Catherine McAuley (1778-1841)

RSS

Catherine McAuley (1778-1841)

Born to upper middle class Irish family
By 1798 & aged 20 y: parents had died
1803: became manager & companion to Callaghans
1822: Callaghans died & Catherine inherited their fortune
1824: Catherine built house for women & children, later named House of Mercy
1831: Sisters of Mercy was founded as official religious order
1841: Catherine died of TB
1831 onwards: Sisters of Mercy proliferated in Ireland and later overseas, including New Zealand
Sisters of Mercy remain dedicated to responding to the needs of the poor

RSS

United Nations Millennium Development Goals

1. Reduction of poverty and hunger
   (Measured by rate of restricted growth in children < 5 y)
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat malaria, HIV/AIDS, and other diseases
7. Ensure environmental sustainability
8. Develop a global partnership for development

RSS

Zinc deficiency: etiology, health consequences, and future solutions

Rosalind S Gibson
Research Professor
Department of Human Nutrition,
University of Otago, Dunedin, New Zealand
Member of International Zn Nutrition Consultative Group

RSG

Outline

- Etiology of zinc deficiency
- Adverse health consequences: the evidence
- How to identify population groups at risk
- Future solutions to reduce the risk of zinc deficiency
- How can Zn interventions help achieve MDGs?
- Next steps for mainstreaming Zn in public health programs

RSG

Prevalence of micronutrient deficiencies by region

Region	Vitamin A (%)[a]	Iodine (%)[b]	Anemia (%)[c]	Zinc? (%)[d]
Africa	49	43	46	
SE Asia	69	48	57	
Americas	20	25	19	
Europe	N/A	32	10	

[a] Proportion with clinical eye signs &/or low serum retinol in children <5y
[b] Proportion with low urinary iodine
[c] Proportion with low hemoglobin values From Allen et al (2006)

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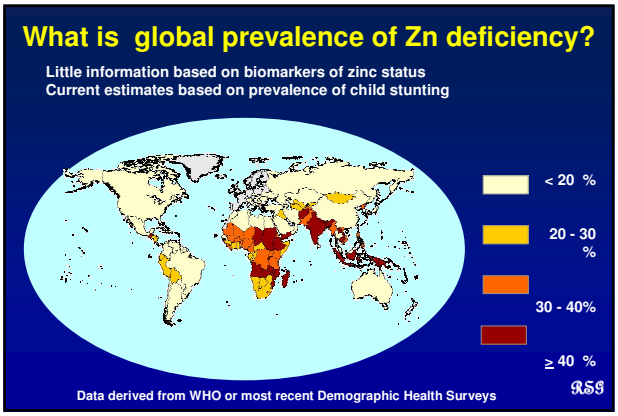
First cases of human Zn deficiency in 1960's in Middle East
•Male adolescent dwarfs
Clinical features
•Stunting
•Little or no secondary sexual development
Diet
•Unleavened wheat bread
•Low intake of flesh foods
•Practiced geophagia
RSS


WHO Global burden of disease – disability adjusted life years (2000)
Illicit drugs
Occupational risk factors for injury
Vitamin A deficiency
Zinc deficiency
Iron deficiency
High cholesterol
Alcohol
High blood pressure
Underweight
0
40000
80000
120000
160000
From Ezzati et al.(2002)
RSS


What is global prevalence of Zn deficiency?
Little information based on biomarkers of zinc status
Current estimates based on prevalence of child stunting
< 20 %
20 - 30 %
30 - 40%
≥ 40 %
Data derived from WHO or most recent Demographic Health Surveys
RSS

What are the functions of zinc?

- > 300 enzymes require Zn for function or regulation
- Biosynthesis of nucleic acids, amino acids, proteins, including specific hormones
  - –insulin; adrenal corticosteroids; testosterone
- Growth
- Immune function
- Vitamin A metabolism: night vision
- Reproduction
- Neuro-behavioural function

RSS

What is the etiology of zinc deficiency?

