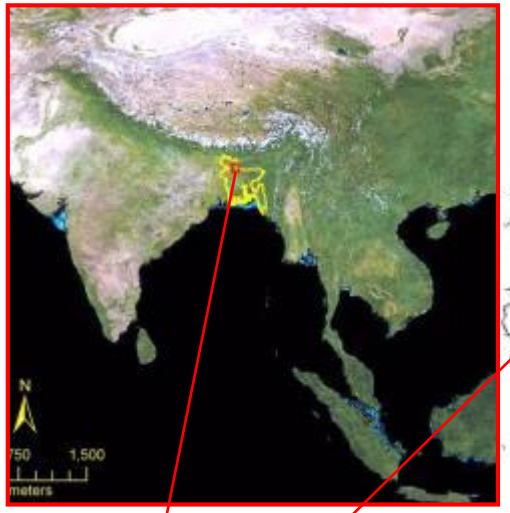

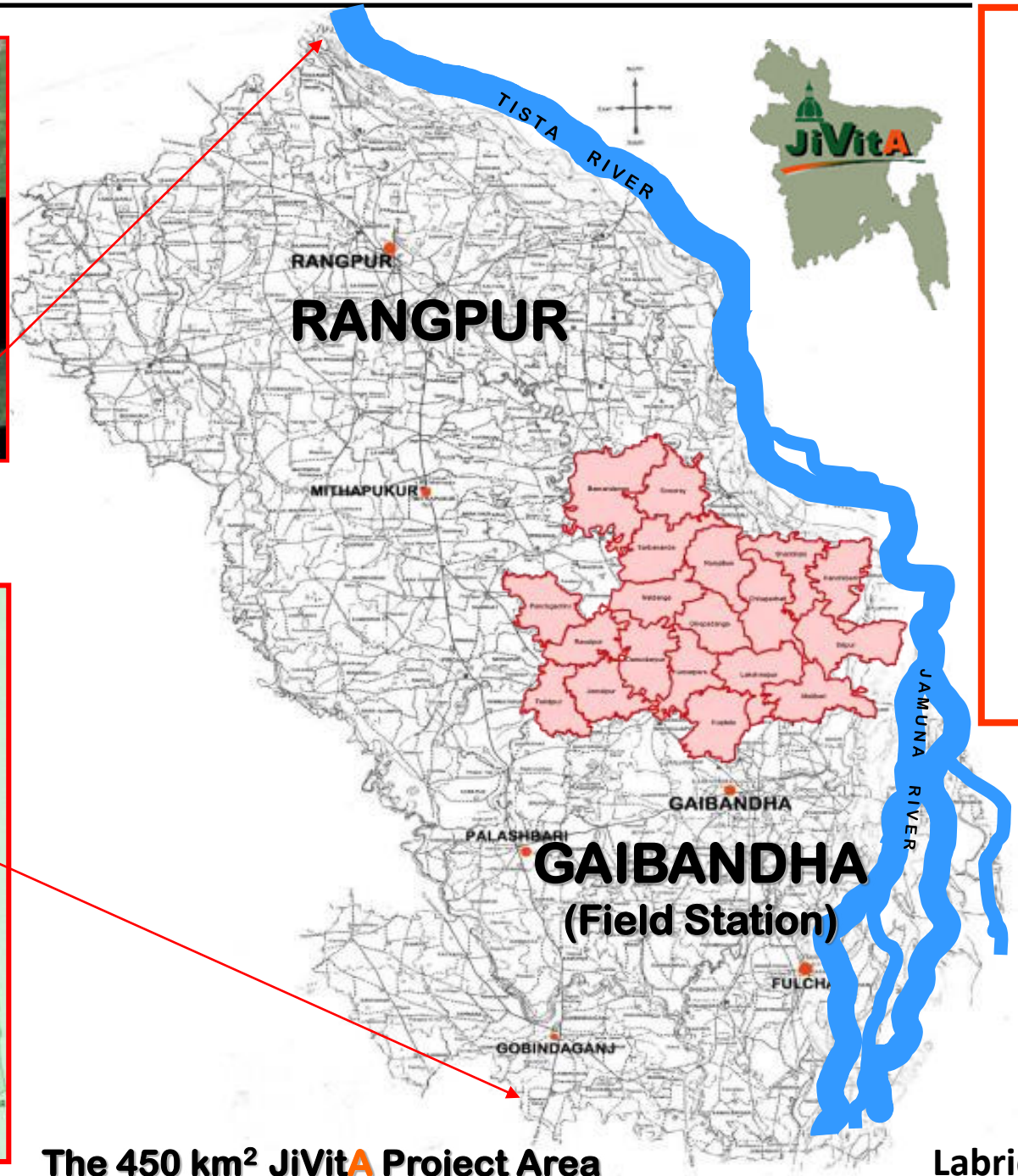

Established 2000
(under GH 614: 2000-2016)

18 Unions

4 x area of Wash DC

Population: ~600,000

Density: 1130 /km²

60 Field Offices

750 Project Staff

Registered under JHUB

With NGO Affairs Bureau

MOA with MOHFW

Registered with DGDA

The 450 km² JiVitA Project Area

Labrique AB et al BMC Trials 2011

Original Investigation

