The impact of improving nutrition during early childhood on cognitive skills over the life course

PRE-ANALYSIS PLAN

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1. RESEARCH QUESTION

This study assesses whether exposure to a nutrition supplementation trial in early life improves cognitive skills over the life course. We assess whether: (a) results are sensitive to how cognitive skills are measured; and (b) changes in cognitive skills during adulthood are affected by early life exposure to this supplementation trial.

2. STUDY DESIGN AND SAMPLE

In the mid-1960s, protein deficiency was seen as the most important nutritional problem facing the poor in developing countries, and there was considerable concern that this deficiency affected children's ability to learn. The Institute of Nutrition of Central America and Panama (INCAP) was the locus of a series of studies on this subject, leading to the implementation of a nutritional supplementation trial that began in rural eastern Guatemala in 1969. Two sets of village pairs (one pair of "small" villages with about 500 residents each and another pair of "large" villages with about 900 residents each) - similar in terms of a variety of nutritional, social, and economic outcomes – were identified as sites for the study. Two of the villages, one from within each pair matched on population size were (based on a coin flip) randomly assigned to receive as a dietary supplement a high protein-energy drink called *atole*. In the remaining villages, an alternative supplement, *fresco*, was provided. The nutritional supplements (i.e., *atole* or *fresco*) were distributed in each village in centrally-located feeding centres and were available twice daily, to all members of the village on a voluntary basis, for two to three hours in the mid-morning and two to three hours in the mid-afternoon, times selected to be convenient to mothers and children, but that did not interfere with usual meal times. All residents of all villages also were offered high quality curative and preventative medical care free of charge throughout the intervention. Preventative services, including immunization and antiparasites campaigns, were conducted simultaneously in all villages. To ensure that the results were not systematically influenced by the characteristics of the health, research, or survey teams, all personnel were rotated periodically throughout the four villages.

From 1969 to 1977, INCAP implemented the nutritional supplementation trial and medical care. While the supplement was freely available to all village residents (as described above), the associated observational data collection focused on children between zero and seven years of age at any point during the intervention period. Thus, our population of interest are individuals who were under seven years of age residing in the villages at the start of the intervention, as well as those born in the villages during the intervention, a total of 2392 individuals.

Subsequent to the completion of the nutrition supplemental trial, four surveys were fielded that traced and interviewed these individuals. These surveys took place in 1988-89 (when

participants were 11-26 years of age), 2002-04 (when participants were 26-42y), 2015-2017 (when participants were 38-54y), and 2024-26 (when participants were 47-63y). When analyzing data from each round, we: (a) use all data available from that round (to maximize sample size); and (b) restrict the sample to individuals appearing in all rounds (to address concerns about how changes in sample composition across rounds might affect our results).

3. TREATMENT AND CONTROLS

Black et al (2013) emphasize that the first two years of life are critical for children's physical and neurological development. Accordingly, we define treatment as being exposed to the *atole* supplement at any point between birth and two years of age. Controls consist of: (a) children exposed to *fresco* at any point between birth and two years of age; and (b) children outside this age range who lived in a village receiving either *atole* or *fresco*. As such, we estimate intent-to-treat (ITT) effects.

We note that these four study villages were a minimum of 10 kilometers apart at a time when road networks and public transport were minimal. For this reason, not surprisingly, we have no evidence that children in fresco villages travelled to an *atole* village to consume the *atole* supplement; put differently, there is no evidence of treatment spilling over to controls.

4. OUTCOMES

Our primary outcome is the percent correct answers on Raven's Progressive Matrices tests administered during the 1987-88, 2002-04, 2015-17, and 2024-26 survey rounds.

We have two sets of secondary outcomes: (a) percent correct answers on reading comprehension and vocabulary as measured by the *Serie Interamericana* or SIA test. SIA was administered in 1987-88, 2002-04, 2015-17, and 2024-26; and (b) scores on the NIH Toolbox Cognition Battery, specifically the Total Cognition Composite, the Fluid Composite, and the Crystallized Composite. These tests were fielded in the 2015-17 and 2024-26 survey rounds. We are aware that similar processing tests were administered during the 1988-89 survey round; if we are able to recover these data in a usable form, we will include them as part of this secondary analysis.

We will also assess changes in scores over time – for both primary and secondary outcomes – where we have the data to do so.

5. ESTIMATION STRATEGY

We will estimate the following model, noting that it is identical to that used in Maluccio et al (2009).

$$Y_{i,PT} = \alpha + \beta_1 \cdot N_i + \beta_2 \cdot N^A_i + \boldsymbol{\beta_{3C}} \cdot \mathbf{C_i} + \boldsymbol{\beta_{4P}} \cdot \mathbf{P_i} + \boldsymbol{\beta_{5VF}} \cdot \mathbf{VF} + \boldsymbol{\beta_{6VV}} \cdot \mathbf{VV} + \varepsilon_{i,PT}$$

where:

$Y_{i,PT}$ are our post-treatment (PT) outcome measures of cognitive skills for the i^{th} person in our sample.

N_i and N^A_i are dummy variable controls for cohort effects and exposure to the *atole* treatment for a cohort. These are based on the birth date of the individual, the dates of operation of the

interventions, and the village in which the child resided. For each individual, we determined whether he or she was exposed to *either* intervention for the entire period from birth to 24 months of age. This dummy variable indicator (N_i) represents a cohort effect that captures factors common to all children in any of the villages in this age range, including improved health care services and increased social stimulation present under either the *atole* or the *fresco* interventions. The *atole* intervention indicator is then calculated by multiplying the cohort measure (N_i) by a dummy variable indicator of whether or not the child lived in one of the two *atole* villages. This second measure (N^A_i), exposed to *atole* from 0–24 months, captures the differential effect in the two *atole* villages in comparison with children in the same cohort in the two *fresco* villages.

