Food Fortification : Benefits and Challenges

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Expert Consultation on Nutrient Risk Assessment for Determination of Safe Upper Levels for Micronutrients
December 4, 2015 , Hotel Le Meridien, New Delhi

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Presentation out line

- Benefits of fortification strategy - efficacy and effectiveness (global)- folic acid, iron, iodine, vitamin D
- India- salt, rice, wheat, milk and point of use fortification with MMP
- Challenges

Global data on prevalence of major micronutrient deficiencies

	Anaemia		Night blindness (VAD)*		Inadequate Zinc intake	Hypo vitaminosis D
	Children <5 years	Pregnant women	Children <5 years	Pregnant women		
Africa	53	39	2.1	9.4	22	40-91
Asia	40	36	0.5	7.8	26	25-80
Europe	26	24	0.7	2.9	10	15-83
LA & Caribbean	33	27	0.6	4.4	17.0	27-67
Oceania	43	36	0.5	9.2	22	25-80
Global	43	38	0.9	7.8	17	30-90

Prevalence of subclinical forms of vitamin A deficiency is 33.3 % in preschool children and 15.3 % among pregnant women. Severe anemia amounts to 1.1 % globally among non pregnant women and 0.9 % among pregnant women

Stevens et al *Lancet Glob Health* (2013) **1**: e16–25;WHO, 2009;
Wessells *Plos one* (2012) **7**(11): e50568;
Arabi et al *Nat Rev Endocrinol* (2010) **6**: 550–561.

Micronutrients and human brain development

- Effects of iodine, folic acid and iron have received appreciable attention

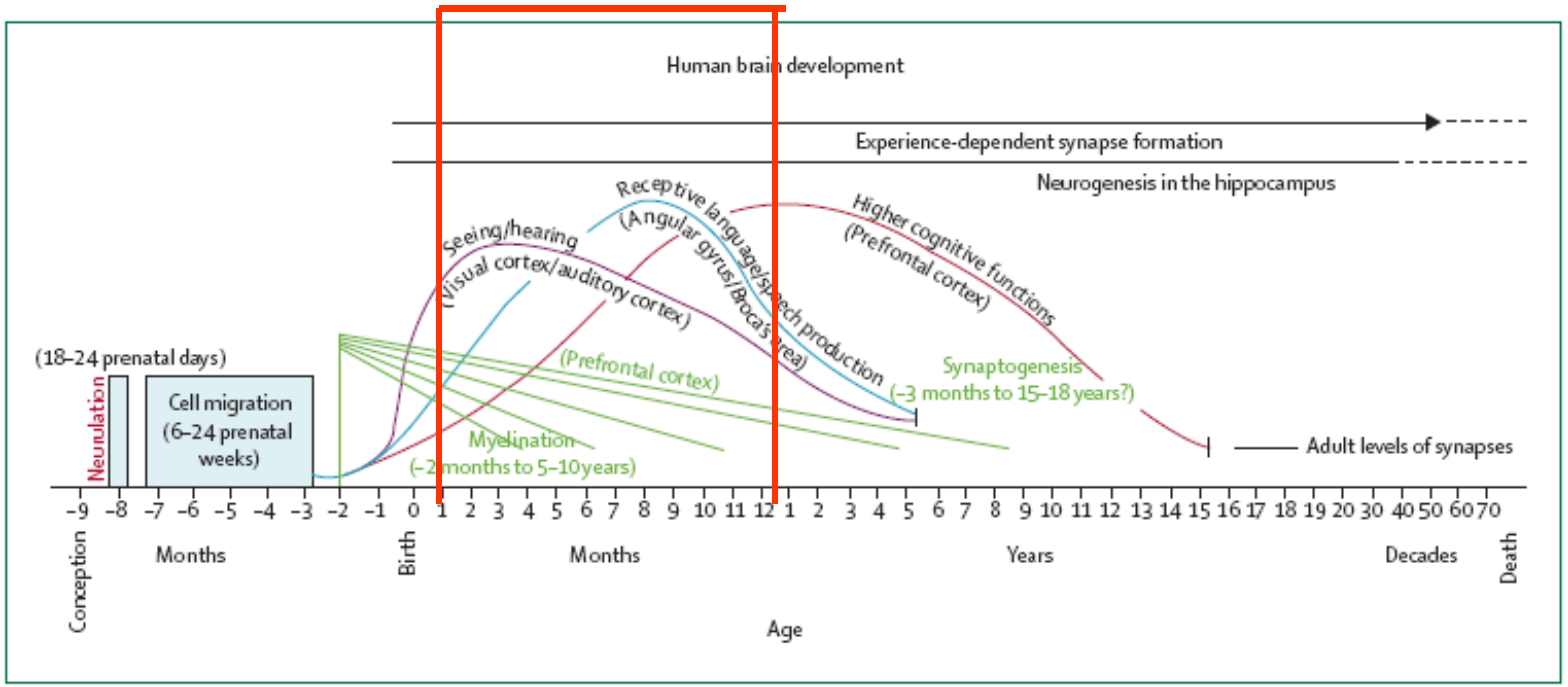
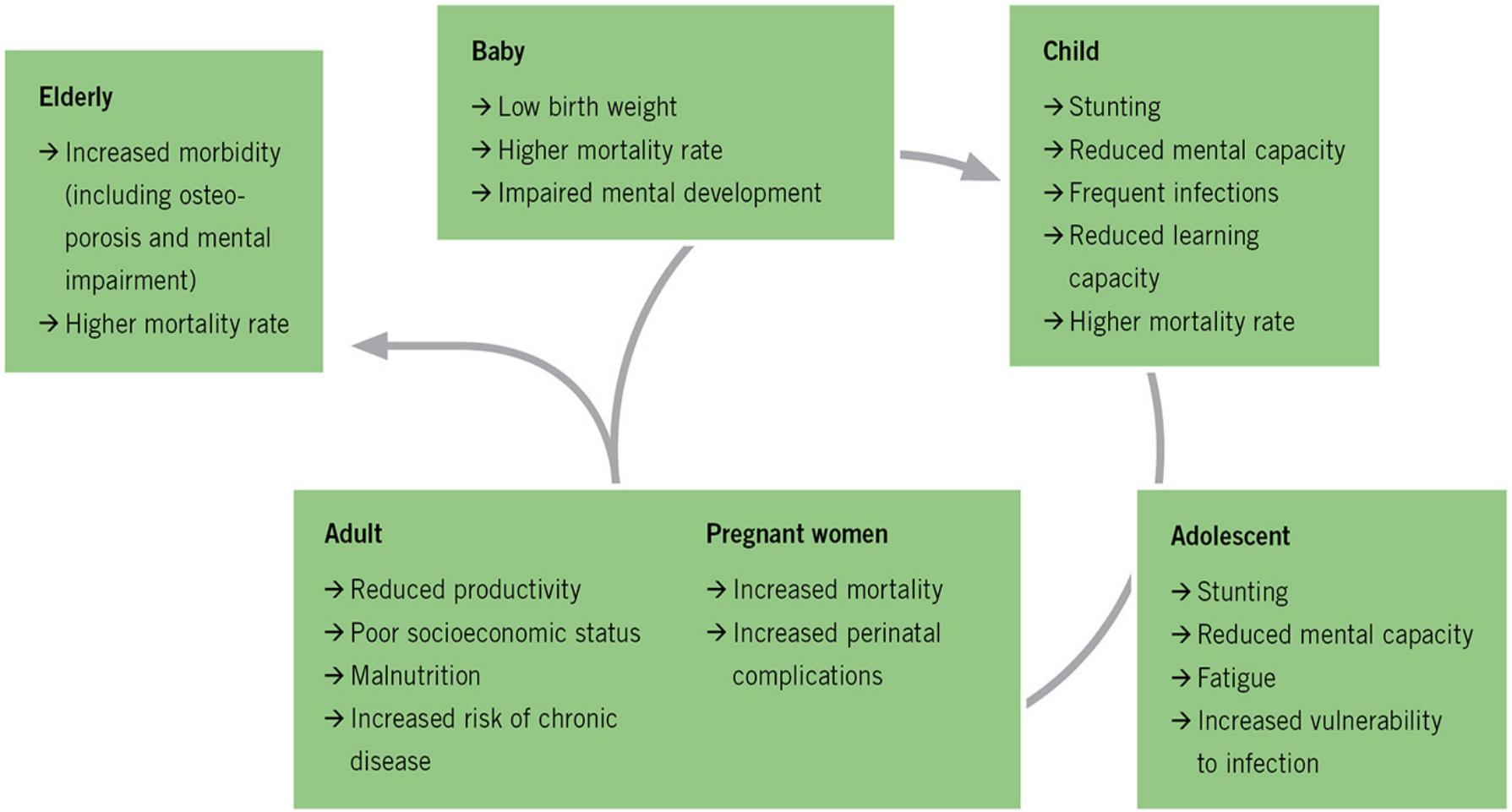