Effect of Maternal Multiple Micronutrient vs Iron–Folic Acid Supplementation on Infant Mortality and Adverse Birth Outcomes in Rural Bangladesh

The JiVitA-3 Randomized Trial

JAMA 2014;312(24):2649-2658.

Funded by the Bill and Melinda Gates Foundation
GH614 Global Control of Micronutrient Deficiency

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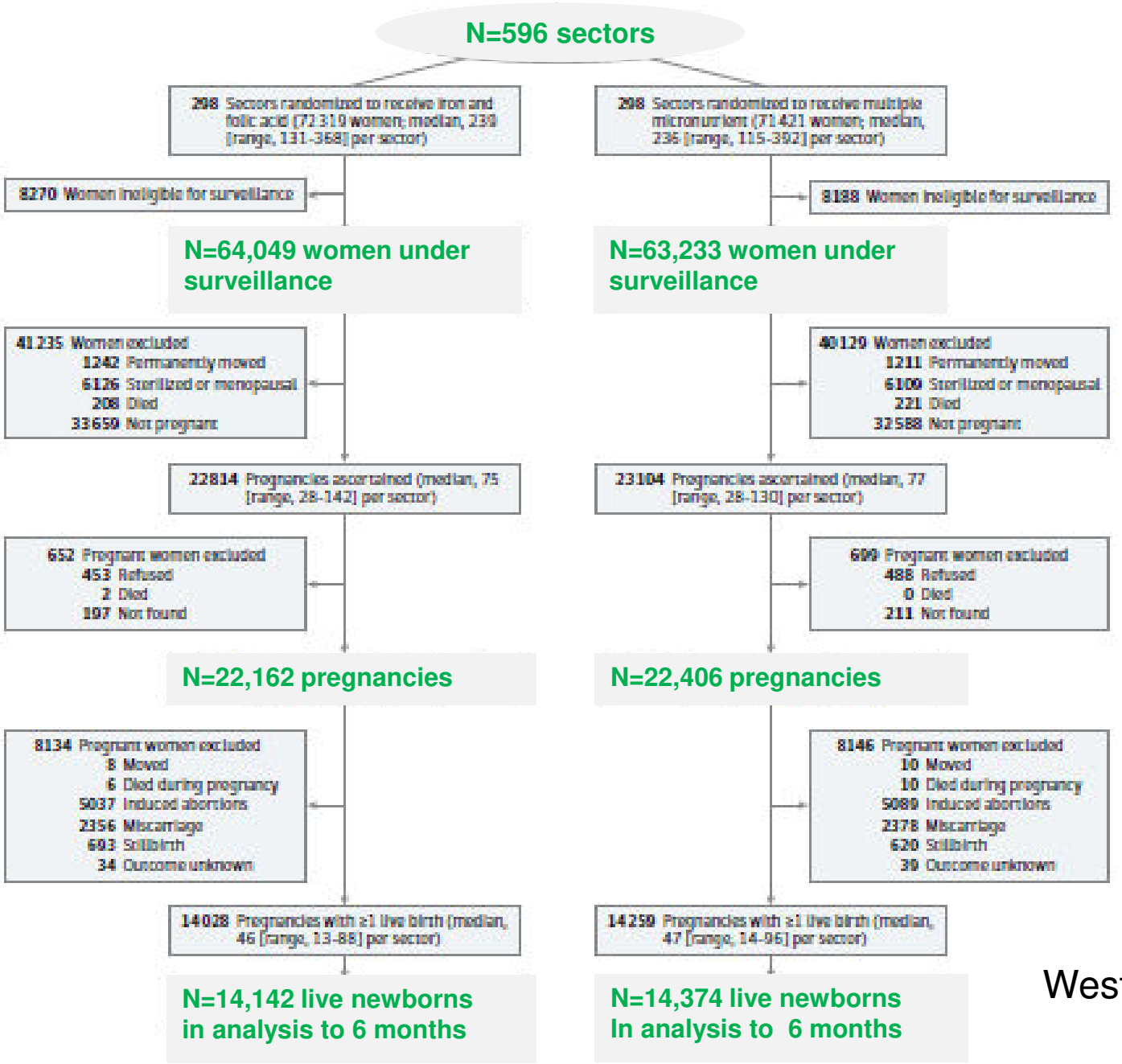
Maternal Multiple Micronutrient vs Iron-Folic Acid Supplementation Trial (JiVitA-3)



