Published in final edited form as:
Cad Saude Publica. 2003 ; 19(5): 1241–1256.

The Pelotas Birth Cohort Study, Rio Grande do Sul, Brazil, 1982-2001

Cesar G. Victora[1], **Fernando C. Barros**[1,2], **Rosângela C. Lima**[1], **Dominique P. Behague**[1,3], **Helen Gonçalves**[1], **Bernardo L. Horta**[1,4], **Denise P. Gigante**[1], and **J. Patrick Vaughan**[3]

[1] Faculdade de Medicina, Universidade Federal de Pelotas. C. P. 464, Pelotas, RS 96001-970, Brasil.

[2] Centro Latinoamericano de Perinatología y Desarrollo Humano. Casilla de Correo 627, 11000, Montevideo, Uruguay.

[3] London School of Hygiene & Tropical Medicine. Keppel Street, London WC1E 7HT, UK.

[4] Escola de Medicina, Universidade Católica de Pelotas. Rua Félix da Cunha 412, Pelotas, RS 96010-000, Brasil.

Abstract

Given the growing recognition of the importance of the life course approach for the determination of chronic diseases, birth cohort studies are becoming increasingly important. This paper describes the methods used in the 1982 Pelotas (Brazil) birth cohort study, one of the largest and longest studies of this type in developing countries. All 5,914 hospital births occurring in Pelotas in 1982 (over 99% of all deliveries) were studied prospectively. The main stages of the study took place in 1983, 1984, 1986, 1995, 1997, 2000, and 2001. More than two thousand variables are available for each subject who participated in all stages of the study. Recent phases of the study included the examination of 2,250 males when presenting for the army recruitment exam in 2000, the study of a 27% sample of men and women in 2001 through household visits, and the study of over 400 children born to the cohort women. Follow-up rates in the recent stages of the cohort were 78.9% for the army examination and 69.0% for the household visits. Ethnographic and oral health studies were conducted in sub-samples. Some recent results on blood pressure, adolescent pregnancy, and asthma are presented as examples of utilization of the data. Suggestions on lessons learned for other cohort studies are proposed.

Keywords

Cohort Studies; Growth; Life Cycle Stages; Adolescent; Child

Introduction

Birth cohort studies from developed countries have contributed enormously to the understanding of the long-term consequences of conditions in early life. The first prospective national birth cohort study was started in the United Kingdom in 1946 (Wadsworth, 1991), and new cohorts were started in 1958, 1970, and 2000 (Smith & Joshi, 2002). In the United States, a large birth cohort will be started in 2004 (see http://www.nichd.nih.gov/despr/cohort).

Correspondence to: Cesar G. Victora.
cvictora@terra.com.br

Europe PMC Funders Author Manuscripts

However, large birth cohort studies are rare outside developed countries. Harpham et al. (in press) have recently reviewed longitudinal studies from developing countries with samples of 1,000 or more children. Of these, only three birth cohorts were followed for 10 years or more. In chronological order, these include the 1982 Pelotas (Brazil) cohort of approximately 6,000 births; the 1983-1984 Cebu (Philippines) study with approximately 3,000 newborns (CHLNS, 2002); and the 1990 Johannesburg (South Africa) *Birth to Ten Study* of some 4,000 births (Richter et al., 1995). With the exception of the Cebu study – terminated in 1999 – the other two cohorts are still being followed. A smaller study is being conducted in Guatemala, where about 400 subjects born from 1969 to 1977 are still being followed (Stein et al., 2002).

In this paper we provide an update on the *Pelotas and Birth Cohort Study*, with emphasis on the design and methods used in recent phases of the study. The importance of birth cohort studies and their main methodological challenges are highlighted. Special attention is given to the issue of losses to follow-up, possible strategies for improving response rates in cohort studies, and integration of longitudinal epidemiological and ethnographic methods.

Methods

The study was carried out in the Brazilian city of Pelotas, Rio Grande do Sul State. The urban population grew from 214,000 in 1982 to 320,000 in 2000. This is a relatively affluent area of Brazil, near the Southern border with Uruguay and Argentina, with a per capita gross domestic product of US$ 2,700 (Klering, 1992) in the 1990s. The population descends mostly from Portuguese and Spanish settlers, Amerindians, and Africans brought as slaves; German immigrants are also represented. Inter-racial marriages are common. The main economic activities are agriculture (mostly rice farming and cattle-raising), commerce, and education (the city is home to two large universities). Over 90% of the households are connected to the public water supply and half to the sewage disposal network. When the study began, the infant mortality rate in the city was some 40 deaths per thousand live births. There is one physician for each 260 inhabitants, health care being provided free of charge at 32 basic health facilities, five specialized health centers, and five general hospitals.

Early phases of the study: 1982-1986

The methods used in the early phases of the cohort have been described elsewhere (Barros et al., 1990, 2001; Victora et al., 1992). The study began as a perinatal health survey (Barros, 1986) including all 6,011 infants born in three maternity hospitals (accounting for 99.2% of all births in the city). The 5,914 live-born infants were weighed with regularly calibrated pediatric scales (Filizolla, Brazil) to the nearest 10g. Birth length was not recorded. Mothers were weighed and measured and answered a short questionnaire on socioeconomic, demographic, and health-related variables.

The cohort children were followed up at several points in time (Table 1). Initially, those born from January to April 1982 were targeted in the *1983 Follow-up Study* through the addresses obtained during the hospital interview, when they were aged 8-16 months (mean age 11.3 months).

To calculate the proportion of children located in each follow-up visit, those known to have died were added to those examined. In 1983, 66 of the 1,919 children born from January to April 1982 were know to have died; added to the 1,457 whose mothers or caretakers were interviewed, these accounted for 79.3% of the children who were targeted. Address errors were the main reason for non-response. Non-response rates quoted in the present paper are slightly different from those presented in earlier publications (Barros et al., 1990), since they did not fully account for children who had died.

The subsequent phases included the *1984 Follow-up Study* (January-April 1984), when the mean age was 19.4 months (range 12-29), and the *1986 Follow-up Study* (December 1985-May 1986) (mean age 43.1 months; range 35-53). To minimize losses to follow-up, in each round the approximately 70,000 urban households were visited in search of children born in 1982. After the census was completed, children who still had not been located were searched for at their last known address. This approach resulted in locating 87.2% and 84.1% of the original cohort, respectively.

During each visit, the mother or caretaker answered pre-coded, standardized questionnaires (see Table 2 for a list of the main variables collected). Children were weighed with portable spring scales (CMS, United Kingdom) and were measured with locally made AHRTAG stadiometers (Barros & Victora, 1998). Standard weighing and measuring methods were used (Jelliffe, 1966), and the interviewers were extensively trained before fieldwork. Quality-control measures included repeating some 5% of the interviews and measurements by a fieldwork supervisor, standardization sessions, and double data entry.