Figure 1: **Human brain development**
Reproduced with permission of authors and American Psychological Association[37] (Thompson RA, Nelson CA. Developmental science and the media: early brain development. *Am Psychol* 2001; 56: 5–15).

CONSEQUENCES OF MICRONUTRIENT DEFICIENCIES THROUGHOUT LIFE CYCLE



ACC/SCN, 2000

Codex General Principles for the Addition of Essential Nutrients to Foods

Fortification / Enrichment:

Addition of one or more essential nutrients to a food whether or not it is normally contained in the food, **for the purpose of preventing or correcting a demonstrated deficiency** of one or more nutrients in the population or specific population groups.

Best global welfare investment

Food fortification has a successful track record in many countries

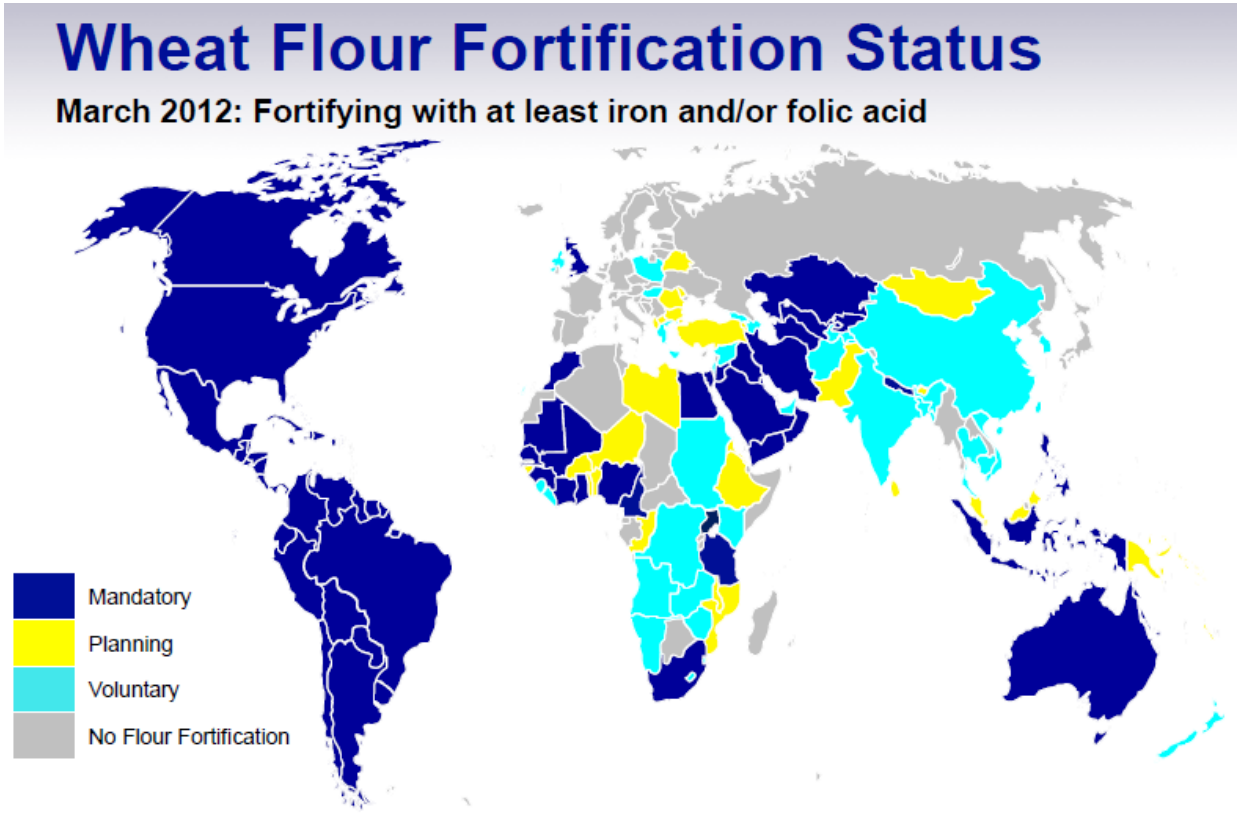
Long history in many countries for successful control of deficiencies of vitamins A, D, several B vitamins, iodine and iron.

1923:	**Mandatory iodization of salt in Switzerland and USA**; now available in most countries.
1933:	**Mandatory fortification of flour with** Vitamin B1 **in Canada** and virtual elimination of Beriberi.
1941:	**Mandatory fortification of flour with** Vitamin B3 **in the USA** and virtual elimination of pellagra
early 40ies:	**Fortification of cereal products** with Vitamin B1, B2 and B3 became common practice **in many countries.**
1954:	**Flour fortified in Chile with** B-vitamins and iron. Country has now very low prevalence for anemia.
1974:	**Beginning of sugar fortification with** Vitamin A **in Guatemala**. Vitamin deficiency diminished to one third.
1992:	**Wheat and maize flour fortification in Venezuela**. Vitamin A sufficiency in general population and important reduction in anemia in children.
1998:	Folic Acid **fortification mandated in the USA**. Now implemented in 60 countries.
2000:	Vitamin D **fortification of milk and dairy products in US and Canada started**

WHO Guidelines
Micronutrient levels for wheat flour fortification (mg/100g)