West KP et al JAMA 2014

Antenatal Multiple Micronutrient vs Iron-Folic Acid Supplementation …

1. Extended gestation age by 0.30 weeks (~2 days)
2. This led to significant increases in infant size at birth: in …
   weight (54 g) and length (0.2 cm);
   arm, chest and head circumferences (0.1-0.25 cm); and Ponderal Index (0.2)

Table 4. Gestational Age and Newborn Size in Singleton Births by Maternal Supplement Allocation

	Iron-Folic Acid Group		Multiple Micronutrient Group			
	No. of Live Births	Mean (SD)	No. of Live Births	Mean (SD)	Difference (95% CI)[a]	Effect Size[b]
Gestational age, wk[c]	13 333	38.58 (3.08)	13 475	38.88 (2.95)	0.30 (0.21-0.40)	0.10
Birth size[d]						
Weight, g	10 530	2531 (415)	10 642	2585 (407)	54 (41-66)	0.13
Length, cm	10 332	46.46 (2.26)	10 442	46.67 (2.17)	0.20 (0.13-0.27)	0.10
Arm circumference, cm[e]	10 510	9.46 (0.85)	10 617	9.56 (0.82)	0.10 (0.07-0.13)	0.12
Chest circumference, cm	10 468	30.70 (2.08)	10 575	30.95 (2.01)	0.25 (0.18-0.31)	0.12
Head circumference, cm	10 445	32.49 (1.57)	10 563	32.69 (1.51)	0.20 (0.15-0.25)	0.13
Ponderal index[f]	10 331	25.11 (2.41)	10 442	25.32 (2.41)	0.20 (0.12-0.29)	0.09

West KP Jr, Shamim AA, Mehra S et al JAMA 2014

Table 3. Risks of Preterm and Low-Weight Births Among Singletons by Maternal Supplement Allocation

	Iron–Folic Acid Group	Multiple Micronutrient Group
Preterm (gestational age <37 wk)		
No. with gestational age known	13 333	13 475
No. born preterm	2912	2510
Rate per 100 live births	21.8	18.6
Relative risk (95% CI)	1 [Reference]	0.85 (0.80-0.91)
P value[a]		<.001
Low birth weight (<2500 g)[e]		
No. with birth weight known	10 530	10 642
No. with birth weight <2500 g	4809	4275
Rate per 100 live births	45.7	40.2
Relative risk (95% CI)	1 [Reference]	0.88 (0.85-0.91)
P value[a]		<.001
Small for gestational age[f]		
No. with gestational age and size known	10 099	10 161
No. born small for gestational age	6479	6405
Rate per 100 live births	64.2	63.0
Relative risk (95% CI)	1 [Reference]	0.98 (0.96-1.01)
P value[a]		.13

West KP Jr, Shamim AA, Mehra S et al JAMA 2014

The extended gestation led to a…

15% reduction in preterm birth

Extended gestation increased birth size and led to a…

12% reduction in LBW

But no significant effect on SGA (ie, no acceleration in fetal growth)

