Combating micronutrient deficiencies during early childhood in low income countries: supplementation vs. fortification vs. food-based interventions

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Outline

- Prevalence of MN deficiencies
- Adverse health consequences
- Etiology of MN deficiencies
- Interventions to combat MN deficiencies with examples
  - Supplementation
  - Fortification
  - Dietary diversification & modification
  - Biofortification
- Barriers to the success of each micronutrient intervention
- Conclusions

Prevalence of micronutrient deficiencies by region

Region	Vitamin A (%)[a]	Insufficient iodine intake (%)[b]	Anemia (%)[c]	Zinc (%)[d]
Africa	49	43	46	71
Southeast Asia	69	48	57	68
Americas	20	25	19	46
Europe	N/A	32	10	8

[a] Proportion with clinical eye signs &/or serum retinol <0.70 μmol/L in children < 5 y

[b] Proportion with urinary iodine <100 μg/L

[c] Proportion with low hemoglobin

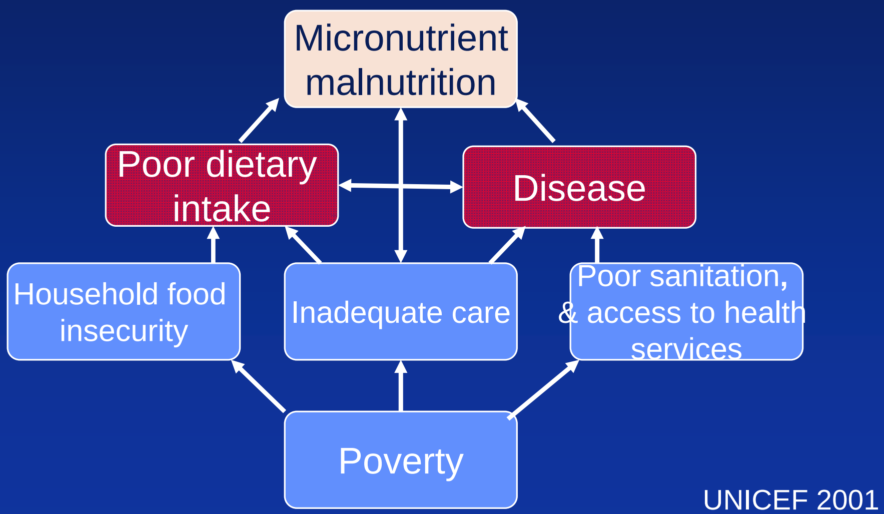
[d] Risk of inadequate intake: food balance sheet data adjusted for phytate : Zn ratio.

From Allen et al (2006) & IZiNCG (2004)

Adverse health effects of micronutrient deficiencies

Function affected	Iron	Zinc	Iodine	Vit A	Vit B-12
Anaemia	+++	0	0	+	+++
Decreased resistance to infections	++	+++	0	+	+
Intra-uterine malnutrition	+	++		0	+
Impaired growth	+	+++	+++	+	0
Reduced activity	+++	++	-	0	0
Lower work capacity & endurance	+++	0	0	0	0
Impaired cognition	+++	++	+++	0	+

Etiology of micronutrient malnutrition in infants and young children



UNICEF 2001

Reasons for poor dietary intake during early childhood

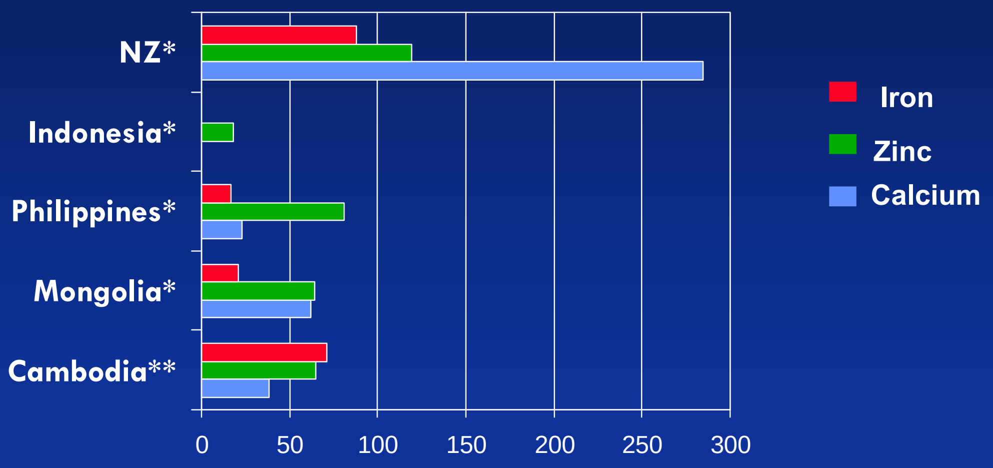
Deficits in quantity

- **Limited gastric capacity**
- **Poor child feeding practices**
- **Anorexia**

Deficits in quality

- **Mainly plant based**
- **Low content & bioavailability of MNs**
- **Low % of energy from animal source foods**
- **Low dry matter content**

Are intakes of micronutrients from CFs meeting the WHO estimated needs?



