SecureNutrition Seminar

Date: November 16th 2017

Title: Cracking the Egg’s Potential to Improve Child Growth and Development
Presenters

Chessa Lutter
Senior Nutrition Researcher, RTI
Visiting Research Professor, UMD

Christine Stewart
Associate Professor, UC Davis

Lora Iannotti
Associate Professor & Associate Dean, Washington University

Discussant

Franck Cesar Jean Berthe
Sr. Livestock Specialist, WBG

Chair

Emanuela Galasso
Senior Economist, WBG

Q&A (remote)
Cracking the egg potential to improve child growth and development

Chessa Lutter, PhD
Senior Nutrition Researcher, RTI International
Visiting Research Professor, UMD School of Public Health

Christine Stewart, PhD
Associate Professor, Department of Nutrition
University of California, Davis

The World Bank, November 16, 2017
Stunting prevalence 2015
Percentage of stunted children under 5, by UN sub-region


Note: *Eastern Asia excluding Japan; **Oceania excluding Australia and New Zealand, *** Australia and New Zealand, regional average based on Australian data, ****Northern America regional average based on United States data. These maps are stylized and not to scale and do not reflect a position by UNICEF, WHO or World Bank Group on the legal status of any country or territory or the delimitation of any frontiers.
Regional Trends – stunting numbers affected
Number (millions) of stunted children under 5, 2000 and 2015

Note: *Asia excluding Japan; **Oceania excluding Australia and New Zealand.
Improving young child nutrition as a key component of economic development

“The effects of stunting have life-long consequences not only for the individual, but for countries as well. How will countries compete … in a global economy in the future when 30 to 45 percent of their children do not have as many neuronal connections in their brain…. “

Jim Young Kim, President, World Bank, April 2016

Credit: UNICEF, Peru
Starchy complementary feeding diets, poor feeding practices

Credit: PAHO (Colombia)

Credit: Reyna Lira (Peru)

Credit: PAHO (Colombia)
Effects of complementary feeding interventions

Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost?

Bhutta ZA¹, Das JK², Rizvi A², Gaffey MF³, Walker N⁴, Horton S⁵, Webb P⁶, Lartey A⁷, Black RE⁸; Lancet Nutrition Interventions Review Group, the Maternal and Child Nutrition Study Group.

Overall, the provision of complementary foods in food insecure populations was associated with significant gains in HAZ (SMD 0.39; 95% CI: 0.05-0.73)

Complementary Feeding Interventions Have a Small but Significant Impact on Linear and Ponderal Growth of Children in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis.

Panjwani A¹, Heidkamp R².

“Complementary food supplementation interventions with or without nutrition education also had a small, significant effect in food-insecure settings on both LAZ (SMD: 0.08; 95% CI: 0.04, 0.13) and WLZ (SMD: 0.05; 95% CI: 0.01, 0.08).”
Food products used to reduce undernutrition

Fortified complementary food, Ecuador

Lipid-based nutrient spread (Plumpy Nut)

No usar este sobre si está dañado o roto. Mantener en lugar fresco y seco.

Dosis: Un sobre diaria

Forma de uso: Mezcle todo el contenido del sobre en una porción individual de comida. Inmediatamente antes de servir.

Formulación para mujeres embarazadas

<table>
<thead>
<tr>
<th>Ingredientes</th>
<th>Contenido</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hierro (Ferromarto)</td>
<td>15 mg</td>
</tr>
<tr>
<td>Zinc (Glucinato de zinc)</td>
<td>15 mg</td>
</tr>
<tr>
<td>Acetil félico</td>
<td>100 µg</td>
</tr>
<tr>
<td>Vitamina C (Ácido Ascorbico)</td>
<td>100 mg</td>
</tr>
<tr>
<td>Póleo (Pentóbio de yodo)</td>
<td>100 µg</td>
</tr>
<tr>
<td>Vitamina E (como Acetato)</td>
<td>10 mg ET</td>
</tr>
<tr>
<td>Vitamina B12 (cyanocobalamina)</td>
<td>7,5 µg</td>
</tr>
<tr>
<td>Vitamina B6</td>
<td>1,2 µg</td>
</tr>
<tr>
<td>Vitamina A</td>
<td>150 µg</td>
</tr>
<tr>
<td>Vitamina D</td>
<td>400 UI</td>
</tr>
</tbody>
</table>

