Long-Term Effects of an Early Life Intervention in Guatemala

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Millennium Development Goal 2: Achieve Universal Primary Education

Target
Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary education

Why do we care about schooling?

• Importance for child health and nutrition
• Gender equity and empowerment
• Long term health benefits to individuals
• Earnings

The average rate of return to income of another year of schooling

<table>
<thead>
<tr>
<th>Region</th>
<th>Rate of Return</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latin America &amp; Caribbean</td>
<td>12.0%</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>11.7%</td>
</tr>
<tr>
<td>Asia</td>
<td>9.9%</td>
</tr>
<tr>
<td>World average</td>
<td>10.0%</td>
</tr>
</tbody>
</table>


Gestation and the first 2 years of life represent a window of vulnerability for human development

• High nutritional requirements
• Rapid growth and development
• Greater susceptibility to infections
• Fully dependent on others for care

Height for age by region, children < 5 years

Human brain development

INCAP
Instituto de Nutrición de Centro América y Panamá

INCAP longitudinal study, 1969-77

- Community-randomized supplementation trial (2 large and 2 small villages).
- Two villages (1 large, 1 small) received Atole, a nutritious supplement made from Incaparina, milk and sugar, and two (1 large, 1 small) received Fresco, a less nutritive drink.

Children included in the Longitudinal Study (1969-77)

- All children < 7 y in 1969 were followed until they turned 7 y or to the study end.
- All newborns were followed until they turned 7 y or to the study end.
- Mothers included during pregnancy and lactation.

Impact on total nutrient intakes and on growth

- Supplement and home dietary intakes measured.
- Total diets of young children < 3 y from Atole villages were greater by 9 g of protein, 100 kcal/day and in micronutrients when compared to diets of children from Fresco villages.
- Length was increased by 3 cm in Atole vs. Fresco but only in the first three years of life.
The preschool battery of the 1969-77 longitudinal study*

Preschool battery (cognitive development as well as Piagetian concepts).
- 10 tests given annually to all children 3-7 yrs of age.
- 12 tests given annually to all children 5-7 yrs of age.

Factor analysis
- Factor 1: General perceptual – organizational (embedded figures, incomplete figures, odd figures, block design, memory for designs) and verbal (verbal analogies, memory for objects, vocabulary recognition) factor.
- Factor 2: Memory (digit, sentence)

Comment about effects seen in preschool children in the 1969-77 longitudinal study

“…there were a few moderately beneficial effects from exposure to the Atole supplement”

Specific studies emphasized in this presentation
- Longitudinal study 1969-77 (children < 7 yrs; n = 2392)
- Follow-up study 1988-89 (youth 11-26 yrs; n = 1574; included migrants to nearby villages and Guatemala City)
- Nutrition, human capital and economic productivity, 2002-2004 (adults 25-40 years; n = 1560; migrants to anywhere in the country)

Definition of cohorts based on timing of exposure to supplementation

<table>
<thead>
<tr>
<th>Cohort number</th>
<th>Birth cohorts</th>
<th>Exposure period</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>≥ 1 Mar 1974</td>
<td>Gestation, partial birth to 3 y</td>
</tr>
<tr>
<td>II</td>
<td>1 Mar 1969 – 28 Feb 1974</td>
<td>Partial during gestation, all birth to 3 y</td>
</tr>
<tr>
<td>III</td>
<td>1 Jan 1966 – 28 Feb 1969</td>
<td>Partial birth to 3 y</td>
</tr>
<tr>
<td>IV</td>
<td>≤ Jan 1966</td>
<td>No exposure during gestation or birth to 3 y</td>
</tr>
</tbody>
</table>

The 1988-89 Follow-up Study results
- Impact largest and more consistent for Cohort II
- Youth in Atole villages taller, greater fat free mass and greater work capacity (males).
- Performance on tests of knowledge, numeracy, reading, comprehension and vocabulary better in Atole villages.

The 1988-89 Follow-up subjects were 11 to 26 years and this limited our ability to properly assess human capital formation and to link it to economic productivity
- Some had not yet finished growing.
- Some had not yet finished studying.
- Some had not chosen an occupation.
- Some had not yet married or formed unions


Human Capital Study
2002-04: age ≈ 32 years

• Original sample: 2393

• Possible sample: 1856*, **

• Achieved: 1560 (84 % )

* Subjects living in Guatemala in 2002.
** 272 died, mostly in early childhood, 163 left the country, 102 were lost to follow up.

