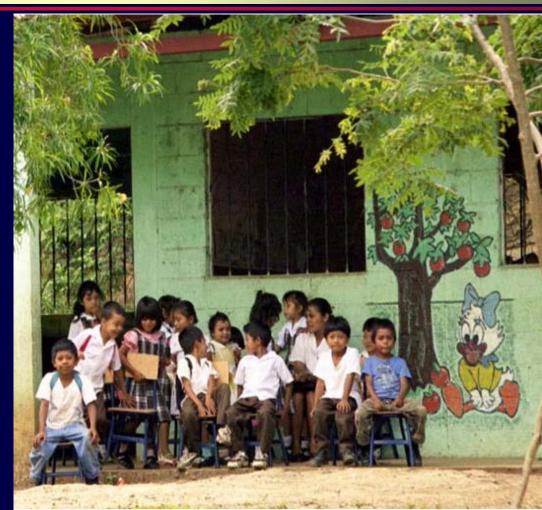
Early Growth and Adult Health and Human Capital: Pooled Analyses from Five Cohorts from Developing Countries

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On behalf of the INCAP and COHORTS Groups



The first 1000 days of life represent a window of vulnerability for human development

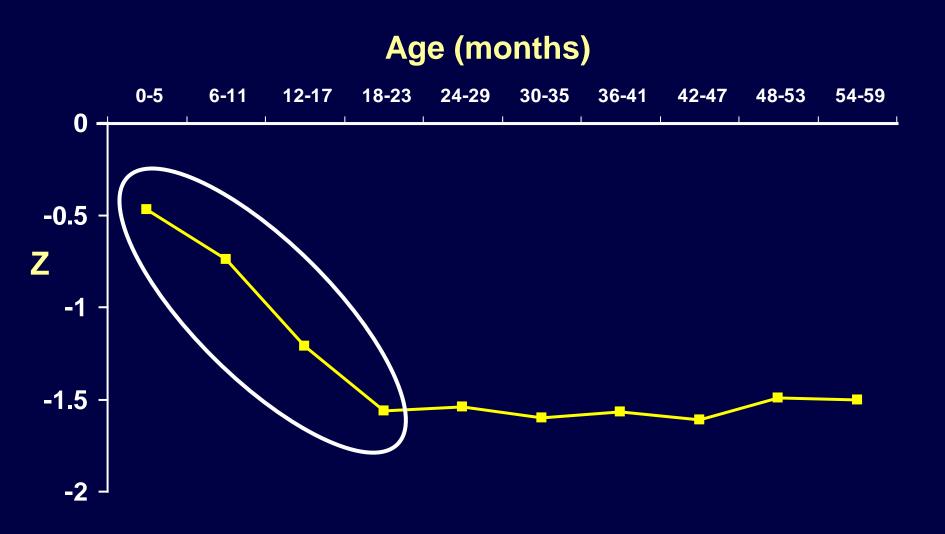
- High nutritional requirements
- Rapid growth and development, including brain growth
- Greater susceptibility to infections
- Fully dependent on others for care



Mean Z-scores for height-for-age relative to the 2006 WHO standards for Peru, 2000



Mean Z-scores for height-for-age relative to the new WHO standards for Peru, 2000







Consortium of Health Orientated Research in Transitioning Societies

Brazil Guatemala India Philippines South Africa

INCAP longitudinal study, 1969-77

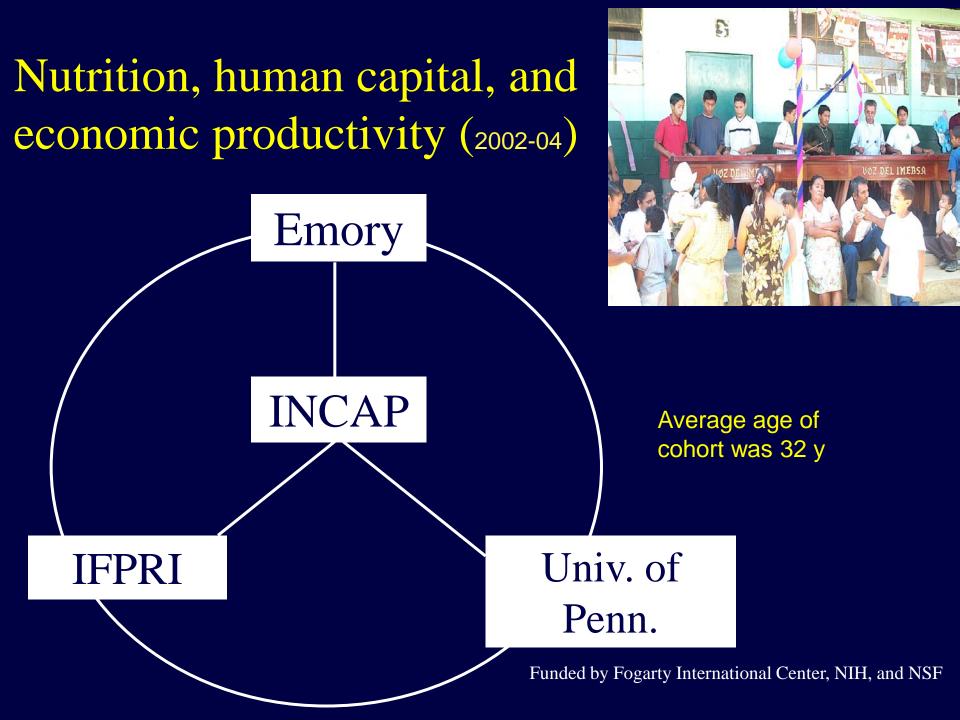
- Community-randomized supplementation trial (2 large and 2 small villages).
- Two villages (1 large, 1 small) received
 Atole, a nutritious supplement made from
 Incaparina, milk and sugar, and two (1
 large, 1 small) received Fresco, a less
 nutritive drink
- Included all children 7 y or younger in 69 and all births 69-77