Maternal MM vs IFA supplementation…

Table 2. Risk of Infant Mortality to Age 6 Months (180 Days) and Stillbirth by Maternal Supplement Allocation

	Iron-Folic Acid Group	Multiple Micronutrient Group
Stillbirths		
No. of live and stillbirths	14 858	15 022
No. of stillbirths	716	648
Rate per 1000 live and stillbirths	48.2	43.1
Relative risk (95% CI)	1 [Reference]	0.89 (0.81-0.99)
P value[a]		.02
Mortality at age ≤6 mo (≤180 d)		
No. of live births	14 142	14 374
No. of deaths	764	741
Rate per 1000 live births	54.0	51.6
Relative risk (95% CI)	1 [Reference]	0.95 (0.86-1.06)
P value[a]		.36
Neonatal mortality (≤28 d)		
No. of live births	14 142	14 374
No. of deaths	625	626
Rate per 1000 live births	44.2	43.6
Relative risk (95% CI)	1 [Reference]	0.98 (0.88-1.20)
P value		.78
Postneonatal mortality (age 29-180 d)		
No. of live births	13 517	13 748
No. of deaths	139	115
Rate per 1000 live births	10.3	8.4
Relative risk (95% CI)	1 [Reference]	0.81 (0.63-1.04)
P value		.11

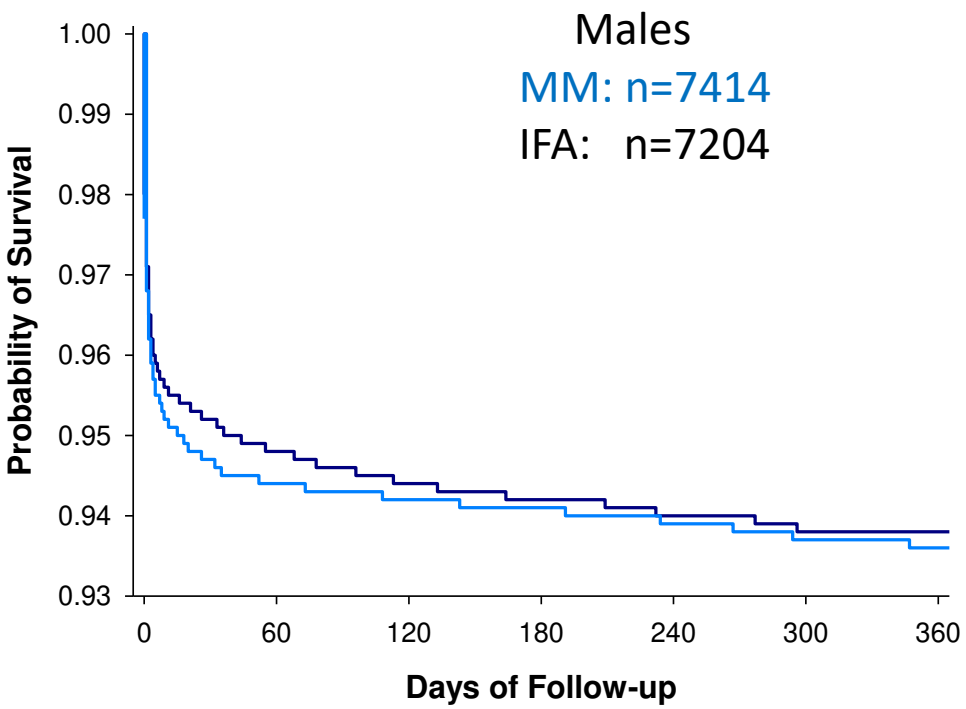
reduced risk of still birth by 11% (RR=0.89, p=0.02)