- Inadequate dietary intakes
- High physiological requirements
- Excessive losses
- Combination of factors

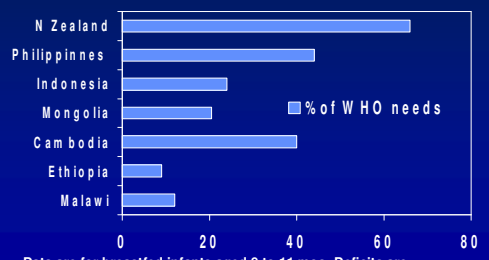
RSS

What are the factors associated with inadequate intakes of Zn?

- Low zinc intakes
  - –complementary foods in LICs low in energy & Zn
  - –diets based on roots & tubers: cassava, sweet potatoes, sago, enset
  - –diets low in cellular animal foods: rich sources of Zn
- Poor bioavailability of zinc
- Environmental factors

RSS

Zinc intakes for breast fed infants from complementary foods compared to WHO estimated needs (as %)



Data are for breastfed infants aged 9 to 11 mos: Deficits are comparable for those aged 6 to 8 and 12 to 23 mos

RSS

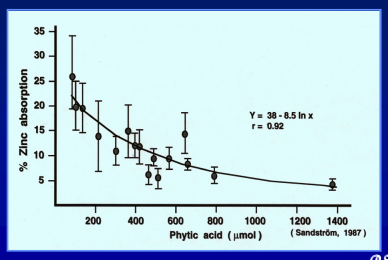
What are the factors associated with inadequate intakes of Zn?

- Low zinc intakes
- Poor bioavailability of zinc:
  - diets based on unrefined cereals & legumes
    - » high in phytate: potent inhibitor of Zn absorption
  - diets low in cellular animal foods
    - » meat, fish, poultry: rich sources of absorbable zinc
- Environmental factors

RSS

Effect of phytate content of diets on Zn absorption in adults

- Phy:Zn molar ratios are used to estimate bioavailability of dietary zinc
- Phy:Zn molar ratios > 18 indicate very low bioavailability of Zn in diets



RSS

Comparison of daily intakes of zinc & phytate by diet type for Ethiopian women

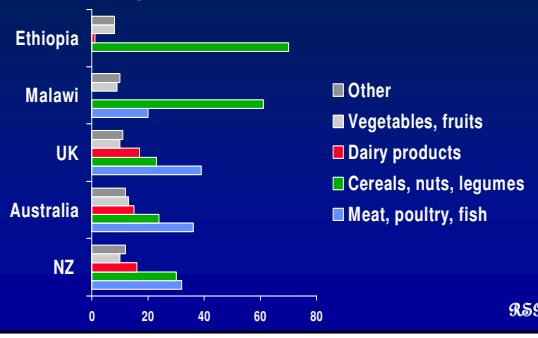
Variable	Maize	Enset
Flesh foods (g)	0	0
Zn mg (mg)	6.3	3.7*
Phytate (mg)	1356	446*
Phy:Zn molar ratio	21	11*

Enset (*Enset ventriosum*)

* $p<0.05$

RSS

Food sources of zinc (as %) in diets of women from Ethiopia, Malawi, UK, Australia & NZ



RSS

What are the factors associated with inadequate intakes of Zn?

- Low zinc intakes
- Poor bioavailability of zinc
- Environmental factors
  - Soils with a low Zn content:
    - » Egypt , Iran, Turkey, Pakistan, NE Thailand
  - Staples grown on low zinc soils will have a low zinc content

RSS

Comparison of Zn levels in soils and rice in three regions of Thailand

Region	Soil Zn (µg/g)	Rice Zn (µg/g)
Central	1.35	77.0
South	1.7	31.9
N East	0.8	20.1

Diets of NE Thai school children

- 8% energy from animal-source foods
- 51% energy from rice grown on low Zn soils
- Zn intakes below requirements

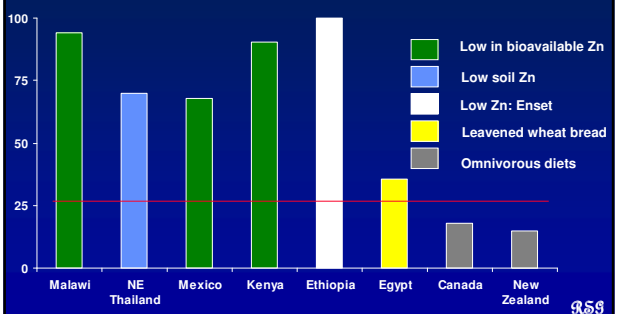
Biochemical Zn status

- 54% had low serum Zn values indicative of Zn deficiency

From Katyal and Vlek (1985)

RSS

Prevalence of inadequate intakes of Zn in children and pregnant women (as %)



RSS

What is the etiology of zinc deficiency?