Martorell R, Habicht J-P, Rivera JA. History and design of the INCAP longitudinal study (1969-77) and its follow-up (1988-89). Journal of Nutrition 125(Suppl. 4S):1027S-1041S, 1995.

Impact on total nutrient intakes and on growth

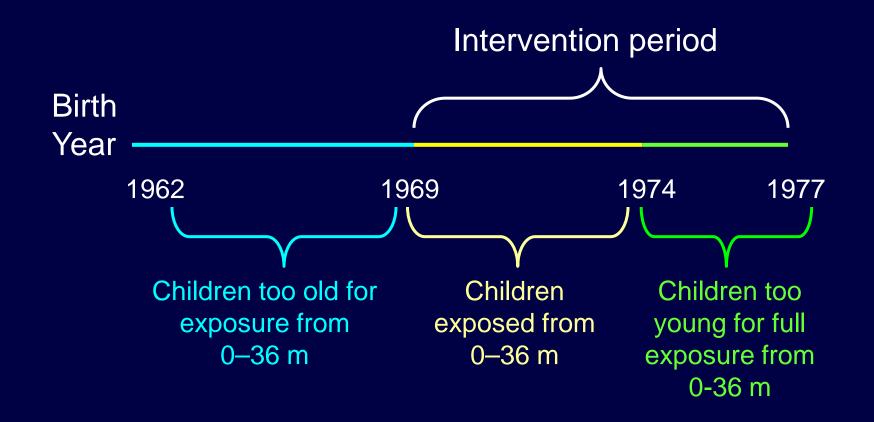
- Supplement and home dietary intakes measured
- Total diets of young children < 3y from Atole villages were greater by 9 g of protein, 100 kcal/day and in micronutrients when compared to diets of children from Fresco villages.
- Length was increased by 3 cm in Atole vs. Fresco but only in the first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



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

- Exploits the fact that children were exposed to the supplements at various ages depending on birthdates
- Focus on testing effects for "windows of exposure" using all subjects to estimate double-differences

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



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

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

Average outcome for those NOT ____ exposed to *atole* 0-36 m completely

Average outcome to fresco 0–36 m completely

Average outcome for those NOT exposed to *fresco* 0-36 m completely

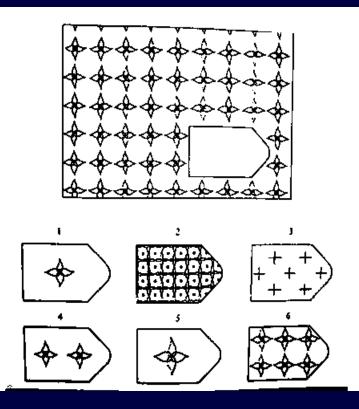
Control variables

- Individual level: age (cohort effects) ; stratified by sex
- Family : SES, parental schooling, mother's age and height

•Community : village fixed effects; historical demographic , social and economic changes in relationship to when the individuals were 7 or 18 y old (e.g. student /teacher ratios when 7y old; producer prize of maize when 18 y old).