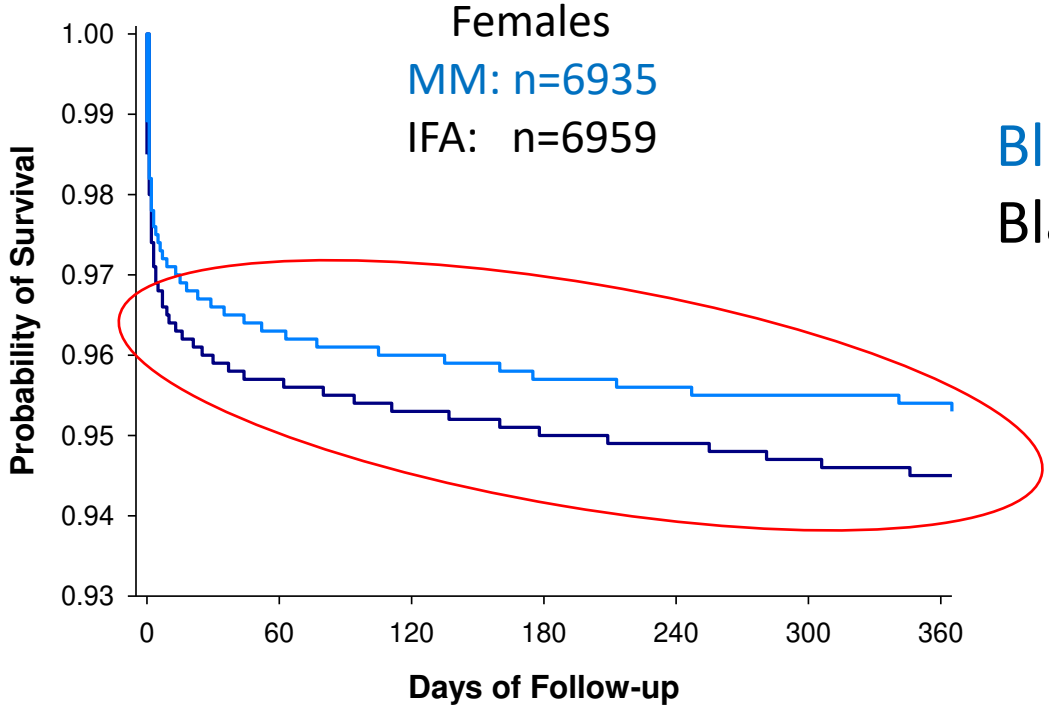
Had no overall effect on infant mortality to 6 mo of age (5% reduction, p=0.36)

or on neonatal mortality (2% reduction, p=0.78),

…or on post-neonatal mortality to 6 mo: a 19% reduction was not SS (RR=0.81, p=0.11)

Effects of MM vs IFA on Infant Mortality
15% lower mortality in girls, not boys





Blue: MM

Black: IFA

Research

Original Investigation

Effect of Maternal Multiple Micronutrient vs Iron–Folic Acid Supplementation on Infant Mortality and Adverse Birth Outcomes in Rural Bangladesh

The JiVitA-3 Randomized Trial

Keith P. West Jr, DrPH; Abu Ahmed Shamim, MSc; Sucheta Mehra, MS; Alain B. Labrique, PhD; Hasmot Ali, MBBS, MPH; Saijuddin Shaikh, PhD, MPH; Rolf D. W. Klemm, DrPH; Lee S-F. Wu, MHS; Maithilee Mitra, MS; Rezwanul Haque, MA; Abu A. M. Hanif, MBBS; Allan B. Massie, PhD; Rebecca Day Merrill, PhD; Kerry J. Schulze, PhD; Parul Christian, DrPH, MSc

