

# Evaluation of Micronutrient Supplementation on Growth and Cognitive Development among Children in Rural Mexico

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March 2008

## Abstract

**Background:** In 1997 a randomized clinical trial was initiated in a small rural community south of Cuernavaca, Mexico. Pregnant women were supplemented with multiple micronutrients (MM) or an iron-only supplement; eligible offspring were randomized into supplementation groups from 3 months to age 2, with MM or iron-vitamin A. The current study, beginning summer 2008, is a follow-up of the children, ages 7 to 9, who received supplements to evaluate their physical and cognitive development.

**Objective:** Conduct nutritional assessments (measure height, weight, head circumference; food frequency analysis; capillary blood draw), assess cognitive function, and identify early childhood experience characteristics of the children being evaluated.

**Methods:** Home visits of families still living in the area will be conducted by the student researcher alongside staff from Mexico's National Institute of Public Health (INSP).

**Significance:** Gestation and the first 2 years of life is a particularly sensitive period for physical growth and cognitive development. Micronutrient supplementation is often recommended during pregnancy to counter inadequate intake from dietary sources. In Mexico, especially in the southern region, micronutrient malnutrition in women of childbearing age and in children under the age of 2 continues to be an important public health problem affecting a child's mental and physical development.

## Background

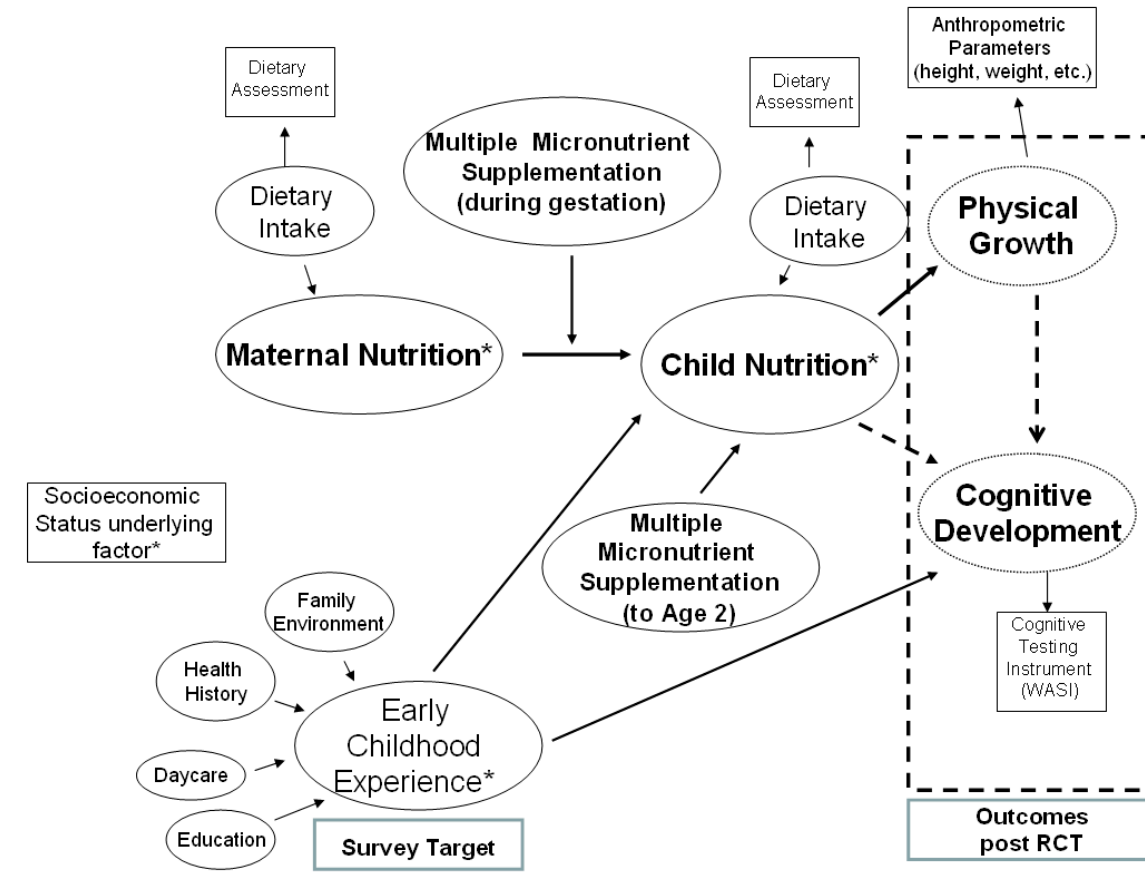
Micronutrient deficiencies and growth impairments are highly prevalent in low-income countries, due to low micronutrient content in the diet and poor bioavailability (8). Growing children and pregnant and lactating women have been identified as the most vulnerable groups to deficiencies (4). Micronutrient supplementation is often recommended during pregnancy to support maternal tissue changes, and offset inadequate dietary intake and the prevalence of associated deficiencies that affect child development (2). Among populations where dietary quality is poor, micronutrient deficiencies co-occur; interventions promoting an increased intake of several growth-limiting micronutrients may be more effective in preventing stunted growth than the intake of only one problem micronutrient (8). In Mexico, previous studies have shown that a lack of micronutrients is a limiting factor for the physical growth of infants (7). Although recent estimates show that the indicators for nutritional status (stunting, wasting, underweight) have improved in Mexico over the years, the number of children under-five years of age who are afflicted by stunting (height for age) is considerable at almost 1.2 million. In comparison to other age groups in Mexico, those with the highest prevalence of anemia, an indicator of multiple micronutrient deficiencies, are 12 to 23 months of age at 37.8% (5).