- Inadequate dietary intakes
- High physiological requirements
  - Low birth weight infants (reduced liver Zn reserve)
  - Malnourished infants: catch up growth
  - Infancy, childhood, adolescence: high growth rates
  - Pregnancy, lactation
- Excessive losses etc
- Combination of factors

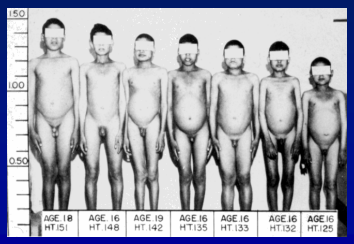
RSS

LBW preterm male infant with acro-orificial dermatitis from severe Zn deficiency

- Fed mother's milk with a very low [Zn]
- Mother had a genetic defect of mammary gland
- +ve response with Zn supplements

RSS

Severe Zn deficiency in adolescence

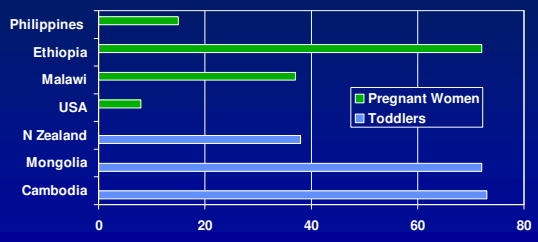


- Impaired linear growth
- Delayed sexual development

Zinc deficient Egyptian dwarfs. From Prasad et al. (1963)

RSS

Prevalence (%) of low serum zinc values among toddlers and pregnant women



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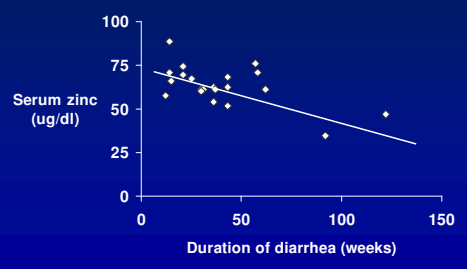
What is the etiology of zinc deficiency?

- Excessive losses
  - Diarrhea during infancy and childhood
  - Abnormal intestinal permeability
    - » chronic infections
- Additional factors
  - Geophagia
  - Hypochlorhydria : Elderly
  - Disease states:
    - » Cystic fibrosis; celiac disease

RSS

Regression plot of serum zinc vs duration of diarrhea



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What are the adverse health consequences of Zn deficiency?

- Impaired growth: MDG # 1
  - Poor linear growth; poor weight gain
- Impaired immune competence: MDG # 4 & 6?
  - Increased morbidity : diarrhoea; ALRI; malaria?
  - Increased mortality
- Adverse pregnancy outcomes: MDG # 5
  - Preterm birth
  - Maternal labour & delivery complications?

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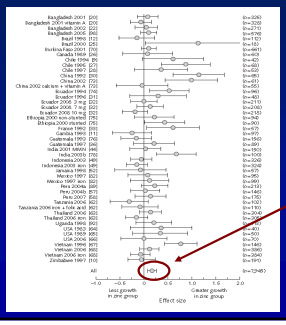
What is the evidence for these adverse health consequences of Zn deficiency?