Two sub-studies were also performed. The *Psychomotor Development Study* (Victora et al., 1990) was performed on a random sub-sample of 360 children born from January to April 1982 who had been seen at all follow-up visits. At the mean age of 4.5 years, they were tested with the Griffiths's scales in six areas of development (locomotor, personal-social, hearing and speech, eye-hand coordination, performance, and practical reasoning).

The *Mortality Study* entailed the identification of all deaths occurring among cohort children. All hospitals, cemeteries, civil records offices, and the Regional Secretariat of Health were regularly visited from 1982 to 1982 to detect deaths of children and adolescents belonging to the 1982 cohort; from 1987 onwards, it became clear that civil records offices were detecting all deaths, and thus other sources were no longer monitored. Causes of death were investigated by reviewing case notes from outpatient clinics and hospitals, in addition to interviewing family members and the attending physicians. During the interviews a full history of the events preceding the death was obtained with the help of a questionnaire based on that used during the *Inter-American Investigation of Mortality in Childhood* (Puffer & Serrano, 1973). Two independent referees assigned the causes of death using this information; in case of discordance a third senior referee made the final decision. Causes of death were coded according to the Portuguese edition of the International Classification of Diseases, 9th version (OMS, 1980). This study is still ongoing.

The 1995 Follow-up Study

In early 1995 we attempted to locate a sub-sample of the cohort children, aged 12-13 years at the time, using the addresses available from earlier phases of the study. The main objectives of this phase were to assess their school performance and knowledge about HIV/AIDS transmission and prevention. Of a random sample of 1,100 adolescents from the original cohort, 715 (69.9%) were located. It was not possible to improve the rate of follow-up due to the high mobility of the population and to the long time elapsed since their home addresses had been recorded.

The 1997 Follow-up Study

In 1997, an attempt was made to visit a sub-sample of the cohort. Given the high rate of non-response in 1995 when adolescents were searched for at their last known addresses, a different sampling strategy was adopted. This entailed systematically selecting 70 of the 265 census tracts in the city, corresponding to 27% of all households. Census tracts include an average of 300 households and are numbered consecutively from the central area of the city to the suburbs, following a spiral pattern. Because socioeconomic status is strongly related

to place of residence, this systematic procedure was expected to result in a sample that would be representative of the entire urban area.

In each tract, all households were visited and adolescents born in 1982 were interviewed and later linked to their cohort records. In all, 1,076 adolescents belonging to the 1982 cohort were interviewed, resulting in a response rate of 71.8% (Table 1). All adolescents were interviewed (Table 2), weighed, and measured and their blood pressure was verified twice, at the beginning and end of the interview. There was also a short interview with their mothers or caretakers. Analyses from this phase of the cohort study have been partially published (Barros & Victora, 1999; Horta et al., 2003).

The 1997 visit provided the sampling frame for two component studies:

- The *Oral Health Study* included a visit to a simple random sample of 900 of the 1,076 adolescents located in 1997. A standardized oral health examination (WHO, 1997) was performed in 893 (99.2%) of these adolescents, who also answered a detailed questionnaire on oral hygiene practices and relevant risk factors.
- The *Adolescent Over-Nutrition Study* covered all those who, in 1997, were in the top quartile of body mass index (BMI; weight in kg over height in m2), and a simple random sample of one third of the remaining subjects. Of 528 adolescents searched for, all but 25 were located; another 10 girls were excluded due to pregnancy. In addition to weight and height, subscapular and triceps skinfolds were measured using a caliper (Cescorf®, Porto Alegre, Brazil) with a precision of 0.1mm. The combination of these measurements allowed the identification of obese subjects using World Health Organization classification criteria (WHO, 1995). A detailed questionnaire was applied covering risk factors for obesity, including diet and physical activity.

The 1997-2001 Ethnographic Study

The *Ethnographic Study* aimed to describe patterns of emotional, social, and reproductive development among a sub-sample of the cohort adolescents. The study was based on intensive, repeated contacts with the same adolescents in two main phases: from the time they were aged 15 to 17 years and again at ages 18 to 20. Special attention was given to the development of social and gender-related identities in order to understand the role of adolescent development in influencing young people's sexual high-risk behaviors. The relationship between sexuality and other potentially negative experiences (smoking, alcohol, illicit drugs, school failure, and violence) was a main objective of the project. Several influences accounting for differences in young people's developmental processes were investigated, including family structure and dynamics, the role of peers and key adult figures, the importance of the young person's own views on how to achieve a clear and productive socioeconomic role in society, and the various institutions with which adolescents and their families interacted (health-care, psychological, and educational institutions).

The census tracts included in the 1997 sample were divided into four socioeconomic strata according to the mean family income level; two tracts were randomly selected from each stratum. In each tract, six boys and six girls were chosen randomly from those located in the 1997 survey, totaling 96 adolescents. These youths and their families were visited prospectively between 1997 and 2001; on average, each subject was visited six times, including an average of four tape-recorded in-depth interviews. The number of visits varied according to how many visits were required to gain sufficient proximity and cover the interview schedule. Two anthropologists and three trained research assistants conducted open-ended interviews, using a range of methods including participant observation, informal

conversation, and structured questioning. In 39 cases, formal interviews were conducted with the adolescents' parents, and in 22 cases close friends were also interviewed. The prospective design with frequent contacts led to the development of a trusting relationship between the adolescents and the researchers, thus allowing the collection of information on personal experiences and life trajectories that would be difficult to obtain through structured questionnaires. Formal and informal interviews were also performed with some 50 health care personnel as a way of ascertaining the various institutional cultures within which adolescents develop. Analyses from this phase of the cohort study have been partially published (Behague et al., 2000).

The 2000 Army Enlistment Study

From January to April 2000, all males born in 1982 were legally required to enlist in the Army. A research assistant was deployed at the recruitment office to interview all draftees and to verify if they belonged to the original cohort, since individuals born outside Pelotas could also enlist in the city. Of the 3,037 boys in the cohort, 2,890 were presumed to be alive; 2,047 were identified when enlisting and traced to their birth records.

In July and September, all those who had enlisted were subjected to a medical examination for selection purposes. A research team was present on this occasion, and cohort members who gave their written informed consent underwent the following procedures:

- an interviewer-applied questionnaire covering non-sensitive issues (Table 3);
- a self-applied confidential questionnaire on sensitive topics (Table 3); this included an identification number and was placed by the responder himself in a ballot-box; this information was not traced to the identification details;
- measurement of blood pressure using mercury sphygmomanometers (Sankey; São Paulo, Brazil);
- anthropometric examination including measurement of:

  (a) standing and sitting height using a CMS (London, United Kingdom) stadiometer, to the nearest mm;

  (b) weight: subjects weighed in their shorts using an electronic Tanita Body Fat Analyzer scale (model TBF-305; Tokyo, Japan), which also provided information on body composition through bioimpedance;

  (c) subscapular and triceps skinfolds using a Holtain skinfold caliper with 0.2mm precision (Dyfed, United Kingdom);

  (d) arm circumference using a non-extensible metallic tape with 1 mm precision (CMS, London, United Kingdom);

  (e) fat mass and fat-free mass, estimated through bioimpedance.