Furthermore, gestation and the first 2 years of life is a particularly sensitive period for rapid brain growth and cognitive development (3). Research has shown that water soluble vitamins, like B and C, and calcium, magnesium, and zinc are most relevant to brain functions and cognition (4). Specifically, iodine, zinc, iron, and B<sub>12</sub> have also been linked to cognitive processes in infants and young children (1). Marginal deficiencies of one or more of these micronutrients are not uncommon, even in developed countries (1,4). A previous study in Central America displayed strong evidence that supplementing children with increased caloric and protein intake produced better outcomes in psychoeducational testing (9).

Socioeconomic status and family environment are also contributing factors to child growth and developmental outcomes (3). The CEPAL survey showed that in Mexico in 1999 there were more than 44.7 million poor people, and about 17.6 million people living in extreme poverty situations (15). The inter-relationships between nutrition, the brain, and behavior are complex, but potential interactions of early childhood experience will be considered in the current study.

## Conceptual Framework

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## Significance

In the context of poverty, multiple micronutrient deficiencies often co-occur, and to date, little is known about the impact of multiple micronutrients on cognitive development (1).

The setting of the current follow-up study is rural southern Mexico. Nutritional status is not equal between Mexico's rural and urban regions; rural areas are worse off in all three indicators. According to the ENSUT nationwide survey, the greatest differences between rural and urban areas in undernutrition occur in southern Mexico; furthermore, rural southern Mexico has the highest rates of stunting in all of Mexico (5). The need is here in this region of proposed study, and so is the opportunity for greatest impact.

Effective prevention programs that begin prenatally or early in life through periods of vulnerability are important; this follow-up study will fill the gap in a concentration where more research is necessary in terms of long-term consequences.

## Problem Statement

Micronutrient supplementation is often recommended during pregnancy to counter inadequate intake from dietary sources. In Mexico, micronutrient malnutrition in women of childbearing age and in children under the age of 2 continues to be an important public health problem affecting a child's mental and physical development.

### Overall Objective

To conduct a post intervention follow-up study to assess the impact of maternal micronutrient supplementation during gestation and micronutrient supplementation during the first two years of life, on cognitive performance and development in rural Mexican children, ages 7 to 9 years old.

