

## COHORT PROFILE

# Cohort Profile: The Cebu Longitudinal Health and Nutrition Survey

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## How did the study come about?

The Cebu Longitudinal Health and Nutrition Survey (CLHNS) was originally conceptualized as an interdisciplinary study of infant-feeding patterns, particularly the overall sequencing of feeding events (milks and complementary foods), the factors affecting feeding decisions and how feeding patterns affect the infant, mother and household. The idea was to study these topics within as natural a setting as possible and to analyse how infant-feeding decisions interacted with social, economic and environmental factors to affect health, nutritional, demographic and economic outcomes. The study was subsequently expanded to cover a wide range of maternal and child health and demographic issues that could be well studied using a prospective, community-based sample.

The study was initially the product of collaboration among researchers at the Carolina Population Center at the University of North Carolina at Chapel Hill (led by B.M.P. with J.S.A. and D.K.G.), The Office of Population Studies Foundation at the University of San Carlos in Cebu, Philippines (led by the late Director Wilhelm Fleiger) and the Nutrition Center of the Philippines (led by Florentino Solon). L.S.A. took the lead for follow-up surveys beginning in 1990. Later, the study team was expanded to include researchers presently at the Northwestern University (C.W.K. and T.M.D.) and Johns Hopkins University (M.J.H.). The study was initiated with cooperation and approval from the Cebu Department of Health. The CLHNS website includes a full list of investigators and their affiliations.

The CLHNS was one of the first large-scale, population-based surveys designed with a conceptual

framework in mind. The guiding framework was adapted from Mosley and Chen's health determinants model,<sup>1</sup> which posits that underlying community-, household- and individual-level variables affect a set of proximate health behaviours which, in turn, influence health outcomes such as growth and infectious disease morbidity and mortality. The study was designed by a highly interdisciplinary group of economists, sociologists, nutritionists, demographers and physicians.

The CLHNS has been funded by a large number of government and non-government organizations (listed in the Funding section).

## What does it cover?

The CLHNS covers a wide range of health-related topics specific to each stage of the life cycle. In the prenatal period, this included social, environmental, demographic, health services and nutritional factors that influence birth outcomes. In the first 2 years after birth, the focus was on infant feeding, morbidity and growth, and mothers' health and nutritional outcomes and birth spacing. During the 1991 follow-up, the focus was on childhood stunting, intellectual development and entry into school. As the cohort entered adulthood, emphasis was on early-life factors that predict schooling and academic achievement, and the development of obesity and cardiovascular disease (CVD) risk. Throughout, data were collected to enhance understanding of how changing community and household factors influence health outcomes. In parallel with the focus on following the original birth cohort, CLHNS mothers were followed to learn about their long-term patterns of health, birth spacing,

family planning, diet, nutritional status, physical functioning, status, parent-child relationships and work patterns.

Core questionnaire modules related to household socio-economic status (employment, education, income, assets, etc.), demographics and environment were retained to allow comparability over time. Additional items were added to modules to account for changing environments (e.g. the list of assets was expanded to include items such as cellular telephones and personal computers, which no household possessed at the time of the baseline survey). New modules were added over time to address age-appropriate and novel topics (e.g. the 1998 survey added an adolescent reproductive health module). Community surveys were related to health-care facilities, water sources, sanitation and food and commodity prices, and a wide array of other community infrastructure and service measures.

In 1998, two subsamples of adolescents participated in additional studies. CLHNS adolescents with a birth weight of  $<2.6$  kg, plus a random sample of those with birth weight of  $\geq 2.6$  kg, participated in a clinic study which collected fasting blood samples ( $n = 619$ ). In 100 of these adolescents, antibody response to a typhoid immunization was tracked. Qualitative research has also been conducted with subgroups of participants, related to women's status and decision making and family planning. In 2002 and 2005, a life-event history matrix was collected from the index young adults.

In 2005, fasting blood samples were collected from all index young adults and their mothers, and saliva was collected for measurement of steroid hormones. The deoxyribose nucleic acid (DNA) was extracted from blood, and plasma was stored for subsequent laboratory analysis of selected biomarkers.

As the original birth cohort has entered adulthood, several studies have focused on reproduction and reproductive biology. In males, samples and data collected in 2005 were used to evaluate multiple sex steroids and measures of testicular function, which were related to parenting and fatherhood.

A 2009–11 study is identifying new pregnancies and birth outcomes among index female young adults, thus making the CLHNS a three-generation study.