*Infants 9 - 11 mos **Young children aged 12 - 23 mos

Interventions to combat micronutrient deficiencies in childhood

- Supplementation
  - single micronutrients
- Food Fortification
  - Targeted: e.g. complementary foods
  - National
- Dietary diversification and modification (DDM)
- Biofortification

Supplementation during early childhood

- Single micronutrient supplements for prevention
  - Vitamin A capsules for children 6-59 mos
  - Fe supplements for infants
- Single micronutrients for treatment
  - Fe supplements for anemia
  - Iodine supplements for goitre
  - Vitamin D supplements for rickets
  - Zn supplements for diarrhea treatment
- No national supplementation programs for multi-micronutrients in LICs to date

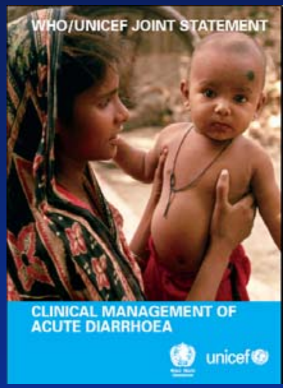
How effective are supplementation programmes for preventing micronutrient deficiencies?

Iron supplements from 6 to 12 mos	Iron deficiency anemia Hb < 110 g/L + serum ferritin < 12 µg/L	16%
Vitamin A capsules from 6 to 59 mos	Vitamin A deficiency Serum retinol< 0.7 µmol/L	33%
Vitamin D supplements from 1 to 35 mos of age	Vitamin D deficiency Serum 25 OHD < 25 nmol/L	61%
No Zn supplements for prevention or treatment	Zinc deficiency Serum Zn < 9.9 µmol/L	74%

Study of Mongolian children aged 6 to 36 mos

Zinc supplementation in treatment of diarrhea

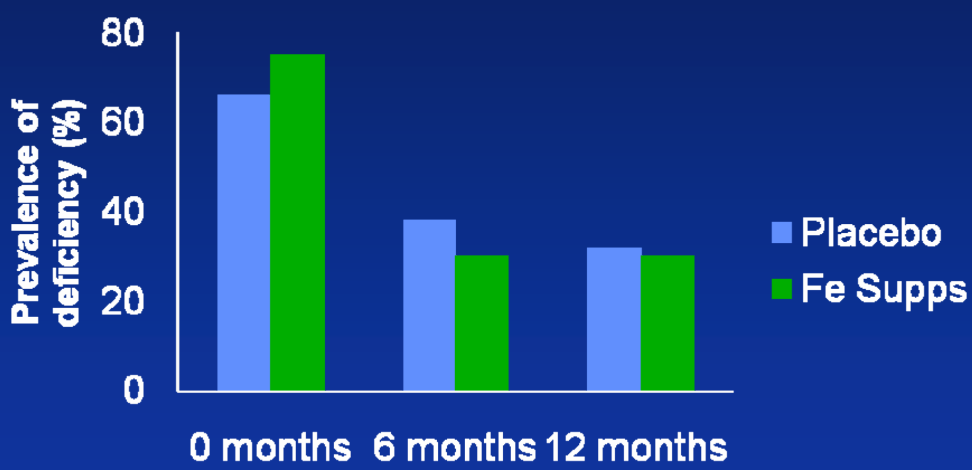
- WHO/UNICEF joint statement for zinc in the treatment of diarrhea:
- Twice age-specific RDA/day (10-20 mg) for 10-14 day distributed with ORS



Ranked 1st investment (with VAC) by 2008 Copenhagen Consensus for prevention of undernutrition in children < 2y

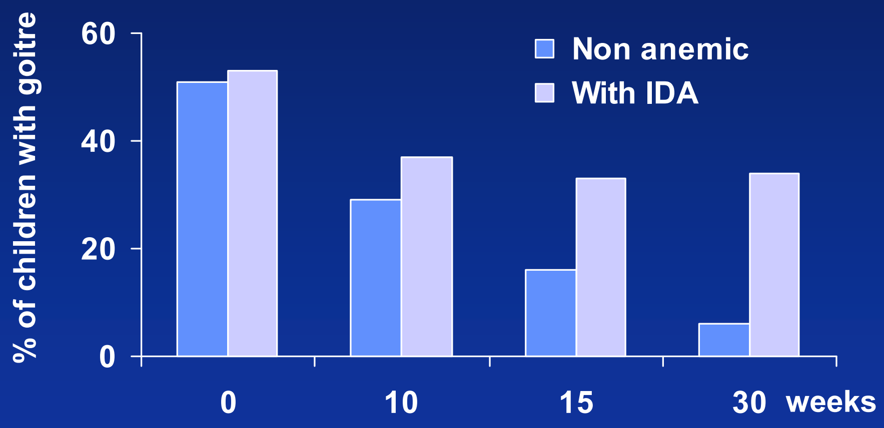
But few countries initiated programmes at scale because of problems with supply & delivery