Analytic approach of the Human Capital Study (2002-04)

• Less emphasis on four birth cohorts (e.g. Cohort II)

• Focus on testing “windows of exposure” using all subjects to estimate double-differences

Double-difference estimate for exposure from 0-36 months of age

Average outcome for those exposed to atole 0–36 m completely – Average outcome for those exposed to fresco 0–36 m completely

Average outcome for those NOT exposed to atole 0–36 m completely – Average outcome for those NOT exposed to fresco 0–36 m completely

Example: assessing exposure to either Atole or Fresco from 0-36 months

Birth Year


Intervention period

Children too old for exposure from 0–36 m

Children exposed from 0–36 m

Children too young for exposure from 0–36 m

Human Capital measures

• Schooling

• Intelligence (Raven test)

• Reading ability (Inter-American Reading test)
Exposure to improved nutrition from 0–3 years of age and education (n=1471)†

• Schooling: Effects found in women only
  – Improved by 1.2 years (36% of SD)

• Reading: Effects found in men and women
  – Improved scores by 28% of SD++

• Cognition: Effects found in men and women
  – Improved Raven scores by 24% of SD+++


++ Raven Progressive Matrices

+++ Inter-American Reading Series

Impact of exposure to atole during early life on income (in US$) earned per hour; n = 602 men; age ~32 years*

Long term effects of a nutrition intervention carried out in Guatemala in 1969-77

Improved nutrition before, but not after 3 years of age, increased wages in men by 46% and annual incomes by $914

Hoddinott, Maluccio, Behrman, Flores and Martorell. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults (The Lancet, 2008).


• 20 million people died in the 1959-62 famine in China (Great Leap Forward)

• Survivors born in 1959-62 (exposed early in life) were compared to cohorts born before or after the famine.

• Famine exposure in early life was associated with a reduction in:
  – Adult height, 3 cm
  – Annual per capita income, 3% lower.

Is there a tradeoff from improving nutrition in malnourished infants between

- improved human capital (IQ, schooling, income, etc.)
- but poor adult health (increased cardiovascular disease risk, abdominal obesity, etc.)?
Conclusion
Interventions designed to address nutrient deficiencies and ameliorate stunting that are targeted at pregnant women and young children are unlikely to increase cardiovascular disease risk later in life and may instead lower the risk.

Intergenerational Effects (Behrman, Calderón, Preston, Hoddinott, Martorell & Stein; AJCN, 2009)
- Offspring of women exposed to Atole (vs. Fresco) were heavier at birth (116g) and were taller (1.3 cm) and had greater head circumferences (0.6 cm) in childhood. No effects on measures of adiposity. Effects were greater in sons.
- Father’s exposure to the supplements in early life, on the other hand, did not influence their offspring’s characteristics.

Cohorts meeting in South Africa

- Review of the literature and original analyses of 5 cohorts (Brazil, Guatemala, India, Philippines and South Africa).
- Poor fetal growth or stunting in the first two years of life linked to irreversible damage including:
  - shorter adult height
  - lower attained schooling
  - reduced adult income
  - decreased offspring birthweight
- Striking consistency of relationships across sites.
Rapid Weight Gain After Being Undernourished Increases Chronic Disease Risk as Adults

Children whose early growth is restricted and gain weight rapidly later in later childhood are more likely to have high blood pressure, diabetes and both cardiovascular and metabolic disease.

No evidence that rapid weight or length gain in first 2 years increases risk of chronic disease later in life.

By supporting early nutrition and growth, incidence of chronic disease could be reduced.

Statistical models

- Used conditional weight gain variables (0-2 and 2-4 y) that were uncorrelated with each other and with birthweight.
- The basic model adjusted for site (except for age at school entry) and sex.
- The fully adjusted model also included household socioeconomic status (when participants were children), maternal years of schooling and whether the subject was still in school (for highest grade attained).