## Who is in the sample?

Participants are residents of Metropolitan Cebu in the Philippines. With a population approaching 2 million, Metro Cebu is the country's second-largest metropolitan area. Located on the east coast of Cebu Island in the Visaya's region, it comprises four cities (Cebu City, Mandaue, Lapu-Lapu and Talisay) and seven municipalities in surrounding areas. Metro Cebu includes 270 administrative units (barangays), which are villages in the rural areas or neighbourhoods in urban areas. The urban core extends along the

seacoast, and to the base of nearby mountains. The study area is ecologically diverse, with high-density urban neighbourhoods, less dense peri-urban areas, rural towns and more isolated mountain and island rural communities.

In 1983, a single-stage cluster-sampling procedure was used to randomly select 17 urban and 16 rural barangays from among the 243 barangays of Metro Cebu identified in the 1980 census. The selected barangays, representing approximately 28 000 households, were surveyed to locate all pregnant women, who were asked, in person, to join the study. Fewer than 4% refused. Those who gave birth between 1 May 1983 and 30 April 1984 were included in the sample. A baseline interview was conducted among 3327 women during pregnancy. Of these, 3080 gave birth to a single live infant, 26 had multiple births, 42 had a stillbirth or miscarriage, 17 refused further participation after the baseline survey and 136 were out-migrants. The survey initially followed only the singleton index children and their mothers through the first 2 years of life. Demographic and socio-economic differences between the 3080 mothers of singletons and those initially excluded from the sample were minimal, with younger age and lower parity being the only significant predictors of being in the excluded group. Twins and mothers whose infant died were later re-incorporated into the survey. The infants are a representative sample of births in Metro Cebu during a 1-year period. Their mothers are not representative of the Metro Cebu adult female population of childbearing age, owing to the fact that pregnancy was a requisite for entry into the study. Demographic characteristics of the women and infants are presented in Table 1.

## How often have they been followed up?

Surveys were conducted in the second to third trimester of pregnancy, immediately after birth and then every 2 months for 24 months. Subsequent follow-up surveys took place in 1991–92, 1994–95, 1998–99, 2002 and 2005. A more limited tracking survey of mothers was completed in 2007, and index children and their offspring were tracked in 2009.

## What has been measured?

CLHNS individual and household data are collected during in-home interviews. The only exception is the 1998 biomarker sub-study, which was conducted in local health clinics. Community data are collected from key informants, who are typically the elected barangay leaders.

**Table 1** Selected characteristics of CLHNS mothers at baseline and infants at birth

	Mean (SD)	Range
<b>Mothers (<i>n</i> = 3327)</b>		
Height (cm)	0	132.5–169.2
Age (years)	26.0 (6.0)	14–47
Household size	5.6 (2.8)	1–21
Parity	2.2 (2.2)	0–14
First pregnancy (%)	23.1	
Rural resident (%)	23.2	
Household has electricity (%)	50.0	
Completed elementary school or less (%)	61.5	
Schooling beyond high school (%)	12.7	
<b>Children</b>		
Birth weight (g)	2987 (442)	907–4800
Birth length (cm)	49.1 (2.1)	38.5–59.0
Gestational age (weeks)	38.7 (2.1)	30–44
Female (%)	47.0	
Low birth weight, <2.5 kg (%)	11.6	
Preterm, <37 weeks (%)	17.5	

SD = standard deviation.

Table 2 summarizes the main topics for each survey round. Complete questionnaires and codebooks for each year are available on the CLHNS website.

## What is attrition like?

Of the 3327 women included at baseline, 3080 remained in the study and had singleton live births during the 1-year period of eligibility. In the 2007–08 tracking survey, 63% of these 3080 mothers who were present at the birth information survey were located and interviewed, and 59% of the 3080 singletons were located and interviewed (Table 3). Attrition was largely due to out-migration (e.g. 78% of the women not interviewed in 2007 have migrated outside sample area). Refusal rates at each survey ranged from 9 to 11% during the first year of data collection but substantially decreased over the years (5% in 2007) as rapport between participants and study team strengthened. To date, 232 of the 3080 index children, and 162 mothers of singletons are known to have died. The vast majority of child deaths occurred within the first 2 years of life. Compared with those lost to follow-up, women who participated in the 2007 survey were less educated, of higher parity and came disproportionately from rural, poorer households. Given that permanent migrants from the Metro Cebu area were not followed, the remaining sample is therefore selective of households with more residential stability. For example, 68% of the women in the 2007 survey have resided in the same barangay since baseline.

## What has been found?

More than 125 scholarly works based on the CLHNS and written by current collaborators have been published in demography, economics, epidemiology, bio-medical, human biology, nutrition, public health and women's studies journals (a complete list of publications is available on the CLHNS web site). Additional papers have been published by other researcher groups who accessed the data from the CLHNS web site. The key findings relate to the following topics.