Human Capital measures

- Schooling
- Intelligence (Raven test)
- Reading ability (Inter- American Reading test)



Exposure to improved nutrition from 0-3years of age and education $(n=1471)^+$

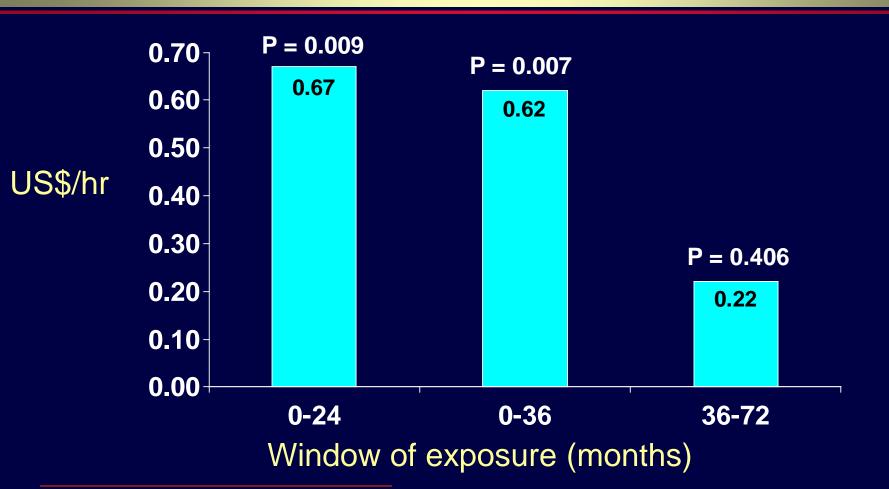
- Schooling: Effects found in women only

 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⁺⁺⁺
- Maluccio J, Hoddinott J, Behrman JR, Martorell R, Quisumbing A, and Stein A. The impact of improving nutrition during early childhood on education among Guatemalan adults . The Economic Journal, 119:734-763. 2009.
 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⁺



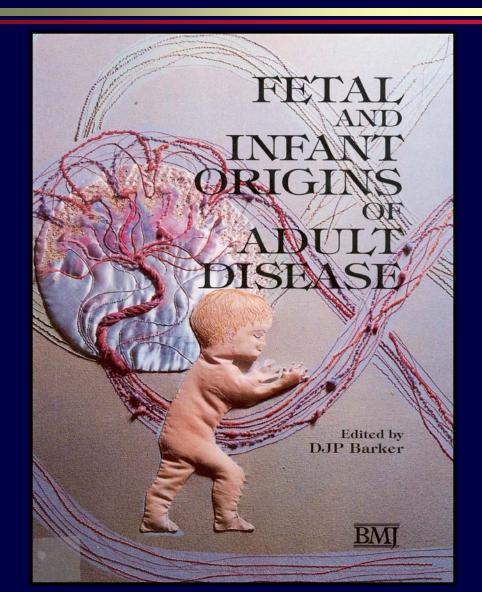
+ Hoddinott, Maluccio, Behrman, Flores and Martorell. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults (The Lancet, 2008).

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?

Stein AD, Wang M, Ramirez-Zea M, Flores R, Grajeda R, Melgar P, Ramakrishnan U, Martorell R. Exposure to a nutrition supplementation intervention in early childhood and risk factors for cardiovascular disease in adulthood: evidence from Guatemala. *Am J Epidemiol 2006*; 164:1160-1170.



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.