Persistent anemia (%) in Mexican preschoolers despite iron supplements



From Allen et al. (2000)

Efficacy of iodine supplement on goitre in children with & without iron deficiency anemia



From Zimmermann et al.(2000)

Effect of setting on response to Fe + Folic acid with or without Zn

- Non malarial area in Nepal (n=25,490)
- Cluster-double blind RCT: 1-36 mo
- No diff in mortality with Fe+FA +/-Zn vs. placebo
- Fe + FA +/-Zn might protect against diarrhea, dysentery, ARI

Tielsch et al. (2006)

- Malaria area in Zanzibar (n=24,076)
- Cluster-double blind RCT: 1-36 mo
- Higher risk to die or need of treatment in hospital in Fe + FA +/- Zn vs. placebo (diff=12%, 95th CI 2-23)

Sazawal et al. (2006)

Supplementation: barriers to success

- Assured supplies, delivery, compliance
- Need social marketing & community mobilization for high coverage
- Formulation & optimal doses for young children not always known
- Variable responses with:
  - Baseline MN status
  - Setting
  - Age
- Safety: issue for settings with high rates of infection
  - Iron supplements and malaria

Food fortification

Targeted fortification for complementary foods

- Centrally processed fortified complementary foods
- Home-based fortification
  - fortified spreads; micronutrient powders or crushable tablets

National fortification

- Maize or wheat flour : Fe, Zn, B-vitamins
- Condiments
  - Salt: iodine
  - Sugar: vitamin A; Oil or margarine: vitamin A
  - Seasoning powder; Fish sauce: iron

Note : Fortification levels for national programmes are *NOT* designed to meet the high needs of infants & young children

Examples of targeted fortification for infants and young children

- centrally processed fortified porridge
- Fortified lipid-based spread: energy + EFAs
- Sprinkles: micronutrient powders in serving size sachets

Does fortification of centrally processed CFs work?

Mixed results

- Efficacy trials have shown that CFs fortified with Fe (+/-other MNs) can improve Fe status and motor development
- *But* Fortified cereal-based CFs in Latin American programmes have not consistently improved Fe status
- Cereal-based CFs fortified with zinc have NOT improved serum Zn: bioavailability issues?
- Fortified milk-based CFs *increased* morbidity in infants aged 4 mos in peri-urban slums, South Delhi !
- Only fortified *milk* has improved linear growth and reduced morbidity in one study of Indian toddlers

Choice of fortificant: experience with MN fortified, milk-based CF in Mexico

Four mos RCT on infants 4-12 mos

- Efficacy of milk-based CF ‘Nutrisano” fortified w. reduced Fe (+ other MNs) vs. supplementation w. MN syrup
- Iron deficiency sig. lower in syrup vs. Nutrisano (12.5 vs. 37.5%)
- No difference in anaemia prevalence in two groups

Stable isotope studies of Fe absorption from Nutrisano:

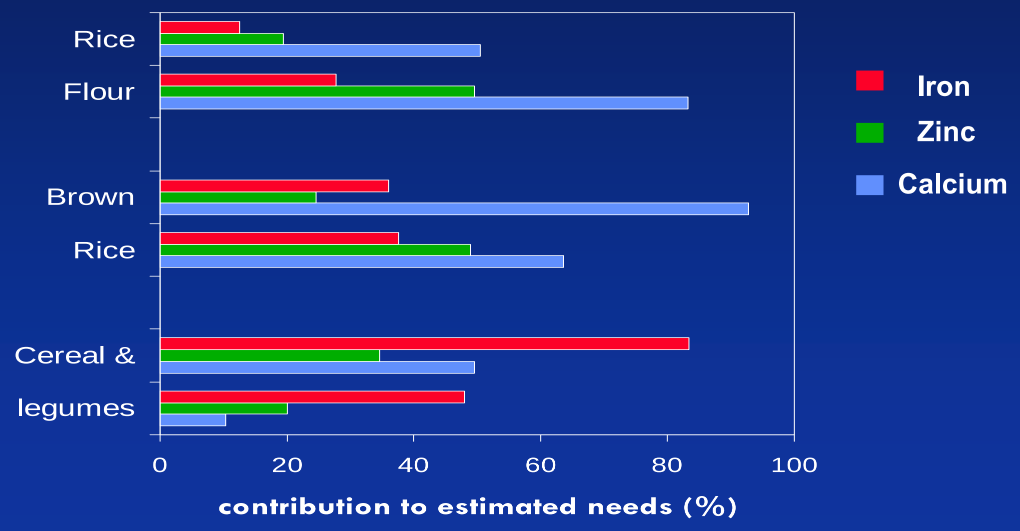
- Reduced Fe 1.4%; ferrous fumarate 2.4%; ferrous sulphate 7.9%

Organoleptic tests & acceptability by infants:

Fe fortificant changed from reduced iron to ferrous fumarate

Are fortificant levels for Fe, Zn, & Ca in centrally processed fortified CFs meeting the WHO needs?

