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Cohort Profile: The Consortium of Health Orientated Research in Transitioning Societies (COHORTS)

How did the collaboration come about?

In 2005 plans were made for a series of papers on maternal and child undernutrition for publication in *The Lancet*. The second paper of the series aimed to describe the long-term consequences of maternal and child undernutrition for health and human capital. The focal person for this article - Cesar Victora from the Federal University in Pelotas, Brazil – decided to bring together available long-term data from low- and middle-income countries. He identified the five largest prospective birth cohort studies from these regions, all of which had at least 15 years of follow-up and an initial sample size of 2000 or more newborns. The principal investigators were approached, and all agreed to join the writing team.

The five studies included the 1982 Pelotas (Brazil) Birth Cohort Study,¹ the Institute of Nutrition of Central America and Panama Nutrition Trial Cohort (INTC; Guatemala),² the New Delhi Birth Cohort (India),³ the Cebu Longitudinal Health and Nutrition Survey cohort (CLHNS; Philippines),⁴ and the Birth-to-Twenty (Bt20; Soweto-Johannesburg, South Africa) cohort.⁵ All the studies were population based and started recruitment during gestation or at delivery; they have long follow-up periods; their study populations experienced high rates of maternal and/or child undernutrition, and all are currently undergoing rapid demographic, nutritional and epidemiological transitions.

The experience of working together on the original paper, which was published in 2008,⁶ was highly positive. This motivated Cesar Victora, on behalf of the principal investigators, to apply for a research grant from the Wellcome Trust aimed at establishing a long-lasting collaborative network among the five cohorts. With funding, the group, named the Consortium of Health Orientated Research in Transitioning Societies (COHORTS) was formed and a logo created (Figure 1).

What does the collaboration cover?

The overall objectives of the consortium include: (a) to strengthen the collaboration among five of the largest and longest running birth cohort studies in low and middle-income countries, including capacity building among young scientists, epidemiologists and statisticians in the cohort teams; (b) to jointly produce high-quality scientific evidence on the early origins of chronic diseases and human capital by analyzing data from five cohort studies from low and middle-income countries; and (c) to disseminate the findings of the collaboration through scientific meetings and journal articles.

The collaboration has developed through three main phases:

Phase 1 (2006-2007) included the preparation and publication of the original *Lancet* article on the long term consequences of maternal and child undernutrition.⁶

Phase 2 (2007-2009) was aimed principally at answering two broad research questions: (a) What is the effect of weight gain during infancy and early childhood on adult health and human capital? In particular, which period of weight gain has a stronger effect on each

outcome? (b) How does infant feeding (duration of breastfeeding and age of introduction of complementary foods) relate to later health outcomes?⁷⁻⁹

Phase 3 (2009-2011) is directed at answering three main research questions: (a) What is the association between the physical and social environment in early childhood and adult indicators of health and capacity?; (b) What is the influence of the physical and social environment in early childhood on growth in the first two years of life?; (c) How does the physical and social environment in early childhood moderate the relationships between growth in the first two years of life and adult indicators of health and capacity?

All three phases have been supported by grants from the Wellcome Trust. Since the beginning of the collaboration, a schedule of annual meetings has been held, at the cohort study sites - Brazil (2006), South Africa (2008) and India (2010) – or coincident with the World Congress on Developmental Origins of Health and Disease - DOHaD (Australia 2007, Chile 2009). In addition to these whole team meetings, smaller subgroup data analysis and writing meetings also take place as needed, sometimes several times a year.

From 2010, COHORTS is also being supported by a grant from the Bill and Melinda Gates Foundation for secondary analyses of the data to address the following issues: preterm birth, subsequent growth, and human capital and health; health postnatal growth, in particular, by attempting to disentangle a) the effects of rapid weight gain versus rapid linear growth during early life on adult human capital and health, as well as consequences of rapid subsequent weight gain in relation to stunting at 2 years, and b) the relationship between early growth failure, delayed menarche, and attained final stature; intergenerational influences on child growth and its consequences, specifically, the differential impact of poverty and low parental schooling on growth before and after age 2 years, and estimating the intergenerational constraints on birth size and infant growth; and lastly, breastfeeding duration and achieved schooling.