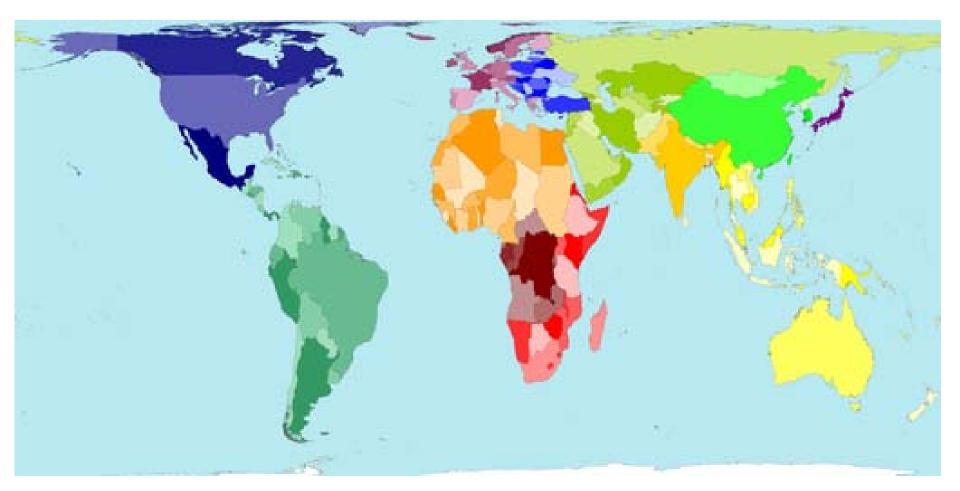




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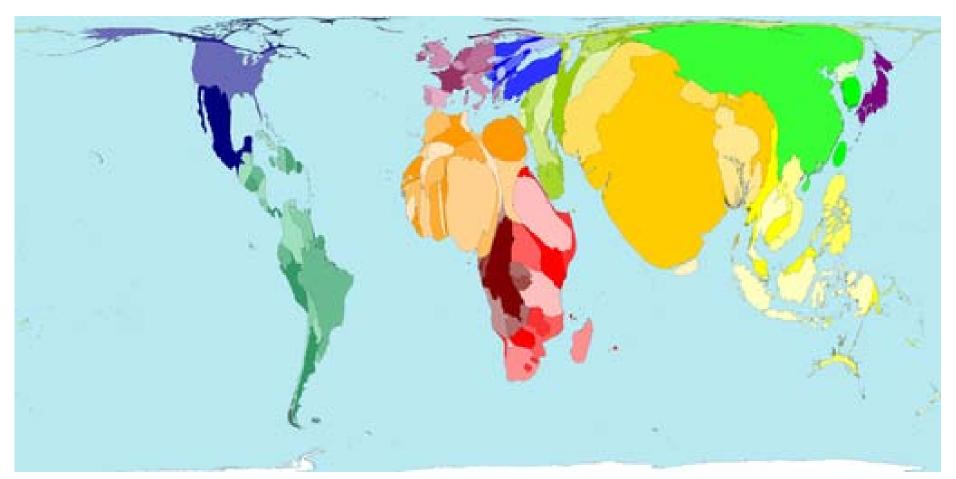
Brazil Guatemala India Philippines South Africa

Land area



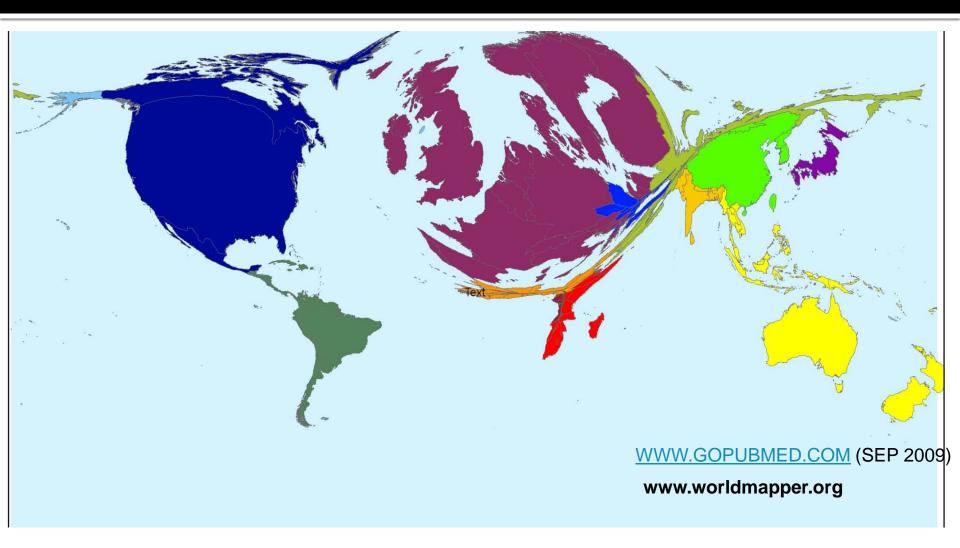
Source: www.worldmapper.org

Total births, 2000



Source: www.worldmapper.org

Birth cohort publications



Why do we need cohorts in LMICs?

- Higher frequency of some exposures (and lower frequency of others)
- Different nature of some exposures
- Different confounding patterns
- Marked social disparities within LMIC cohorts
- LMIC cohorts growing up under the epidemiological and nutrition transitions
 High potential for "mismatch"

Sample

Study	Cohort inception	Who was enrolled?
Pelotas Brazil	1982	Births during 1982. All social classes
INCAP Nutrition Trial Cohort Guatemala	1969-77	Participants in nutrition supplementation intervention trial in 4 rural villages
New Delhi Birth Cohort Study India	1969-72	Births to married women from defined area of Delhi. Primarily middle-class
Cebu Longitudinal Health & Nutrition Survey Philippines	1983-84	Births in 33 randomly selected communities of Metro Cebu; 75% urban. All social classes
Birth to 20 South Africa	1990	Infants from a delimited urban area (Soweto, Johannesburg). Predominantly poor, black

Richter et al., IJE 2011

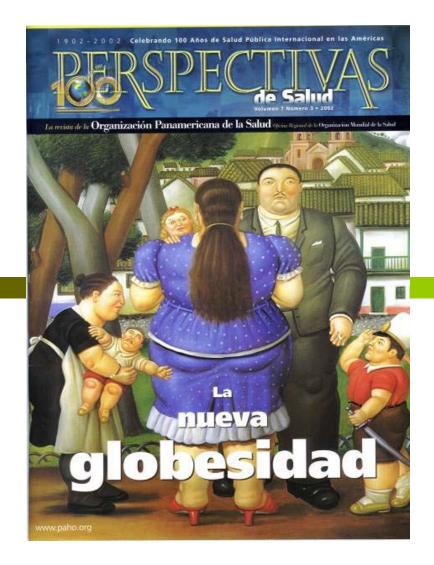
Phase I : How do birth weight and stunting size at age 2 yr relate to young adult health and human capital ?