Assuming 40g dry weight daily intake of complementary food



Does home-based fortification work?

Efficacy of Sprinkles (SP), Nutritabs (NR) & lipid-based spread (LBS) for 6 mo on Ghanaian infants aged 6 mos

Iron status

- Sig lower prevalence of anemia & ID in all 3 grps vs. NI
- **Zinc status**
- No sig diff in plasma Zn or % w. low values between 3 grps & NI

Growth

- Only LBS affected growth: greater weight and length gain

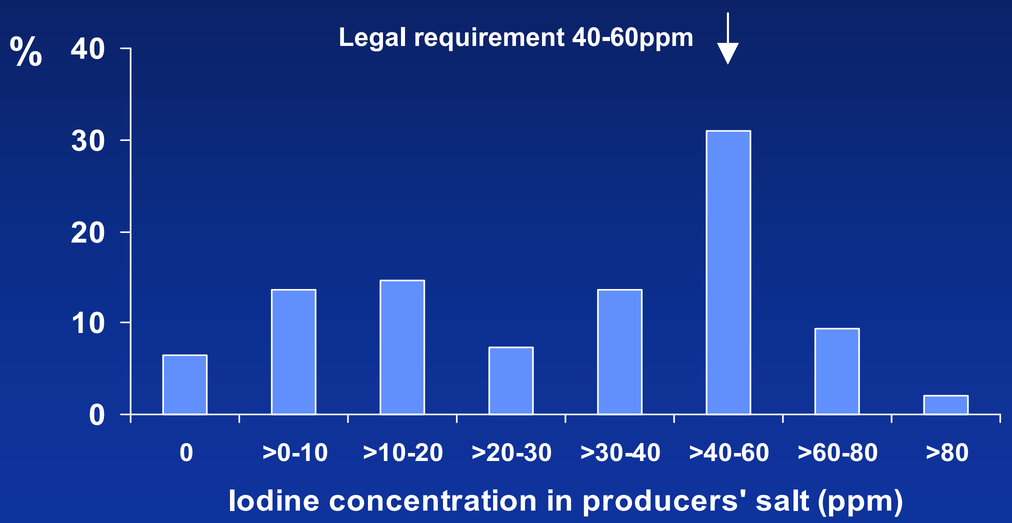
Other outcomes

- More walked independently in all 3 grps at 12 mos vs. NI
- No sig diff in morbidity across groups

NI: Non intervention

Adu-Afarwuah et al. (2007; 2008)

On-going quality assurance: Relative distribution of iodine concentration in table salt at production level in South Africa



From Jooste (2003)

Fortification: barriers to success

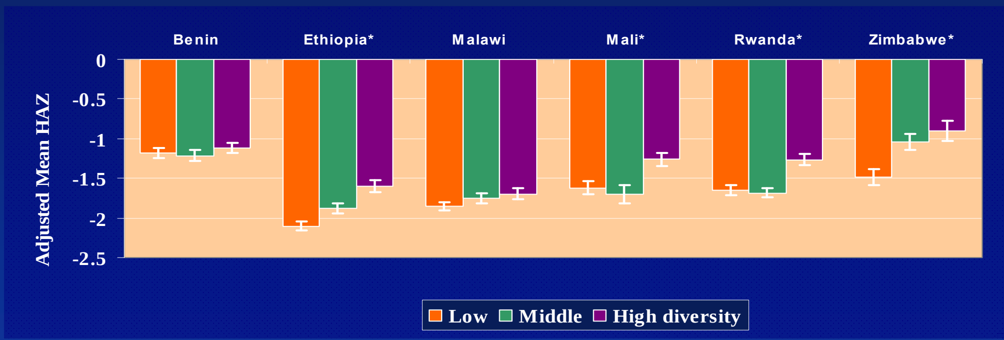
- Chemical form of fortificant; optimal levels; sensory properties
- Choice of food vehicles — cereal-based CFs often high in phytate
- Creating consumer demand among poor families:
  education; social marketing
- Quality assurance: at level of production & point of purchase
- On-going coordination, regulation, enforcement & monitoring by Governments
- Clear policy support & advocacy for resources for fortified CFs by government
- Build human resource capacity

Dietary diversification and modification (DDM)

Changes in food production and food selection patterns, as well as traditional household methods for preparing and processing indigenous foods

Overall goal to enhance availability, access, and utilization of foods with high content and bioavailability of micronutrients

Why is DDM important?: Adjusted mean height-for-age Z-scores by diet diversity tercile in six African countries (DHS data)



Means adjusted for child age, maternal height and BMI, # children < 5 y, and 2 wealth/welfare factor scores

Arimond & Ruel (2004)