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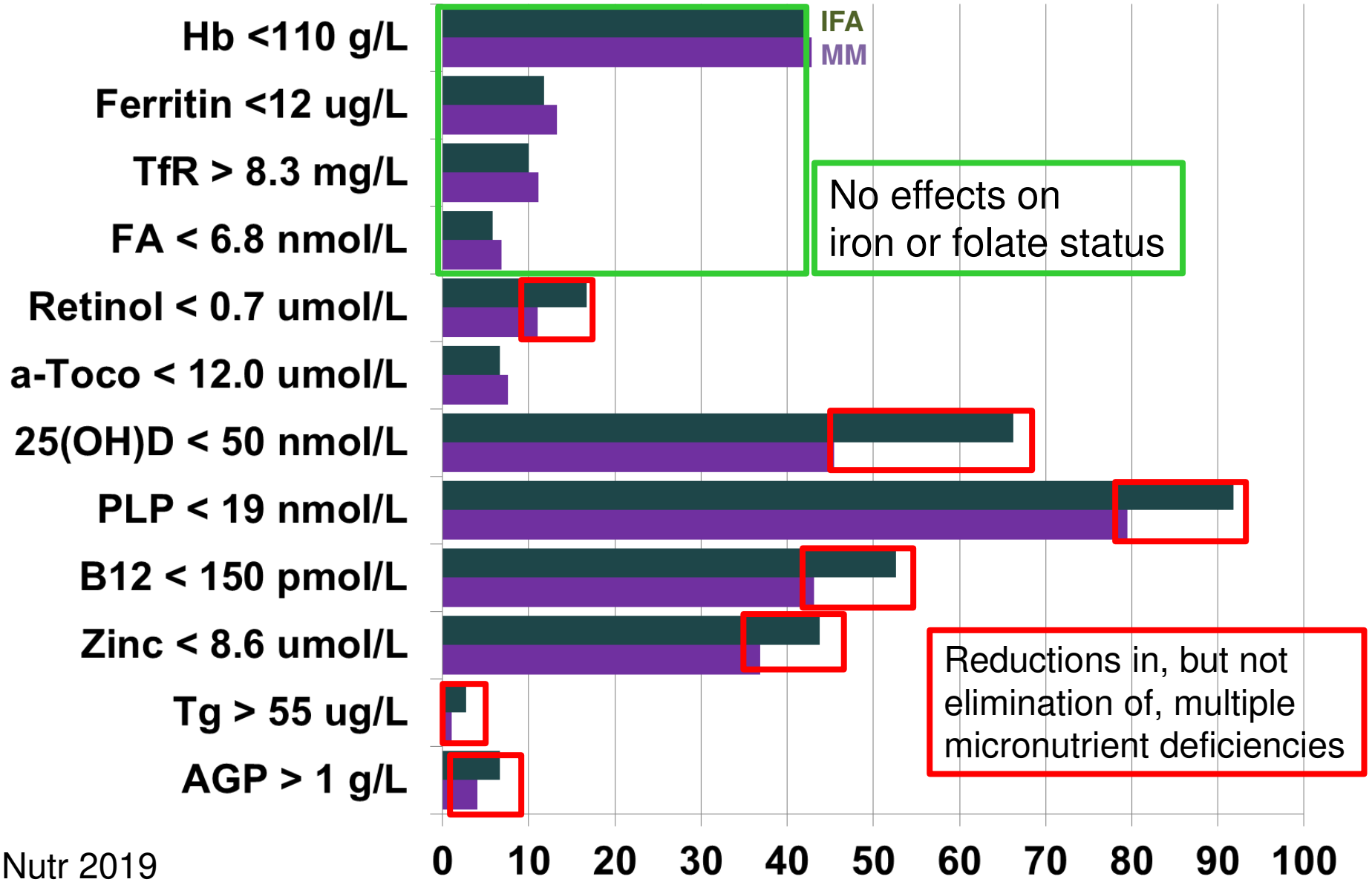
Funded by the Bill and Melinda Gates Foundation

DSM through Sight & Life produced 16 m supplements & provided technical assistance

