AFRICAN NUTRITION GRADUATE STUDENTS NETWORK (AGSNet)
(Contributing together to better health and nutrition in Africa)

Report

of the Inaugural Conference of AGSNet

Held at

Beach Hotel – Good Leisure Gardens, Durban, South Africa

On

September 19, 2005

THEME:

NUTRITION AND INFECTION IN AFRICA

Compiled by

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Mohamed Ag Ayoya
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Folake Samuel

The conference was funded by

The United Nations University Food and Nutrition Program
International Nutrition Foundation/Kraft foods/Unilever
German Development Service (GTZ)
Cornell University, USA
Wageningen University, The Netherlands
University of Southampton, UK
Université Cheick Anta Diop, Senegal

Program for the AGSNet Inaugural Conference

Meeting facilitator: Joseph Mensah-Homiah (Ghana)

September 19, 2005

- 08:00am -8:30am: Session 1: Welcome and introduction Chair: Nkosinathi Mbuya (Zimbabwe)
  - ✓ Rationale and objectives of the meeting
- 08:30am - 10:30pm: Session 2: Business Session I Chair: Adama Diouf (Senegal)
- 10:30am - 10.45am : Tea break
- 10:45am – 12:30pm: Business Session II Chair: Susan Keino (Kenya)
- 12:30pm -1:00pm: Solidarity Messages (Kraft/UNU/GTZ) Chair: Richard Kajura (Uganda)
- 1:00pm – 2:00pm: Lunch
- 2:00pm – 3:00pm: Session 4: Keynote address By Dr. Wafaie Fawzi, Topic: Nutrition and Infections Chair: Mohamed Ag Ayoya (Mali)
  - ✓ 30 minutes talk
  - ✓ 30 minutes for discussions
- 3:00pm – 3:15pm: Tea break
- 3:15pm – 3:30pm INAUGURATION OF THE NETWORK (Tola Atinmo/Pauline Kuzwayo) Chair: Nkosinathi Mbuya (Zimbabwe)
- 3:00pm – 4:00pm: Group Session Chair: Arno (South Africa)
- 4:00pm – 5:00pm: Closing discussions
  - ✓ Future direction for the African graduate student network Chair: Reginald Annan (Ghana)
  - ✓ Election of the steering committee Chair: Nkosinathi Mbuya (Zimbabwe)

7:30pm Dinner /Closing Ceremony

- ✓ Presentation of the steering committee

PROCEEDINGS OF THE AGSNET INAUGURAL CONFERENCE

The meeting started around 9:00am. It was held at the Good Leisure Resort, Beach Hotel, Durban, South Africa, on the 19th of September, 2005.

1. Welcome and Introduction

This session was chaired by Nkosinathi Mbuya, Coordinator of the Network.

Joseph Mensah-Homiah, one of the three Co-ordination Team members from Cornell University warmly welcomed participants to the Conference. He introduced the other members of the Co-ordination Team, namely Nkosinathi Mbuya and Mohamed Ag Ayoya. He also introduced our advisors and other dignitaries present. They included Prof. Pauline Kuzwayo (South Africa), Mrs. Rosina Agble (Ghana), Mrs. Julia Tagwireyi (Zimbabwe), Dr. Robert Mwadime (Kenya, now in Uganda), Prof. Michael Latham (Cornell, USA), Dr. Godwin Ndossi (Tanzania), Dr. Romain Dossa (Benin), Dr. Abraham Todd (Kraft Foods, USA), Dr. Barbara Lyle (Kraft Foods, USA), Dr. Wafaie Fawzi (Harvard University, USA) – Speaker, Dr. Fre Pepping (Wageningen University, The Netherlands) and Dr. Frans Kok (Wageningen University, The Netherlands).

Following this, Nkosinathi Mbuya provided a brief background of the Network.

Business session I

This session was chaired by Adama Diouf (Senegal)

2. Objectives of the Network

The objectives of the Network were considered. It was pointed out that the word "sub-Saharan" should be deleted from the objective statement in view of the fact that the Network is for the whole of Africa.

3. The Activities of the Network

The house discussed the types of activities that AGSNet should be involved in. These include:

- Providing access to journals though websites such as AGORA and Enlink;
- Creating an e-group or discussion board for members of the Network to discuss issues of interest including the nutrition situation in Africa. This would be exclusively for members
- Sharing of information as regard to fellowships, job opportunities, short-term consultancies, conferences, scholarships, internships, etc.
- Sharing of issues on cutting-edge research
- Sharing of experiences from programmatic activities that may not be found in journals. The network should link up with networks or organized groups that are involved in such program information. Such linkages will assist in keeping the research agenda (of AGSNet members) relevant to the needs of Africa.

The first session broke up for a tea at 10:50am.

Business Session II

This session was chaired by Susan Keino (Kenya)

4. Membership

To guard against duplication of efforts of other nutrition societies in Africa, and to prevent pluralization of interests, it was decided that we should retain the name African Nutrition Graduates Students Network (AGSNet). This will provide a strict definition of the aim of the society, that is, to specifically address the needs of Graduate African students.

After extensive debate, the house agreed on the following categories of members;

i. Full membership
ii. Student Associate Membership
iii. Alumni Membership

iv. Associate Membership

4a. CRITERIA FOR MEMBERSHIP

Full membership

- Must be African
- Must be enrolled for graduate study in nutrition or nutrition related courses
- Must be willing to actively participate in the activities of the Network.

In view of this, it was decided that the Network should come up with indices of participation, which will be measurable.

Student Associate Membership

- Must be African
- Must be an undergraduate nutrition or nutrition related discipline
- Must be willing to actively participate in the activities of the Network.

Alumni Membership

- These are former members of AGSNet, who have concluded studies, but are still willing to actively participate as members of the Network.

Associate Membership

- Must have an interest in promoting good nutrition on the African Continent.
- Must either be a graduate student in any of the nutritional sciences or must have completed graduate studies in any of the nutritional sciences.
- Must be willing to actively participate in the activities of the Network.

Only Full Members have voting rights and can hold executive positions.

4b. Dues

The membership dues were decided upon, according to membership categories as follows:

- Full members ($25 per year)
- Student Associates ($5 per year)
- Alumni ($50 per year)
- Associate members ($50 per year)

It was also agreed that the dues should be paid by December 31 each year. The modalities for payment should be discussed with the regional representatives.

5. Governance

On issues of governance, that is. the administrative structure of the Network, the house decided that there will be a general assembly, which will be the highest decision making body. The General Assembly will meet every two years. The next meeting will take place in 2007, in Morocco to coincide with the Federation of African Nutrition Societies (FANUS) Conference.

There shall be a Coordination Team which will be from one institution or geographical area to facilitate effective communication and administration for a term of two years. The Coordination Team will be responsible for the day-to-day administration of the Network.

The Network's account is still lodged at Cornell University and administered by the University Accounting System hence there must be always one member of the Coordination Team from Cornell University who will serve as a signatory to the account even if the rest of the Coordinating team is based in another institution.

There will be regional representatives elected at the Biennial Conference who will be responsible to coordinating activities in the various regions.

For the next two years however, Cornell University will host the coordinating team. This is to allow the Network to stabilize at this teething stage of its existence.

6. KRAFT FOODS REPRESENTATIVES

Dr. Abraham Todd and Dr. Barbara Lyle, both representatives of Kraft Foods, the second largest food company in the world after Nestlé and the first in the USA addressed the house. Dr. Todd spoke on issues of leadership.

After the talk, the house broke up for a short lunch session.

7. Scientific Session: Chaired by Mohamed Ag Ayoya (Mali)

7a. Keynote Address

Dr. Wafaie Fawzi, gave the keynote lecture on Nutrition and Infections, after which the Network broke up into three groups for discussions on assigned topics. See Appendix for the slides of the presentation.

7b. Plenary Session

Plenary Session: Chaired by Arno Greyling (South Africa)
Sequel to the presentation, a plenary session on the discussions took place.
Members opted for one of the three groups for discussions. The theme for the group discussions were as follows:

Group 1:

Nutrition and HIV infection: it would be good to incorporate findings from research in Africa related to nutrition and HIV infection. These include findings related to the role of

micronutrient supplements among HIV infected individuals, and knowledge on infant feeding practices including the role of exclusive breastfeeding. General approaches to improving nutrition (nutrition education) and long-term strategies such as fortification are also needed.

How can we get such findings to be incorporated in nutrition practices?

Group 2:
Investment in Essential Health Research by governments - including operations research as well as other forms of research (observational studies and randomized trials) that can be piggy backed onto programs and provides solutions in the African context

How can we get African governments to invest in health research?

Group 3:
Too often nutrition is sidelined and the assumption is made that everyone can/will take care of it, but it ends up being neglected. A proposal is to incorporate nutrition into all MCH programs, and other public health programs at the district level. Consider introducing a cadre of nutrition officers at the district level to cater for such interventions.

How can nutrition be incorporated in all Maternal and Child Health (MCH) programs?

Feedback from Group discussions

Group 1: Incorporating Research findings into Nutrition Practice

- Research findings are available, for example.
  - Breastfeeding is linked to HIV infection
  - Micronutrient deficiency and HIV
  - Characteristics of HIV patients

- Infiltrate Governments and policy makers to get findings incorporated into Nutrition Practice
  - Education at all levels, using appropriate language at appropriate time
  - Simplify information
  - Advocacy information (direct message using PROFILES style)
  - Quantification of the effect of the problem
- Community based interventions
  - Guidelines
  - Include policy makers, community leaders
  - Use locally available materials as much as possible to get to the people
- Be proactive
  - Radio, journals, various publications such as local magazines
  - Target both women and men

Group 2: African governments to invest in health research?