Advantages of dietary diversification and modification

- Designed to be sustainable
- Culturally acceptable and safe
- Community-based
  - ability to empower community to help themselves
- Prevent concurrent micronutrient deficiencies
- Limited risk of antagonistic interactions
- Enhance MN status of entire household & across generations
- Minimal inputs once behavior change achieved

Dietary diversification and modification strategies

1. Increase dry matter content of porridges
2. Increase intakes of absorption enhancers
3. Reduce intakes of absorption inhibitors
4. Increase production & consumption of animal-source foods
5. Promote exclusive breastfeeding to 6 mos
6. Promote safe & appropriate complementary foods at 6 mos + breastfeeding to $\geq$ 2 y

Note: All require *effective* behavior change strategies and community participation

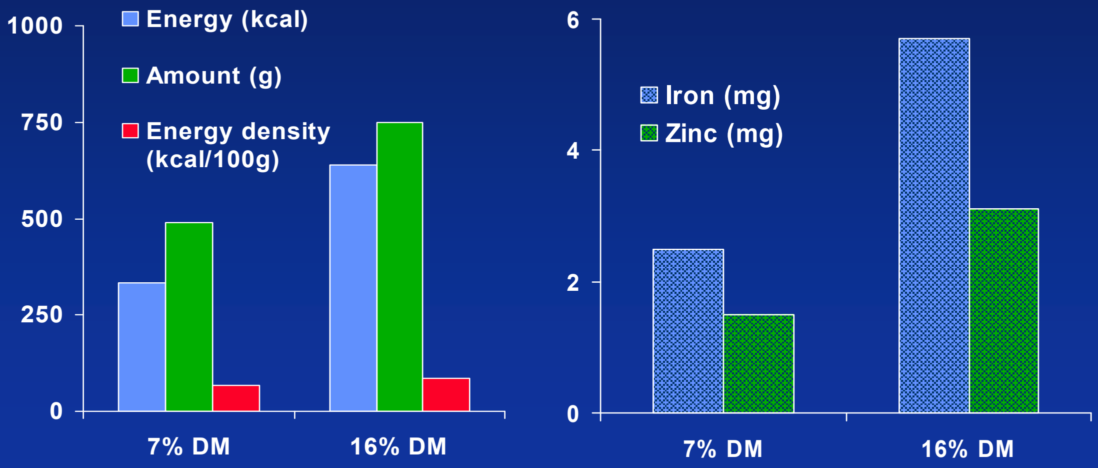
Experiences with dietary diversification & modification in rural Malawi: two case studies

- Infants and toddlers aged 6-23 mos
  - three intervention villages; one control village
- Children aged 36-84 mos; median 48 mos
  - two intervention villages; two control villages

- Quasi-experimental designs with non-equivalent control group

1. Increase dry matter (DM) content:

Energy, Fe & Zn intakes of Malawian infants fed 7% & 16% (DM) maize porridges

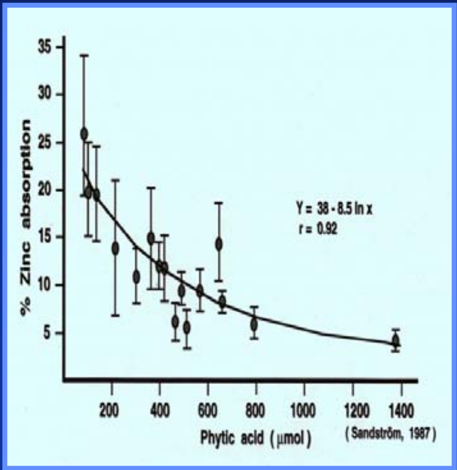


2. Increase intakes of absorption enhancers

- **Protein, especially meat & fish**
  - Enhance absorption of non-haem Fe & Zn by forming soluble ligands
  - Effect on non-haem Fe highest for beef>lamb>pork>liver>chicken>fish
- **Ascorbic acid: enhances non-haem Fe absorption**
  - Forms iron-ascorbate chelate: prevents formation of complex with phytate or tannin
  - Magnitude of effect depends on: level of vit C; meal composition; larger effect for meals containing Fe inhibitors
  - *BUT* a positive effect on iron status in *community* studies not shown
- **Organic acids from fermented foods**
  - May facilitate absorption of non-haem Fe & Zn, although impact on Fe absorption less than vit C
- **Dietary fat**
  - Facilitate absorption of fat-soluble vitamins & carotenoids

3. Reduce intake of absorption inhibitors

Inhibitory effect of phytate on Zn absorption



From Sandberg & Sandström (1992)

Household strategies to reduce phytate content

- Soaking cereal flours

  Passive diffusion of water-soluble phytate
- Fermentation of porridges

  Phytate hydrolysis via microbial phytase
- Addition of germinated cereal flours (ARF)

  Phytate hydrolysis via endogenous phytase

4. Increase production & consumption of ASFs: Supply of meat per capita (kg/y)

Country/continent	All meat (kg/y per person)*
Asia	26
Africa	38
China	55
Latin America + Caribbean	59
European Union	92
New Zealand	110
Australia	118
United States	124