Eight interviewers applied the questionnaires and measured blood pressure; these measurements were standardized against an experienced cardiologist. A single field worker, trained by an experienced anthropometrist, took each of the other anthropometric measures. The weighting scale was calibrated daily.

Blood samples were collected from consenting subjects (98.2% of the sample). Sera samples were stored in test tubes labeled with the subject's identification number and frozen at −80°C for subsequent analyses. Analyses are now under way for herpes virus type II antibodies and for serum cholesterol.

Of the 2,047 cohort members who had enlisted, 198 failed to attend the Army exam. They were invited through correspondence and phone calls to attend an examination at the School of Medicine, and 97 agreed to do so. A mobile team attempted to locate those who did not attend; this resulted in an additional 101 subjects being included in the study. Thus, it was possible to examine all of those who had enlisted.

At the end of the Army enlistment period, 843 cohort subjects who were presumably alive had not been located. They were then searched for at their last known address, and an additional 216 subjects were identified. Of these, 111 were examined at the School of Medicine and 68 at home, the latter by a mobile examination team. Another 37 subjects who had been identified could not be examined; 10 have severe mental or physical handicaps, and the other 27 refused.

Thus, 2,250 cohort members were interviewed. Added to the 147 who were known to have died, they comprised 78.9% of the 3,037 males in the cohort.

Of the subjects who were examined, all those who had presented low birth weight were invited to participate in lung function tests. Two subjects who did not present low birth weight were matched to each of the former. Forced expiratory volume and forced vital capacity were measured with an S-model spirometer (Vitalograph, Buckingham, England), which was calibrated daily. Three measurements were taken on each subject, and the highest result was selected. A single observer, trained by a pulmonologist (A.M.B.M.), performed all examinations.

Early results from this phase of the study will soon be available (Lima et al., in press; Victora et al., in press).

The 2001 Follow-up Study

Since the *2000 Army Enlistment Study* was restricted to males, it was desirable to obtain similar information for the female adolescents in the cohort. In addition, the Army examination setting limited the time available for interviewing subjects and constrained the investigation of sensitive topics requiring a more private environment. For this reason, a home visit to a sample of boys and girls from the cohort was planned for early 2001, soon after the Army study was completed.

The sampling approach used in 1997 was repeated. The same 70 census tracts were visited, and all adolescents living in these tracts were contacted. This resulted in locating 1,031 subjects, a contact rate of 69.0% (Table 1); of these, 794 had also been included in the 1997 follow-up. Adolescents who had been interviewed in the same census tracts in 1997 but who were no longer living in the same area were actively searched for at their new addresses. This led to interviewing 250 more adolescents. Therefore, a sub-cohort of adolescents seen both in 1997 and 2001 was assembled by including the 794 subjects who had not moved and the 250 who had moved but could be traced, totaling 1,044 subjects.

Of the 1,031 adolescents contacted in the original census tracts, it was possible to interview all but 21. It was also possible to interview 1,019 mothers. The interview with the mothers included socioeconomic information, household composition, migration patterns, mothers' intimate, marriage, and reproductive histories, major positive and negative life-changing events affecting members of the household in the past year, mothers' child-rearing patterns and preferences, adolescents' school history, and basic indicators of mothers' current physical and mental health status.

Males who had been interviewed in the Army answered a short questionnaire with variables that had not been not previously collected from them. Females, plus 21 males who had not been interviewed in the Army, answered a longer version of the interviewer-applied questionnaire, as well as the same self-applied confidential questionnaire used in the Army study.

The 2001 questionnaires had a strong input from the longitudinal 1997-2001 *Ethnographic Study*. The *Ethnographic Study* generated an average of 30-80 pages of transcribed interviews and observational notes for each adolescent and his/her family and friends. By using an inductive analytical process with this material, a list of variables and values, which were known to capture meaningful heterogeneity, were generated. This analytical process was useful for identifying new explanatory concepts (and possible determinants) as well as for operationalizing predetermined variables. For each variable, we devised several questions and their values, based on wording and conceptualizations found to be effective in open-ended interviews, piloted them in a questionnaire format, and then selected the one that gave the most ethnographically valid and meaningful responses. In addition to standard questions on health, education, and work, several topics were included on intimacy and intimate relationships, friendship patterns, community & political participation, recall of major life-impacting events, and recent positive and negative events experienced by family and household members (Table 3).

Weight, height, and blood pressure were measured at home on all subjects, except for boys who had already been examined in the Army.

Case-Control Study of Adolescent Parity

Teenage pregnancy is an important problem in Pelotas, and a component study was designed to address this issue. The city health authorities monitor all live births through the Live Birth Information System (*Sistema de Informações sobre Nascidos Vivos* or SINASC). Stillborns are identified through the Mortality Information System (*Sistema de Informações sobre Mortalidade* or SIM). Coverage of both systems is considered to be close to 100%, as it is not possible to register a birth or bury a stillborn child without a copy of these documents.

The information systems record maternal age (but not maternal date of birth) and the child's date of birth. All mothers giving birth from January 1995 to March 2001 whose age was compatible with having been born in 1982 were flagged in the system. Hospital delivery records were then sought in the five maternity hospitals in the city, to obtain information on maternal date and place of birth. If needed, an attempt was made to visit these women to confirm that they belonged to the original cohort. In all, 446 parous adolescents belonging to the 1982 cohort were identified. They account for 16.2% of the original cohort (those known to have died were removed from the denominator). Among those identified, there were three refusals, and 23 adolescents could not be located. This resulted in a sample of 420 parous teenagers (94.2% of those identified) who had delivered at least one live or stillborn child. It is important to stress that this study does not refer to adolescent pregnancies in general, since many of these may have led to abortions that are frequent, albeit illegal.

Parous adolescents answered a detailed questionnaire on pregnancy-related variables, as well as the same standard questionnaire used in the 2001 visit to the 27% sample of the whole cohort. This allows a case-control analysis in which cases are the 420 parous teenagers, and controls were the 411 adolescents who, being part of a representative sample of the birth cohort, had not delivered an infant by March 2001.

Parous adolescents and their mothers answered the general questionnaire used in the 2001 follow-up visit. Additional information was collected from parous adolescents on date of

menarche, number of gestations and deliveries, and selected questions on morbidity. A separate questionnaire addressed the health of their children (see below).

Twenty-six parous adolescents residing in the census tracts selected for the 1997-2001 ethnographic study were selected for an ethnographic study. An anthropologist conducted an average of three in-depth interviews with each of them. Semi-structured interviews and participant observation were also used. All interviews were recorded and transcribed. The main topics included knowledge about reproduction and contraception; parenthood and desire to become pregnant; pressure and negotiation with sex partners; family relations and familial reproductive patterns; and health services utilization. Informal conversations with other family members were also used to capture their attitudes and experiences with reproductive issues – including the teenager's pregnancy – as well as to record relevant aspects of their life histories.