- AGSNet members should invest time and efforts into quality research proposals
- Members should advocate in our various countries
- Representatives (e.g. associate members) in nutrition depts./units/ministries in all countries
- Improve associate members (bring in more membership)
- Advocacy messages using PROFILES style
- Publish in scientific journals and other sources such as media, communities, etc
- Collaborative research
- Funding from other sources for multi-country research
- Integrate nutrition into existing programmes
- Do simple things that have been shown to work
- Need a stronger voice

Group 3: Incorporating nutrition in all MCH programs?

- Components of MCH
  - Ante natal

  - Post natal
  - Growth monitoring, etc

Challenges

- Little elements of nutrition, no complete package
- Lack manpower and knowledge
- Lack of training and models
- Lack of appropriate and simple nutrition solutions

Solutions

- Empower women by focusing on MCH issues
- Develop generic aids
- Draw more support from all levels
- Influence action on matters at our various locations
- Develop simple and appropriate indicators
- Go to health facilities for help
- Help girls (from 15 yrs and above)
- Need for knowledge of members about PROFILES (organize a workshop at the next General meeting?)

8. Future Directions

Chaired by Reginald Annan (Ghana)

A number of issues were raised for the future directions of AGSNet among which are:

- Double our membership by 2007; every member is to bring at least a new member on board by 2007.
- Draw up a plan of specific activities and a time frame
- Member countries should organize educative programmes/activities
- The Network's website should be updated to include more information as outlined in our activity plans
- Members should resolve to "stand on their feet" ready to move forward

- Continue discussions via e-mail as regards the constitutions. A time frame of 6 months (May, 2006) was given to conclude the constitution.

9. Election of Regional Representatives

The Network has six (6) regions and officers were elected to the position of regional representatives

North Africa – Nada Benajiba

Central Africa – Demasse Mawamba F. Adelaide

West Africa – Adama Diouf

East Africa – Susan Keino

Southern Africa – Cornelie Nienaber

Europe – Reginald Annan

The conference ended at 6:45pm after which members proceeded for a Dinner.

10. Breakfast Meeting with representatives of the International Nutrition Foundation (INF) and Kraft Foods.

A breakfast meeting was organized by INF/Kraft Foods for the Travel Grant Fellows (Members who were sponsored by INF/Kraft Foods at the Royal Hotel, Durban, South Africa on Thursday, September 22, 2005. In view of the massive support given by INF/Kraft Foods to AGSNet for the organization of the Conference, all members present in Durban participated in the Breakfast session to interact with the representatives of INF and Kraft Foods.

The discussions centered on how Kraft Foods could push the agenda of improving nutrition on the continent further. The representatives of Kraft Foods primarily listened to ideas that members of AGSNet had to offer in improving nutrition.

Representatives of the International Nutrition Foundation present included Dr. Nevin Scrimshaw and Dr. Shibani Ghosh. Drs Lyle and Ruft represented Kraft Foods.

RESOLUTION OF THE INAUGURAL CONFERENCE OF THE AFRICAN NUTRITION GRADUATE STUDENTS NETWORK

We, graduate students studying nutrition and meeting here at Durban, South Africa, and discussing Nutrition and Infection in Africa declare forming a Network which shall be called the African Nutrition Graduate Students Network (AGSNet).

We acknowledge that we have a principal role to play in solving Africa's nutrition problems.

We resolve to stand up, network and contribute together in moving the agenda of solving Africa's nutrition problems forward.

We resolve to take our studies serious, conduct quality research that is relevant to the Continent and publish in good international journals.

We pledge to reach to other graduate students studying nutrition related courses so as to double our membership by 2007.

Members should organize educative programmes/activities, at least one, in their various countries.

We call on African Governments to incorporate Research findings into Nutrition Practice. We acknowledge that relevant research findings are available, such as Breastfeeding is linked to HIV infection; Micronutrient deficiency and HIV; Characteristics of HIV patients.

We encourage African governments to invest in health research.

AGSNet urges African Governments to incorporate nutrition in all Maternal and Child Health programs. We acknowledge the challenges of not having a complete nutrition

package, lack of nutrition manpower and knowledge in Africa, lack of training and models, and the lack of appropriate and simple nutrition solutions. We propose the empowering of women by focusing on MCH issues, the development of generic nutrition aids, and the development of simple and appropriate indicators.

Members of AGSNet resolve to contribute to reducing the incidence of infection and malnutrition by going to health facilities to support public health activities.

International agencies and organizations must consider African expertise for their expatriate job positions and internships.

African Nutrition Graduate Students in conjunction with experienced advisors are also prepared to take on short-term consultancies on the continent.

Members of AGSNet presently studying abroad pledge to come back to the continent and bring their expertise for African needs.

Appendix 1

In attendance:

a. Coordination Team

1. Nkosinathi Mbuya (Zimbabwe)
2. Mohamed Ag Ayoya (Mali)
3. Joseph Mensah-Homiah (Ghana)

b. Members

4. Adama Diouf (Senegal)
5. Khaly Mbodji (Senegal)
6. Aissatou Dioum (Senegal)
7. Aita Sarr Cisse (Senegal)
8. Amadou Lamine Gueye (Senegal)
9. Adekoya Adeniyi Samuel (Nigeria)
10. Folake Samuel (Nigeria)
11. Ohuruogu Victor U. (Nigeria)
12. Akoto Osei K. (Ghana)
13. George Amponsah Annor (Ghana)
14. Grace Achindiba Abbey (Ghana)
15. Joseph Ashong (Ghana)
16. Robert Ackatia-Armah (Ghana)
17. Frederick Kobina Ebo Grant (Ghana)
18. Nada Benajiba (Morocco)
19. Mitchikpe Comlan Evariste (Benin)
20. Nana Constance P. (Burkina Faso)
21. Dossa Romain A. (Benin)
22. Susan Keino (Kenya)
23. Lukwago Fred Brany (Uganda)
24. Richard Kajura (Uganda)
25. Ismael Ngrie Teta (Cameroon)
26. Demasse Mawamba F. Adelaide (Cameroon)
27. Jeanne Ejigui (Cameroon)
28. Nanama Simeon (Burkina Faso)
29. Joseph Mutuku (Kenya)
30. Jecinter Oketch (Kenya)
31. Constance Gewa (Kenya)
32. Arno Greyling (South Africa)
33. Lisa Davis (South Africa)
34. Rachelle Pretorius (South Africa)
35. Cornelie Nienaber (South Africa)
36. Reginald Annan (Ghana)
37. Joseph Waweru (Kenya)
38. Daisy Chasauka (Zimbabwe)
39. Kgomotso G. Moruisi (Botswana)

c. Advisors

40. Julia Taguireyi (Zimbabwe)
41. Pauline Kuzwayo (South Africa)
42. Rosanna Agble (Ghana)
43. Robert Mwademe (Tanzania)

Invited Guests

44. Michael Latham (USA/UK/Tanzania)
45. Abraham Todd (Kraft Foods, USA)
46. Barbara Lyle (Kraft Foods, USA)
47. Wafaie Fawzi (Harvard University, USA)
48. Fre Pepping (Wageningen University, The Netherlands)
49. Frans Kok (Wageningen University, The Netherlands)
50. Godwin N'Dossi (Tanzania)

Appendix 2

Presentation of Nutrition and Infection in Africa, by Prof. Wafaie Fawzi

Nutrition and Infection

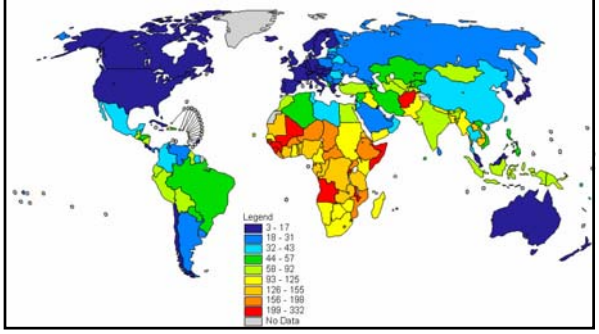
Wafaie Fawzi
Harvard School of Public Health

Inaugural Meeting of African Graduate Nutrition Students Network
Durban, South Africa
September 19, 2005

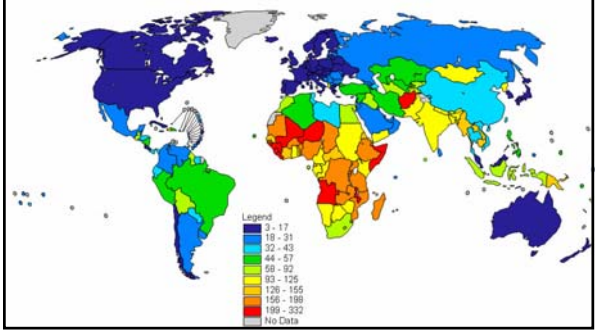
Overview

- Infections and Malnutrition in Africa
- HIV Infection
- TB
- Malaria
- Childhood Infections
- Paradoxical Effects of Micronutrients
- Concluding Remarks