Nutrient	Compound	<75 g/d	75 – 149 g/d	150 – 300 g/d	>300 g/d[3]	EAR[2]
Iron[1]	Micronized ferric pyrophosphate	12	12	7	7	Not specifiable
Folic Acid	Folic acid	0.50	0.26	0.13	0.10	0.192
Vitamin B12	Cyanocobalamin	0.004	0.002	0.001	0.0008	0.002
Vitamin A	Vitamin A palmitate	0.59	0.3	0.15	0.1	0.357 (f) 0.429 (m)
Zinc	Zinc oxide	9.5	8	6	5	8.2 (f) 11.7 (m)
Thiamin	Thiamin mononitrate	2.0	1.0	0.5	0.35	0.9 (f) 1.0 (m)
Niacin	Niacin amide	26	13	7	4	11 (f) 12 (m)
Vitamin B6	Pyridoxine hydrochloride	2.4	1.2	0.6	0.4	1.1

WHO Consultation, Geneva, 2005



Flour Fortification Initiative

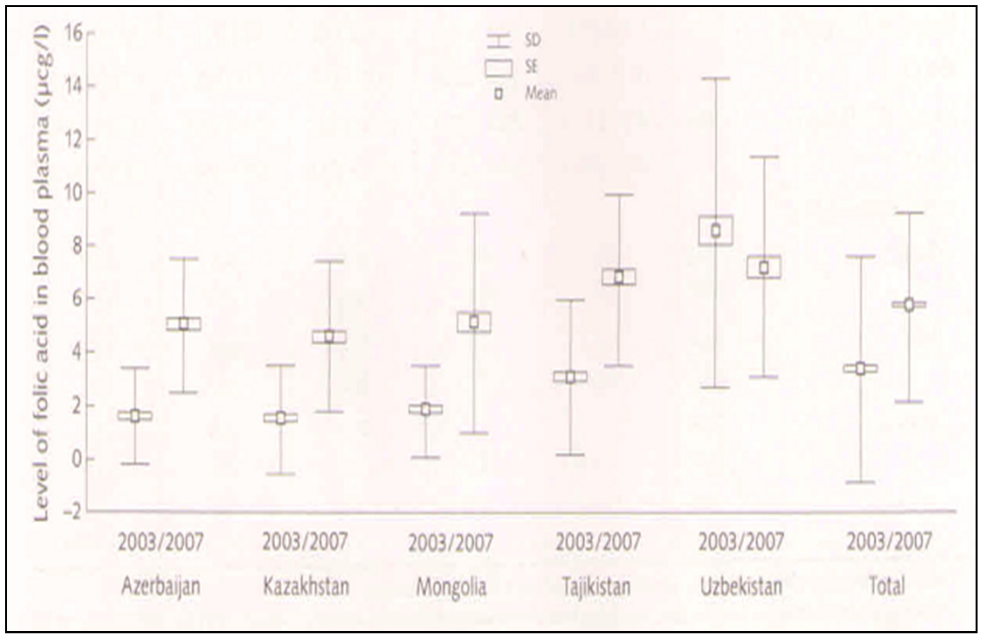
Table 1. Levels of folic acid fortification in countries with mandatory fortification programs.

Country	Fortification level	Date of implementation
United States [25]	140 µg/100 g	1998
Canada [33]	150 µg/100 g	1998
Costa Rica [34]	180 µg/100 g	1998
Chile [35]	220 µg/100 g	2000
South Africa [36]	150 µg/100 g	2003

Levels highly successful in preventing folate related NTD

Crider et al , Nutrients 2011, 3

Serum folate concentration at baseline and end line by country



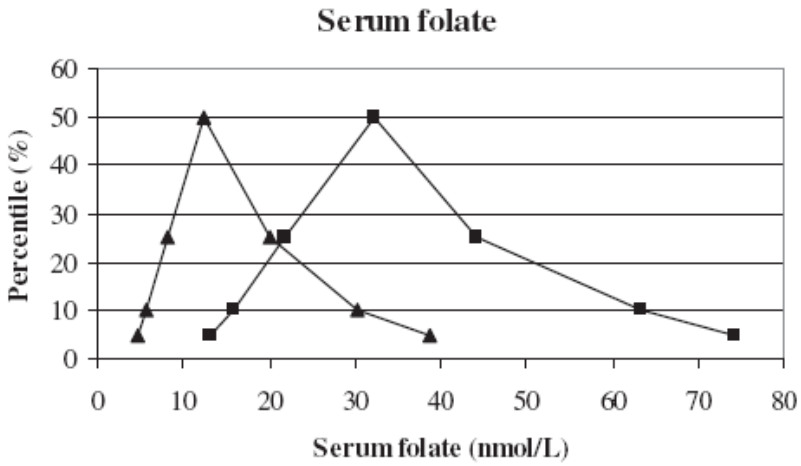
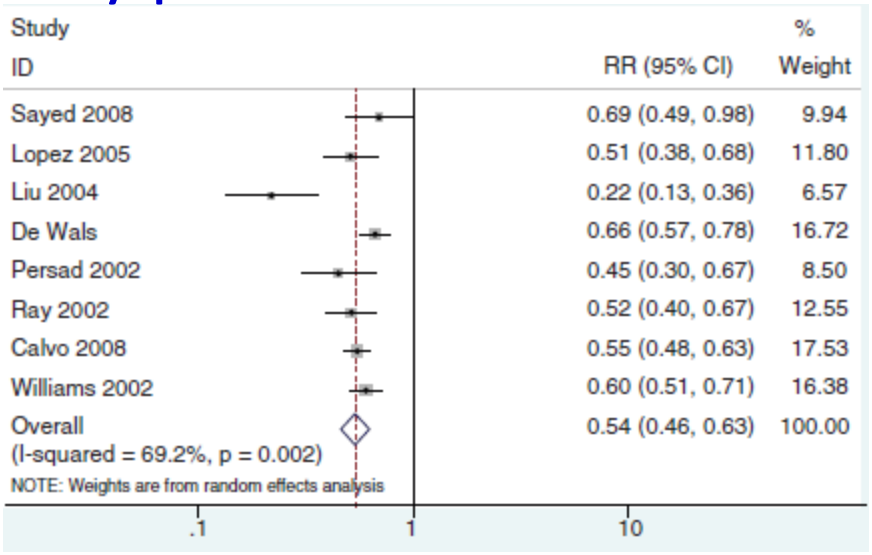


FIGURE 5. Frequency distribution of serum folate for persons aged ≥3 y in 1999–2000 (■) and for persons aged ≥4 y in 1988–1994 (▲) in the United States. Reprinted with permission from Pfeiffer et al (26).

Primary prevention of neural tube defects



- Shamil *et.al* Food and Nutrition Bulletin, The United Nations University 2008.. Vol. no. 29 (4); pp 255-65
- Pfeiffer et al; AJCN, 2005; 82:442-50
- Blencowe et al *Int J Epidem* 2010;39:i110–i121

The benefits of food fortification-folic acid

- Prevent approximately half of all neural tube defects.
- Human and financial perspectives.
- Helped other segments of the population by greatly reducing rates of folate deficiency.
- No important adverse effects have been identified to date, probably because a modest level of fortification in preventing birth defects.
- Attempts to reduce recurrence of cardiovascular disease with folic acid and related B vitamins have produced largely negative results but have shown no adverse.