RSS

Effect of zinc supplementation on children's linear growth (n = 47 comparisons; 7,945 children)



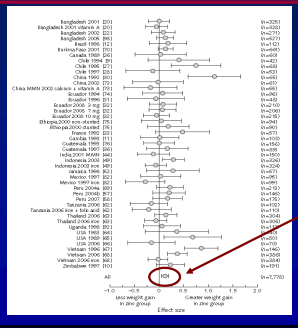
Small but significant increase in linear growth

Mean effect size = 0.17

(CI = 0.08, 0.26), p=0.001

RSS

Effect of zinc supplementation on children's weight gain (n = 45 comparisons; 7,778 children)



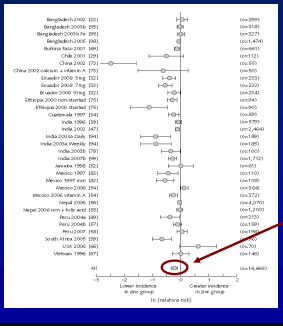
Zinc supplementation produced a significant increase in weight gain

Mean effect size = 0.12

(CI = 0.05, 0.19), p=0.002

RSS

Effect of zinc supplementation on diarrhea incidence (n = 33 comparisons; 16,665 children)



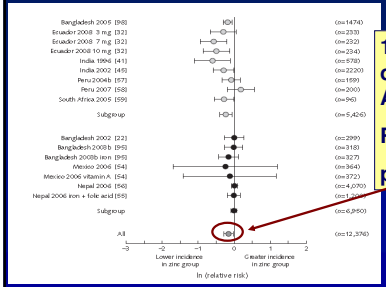
20% reduction in overall diarrhea incidence

RR = 0.80 (0.61,0.87)
p=0.0004

27% reduction for children ≥ 12 mos

RSS

Effect of zinc supplementation on incidence of acute lower respiratory infections (ALRI) (n = 16 comparisons; 12.376 children)



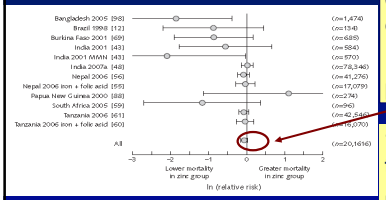
15% reduction in overall incidence of ALRI

RR =0.85 (0.75, 0.97)

p=0.017

RSS

Effect of zinc supplementation on child mortality (n = 13 comparisons; 201,616 children)



6% reduction in overall child mortality

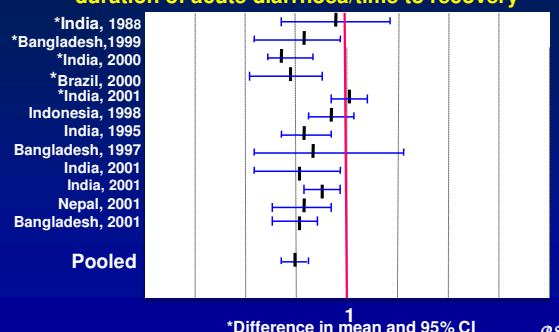
RR = 0.94 (0.86, 1.01)
p=0.11

18% reduction for those ≥ 12 mos

No effect in those less than 12 mos

RSS

Therapeutic effect of zinc supplementation on duration of acute diarrhoea/time to recovery



*Difference in mean and 95% CI
Relative Hazards and 95% CI

RSS

Effect of Zn supplementation during pregnancy

Meta-analysis of 13 Zn supplementation studies

- Overall: 14% reduction in preterm births
- Women with BMI< 18.5 & low Zn intakes:
  - Positive effect on birth weight?
- Maternal labor & delivery complications: variable
- Postnatal growth & risk of infection: inconsistent

Consider supplemental Zn in high risk areas
- Stunting < 5 yr > 20%; maternal BMI < 18.5

IZiNCG Recommended dose: 20 mg Zn/d

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Effect of Zn supplementation on malaria, HIV/AIDS, and other diseases

Preventive effect

- Malaria: only 3 RCTs
  - Zn may reduce incidence of malaria, especially more severe cases resulting in clinic attendance
- HIV-positive children
  - Zn may reduce diarrhea & pneumonia in HIV-positive children: often complicate HIV infections

Therapeutic effect

- Malaria or pneumonia: Insufficient evidence
- Tuberculosis: no studies to date

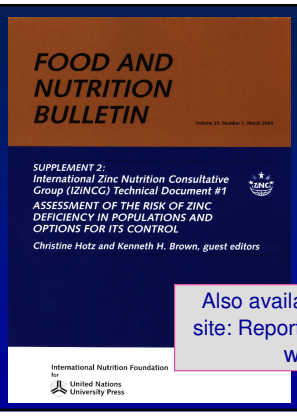
From Haider & Bhutta (2009)

RSS

Why is it taking so long for LICs to have national policies for reducing risk of Zn deficiency?