Who is in the sample?

The 1982 Pelotas (Brazil) Birth Cohort study originally included all 5914 children born in the city's hospitals during the 1982 calendar year. At that time, over 99% of all deliveries in the city took place at hospitals. Because the sample is representative of the city's population, it includes participants from all social classes.¹

The INTC study in Guatemala was originally an intervention trial in four villages. All children younger than 7 years in 1969, and all children born between 1969 and 1977, were enrolled (N=2392) and followed up until 7 years of age or until the end of the study in 1977.² For the COHORTS analyses, only children enrolled at birth were included in the analyses, irrespective of whether they were born in the intervention or control villages (a dummy variable for treatment arm was included in all analyses).

The New Delhi Birth Cohort in India recruited all married women living in a defined area of the city from 1969 to 1972. Pregnancies were identified and the newborns were enrolled (N=8181) and followed up. The cohort is primarily middle-class.³

The CLHNS in the Philippines recruited pregnant women living in 33 randomly selected neighbourhoods of the metropolitan Cebu area in 1983 and 1984. Data collection started at the 30th week of gestation. Cohort members (N=3080) are from all social classes.⁴

Finally, the Bt20 study in South Africa identified pregnant women with gestational age of 26-40 weeks living in the largest urban area (Soweto-Johannesburg) in 1990. The sample enrolled (N=3273) was predominantly Black and generally poor.⁵

How often have cohort members been followed up?

Table 1 shows all waves of follow up for each site included in the COHORTS collaboration. All sites have some data available at birth, one and two years of age, mid-childhood and late adolescence or adulthood. In the last follow up visits (2009), participants had an average age of 23 years in Brazil, 32.7 years in Guatemala, 36 years in India, 21.5 years in the Philippines and 18.5 years in South Africa.

What has been measured?

Detailed lists of what has been measured in each cohort are available elsewhere.^{1;2;5;10;11} We provide here key variables that are common in most if not all cohorts.

Growth-related variables: Information on birthweight is available for all sites. Birth length is available for three out of five sites (Delhi, Guatemala and Cebu). Data on weight and length/height is available for all cohorts throughout infancy and childhood. In the late adolescence or adult visits, all cohorts collected data on weight and height and some indicator of body composition.

Early-life socioeconomic, infrastructure and environment variables: All cohorts except Delhi allow calculation of household asset scores in early life (e.g. TV, fridge, car, radio, telephone). Information on maternal and paternal education is available for all sites, as are a range of variables related to family income and paternal employment. All studies have common data on basic services (e.g. water, electricity and toilets), and all sites have information on the size of the household and the quality of building materials used.

Human capital: Socioeconomic indicators continued to be collected in all sites, from initiation and throughout adolescence and adulthood. Information on schooling attainment is available for all sites, and individual income at follow up is available in three out of the five sites (Pelotas, Guatemala and Delhi).

Behavioural variables: Feeding patterns in infancy were collected in all sites. In three of the sites, data are available on the age of first alcohol intake. All sites have data on smoking and physical activity, either in adolescence or adulthood. In addition to variables on the behaviour of cohort members, some information is available about their parents (e.g. maternal smoking during pregnancy).

Chronic disease-related variables: In late adolescence or adulthood, all sites have data on blood pressure, plasma/blood glucose concentrations, lipids and body composition.

What was attrition like?

The current COHORT analyses are based on close to 11000 individuals. The numbers of people not traced into adulthood varies from 1 percent in the Philippines to 17 percent in Pelotas. Other reasons for loss of participants are known deaths and established movements out of the study area. Table 2 presents attrition information by site.

What has COHORTS collaboration found to date?

Phase 1: The group carried out a comprehensive literature review on the long term consequences of 12 exposure variables on 14 adult outcomes, and conducted meta-regression analyses from the five cohorts on the effects of six exposure variables on seven adult outcomes.⁶ Our main findings were: (a) intra-uterine growth retardation and stunting in the first years of life is associated with shorter adult height, lower attained schooling, reduced adult income and lower offspring birthweight; (b) there were no associations

between anthropometric status at two years of age and the risk of chronic disease, even in children with intra-uterine growth retardation; (c) children who are undernourished in early life and then gain weight rapidly after infancy are at high risk of chronic diseases. The findings suggest that the prevention of maternal and child undernutrition is a long-term investment that will benefit both the current generation and their children.