Probability of Dying (per 1000) under 5 years of age, males 1998



Probability of Dying (per 1000) under 5 years of age, males 1999



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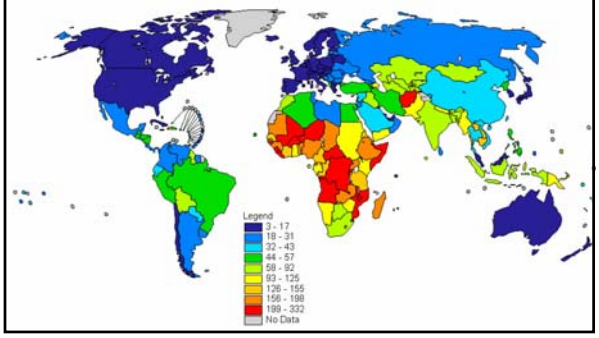
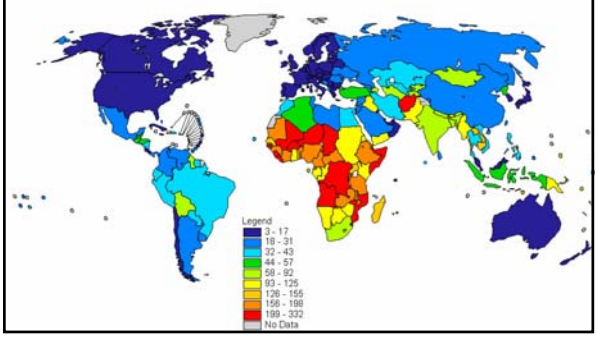
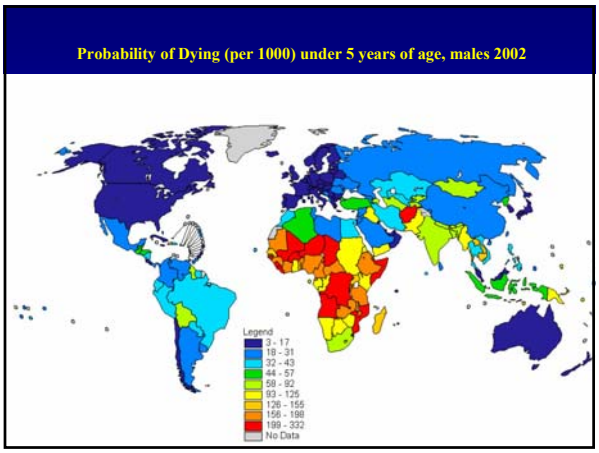


Probability of Dying (per 1000) under 5 years of age, males 2001




Probability of Dying (per 1000) under 5 years of age, males 2002
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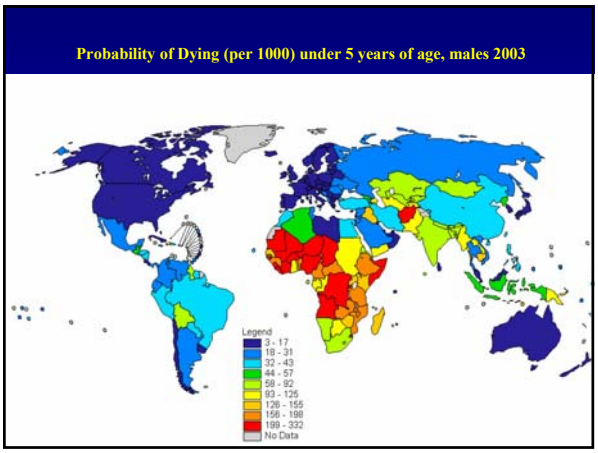
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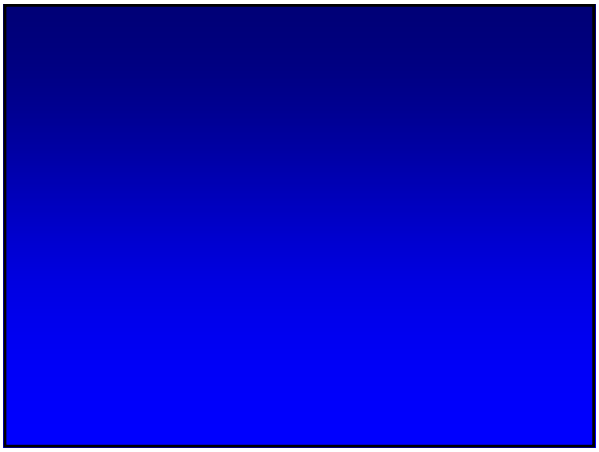

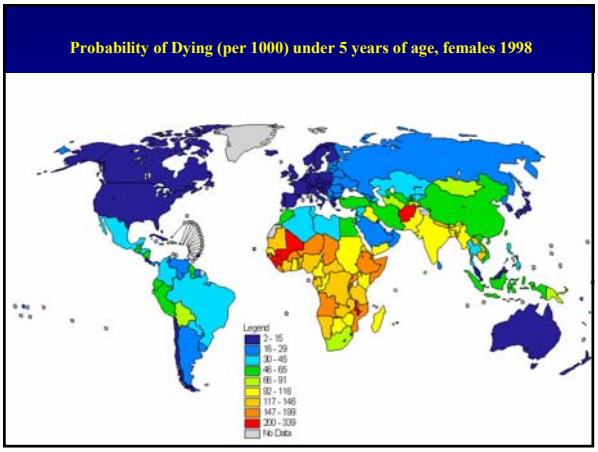
Probability of Dying (per 1000) under 5 years of age, females 1998
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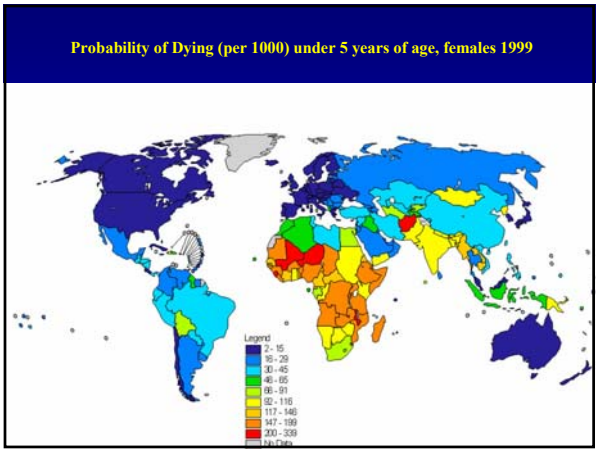
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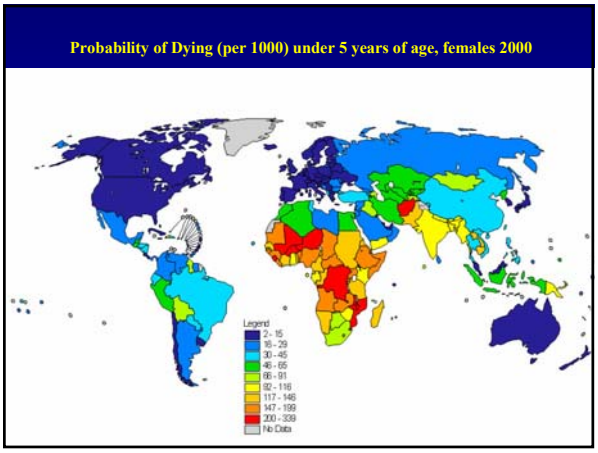
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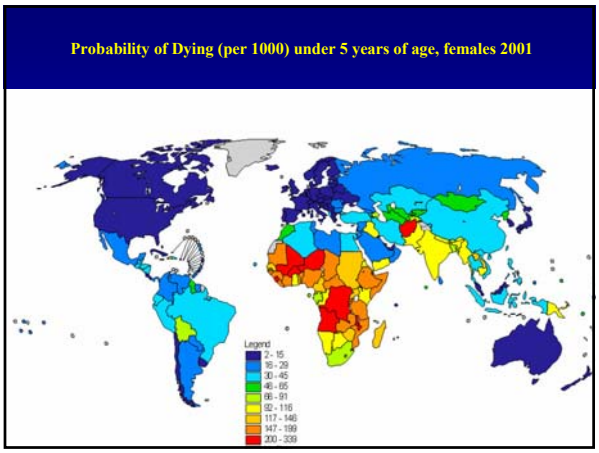
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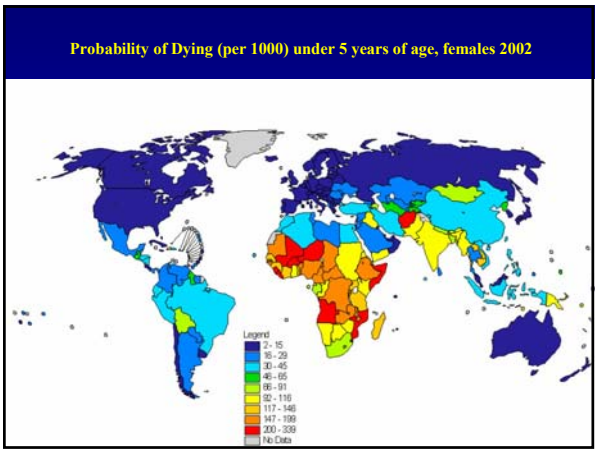
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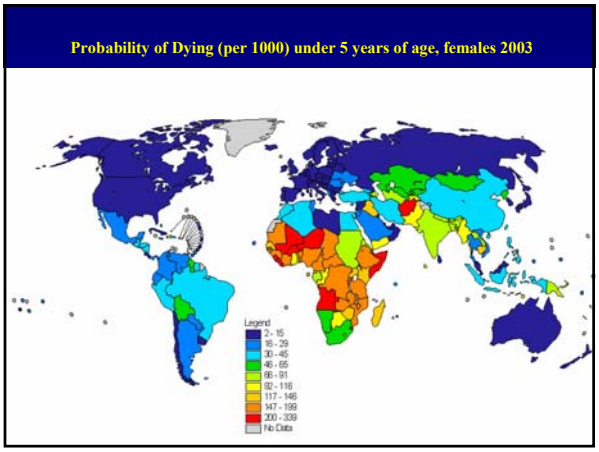
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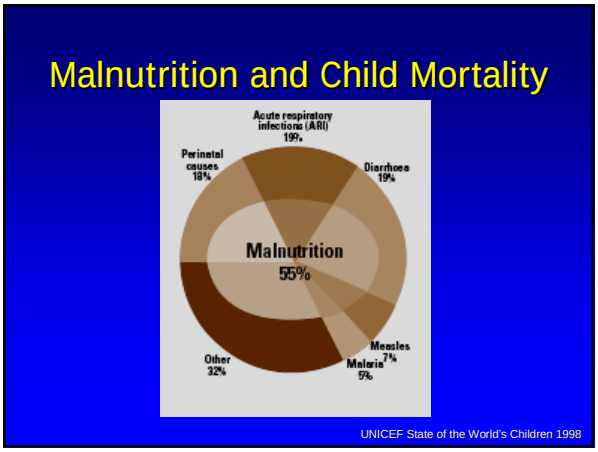
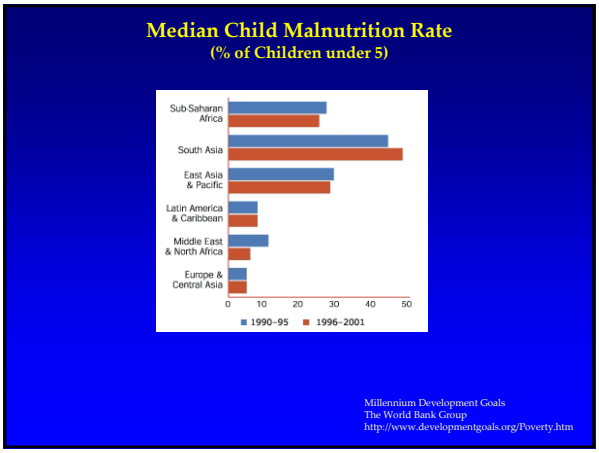

