


BMJ Open Cohort profile: the Maternal and Child Health and Nutrition in Acre, Brazil, birth cohort study (MINA-Brazil)

Marly Cardoso ¹, Alicia Matijasevich,² Maira Barreto Malta,¹ Barbara Hatzlhofer Lourenco,¹ Suely G A Gimeno,¹ Marcelo U Ferreira,³ Marcia C Castro,⁴ On behalf of the MINA-Brazil Study Group

To cite: Cardoso M, Matijasevich A, Malta MB, *et al.* Cohort profile: the Maternal and Child Health and Nutrition in Acre, Brazil, birth cohort study (MINA-Brazil). *BMJ Open* 2020;**10**:e034513. doi:10.1136/bmjopen-2019-034513

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2019-034513>).

Received 23 September 2019

Revised 08 January 2020

Accepted 28 January 2020



© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Nutrition, Universidade de São Paulo, São Paulo, Brazil

²Departamento de Medicina Preventiva, Universidade de São Paulo, São Paulo, Brazil

³Department of Parasitology, University of São Paulo, São Paulo, Brazil

⁴Department of Global Health and Population, Harvard University T H Chan School of Public Health, Boston, Massachusetts, USA

Correspondence to

Dr Marly Cardoso;
marlyac@usp.br

ABSTRACT

Purpose Maternal and Child Health and Nutrition in Acre, Brazil (MINA-Brazil) is a longitudinal, prospective population-based birth cohort, set-up to understand the effects of early environmental exposures and maternal lifestyle choices on growth and development of the Amazonian children.

Participants Mother–baby pairs (n=1246) were enrolled at delivery from July 2015 to June 2016 in Cruzeiro do Sul, Acre, Brazil. Mothers of 43.7% of the cohort were recruited in the study during pregnancy from February 2015 to January 2016. Study visits took place during pregnancy, delivery, at 1 month, 6 months, 1 year and 2 years after delivery. In addition to clinical and epidemiological data, samples collected by the MINA-Brazil study include plasma, serum and extracted DNA from blood and faeces, which are stored in a biobank.

Findings to date Key baseline reports found a high prevalence of gestational night blindness (11.5%; 95% CI 9.97% to 13.25%) and maternal anaemia (39.4%; 95% CI 36.84% to 41.95%) at delivery. Antenatal malaria episodes (74.6% of *Plasmodium vivax*) were diagnosed in 8.0% of the women and were associated with an average reduction in birth weight z-scores of 0.35 (95% CI 0.14 to 0.57) and in birth length z-scores of 0.31 (95% CI 0.08 to 0.54), compared with malaria-free pregnancies. At 2-year follow-up, data collection strategies combined telephone calls, WhatsApp, social media community and home visits to minimise losses of follow-up (retention rate of 79.5%).

Future plans A 5-year follow-up visit is planned in 2021 with similar interviews and biospecimens collection. The findings from this prospective cohort will provide novel insights into the roles of prenatal and postnatal factors in determining early childhood development in an Amazonian population.

INTRODUCTION

In 2010, Brazil ranked as the 10th country in number of preterm births,¹ with marked regional differences.² Although Brazil has intensified actions towards pregnant women's health, and has a comprehensive protocol for antenatal care, the coverage and quality at the primary care level remain as concerns.¹ The Maternal and Child Health and Nutrition in Acre, Brazil (MINA-Brazil) study,

Strengths and limitations of this study

- The Maternal and Child Health and Nutrition in Acre, Brazil birth cohort is the first population-based study with longitudinally collected biospecimens (plasma, serum and extracted DNA from blood and faeces) and measurements carried out in the Amazon.
- Mother–baby pairs (n=1246) were enrolled at pregnancy between February 2015 and January 2016 (44%) or at delivery from July 2015 to June 2016 in Cruzeiro do Sul, Acre, Brazil.
- Repeated assessments and health outcomes took place during pregnancy, at 1 month, 6 months, 1 year and 2 years after delivery.
- Potential limitation includes generalisability of the study results since the cohort population was limited to suburban and urban area residents due to difficult access to Amazonian rural areas.

is the first population-based birth cohort followed in the Amazon. Cruzeiro do Sul, the study site, is a municipality with 82 000 inhabitants (2017 estimate) located in Juruá Valley, the main malaria hotspot of Brazil. The local female population is highly vulnerable as in the Amazonian region the odds of a preterm delivery are among the highest in Brazil, with poor antenatal care indicators (eg, in 2010, 22% of the women did not attend to any antenatal care visit, and 23% attended only 1–3 visits) and significant social and health inequalities.²

Previous studies among Amazonian children found that ever-use of a feeding bottle, having a single mother and belonging to the low economic status were associated with a shorter breast feeding duration,³ higher exposure to infections, anaemia, micronutrient deficiencies and an increased risk of being overweight.^{4–6} Early exposures—both biological and social—are known to influence trajectories of health and well-being throughout life, including the double burden of disease seen in low-income and

middle-income countries.^{7 8} International longitudinal studies on health and nutrition status are relevant to facilitate cross-cohort comparisons⁹ and plan evidence-based interventions aimed at improving maternal and child health.

The MINA-Brazil cohort was set-up to better understand the effects of early environmental exposures and maternal lifestyle choices on growth and development of the Amazonian children. It was conducted with a focus on the first 1000-day window of vulnerability and opportunities for the child's cognitive and physical development. It integrated clinical and epidemiological research on health conditions and nutrition in an endemic malaria region. The MINA-Brazil study aimed to investigate risk factors during the prenatal–early childhood period for the nutritional status and developmental trajectories of children. The cohort was established to cover measurements over the first 2 years of life, with planned follow-up assessments as long as possible during childhood.