Fabricado por Ped-Med Ltd, Canadá

Multi-micronutrient powders
“Eggs have been consumed throughout human history, though the full potential of this nutritionally complete food has yet to be realized in many resource-poor settings around the world.”

“It should not be surprising that a simple egg, which provides a chicken embryo nutritive support from conception to the time it hatches, might also be important food to support fetal growth and development during pregnancy.”
Eggs: provides >50% of nutrients (+++) and 20-50% (+) for breastfed infants 7-12 months

Iannotti et al. *Nutrition Reviews* 2014
Food is biologically complex. It consists of cells, other non-cellular material and their molecular constituents.

“Foods (are) complex, non-random mixtures of natural compounds, developed under biological evolitional control.”
lulun project

Universidad San Francisco de Quito  |  Washington University in St. Louis
Pan American Health Organization  |  University of California, Davis  |  The Mathile Institute

G. Reinhart photo 2014
Stunting in Ecuador

**Stunting over time**

- 1986: 40.2%
- 2004: 33.5%
- 2012: 25.3%

**Stunting by ethnic group (2012)**

- Indigenous: 42.3%
- Afro-Ecuadorian: 17.7%
- Montubio: 21.3%
- Mestizo, white, and other: 24.1%

Lulun Project

- **Objective:** Test the efficacy eggs introduced early in 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
- **Approved** by IRBs at USFQ, Washington University, PAHO
Lulun Project: study design

- **RCT (Mar–Dec 2015)**
  - **Cotopaxi Province**: mixed indigenous community, high baseline stunting
  - **Intervention**: 1 egg per day for 6 months (eggs purchased locally, and delivered weekly during surveillance visits)
  - **Longitudinal follow-up**: baseline (6-9 mo) and endline (12-15 mo)

- **Mixed methods**
  - **Qualitative**: grounded theory, structured observations, focus groups, and in-depth interviews
  - **Quantitative**: caregiver surveys, anthropometry, GPS/GIS
  - **Biomarkers**: LC/MS/MS at Washington University in St. Louis, ELISA (vitamin B12) at NETLAB
Social marketing: ownership, participation, and adherence
Consort diagram

Assessed for eligibility (n= 175)

Excluded (n= 12)
- Not meeting inclusion criteria (n=4)
- Declined to participate (logistics or moving from area, apprehension about blood draw, unknown reasons) (n=8)

Randomized (n=163)

Allocated to control group (n= 83)
Lost to follow-up (n=8)
- Temporary relocation (n=5)
- Moved permanently (n=1)
- Unknown reason (n=2)

Baseline Analyzed (n= 82)
- Missing anthropometry (n=1)

Endline Analyzed (n=73)
- Missing anthropometry (n= 1)

Allocated to egg group (n= 80)
Lost to follow-up (n=3)
- Refused final blood draw (n=1)
- Temporary relocation (n=1)
- Moved permanently (n=1)

Baseline Analyzed (n= 78)
- Missing anthropometry (n= 2)

Endline Analyzed (n=75)
- Missing anthropometry (n=5)
Growth effects: GLM models

47% reduction in stunting

Growth Effect: change in LAZ, baseline (dashed) to endline (solid)