Malnutrition and Child Mortality
Acute respiratory infections (ARI) 19%
Perinatal causes 18%
Diarrhoea 19%
Malnutrition 55%
Other 32%
Measles 7%
Malaria 5%
UNICEF State of the World's Children 1998


Median Child Malnutrition Rate
(% of Children under 5)
Sub-Saharan Africa
South Asia
East Asia & Pacific
Latin America & Caribbean
Middle East & North Africa
Europe & Central Asia
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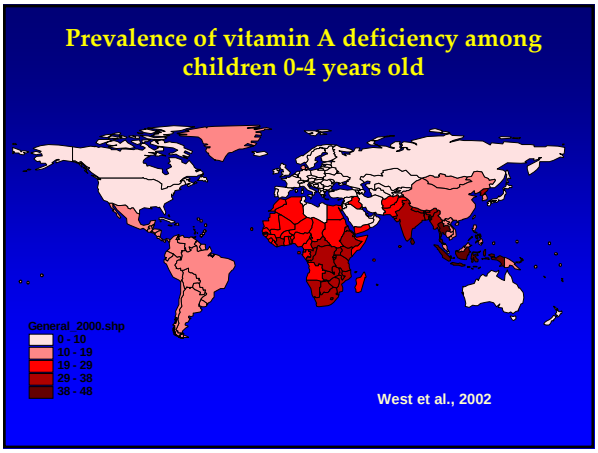
50
1990-95
1996-2001
Millennium Development Goals
The World Bank Group
http://www.developmentgoals.org/Poverty.htm


Prevalence of vitamin A deficiency among children 0-4 years old
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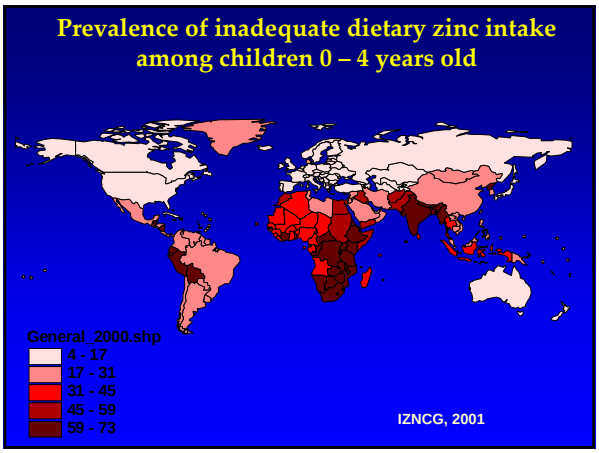
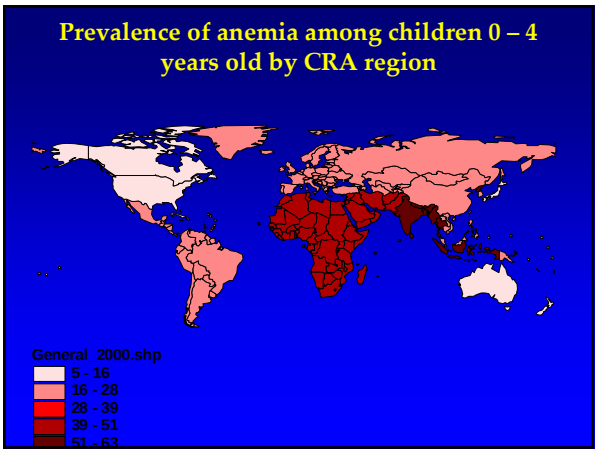
38 - 48
West et al., 2002





Infection → Malnutrition

Impact of ARI on Nutritional Status

- Febrile respiratory infections increase likelihood of stunting
  - Adair LS, Guilkey DK. J Nutr 1997;127:314-20.
- ALRI positively associated with:
  - low weight-for-age (<80% of expected)
  - Stunting (<90% of expected)
    - Ballard TJ, Neumann CG. J Trop Pediatr 1995;41:8-13.
- Frequent episodes of ARI increase risk of vitamin A deficiency (2X risk of xerophthalmia)
  - Sommer A et al. Am J Clin Nutr 1987;45:977-80.

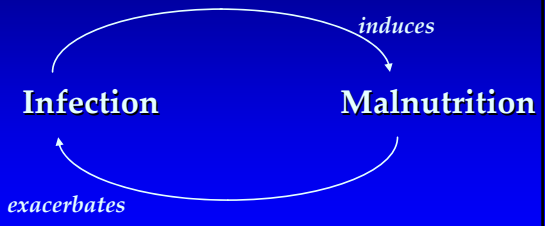
Impact of Measles on Nutritional Status

- Measles associated with a negative effect on nutritional status
  - Fever leads to increased need for protein and energy
  - Increased fecal protein losses
  - Anorexia

Impact of Malaria on Nutritional Status

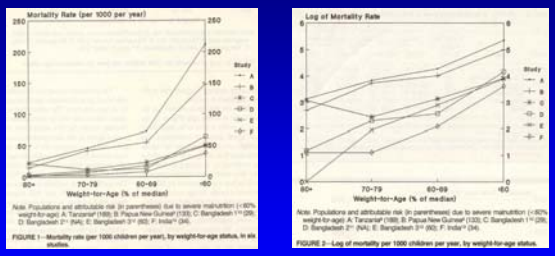
- Malaria associated with lower weight gain in Gambian childrenRowland et al. Br J Nutr 1977;37:441-50
- Malaria attacks associated with decreased linear growth of Zambian children
- Weekly chloroquine prophylaxis in Nigerian children was associated with:
  - Fewer deaths from malnutrition; Greater weight and height gain
- Combining chemoprophylaxis with insecticide spraying led to increased weight gain in <5 y/o
  - Molineaux WHO 1980
  - Hautvast Acta Pediatr 2000)

Interaction of Infection and Malnutrition



Scrimshaw, WHO 1968
Scrimshaw, AJCN 1997:664645

Underweight and all-cause mortality



55% of deaths attributable to PEM

(Pelletier et al)

Relative Risk (95%CI) of Mortality Overall and by Cause Associated with Low Weight-for-Age

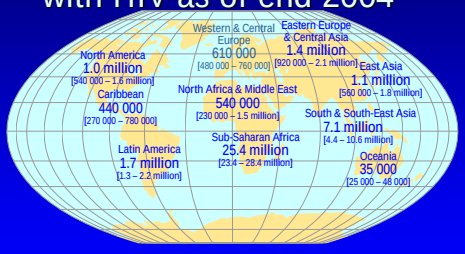
Cause of death	<-3 SDs[1]	-2 to -3 SDs	-1 to -2 SDs	>-1 SDs
Diarrhea	12.50 (7.19, 21.73)	5.39 (3.73, 7.79)	2.32 (1.93, 2.79)	1.0
Pneumonia	8.09 (4.36, 15.01)	4.03 (2.67, 6.08)	2.01 (1.63, 2.47)	1.0
Malaria	9.49 (5.25, 27.66)	4.48 (2.20, 9.15)	2.12 (1.48, 3.02)	1.0
Measles	5.25 (2.29, 11.88)	3.01 (1.74, 5.21)	1.73 (1.32, 2.28)	1.0
All causes	8.72 (5.55, 13.72)	4.24 (3.13, 5.53)	2.06 (1.77, 2.39)	1.0

[1] Calculated at -3.5, -2.5, and -1.5 compared with 0.5 SD weight-for-age from weighted random-effects models. A significant test for trend is evidenced by a statistically significant ($P < 0.05$) coefficient for weight-for-age in each model.