### Aims

- Conduct nutritional assessments on the children in each study group (supplemented with multiple micronutrients vs. control of supplementation with iron-vitamin A), including:
  1. Anthropometrics assessment (weight, height, head circumference)
  2. Dietary assessment (food frequency analysis)
  3. Biochemical exams (blood test)
- Measure cognitive functioning among children in each study group using a modified version of the Weschler Abbreviated Scale of Intelligence.
- Identify characteristics of early childhood experience: family environment, education, and health history of child.

### Hypothesis

Maternal and early childhood micronutrient supplementation is associated with positive physical and cognitive development outcomes among children in rural Mexico, 5 to 7 years following a multiple micronutrient intervention.

### Methods

#### *Design and Setting*

This project is nested in a randomized double-blinded clinical trial that was first initiated July 1997 in a small rural community in the state of Morelos, Mexico. The National Institute of

Public Health in Cuernavaca, Mexico (INSP) and Emory University, Atlanta, Georgia are partnered in this research. Eight hundred and seventy-three pregnant women, at 13 weeks gestation, were randomized into two groups receiving multiple micronutrients (1.0-1.5 RDA of vitamins A, D, E, C, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, and B<sub>12</sub>, niacin, folic acid, magnesium and zinc) or an iron-only supplement. The women were supplemented 6 days per week until giving birth (6). At 3 months of age, 650 children from the original study group of pregnant women were recruited for participation for a supplementation study up to age 2 years from December 1999 to December 2001. The children were randomly assigned to receive daily supplements of multiple micronutrients (See Appendix A for nutrient combination) or iron-vitamin A until 2 years of age. Child supplements were administered by trained personnel during household visits 6 days per week; rates of compliance were documented by field workers. Four hundred and sixty seven children completed the intervention (11). An estimated eighteen thousand people live in this community, which is located about 40 km away from the closest urban center of Cuernavaca.

### *Data Collection*

With a team of two INSP employees, I will assist in follow-up with approximately 350 families that are still in the area within a 10-week period. Home visits will be conducted to perform nutritional assessments, measure cognitive function in children, and to survey the mothers for additional background information.

- 1) Weight, height, and head circumference measurements will be taken according to established standardized methods (10). Weight will be measured with a digital scale (Tanita scale model 1582, Tanita, Arlington Heights, IL) without shoes to the nearest 100g, and standing height will be measured using a portable stadiometer (Schorr Industries, Glen Burney, MD) and recorded to the nearest millimeter. Head circumference will be measured to precision of 1mm.
- 2) Dietary intakes will be measured using a food frequency survey.
- 3) Trained field personnel will take a capillary blood sample using a Hemocue analyzer (Hb 201 Plus, Ängelholm, Sweden) to measure Hemoglobin concentration.
- 4) Cognitive functioning among children in each study group will be measured using the Weschler Abbreviated Scale for Intelligence (WASI, Psychological Corporation, 1999). Although some research cautions the use of WASI (12), it has been successfully used as a brief and reliable, culturally-adaptable measure where a longer, more comprehensive cognition test is not possible (13, 14).
- 5) Survey questions will be added to existing questionnaire material. This survey will be administered to the mother of the child, to document the child's early childhood experience: health history, education, and family environment (See Appendix B for draft Family Environment survey module).

### *Data Analysis*

Anthropometric measurements (height and weight) will be converted to standard deviation units (Z-scores), examining height- and weight-for-age results. Body Mass Index can also be calculated using these measurements: weight (kg)/length (m<sup>2</sup>).

SAS version 9.1 (SAS Institute Inc., 2002-2003) will be used to clean and analyze the quantitative data. Univariate frequencies of select variables will be examined. T-tests will be used to determine mean differences in height from the end of early child supplementation to present, and also compare differences between intervention groups (multiple micronutrients vs. iron-vitamin A). Cognition testing scores from each group will be compared using t-tests as well. Family environment variables will be considered in later analysis to assess effects on growth and developmental outcomes.