* Includes poultry and fish

FAO Food Balance Sheet Data 2003: Note supply is always higher than actual intake

Dietary intakes by tercile of % energy from animal products: Guatemalan infants 9-11mos

	Lower	Middle	Upper	Needs
AFS % energy	2	15	40	
Ca (mg)	56	84	245*	356
Fe (mg)	1.51	1.89	2.12*	10.8
Zn (mg)	0.54	0.52	0.89	2.3
Vit A (µg RE)	145	215	340	42-165
Riboflavin (mg)	0.08	0.16	0.41*	0.2
Niacin (mg)	1.18	1.35	1.54	4

* Adapted from Brown et al. (2002)

Additional reasons why animal source foods should be included in diets of infants & toddlers?

- Improve growth: weight, MUAC, head circumference[3]
- Improve cognitive performance
- Trend for a higher behaviour index & positive association with psychomotor development
- Rich source of readily absorbable Fe & Zn, vit A (liver), plus other micronutrients: B-12, niacin; B-2 (dairy)
- Meat: Enhancer of nonhaem iron & zinc absorption

Morgan et al. (2004); Grillenberger et al. (2003); Krebs et al. (2006); Neumann et al. (2007); Engelmann et al. (1998); Hallberg et al. (2003); Lönnderdal. (2000).

Efficacy of animal source foods on child development in Kenyan school children

- 3 snacks given to 554 Kenyan children in 12 schools for 2 y:
- **Energy**: 250 kcal from githeri (maize and beans) + oil
- **Meat**: 250 kcal from githeri + 60-80 g beef
- **Milk**: 250 kcal from githeri + cup of milk
- No intervention: (goat given after study)

Meat snack improved:

cognitive performance

physical activity

initiative and leadership behaviors

school test scores

Milk snack improved:

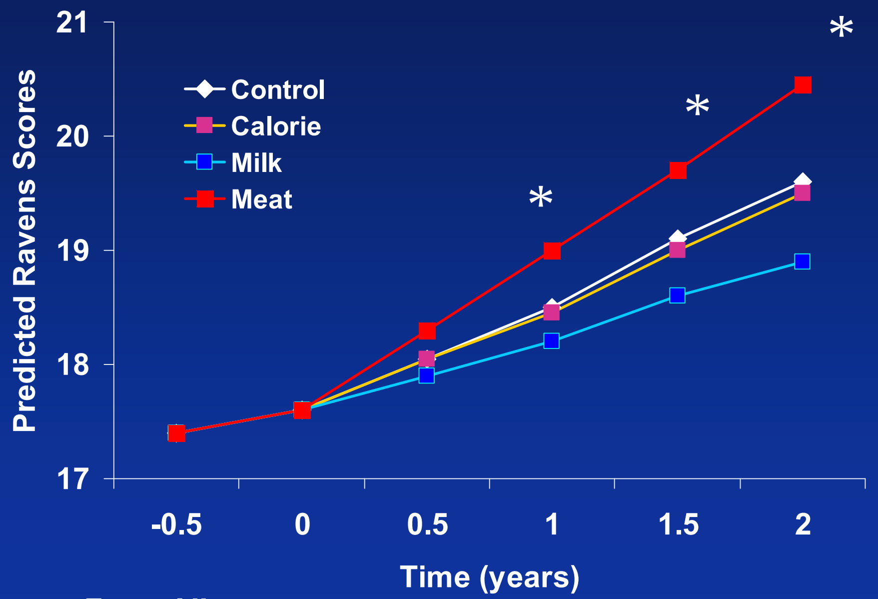
linear growth of stunted children

Milk & meat improved:

biochemical vitamin B-12 status

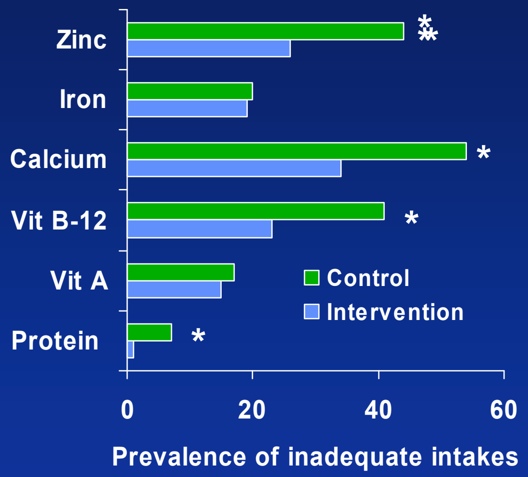
From Allen et al.