AJCN 2004;80(1):193-8

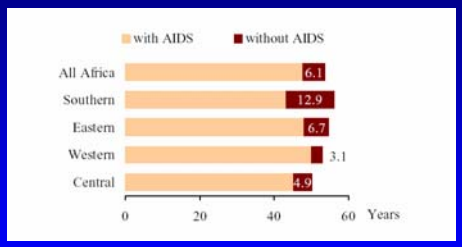
Nutrition and HIV/AIDS

Adults and children estimated to be living with HIV as of end 2004



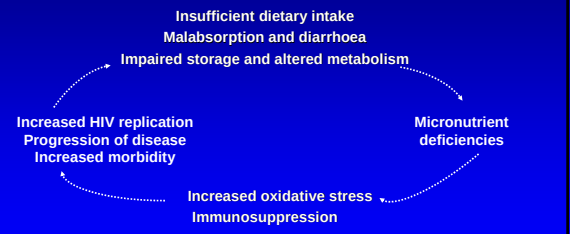
Total: 39.4 (35.9 – 44.3) million

Life Expectancy With and Without HIV/AIDS in Africa, 2002



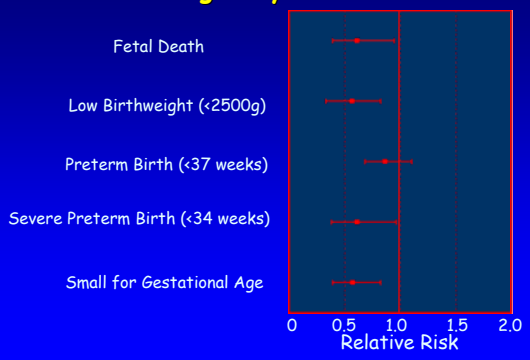
WHO
World Report 2004

Micronutrient Deficiencies and HIV Disease



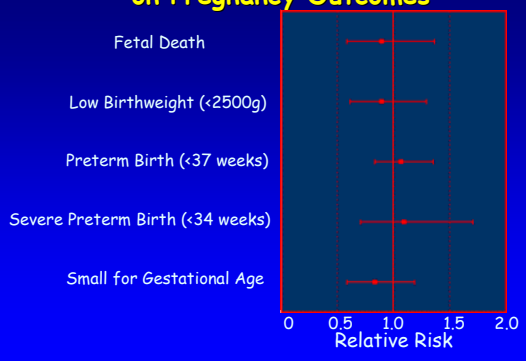
Semba & Tang,1999

Effect of Multivitamins on Pregnancy Outcomes



Fawzi, Lancet 1998;351:1477

Effect of Vitamin A on Pregnancy Outcomes



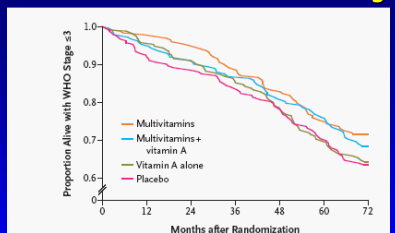
Fawzi, Lancet 1998;351:1477

Effect of Maternal Vitamin Supplements on Child Morbidity

	Multivitamins RR (95% CI)	Vitamin A RR (95% CI)
Diarrhea	0.83 (0.71-0.98)	0.95 (0.81-1.12)
Cough	1.05 (0.93-1.19)	1.04 (0.92-1.18)

Fawzi, CID 2003;36:1053

Multivitamins and HIV Disease Progression



No. at Risk

Multivitamins	271	195	157	119
Multivitamins+ vitamin A	267	181	143	102
Vitamin A alone	272	190	147	104
Placebo	267	173	145	101

Figure 1. Kaplan–Meier Estimates of the Proportion of Women Alive with Disease at WHO Stage 3 or Lower.

Fawzi, NEJM 2004;351:23

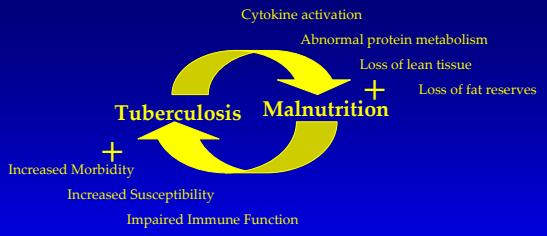
Multivitamins and HIV-Related Complications

Complication	Episodes†	Relative Risk in Placebo Group	Multivitamins		Vitamin A Alone	
			Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
Thrush	0.14±0.48	1.0	0.47 (0.30–0.73)	<0.001	0.69 (0.44–1.07)	0.10
Gingival erythema	0.02±0.14	1.0	0.22 (0.06–0.83)	0.02	1.00 (0.40–2.46)	0.99
Angular cheilitis	0.11±0.48	1.0	0.45 (0.25–0.79)	0.006	1.54 (0.95–2.51)	0.08
Oral ulcer	0.10±0.30	1.0	0.44 (0.28–0.68)	<0.001	0.94 (0.59–1.48)	0.78
Reported mouth and throat ulcers	0.28±0.93	1.0	0.47 (0.33–0.66)	<0.001	1.01 (0.74–1.38)	0.93
Painful tongue or mouth	0.31±0.98	1.0	0.46 (0.33–0.66)	<0.001	1.03 (0.76–1.40)	0.85
Difficult or painful swallowing	0.16±0.55	1.0	0.41 (0.26–0.63)	<0.001	1.25 (0.88–1.77)	0.21
Nausea and vomiting	0.38±1.14	1.0	0.69 (0.50–0.97)	0.03	0.98 (0.71–1.35)	0.91
Diarrhea	0.55±1.25	1.0	0.83 (0.63–1.09)	0.18	0.95 (0.72–1.25)	0.71
Dysentery	0.19±0.71	1.0	0.66 (0.45–0.95)	0.03	0.90 (0.62–1.28)	0.54
Fatigue	0.59±1.43	1.0	0.64 (0.49–0.86)	0.003	1.04 (0.79–1.35)	0.79
Rash	0.96±1.76	1.0	0.74 (0.57–0.96)	0.02	0.83 (0.64–1.06)	0.13
Acute upper respiratory tract infection	0.83±1.13	1.0	0.79 (0.66–0.96)	0.02	0.96 (0.80–1.14)	0.62

Fawzi, NEJM 2004;351:23

Nutrition and TB

Malnutrition and Tuberculosis



The Problem

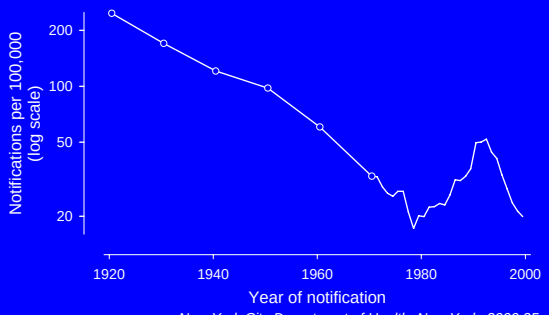
- 1/3 of world's population Tb infected
- 30 million Tb deaths in last decade
- 1.8 million deaths in 2002

Contribution of Nutrition Research to Solve the Problem (1999)

- 1017 papers on Tb in humans
  - 9 addressed wasting/nutrition
  - 6 contained original data

Macallan, Diagn Microbiol Infect Dis 1999; 34:153

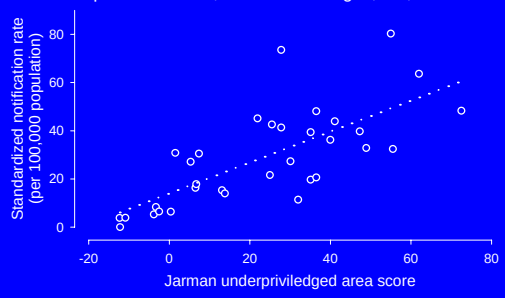
Tuberculosis Notification Rates in New York City, 1920 - 1999



New York City Department of Health, New York, 2000:25

International Union Against Tuberculosis and Lung Disease

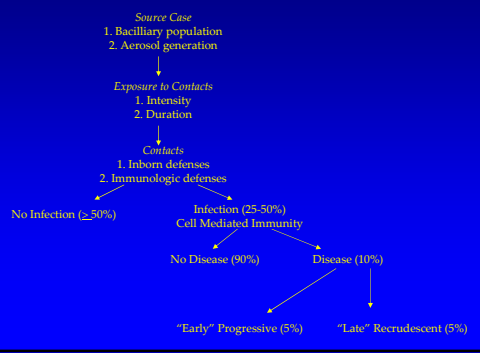
Standardized Tuberculosis Notification Rates by Deprivation Score, London Burroughs, UK, 1996



Bradsley M, et al. Health of Londoners Project, 1998
McKee M, et al. Lancet 2000;356:665-70

International Union Against Tuberculosis and Lung Disease

Major Factors that Determine Transmission of Infection from a Source Case to Contacts and the Natural History of Tuberculosis in Infected Contacts



Malnutrition and Tuberculosis -Anthropometry

Nutritional status using anthropometric measurements in active pulmonary tuberculosis patients and healthy controls[1]

	Patients		Controls	
	Male	Female	Male	Female
n	25	16	25	16
Weight, *kg*	50.6 ± 9.6	40.8 ± 6.5	58.1 ± 7.3**	50.5 ± 9.9**
Height, *cm*	165.1 ± 6.3	151.5 ± 5.3	163.0 ± 5.1	151.5 ± 4.8
Body mass index, *kg/m²*	18.5 ± 3.2	17.8 ± 3.1	21.9 ± 2.8**	21.9 ± 3.5**
Biceps skinfold, *mm*	5.5 ± 2.8	6.3 ± 3.8	7.3 ± 2.6*	8.9 ± 4.4
Triceps skinfold, *mm*	7.0 ± 3.7	12.1 ± 5.4	9.2 ± 3.2*	17.1 ± 5.5*
Subscapular skinfold, *mm*	8.5 ± 3.8	11.0 ± 5.1	11.5 ± 3.9*	14.2 ± 3.9*
Suprailiac skinfold, *mm*	9.2 ± 5.2	11.6 ± 5.4	13.4 ± 5.5*	14.0 ± 5.0
Mid-upper arm circumference, *cm*	24.0 ± 3.4	22.3 ± 3.2	28.4 ± 2.5***	26.6 ± 3.5***
Proportion of fat, *g/100 g body*	13.5 ± 6.3	23.0 ± 6.2	17.3 ± 5.1*	27.9 ± 4.5*
Fat mass, *kg*	7.3 ± 5.0	9.6 ± 3.8	10.4 ± 3.9*	14.4 ± 5.0**
Fat-free mass, *kg*	43.4 ± 5.6	31.2 ± 3.8	47.8 ± 4.4**	36.0 ± 5.2**

[1] Values are mean ± SD. Asterisks indicate significantly different from same sex patients, * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ (independent sample *t* test).

