Effective pathways towards reducing chronic malnutrition

Lora Iannotti, PhD

Symposium: Ensuring children’s cognitive and physical development through animal-source foods
Capitol Hill Club, June 5, 2019
Presentation Outline

1. Introduction
   • The problem: stunting
   • Biological and evolutionary basis of ASF

2. Evidence
   • Ecuador: Lulun Project
   • Kenya: Samburu, coastal areas

3. Conclusion
   • ASF for achieving global milestones
   • Key messages
Malnutrition: prevalence

**Malnutrition in young children**
- 151 million *stunted growth*
- 250 million *stunted development*
- 50 million *wasted*
- 41 million *overweight/obese*

**Hidden hunger globally**
- 33% children *vitamin A* deficient
- 18% children & 19% women *anemic*
- 17.3% world *zinc* deficient;
- 28% world *iodine* deficient

**3.1 million (45%) of deaths to children <5 yr**

(Black et al. *Lancet* 2013)
Periods of greatest risk for chronic malnutrition

FIGURE 1
Mean anthropometric z-scores according to age for all 54 studies, relative to the WHO standard (1 to 59 months).

(Victora et al., Pediatrics 2010)

Sensitive periods and the developing brain

THE LANCET
Advancing Early Childhood Development: from Science to Scale
Hidden hunger & brain development

• “Brain-selective” nutrients
  – Iodine (thyroid hormone), iron (white matter, myelination, neurotransmitter metabolism), zinc (enzymes, neurotransmitter), copper, selenium, DHA, choline, vitamins A and B12
  – Deficiencies → hippocampus insults, ↓ learning and memory, compromised child development across all domains, etc.

Goyal, Iannotti and Raichle Annual Review of Nutrition 2018
Global Stunting

In 7 sub-regions, at least one in every four children under 5 is stunted

Percentage of stunted children under 5, by United Nations sub-region, 2017

UNICEF WHO World Bank 2018
Nutrient disparities: zinc availability (Lancet Planetary Health series 2018)
Stunting: Causes & Consequences

Consequences:
• ↑ risk of mortality
• ↑ risk of infectious diseases (enteric, malaria, respiratory)
• Impaired development
• ↓ schooling
• ↓ adult earnings
• Poor reproductive health
• Intergenerational effects
Evolutionary Nutrition: Theories

• **Discordance theory**
  – Human genome evolved to adapt to conditions that no longer exist. Mismatch leading to ↑ chronic diseases (Eaton & Konner NEJM 1985)
  – Genome-nutrition divergence of divergence across the entire nutrition spectrum, with overlapping region of poor diet quality (Eaton & Iannotti Nutrition Reviews 2017)

• **Shore-based paradigm**
  – Archeological evidence (e.g. shell middens) points to emergence of *Homo sapiens* and anthropometric differences in body and brain, driven by shore-based diets (Cunnane & Crawford 2014)

• **Savanna & Woodland theories**
  – Hominin as hunter on savanna & woodland → grassy woodland (Washburn & Lancaster 1968; Stanford et al. 1999; White et al. 2009)
The *Homo* genus: anatomical differences

- **Homo erectus** (early hominin) ~1.8 mya
  - Anatomical differences from other *hominins* (*Australopithecus garhi* & *Homo habilis*), attributable to diet changes - animal source foods in particular.

**Physical Differences**
- ↑ Brain size – 3x the encephalization quotient (brain mass to body mass) (Broadhurst et al. 1998)
- ↑ Taller height - 15% taller (Walker 1993)
- ↑ Larger body mass
- ↑ Longer legs (bipedalism)
- ↓ Smaller teeth
- ↓ Colon, ↑ small intestine (>56%)

Advent of Agriculture (~10,000 ya)

Offspring numbers increase, by at what cost?

- Life expectancy ↓ from 40 to 20 yr
- Human height ↓
- Infection ↑
- Brain size ↓

H. erectus (1.6 mya), H. heidelbergensis (300,000 ya), H. sapiens Cro-Magnon (30,000 ya), modern H. sapiens (DeSilva et al. unpublished)
### Food matrices: the importance of packaging

<table>
<thead>
<tr>
<th>Limiting nutrient</th>
<th>ASF matrix</th>
<th>ASF vs. plant absorption rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit A →</td>
<td><img src="image" alt="ASF matrix for Vit A" /></td>
<td>12-24x (ug)</td>
</tr>
<tr>
<td>Iron →</td>
<td><img src="image" alt="ASF matrix for Iron" /></td>
<td>2x (mg)</td>
</tr>
<tr>
<td>Zinc →</td>
<td><img src="image" alt="ASF matrix for Zinc" /></td>
<td>2x (mg)</td>
</tr>
<tr>
<td>Choline →</td>
<td><img src="image" alt="ASF matrix for Choline" /></td>
<td>?</td>
</tr>
</tbody>
</table>
E3 Nutrition Lab – animal source foods