$\mathbf{C}_i$ is a vector of characteristics of the study participant, sex and birth year (expressed as a continuous variable ranging in value from 1962 to 1977).

$\mathbf{P}_i$ is a vector of characteristics of the parents of the study participant when the intervention took place (father's age, mother's age, father's grades of schooling completed, mother's grades of schooling completed, household wealth as measured by a Principal Components Index, distance to the feeding center).

VF is a vector of dummy variables for three of the four villages, capturing all fixed characteristics of these localities that might affect cognitive skills-related outcomes. These control for factors such as the initial sizes of the villages and persistent cultural differences or differences in educational or economic alternatives that might result in different educational investments across villages, even in the absence of the interventions.

VV is a vector of dummy variables for time varying village characteristics that might affect cognitive skills-related outcomes. In our initial estimates, these will include the student-teacher ratios at the primary schools located in each village when study participants were aged 7 and 13 years, and whether the school structures were permanent (ie concrete walls, metaled roofs) when study participants were aged 7 and 13 years.

$\varepsilon_{i,PT}$ is a white noise disturbance term.

β_1, β_2, $\boldsymbol{\beta_{3C}}$, $\boldsymbol{\beta_{4P}}$, $\boldsymbol{\beta_{5VF}}$, $\boldsymbol{\beta_{6VV}}$ are parameters to be estimated. We are particularly interested in β_2.

6. INFERENCE

Our data consists of individuals born in different villages over a 15 year period and most individuals in our sample also have siblings that took part in the supplementation trial. Thus, there are multiple levels over which clustering could be considered. In work using earlier rounds of these data, we found that clustering at the mother level produces the largest (ie most conservative) standard errors and so this approach will be our base method for constructing standard errors (also see section 11 for a description of alternative approaches we will use).

We will report significance levels at the 10%, 5% and 1% levels.

Because we have a single primary outcome, we do not intend to undertake multiple hypothesis adjustments.

7. ATTRITION AND MISSING DATA

Our data span more than 60 years, from the birth of our oldest study member in 1962 to the completion of the most recent round of data collection in 2026. Not surprisingly, we expect there to be significant attrition in our sample. We will describe attrition in the following ways:

First, we will document the prevalence of attrition in these data and its primary causes, distinguishing between individuals who attrit because they died, they could not be traced or were traced but declined to be interviewed.

Second, we will assess, by survey round, whether attrition is random or non-random. We will compare mean values of individual and parental baseline characteristics and treatment status. We will estimate models where the outcome variables are whether the subject was successfully in each survey round as a function of the baseline characteristics.

In terms of missing data, we do not undertake any imputation for missing outcome variables. We are missing between 9 and 15 percent of observations on maternal and paternal schooling and ages, household wealth, and distance to feeding center. These missing observations are replaced with sample means.

8. BALANCE

We begin by noting that our study team includes researchers with disciplinary backgrounds in economics and in biomedical sciences. These disciplines have markedly different approaches to the assessment of balance in randomized trials. In the biomedical sciences, the CONSORT guidelines strongly discourage tests of balance, noting that if randomization was correctly implemented (as was the case in our study), any differences in baseline values are essentially the result of chance. By contrast, economists often test for balance as a means of assessing whether treatment and control groups were comparable at baseline.

For the purposes of this work, we will assess balance across selected baseline characteristics (subjects' age and sex; maternal and paternal age and schooling; and household wealth) through pairwise t tests and an omnibus F test (regressing these characteristics on assignment to treatment village) and note these findings.

9. HETEROGENEITY ANALYSIS

We will report results disaggregated separately by sex and by baseline socio-economic status.

10. ROBUSTNESS AND SENSITIVITY ANALYSIS

We will undertake the following robustness and sensitivity analyses:

(1) We will explore whether our results are sensitive to the measurement of outcomes; for example, by constructing z scores and using the number of correct responses (rather than the percent correct) in both level and log terms.

(2) To check the sensitivity of our results to the choice of **VV** variables, we will also apply post-double selection Lasso methods (Belloni et al., 2014) to a wider set of VV variables (for example, measures of school quality at other ages), retaining the N_i , N^A_i , $\mathbf{C}_i$, $\mathbf{P}_i$ and **VF** variables in the amelioration set.

(3) Estimating impact using randomized inference methods.

(4) To assess whether our results are sensitive to how we model exposure to the supplement, we will construct alternative exposure windows to *atole* (for example, exposure between 0 and 36 months; exposure between 0 and 48 months etc).

(5) To assess whether our primary outcome is robust to outliers, we will winsorize at the 2% and 98% levels.

(6) We will assess whether our results are sensitive to attrition through calculation of Lee bounds, Kling and Liebman sensitivity bounds and the use of inverse probability weighting.

(7) Report results based on standard errors that allow for correlations within the 64 village-birth-year cohorts and block-bootstrapped standard errors.

11. TRANSPARENCY

We end by noting that we regard this pre-analysis plan as a "serious statement of intent" but not a binding contract. More specifically, depending on the results we obtain from these analyses, there may be additional statistical work that is warranted and/or additional work suggested/required by journal reviewers, editors and others who read the paper and provide comments. In the paper we write, we will note that such analyses were not included in this pre-analysis plan.