Growth and schooling (Martorell, Horta, Adair et al, J. Nut. 140: 348-354)

- Analyses of the relative importance of birthweight and weight gain between 0-2 y and 2-4 y for three schooling outcomes.
  - Highest grade attained
  - Ever failed a grade
  - Age at school entry

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**Highest grade (y) attained by study site**

<table>
<thead>
<tr>
<th>Yrs</th>
<th>Brazil (Pelotas)</th>
<th>Guatemala (4 villages)</th>
<th>India (New Delhi)</th>
<th>Philippines (Cebu)</th>
<th>South Africa (Soweto)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>13.5</td>
<td>10.8</td>
<td>2.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*+ 43% of participants still in school
++ Almost all participants in school*

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**% stunted (< -2 HAZ) at 2 y, by site**

<table>
<thead>
<tr>
<th>%</th>
<th>Brazil (Pelotas)</th>
<th>Guatemala (4 villages)</th>
<th>India (New Delhi)</th>
<th>Philippines (Cebu)</th>
<th>South Africa (Soweto)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12%</td>
<td>86%</td>
<td>47%</td>
<td>68%</td>
<td>27%</td>
<td></td>
</tr>
</tbody>
</table>

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**Years of increased schooling associated with a standard deviation shift in birth weight and conditional weight gain (0-24 and 24-48m)**

<table>
<thead>
<tr>
<th>coefficient</th>
<th>Birth weight</th>
<th>Weight gain 0-24 m</th>
<th>Weight gain 24-48 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.21, p&lt;0.05</td>
<td>0.43, p&lt;0.05</td>
<td>0.07 (N.S.)</td>
<td></td>
</tr>
</tbody>
</table>

One standard deviation (z) of birth weight = 0.5 kg
weight gain (0-24m) = 0.7 kg
weight gain (24-48m) = 0.9 kg

Martorell et al., 2010
Relationship between stunting at age 2y (1=yes, 0=no) and schooling outcomes in pooled analyses from 5 cohorts**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Coefficient</th>
<th>95% C.I.</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest grade attained (y)</td>
<td>-0.92</td>
<td>-1.08, -0.76</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Ever failed a grade (1=yes, 0=no)</td>
<td>1.20</td>
<td>1.04, 1.39</td>
<td>0.004</td>
</tr>
</tbody>
</table>

** Adjusted for SES and maternal education; Martorell et al, 2010
+++ According to the economic literature, the average rate of return to income of another year of schooling is 10% (Psacharopoulos & Patrinos, 2004)

The findings from our intervention study in Guatemala do not provide the full measure of the impact of nutrition

- The intervention had a modest impact on complementary feeding intakes
- There was no WASH intervention component
- There was substantial stunting remaining among children receiving Atole; micronutrient deficiencies, such as in iron, were also probably common among Atole children
- On the other hand, breastfeeding was common although not practiced exclusively

Breastfeeding and cognitive development score: a meta-analysis of differences with respect to formula feeding*

<table>
<thead>
<tr>
<th>Benefit**</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>5.3</td>
</tr>
<tr>
<td>Adjusted</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>4.5, 6.1</td>
</tr>
<tr>
<td></td>
<td>2.4, 4.0</td>
</tr>
</tbody>
</table>

** Before and after adjustment for confounding


- Available reports are mostly based on observational data. Although these studies consistently show benefits in cognition, residual confounding remains an issue.
- A large cluster-randomized trial of breastfeeding (BF) promotion was conducted in Belarus (Kramer et al, 2008).
- Exclusive BF at 3 mo was 43% for the experimental and 6% for the control group (P<.001). At 6 mo, exclusive BF was 49.8 vs. 36.1%. Duration of any BF was increased.
- Enten to treat analysis: At age 6.5 years, verbal, performance and full IQ (Wechsler) were 7.5, 2.9 and 5.9 IQ points higher, respectively, in the experimental group (all significant)

Possible mechanisms for effects of breastfeeding on cognitive development (Kramer et al, 2008)

- Some constituent of breast milk (e.g. DHA, insulin like growth factor I)
- Physical and social interactions inherent in breastfeeding (might trigger epigenetic changes, as found in animal studies, or might simply increase verbal interaction).
Programs in health and nutrition aimed at women and young children

Better growth and development

Improved Human Capital

Increased Productivity

Repositioning nutrition as central to development (World Bank, 2006)

According to the World Bank (2006), good nutrition is not only a matter of welfare or human rights…it is an economic investment…an engine of economic growth.