Effect of food fortification strategies and programmes on target age-groups: Review of data from 36 countries

Target group	Effect
Prenatal and antenatal	Weighted mean difference in Hb higher ▪ 5.7g/L in women of child bearing age ▪ 6.9g/L in pregnant women 19-64% decrease in prevalence of goiter after universal iodization
Neonates (0-1mo)	65.7% reduces mortality after iodization
Infants (1-12mo)	• 7.36, 2.88-11.84g/L increase in Hb • 56.5% decrease in infant mortality after iodization
Children (12-59mo)	7.36, 2.88-11.84g/L higher Hb

Bhutta et al; Lancet 2008, DOI:10.1016/S0140-6736(07)61693-6

Estimates of the effect of fortification on mortality and stunting

Effect	months	% reduction
Proportional reduction in deaths before	12 24 36	10 11.3 12.1
Relative reduction in prevalence of stunting at	12 24 36	10.3 15.9 17.4
Millions (%) of DALYs averted at	36	12.3

Bhutta et al; Lancet 2008, DOI:10.1016/S0140-6736(07)61693-6

Efficacy studies of iron fortification in foods

Study design: **systematic review**

Foods fortified: **cereals, salt, condiments, and commercially processed foods**

- **41% reduction in anemia and a 52% reduction in iron deficiency [1].**
- **45% reduction in anemia in children and 32% reduction in women [2].**
- **Significant increase in hemoglobin concentration of 5.09 g/L [3].**

1. Gera et al *AJCN* 2012;96:309–24
2. Das et al *Syst Rev*. 2013;2:67
3. Athe et al *PHN* 2013;17(3):579-586

Evidence of the effectiveness of flour fortification for reducing the prevalence of anemia is limited

Countries included: Azerbaijan, Brazil, China, Fiji, India, Iran, Kazakhstan, Mongolia, Nepal, Sri Lanka, Tajikistan, Uzbekistan, and Venezuela

Most reported fortification: wheat flour only (n=10), wheat and maize flour (n=2), and of wheat, maize, and millet flour (n=1) with iron

Population represented= Children ≤ 15 (14 sub groups) and women of reproduction age (12 sub groups)

Biological marker	Children ≤15 y (n = 14 subgroups)			Women of reproductive age (n = 12 subgroups)		
	Yes	No	Not assessed[a]	Yes	No	Not assessed[a]
Increased ferritin[b]	3	3	8	5	0	7
Decreased prevalence of low ferritin	1	5	8	3	0	9
Increased hemoglobin	5	7	2	6	5	1
Decreased prevalence of anemia	4	9	1	4	8	0
Decreased prevalence of IDA	0	0	14	0	2	10

Insufficient evidence to evaluate whether programs that followed WHO iron recommendations for flour fortification have better outcomes

Pachon et al *Nutr Rev* 2015 Nov;73(11):780-95.

In a review of wheat flour fortification programs, only 9 of 78 programs were judged to be effective

Hurrell *FNB* 2010;31:S7–21

ULTRA RICE TECHNOLOGY

- Ingredients: Rice flour, shortening (soybean), sodium alginate, Ferric pyrophosphate, citric acid, sodium tri polyphosphate, BHA, BHT, calcium chloride
- Iron .

PATH

Efficacy trials –Iron fortified rice

- Iron fortified rice noodles are efficacious in reducing anaemia and improving haemoglobin and iron status indicators among Vietnamese school children (*Huong 2006*).
- iron fortification reduced the prevalence of iron-deficiency anemia from 100% to 33% among preschool age children (*Angeles-Agdeppa 2008*).
- Reduced the prevalence of anaemia by 80% and iron deficiency by 29% in Mexican women working in a factory (*Hotz 2008*).
- Rice fortified with micronized iron pyrophosphate was more effective than iron drops in decreasing anaemia from 100% to 62% and iron deficiency from 69% to 25% and improving iron status (*Beinner 2010*).

Efficacy of vitamin D fortification

Study design: A meta-analysis

Studies included: 16

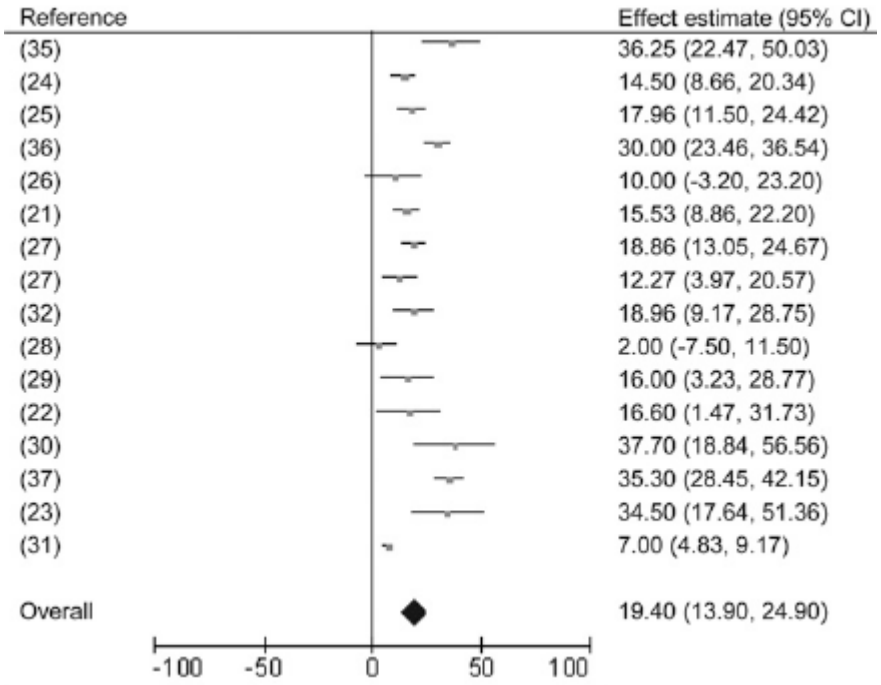
Subjects: Adult men and women

Food vehicle: Twelve studies used dairy products as a food source (and orange juice was used in 2 studies and bread was used once.

Dose: The daily dose of vitamin D in the fortified foods ranged from 3 to 25 µg (per 100 g or serving, or dose achieved from consumption of fortified food): 8 studies used <10 µg .

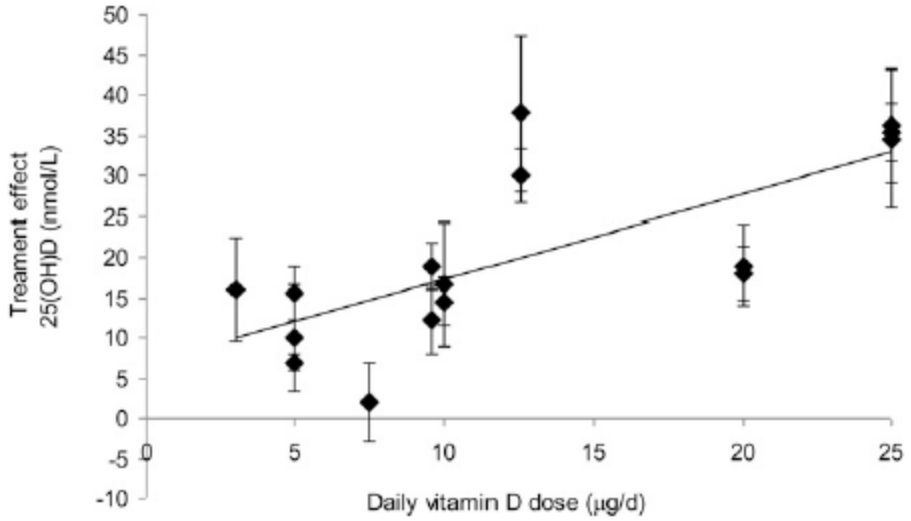
Black *et al* 2012; 2012; 142(6): 1102-1108