COHORT DESCRIPTION

Recruitment

The recruitment of participants took place at two moments: (1) during pregnancy and (2) after delivery. Pregnant women with up to 20 gestational weeks were recruited while booking an appointment for antenatal care in each of the 13 primary healthcare units, covering the entire urban area of Cruzeiro do Sul, from February 2015 to January 2016. Contact information was recorded in a standardised form by the research team. Afterwards, the research protocol was explained to the woman or caregiver (in case of teenage pregnancy), and their participation invited through phone calls. Women were eligible for the study if they intended to give birth at the only maternity hospital in Cruzeiro do Sul. On acceptance of the invitation, a home visit was scheduled to obtain written consent and collect initial socioeconomic and health data. This antenatal visit enrolled 545 participants, corresponding to 43.7% of the total mothers who subsequently delivered babies included in the MINA-Brazil birth cohort (n=1246).

After delivery, baseline data collection for the entire birth cohort included 1881 children who were born from July 2015 to June 2016 at the Women's and Children's Hospital of Juruá Valley, where 96% of all deliveries of the municipality take place (figure 1).¹⁰ Of them, 16 were stillbirths, 112 abortions, 184 mothers refused further participation and 18 births were not captured by the study researchers despite daily visits to the hospital. In the next step, 1551 mothers with live babies were contacted. In this group, 305 living in remote rural areas were excluded due to difficult access. The remaining 1246 participants were eligible for follow-up.

Data collection

The first research assessment of pregnant women was scheduled between 16 and 20 weeks of pregnancy to

collect clinical data, blood samples and additional health and lifestyle information. Ultrasound examinations were carried out to confirm gestational age (GA) and measure foetal growth (figure 2). These assessments took place between March 2015 and March 2016 and were scheduled based on the last menstrual period. The ultrasound examination at the first assessment was used to estimate GA during the follow-up. A second assessment was held from May 2015 to May 2016, at about 28 weeks of pregnancy.

In the delivery phase, all live and stillbirths of women living in Cruzeiro do Sul occurring in the Women's and Children's Hospital of Juruá Valley were identified through daily visits. The research team visited mothers within the first 12 hours after delivery, before hospital discharge, to explain the cohort study protocol and invite them to participate. On acceptance, an interview was held to collect data on socioeconomic, environmental and gestational characteristics and obstetric history. Tablets programmed with CPro (US Census Bureau, ICF International) were used for data entry. Maternal blood samples (~90% of participants) and umbilical cord blood samples of neonates (~50% of participants) were collected.

During follow-up, phone interviews on morbidities and feeding practices were carried out within 30–45 days and at 3 months after delivery, between August 2015 and September 2016. At 6 months (from January to December 2016), 1 year (from August 2016 to July 2017) and 2 years of age (from August 2017 to July 2018), the anthropometric evaluation of infants and their mothers was measured during follow-up visits. A structured questionnaire was administered to children's mothers or guardians to update mother and child's socioeconomic and demographic characteristics, birth-related variables, infant feeding practices and other behaviours. Blood and faecal samples of children were collected at 1 and 2 years. Oral health examination was done by two research paediatric dentists at 2-year follow-up.

Questionnaires and measures

At the maternity hospital, research assistants interviewed each mother before discharge using a semistructured electronic questionnaire. Data were collected on: (1) socio-demographic status: maternal age, self-reported skin colour defined by the Demographic Census of the Brazilian Institute of Geography and Statistics (white, mulatto, black, yellow and indigenous), years of schooling, living with a partner, receiving assistance from the Bolsa Família conditional cash transfer programme, maternal occupation and ownership of household assets; (2) environmental variables: household water supply, sanitation facilities, number of people living in the house and type and number of rooms in the house; (3) clinical and obstetric history: menarche age, previous foetal losses, parity, self-reported morbidity such as diabetes, chronic or gestational hypertension and antenatal urinary tract infections, antenatal micronutrient supplementation