The Second Generation Study

As mentioned above, a questionnaire was applied relative to each child delivered by the 1982 cohort adolescents; 336 had delivered one live-born child, 70 two children, 12 three children and two, four children; 12 adolescents had not delivered a live child. In all, 501 children were still alive when the mother was visited; their mean age was 24.7 months (standard deviation 14.0 months).

Information was collected on gestational age, perinatal morbidity, type of delivery, birth weight and length, delivery care, Apgar score, and breastfeeding duration for each child.

Administrative and ethical aspects of the study

The original 1982 perinatal survey was carried out at the Catholic University of Pelotas. From 1983 onwards, the study headquarters was transferred to the Federal University in Pelotas, affiliated with the Brazilian Ministry of Education. The sources of funding for the study are listed in the Acknowledgments section.

The Ethical Review Boards of the Universities involved, which are currently affiliated with the Brazilian Medical Research Council, approved all phases of the study. Verbal informed consent was obtained from the caretakers in the 1982-1986 phases of the study, as was common practice at that time. In recent phases of the study, written informed consent was procured. Confidentiality was guaranteed in all phases of the study, and computer files with the names of mothers and cohort members are kept separately under restricted access.

In every phase of the study, subjects diagnosed with health problems were referred to the University clinics for free treatment. Since free dental treatment is not routinely available for Brazilian adolescents, the grant for the *1997 Oral Health Study* included funds for setting up a special clinic at the Federal University's Dentistry School to provide care for subjects found to require dental treatment.

Results

Table 4 shows the follow-up rates in the different studies, according to baseline characteristics. The proportion of subjects located did not vary markedly according to sex or birth weight. In terms of family income, fewer subjects in the lowest income category were traced in 1983; in the 1984, 1986, and 1995 follow-ups there was a tendency to locate a higher proportion of the middle-income group; from 1997 onwards, there were no clear trends. Follow-up rates did not vary systematically according to maternal schooling or in terms of maternal skin color. In all phases, children of single mothers were less likely to be

traced. Except for the 1995 study, at least 60% of children in any of the categories in Table 4 were traced.

In spite of these follow-up rates, Table 5 shows that the actual number of subjects available for analyses that combined more than one phase of the follow-up could be sharply reduced. For example, an analysis including data collected in 1982, 1984, 1986, 1997, and 2001 would be based on only 718 subjects. This is mostly due to the fact that the 1997 and 2001 follow-up visits were restricted to 27% of the urban area.

Next, some illustrative results from recent phases of the study are presented, as examples of the analytical possibilities afforded by this dataset.

Intergenerational effects of poverty

When all cohort boys were interviewed at the *Army Enlistment Study* in 2000, it became clear how social characteristics persisted across generations. Figure 1 shows that family income at birth was strongly associated with achieved schooling levels. Eighteen-year-old boys from families earning up to one minimum wage (≤ US$ 50) in 1982 had on average 6.8 years of schooling, while those from families earning more than 10 times the minimum wages (> US$ 500) in 1982 had a mean of 10.5 years. Schooling being one of the major determinants of future earnings, it is clear how poverty tends to be reproduced across generations.

Risk factors for chronic disease at 18 years of age

As cohort members became older, the focus of the study moved from infectious childhood diseases and malnutrition to risk factors for chronic diseases. Preliminary analyses shown in Figure 2 describe the prevalence of selected risk factors measured in the 2001 *Army Enlistment Study*, according to family income level at birth. In contrast to the sharp socioeconomic differences observed for early life risk factors (Victora et al., 1992), the distribution is now more complex (Figure 2). Some risk factors appeared to be more common among those born to the poorest families – daily smoking ($P = 0.08$) and lack of regular exercise during leisure time ($P = 0.06$) – but significance levels were borderline. Mean diastolic blood pressure was significantly lower in the high-income group (data not shown), but there was no difference for systolic pressure. On the other hand, several factors were significantly more common among boys from families in the highest income group: overweight (WHO, 1995), obesity (WHO, 1995), high fat diet (Block et al., 1989), and alcohol intake in the preceding week (the latter with $P = 0.06$). Total cholesterol was 19mg/dl higher among the highest-income boys than among the poorest ($P < 0.001$). In many developed countries, risk factors for cardiovascular diseases used to be more prevalent among the better off, and are now more common among the poor (Chang et al., 2002; Tyroler, 1999). It is possible that our study population is at a transition stage in which some risk factors are still more prevalent among the wealthy.

Blood pressure levels at 15 years of age according to early life characteristics

Hypertension and over-nutrition are two major current public health problems. At the *1997 Follow-up Study*, blood pressure levels were measured on all boys and girls. The early origins of diseases hypothesis (also known as the Barker hypothesis) (Barker, 1999) postulates that adverse conditions in intrauterine and early extrauterine life may lead to chronic disease later in life. Our analyses showed that, after controlling for possible confounding variables, birth weight was negatively associated with systolic blood pressure. One z-score increase in birth weight for gestational age was associated with an average decrease of 1.23mmHg in systolic blood pressure. On the other hand, rapid growth in childhood (catch-up growth, measured by weight gain between birth in 1982 and attained

weight in 1984 and 1986) was also associated with higher blood pressure levels in adolescence (Horta et al., 2003). Catch-up growth was also associated with a greater prevalence of overweight and obesity in 16-year-olds, detected in the *1998 Adolescent Over-Nutrition Study* (Monteiro et al., in press).

The findings on catch-up growth are worrisome. Children who are born small and who catch up by gaining weight rapidly in infancy have lower morbidity and mortality in childhood, as our own study has shown (Victora et al., 2001). On the other hand, these same children present higher prevalence of hypertension, overweight, and obesity in adolescence.

Asthma according to early life characteristics

In the *2000 Army Enlistment Study*, 18.6% of the adolescent boys reported asthma – defined as "wheezing in the chest" – in the past year (Lima et al., in press). The following childhood factors were significantly associated with increased risk of asthma in a multivariate analysis: high socioeconomic status (Figure 3), living in non-crowded households, and breastfeeding for nine months or longer. When a stricter asthma definition (Sole et al., 1998) was used, poor nutrition and a history of helminth infections were also protective. These findings are in agreement with the "hygiene hypothesis", that early exposure to infections helps develop specific components of the immune system that protect against later onset of asthma (Strachan, 1989). Therefore, several exposures and conditions that are well known to be detrimental to young children – such as poverty, malnutrition, crowding, and lack of breastfeeding – appear to protect against asthma in adolescents.

Adolescent pregnancies and childbearing

As mentioned, over 400 girls born in 1982 had already delivered a child by March 2001.

Figure 4 shows that this proportion ranged from 3% in the high-income group, to 24% among the poorest. We also investigated whether or not the pregnancy had been planned – one out of every three children born in the lower income group had reportedly resulted from a desired pregnancy; in the high-income group, not a single child was reportedly planned. The case-control analysis showed that in addition to family income, several other characteristics were independently associated with childbearing: parental schooling, being born to a teenage mother, having siblings from different fathers, and failing in school before the fourth grade (Gigante et al., submitted).