Change in circulating 25(OH)D (nmol/L)



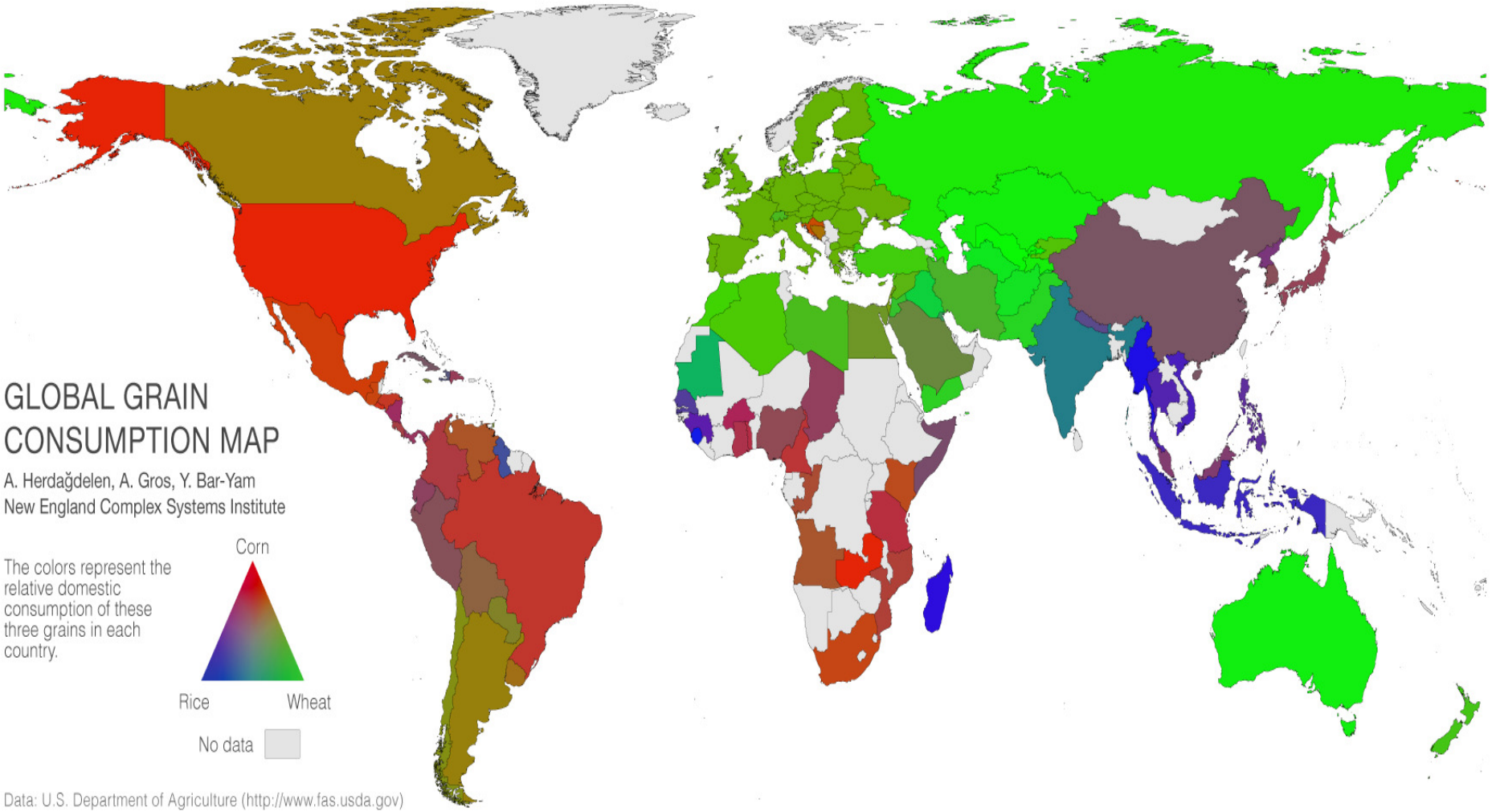
Weighted mean difference in absolute change estimated; mean dose of ~ 11 mg/d; I^2 (variation in effect size attributable to heterogeneity) = 89%; chi-square statistic P value =0.00001; n = 16.

Dose-response of 25(OH)D at doses between 3 and 25 µg/d



Black *et al* 2012; 2012; 142(6): 1102-1108

India


GLOBAL GRAIN
CONSUMPTION MAP
A. Herdağdelen, A. Gros, Y. Bar-Yam
New England Complex Systems Institute
The colors represent the relative domestic consumption of these three grains in each country.
Corn
Rice
Wheat
No data
Data: U.S. Department of Agriculture (http://www.fas.usda.gov)

NIN Double Fortified Salt (Iron + Iodine)

Ingredients	Quantity
Common Salt (g)	1000
$FeSO_4$ $7H_2O$ (g)	5 (Fe 1 mg/g)
KI/KIO_3 (mg)	52 (40 µg/g)
SHMP (g)	10 (10 mg/g)

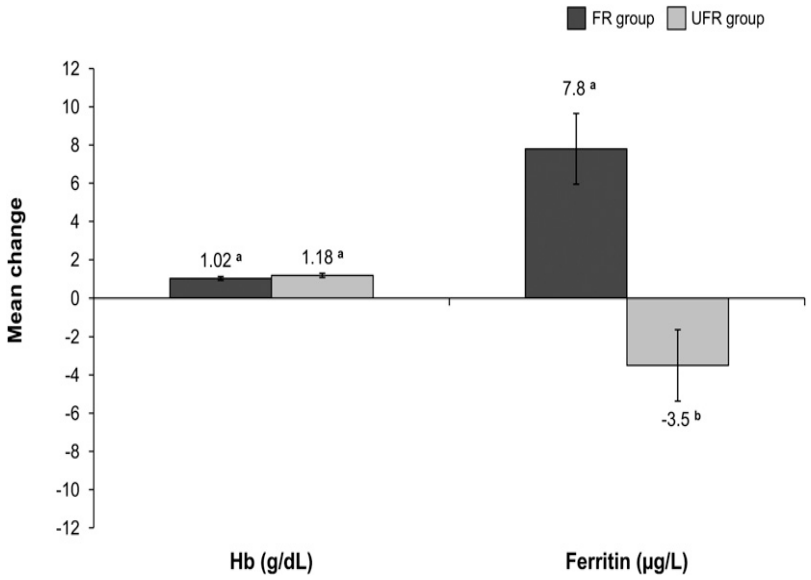
Nair KM et al. Indian J Med Res , 108: 203-211.1998;
Sivakumar et al Brit. J. Nutr.85: S167-S173. 2001;
Sivakumar et al Indian J Pediatrics 69: 617-623, 2002