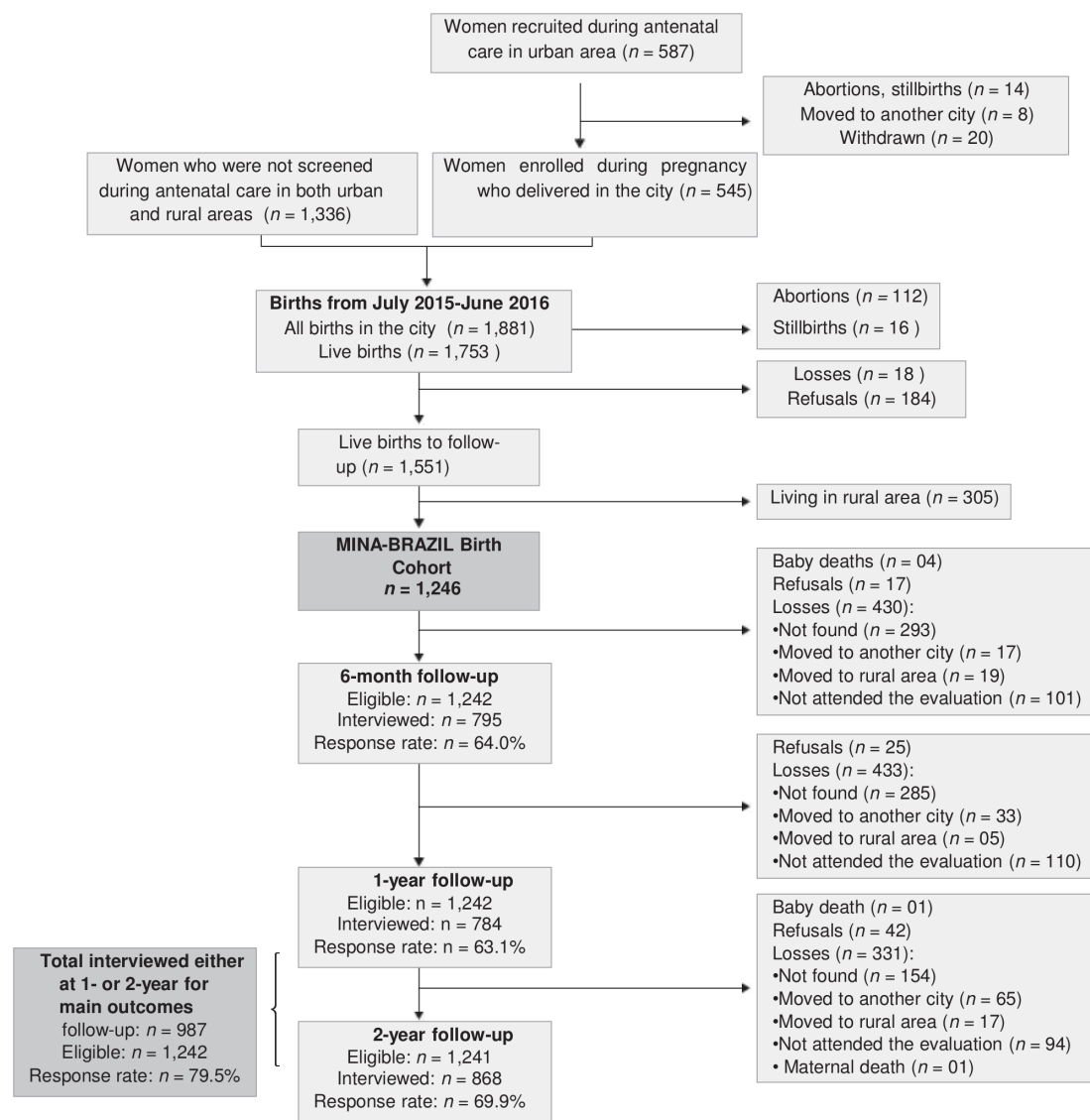


Figure 1 Flowchart of the MINA-Brazil cohort participation. A total of 20 of the 1246 participating children were twins. MINA-Brazil, Maternal and Child Health and Nutrition in Acre, Brazil.

(none, iron-folic acid or multiple micronutrients), number of antenatal care visits and maternal smoking and alcohol consumption.

Furthermore, participants consented to the linkage of their MINA-Brazil study data to hospital data. From the hospital records, data were gathered on the total number of antenatal care visits, history of malaria during pregnancy, GA at delivery, type of delivery (vaginal or caesarean) and the child's sex, birth weight and length. All maternity staff involved in newborn care received training from the research investigators on newborn anthropometric measurements.¹¹ The newborn birth weight was measured to the nearest 0.005 kg using a Toledo *Júnior* portable scale (São Bernardo do Campo, Brazil) with 15 kg capacity. Length and head circumference were measured with an inextensible measuring tape (SECA, model 218).

Information on household assets was used to calculate a wealth index from principal component analysis, which

was divided into quintiles, as a proxy of socioeconomic status for each household.¹² Total gestational weight gain was calculated by subtracting the reported prepregnancy weight from the prebirth weight and further categorised according to the prepregnancy body mass index (BMI) as insufficient, adequate or excessive based on Institute of Medicine protocol.¹³ Regarding GA, an ultrasound-confirmed antenatal estimate taken by our research team was available for 34% of the mothers, with an acceptable mean difference in comparison with hospital records (0.43 week; 95% CI 0.32 to 0.53, according to Bland-Altman analysis).¹⁰ Z-scores for birth weight, length and head circumference were obtained using the Intergrowth-21st Project references for GA and sex.¹⁴

Table 1 summarises the information collected by questionnaires, physical measurements and estimates of biological samples from mothers and children of the MINA-Brazil birth cohort study. Field nurses and research assistants were trained by study investigators to carry out