- Lack of information on prevalence of Zn deficiency
  - Difficult to identify Zn deficiency: Type 2 nutrient
  - No unique clinical symptoms: poor growth; wasting
- Lack of understanding on importance of Zn deficiency
- Lack of guidance by UN agencies on need to control Zn deficiency
- Lack of funds by donor agencies

RSS



How can we identify risk of Zn deficiency in populations?

Also available on the IZiNCG web site: Report on Zn status indicators: www.izincg.org

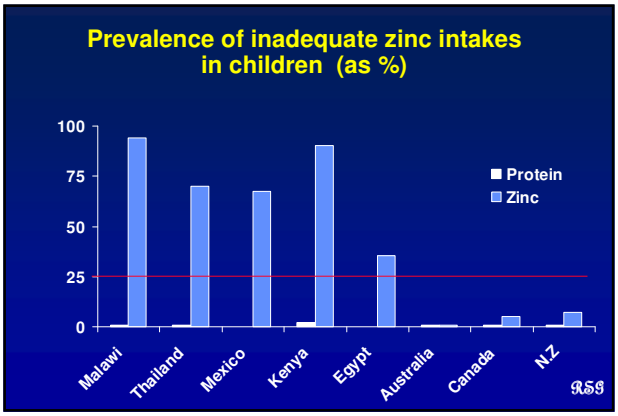
RSS

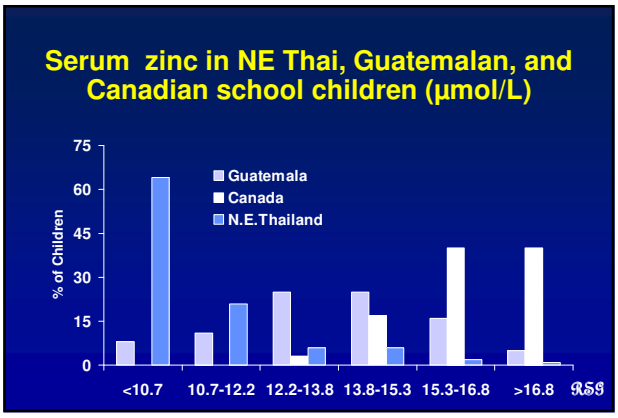
How can we identify risk of zinc deficiency in populations?

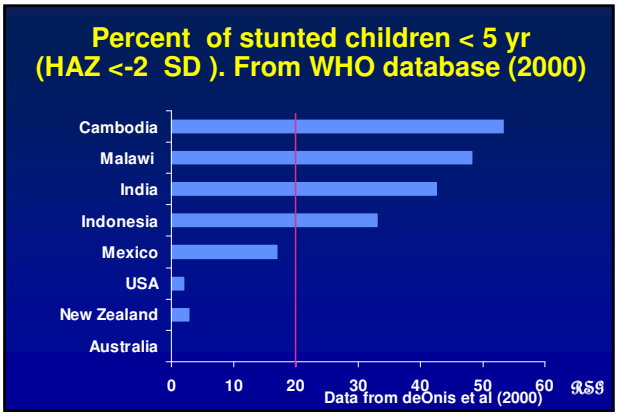
1. **Dietary indicator**
   Percent with Zn intakes below Estimated Average Requirement (EAR)
   High risk: public health concern > 25%
2. **Biochemical indicator**
   Percent with low serum Zn concentrations
   High risk: public health concern > 20%
3. **Functional indicator**
   Percent of children < 5 y with HAZ score < - 2.0 SD
   High risk: public health concern > 20%

From WHO/UNICEF/IAEA/IZiNCG (2007)

RSS


Prevalence of inadequate zinc intakes in children (as %)
100
75
50
25
0
Protein
Zinc
Malawi
Thailand
Mexico
Kenya
Egypt
Australia
Canada
N.Z