<table>
<thead>
<tr>
<th>Amino acid composition</th>
<th>% of infant amino acid requirements met by the egg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lulun egg</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>52</td>
</tr>
<tr>
<td>Tryptophan (mg)</td>
<td>110</td>
</tr>
<tr>
<td>Cystine (mg)</td>
<td>141</td>
</tr>
<tr>
<td>Methionine (mg)</td>
<td>225</td>
</tr>
<tr>
<td>Threonine (mg)</td>
<td>309</td>
</tr>
<tr>
<td>Valine (mg)</td>
<td>466</td>
</tr>
<tr>
<td>Isoleucine (mg)</td>
<td>367</td>
</tr>
<tr>
<td>Leucine (mg)</td>
<td>603</td>
</tr>
<tr>
<td>Tyrosine (mg)</td>
<td>288</td>
</tr>
<tr>
<td>Phenylalanine (mg)</td>
<td>377</td>
</tr>
<tr>
<td>Total Lysine (mg)</td>
<td>514</td>
</tr>
<tr>
<td>Histidine (mg)</td>
<td>168</td>
</tr>
</tbody>
</table>

1. Institute of Medicine, Dietary Reference Intakes for Energy, Carbohydrates, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids
2. Calculated based on median infant weights of 7.630 kg at baseline and 9.275 kg at endline in the Lulun study cohort
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Unit</th>
<th>Lulun Egg</th>
<th>% of RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>kcal</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>g</td>
<td>6.8</td>
<td>61.8</td>
</tr>
<tr>
<td>Lipids (total)</td>
<td>g</td>
<td>5.93</td>
<td>19.8</td>
</tr>
<tr>
<td>LA</td>
<td>g</td>
<td>0.71</td>
<td>15.4</td>
</tr>
<tr>
<td>ALA</td>
<td>g</td>
<td>0.02</td>
<td>4.0</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>g</td>
<td>0.57</td>
<td>0.6</td>
</tr>
<tr>
<td>Vitamin A, RAE</td>
<td>μg</td>
<td>54.5</td>
<td>10.9</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>μg</td>
<td>0.33</td>
<td>66.0</td>
</tr>
<tr>
<td>Folate, DFE</td>
<td>μg</td>
<td>15.1</td>
<td>18.9</td>
</tr>
<tr>
<td>Choline</td>
<td>mg</td>
<td>192.8</td>
<td>128.5</td>
</tr>
<tr>
<td>Vitamin E (α-tocopherol)</td>
<td>mg</td>
<td>1.9</td>
<td>38.0</td>
</tr>
<tr>
<td>Calcium</td>
<td>mg</td>
<td>30</td>
<td>11.5</td>
</tr>
<tr>
<td>Iron</td>
<td>mg</td>
<td>1</td>
<td>9.1</td>
</tr>
<tr>
<td>Magnesium</td>
<td>mg</td>
<td>6</td>
<td>8.0</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>mg</td>
<td>100</td>
<td>36.4</td>
</tr>
<tr>
<td>Potassium</td>
<td>mg</td>
<td>68</td>
<td>9.7</td>
</tr>
<tr>
<td>Selenium</td>
<td>μg</td>
<td>19</td>
<td>95.0</td>
</tr>
<tr>
<td>Sodium</td>
<td>mg</td>
<td>70</td>
<td>18.9</td>
</tr>
<tr>
<td>Zinc</td>
<td>mg</td>
<td>0.58</td>
<td>19.3</td>
</tr>
</tbody>
</table>
Biomarkers measured

• Amino acids, choline, betaine, TMAO, fatty acids, retinol, phosphatidyl cholines, sphingomyelins
  – LC-MS/MS, Washington University, St. Louis Metabolomics Core Facility

• Vitamin B12
  – Chemiluminescent immunoassay, NETLAB in Ecuador
## Effects on amino acids