Karyadi, AJCN 2000;130:2953

Effect of Co-infection with HIV and Tuberculosis on Nutritional Status

	Control HIV-	Tuberculosis HIV-	Tuberculosis HIV+
Number	85	56	27
Arm fat area (% of control)	100	64	57
Arm muscle area (% of control)	100	74	71

Results for men are shown; similar results were found in women.

Scalcini et al., 1991

Malnutrition and Tuberculosis -Micronutrient Status

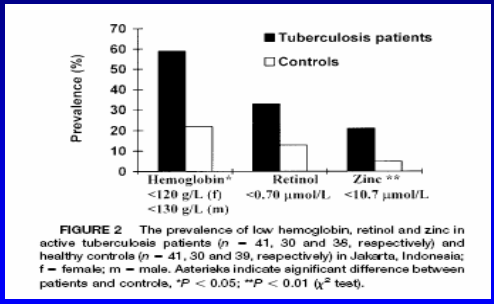


FIGURE 2 The prevalence of low hemoglobin, retinol and zinc in active tuberculosis patients (n = 41, 30 and 36, respectively) and healthy controls (n = 41, 30 and 39, respectively) in Jakarta, Indonesia; f = female; m = male. Asterisks indicate significant difference between patients and controls. *$P < 0.05$; **$P < 0.01$ (χ^2 test).

Karyadi, *AJCN* 2000;130:2953

Effect of Carotene on Course of *B. Tuberculosis* Infection of Mice

	Carotene		No Carotene	
	Infected with *B. Tuberculosis*	Uninfected	Infected with *B. Tuberculosis*	Uninfected
Total Enrolled	Total N = 20	Total N = 20	Total N = 20	Total N = 20
Deaths	6 died within 44 days; all died within 74 days	No	All died within 44 days	None
Xerophthalmia	No	No	Yes	No

Finkelstein, 1931

Prospective Relationship of Plasma Vitamin C Levels and Risk of Tuberculosis Among Black Men in Philadelphia

Plasma Vitamin A (IU per 100 ml)	Remained Non-tuberculosis	Developed Active Disease
< 0.60	896	15 (1.65%)
≥ 0.60	117	0 (0%)

Gertz et al, 1951

Role of Vitamin C in Experimental TB

Group	No. of Animals	Average Weight Loss	Average Period of Survival (day)
Scurvy	3	140	26
Scurvy + TB	4	112	21
No Scurvy + TB	4	70	64
Vitamin C suppl + TB	4	21	68

Gangadharam and Sirsi, 1953

Malnutrition and Tuberculosis Vitamin D

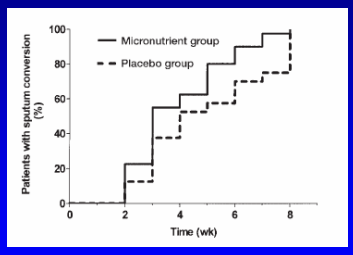
	Tuberculosis contacts (n=42)	Tuberculosis patients (n=103)	Odds ratio (95% CI) for disease	p
25-hydroxycholecalciferol concentration				
Undetectable	1 (2%)	20 (19%)	9·9 (1·3–76·2)	0·009
≤10 nmol/L	10 (24%)	49 (48%)	2·9 (1·3–6·5)	0·008
>10 nmol/L	31 (74%)	34 (33%)	0·17 (0·07–0·39)	<0·0001
Median (IQR) concentration (nmol/L)	17 (11·0–25·8)	12 (6·0–20·5)		0·002

Data are number (%) unless otherwise indicated.

Table 1: **25-hydroxycholecalciferol concentrations in untreated tuberculosis patients and tuberculosis contacts**

Wilkinson, Lancet 2000;355:618

Proportion of patients in the micronutrient (n = 40) and placebo (n = 40) groups with sputum smears converting to negative during the first 8 weeks of anti-tuberculosis treatment



There was a significant difference between the groups. P = <0.05 (log rank test)

Am J Clin Nutr.2002;75:720-27

Drug Resistant TB

- Drug-resistant TB transmitted the same way as drug-susceptible TB
- Drug resistance is divided into two types:
  - Primary resistance develops in persons initially infected with resistant organisms
  - Secondary resistance (acquired resistance develops during TB therapy)

Nutrition and Malaria

Current Worldwide Status of Malaria

- *Plasmodium falciparum* malaria causes 1-2 million deaths yearly
  - A death from malaria occurs every 30 seconds
- Vast majority of morbidity and mortality occurs in sub-Saharan Africa
- Number of malaria cases is increasing
- Drug-resistant parasites are widespread
- Insecticide-resistant mosquitoes are common

Vitamin A and Malaria *In Vitro* Studies

- Retinol inhibited growth of isolates of *P. falciparum* in tissue culture in concentrations comparable to retinol levels in normal human serum
  - Davis Acta Tropica 1998
- 9-cis-retinoic acid reduces malaria induced TNFα secretion from human monocytes AND
- Upregulates CD36 expression on human monocytes/macrophages (leading to increased phagocytosis of infected erythrocytes
  - Serghides Lancet 2001.

Evidence Linking Vitamin A Status and Malaria Morbidity

- Tanzania: Low serum retinol levels in children were associated with subsequent *Pf* parasitemia (Sturchler et al. Acta Tropica 1987)
  Chicken or egg?
- Senegal, Congo, Thailand, Ghana: Low serum retinol levels assoc. with higher *Pf* parasitemia densities
  - (Samba Gast Clin Biol 1989, Galan Int J Vi Nut Res 1990, Thurnham Trans R Soc Trop Med Hyg 1991, Filteau AJCN 1993)

Vitamin A Supplementation and Malaria

- Ghana VAST Study: 2 companion vitamin A supplementation trials reported no effects on:
  - *Pf* malaria parasitemia
  - *Pf* density
  - Probable malaria illness
  - Malaria-associated mortality
- However, vitamin A supplemented children had 32% and 23% ↓ slide-confirmed malaria
  - Binka et al. AJCN 1995

Vitamin A Supplementation and Malaria Morbidity in Papua New Guinea

- RCT of VA (200,000 IU every 3 mo) in children aged 6-60 mo found:
  - 30% reduction in *P. falciparum* clinical episodes
  - 36% reduction in *P. falciparum* density

AH Shankar et al. Lancet 354:203, 1999

Evidence Linking Zinc Status and Malaria Morbidity

- Animal studies:
  - Murine models indicate that zinc deficiency can exacerbate malaria parasitemia, mortality, and lipid peroxidation during infection
    - Arif et al. Ind J Mal 1987, Shankar FASEB J 1995
- Papua New Guinea and Malawi:
  - Associations between zinc status, anemia, and malaria suggest that zinc status is inversely correlated with *Pf* malaria
    - Gibson et al. AJCN 1991, Gibson et al. AJCN 1998

Zinc and Prevention of Malaria Placebo-Controlled Trials (1)

- The Gambia:
  - N = 110 children aged 6 to 28 months
  - Twice weekly supplementation with 70 mg zinc reduced *Pf* malaria-attributable health center attendance by 30% (p=.09)
  - Impact greatest after the first month (p=0.054)
    - Bates et al. Brit J Nutr 1993;69:243-55.

Zinc and Prevention of Malaria Placebo-Controlled Trials (2)

- Papua New Guinea:
  - N = 274 children aged 6 to 60 months
  - Zinc gluconate (10 mg/d given 6 days/week) for a total of 46 weeks
- 38% reduction in *Pf*-attributable health center attendance
- 69% reduction in *Pf* attacks with parasitemia >100,000/μL
- No consistent effects on parasite density, hemoglobin, spleen rates, or prevalence, and no evidence of age specificity
  - Shankar AS et al. Am J Trop Med Hyg 2000;62:663-9.

Zinc and Prevention of Malaria Placebo-Controlled Trials (3)

- Burkina Faso:
  - N = 709 children between 6 to 31 months of age
  - Zinc sulfate (12.5 mg/day given 6 days/week) supplemented during the rainy season (about 6 months)
  - Primary outcome: clinical episodes of *Pf* malaria defined as axillary temperature ≥37.5ºC and ≥5,000 parasites/μL
    - Muller O et al. Brit Med J 2001;322:1-6.

Burkina Faso Study Results

- No difference in *P. falciparum* incidence, even when different parasitemia cutoff points were used
- No difference in duration or severity of malaria episodes
- Fewer children died in the Zn than in the P group
  - (5/341 vs. 12/344; p = 0.1)
- Serum zinc was significantly higher in the zinc group after 3 months of supplementation
  - 15.3 μmol/L (Zn) vs. 12.4 μmol/L (P)

Why Are There Conflicting Results?