### Birth outcomes

Early papers focused on determinants of birth weight, length and gestational age, finding important roles for prenatal care,<sup>2,3</sup> maternal age,<sup>4</sup> parity and current and past nutritional status.<sup>5,6</sup> Perinatal mortality was higher among low (<2.5 kg) and high (>4 kg) birth-weight infants.<sup>7</sup>

### Infant feeding, growth and health

Infant feeding was the centre-piece of the original CLHNS. Studies identified factors that influenced women's initial infant-feeding decisions,<sup>8–10</sup> initiation and duration of breastfeeding<sup>11</sup> and the consequences of feeding for infant health<sup>12</sup> and birth spacing.<sup>13</sup> Structural models related underlying individual, household and community characteristics to health behaviours and infant morbidity, mortality and growth.<sup>14,15</sup> Detailed longitudinal data enabled extensive studies of child growth dynamics.<sup>16,17</sup>

**Table 2** CLHNS surveys and measurements

Phase	Measurements: mothers	Measurements: offspring
<b>Original CLHNS</b>		
1983–84 Pregnancy	Anthropometrics, diet (24-h recall, physical activity (time use), prenatal care, socio-demographic characteristics)	Not applicable
1984–86: 12 postpartum/infancy bi-monthly surveys	Anthropometrics, diet (24-h recall at 3, 6 and 14 months postpartum only), physical activity, work and earnings, pregnancies, births, family planning, major illnesses	Weight and length measured, breastfeeding, complementary feeding, morbidity, preventive and curative health care reported by mothers
<b>Follow-up surveys</b>		
1991	Anthropometrics, diet (quantitative food frequency questionnaire), physical activity, work and earnings, pregnancies, births, family planning, major illnesses	Anthropometrics, diet (quantitative food frequency questionnaire), major illnesses, non-verbal IQ test, schooling
1994	Anthropometrics, diet (24-h recalls), physical activity, work and earnings, pregnancies, births, family planning, major illnesses, status and autonomy, memory, physical functioning (ADL and IADL)	Anthropometrics, diet (24-h recalls), major illnesses, IQ, school attainment, math and language achievement tests, physical activity
1998	Anthropometrics, diet, physical activity, work and earnings, pregnancies, births, family planning, major illnesses, parent–child communication, blood pressure (BP), memory, physical functioning	Anthropometrics, self-assessed pubertal development, diet, major illnesses, physical activity, school attainment, parent–child communication, reproductive health, BP. Fasting blood drawn for CVD biomarkers in selected subsample ( $n = 612$ )
2002	Anthropometrics, diet, physical activity, work and earnings, pregnancies, births, family planning, major illnesses, status and autonomy, BP, memory, physical functioning	Anthropometrics, diet, major illnesses, physical activity, school attainment, reproductive health, marriage/cohabitation, reproductive history, mental health, work and earnings, BP
2005	Anthropometrics, diet, physical activity, work and earnings, pregnancies, births, family planning, major illnesses, memory, physical functioning, grip strength, BP, fasting blood drawn for CVD biomarkers and genetics	Anthropometrics, diet, major illnesses, physical activity, school attainment, marriage/cohabitation, reproductive history, BP, grip strength, fasting blood drawn for CVD biomarkers and genetics, saliva collected for cortisol and sex steroids
2007	Anthropometrics, work and earnings, memory, physical functioning, blood pressure, illnesses	Anthropometrics, work and earnings, marriage/cohabitation, morbidity and reproductive health, stress, birth outcomes for offspring, blood pressure. Breast milk for compositional analysis (females)
2009		Anthropometrics, work and earnings, marriage/cohabitation, fatherhood, morbidity and reproductive health, blood pressure, birth outcomes in offspring (females), grip strength and saliva samples for steroid analysis (males)

ADL: activities of daily living; IADL: instrumental activities of daily living scale.

**Table 3** The CLHNS sample over multiple survey waves

	1983–84	Birth	1984–85	1985–86	1991	1994	1998	2002	2005	2007
<b>Women</b>										
<i>N</i>	3327	3120	2661	2565	2395	2279	1989 <sup>a</sup>	2102	2018	1977
Age (SD)	26.6 ± 6.0				35.5 ± 6.1	38.5 ± 6.1	42.5 ± 6.1	45.2 ± 6.1	48.4 ± 6.1	50.9 ± 6.0
<b>Offspring</b>										
<i>N</i>	NA	3080	2600	2462	2264	2186	2089	2023	1888	1817
Age (SD)	NA	0	1.0 ± 0.01	2.0 ± 0.01	8.5 ± 0.1	11.5 ± 0.4	15.5 ± 0.6	18.7 ± 0.3	21.5 ± 0.3	23.6 ± 0.5

SD: standard deviation; NA: not applicable, pregnancy survey.

<sup>a</sup>Only mothers with surviving offspring were followed.