<table>
<thead>
<tr>
<th>Effect size</th>
<th>(95% CI)</th>
<th>p-value</th>
<th>Corrected p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartic acid</td>
<td>0.43 (0.17,0.69)</td>
<td>0.001</td>
<td>0.021</td>
</tr>
<tr>
<td>Ornithine</td>
<td>0.41 (0.13,0.70)</td>
<td>0.005</td>
<td>0.052</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.35 (0.04,0.65)</td>
<td>0.028</td>
<td>0.143</td>
</tr>
<tr>
<td>Histidine</td>
<td>0.31 (-0.01,0.63)</td>
<td>0.054</td>
<td>0.158</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>0.31 (0.03,0.60)</td>
<td>0.034</td>
<td>0.143</td>
</tr>
<tr>
<td>Serine</td>
<td>0.28 (-0.06,0.61)</td>
<td>0.101</td>
<td>0.182</td>
</tr>
<tr>
<td>Proline</td>
<td>0.26 (-0.06,0.59)</td>
<td>0.113</td>
<td>0.182</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>0.26 (0.05,0.46)</td>
<td>0.013</td>
<td>0.091</td>
</tr>
<tr>
<td>Alanine</td>
<td>0.24 (-0.07,0.54)</td>
<td>0.130</td>
<td>0.182</td>
</tr>
<tr>
<td>Glycine</td>
<td>0.24 (-0.05,0.54)</td>
<td>0.105</td>
<td>0.182</td>
</tr>
<tr>
<td>Valine</td>
<td>0.24 (-0.05,0.53)</td>
<td>0.097</td>
<td>0.182</td>
</tr>
<tr>
<td>Leucine</td>
<td>0.23 (-0.07,0.52)</td>
<td>0.129</td>
<td>0.182</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>0.23 (-0.05,0.51)</td>
<td>0.109</td>
<td>0.182</td>
</tr>
<tr>
<td>Lysine</td>
<td>0.21 (-0.10,0.53)</td>
<td>0.187</td>
<td>0.231</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>0.13 (-0.16,0.42)</td>
<td>0.377</td>
<td>0.440</td>
</tr>
<tr>
<td>Threonine</td>
<td>0.09 (-0.20,0.38)</td>
<td>0.554</td>
<td>0.582</td>
</tr>
<tr>
<td>Citrulline</td>
<td>-0.05 (-0.30,0.23)</td>
<td>0.786</td>
<td>0.786</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>-0.10 (-0.37,0.16)</td>
<td>0.437</td>
<td>0.483</td>
</tr>
<tr>
<td>Glutamine</td>
<td>-0.21 (-0.42,0.01)</td>
<td>0.060</td>
<td>0.158</td>
</tr>
<tr>
<td>Asparagine</td>
<td>-0.21 (-0.43,0.01)</td>
<td>0.056</td>
<td>0.158</td>
</tr>
<tr>
<td>Arginine</td>
<td>-0.24 (-0.56,0.08)</td>
<td>0.141</td>
<td>0.185</td>
</tr>
</tbody>
</table>
## Effects on choline pathways & DHA

<table>
<thead>
<tr>
<th></th>
<th>Effect size</th>
<th>(95% CI)</th>
<th>p-value</th>
<th>Corrected p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatty acids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docosahexaenoic acid (DHA)</td>
<td>0.42</td>
<td>(0.13,0.71)</td>
<td>0.005</td>
<td>0.015</td>
</tr>
<tr>
<td>Linoleic acid (LA)</td>
<td>0.23</td>
<td>(-0.05,0.50)</td>
<td>0.108</td>
<td>0.162</td>
</tr>
<tr>
<td>Alpha-linolenic acid (ALA)</td>
<td>0.10</td>
<td>(-0.17,0.38)</td>
<td>0.459</td>
<td>0.459</td>
</tr>
<tr>
<td><strong>Choline pathways</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimethylamine</td>
<td>0.40</td>
<td>(0.11,0.71)</td>
<td>0.009</td>
<td>0.034</td>
</tr>
<tr>
<td>Choline</td>
<td>0.34</td>
<td>(0.11,0.55)</td>
<td>0.004</td>
<td>0.032</td>
</tr>
<tr>
<td>Trimethylamine-N-oxide</td>
<td>0.33</td>
<td>(0.07,0.58)</td>
<td>0.013</td>
<td>0.034</td>
</tr>
<tr>
<td>Betaine</td>
<td>0.29</td>
<td>(0.01,0.56)</td>
<td>0.041</td>
<td>0.082</td>
</tr>
<tr>
<td>Dimethylglycine</td>
<td>0.03</td>
<td>(-0.20,0.27)</td>
<td>0.769</td>
<td>0.772</td>
</tr>
<tr>
<td>Trimethylamine</td>
<td>-0.04</td>
<td>(-0.4,0.26)</td>
<td>0.772</td>
<td>0.772</td>
</tr>
</tbody>
</table>
Pathways mediating the growth effect