Consequences for Adult Health and Human Capital



CG Victora, L Adair, C Fall, PC Hallal, R Martorell, L Richter, HS Sachdev and Maternal and Child Undernutrition Study Group

(The Lancet, Jan 2008)



Phase II: Early growth and adult outcomes

- Human Capital
- Adult Health

COHORTS III will focus on the physical and social environment in early childhood



- How it relates to early childhood growth.
- Its relationship with adult indicators of health and capacity.
- How it moderates relationships between growth in the first two years of life and adult indicators of health and capacity.

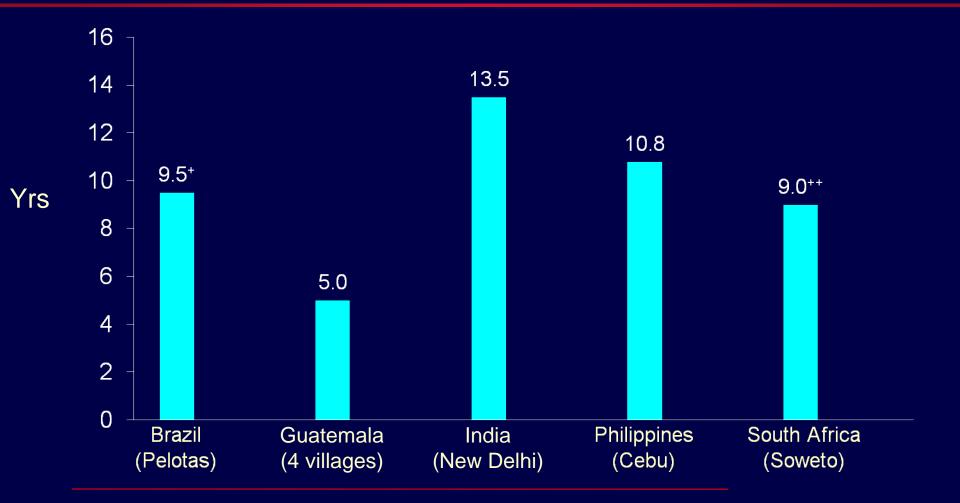
Phase II : Schooling analyses

What is the relative importance of birthweight and weight gain between 0-2 y and 2-4 y for schooling outcomes?