- Population studied in Burkina Faso had lower levels of subclinical zinc deficiency
  - Mean baseline plasma zinc concentration = 77.0 μg/dL and was even higher after 3 months of supplementation (in contrast to deficiency cutoff point of 60 μg/dL)
- Duration of supplementation may have been too short in Burkina Faso (6 mo vs. 48 weeks in PNG)
- Possible benefit seen in Burkina Faso in terms of malariometric indices (*Pf* prevalence and density of parasitemia)

Zinc as Adjunctive Treatment

- 1087 children ages 6 mo- 5 years with acute falciparum malaria enrolled at five sites (Ecuador, Ghana, Tanzania, Uganda, and Zambia)
- Randomized to 10-20 mg zinc per day x 4 days
- Follow-up until hospital discharge and at 4 weeks

ZAP Study Group. Am J Clin Nutr, 2002; 76: 805

ZAP Study: Zinc in Acute Malaria

- Zinc and placebo groups were similar at baseline
- Zinc sulfate was well tolerated
- Time to resolution of fever was similar in the two groups
  - Zinc = 24.2 and placebo = 24.0 hours (p= 0.37)
- Proportion of children with reduction of parasitemia by ≥75% was similar in the two groups
  - Zinc = 73.4% and placebo = 77.6% (p= 0.11)

Predicted Effects of Micronutrient Deficiencies on Malaria Parasitemia

(based on composite data from malaria studies in human, animals, and/or in vitro)

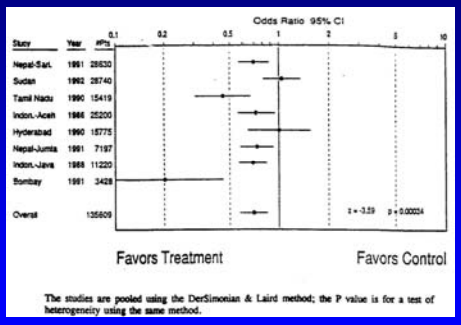
Nutrient Deficiency	Parasitemia
Folic acid	↓?
Iron	↓
Magnesium	↓
Pantothenic acid	↑
Pyridoxine (B6)	↓
Riboflavin (B2)	↓
Selenium	0
Thiamin (B1)	↑
Vitamin A	⇑
Vitamin C	↓
Vitamin E	⇓
Zinc	⇑

Childhood Infections

Childhood Mortality

- Acute respiratory infections (ARI) and diarrheal diseases (DD) are the two leading causes of death of children worldwide
- Malaria is a leading cause in some areas, especially sub-Saharan Africa
  - ARI = 4.4 million deaths/y in children <14y
  - DD = 3.1 million deaths/y
    - Science 1996;272:1269
  - Malaria = 1-2 million deaths/y

Vitamin A Supplementation and Child Mortality in Community Based Trials



The studies are pooled using the DerSimonian & Laird method; the P value is for a test of heterogeneity using the same method.

(studies arranged by descending quality score)

Effect on Mortality Among Subgroups in Community-based Studies

Subgroup	Studies Pooled	Total no. of subjects	D&L OR (Clustering-adjusted 95% CI)	P valu
Mortality by cause of death:				
Diarrhea	1-3,6	79,986	0.69 (0.57,0.84)	0.000
Pneumonia	1-3,6	79,986	0.96 (0.65,1.42)	0.84
Measles	1-3,6	79,986	0.61 (0.32,1.15)	0.13

Vitamin A Supplementation and Hospital Mortality Among Children with Measles

No.	Trial	Vitamin A Deaths/1000	Control Deaths/1000	Odds ratio (95% CI)	Risk difference per 1000 (95% CI)
1	S.Africa (Cape Town)	2/92	10/97	0.19 (0.04,0.91)	-81.4 (-148.8,-13.9)
2	Tanzania	6/88	12/92	0.49 (0.17,1.36)	-62.3 (-148.9,24.4)
3	S.Africa (Durban)	0/29	1/31	0.34 (0.01,8.80)	-32.3 (-94.5,29.9)
4	London	11/300	26/300	0.40 (0.19,0.83)	-50.0 (-88.3,-11.7)

(studies arranged by descending quality score)

Zinc Deficiency and ALRI

- Mean prevalence rate of ALRI 3.5X higher in children with low plasma zinc
- No significant difference in the number of episodes of ALRI
  - Bahl R et al. Am J Clin Nutr 1998;68(suppl)414S.
- Increased respiratory morbidity in zinc-deficient children (low hair or plasma zinc)

ZINC FOR THE PREVENTION OF ARI IN CHILDREN

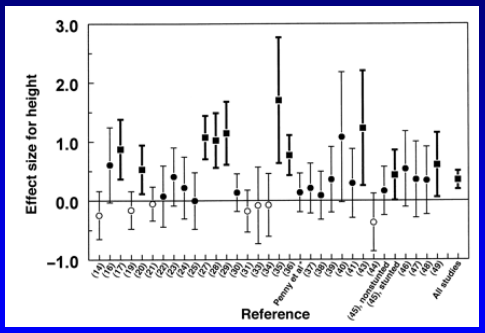
- 45% (95% CI 10-67%) reduction in incidence of ALRI in supplemented children
  - Sazawal et al. Pediatrics 1998;102:1-5.
- 2.5-fold reduction of relative risk of respiratory infection
  - Ninh et al. Am J Clin Nutr 1996;63:514-9.
- Reduced fever, cough, and upper respiratory tract secretions
  - Sempértegui et al. Eur J Clin Nutr 1996;50:42-6.

Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries

Results from meta-analyses	Zinc Supplements RR (95% CI)
Diarrheal Incidence	0.82 (0.72-0.93)
Probability of continuing diarrhea	0.76 (0.63-0.91)
Pneumonia Incidence	0.59 (0.41-0.83)

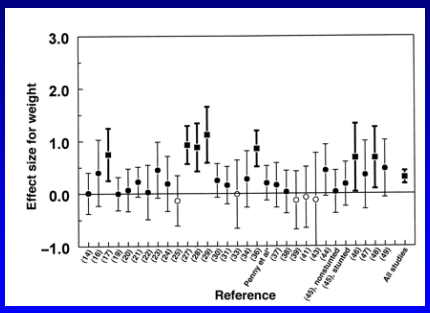
Bhutta, J Ped 1999;135:689
Bhutta, AJCN 2000;72:1516

Zinc supplementation and linear growth



Brown et al., AJCN 2002; 75:1062-1071

Zinc supplementation and weight gain

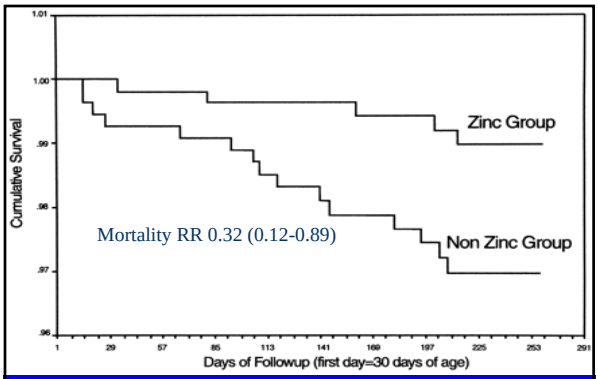


Brown et al., AJCN 2002; 75:1062-1071

Zinc and Mortality

- RCT of 1154 full-term SGA Indian infants randomized to
  - Iron, folate, Ca, P or none
  - Zinc or none
- Daily dose between 30 and 284 days age
- Household visits 6x/week

Sazawal et al., Pediatrics 2001; 108:1280



Sazawal et al., Pediatrics 2001; 108:1280

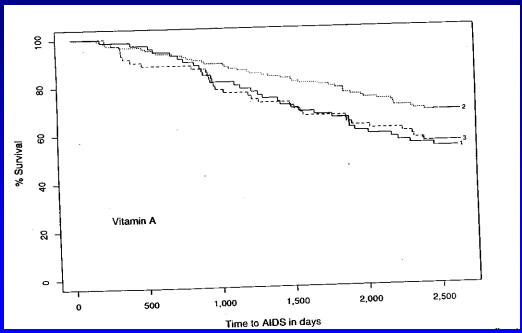
Paradoxical Effects of Micronutrients

Supplementation as a double-edged sword

Paradoxical Effects of Micronutrients

Vitamin A,
HIV-related outcomes, and ARI

TOTAL DIETARY INTAKE OF VITAMIN A AND AIDS-FREE SURVIVAL AMONG HIV-1-INFECTED MEN



Tang, Am J Epidemiol 1993;138:937

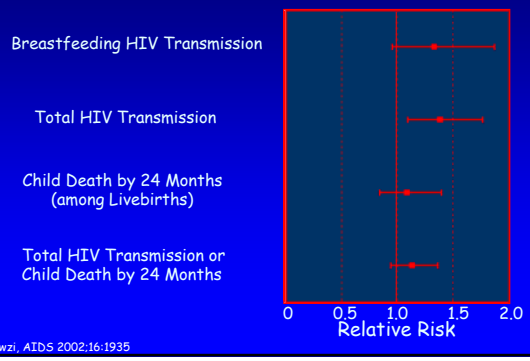
MULTIVARIATE ANALYSIS OF RISK FACTORS ASSOCIATED WITH HIV-1 SEROCONVERSION USING COX REGRESSION

	Hazard Ratio	95% CI	P
Retinol > 20 μg/dl	2.43	1.25-4.70	0.009
Circumcision	0.46	0.23-0.93	0.03
H. ducreyi	3.49	1.03-11.7	0.04

Lifetime number of sex partners, history of condom use and sex worker contact were not significant

MacDonald, AIDS 2001;15:833

Effect of Vitamin A on Child HIV Status and Mortality



Fawzi, AIDS 2002;16:1935

Paradoxical Effects of Vitamin A on ALRI in Indonesia

Study design

- Community-based study of children aged 6-47 months (n = 1,407)
- VA supplements given every 4 months

Results

- Significantly ↑ risk of ARI and ALRI overall
  - VAS significantly ↓ the risk of ALRI in stunted children (RR = 0.71, 95% CI 0.375-1.331) but
  - ↑ALRI risk in nonstunted children (RR = 1.83, 95% CI 1.257-2.669).
    - **Dibley et al. J Nutr 1996;126:434-42.**

ARI/ALRI Increased by VAS esp. well nourished (Nepal)

- West et al (1995) 11,918 children < 6 mos. given VA. RR of ARI was nonsignficantly increased by VAS (RR = 1.11, 95% CI 0.86-1.42).
- A "perplexing, dose-responsive" tendency for the RR of death to rise with improved nutritional status. RR of ALRI was higher in the supplemented children (RR = 1.21, 95% CI 0.81-1.82).