Phase 2: The second set of analyses investigated associations between weight gain and linear growth (first year of life vs. second year vs. 2 years in early to mid-childhood) and two sets of outcomes measured among young adults. The first set included risk factors for complex chronic diseases, including blood pressure, body composition and glucose. The second set included human capital outcomes, namely achieved schooling and adult height. All analyses used conditional growth modelling in order to remove the correlation between growth measured in different age ranges.¹³ Our main findings so far are the following:

Schooling⁸: Growth during the first two years of life was found to be the most critical period for schooling outcomes, followed by status at birth; but growth from 2 to 4 years has little relationship to schooling outcomes. Stunting was associated with a reduction in attained schooling of 1.8 years and 0.9 years before and after controlling for confounding, respectively. In fully adjusted models, one z-score of birthweight, weight gain between 0 and 24 months and 24 to 48 months were each associated with 0.21, 0.43 and 0.07 additional years of schooling, respectively.

Height⁹: The five cohorts differed in their patterns of child growth in length/height, with Guatemala and Cebu showing marked growth failure in early childhood, Pelotas showing growth quite similar to international standards, and South Africa and India showing intermediate patterns. Nonetheless, across the five cohorts, linear growth failure was associated with reduced adult height. In the cohorts with measured length at birth (Guatemala, India, Cebu), linear growth failure during the period from 0-12 months was most strongly associated with attained height whereas growth failure in the periods 12-24 months or from 24 months through to mid-childhood was not associated with attained adult height.

Blood pressure⁷: Weight gain in childhood was associated with increased blood pressure and the risk of pre-hypertension and hypertension, and this association was mediated through adult body mass index (BMI). After adjustment for adult height and BMI, systolic blood pressure and risk of hypertension and pre-hypertension were inversely associated with birth weight, but not with any of the conditional weight gain measures. Relationships were similar in adults who had been born small for gestational age and those with normal birth weight. These analyses suggest that rapid weight gain in infancy does not pose a higher risk for elevated blood pressure than gains at other ages.

Long term consequences of breastfeeding: There were no differences in outcomes related to chronic-disease between children whose mothers initiated breastfeeding compared to children who were never breastfed¹⁴. Associations with duration of breastfeeding were most U-shaped and of small effects. Children who started complementary foods later in infancy were less adipose in adult life. These associations remained significant after adjusting for the confounding factors, indicating that delayed introduction of complementary foods until child age of six months may protect against later overweight.

Analyses are underway on the association between early growth and later glucose and body composition. A paper on the methods used in the DOHaD field is also under preparation.

Taken together, the series of analyses on the timing of early weight and/or height gains show that children from low and middle income countries with greater gains in the first and

possibly in the second year of life show improved human capital indicators as adults, and no evidence of increased risk of chronic diseases in later life.

What are COHORTS main strengths and weaknesses?

The main strengths of the collaboration include: (a) the possibility of confirming individual-site findings by verifying whether they are also observed in other low- and middle-income contexts; (b) the enhanced statistical power obtained by pooling five datasets; (c) the high prevalence of maternal and child undernutrition in our cohorts as compared to studies from high-income countries, which allows studying their long-term consequences; (d) for selected exposures and outcomes, the different patterns of confounding as compared to high-income country cohorts (for example, breastfeeding being more common among the poor in most of the five cohorts, or overweight/obesity being more common among the better off) and (e) the avoidance of publication bias by agreeing a priori on which analyses are to be undertaken and jointly publishing the results for the five cohorts.

Some of the weaknesses include: (a) differences in variable definitions, or in measurement techniques across sites (this affects exposures, outcomes and confounding variables) which means that major effort has gone into producing a common dataset; (b) the different ages of individuals across the five cohorts and the different time periods they reflect; (c) the different ages for which data are available throughout infancy and childhood; (d) heterogeneity in the results for some of the analyses, for example those on body composition. In order to overcome these limitations, we have restricted potential analyses to those including variables collected consistently across the cohorts; likewise, we have limited the analyses to ages with data available for all (or most) cohorts. In some analyses, different outcome variables have been used (for example, pre-hypertension for adolescents and hypertension for adults)⁷ because of the different ages of the individuals across cohorts.