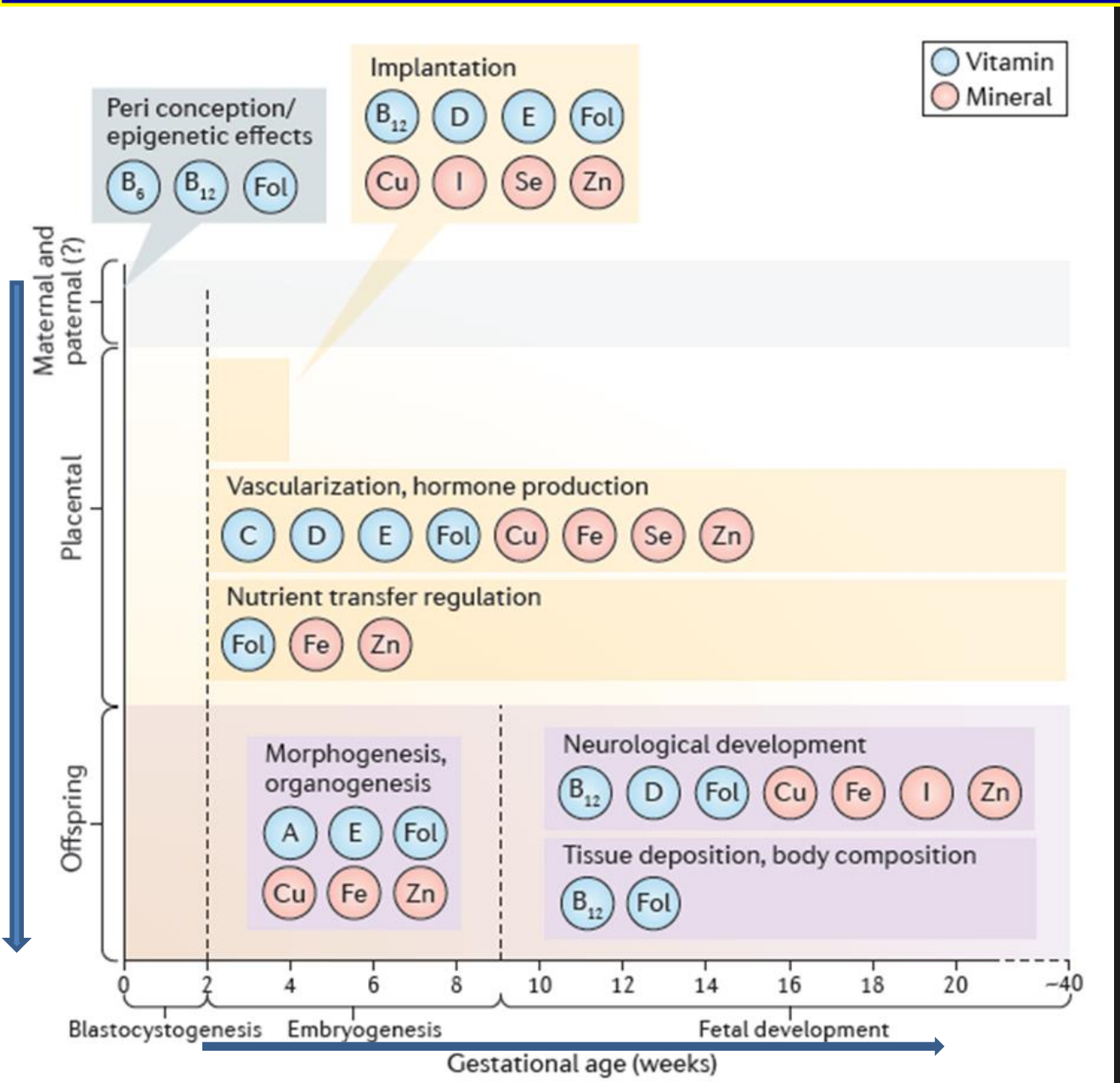
- **RDA amounts of vit A, D, E, B1, B2, B3, B6, folic acid, B12, C, Fe, Zn, Cu, Se, I vs Fe and folic acid alone (MM vs IFA)**
- **44,567 pregnancies; 28,516 live births**
- **Increased GA by 0.3 weeks and thus: birth weight by 54 g, therefore -**
  - **Reduced preterm by 15%**
  - **Reduced LBW by 12%**
  - **Reduced still birth by 11%**
  - **Reduced infant mortality – in girls but not boys**
  - **Led to a healthier pregnancy & infant**

Micronutrient Deficiencies in 3rd Trimester by Supplement Group, JiVitA-3, Bangladesh