Availability of data on children born to the cohort teenagers allows the comparison of perinatal factors across generations. Figure 5 shows the mean birth weight of these children, according to their mothers' birth weight recorded in 1982. Mothers born with a birth weight under 2,500g had babies who, on average, weighed 2,922g, compared to 3,259g for infants whose mother weighed 3,500g or more at birth. This finding suggests that, like poverty, several risk factors persist across generations.

Discussion

According to the recent review by Harpman et al. (submitted), ours is the largest and longest running birth cohort study in a developing country. For subjects who were seen in all phases of the study, over 2,000 different variables are available covering many aspects of the social, behavioral, and health dimensions of life.

Given the recent interest in the life-course approach to the determination of health (Barker, 1999), birth cohort studies are invaluable. New, large birth cohorts are being launched in developed countries. The National Institute of Child Health and Development is launching a large multi-center cohort in the United States (see http://www.nichd.nih.gov/despr/cohort),

and in the United Kingdom the tradition of national cohorts is being continued with the *Millennium Cohort Study* (Smith & Joshi, 2002). Of particular value are cohorts, such as ours, in which children underwent anthropometric measurements not only at birth but also on different occasions in childhood. Very few cohorts, anywhere in the world, have such measurements (D. J. Barker, personal communication), which allow the investigation of the influence of prenatal and postnatal growth on adult outcomes.

It is regrettable that only three large-scale birth cohorts lasting 10 years or more are available from less-developed countries, as discussed in the *Introduction*. Findings from developed country cohorts cannot be automatically extrapolated to populations where the prevalence of intrauterine growth retardation and pre-term deliveries is considerably higher, where childhood infections are highly prevalent, and where malnutrition takes a heavy toll. Regarding bi-generational studies in developing countries, the only other known study includes approximately 200 mother-infant pairs in Guatemala (Ramarkrishnan et al., 1999).

In the above results, we highlighted some of the potential analyses that may be carried out in our dataset. In particular, results on risk factors for asthma and on the consequences of catch-up growth suggest possible tradeoffs between early life gains and later prevalence of health problems. It will be difficult, if not impossible, to study these public health dilemmas in developed country cohorts where severe infections and malnutrition are uncommon in childhood.

The reasons for the success of the Pelotas cohort are largely related to the characteristics of the city. Pelotas is a middle-size city with relatively low rates of in- and out-migration. The number of annual births provides sufficient statistical power for the study, while being still logistically manageable. Also, concerns with personal and home security are not as manifest as in larger Latin American cities, and the local population has been extremely generous in welcoming our interviewers and answering our often too numerous questions.

Several lessons were learned from the Pelotas cohort that may be relevant to other studies. A critical issue in all cohorts is that of losses to follow-up. Two successful strategies were used in our study: household sampling and Army enlistment. The first entailed visiting a sample of the city's households, identifying individuals born in 1982, and later tracing them to their cohort records. The second included taking advantage of the compulsory Army enlistment process. Both attempts at locating cohort members using available addresses (both in 1983 and in 1995) led to higher rates of losses to follow-up.

An epidemiological maxim states that "*the best solution to losses to follow-up is not to have them*" While this is certainly true, documentation that follow-up rates did not vary markedly according to key baseline variables (Table 4) is reassuring. Outside a few developed countries, particularly in Northern Europe, where computerized databases and unique identification numbers for every citizen allow "passive" cohort studies to be carried out, our labor-intensive approach in an active cohort study will necessarily lead to higher rates of loss.

One disadvantage of the household sampling approach is that subjects who are identified in a given phase of the study are not necessarily the same as those identified in other phases using the same strategy. For example, 1,076 individuals were interviewed in 1997 and 1,031 in 2001 in the same census tracts, but only 794 were present on both occasions (as mentioned, an additional effort resulted in including another 250 subjects seen in 1997). The results presented in Table 5 show how rapidly the number of subjects available for analysis may decrease when combining variables from several phases of the study.

Several lessons can also be learned from the administrative and financial aspects of the study. Funding agencies are subject to “donor fatigue”, and even though the study was conducted successfully and many publications were produced, funding agencies were prepared to support only one, or at most two, phases of the cohort. Lack of funding precluded a more regular schedule of visits, and more than once the sampling fractions were determined by availability of funds rather than by scientific principles, as for example in the 1983 and 1995 follow-ups. Large birth cohort studies present specific funding issues that should deserve special treatment by grant-making agencies, who usually function on relatively short funding cycles. A related problem is that funding is more easily available for new data collection than for analyses of existing data. This is a problem that our cohort is still facing, with enormous amounts of data that cannot be fully explored.

From the logistic standpoint, some important differences exist between developing and developed country cohorts. In many of the latter, national databases are available that allow passive follow-up of cohort subjects by linking birth records with records belonging to census, hospital admissions, and death certificates. Investigators with access to these databases can conduct “passive” cohort studies – examples include studies from Scandinavia and the United Kingdom. Cohorts in developing countries, on the other hand, have to be active, with the investigators being directly in charge of all data collection.

Another important difference is that because of relatively low educational levels among part of the city's population, it is not possible to use complex or extensive self-applied questionnaires like most developed country cohorts do. This adds tremendously to the cost of follow-ups, making them less frequent and less comprehensive. Among the problems faced by our field workers were the high frequency of address changes, the fact that many low-income families did not have telephones, and also frequent changes in telephone numbers, reportedly due to unpaid bills.

The future for the Pelotas study is unclear. As cohort members reach adult age, it is likely that they will increasingly move out of the city, where job opportunities are scant due to its poor local economy. Alternative approaches will have to be conceived, including “passive” follow-up through death certificates and nested case-control studies, among others. Nevertheless, the large amount of data already available from the study will certainly lead to many additional analyses on health, behavior, and development in childhood and adolescence.

A second birth cohort study was launched in Pelotas in 1993, eleven years after the original study. Sub-samples of these children were followed up at ages 1, 3, 6, and 12 months, and again in 1998 (Barros et al., 2001), and a new visit to the entire cohort is planned for 2004. We are also applying for funding to start a third birth cohort in 2004, again by enrolling all births in the city. If successful, we will have three birth cohorts at 11-year intervals, allowing the study of secular trends in child, adolescent, and eventually adult health indicators.

Acknowledgments

The early phases of the cohort study were financed by the International Development Research Center of Canada (1982 study), the World Health Organization (1983), and the United Kingdom Overseas Development Administration (1984-1986). The 1995 study was financed by the United Nations Development Fund for Women. The 1997-2001 phase was financed by the National Program for Centers of Excellence (PRONEX), the Brazilian Ministry of Health (National Health Foundation), and the World Health Organization (Division of Child and Adolescent Health and Development). The Pan-American Health Organization supported the Ethnographic Study from 1997 onwards, and the Rio Grande do Sul State Research Foundation (FAPERGS) supported the Teenage Pregnancies Study. The 2000 study was made possible by the logistic support of the Brazilian Army, in particular Colonel J. C. Poppe, Major L. M. Coutinho, Captain J. L. Barros, and Mr. O. Petiz. Several scholarships and

training fellowships were provided during the study by the Brazilian National Research Council (CNPq), FAPERGS, and the United States National Science Foundation (D. Behague).