### Timeline of Activities

Activity	March 2008	April	May	June	July	August	September	October
Literature Review	X	X						
Budget Assessment	X	X						
Survey Development	X	X						
IRB review submission	X	X						
Finalize research methods		X	X					
Translate finalized survey and cognitive tests			X					
Pilot test survey			X					
Orientation with INSP Cuernavaca, Mexico				X				
Begin Follow-up with intervention cohort				X				
Data collection				X	X			
Data entry				X	X			
Data analysis in Atlanta, Georgia						X	X	X

### Feasibility

Dr. Usha Ramakrishnan is the principal investigator of this follow-up study. She is a faculty member in the department of global health at Emory University's Rollins School of Public Health (RSPH) and has been involved in the intervention since its commencement in 1997. She will provide close supervision during the planning process as well as guidance throughout the course of the project to the proposed MPH candidate to assist in research in Mexico. By May 2008, the MPH candidate will have completed two semesters of Biostatistics coursework, including SAS 9.1 software training, a Survey Methods course, EPI INFO coursework, and a Proposal Development class. The aforementioned MPH candidate has a strong working knowledge of the Spanish language, has fieldwork experience, and has become familiar with issues regarding nutrition and health in Latin American countries. This project is in partnership with the National Institute of Public Health (Instituto Nacional de Salud Pública- INSP) in Cuernavaca, Mexico. The MPH candidate will work alongside INSP employees in the field and with the Principal Investigator, Dra. Lynnette Neufeld, in the INSP office in Cuernavaca.

## Human Subjects and Ethical Considerations

Participants in this longitudinal study have consented periodically for the purposes of follow-up evaluations. Parental (i.e., mother) written consent will be attained for the children, ages 7 to 9, that will be tested and measured during summer 2008. Respondent's data will be matched to previous evaluations by name and I.D. number. Collected information is confidential and may be accessed only in INSP data system by password. Names and addresses of individuals will be removed from all documentation and data before transporting to the United States or analyzing on a personal computer.

The IRB application for this study will be submitted for approval by Emory University. Acceptance of funds granted will be contingent on IRB approval.

## Project Budget

	<b>Item</b>	<b>Number</b>	<b>Amount of Time</b>		<b>Cost per Unit</b>		<b>Total Cost</b>	<b>In Kind/ Facilitated</b>
	<b>Base Compensation</b>							
1	Principal Investigator	1	18	weeks	500	per week	9000	9000
2	Co- Principal Investigator	1	18	weeks	500	per week	9000	9000
3	Student Researcher	1	16	weeks	300	per week	4800	4800
4	Fieldwork Assistant	2	10	weeks	200	per week	4000	4000
5	Data entry operator	1	9	weeks	150	per week	1350	1350
6	Driver	1	10	weeks	150	per week	1500	1500
	<b>Travel Allowances</b>							
7	Student Researcher	1	70	days	40	per day	2800	
8	Fieldwork Assistant	2	70	days	15	per day	2100	2100
9	Driver	1	70	days	15	per day	1050	1050
	<b>Materials</b>							
10	Vehicle rental	1	70	days	40	per day	2800	2800
11	Fuel	1	10	weeks	150	per week	1500	1500



12	Data entry/analysis computer	1	-	-	1000	-	1000	1000
13	Computer office/supplies	-	10	weeks	30	per week	300	300
14	HemoCue Hb 201 Plus Analyzer	1	-	-	800	-	800	800
15	Hemoglobin 201 microcuvette	4	-	-	255	-	1020	1020
16	Lancets 1.8mm	7	-	-	21	-	147	147
17	Gloves for hemoglobin test	13	-	-	32.2	-	418.6	418.6
18	Schorr Industries Stadiometer	1	-	-		-	0	
19	Tanita Digital Scale	1	-	-		-	0	
20	Cell phones	6	-	-	100	-	600	600
21	Cell phone minutes	800	-	-	2	per min	1600	1600
	<b>Printing Costs</b>							
22	Questionnaires	650	-	-	2	-	1300	1300
	<b>Consultant</b>							
23	Local consultants (in Mexico)	2	4	person-wks	300	per week	2400	2400
24	International air travel	1	-	trip	450	-	450	
	<b>Total</b>						49935.6	
	<b>Total In Kind/Facilitated Funds</b>							46685.6
	<b>TOTAL NEEDED after In Kind/Facilitated</b>							<b>\$3,250.00</b>