Highest grade attained

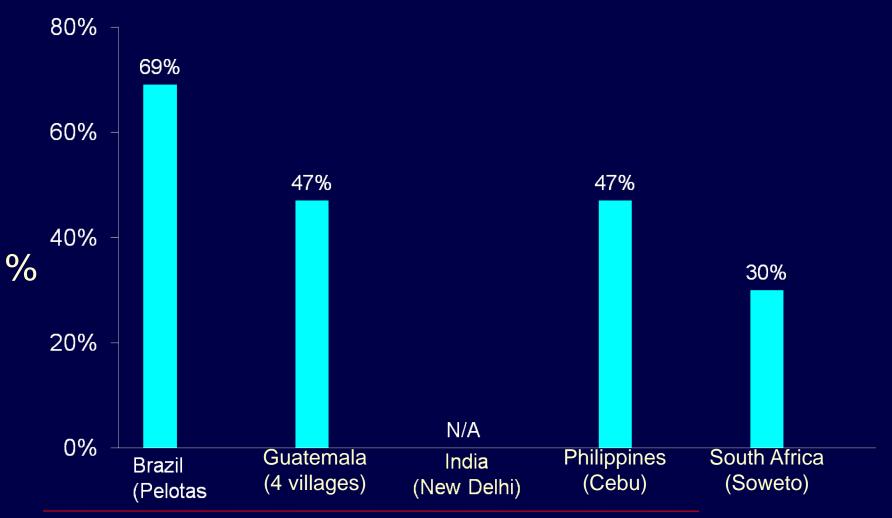
- Ever failed a grade

Highest grade (y) attained by study site



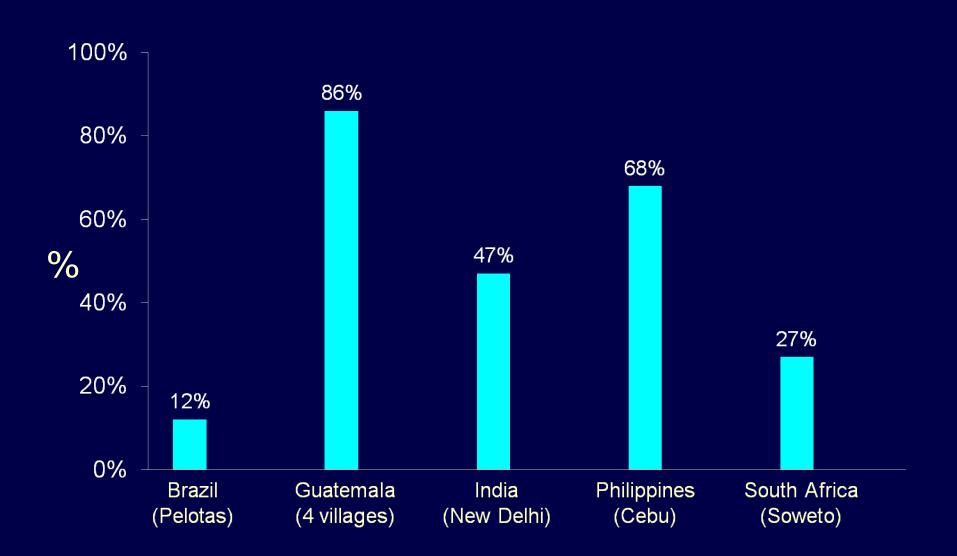
+ 43% of participants still in school ++ Almost all participants in school

Ever failed a grade (%) by site



+ N/A = Not Available

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



Methods

- Used conditional weight gain variables (0-2 and 2-4 y) that were uncorrelated with each other and with birthweight.
- Tested for interactions with sex and found none.
 Therefore, results for males and females were pooled.
- No significant interactions by site for highest grade attained and ever failed a grade. Therefore, these analyses were pooled by site.

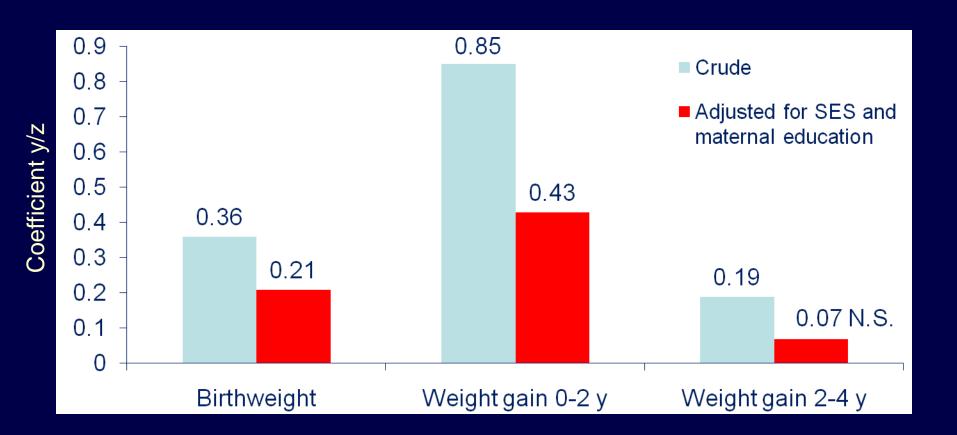
Data availability

- Brazil, Guatemala and the Philippines provided data for all schooling outcomes.
- Data for *highest grade attained* were not included for South Africa because virtually all were still in school, providing little variability.
- Only highest grade attained was available for New Delhi.
- Weight measures were available for all sites. Birth length was not available for South Africa and Brazil.
 Used weight measures as the exposure variables.

Statistical models

- 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).

Years of increased schooling associated with a standard deviation shift in birth weight and conditional weight gain (0-2y and 2-4y) in 5 cohort studies



One standard deviation (z) of birth weight =0.5 kg weight gain (0-2 y) = 0.7 kg weight gain (2-4y) = 0.9 kg

Martorell et al., 2010

Reduced probability of failing a grade associated with a standard deviation shift in birth weight and conditional weight gain (0-2 and 2-4 y) In 5 cohort studies

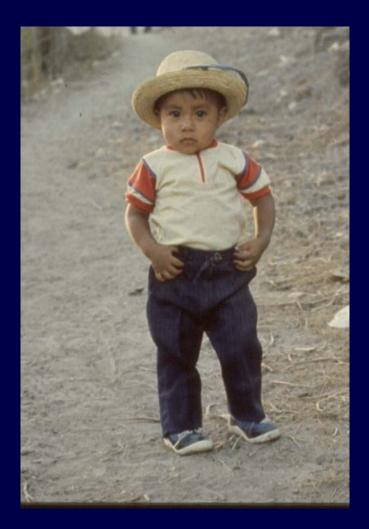
	Reduction in probability in failure			
Variable (z)	<u>Crude</u>	Adjusted +		
Birthweight	11%	8%		
Weight gain 0-2 y	21%	12%		
Weight gain 2-4 y	5%	2% (N.S.)		