We would also like to thank our many colleagues who participated in the several phases of the study, particularly Ana Maria Borges Teixeira, Angela Maas, Angela Oliveira, Ari Lemos Jr., Beatriz Guimarães, Cintia Lombardi Nash, Cora Post, Jorge Umberto Béria, José Carlos Martines, Luciana Anselmi, Magda Damiani, Paulo Orlando Monteiro, Paulo Post, Pedro Olinto, and Sharon Huttly.

References

BARKER DJ. Fetal origins of cardiovascular disease. Annals of Medicine. 1999; 31(Sup. 1):3–6. [PubMed: 10342493]

BARROS, FC. The Epidemiology of Perinatal Health in Southern Brazil: A Study of Perinatal Mortality, Low Birth Weight and the Utilisation of Health Care. University of London; London: 1986. Ph.D. Thesis

BARROS, FC.; VICTORA, CG. Epidemiologia da Saúde Infantil: Um Manual para Diagnósticos Comunitários. Fundo das Nações Unidas para a Infância/Editora Hucitec; São Paulo: 1998. 3ª Ed.

BARROS FC, VICTORA CG. Increased blood pressure in adolescents who were small for gestational age: A cohort study in Brazil. International Journal of Epidemiology. 1999; 28:676–681. [PubMed: 10480695]

BARROS FC, VICTORA CG, VAUGHAN JP. The Pelotas Birth Cohort Study, 1982-1987. Strategies for following up 6,000 children in a developing country. Paediatric and Perinatal Epidemiology. 1990; 4:267–282.

BARROS FC, VICTORA CG, VAUGHAN JP, TOMASI E, HORTA BL, CESAR JA, MENEZES MB, HALPERN R, POST CL, DEL MAR GARCIA M. The epidemiological transition in maternal and child health in a Brazilian city, 1982-93: A comparison of two population-based cohorts. Paediatric and Perinatal Epidemiology. 2001; 15:4–11. [PubMed: 11237113]

BEHAGUE, DP.; VICTORA, CG.; GONÇALVES, HD. Sexual Intimacy Among Young Teenagers in Pelotas, Brazil: Achieving Maturity in a Diversified World. Pan American Health Organization; Washington, DC: 2000. Research in Public Health Technical Papers, Priority Themes in Public Health 25

BLOCK G, CLIFFORD C, NAUGHTON MD, HENDERSON M, McADAMS M. A brief dietary screen for high fat intake. Journal of Nutrition Education. 1989; 21:199–207.

CHANG CL, MARMOT MG, FARLEY TM, POULTER NR. The influence of economic development on the association between education and the risk of acute myocardial infarction and stroke. Journal of Clinical Epidemiology. 2002; 55:741–747. [PubMed: 12384187]

CLHNS (Cebu Longitudinal Health and Nutrition Survey). Cebu Longitudinal Health and Nutrition Survey. Nov 13.2002 2002 <http://www.cpc.unc.edu/cebu/about.html>

GIGANTE DP, VICTORA CG, GONÇALVES HD, BEHAGUE DP, LIMA RC, BARROS FC, RASSMUSSEN K. Risk factors for childbearing during adolescence in a population-based birth cohort. submitted. (submitted for publication).

HARPHAM T, HUTTLY S, DE WET T, WILSON E. Linking public issues with private troubles: Panel studies in developing countries. Journal of International Development. in press.

HORTA BL, BARROS FC, VICTORA CG, COLE JT. Early and late growth and blood pressure in adolescence. Journal of Epidemiology and Community Health. 2003; 57:226–230. [PubMed: 12594200]

JELLIFFE, DB. The Assessment of the Nutritional Status of the Community. World Health Organization; Geneva: 1996. Monograph Series 53

KLERING LR. Análise do desempenho dos municípios do Rio Grande do Sul em 1991. Análise (Porto Alegre). 1992; 3:211–253.

LIMA RC, VICTORA CG, MENEZES AMB, BARROS FC. Risk factors for childhood infection and malnutrition protect against asthma in Brazilian male adolescents. American Journal of Public Health. in press.

MONTEIRO POA, VICTORA CG, BARROS FC, MONTEIRO LA. Birth size, early childhood growth and adolescent obesity in a Brazilian birth cohort. International Journal of Obesity. in press.

OMS (Organização Mundial da Saúde). Classificação Internacional de Doenças. Revisão 1975. Centro da OMS para Classificação de Doenças em Português; São Paulo: 1980.

PUFFER, RR.; SERRANO, CV. Patterns of Mortality in Childhood: The Inter-American Investigation of Mortality in Childhood. PanAmerican Health Organization; Washington, DC: 1973. Scientific Publication 262

RAMARKRISHNAN U, MARTORELL R, SCHROEDER DG, FLORES R. Role of intergenerational effects on linear growth. Journal of Nutrition. 1999; 129(Sup. 2):544S–549S. [PubMed: 10064328]

RICHTER L, YACH D, CAMERON N, GRIESEL R, DE WET T. Enrolment into birth to ten: Population and sample characteristics. Paediatric and Perinatal Epidemiology. 1995; 9:109–120. [PubMed: 7724410]

SMITH K, JOSHI H. The Millennium Cohort Study. Population Trends. 2002; 107:30–34. [PubMed: 12152184]

SOLE D, VANNA AT, YAMADA E, RIZZO MC, NASPITZ CK. International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire: Validation of the asthma component among Brazilian children. Journal of Investigational Allergology & Clinical Immunology. 1998; 8:376–382. [PubMed: 10028486]

STEIN AD, CONLISK A, TORUN B, SCHROEDER DG, GRAJEDA R, MARTORELL R. Cardiovascular disease risk factors are related to adult adiposity but not birth weight in young Guatemalan adults. Journal of Nutrition. 2002; 132:2208–2214. [PubMed: 12163664]

STRACHAN DP. Hay fever, hygiene, and household size. BMJ. 1989; 299:1259–1260. [PubMed: 2513902]

TYROLER HA. The influence of socioeconomic factors on cardiovascular disease risk factor development. Preventive Medicine. 1999; 29:S36–40. [PubMed: 10641816]

VICTORA CG, BARROS FC, HORTA BL, MARTORELL R. Short-term benefits of catch-up growth for small-for-gestational-age infants. International Journal of Epidemiology. 2001; 30:1325–1330. [PubMed: 11821340]

VICTORA CG, BARROS FC, LIMA RC, HORTA BL, WELLS J. Anthropometry and body composition of 18-year-old males according to breastfeeding duration: A birth cohort study from Brazil. BMJ. in press.

VICTORA, CG.; BARROS, FC.; VAUGHAN, JP. Epidemiología de la Desigualdad. Pan American Health Organization; Washington, DC: 1992.