Serum zinc in NE Thai, Guatemalan, and Canadian school children (µmol/L)
% of Children
75
60
45
30
15
0
Guatemala
Canada
N.E.Thailand
<10.7
10.7-12.2
12.2-13.8
13.8-15.3
15.3-16.8
>16.8


Percent of stunted children < 5 yr (HAZ <-2 SD). From WHO database (2000)
Cambodia
Malawi
India
Indonesia
Mexico
USA
New Zealand
Australia
0
10
20
30
40
50
60
Data from deOnis et al (2000)

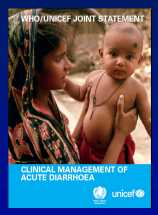
Interventions to reduce risk of Zn deficiency

- Supplementation
  - Therapeutic: diarrhea: only ~6 countries
  - Preventive : no programmes to date
    - Potential target groups: infants; toddlers pregnant & lactating women
- Food fortification
- Dietary diversification and modification

RSS

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 Copenhagan Consensus for prevention of undernutrition in children < 5y

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Impact of preventive Zn supplementation in children

- Increased growth and weight gain
- Reduced incidence of diarrhea
- Reduced incidence of ALRI
- Decreased death rate

IZiNCG Recommended dose for Zn:
7 mos- 36 mos: 5 mg Zn/d,
> 3 yr : 10 mg Zn/d

•BUT: Preventive Zn supplementation in children is not yet practiced in any low income countries

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Experience with preventive Zn supplementation: RCTs

- Canada: School boys with low height percentiles
- Guatemala: School children
- Chile: Pre-school children*
- Chile: Infants w. birth weight > 2300g*
- S Ethiopia: Planned: Pregnant women

* Former PhD student

RSS

Interventions to reduce risk of Zn deficiency

- Supplementation
- Food Fortification
  - Mass: cereal staples
  - Targeted: infant foods; school meals
    - Commercially processed
    - Household level
- Dietary diversification and modification

RSS

Experience with targeted food fortification: RCTs

- Malawi: MN fortified therapeutic complementary food (CF) for malnourished children in hospital
- NE Thailand: MN fortified seasoning powder on school children in 10 low SES schools
- Zambia: MN fortified locally-produced maize-based CF on infants: Serum Zn analysis
- Cambodia: Fortifying CFs with MN Sprinkles : Serum Zn to be analyzed

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Fortification of seasoning powder in Thailand: RCT

- Fortified with or without Zn (5 mg), Fe (5 mg), vit A (270 ug), & I (50 ug)
- Mixed in school lunch to 580 children from 10 schools for 31 wks

Results: Intervention vs. control

- Sig ↑ in hemoglobin (1ary outcome)
- Sig ↓ in biochemical Zn & I deficiencies
- Sig ↓ incidence of respiratory illnesses
- Sig ↓ symptoms of cough, runny nose, diarrhea
- Sig higher cognitive scores for short-term memory & attention
- No effect on growth

Interventions to reduce risk of Zn deficiency

- Supplementation
- Food Fortification
- Dietary diversification and modification (DDM)
  - Changes in food production, food selection, & traditional methods for preparing and processing indigenous foods

Experience with dietary diversification/modification in rural Malawi: two pilot studies

- Breast-fed children aged 6-23 mos
- Children aged 36-84 mos; median 48 mos
- Quasi-experimental designs with non-equivalent control groups

Dietary diversification & modification strategies used in Malawi

- Increase production & consumption of Zn-rich foods, especially cellular animal protein
- Reduce phytate via household processing
  - soaking; germination; fermentation
- Promote exclusive breastfeeding to 6 mos
- Promote safe & appropriate complementary foods at 6 mos + continued breastfeeding to ≥ 2 y

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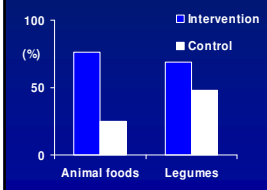
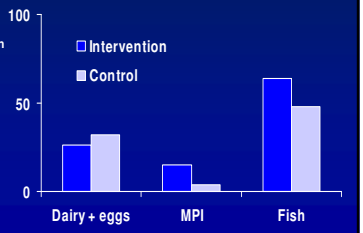
Increase consumption of Zn-rich foods