Difference in LAZ: 0.63 (0.38, 0.88), p<0.001
Mediation analysis

Difference in LAZ: 0.63 (0.38, 0.88), p<0.001

15% of the effect of the intervention on LAZ could be attributed to choline (p=0.007)
Mediation analysis

Difference in LAZ: 0.63 (0.38, 0.88), p<0.001

15% of the effect of the intervention on LAZ could be attributed to choline (p=0.007)
4.5% of the effect attributed to DHA (p=0.07)
Mediation analysis

Difference in LAZ: 0.63 (0.38, 0.88), p<0.001

15% of the effect of the intervention on LAZ could be attributed to choline (p=0.007)
4.5% of the effect attributed to DHA (p=0.07)
4.2% of the effect attributed to histidine (p=0.10)

Combined: 24% of the effect attributed to choline, DHA, and histidine together
Choline

- Conditionally essential nutrient. Requirements are higher during pregnancy and early infancy.
- Intrinsic to the neurotransmitter acetylcholine and plays an important role in the development of the hippocampus, critical for declarative memory formation.
- Involved in the one-carbon metabolic cycle for DNA methylation and may be particularly important in the context of B12 deficiency.
Docosahexaenoic acid (DHA)

- Long-chain polyunsaturated omega-3 fatty acid
- Can be produced in a series of elongation, desaturation, and β-oxidation steps from alpha-linolenic acid (ALA)
- Predominant omega-3 PUFA in the brain
- Neurogenesis, neurotransmission, myelination, synaptic plasticity, among other functions
Summary

• Lulun Project showed a significant effect on LAZ (0.63) and stunting reduction (47%)
  – Comparatively much larger than the global average for other CF interventions

• Biomarker analyses suggest important pathways affected
  – Choline pathways, several amino acids, and DHA
New Project: The Mazira Study
Study area: Lungwena, Mangochi District
Research Objectives

1. To evaluate the impact of eggs on child growth and prevalence of stunting
2. To explore the metabolic pathways through which eggs may improve growth and development
3. To explore the effect of eggs on gut health and the microbiome
4. To evaluate the effect of eggs on child development
Study Design

• Randomized controlled trial with 2 groups
  – **Egg group:** 1 egg per day for 6 months of time
  – **Control group:** Usual diet with a delayed intervention food basket after 6 months

• N=331 children per group
Future interests

• Proof of concept of the effects of eggs during pregnancy on maternal nutrition, birth weight and infant growth

• Examine the effectiveness of an enhanced village poultry production and behavioral change communication/social marketing model on:
  – Flock size and egg production
  – Viral and bacterial pathogen exposures associated with poultry production
  – Egg consumption among women and young children
  – Child growth and development
  – Improved livelihoods and empowerment among women
Conclusions

• Eggs are among nature’s first foods, providing a holistic package of nutrients and other bioactive factors
  – Eggs were integral to our evolutionary history

• Eggs may be a locally available and feasible option for poor households, with uncracked potential to address the most salient issues of undernutrition
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UC-Davis
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Rebecca Young

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Chessa Lutter

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Gregory Reinhart
Ana Palacios

University of Malawi
College of Medicine
Ken Maleta

Community of Pastocalle

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