costs 18 to 20 cents per person per year

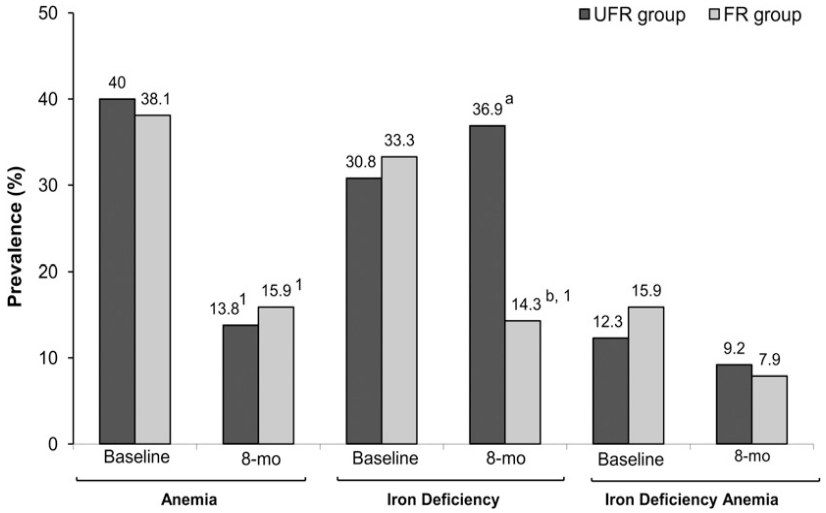
Other formulations of fortified salt

Nutrients	Technology	Country	Target Population	Impact	Reference
Fe, I	MI	South India	Community trial Children (5-15y)	Effective in reducing prevalence of anemia & Fe deficiency	Am J Clin Nutr, 88: 1378-87
Fe, I, Ca Vit A, B1, B2, B12, B6, Folic acid, niacin,	Sundar Serendipity Foundation, Chennai	South India	Children (5-15y)	Effective in improving Hb, Vitamin A	Eur. J Clin Nutr, 63:437-445(2009)
Micro-encapsulated I, Fe and vit A	Swiss federal institute of technology	South India	10-mo, randomized, double-blind trial in goitrous schoolchildren (n = 157)	Efficacious in reducing the prevalence of iron, iodine, and vitamin A deficiencies	Am J Clin Nutr 80:1283-90, 2004

Micronized ferric pyrophosphate supplied through extruded rice kernels improves body iron stores in children: Midday meal feeding trial in Indian schoolchildren



Mean (changes from baseline in hemoglobin (Hb) and ferritin concentrations in the fortified rice and unfortified rice groups



Changes in prevalence of anemia, iron deficiency, and iron deficiency anemia in the fortified rice and unfortified rice groups.

Radhika , Naie et al Am J Clin Nutr 2011;94:1–9

Efficacy of Hot Extruded Fortified Rice

Study Design:

Iron depleted Children 6-13 y
Double-blind, 7-months, school-based feeding trial in Bangalore.
70 children per group (20 mg iron/100g raw rice in each meal)

	Baseline	Endpoint
Hemoglobin (g/L)		
Iron group	121 ± 12[a]	119 ± 9[a]
Control	121 ± 13[a]	116 ± 11[b]
Serum ferritin (µg/L)		
Iron group	16.8 ± 17[a]	26.3 ± 19[b,]
Control	15.4 ± 13[a]	17.7 ± 17[b]

Moretti et.al AJCN(2006), 84,4,822-829

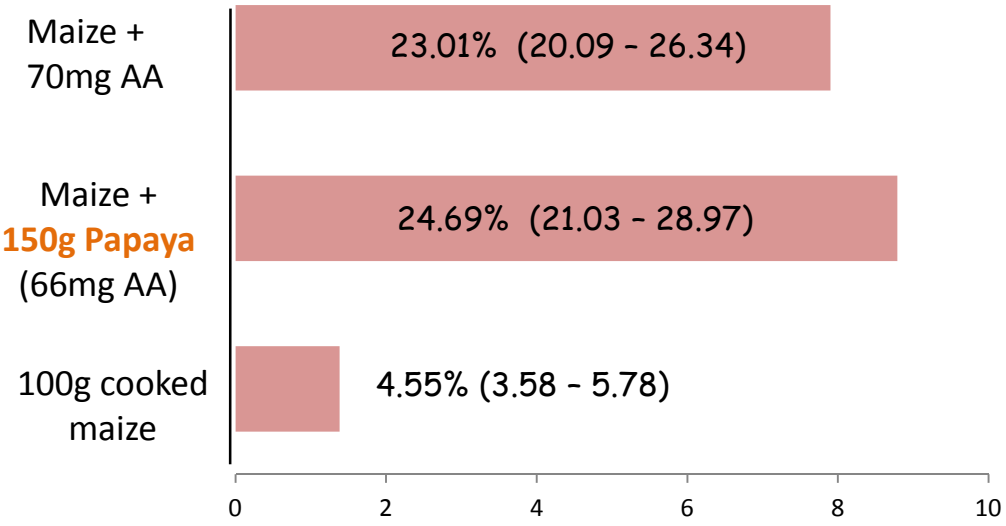
Means in a row with different superscript letters are significantly different, *P<0.001 (Tukey's* tests).

Challenge

How to enhance bioavailability of fortificant iron from low bio available habitual diet (cereal-pulse diet/ whole wheat atta / rice/ millets