Can I get hold of the data? Where can I find more?

Individual sites have extensive collaborations with groups outside of COHORTS. Further information is available on the websites of the individual birth cohort projects (table 3). A website for the collaboration is in the making and the contact details of the Principal Investigators and individual study websites are shown in Table 3. For further information, please e-mail L.Richter@hsrc.ac.za (principal investigator of the current Wellcome Trust grant), prchallal@gmail.com (data manager) or aryeh.stein@emory.edu (coordinator of the Gates Foundation funded analyses)

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Figure 1.
Logo of the Consortium of Health Orientated Research in Transitioning Societies (COHORTS) collaboration.

Table 1

Data collection waves in the individual studies in the Consortium of Health Orientated Research in Transitioning Societies (COHORTS) collaboration.

Country	Follow up visits
Brazil	All cohort members were sought at birth and at the mean ages of 2, 4, and 23 years. Subsamples were seen at 1, 15, 18, 19 and 26 years of age.
Guatemala	After recruitment, follow up studies took place in 1988-99, 1996-99, 2002-04 and 2005-07.
India	All cohorts were included from conception and then followed-up from birth at 3 monthly intervals (+7 days) until 1 year, and at six monthly intervals (\pm 15 days) thereafter till 20 years. Subsequently as adults they were followed-up once each between 29 and 32 years and 37 and 40 years of age. These phases of follow up were conducted in 1969-1973; 1975-1980; 1983-1987; 1988-1990; 1998-2002; and 2006-2010.
The Philippines	Women were recruited in pregnancy (1983-84), and their children were assessed at birth, at 2-month intervals until age 2 years, and then in 1991, 1994, 1998, 2002 and 2005.
South Africa	All cohort members were sought during pregnancy, at birth, 6 months, 1, 2, 3.5, 5, 7.5, 9.5, 11.5, 13, 14, 15, 16, 17.5 and 18.5 years of age.

Table 2

Attrition information by site

Attrition information	Brazil	Guatemala	India	The Philippines	South Africa
Original cohort size	5914	2392	8181	3080	3273
Known to have died	282	274	590	237	47
Moved out of study area	334	162 ²	3918	724	292 ⁵
Not traced	1001	101	1311	24	441 ⁶
				63 ⁴	
Sample size available for main COHORTS analyses	4297	1571 ¹	1526 ³ (2002) 1149 (2009)	2032	1869 ⁷

¹ 1,571 completed at least one interview in the 2002-4 study² 162 left Guatemala³ 2,362 available; numbers analyzed based on consent and eligibility⁴ Refused, institutionalized, physically/mentally ill, pregnant in 2002 or 2005, invalid baseline/birth data⁵ An additional 498 moved to an unknown address, either within or outside of the study area.⁶ The cumulative attrition over 20 years for all reasons was 961, of which 441 were deemed as "not traced", having only been seen once in the first year of the study and never contacted again. ¹²⁷ At age 18/19, 1869 had data collected, 2312 had true contact.

Table 3

Contact information for each study in the Consortium of Health Orientated Research in Transitioning Societies (COHORTS) collaboration.

Site	Principal investigator for the COHORTS collaboration	Email	Website
Pelotas (Brazil)	Cesar G Victora	cvictora@gmail.com	http://www.epidemiologia-ufpel.org.br/_projetos_de_pesquisas/coorte1982/
NTCS (Guatemala)	Reynaldo Martorell	rmart77@sph.emory.edu	http://www.sph.emory.edu/humanecapital/index.php
New Delhi (India)	Santosh Bhargava	dskbhargava@yahoo.com	No website
Cebu (the Philippines)	Linda Adair	linda_adair@unc.edu	http://www.icpsr.umich.edu/cocoon/DSDRSTUDY/00178.xml
Birth-to-twenty (South Africa)	Linda Richter	LRichter@hsrc.ac.za	http://web.wits.ac.za/Academic/Health/Research/BirthTo20/