Malawi infants: Proportion consuming animal foods & legumes post-intervention



Malawi children: Intake of animal-source foods (g/day) post-intervention



MPI: meat, poultry, insects

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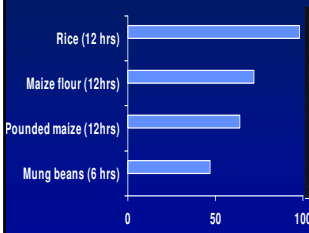
Reduce phytate via soaking



Pound maize
Mix 1 part maize with 4 parts water
Soak overnight
Dry in sun

Significant increase in Zn absorption w. LP maize with 60% loss of phytate

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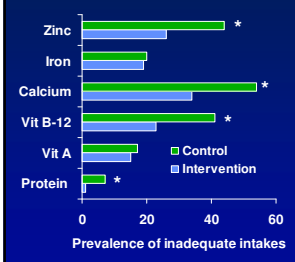
Efficacy of dietary strategies on Malawian children



Impact on other outcomes

Intervention vs. controls had:

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

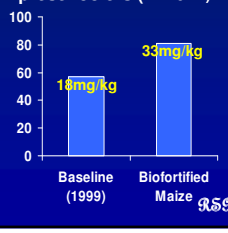
* P<0.05

From Yeudall et al. (2002, 2007)

Future: Biofortification of plant-based staples

- Zn fertilizers on low Zn soils
- Plant-breeding to increase:
  - Zn in rice; wheat; maize
- Genetic modification to:
  - to decrease grain phytate
  - to decrease phytate & increase Zn content of cereal staples

Simulated impact of biofortified maize on prevalence of *adequate* Zn intakes in Mexican preschoolers (n=1072)



How can Zn interventions help achieve MDGs?

- **MDG # 1: Reduce poverty & hunger:** Restricts growth
  - Improve linear growth & weight gain
- **MDG # 4: Reduce child mortality**
  - Reduce diarrhea ~ 20% & ALRI ~15%
  - Reduce child mortality for those ≥ 12 mos ~ 18%
- **MDG # 5: Reduce maternal mortality**
  - May reduce protracted labour
- **MDG # 6: combat malaria, HIV/AIDS**
  - May reduce severity of malaria
  - May reduce risk of diarrhea & pneumonia in HIV +ve children

More research needed

Galvanizing action: next steps for mainstreaming Zn in public health programs

- Collect information on population Zn status in LICs
- Mobilize interest in Zn nutrition
- Determine how best to deliver Zn interventions *within* existing Public Health programs eg:
  - Zn supplements in growth monitoring
  - Add Zn to Fe supplements for high risk pregnant women
  - Use appropriate levels of Zn in fortification
  - Use *effective* behaviour change with dietary interventions
- Scale up therapeutic Zn supplementation for diarrhea (only in ~6 LICs)

RSS

Acknowledgements

PG students: Canada, New Zealand, Norway, Thailand, Philippines

Collaborators:

Dr N Solomons: Guatemala
Dr P Heywood: Papua New Guinea
Dr B Mitimuni & Prof T Cullinan: Malawi
Dr P Winichagoon: Thailand
Dr S Jack: Servants & WHO: Cambodia
Drs L Lasonka & E Kafwemba: Zambia
Dr Y Abebe: Ethiopia
Dr Enkjargal: Mongolia
plus many other researchers & all the participants!

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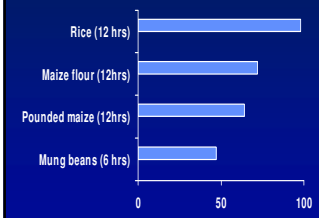
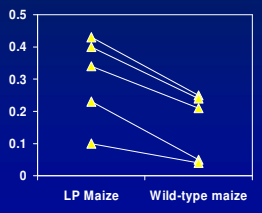
Reduce phytate via household processing

Loss of phytate via soaking



Fractional absorption of Zn in polenta



Significant increase in Zn absorption w. LP maize with 60% loss of phytate

RSS