Ravens scores over time for four groups of Kenyan school children



From Allen, pers.com

Efficacy of DDM strategies on Malawian children



Impact on outcomes

Intervention vs. controls had:

- Lower prevalence of inadequate intakes*
- More diverse diets which were of higher quality*
- Lower prevalence of anemia (62 vs. 80%)*
- Lower morbidity*
- Greater muscle mass*
- But: No effect on growth

* P<0.05

From Yeudall et al. (2002, 2007)

Dietary diversification & modification: barriers to success

- Conduct of efficacy trials expensive; difficult to double-blind
- Need longer time to show change
- Require effective behavior change & communication
- Inclusion of animal source foods essential but they are expensive: may not be accessible to poor
- Difficult to meet MN needs during infancy: limited gastric capacity so may need to include fortificants as well
- Designs often too weak to provide convincing evidence
- Often fail to include monitoring & evaluation

↑ Production ≠ ↑ Consumption ≠ ↑ Nutrition

<Food -----Care------Health>

Integrated programmes: World Vision Malawi MICAH

Public health interventions
- Nutrition & health education
- Water & sanitation
- Control of common illnesses
- Control of parasitic infections
- Promotion of exclusive breast feeding

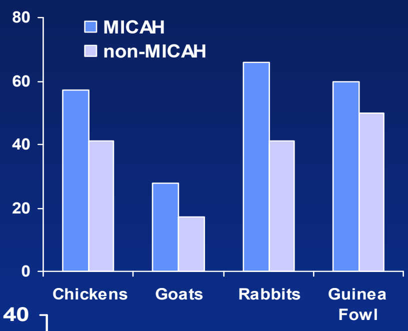
Vit A & Fe supplements

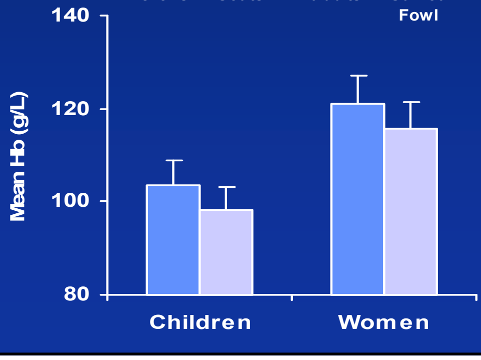
Dietary diversification

Small-animal revolving fund: goats, chickens, guinea fowl; rabbits

MICAH HHs vs. comparison group

↑ : small animal husbandry
↑ : % HHs eating ASFs
↑ : mean Hb in children & women
↓: (modest) in stunting





From AA Kalimbira

In the future: Biofortification

More accessible to HHs who consume staple foods from local or self-production

- **Soil (Zn, I, Se) or foliar fertilizers (Fe)**
  - ↑ grain MN content
- **Plant-breeding**
  - ↑ Zn & Fe in cereals
  - ↑ ß-carotene in sweet potatoes, maize, cassava
- **Genetic modification**
  - ↑ ß-carotene in rice, cassava, banana
  - ↓ phytic content & increase Fe & Zn

NB: Nutrient density not sufficient for diets of infants & toddlers

Taste tests to determine taste & appearance preferences of sweet potatoes by Mozambique consumers Lowe et al. (2007)

Conclusions

- Mixed responses to supplementation & fortification
  - Need to optimize form, level, & combination of MNs
  - Need to increase coverage of supplements
  - Need to strengthen quality control of fortified foods
- DDM can be successful if animal-source foods are included & BCC is effective
- Design of DDM studies need to be improved
  - duration should be increased
  - monitoring & evaluation must be included
- DDM should be integrated with care & health components to enhance effectiveness
  - Nut education; Immunization; MCH; antenatal health care etc

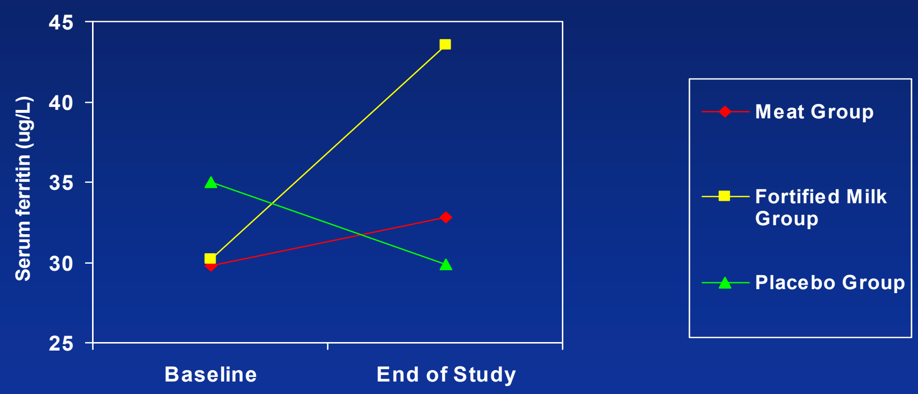
What is the prevalence of micronutrient deficiencies in early childhood?