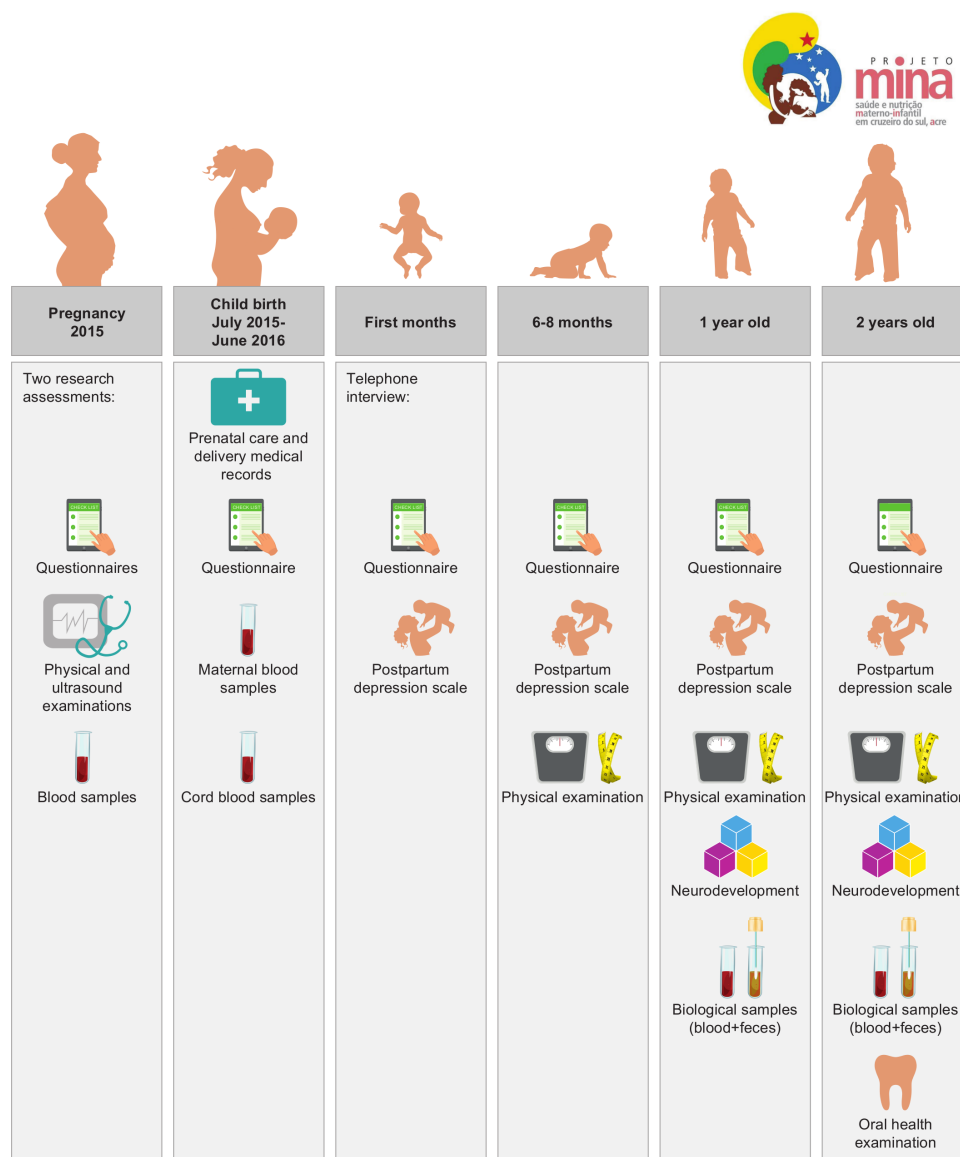


Figure 2 Schematic representation of the MINA-Brazil cohort design and measures. MINA-Brazil, Maternal and Child Health and Nutrition in Acre, Brazil

interviews, anthropometric measurements and biological samples collection and processing. Supervisors routinely checked all information and gave feedback to research team members to correct inconsistencies whenever necessary. In addition to clinical and epidemiological data, samples collected by the MINA-Brazil study include plasma, serum, and extracted DNA from blood and faeces, which are stored in a biobank.

Study visits during pregnancy

During pregnancy, two clinical, anthropometric and laboratory assessments were conducted, including collecting obstetric history, personal and family history of disease, height, weight, blood pressure and blood tests. The Self-Reporting Questionnaire-20 for assessment of common mental disorders among pregnant women^{15 16} was applied by trained research assistants. We assessed maternal anthropometry, biochemical measurements

(haemoglobin concentrations and blood count, fasting plasma glucose, insulin, C-reactive protein, alpha-1-acid glycoprotein (AGP) and serum retinol, vitamin D, β -carotene and ferritin) and conducted ultrasound exams. Maternal height was measured to the nearest 0.1 cm, and the pre-pregnancy BMI (kg/m^2) was calculated following the WHO recommendations.¹⁷

The ultrasound examination was performed by trained physicians using a portable SonoSite Titan equipment (SonoSite, Bothell, Washington, USA). An expert obstetrician not involved with the fieldwork reviewed all images. In each ultrasound examination, field physicians were aware of participant's last menstrual period and ascertained foetal biometric parameters in cephalic (biparietal diameter, occipitofrontal diameter and head circumference), abdominal (transverse abdominal diameter, anterior-posterior abdominal diameter and abdominal

Table 1 Number of participants and information collected by questionnaires, physical measurements and biological samples from mothers and children of the MINA-Brazil birth cohort study

Variables	Pregnancy	Delivery	Children's follow-up			
			30–90 Days	6 Months	1 Year	2 Years
Number of participants	545	1246	964	795	784	868
General characteristics, lifestyle and morbidity questionnaires	√	√	√	√	√	√
Maternal blood pressure, prepregnancy weight, gestational weight gain	√	√				
Maternal screening depression questionnaire	√					
Fetal growth measures	√					
Length, weight and head circumference		√		√	√	√
Breast feeding and complementary feeding practices		√	√	√	√	√
MOS questions			√			
The Edinburgh Postnatal Depression Scale (mothers)			√	√	√	√
Denver II Screening Test for neuropsychomotor development					√	√
Oral health screening						√
Dietary intakes and lifestyle (mothers)	√					√
Blood collection (mothers)	100%	~90%				
DNA samples and biochemical indicators	√	√				
Blood collection (children)	–	~50%			~70%	~80%
DNA samples and biochemical indicators		√			√	√
Retal swab for microbiome analysis					√	√

MINA-Brazil, Maternal and Child Health and Nutrition in Acre, Brazil ; MOS, Medical Outcomes Study.

circumference) and femoral (femoral length) planes, following standardised procedures,¹⁸ using a self-scoring system for quality criteria for image acquisition.¹⁹

Childhood follow-up

Information including the mother's history of disease, socioeconomic and lifestyle factors and illicit drug use was updated during childhood follow-up assessments. The Medical Outcomes Study questions,²⁰ which have been validated in Brazil,²¹ were applied to register mother's perception of social support during the puerperium follow-up. The Edinburgh Postnatal Depression Scale,²² a set of 10 questions previously validated in Brazil,²³ was used in the 3 month, 6 month, 1 year and 2-year follow-up assessments for screening mother's depression symptoms. Maternal habitual diets were assessed only at two visits

(during pregnancy and at 2-y follow-up) to avoid information overload.