	<b>Notes</b>
1	Dr. Usha Ramakrishnan: Principal Investigator, Emory University. In Kind/Facilitated
2	The co-Principal Investigator will be at the National Institute of Public Health in Cuernavaca, Mexico. In country organizing. Facilitated by INSP
3	I will be assigned data and fieldwork. Donated time
4	Will assist in data collection. Both to be trained to administer capillary blood samples, taking physical measurements, as well as interviewing.
5	Donated Time
6	One driver for daily commute from Cuernavaca to 1 hour south rural town. Facilitated by INSP
7	Max per diem rate for Cuernavaca, Mexico, the closest urban town to survey destination, is \$211 US per day ( <a href="http://www.state.gov">www.state.gov</a> ). Includes all living expenses incurred (housing and food).
8	Field workers live in Cuernavaca. Per diem covers food only. Facilitated by INSP
9	Driver lives in Cuernavaca. Per diem covers food only. Facilitated by INSP
10	<a href="http://www.mexicocar.net/">http://www.mexicocar.net/</a> . Facilitated by INSP
11	Facilitated by INSP
12	Facilitated by INSP
13	Printer, scanner, fax, printer cartridges, paper, and other miscellaneous. Costs estimated. Facilitated by INSP in Cuernavaca, Mexico.

14	Portable device analyzes hemoglobin. Spoke with Joanie in customer service@ Hemocue 949-859-2630. Facilitated by INSP
15	Packages of 200(4x50). Disposable. Facilitated by INSP
16	100 count. Item 139001. Designed for use with children. Facilitated by INSP
17	100 gloves /box. SAFESKIN® Hypoclean™ Powder-Free Disposable Nitrile Gloves. www.labsafety.com
18	Portable device measures standing height. Facilitated by INSP
19	Measures weight. Facilitated by INSP
20	For field personnel, including driver, manager and project supervisor, and one for data entry staff.www.mobalrental.com
21	Project communication only. Estimated minutes
22	Surveys will be printed up in Mexico after being approved by IRB in U.S. Facilitated by INSP.
23	In Kind
24	Flight to Mexico City, Mexico from Atlanta, Ga. Roundtrip.
	Currency converter 1.00 USD=10.7151 MXN (Mexico Peso) www.xe.com February 29,2008
	<b>* All estimates in US dollars</b>

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Appendix A

**TABLE 1: Nutrient Composition of the multiple micronutrient supplement<sup>1</sup>**

<b>Nutrient</b>	<b>3-11 mo of age  (per dose, 20 ml)</b>	<b>12-24 mo of age  (per dose, 30 ml)</b>
Vit A, IU	450	480
Vit D, IU	400	400
Vit E, IU	4.0	6.0
Vit B6, mg	0.60	0.10
Vit B 12, µg	0.75	1.05
Vit C, mg	52.5	60.0
Niacin, mg	6.0	9.0
Folic Acid, µg	35.0	50.0
Vit B1, mg	0.40	0.70
Vit B2, mg	0.75	1.20
Iron, mg	15.0	15.0
Zinc, mg	7.5	15.0

Magnesium, mg	60.0	80.0
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<sup>1</sup>the control group received a supplement containing similar amounts of vitamin A and iron

Appendix B

Draft Survey Format and Questions  
Sample Family Environment Module

The mothers of the children being evaluated should be sought out as respondents.

**READ EACH QUESTION AS WRITTEN. Additional instructions for the interviewer are in bold font.**

Response codes are also in **bold** font.

1. What is the total household income?

- 1.1**     0-20,000
- 1.2**     20,001-35,000
- 1.3**     35,001-55,000
- 1.4**     55,001-75,000
- 1.5**     75,000+
- 1.8**     Don't know
- 1.9**     Refuse to answer

2. How many people live in the household that are 18 years of age and older? **2.1** \_\_

3. How many children live in the household that are 14 years of age and younger? **3.1** \_\_

4. Please list out the ages of the children in the household that are 14 years and younger, including the child being tested for growth and development.