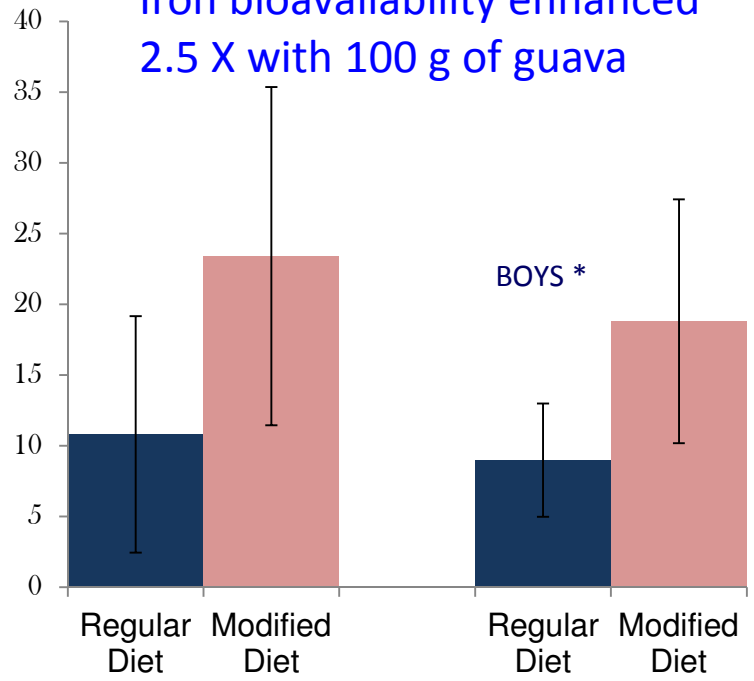
Food synergy

Food synergy to improve Iron Bioavailability



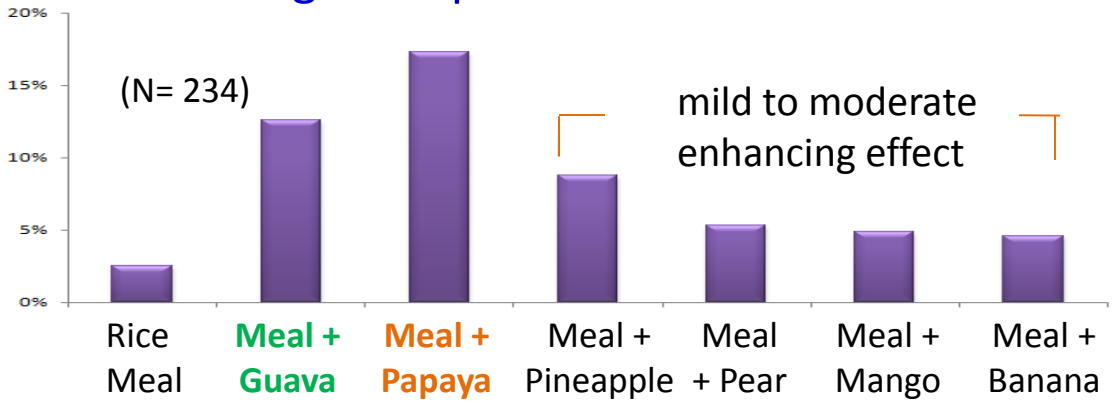
Layrisse et.al. 1974; AJCN, 27: 152-162

Iron bioavailability enhanced 2.5 X with 100 g of guava



Nair et. al, J Nutr 2013, 143: 852-858

Rice meal among 22–74y aged Durban-Indian women using incorporation of radioactive ^{59}Fe in Hb

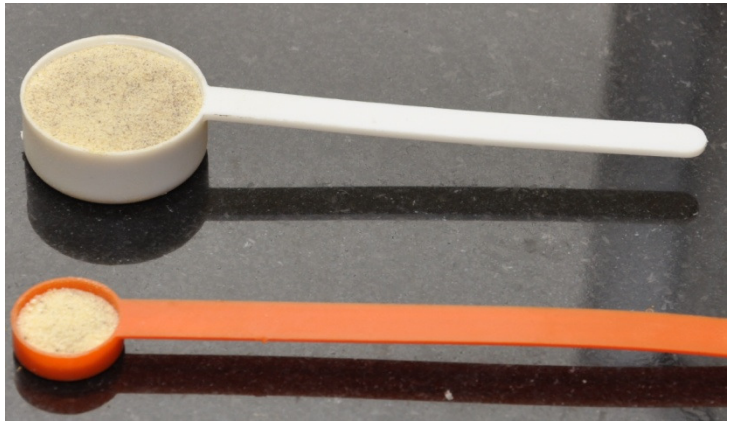


Fe bioavailability and the ascorbic acid content of the fruits *(r* = 0.738, *P < 0.0001).*

Ballot et.al 1987. BJN, 51: 331-343

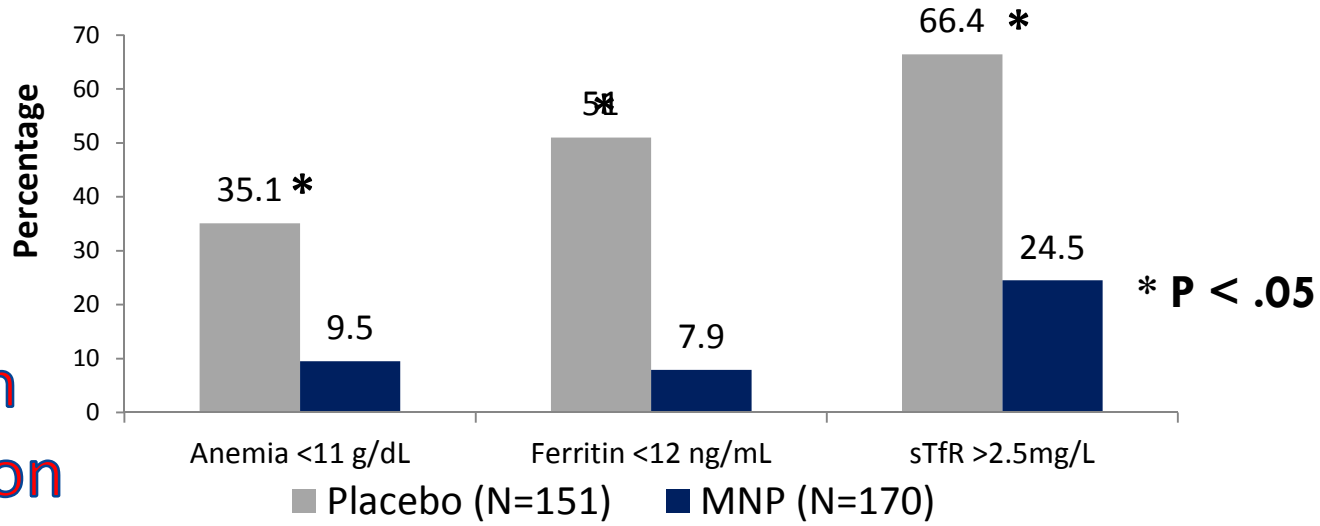
Point of use fortification with multiple micronutrient powders

- Powders of premix in small packets adequate for one /multiple serving.
- Provide an easy to use formulation for improving vitamin and mineral content of diet by mothers and caregivers.



Effect of MNP on Anemia and Deficiencies of Iron

Effect of MNP on Biomarkers of Iron



Biomarkers	Placebo (N=149)	MNP (N=167)	P
Hb g/dL	11.2 ± 0.15	12.1 ± 0.15	<0.0001
Ferritin µg/L	15.6 ± 1.19	24.3 ± 1.19	<0.0001
sTfR mg/L)	3.2 ± 0.007	2.3 ± 0.007	<0.0001

Effect on cognitive functions: expressive language and inhibitory control

World Health Organization

Guideline:

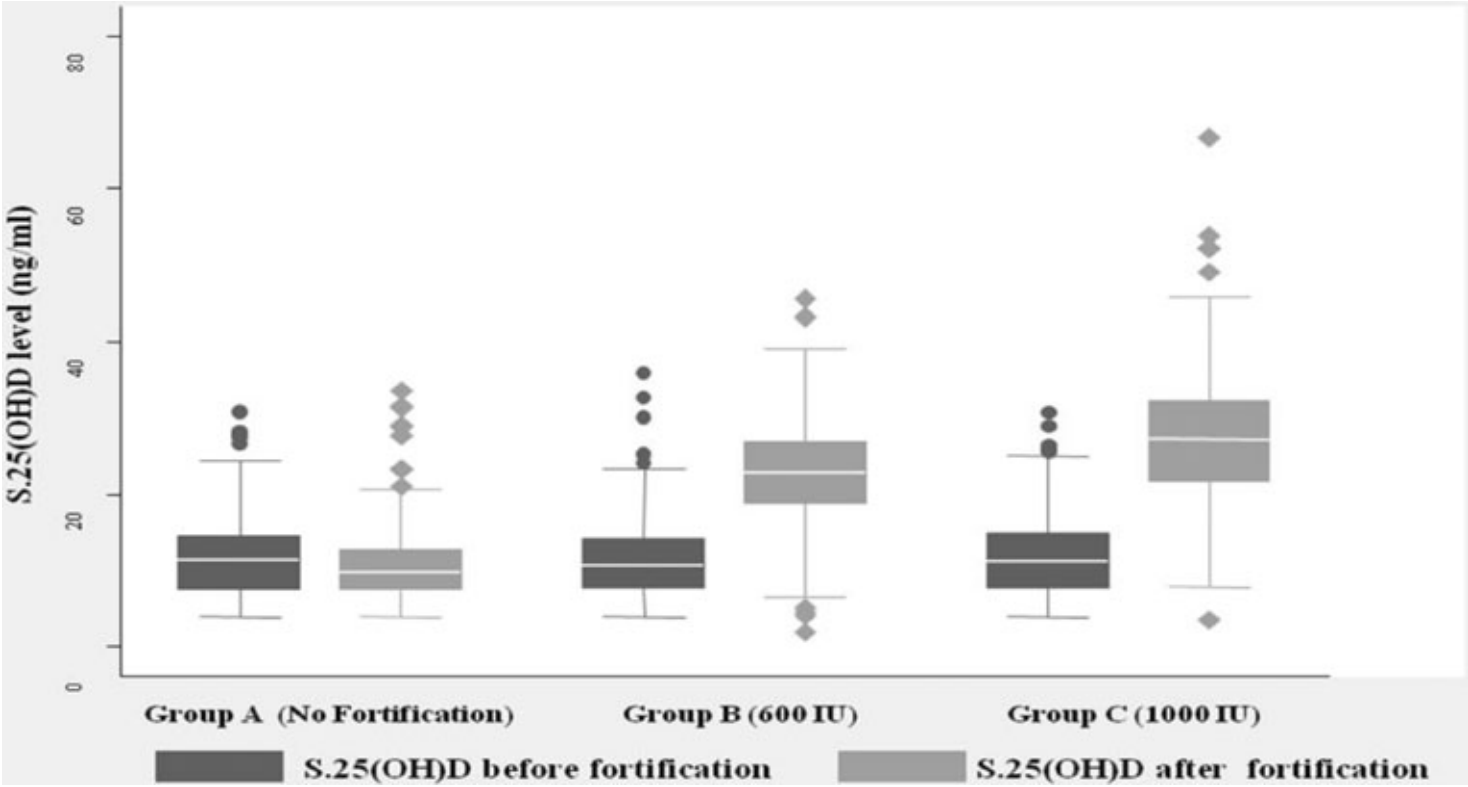
Use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 months of age

Effect of fortified milk on morbidity in young children in North India

	Intervention (n=316)	Control (n=317)	RR/ Odds ratio (95% CI)	P value
GI MORBIDITY				
Episodes of diarrhoea:	1408	1700	0.82 (0.73-0.93)	0.002
Days of diarrhoea	3277	4010	0.81* (0.77-0.85)	0.00
RESPIRATORY MORBIDITY				
Episodes of acute respiratory illness	195 71	262	0.74 (0.57-0.97)	0.03
Severe episodes of ALRI	79	110	0.72 (0.49-1.05)	0.09
Febrile illness and others	530	621	0.85* (0.76-0.95)	0.006
Days with high fever	2899	3099	0.93* (0.88-0.98)	0.005
Measles	1	8	0.12 (0.02-0.99)	0.05
Antibiotic consumed (doses)	7166	7437	0.96* (0.92-0.99)	0.01

Sazawal et al; bmj.39035.482396.55, 2006, * Odds ratios

Impact of vitamin D fortified milk - healthy school children aged 10–14 years



Group A Control (n = 237) received 200 ml of unfortified milk per day. Group B (n = 243) and group C (n = 233) received 200 ml of milk fortified with 600 IU (15 µg) and 1,000 IU (25 µg) of vitamin D per day for 12 weeks.

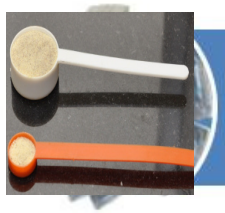
Khadgawat *et al Osteoporos Int* 2013; 24(8):2335-43

Scale-up of the translatable technologies and integrating into the National programme

National Iron +

Iron fortified iodized salt

Wheat and rice flour fortification



Fortification with multiple micronutrient powder

Dietary diversification strategies

PLATFORMS

SERVICE DELIVERY

Food

Security

National Rural Health Mission

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MONITORING PLA

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B. in regulation 2.4.1, for sub-regulation 2 relating to Fortified atta, the following shall be substituted, namely:
"2. Fortified atta means the product obtained by adding one or more of the following nutrients to atta, namely:

S. No	Nutrient	Level of fortification per Kg of atta (*Not more than*)
1.	**Calcium-** Calcium carbonate, Calcium chloride, Calcium citrate, Calcium phosphate monobasic, Calcium phosphate dibasic, Calcium phosphate tribasic;	1500mg
2.	**Iron-** (a) Ferrous citrate, Ferrous lactate, Ferrous sulphate, Ferric pyrophosphate, electrolytic iron, ferrous fumarate; (b) Sodium Iron (III) Ethylene Diamine tetra Acetate, Trihydrate (Sodium Feredetate- Na Fe EDTA)	60mg 25mg
3.	**Zinc-**Zinc Sulphate	30mg
4.	**Vitamin A-** Retinyl acetate, Retinylpalmitate, Retinylpropionate;	1500 µg RE
5.	**Ascorbic Acid (Vitamin C)** – Ascorbic acid, sodium ascorbate, calcium ascorbate, ascorbyl- 6-palmitate;	100 mg
6.	**Thiamine (Vitamin B1)** – Thiamine hydrochloride, Thiamine mononitrate;	3.5mg
7.	**Riboflavin (Vitamin B2)** – Riboflavin, Riboflavin 5'-Phosphate sodium;	4.0mg
8.	**Niacin** – Nicotinamide, nicotinic acid;	45mg
9.	**Pyridoxine (Vitamin B6)** – Pyridoxine hydrochloride;	5.0mg
10.	**Folic acid-** Folic acid;	250µg
11.	**Vitamin B12-** Cyanocobalamine, hydroxycobalamin;	2.5µg
12	**Vitamin D-** Cholecalciferol, Ergocalciferol	1000 IU

Note: It shall be free from any extraneous matter including rodent hair and excreta.";

12th Five year Plan Goals 2013-2017

Reproductive, Maternal & Child Health and Nutrition

To achieve the overall goal of preventing and reduction of underweight children under 3 to less than 23% and anemia among women aged 15-49 years to 28% by the end of the plan period.

The priority areas in nutrition include

1. Inclusion of multi-stakeholders strategies including community participation to maximize nutritional benefits from locally available foods, food fortification, micronutrient supplementation.

2. The three important public health interventions (i) national iron + initiative NRHM (ii) Universal use of iodine and iron fortified salt and (iii) vitamin A supplementation for children aged 6 to 59 months

3. Improve iron bioavailability from Indian diet and micronutrient status

The Challenges

- Policy : Efforts to create a policy environment for making compulsory fortification a national agenda,
- Integrating into the National nutrition programmes National iron + initiative etc
- Setting standards- RDA of micronutrients as standards or choosing a level that will prevent clinical signs or reduce inadequacy of specific biomarkers.
- Selecting the best combinations of micronutrients that will reduce anaemia and improve functional outcomes
- Partnership with Industry to –Scale up the translatable technologies
- How to engage unorganized sector + addressing the financial implications, including start-up costs and premix procurement.

The Challenges

- How to mitigate stakeholders reluctance to change- Behavioral Change Communication
- Shelf life and Packaging for fortified rice (stored rice)
- Capacity building in inspection and enforcement (training of inspectors, establishing a regional reference laboratory, -spot tests etc.)
- Effective Monitoring - require careful consideration of the effect of other fortified foods and supplements without exposing the population to levels above UL.

THANK YOU