During childhood follow-up (figure 2), trained field-workers updated socioeconomic and demographic information, assessed infant feeding practices (including bottle and pacifier use) and recorded the occurrence of morbidities since birth. Anthropometric measurements were acquired in duplicate from children and their mothers, using standardised procedures and calibrated equipment.¹⁷ Participants were barefoot and wearing light clothes for all measurements; diapers were removed from children. Child's recumbent length was measured to the nearest millimetre on a horizontal infant measuring board laid on a flat and firm surface. Maternal height and weight were measured, respectively, with a

portable stadiometer with 0.1 mm precision and a digital electronic scale with 150 kg capacity and 100 g precision (UM061, Tanita Corporation). Then, a combined weight of mother and child was obtained; child's weight was calculated from the difference between the combined weight measure and maternal weight. The head circumference was measured in duplicate with an inextensible tape (SECA, model 218), passed through the widest part of the child's head reaching to the top of the eyebrow.²⁴ Between duplicates, maximum differences of 0.2 mm and 100 g were allowed for length/height/head circumference and weight measurements, respectively, and the mean values were calculated. Child anthropometric indexes in z-scores were calculated according to age and sex with the WHO Child Growth Standards.²⁵ At 1-year and 2-year follow-up assessments, neuropsychomotor development was evaluated using the Denver II screening test,^{26 27} adapted to the Brazilian population.²⁸

Blood samples were collected for biochemical measurements (haemoglobin concentrations and blood count, plasma C-reactive protein and AGP and serum retinol, vitamin D, folate and ferritin) and blood DNA extraction at both 1-year and 2-year follow-up assessments. We also collected stool samples from children's anal swabs during clinic study visits at 1-year and 2-year follow-ups for gut microbiota analyses (table 1). The DNA extraction from stool samples was performed using the ZymoBiomix™ DNA Miniprep Kit (Zymo Research Corp, Irvine, California, USA) following the kit instructions. The DNA quality control and library preparation, and sequencing of the V4 region of the 16S ribosomal RNA gene on a MiSeq sequence (Illumine Inc) were performed using standard procedures in a blinded fashion by MacroGen Inc (MacroGen Korea, Seoul, Republic of Korea).

At 2-year follow-up, two research paediatric dentists performed oral health examinations. Dental caries was diagnosed according to the WHO criteria²⁹ and calculated in terms of decayed deciduous teeth, extracted due to caries or sealed. Defects of enamel on primary teeth were classified according to the modified index proposed by the International Dental Federation.³⁰

Malaria status

Information about the number of malaria episodes experienced by mothers during pregnancy and by infants over their first years of life was retrieved from the electronic malaria notification system of the Ministry of Health of Brazil.¹⁰

Communication strategies

The following strategies were implemented to establish project identity, promote high participation and retain participants in all study waves to minimise loss to follow-up:

1. Information folders were distributed in all health facilities, cohort member cards (with the project's logo) were provided for each mother and child and all

personnel working on the project wore t-shirts with the project's logo.

2. Trained interviewers made telephone calls to reach the participants or their relatives on different time and days of the week, including weekends and holidays, for scheduling the assessments. Text messaging was sent to the participants 1 day before the scheduled clinic visit as a reminder.
3. The research team provided personalised feedback about the child's nutritional evaluations to each mother or caregiver. Children with anaemia, overweight, underweight, stunting and/or suspected neurodevelopmental delay were scheduled for additional appointments with research clinicians for treatment or complementary healthcare in partnership with the local community health workers.
4. At 2-year follow-up, a social media community was created on Facebook to strengthen interactions with and between the study participants (n=450).
5. Research assistants were trained to keep regular communication with the families and promptly respond to any questions. For the families we could not reach by telephone calls/WhatsApp or Facebook, a local post office worker was trained by the research team to visit reported addresses and schedule home visits with the participant's family or their relatives and friends. These combined strategies (telephone and home visits) implemented at 2-year follow-up improved the response rate from 63.1% to 69.9%.
6. During 1-year and 2-year follow-ups, children who provided biological samples received laboratory results by regular mail, WhatsApp or Facebook messages.

Patient and public involvement

The patients had no role in the design, recruitment and conduct of the study. Participants (children's mothers or guardians) have been informed on the project's main results by flyers, WhatsApp or Facebook messages.

FINDINGS TO DATE

Baseline characteristics

Table 2 shows the characteristics of the MINA-Brazil study participants: mothers and their children at prenatal and early childhood assessments. At birth, the mean maternal age was 24.8 years (19% were adolescents, aged from 13 to 19 years old), with an average of 10.4 years of schooling. Compared with participants at birth, the proportion (95% CI) of participants from poorest families declined from 24.9% (22.5 to 27.4) at birth to 19.3% (16.8 to 22.1) at 2 years; however, average years of maternal schooling, proportion of primiparous mothers, type of delivery, child's sex, low birth weight, and preterm birth were similar among participants who remained in the study and those lost to follow-up at each survey wave. Maternal working status was updated over time, increasing the proportion (95% CI) of paid job from 30.2% (27.7 to 32.9) at birth to 40.5% (37.2 to 43.8) at 2 years. At baseline, 78% of the

Table 2 Characteristics of mother–child pairs enrolled in the MINA–Brazil birth cohort study