Ecuadorian Study: Logistical regression analysis of ALRI in children who took Vitamin A or placebo by WAZ strata

WAZ Stratum	Relative Risk of ALRI (95% CI)
≤ -2 SD	0.15 (0.034-0.63) p = 0.01
> -2 and ≤ -1 SD	1.66 (0.699-3.94) p = NS
> -1 and ≤ 0 SD	2.51 (1.24-5) p = 0.005

Paradoxical Effects of Micronutrients

Iron,
Anemia and Malaria

Malaria and Anemia

- Prevalence of anemia (Hb < 11 g/dL) is high in children under the age of 5 years in sub-Saharan Africa
  - Range of 11-75% or more
- Children under the age of 2 years most greatly affected
- Contributing factors (besides malaria):
  - Intestinal nematodes (esp. hookworms)
  - Schistosomiasis – Sickle cell disease
  - Inadequate dietary iron intake of child or mother during pregnancy/breastfeeding

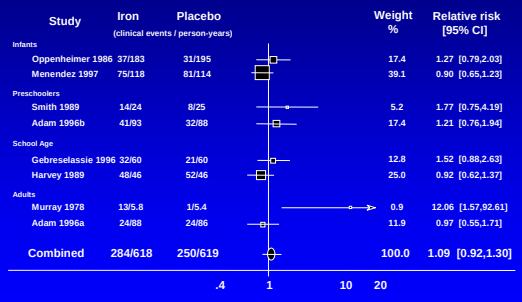
Negative Consequences of Iron Deficiency Anemia

- Impaired height and weight gain
- Low birth weight
  - if malaria occurs during pregnancy
- Impaired cognitive development
- Decreased physical exercise tolerance

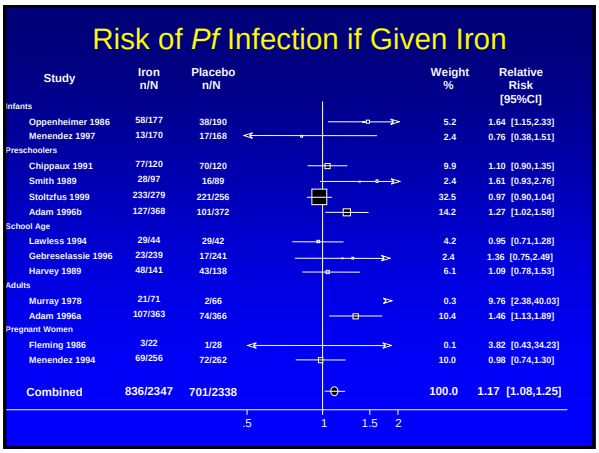
Influence of Iron Supplementation on Malaria Morbidity

- Iron supplementation of Somali nomads during famine suggested that oral iron supplements may activate latent *Pf* malaria (Murray et al. BMJ 1978)
- Studies in Papua New Guinea indicated that parenteral iron can exacerbate *Pf* parasitemia and morbidity (Oppenheimer TRSTMH 1986)
- More recent work in Tanzania and Zanzibar did not find an increased risk for *Pf* malaria in children given iron (Menendez et al. Lancet 1997, Stoltzfus et al. unpub 2000)

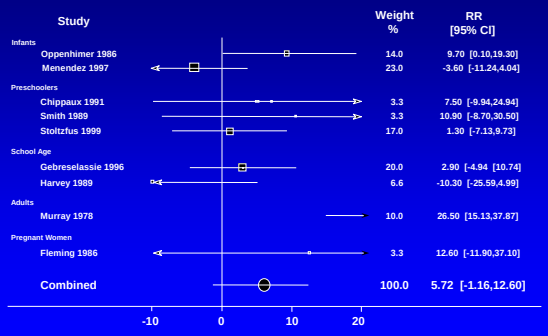
Risk of Clinical *Pf* Malaria if Given Iron



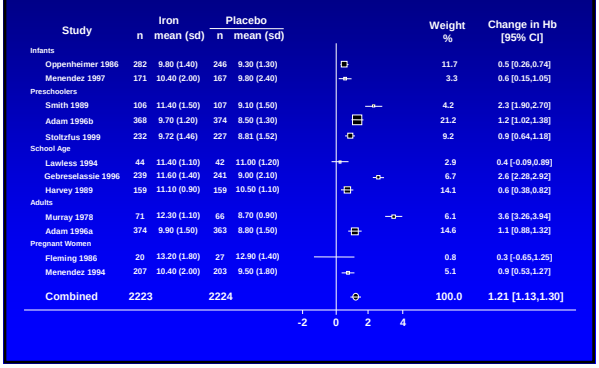
Risk of *Pf* Infection if Given Iron



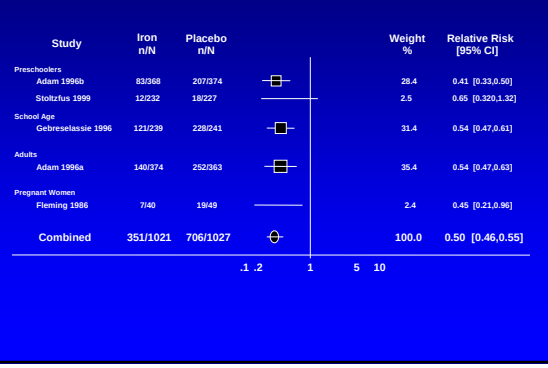
% Change in *Pf* Prevalence if Given Iron



Change in Hemoglobin Level if Given Iron



Risk of Severe Anemia if Given Iron



Paradoxical Effects of Micronutrients

Other examples:
Beta-carotene and Lung Cancer
Selenium and Genital HIV shedding
Zinc and HIV Disease Progression

Concluding Remarks – Next Steps in Research and Practice

Issues Requiring Further Study

- What are the underlying immunological mechanisms of nutritional interventions ?
- Can synergistic effects be obtained by the combined use of nutritional and other interventions such as therapeutic drugs, and experimental vaccines?
- What role does nutrition play in the evolution of drug resistance ?
  - Need to Invest in Essential Health Research

From Epidemiology to Practice (1)

- Multiple Approaches to Addressing Micronutrient Malnutrition
  - Supplementation
  - Food Based Interventions
    - Diet diversification
    - Fortification, Bio-fortification

Quintiles of Dietary Vitamin A Intake in Relation to Risk of Xerophthalmia at Round 4

Pre-formed Vitamin A:	Quintiles of Intake					Trend
	1	2	3	4	5	
Range of intake Median intake	<44 43		44-65 65	66-91 73	>91 102	
Child-periods No. of cases	5416 41		9577 60	4855 24	5130 15	
Age-adjusted RR 95 percent CI	1.00		0.85 (0.57,1.27)	0.66 (0.40,1.09)	0.40 (0.22,0.72)	P=0.002
Multivariate RR 95 percent CI	1.00		0.76 (0.50,1.16)	0.70 (0.41,1.20)	**0.43** **(0.23,0.80)**	P=0.01

Relative Risk of Mortality According to Quintile of Dietary Vitamin A Intake

Total Vitamin A	Quintiles of Intake[1]					P for Trend[2]
	1	2	3	4	5	
cases child periods	59 17,452	86 17,975	43 15,606	26 12,946	18 16,125	
Age & sex-adjusted RR[2] (95 % CI)	1.00	1.21 (0.86,1.69)	0.78 (0.52,1.16)	0.59 (0.37,0.95)	0.35 (0.21,0.60)	P <0.0001
Multivariate RR[2] (95 % CI)	1.00	1.33 (0.94,1.89)	1.05 (0.68,1.62)	0.86 (0.52,1.41)	0.53 (0.30,0.93)	P=0.002

From Epidemiology to Practice (2)

- Evidence-based Nutrition Practice
- Nutrition Integrated in Health Programs
- Strong Monitoring and Evaluation
- Food Security and Beyond
- Plan for Long-term Sustainability
- High Level Political Commitment (e.g. South Africa)

From Epidemiology to Practice (3)

- Development of Future Leaders in Nutrition for Africa
- Training Programs in Africa – Strengthen/ Integrate Nutrition in Existing Research, Teaching, and Policy Institutions
- Twinning: North-South, South-South
- Key to Develop Skills in Proposal Development, Data Analyses, and Report Writing. Theory and Practice.