Economically affordable
Evolutionarily appropriate
Environmentally sustainable

Eggs, Milk, Fish

• First foods: designed to sustain and support early life, entirely
• Complete set of nutrients and other bioactive factors
Egg = >50% of daily nutrients (++) and 20-50% (+) for breastfed infant

Source: Iannotti et al. *Nutrition Reviews* 2014
Synthesized evidence

• **Lancet Series: Maternal and Child Nutrition** *(Bhutta et al. 2013)*
  - Assessed 43 nutrition-related interventions
  - Literature *replete for nutrition-specific* (micronutrient supplementation, fortification, LNS, breastfeeding), but *limited for nutrition-sensitive* (food/diet, agriculture/livestock, education, etc.)
  - Provision of complementary food in food insecure populations *0.39 SMD in HAZ*; no effects on stunting reduction

• **Cochrane Review ASF for growth in children 6-59 mo** *(Eaton et al. 2019)*
  - Only 6 studies (*n=3,076 children*) from China, DRC, Ecuador, Guatemala, Pakistan, US, and Zambia
    - 3 reported increased height & weight with ASF vs. cereal-based foods/no intervention
    - 1 reported growth in height & weight gain in meat vs. dairy
Lulun Project

- **Objective:** Test the efficacy of eggs introduced early in the complementary feeding period on growth and nutrient biomarker outcomes (n=163)
  - **Primary outcomes:** biomarkers of choline, betaine, vitamin B$_{12}$, fatty acids, anthropometry, and growth
  - **Secondary outcomes:** acceptability, dietary intakes, and morbidities, amino acids, growth factors
The Lulun Project

• RCT
  – **Cotopaxi**: mixed indigenous, high baseline stunting
  – **Intervention**: 1 egg/day for 6 mo, eggs purchased locally
  – **Longitudinal follow-up**: baseline (6-9 mo), endline (12-15 mo)
  – **Social marketing**: ownership, participation, compliance

• Mixed methods
  – **Quantitative**: caregiver surveys, anthropometry, GPS
  – **Biomarkers**: LC/MS/MS at Wash U, ELISA at NETLAB
  – **Qualitative**: grounded theory, structured observations, focus groups, and in-depth interviews
Social marketing: ownership, participation, and adherence
# Growth effects: GLM models

## Table 2: Effect of the Intervention on Child Growth in a Randomized Controlled Trial of Eggs in Ecuador

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End Point</th>
<th>Effect Size or PR</th>
<th>Effect Size or PR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n = 82)</td>
<td>Egg (n = 78)</td>
<td>Control (n = 73)</td>
<td>Egg (n = 75)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>LAZ (SD)</td>
<td>-1.71 (0.92)</td>
<td>-2.09 (1.08)</td>
<td>-1.71 (1.00)</td>
<td>-1.39 (1.35)</td>
</tr>
<tr>
<td>WAZ (SD)</td>
<td>-0.40 (0.92)</td>
<td>-0.91 (1.24)</td>
<td>-0.55 (0.85)</td>
<td>-0.34 (1.06)</td>
</tr>
<tr>
<td>WLZ (SD)</td>
<td>0.86 (0.99)</td>
<td>0.55 (0.99)</td>
<td>0.36 (0.81)</td>
<td>0.45 (0.84)</td>
</tr>
<tr>
<td>BMIZ (SD)</td>
<td>0.80 (1.00)</td>
<td>0.42 (1.10)</td>
<td>0.64 (0.82)</td>
<td>0.68 (0.85)</td>
</tr>
<tr>
<td>Stunted</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Underweight</td>
<td>26 (32)</td>
<td>37 (47)</td>
<td>29 (40)</td>
<td>21 (28)</td>
</tr>
<tr>
<td></td>
<td>4 (5)</td>
<td>10 (13)</td>
<td>5 (7)</td>
<td>4 (5)</td>
</tr>
</tbody>
</table>

Table shows results for end-point mean (SD) anthropometric measures and prevalence (no. (%)) of undernutrition, as well as GLM modeling for unadjusted and adjusted effect size and PR for anthropometric outcomes, by group.

<sup>a</sup> Adjusted for child age, sex of the child, and baseline anthropometry for the same dependent variable.

<sup>b</sup> PR was estimated using GLM with robust Poisson.
Egg increased linear growth by 0.63 LAZ, reduced stunting 47%
Egg increased biomarkers of brain development

- **Choline → 0.35** (95% CI: 0.12, 0.57)
  - cell membrane (phosphatidylcholine); neurotransmission (acetylcholine);
  - memory & learning (hippocampus); gene expression (betaine to methionine)

- **Docosahexaenoic acid (DHA) → 0.43** (95% CI: 0.13, 0.73)
  - predominant n-3 fatty acid in the brain
  - neurogenesis, neurotransmission, myelination, synaptic plasticity

- Methionine, betaine, TMAO, DMA, amino acids

(Iannotti et al. AJCN 2017)
## Pilot study – Ecuador (preliminary, unpublished results)