Characteristics	Pregnancy*		Birth		Puerperium		6Months		1 Year		2 Years	
	N	Percent or mean (95% CI)	N	Percent or mean (95% CI)	N	Percent or mean (95% CI)	N	Percent or mean (95% CI)	N	Percent or mean (95% CI)	N	Percent or mean (95% CI)
Maternal age (years)	545	24.8 (24.2 to 25.3)	1224	24.9 (24.5 to 25.2)	964	24.9 (24.5 to 25.3)	781	26.0 (25.5 to 26.4)	774	26.6 (26.1 to 27.0)	854	27.5 (27.1 to 27.9)
Maternal schooling at delivery (years)	523	10.5 (10.2 to 10.7)	1155	10.4 (10.2 to 10.6)	820	10.0 (9.8 to 10.2)	745	10.8 (10.4 to 11.1)	744	10.7 (10.5 to 10.9)	817	10.9 (10.6 to 11.0)
Wealth index at delivery												
Poorest	136	25.0 (21.5 to 28.8)	296	24.9 (22.5 to 27.4)	204	23.6 (20.9 to 26.6)	167	21.8 (19.0 to 24.8)	145	19.0 (16.4 to 22.0)	162	19.3 (16.8 to 22.1)
Second	139	25.6 (22.1 to 29.4)	299	25.1 (22.7 to 27.7)	215	24.9 (22.1 to 27.9)	189	24.6 (21.7 to 27.8)	198	26.0 (23.0 to 29.2)	212	25.3 (22.5 to 28.3)
Third	133	24.4 (21.0 to 28.5)	297	25.9 (22.6 to 27.5)	223	25.8 (23.0 to 28.8)	200	26.1 (23.1 to 29.3)	196	25.7 (22.7 to 29.0)	217	25.9 (23.0 to 28.9)
Wealthiest	136	25.0 (21.5 to 28.8)	299	25.1 (22.7 to 27.7)	222	25.7 (22.9 to 28.7)	211	27.5 (24.5 to 30.8)	223	29.3 (26.1 to 32.6)	248	29.5 (26.6 to 32.7)
Maternal working status												
Paid job	177	32.5 (28.7 to 36.6)	360	30.2 (27.7 to 32.9)	257	29.7 (26.7 to 32.8)	243	31.1 (28.0 to 34.5)	260	34.2 (30.9 to 37.6)	345	40.5 (37.2 to 43.8)
Not working	367	67.5 (63.4 to 71.3)	831	69.8 (67.1 to 72.3)	609	70.3 (67.2 to 73.3)	538	68.9 (65.5 to 72.0)	501	65.8 (62.4 to 69.1)	507	59.5 (56.2 to 62.8)
Parity												
Primiparous	241	44.3 (40.2 to 48.5)	498	41.8 (39.0 to 44.6)	357	41.2 (38.0 to 44.5)	312	40.7 (37.3 to 44.2)	322	42.3 (38.8 to 45.8)	343	40.9 (37.6 to 44.3)
Multiparous	303	55.7 (51.5 to 59.8)	693	58.2 (55.4 to 61.0)	509	58.8 (55.5 to 62.0)	455	59.3 (55.8 to 62.8)	440	57.7 (54.2 to 61.2)	839	59.1 (55.8 to 62.4)
Delivery												
Vaginal	295	54.1 (49.9 to 58.3)	660	53.9 (51.1 to 56.7)	544	56.4 (53.3 to 59.5)	406	52.0 (48.5 to 55.5)	402	51.9 (48.4 to 55.5)	452	52.9 (49.6 to 56.3)
C-section	250	45.9 (41.7 to 50.1)	564	46.1 (43.3 to 48.9)	420	43.6 (40.5 to 46.7)	375	48.0 (44.5 to 51.5)	372	48.1 (44.6 to 51.6)	402	47.1 (43.7 to 50.4)
Child's sex												
Female	265	49.0 (44.8 to 53.2)	618	50.5 (47.7 to 53.3)	492	51.0 (47.9)	406	52.0 (48.5 to 55.5)	404	52.2 (48.7 to 55.7)	427	50.0 (46.7 to 53.4)
Male	276	51.0 (46.8 to 55.2)	606	49.5 (46.7 to 52.3)	472	49.0 (45.8 to 52.1)	375	48.0 (44.5 to 51.5)	370	47.8 (44.3 to 51.3)	427	50.0 (46.7 to 53.4)
Birth weight (g)												
<2500g	43	8.0 (6.0 to 10.6)	86	7.0 (5.7 to 8.6)	66	6.9 (5.4 to 8.6)	55	7.0 (5.4 to 9.1)	49	6.3 (4.8 to 8.3)	58	6.8 (5.3 to 8.7)
2500–3499	342	63.5 (59.3 to 67.4)	775	63.4 (60.6 to 66.0)	627	65.2 (62.1 to 68.1)	485	62.1 (58.6 to 65.5)	485	62.7 (59.3 to 66.1)	533	62.5 (59.2 to 65.7)
≥3500	154	28.6 (24.9 to 32.6)	362	29.6 (27.1 to 32.2)	269	28.0 (25.2 to 30.9)	241	30.9 (27.7 to 34.2)	239	30.9 (27.8 to 34.3)	262	30.7 (27.7 to 33.9)
Preterm birth	44	8.1 (6.1 to 10.8)	104	8.5 (7.1 to 10.2)	78	8.1 (6.5 to 10.0)	60	7.7 (6.0 to 9.8)	60	7.8 (6.0 to 9.4)	68	8.0 (6.0 to 9.4)
Breast feeding	–	–	1153	94.2 (92.7 to 95.4)	942	97.7 (96.6 to 98.5)	648	83.0 (80.2 to 85.5)	537	69.4 (66.0 to 72.5)	295	34.5 (31.4 to 37.8)
Total	545		1224		964		781		774		854	
Twins	–		22		14		14		10		14	

*Data for the subsample of participants whose mothers were recruited during pregnancy. MINA–Brazil, Maternal and Child Health and Nutrition in Acre, Brazil.

mothers were living with a partner; of them, 54% had less than 9 years of schooling. Based on information updated during follow-up, maternal education also improved, with the mean years of schooling increasing from 10.4 (10.2 to 10.6) at birth to 11.8 (11.6 to 12.1) at 2-year follow-up (data not shown in table).

The MINA-Brazil study is ongoing. To date, we have published few papers on baseline data.^{10 11 31–34} Key reports included poor serum retinol status observed throughout pregnancy³¹ found to be negatively associated with maternal haemoglobin (β -3.30 g/L; 95% CI -6.4 to -0.20) and newborn birth weight (β -0.10 kg; 95% CI -0.20 to -0.00).¹¹ According to WHO, 7.8% and 41.8% of all pregnancies worldwide are affected by gestational night blindness and anaemia, respectively.^{35 36} In the MINA-Brazil study, a high prevalence of gestational night blindness (11.5%; 95% CI 9.97% to 13.25%) and maternal anaemia (39.4%; 95% CI 36.84% to 41.95%) was found at delivery.³² Maternal anaemia was associated with maternal age <19 years (adjusted prevalence ratio 1.18; 95% CI 1.01 to 1.38), not taking micronutrient supplements during pregnancy (1.27; 95% CI 1.01 to 1.62), attending <6 antenatal care visits (1.40; 95% CI 1.15 to 1.70) and gestational malaria (1.22; 95% CI 1.01 to 1.49).³² Antenatal malaria episodes (74.6% of *Plasmodium vivax*) were diagnosed in 8.0% of the women and were associated with an average reduction in birth weight z-scores of 0.35 (95% CI 0.14 to 0.57) and in birth length z-scores of 0.31 (95% CI 0.08 to 0.54), compared with malaria-free pregnancies.¹⁰ At 30 days of age, 36.7% of the studied children (95% CI 33.6% to 39.8%) were exclusively breastfed, with a median duration of 16 days. The use of a pacifier and the occurrence of wheezing were associated with a reduced time ratio (TR) for exclusive breast feeding duration by 33% (TR 0.67; 95% CI 0.58 to 0.77) and 19% (TR 0.80; 95% CI 0.70 to 0.93), respectively.³³ At 1 year of age, 2.2% of children were stunted and 6.6% overweight. Maternal height and BMI were positively associated with infant linear growth (p for trend <0.001). Children with at least one reported malaria episode within the first year of life were 0.58 (95% CI 1.05 to 0.11) z-score shorter. Other reports are under review or in preparation.