Schulze et a J Nutr 2019

Micronutrients are Essential Throughout Pregnancy & Gestation



Gernand A et al Nature Rev Epidemiol 2016

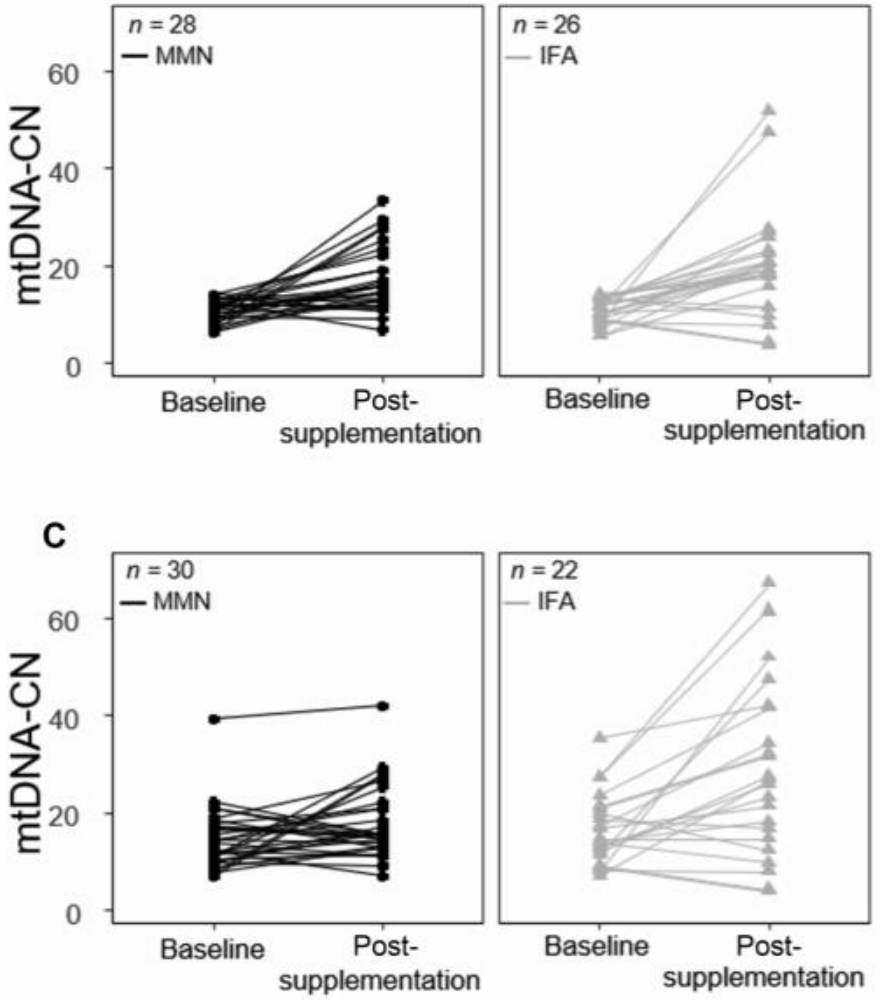
Maternal Multiple Micronutrient Supplementation Stabilizes Mitochondrial DNA Copy Number in Pregnant Women in Lombok, Indonesia

J Nutr 2019

Lidwina Priliani,[1,2] Elizabeth L Prado,[3,4] Restuadi Restuadi,[1,5] Diana E Waturangi,[2] Anuraj H Shankar,[3,6] and Safarina G Malik[1]

TABLE 3 The Δ mtDNA-CN proportions of 108 pregnant women enrolled in the Supplementation with Multiple Micronutrients Intervention Trial study by supplementation group

	Supplement	
MtDNA-CN change[1]	MMN ($n = 54$)	IFA ($n = 54$)
>10% decrease	14 (25.9)	13 (24.1)
No change	12 (22.2)	3 (5.6)
>10% increase	27 (51.9)	38 (70.4)
P^2	0.021	



Antenatal Micronutrients and the Mitochondrial Genome: A Glimpse of Future Nutritional Investigation

J Nutr 2019

Sun Eun Lee,[1] Michael F Fenech,[2] and Keith P West, Jr[1]

MMS may improve health of materno-placental mitochondria and, thus, bioenergetics of pregnancy

Policy Implications: Antenatal Multiple Micronutrient vs IFA Supplementation

- **Antenatal MMN supplementation** –
  - Extends gestation by 2-3 days, thus reducing risks of preterm birth, low birth weight and still birth by ~10-15%
  - May also reduce mortality by 10-15%
  - May have long term effects on offspring: on cognition, metabolic syndrome and growth
- Multiple micronutrient supplementation should be combined with adequate prenatal and essential obstetric and neonatal care

Acknowledgements

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