<table>
<thead>
<tr>
<th></th>
<th>Mean Z Scores (SD)</th>
<th>WHO Mean Percentiles (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n = 25)</td>
<td>Female (n = 20)</td>
</tr>
<tr>
<td>Biparietal Diameter</td>
<td>-0.65 (1.00)</td>
<td>-1.32 (1.19)</td>
</tr>
<tr>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head Circumference</td>
<td>0.45 (0.87)</td>
<td>-0.02 (1.07)</td>
</tr>
<tr>
<td>Abdominal Circumference</td>
<td>0.06 (0.86)</td>
<td>0.08 (1.00)</td>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femur Length</td>
<td>-0.21 (0.86)</td>
<td>-0.30 (1.39)</td>
</tr>
<tr>
<td>Humerus Length</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated Fetal Weight</td>
<td>39.90 (31.75)</td>
<td>45.25 (33.86)</td>
</tr>
</tbody>
</table>

Regression modeling:
- head circumference, biparietal diameter, & cerebellar diameter associated with dietary intake of animal source foods (seafood, eggs)
KENYA
Pastoralists & milk nutrition

- 200 million pastoral and agro-pastoral people in drylands (ILRI)

- 1980s-1990s milk >50% of diets Turkana, Rendille, Maasai, and Borana; 30% in other agro-pastoralist populations of Sudan and Afghanistan

- Milk provides calcium, magnesium, zinc, selenium, riboflavin, vit B12, whey/casein proteins, linoleic acid and α-linolenic fatty acids, IGF-1
Pathways to nutrition impacts

- Livelihood transition: ↓ Land access & ↑ Sendentarization
- 2 comparable communities: Siambu, livestock; Mbaringon: cultivation
Maize dependency - % daily kcals
## Food source of nutrients

### Table 3. Food group source of nutrients (%), 2010

<table>
<thead>
<tr>
<th></th>
<th>Energy</th>
<th>Vitamin A</th>
<th>Vitamin B&lt;sub&gt;12&lt;/sub&gt;</th>
<th>Vitamin C</th>
<th>Folate</th>
<th>Iron</th>
<th>Zinc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maize</td>
<td>49</td>
<td>34</td>
<td>0</td>
<td>0</td>
<td>27</td>
<td>60</td>
<td>51</td>
</tr>
<tr>
<td>Rice</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Potatoes</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Beans</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>57</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>Meat</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Milk</td>
<td>10</td>
<td>57</td>
<td>94</td>
<td>50</td>
<td>6</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Vegetables</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>17</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fat</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sugar</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Iannotti and Lesorogol *Current Anthropology* 2014
Livestock ownership improves nutrient intake

• Findings:
  – Livestock ownership increased nutrient adequacy for vitamin A, B\textsubscript{12}, and zinc (P<0.001) (Iannotti and Lesorogol CA 2014)
  – Milk consumption increased BMI z scores among youth (P<0.001) (Iannotti and Lesorogol AJPA 2014)
  – Cattle and chicken ownership increased dietary diversity (P<0.001)

• Conclusion:
  – Support livestock development among pastoralist households for child milk consumption and nutrition

• Next steps:
  – Samburu study to examine mineral status of adolescent pastoralists – highlands vs lowlands
SecureFish Kenya - FIL

• Problem
  – Coastal communities stunting 39% (26% national average) (DHS)
  – Kenyan coastal fisheries overexploited; ↓4x in catch since 1980s (Samoilys et al. 2017)

• Design & Methods
  – Site inclusion criteria: proximity to Marine Protected Area; Beach Management Units divided by coastal highway
  – Fishers (n=100) and non-fishers (n=100)
  – Mixed methods: qualitative, quantitative, Wildlife Conservation Society data

Partners: Wash U, University of Rhode Island, Egerton University, Pwani University, MSU
ASF Research – context matters

- **Malawi**
  - Mazira RCT replication study: egg effects on growth, biomarkers, and child development → no effect on LAZ or stunting
  - High fish consumption; maize staple; limited social marketing

- **Ecuador**
  - Lulun II follow-up cohort → effect no longer present after 2 years; ASF interventions should be continued through childhood
  - Sustainability and scalability of egg nutrition: poultry production → barriers include soil quality, climate change
  - Evolutionary nutrition trial – fish, eggs, berries/greens in pregnancy
CONCLUSIONS
Global Nutrition Targets 2025 – ASF Contribution

1) Stunting →

2) Anemia →

3) Low birthweight→
Key messages

1) Globally, 151 million young children have stunted growth & 250 million stunted development. Malnutrition primarily risk factor in 45% of all childhood deaths globally.
   - Biological and evolutionary rationale underpin the need for ASF in human nutrition

2) Evidence is limited for ASF
   - Previous studies focused on nutrient supplements, LNS, & fortification - with a small effect size of 0.39 HAZ
   - Lulun Project of one egg/d ↑ LAZ by 0.63; ↑ biomarkers of brain development
   - Context matters: milk pastoralists; Mazira; fish coast; etc.

3) ASF show great potential for alleviating stunting
   - Global community strive for nutrition equity for planetary health
   - ASF contribute to Global Nutrition Targets & SDGs
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