Future plans

Similar interviews, anthropometric measurements and biospecimens collection are planned at the 5-year follow-up visit in 2021. Based on the retention rate of the first 2 years of follow-up (79.5%) and our previous research experience in the Amazon region, we expect to achieve an average retention rate around 70%.

Given the dataset available, the MINA-Brazil cohort study aims at continuing the use of a life-cycle approach to recognise the importance of nutrition from early stages of life. A major challenge for current scientific knowledge and evaluation of actions in child health is the investigation of early determinants (exposures in pregnancy and in the first 2 years of life) for promoting adequate growth and development without excessive weight gain

throughout childhood. The findings may provide new insights into biological mechanisms linking the prenatal and postnatal risk factors for childhood development. Collaboration with other independent birth cohorts from different regions and ethnicities will provide an innovative effort to validate the results and increase their generalizability.

Strengths and limitations

The MINA-Brazil cohort is the first population-based delivery sampling frame with longitudinally collected biological samples and measurements carried out in the Amazon. At delivery, women living in rural settings were enrolled in the study allowing prevalence estimates of important maternal and child health indicators. However, at follow-up visits, the cohort population was limited to suburban and urban area residents due to difficult access to Amazonian rural areas. Nevertheless, scheduling follow-up assessments was challenging for all participants due to the local context (ie, poor internet connection, lack of street labels for many addresses and intermittent mobile signal). Additionally, loss to follow-up was more likely among poorer families. This may be attributable to the fact that poor families move more often than wealthier families. At 2-year follow-up, data collection strategies combining telephone calls, WhatsApp, social media community and home visits minimised losses of follow-up.

COLLABORATION

The MINA-Brazil data are not yet openly available. A repository database is being organised at the University of São Paulo where future published papers will be made available (<https://uspdigital.usp.br/repositorio/>). Researchers who are interested in potential collaboration should contact the principal investigator Marly A Cardoso (marlyac@usp.br) to complete a research plan for evaluation by the MINA-Brazil study steering committee.

Acknowledgements The authors thank all women and children who have taken part in the MINA-Brazil Study. The establishment of this cohort involved a large number of professional health workers, research team members, and different institutions, with special acknowledgements to the Maternity Hospital and Primary Health Care Units of Cruzeiro do Sul, Acre, Brazil. Members of MINA-Brazil Study Group: Alicia Matijasevich, Bárbara Hatzlhofer Lourenço, Jenny Abanto, Maira Barreto Malta, Marly Augusto Cardoso, Paulo Augusto Ribeiro Neves, Suely Godoy Agostinho Gimeno (University of São Paulo, São Paulo, Brazil); Ana Alice Damasceno, Bruno Pereira da Silva, Rodrigo Medeiros de Souza (Federal University of Acre, Cruzeiro do Sul, Brazil); Simone Ladeia Andrade (Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil); Marcia Caldas de Castro (Harvard T.H. Chan School of Public Health, Boston, USA).

Contributors MC, AM, BHL, MBM, SGAG, MUF and MCC worked in the planning of the cohort. MAC, MCC, BHL and MBM coordinated the fieldwork and supervised data management and analysis. MC wrote the manuscript with input from all authors. All authors have read and approved the final version of the manuscript.

Funding The MINA-Brazil Study has been funded by the Brazilian National Council for Scientific and Technological Development (CNPq, grant number 407255/2013-3); the Maria Cecília Souto Vidigal Foundation; and the São Paulo Research Foundation (FAPESP, grant number 2016/00270-6). MAC, AM, SGAG and MUF are recipients of CNPq senior research scholarships; MBM is supported by a FAPESP

postdoctoral scholarship (grant number 2017/05019-2); and MCC was supported by CNPq Special Visiting Scholar (grant number 407255/2013-3).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the ethical committee of the School of Public Health, University of São Paulo, Brazil (872.613/2014 and 2.358.129/2017). Each participating mother or caregiver (in case of a teenage pregnancy) provided written informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Additional data are available on reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Marly Cardoso <http://orcid.org/0000-0003-0973-3908>