### **Developmental origins of young adult disease risk**

Studies have examined how prenatal maternal nutrition, infant size at birth and/or early infant growth relate to age at menarche,<sup>18</sup> blood pressure,<sup>19–21</sup> antibody response to immunization and thymic function<sup>22–24</sup> and lipid profiles.<sup>25,26</sup>

### **Child development, schooling and young adult work status**

Early-childhood growth deficits were related to lower intelligence quotient (IQ) at age 8 years and achievement test scores at age 11 years<sup>27</sup> as well as later age at entry into school, more grade repetition and lower completed school attainment.<sup>28,29</sup> Early linear growth retardation was also associated with reduced likelihood of working in the formal wage sector, and thus reduced earning capacity of young adults.<sup>30</sup>

### **Reproductive health, sexual behaviour**

A series of studies examined parental and peer influences on adolescent and young adult sexual behaviour<sup>31–33</sup> and adolescent risk behaviours.<sup>34</sup>

### **Family dynamics and intimate partner violence**

Studies have examined the impact of household power and gender on schooling outcomes<sup>35</sup> and women's birth intervals.<sup>36</sup> The CLHNS is one of the few sources for longitudinal analysis of intimate partner violence<sup>37</sup> and its determinants and consequences for women and for young adults.<sup>38,39</sup>

## **The CLHNS mothers**

### **Health and nutrition**

Studies initially focused on undernutrition in the postpartum period and how it relates to lactation and birth spacing.<sup>13,40,41</sup> The rapidly changing environment in Cebu is now associated with dramatic increases in overweight and prevalence of hypertension and other CVD risk factors.<sup>42</sup>

### **Genetics**

Maternal DNA was subjected to a genome-wide scan. The initial focus of genetic analysis has been on obesity and CVD-related phenotypes.

### **Work, status, earnings**

Detailed work and reproductive histories provide data for the study of interrelationships of childbearing and women's work.<sup>43–45</sup> Additional children born after the index child reduced maternal work hours and earnings.<sup>46,47</sup>

### **Urbanization**

Rapid changes in Cebu make it a good laboratory for studying urbanization: an urbanization index was developed to track changes over time and relate these changes to health outcomes.<sup>48</sup>

### **Methodological contributions**

Many of the early CLHNS papers used longitudinal structural models to develop causal inferences about health determinants.<sup>14,15</sup> Studies showed the importance of accounting for endogeneity, and CLHNS papers enhanced understanding among epidemiologists of this important source of bias and how to deal with it.<sup>49,50</sup>

## **What are the main strengths and weaknesses?**

### **Weaknesses**

The data represent a single region, rather than the entire country. Annual data throughout the study were not collected, leaving important time gaps for the study of child and adolescent growth. The sample size, while large for a cohort followed for 23 years, may be limiting for genetic studies and studies of smaller subsets of the population. Furthermore, dietary data were initially limited to single 24-h recalls, and in more recent survey years to 2 consecutive days. A key challenge for such a long-running study is to maintain comparability of measures over time, whereas at the same time, adding topics and measures that are timely and age appropriate (e.g. necessary changes in the instruments needed to measure blood pressure, the need to include new sets of assets to measure wealth). Attrition is a concern, especially given the high mobility of the young adult population. Migration of the more educated, urban segment of the original cohort has left us with a sample that is no longer representative of the population from which it was drawn.

### **Strengths**

The CLHNS used the Mosley and Chen proximate-determinants model<sup>1</sup> to guide the design and data collection as well as subsequent data analysis. Detailed data were collected at the community, household and individual levels, allowing for a wide range of analytical approaches. The study has continued for >25 years, providing repeated measures of maternal and child health and nutrition and detailed environment, socio-economic and demographic measures over time. The time depth, breadth and level of detail and quality of the data are important strengths of the study, and make it particularly useful for life-course research. The rapid social and economic changes that have characterized the Philippines over the last 25 years also make this an

important data set. The addition of biomarkers to what was originally an interview-based health survey expands the utility of the study to address the transition from infectious to chronic diseases with a focus on cardiometabolic disease-risk factors. CLHNS index 'children' are now becoming parents, offering opportunities for three-generation studies. The age of the CLHNS mothers now offers an opportunity to study multiple dimensions of healthy ageing.

## Can I get access to the data? Where can I find out more?

Most CLHNS data are publicly available on the CLHNS website housed at the Carolina Population Center at the University of North Carolina at Chapel Hill (<http://www.cpc.unc.edu/projects/cebu>). Some data considered sensitive (e.g. information on pregnancy terminations, illegal drug use) are available only on request. Genetic and biomarker data are not publicly available, but collaborations with other investigators are welcome. The website includes a project description, list of publications by the Cebu study team, questionnaires, codebooks and data.

## Funding

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and implementation of the original birth cohort study and the first decade of collaborative research.

**Conflict of interest:** None declared.

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