Role of Science in Shaping Future Micronutrient Policies and Programs

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Health Problems among the Undernourished

Nutritional Deficiencies

- PEM

- Micronutrient deficiencies:
  - Vitamin A, zinc, iron, iodine, folate, others

- Behavioral Causes:
  - Breast & compl feeding; home diet; low SES, hygiene, and education; markets; global economics

Child and Maternal Health Problems

- Infant or Child
  - Infection
  - Poor growth
  - Impaired mental, motor & behavioral development
  - Mortality

- Mother
  - Short stature
  - Infection/sepsis
  - Obstetric problems
  - Anemia
  - Mortality

Chronic disease, disability, mortality
Essential Nutrient Facts

• Micronutrients must be provided by diet, always
• Perform millions of vital functions
• Deficiencies decrease stores & health deteriorates
• Public health importance depends on prevalence, severity and health consequences
• Roles of science: quantifying deficiency and consequences, assessing public health impact, offering plausible mechanisms, monitoring trends and evaluating approaches to prevention
Success Stories Guided by Science:

Pillars of Public Health

• Iodization of salt to prevent IDD
• Flouride to reduce dental cavities
• Vitamin A to prevent blindness and mortality (VADD)
• Zinc as adjunct to ORS for diarrhea
• Iron to prevent (iron-deficiency) anemia
• Folic acid fortification to prevent NTDs
A Decade of Research on Vitamin A & Child Mortality

Sommer & West, 1996
NVAS and Infant Mortality

In W Java, Indonesia: **Vitamin A (50,000 IU) at birth reduced mortality 64%**

Relative Risk = 0.36 (95% CI: 0.16 to 0.87)

South India: **VA (~50,000 IU) at birth reduced infant mortality by 23%**
Rahmathullah et al BMJ 2003;327:254

Relative Hazard = 0.77 (0.62, 0.96)  p = 0.02

NW Bangladesh: **VA (50,000 IU) at birth reduced infant mortality by 15%**
Klemm et al MF Meeting 2007

Log-rank test: 4.33, p=0.037
A Decade of Trials on Zinc in Treating Diarrhea, Preventing Other Infections

Diarrhea Incidence
9 countries

Diarrheal Prevalence
9 countries

Pneumonia Incidence
4 countries

~25% reduction for diarrhea

~40% reduction for pneumonia

Zinc Investigators’ Collaborative Group
J Pediatrics 1999;135:689
Early Life Micronutrient Nutrition: Influence on Lifelong Health

Maternal Nutrition

- Maternal energy & nutrients
- Fetal energy & nutrients

Health at Birth
- Size
- Physiological Endowment
- Maturity

Infant & Child Nutrition
- Growth & Size
- Resistance to Infection
- Cognition & Development
- Maturity

Health Later in Life
- Childhood
- Adolescence
- Adulthood

Maternal Nutrition Interventions

Newborn/Infant & Early Childhood Nutrition Interventions
## Antenatal Folic Acid Supplementation Reduced Microalbuminuria in Offspring 6-8 Yrs of Age

<table>
<thead>
<tr>
<th>Maternal supplement group</th>
<th>$n$</th>
<th>Microalbuminuria, $n$ (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>653</td>
<td>40 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Folic acid</td>
<td>595</td>
<td>21 (3.5)</td>
<td>0.56* (0.33, 0.93)</td>
</tr>
<tr>
<td>Folic acid + iron</td>
<td>609</td>
<td>29 (4.8)</td>
<td>0.77 (0.49, 1.22)</td>
</tr>
<tr>
<td>Folic acid + iron + zinc</td>
<td>621</td>
<td>21 (3.4)</td>
<td>0.53* (0.32, 0.89)</td>
</tr>
<tr>
<td>Multiple micronutrient</td>
<td>675</td>
<td>30 (4.4)</td>
<td>0.70 (0.44, 1.11)</td>
</tr>
</tbody>
</table>

1. Microalbuminuria = urinary microalbumin : creatinine ratio $\geq 3.4$ mg/mmol. *$P < 0.05$. OR and 95% CI were calculated using a GEE logistic regression model controlling for the child age at follow-up.

Stewart CP et al Journal of Nutrition 2009
Lessons Being Learned
Context Matters

- Populations vary by nutrition and health outcomes, health services, cultures, other resources
- Once studies pass design, power, conduct and analysis criteria, local factors may explain differences in results

**Double blind, cluster randomised trial of low dose supplementation with vitamin A or β carotene on mortality related to pregnancy in Nepal**

**Effects of vitamin A supplementation in women of reproductive age on maternal survival in Ghana (ObaapaVitA): a cluster-randomised, placebo-controlled trial**

MMR ~350, VAD ~15%, XN nil, generally better nutritional status
**No reduction in maternal mortality**

**Effects of Vitamin A or Beta Carotene Supplementation on Pregnancy-Related Mortality and Infant Mortality in Rural Bangladesh**

MMR 230, VAD ~8%, XN ~9%, PEM, diet and care better than in Nepal
**No reduction in maternal mortality**
Lessons Being Learned

- Nutrition is complex: simplify but not too much
- Meta-analysis requires comparable risk profiles
- Extend and blend vs confirm or negate
- Infection: a cause, not a confounder
- Mechanisms count, expand biology, lead to new thinking/approaches, but won’t drive policy
- Surveys establish prevalence, epidemiological studies raise risk factors, trials reveal impact of solutions
- RCTs drive reactions, further research and ... eventually evidence-based programs
Future Directions

• Look beyond survival...improve cognition & function, reduce infection, prevent inflammation, oxidative stress & chronic disease

• Look before birth... to achieve healthy growth

• Look beyond size ... Examine roles of maternal micronutrient intakes on “functional growth and development” of offspring
  – including preventing birth defects

• Look beyond health outcomes ... to change feeding and dietary practices and intakes within resources and seasons
Future Directions

• Discern interactions between infection and nutrition

• Roles of “antinutritionals” (eg, mycotoxins, arsenic, smog) in affecting inflammation, status and health

• Look beyond dietary content ... to hygiene in food processing, home, contaminants and water

• Design and evaluate adequate, balanced nutrient delivery: from food, fortificants, supplements

• Reveal ‘Hidden Hunger’ in all of its breadth, depth and consequence
Future Directions: Assessment

• New “point of population” (PoP) platforms to rapidly assess multiple micronutrient deficiencies to
  – Know what they are, who has them, when and how severely,
  – Act in real time to prevent - specifically
  – Discern population deficiency thresholds for expecting certain health impacts
  – Monitor and evaluate programs addressing broader array of deficiencies
Thank You!