REFERENCES

- WHO. *Born too soon: the global action report on preterm birth*. Geneva: World Health Organization, 2012.
- Miranda AE, Pinto VM, Szwarcwald CL, et al. Prevalence and correlates of preterm labor among young parturient women attending public hospitals in Brazil. *Rev Panam Salud Publica* 2012;32:330–4.
- Kearns AD, Castro MC, Lourenço BH, et al. Factors associated with age at breastfeeding cessation in Amazonian infants: applying a proximal-distal framework. *Matern Child Health J* 2016;20:1539–48.
- Cardoso MA, Scopel KKG, Muniz PT, et al. Underlying factors associated with anemia in Amazonian children: a population-based, cross-sectional study. *PLoS One* 2012;7:e36341.
- Lourenço BH, Gimeno SGA, Cardoso MA, et al. BMI gain and insulin resistance among school-aged children: a population-based longitudinal study in the Brazilian Amazon. *Br J Nutr* 2014;112:1905–10.
- Lourenço BH, Qi L, Willett WC, et al. FTO genotype, vitamin D status, and weight gain during childhood. *Diabetes* 2014;63:808–14.
- Adair LS, Fall CHD, Osmond C, et al. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* 2013;382:525–34.
- Ramakrishnan U, Grant F, Goldenberg T, et al. Effect of women's nutrition before and during early pregnancy on maternal and infant outcomes: a systematic review. *Paediatr Perinat Epidemiol* 2012;26:285–301.
- Brion M-JA, Lawlor DA, Matijasevich A, et al. What are the causal effects of breastfeeding on IQ, obesity and blood pressure? Evidence from comparing high-income with middle-income cohorts. *Int J Epidemiol* 2011;40:670–80.
- Pincelli A, Neves PAR, Lourenço BH, et al. The hidden burden of *Plasmodium vivax* malaria in pregnancy in the Amazon: an observational study in northwestern Brazil. *Am J Trop Med Hyg* 2018;99:73–83.
- Neves PAR, Castro MC, Oliveira CVR, et al. Effect of vitamin A status during pregnancy on maternal anemia and newborn birth weight: results from a cohort study in the Western Brazilian Amazon. *Eur J Nutr* 2018;46.
- Filmer D, Pritchett LH. Estimating wealth effects without expenditure data - or tears: an application to educational enrollments in states of India. *Demography* 2001;38:115–32.
- Institute of Medicine. Implementing guidelines on weight gain and pregnancy [Internet]. IOM. [cited Jan 2018], 2013. Available: <https://www.nap.edu/catalog/18292/implementing-guidelines-on-weight-gain-and-pregnancy> [Accessed 19 Sep 2019].
- Villar J, Ismail LC, Victora CG, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the newborn cross-sectional study of the INTERGROWTH-21st project. *Lancet* 2014;384:857–68.
- Gonçalves DM, Stein AT, Kapczinski F. Performance of the self-reporting questionnaire as a psychiatric screening questionnaire: a comparative study with structured clinical interview for DSM-IV-TR. *Cad Saúde Pública* 2008;24:380–90.
- Rad S, LdC O, Mondin TC, et al. Common mental disorders and self-esteem in pregnancy: prevalence and associated factors. *Cad Saúde Pública* 2010;26:1832–8.
- World Health Organization. Physical status: the use and interpretation of anthropometry [Internet]. WHO. [cited Aug 2017], 1995. Available: http://www.who.int/childgrowth/publications/physical_status/en/ [Accessed 19 Sep 2019].
- Papageorgiou AT, Sarris I, Ioannou C, et al. Ultrasound methodology used to construct the fetal growth standards in the INTERGROWTH-21st project. *BJOG* 2013;120:27–32.
- Salomon LJ, Bernard JP, Duyme M, et al. Feasibility and reproducibility of an image-scoring method for quality control of fetal biometry in the second trimester. *Ultrasound Obstet Gynecol* 2006;27:34–40.
- Harris SR. Measuring head circumference: update on infant microcephaly. *Can Fam Physician* 2015;61:680–4.
- Morgado CMdaC, Werneck GL, Hasselmann MH. Rede E apoio social E práticas alimentares de crianças no quarto mês de vida. *Ciência Saúde Colet* 2013;18:367–76.
- Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. *Br J Psychiatry* 1987;150:782–6.
- Santos IS, Matijasevich A, Tavares BF, et al. Validation of the Edinburgh postnatal depression scale (EPDS) in a sample of mothers from the 2004 Pelotas birth cohort study. *Cad Saúde Pública* 2007;23:2577–88.
- Sherbourne CD, Stewart AL. The MOS social support survey. *Soc Sci Med* 1991;32:705–14.
- de Onis M, Onyango AW, Borghi E. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* 2007;85:660–7.
- Frankenburg WK, Dadds J, Archer P, et al. *The Denver II: technical manual and training manual*. Denver: Denver Developmental Materials Inc, 1990.
- Drachler MdeL, Marshall T, de Carvalho Leite JC. A continuous-scale measure of child development for population-based epidemiological surveys: a preliminary study using item response theory for the Denver test. *Paediatr Perinat Epidemiol* 2007;21:138–53.
- Halpern R, Barros AJD, Matijasevich A, et al. Developmental status at age 12 months according to birth weight and family income: a comparison of two Brazilian birth cohorts. *Cad. Saúde Pública* 2008;24:s444–50.
- WHO Library Cataloguing-in-Publication Data. *Oral health surveys: basic methods*. 5th edn. Geneva: World Health Organization, 2013.
- Commission on Oral Health, Research & Epidemiology, Report of an FDI Working Group. A review of the developmental defects of enamel index (DDE Index). *Int Dent J* 1992;42:411–26.
- Neves PAR, Campos CAS, Malta MB, et al. Predictors of vitamin A status among pregnant women in Western Brazilian Amazon. *Br J Nutr* 2019;121:202–11.
- Neves PAR, Lourenço BH, Pincelli A, et al. High prevalence of gestational night blindness and maternal anemia in a population-based survey of Brazilian Amazonian postpartum women. *PLoS One* 2019;14:e0219203.
- Mosquera PS, Lourenço BH, Gimeno SGA, et al. Factors affecting exclusive breastfeeding in the first month of life among Amazonian children. *PLoS One* 2019;14:e0219801.
- Dal Bom JP, Mazzucchetti L, Malta MB, et al. Early determinants of linear growth and weight attained in the first year of life in a malaria endemic region. *PLoS One* 2019;14:e0220513.
- World Health Organization. *Global prevalence of vitamin A deficiency in populations at risk*. Geneva: World Health Organization, 2009.
- World Health Organization. *Guideline: daily iron and folic acid supplementation in pregnant women*. Geneva: World Health Organization, 2012.