+ Adjusted for maternal schooling and SES status (Martorell et al, 2010)

Conclusions about schooling

 Growth from 0-2 y had the strongest associations with schooling, followed by birthweight. Growth from 2-4 y had little relationship to schooling.

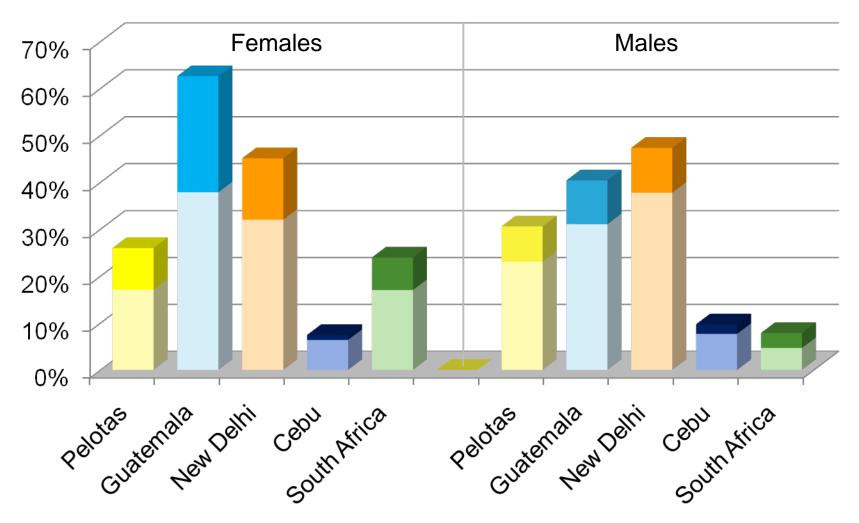
Catch-up growth form 0-2 yin smaller babies benefits schooling.



Is there a trade off between human capital and adult health if investment is made in improving nutrition during gestation and the first two years of life?

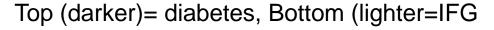
- Promotion of good nutrition in early life is essential for health later in life because either undernutrition or overnutrition can cause lifelong, irreversible damage" Cesar Victora (Lancet, Oct 2009).
 - "...interventions in early life aimed at essential short term gains, such as infant survival, could have longer term effects on individuals throughout their life-course , and such outcomes might not always be beneficial" Gluckman et al (Lancet, May 2009).

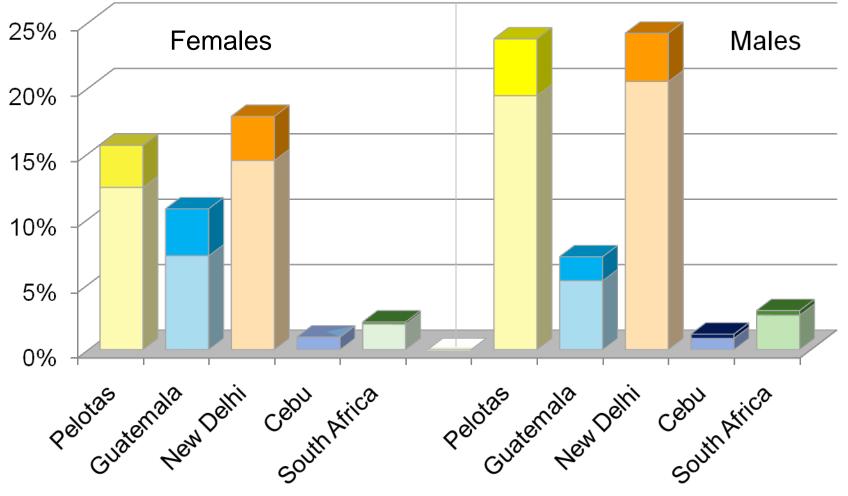
Prevalence of overweight (BMI>25*) and obesity (BMI>30*)