	Bangladesh	Mongolia	Indonesia	Cambodia	NZ[a]
Anaemia	49%	24%	66%	71%	-
Iron deficiency anaemia	-	16%	30%	21%	10%
Zinc deficiency	57%	74%	17%	73%	7%
Vitamin A deficiency	-	33%	54%	28%	-

New Zealand Toddler Food Study

- 1 in 3 NZ toddlers has suboptimal iron status
- Iron stores ↓ during the second year of life
- Both ↑ red meat intake and using an iron-fortified milk prevent this ↓ in iron stores
- Iron-fortified milk increases iron stores in 12-20 month old NZ children

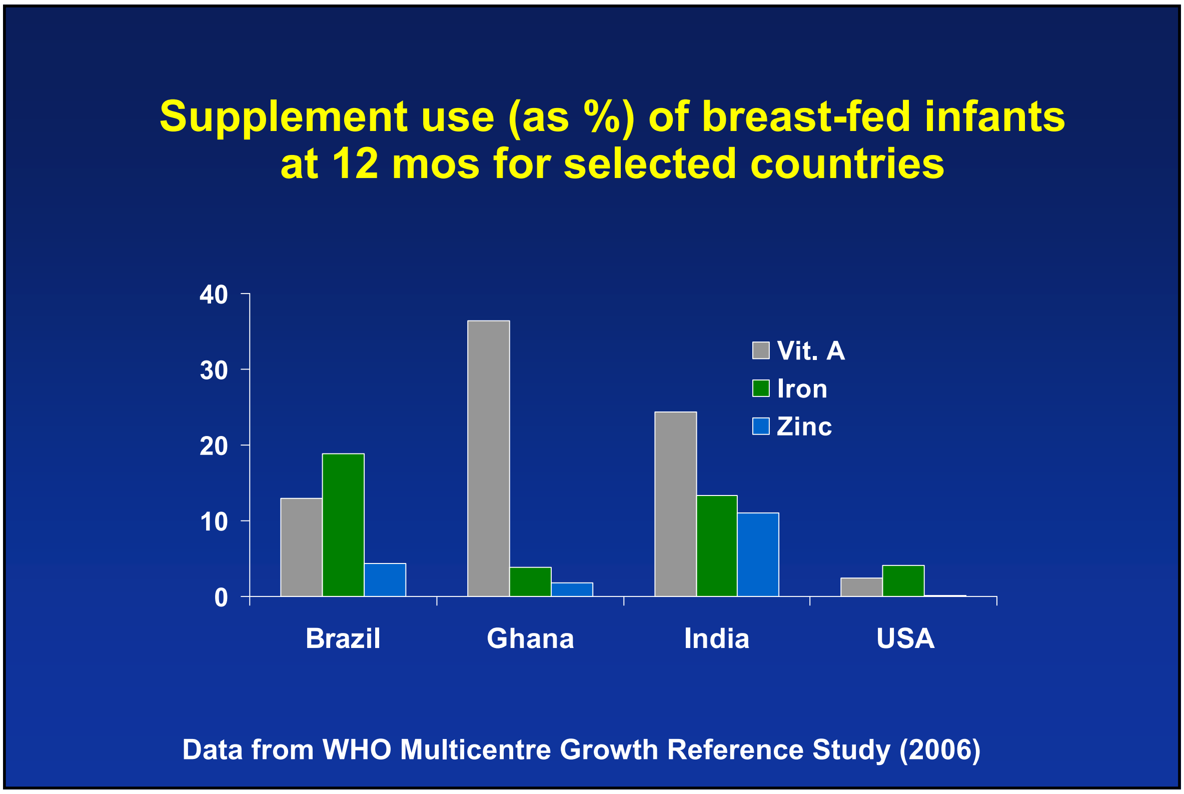
Changes in serum ferritin over 20 weeks in NZ Toddler Food Study



Adjusted for age, sex, age x sex, infection, education, income, ethnicity
a Significant change from baseline P=0.002
b Significant change compared to Placebo Group P<0.05

Examples of successful community-based studies: *integration* of DDM with care & health

Country	Target	Interventions	Outcomes
China (rural)	Infants 4-12 mos Intervention vs control	Nutrition & health education Counseling visits to: ↑ breast-feeding; used thick rice + egg yolk daily; hygiene	↑ intake nutrient-dense foods; ↑ breast-feeding ↓ Anemia ↓ Stunting & wasting
Bangladesh, Cambodia, Nepal, (HKI)	Mothers & children < 5 y HKI HHs vs controls	Home gardens; fish ponds; milking cow Health & nutrition education targeting mothers	↑ Production MN-rich foods ↑ % eating ASFs ↓ Anemia & night blindness
Peru Government	Infants: from birth to 18 mos Intervention vs control	Nutrition & health education to: ↑ feeding behaviour ↑ quality CFs: thick purees + chicken liver, eggs, or fish at each meal	↑ Intake of ASFs ↑ Energy, Fe, Zn intakes ↓ Stunting No change in morbidity


Supplement use (as %) of breast-fed infants
at 12 mos for selected countries
40
30
20
10
0
Vit. A
Iron
Zinc
Brazil
Ghana
India
USA
Data from WHO Multicentre Growth Reference Study (2006)