VICTORA MD, VICTORA CG, BARROS FC. Cross-cultural differences in developmental rates: A comparison between British and Brazilian children. Child Care, Health and Development. 1990; 16:151–164.

WADSWORTH, MEJ. The Imprint of Time: Childhood, History and Adult Life. Clarendon Press; Oxford: 1991.

WHO (World Health Organization). Physical Status: The Use and Interpretation of Anthropometry. WHO; Geneva: 1995. Technical Report Series 854

WHO (World Health Organization). Oral Health Surveys. Basic Methods. WHO; Geneva: 1997. 4th Ed.

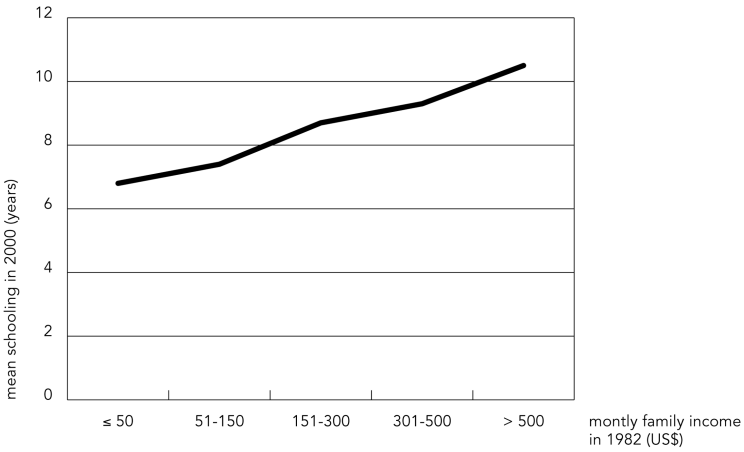

Figure 1.
Mean schooling (years completed with approval) among 18-year-old males according to family income at birth.

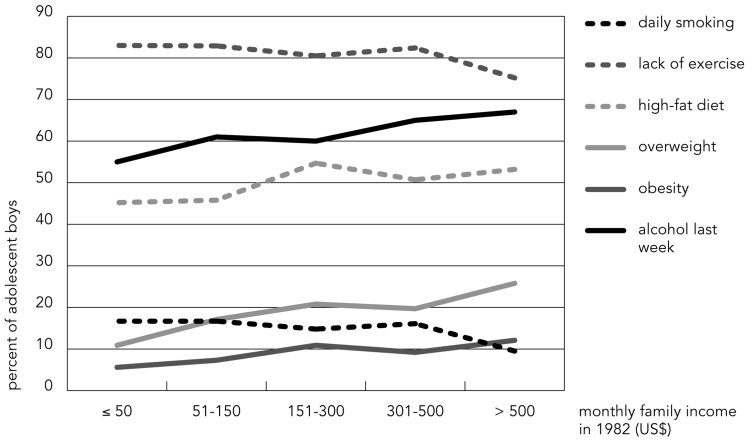

Figure 2.
Percentage of males presenting selected risk factors for chronic disease at 18 years of age.

Europe PMC Funders Author Manuscripts

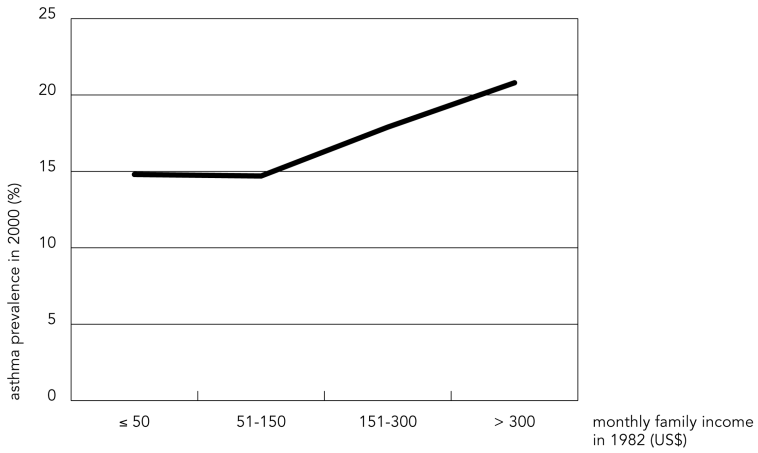

Figure 3.
Asthma prevalence among by 18-year-old males according to family income at birth.

Europe PMC Funders Author Manuscripts

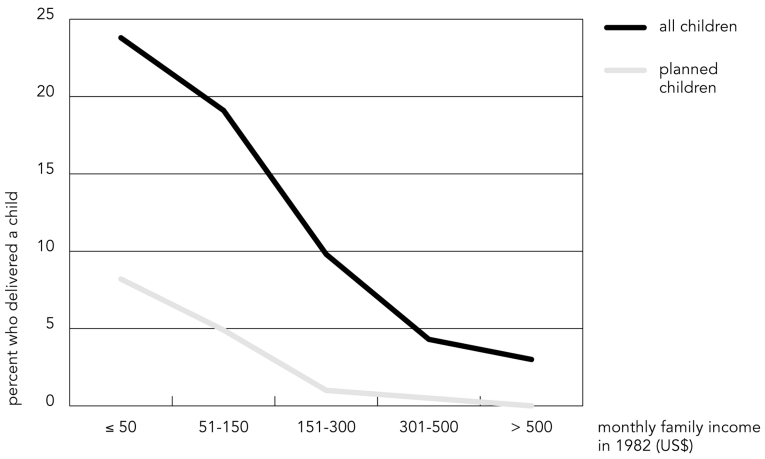

Figure 4.
Percentage of females who had delivered a child by 18 years of age, according to family income at birth.
$p < 0.001$.

Europe PMC Funders Author Manuscripts

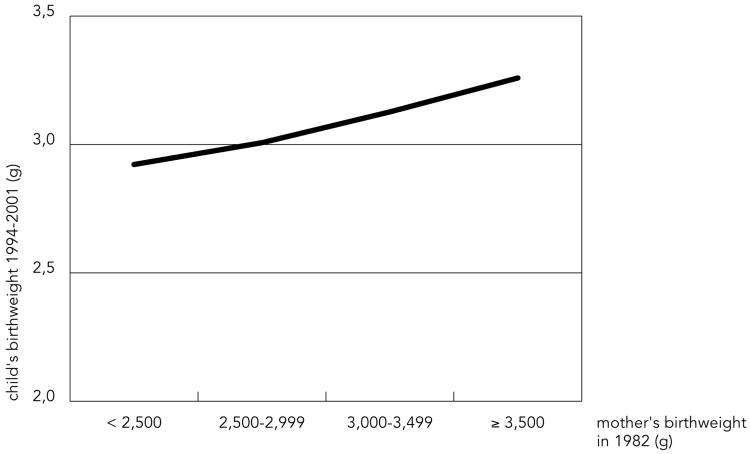

Figure 5.
Mean birth weight of children born to adolescents belonging to the 1982 cohort, according to their mothers' birth weight.
$p < 0.001$.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Table 1

Principal phases of the Pelotas Birth Cohort Study.