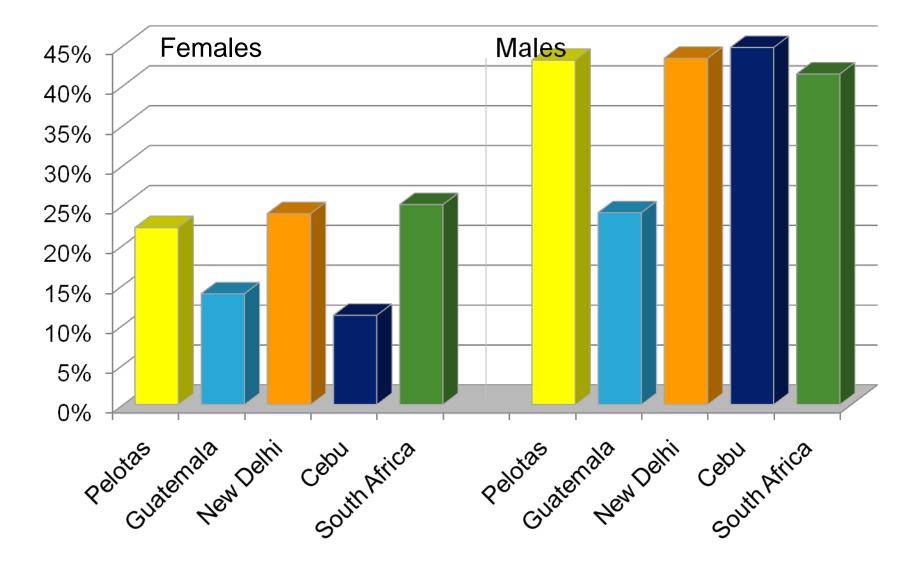
* or >IOTF cupoint if age<18

Prevalence of impaired fasting glucose (>6.1 mmol/ml) or diabetes (>7.0 mmol/ml)





Prevalence of Pre-Hypertension + Hypertension (SBP>130 or DBP>85)



Cardiometabolic outcomes

	Logistic Regression Models			Linear Regression Models	
	Diabetes (OR, 95% CI)	IFG+diabetes (OR, 95% CI)	P/HTN (OR, 95% CI)	Fat mass (effect size)	Lean mass (effect size)
BW	0.88 (0.76-1.01)	0.92 (0.86-0.99)	0.95 (0.90-1.01)	0.15 (0.14-0.16)	0.26 (0.25-0.27)
0-24	0.80 (0.68-0.95)	0.97 (0.89-1.05)	1.12 (1.06-1.18)	0.32 (0.31-0.33)	0.41 (0.39-0.42)
24-48	0.93 (0.79-1.10)	0.99 (0.92-1.07)	1.19 (1.13-1.26)	0.34 (0.33-0.36)	0.36 (0.35-0.37)
48- adult	1.30 (1.14-1.48)	1.29 (1.20-1.38)	1.63 (1.54-1.72)	0.74 (0.73-0.75)	0.68 (0.67-0.69)

Outcomes regressed on CW in 4 age periods, adjusted for sex, site and SES covariates

Conclusions about analyses of weight gain, and adult body composition, blood pressure, IFG/ diabetes)

- Early childhood weight gains are less detrimental than late childhood/adolescent weight gains, and can even be beneficial for some outcomes...likely because early weight gain is more related to higher lean mass
- Later weight gains are consistently associated with adverse outcomes... *likely because they are associated with greater* gains in **fat mass**
- There are beneficial effects of weight gain for short-term morbidity and mortality, as well as for long-term gains as schooling.

Pelotas Cohort Study Cesar G. Victora, Pedro C. Hallal, Fernando C. Barros, Bernardo L Horta and Denise P Gigante Universidade Federal de Pelotas



Birth to Twenty Linda Richter Human Sciences Research Council, Durban, South Africa Shane A. Norris, Daniel Lopez and Mathew Mainwaring Department of Paediatrics, MRC Mineral Metabolism Research Unit, University of the Witwatersrand, Johannesburg, South Africa

New Delhi Birth Cohort Study Santosh K. Bhargava Sunder Lal Jain Hospital, New Delhi, India Harshpal S. Sachdev Sitaram Bhartia Institute of Science and Research, New Delhi, India Caroline Fall, Clive Osmond MRC Epidemiology Resource Centre, University of Southampton, Southampton, UK Andrew Wills: MRC Unit for Lifelong Health and Ageing,

INCAP Nutrition Trial Reynaldo Martorell, Aryeh D. Stein Emory University Manuel Ramirez-Zea Institute of Nutrition of Central America and Panama, Guatemala City



COHORTS analysis funded by the Wellcome Trust Nutrition Survey Linda S. Adair University of North Carolina at Chapel Hill Judith Borja and Nanette Lee Office of Population Studies Foundation, University of San Carlos Cebu, Philippines Chris Kuzawa and Thom McDade Northwestern University Darren Dahly