**4.1** \_\_    **4.2** \_\_    **4.3** \_\_    **4.4** \_\_    **4.5** \_\_    **4.6** \_\_    **4.7** \_\_    **4.8** \_\_

5. Do extended family members (grandparents, aunts, uncles) share the household?

- 5.1**     Yes
- 5.2**     No
- 5.8**     Not sure
- 5.9**     Refuse to answer

6. What type of dwelling do you and your family reside in?

- 6.1     House
- 6.2     Duplex
- 6.3     Apartment
- 6.4     Other \_\_\_\_\_

7. Do you rent or own the dwelling in which you currently reside?

- 7.1     Own
- 7.2     Rent
- 7.3     Other \_\_\_\_\_
- 7.8     Don't Know
- 7.9     Refuse to answer

8. What is the highest level of education you have achieved?

- 8.1     Less than High School
- 8.2     High School or Equivalent
- 8.3     2-Year Degree or Equivalent
- 8.4     4-Year Degree
- 8.5     Master's level and beyond
- 8.8     Don't Know
- 8.9     Refuse to answer

9. What is your marriage status?

- 9.1     Married
- 9.2     Common law marriage
- 9.3     Divorced
- 9.4     Widowed
- 9.5     Never married
- 9.8     Don't know
- 9.9     Refuse to answer

10. Does your partner currently live in the household?

- 10.1    Yes
- 10.2    No
- 10.3    Don't Know
- 10.4    Refuse to answer

**Interviewer: If Yes, proceed to next question. If No, Don't Know, or Refuse SKIP question 11.**

11. What is the highest level of education that the male head of household has achieved?

- 11.1    Less than High School
- 11.2    High School or Equivalent
- 11.3    2-Year Degree or Equivalent
- 11.4
- 11.5
- 11.8

- 4-Year Degree
- Master's level and beyond
- Don't Know
- Refuse to answer

**Interviewer: Insert child's name that is being evaluated. Do not read parentheses.**

12. What type of school does (your child that is being tested for growth and development) attend?

- 12.1** ○ Public
- 12.2** ○ Private
- 12.3** ○ Other \_\_\_\_\_
- 12.8** ○ Don't Know
- 12.9** ○ Refuse to answer

13. Is there an adult present in the home after school to supervise the child's activities?

- 13.1** ○ Yes
- 13.2** ○ No
- 13.8** ○ Don't Know
- 13.9** ○ Refuse to answer

14. Is there a television in the household?

- 14.1** ○ Yes
- 14.2** ○ No
- 14.8** ○ Don't Know
- 14.9** ○ Refuse to answer

15. To your knowledge, how many hours of television does your child watch each day?

- 15.1** ○ None
- 15.2** ○ 1- 2
- 15.3** ○ 3-4
- 15.4** ○ 5 or more
- 15.8** ○ Don't Know
- 15.9** ○ Refuse to answer

16. Is there a computer in the household?

- 16.1** ○ Yes
- 16.2** ○ No
- 16.8** ○ Don't Know
- 16.9** ○ Refuse to answer



17. To your knowledge, how many hours of computer-time does your child have each day?

- 17.1  None
- 17.2  1- 2
- 17.3  3-4
- 17.4  5 or more
- 17.8  Don't Know
- 17.9  Refuse to answer

18. Is the child's computer and TV activity supervised by an adult in the household?

- 18.1  Yes
- 18.2  No
- 18.8  Don't Know
- 18.9  Refuse to answer

19. Is there a table in the household that everyone in the household eats at together?

- 19.1  Yes
- 19.2  No
- 19.8  Don't Know
- 19.9  Refuse to answer

20. How many times per week do you eat together as family at a table?

- 20.1  None
- 20.2  1- 2
- 20.3  3-4
- 20.4  5 or more
- 20.8  Don't Know
- 20.9  Refuse to answer

21. How many hours per week do you work outside the home?

- 21.1  None
- 21.2  1-10
- 21.3  11-20
- 21.4  21-40
- 21.5  40 or more
- 21.8  Don't Know
- 21.9

- Refuse to answer

**Thank You!**

**Interviewer: Thank respondent for their participation and their time.**