Year	Target population		Main sampling strategy	Mean age (range)	Number of subjects		Losses to follow-up (%)*
	Description	Number			Interviewed	Deceased*	
1982	All hospital births in the city from January-December 1982	5,914	Daily visits to all city hospitals	0 mo.	5,914	0	–
1983	All children born from January-April 1982	1,916	Visit to addresses obtained in hospital	11.3 mo. (8-16)	1,457	66	20.7
1984	All cohort children	5,914	Census of all 70,000 households in the city	19.4 mo. (12-29)	4,934	227	12.8
1986	All cohort children	5,914	Census of all 80,000 households in the city	43.1 mo. (35.4-53.0)	4,742	237	15.9
1995	20% of cohort adolescents	1,100	Visits to households based on the addresses collected in previous visits	13.1 yr. (12.5-13.7)	715	47	30.1
1997	27% of cohort adolescents	1,749	Visits to all households in a systematic sample of 27% of the city's census tracts	14.7 yr. (14.0-15.6)	1,076	70	28,2
1997-2001	Ethnographic study	–	Stratified sub-sample of 8 census tracts from those visited in 1997; random sample of 12 subjects in each tract	15-19 yr.	96	–	–
2000	All male cohort adolescents	3,037	Identification of adolescents attending the compulsory Army recruitment examination	18.2 yr. (17.6-19.1)	2,250	143	21.1
2001	27% of cohort adolescents	1,749	Visits to all households in a systematic sample of 27% of the city's census tracts	18.9 yr. (18.1-19.9)	1,031	71	31.0

*This includes those known to be dead at the time of the 1983, 1984, 1986, and 2000 visits, and 27% of those known to be dead at the time of the 1997 and 2001 visits.

Table 2

Principal variables collected in the early phases of the cohort study (1982-1986).

Category	Examples of variables	
Socioeconomic status and demographic variables	Family income	Family structure
	Maternal and paternal education	Number of siblings
	Household assets	
	Parental occupation	
Maternal characteristics	Maternal age	Pre-pregnancy weight
	Reproductive history	Smoking
	Height	Skin color
Pregnancy	Date of last menstrual period	Prenatal care (attendances, when started)
	Inter-gestational interval	Health problems during pregnancy
	Smoking during pregnancy	
	Weight gain during pregnancy	
Delivery	Birth weight	Type of delivery
	Gestational age	Perinatal morbidity
Mortality	Age of death	Cause of death
Environmental characteristics	Water supply	Indoor pollution
	Sanitation	Crowding
	Parental smoking	Type of housing
Health services utilization and morbidity	Medical visits (number, reasons)	Vaccinations
	Growth monitoring	Type of health care provider
	Number and cause of hospital admissions	Use of medicines
		Incidence of selected illnesses
Nutrition	Duration of breastfeeding	Weight and length/height
	Age at introduction of other foods	Sitting height
	24-hour food recall	Head circumference
Child care	Who looks after the child	Role of father in child care
	Day-care attendance	
Maternal health	Minor psychiatric disorders score	Subsequent gestations
	Reported morbidity	
Psychological development	Age of attainment of developmental milestones	Sphincter control

Europe PMC Funders Author Manuscripts

Table 3

Principal variables collected in the late phases of the cohort study (1995-2001).

Instrument	Variables
Interviewed-applied questionnaire	Family situation
	Schooling history, including performance
	Study habits
	Employment/salary
	Participation in household chores
	Friendship patterns
	Leisure activities
	Religious practices
	Dietary habits
	Smoking
	Alcohol consumption
	Physical activity
	Community participation & sense of belonging
	Romantic/intimate relationships: patterns, preferences, history
	Knowledge of contraceptive options
	Recent negative and positive events of households members
	Morbidity history (accidents/violence, asthma, mental health, other health problems)
	Use of health services
Confidential questionnaire	Illicit drug use (self and friends)
	Knowledge about AIDS/STDs
	Exposure to sex education
	Body image
	Self-esteem
	Relationship with parents
	Age at first intercourse
	Number of partners
	Contraceptive practices
	Condom use
	Use of health services
	Reproductive history
	Mental health assessment
Physical examination	Weight
	Standing and sitting height
	Subscapular and triceps skinfolds
	Body composition (bioimpedance)
	Blood pressure
	Oral health

Europe PMC Funders Author Manuscripts

Table 4

Follow-up rates in different phases of the study according to baseline characteristics of the cohort.

Variable	Original cohort (number)*	Percent located**						
		1983	1984	1986	1995	1997	2000	2001
Sex								
Boys	3,037	76	87	84	67	73	79	73
Girls	2,876	83	87	84	72	70	–	65
Birth weight (g)								
< 2,500	534	80	87	84	70	72	79	69
≥ 2,500	5,375	78	89	84	64	67	77	72
Family income (US$)								
≤ 50	1,288	68	84	81	61	61	73	61
51-100	2,789	85	89	86	73	72	80	69
151-300	1,091	81	89	86	71	81	84	78
301-500	382	75	83	80	78	74	79	68
> 500	335	79	83	79	54	80	77	81
Maternal schooling (years)								
0-4	1,960	76	85	83	70	67	76	62
5-8	2,454	80	89	86	70	73	82	73
9-11	654	85	87	84	68	72	76	63
≥ 12	839	84	86	82	68	79	80	81
Maternal skin color								
White	4,851	79	87	84	70	73	79	70
Black	1,060	81	88	87	67	65	78	67
Maternal marital status								
Married	5,424	81	88	85	71	73	79	70
Unmarried	485	68	83	79	52	62	73	62
Total	5,914*	79,3	87,2	84,2	69,3	71,8	78,9	69,1

* Up to 29 subjects had missing information in baseline variables.

** Includes subjects interviewed as well as those who are known to have died; when the follow-up study was restricted to a sub-sample of the cohort, the numbers of subjects located and of deaths were estimated proportionately.

Europe PMC Funders Author Manuscripts

Table 5

Number of subjects available with valid interviews in different combinations of follow-up visits.

Follow-up	Sex	Number of subjects examined
1982 and 1984	Both	4,934
1982 and 1986	Both	4,742
1982, 1984, and 1986	Both	4,476
1982 and 1997	Both	1,076
1982, 1984, and 1997	Both	1,009
1982, 1986 and 1997	Both	1,000
1982, 1984, 1986, and 1997	Both	956
1982 and 2000	Males	2,250
1982, 1984, and 2000	Males	2,067
1982, 1984, 1986, and 2000	Males	1,936
1982, 1984, 1986, 1997, and 2000	Males	481
1982 and 2001	Both	1,031
1982, 1984, and 2001	Both	977
1982, 1984, 1986, and 2001	Both	923
1982, 1984, 1986, 1997, and 2001	Both	718
1982, 1997, and 2001	Both	794