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Cohort Profile: The Amsterdam Born Children and their Development (ABCD) study

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Cohort Profile:

The Amsterdam Born Children and their Development (ABCD) study

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How did the study come about?

In 2000, a study among pregnant women in Amsterdam revealed large ethnic disparities in birth outcomes[1] that were consistent with previous findings in both the Netherlands and other Western countries.[2-7] So far, conventional risk factors such as low maternal socioeconomic status (SES), smoking, or body mass index (BMI) could not explain these disparities. These results, in conjunction with increasing evidence of the long-term implications of adverse

pregnancy outcomes (fetal origins of disease hypothesis)[8] formed the basis of the Amsterdam Born Children and their Development (ABCD) study, which was established in 2003. This large prospective population-based cohort study examines the association between maternal lifestyle, medical, psychosocial, and environmental conditions during pregnancy and children's health at birth as well as in later life. Specific attention is paid to ethnic disparities. Consequently, the study has detailed measurements of ethnic background, including country of birth of the pregnant woman herself, country of birth of her parents, and ethnic identity.

The study is a collaboration between the Public Health Service of Amsterdam and the two university medical centers in Amsterdam (Academic Medical Center (AMC) and VU University Medical Center (VUmc)), and has been implemented in cooperation with hospitals and midwives, Youth Health Care (YHC) centers, primary schools, and the University of Tilburg.

What does the study cover – and how has this changed?

The main objectives of the ABCD study are:

1) to investigate children's health at birth as well as in later life, and ethnic disparities therein;

2) to investigate maternal lifestyle, medical, psychosocial, and environmental conditions during pregnancy, and ethnic disparities therein;

3) to investigate the extent to which (ethnic disparities in) maternal conditions during pregnancy explain (ethnic disparities in) children's health at birth as well as in later life.

However, a fourth objective has been added over the past few years, following mounting evidence that also postnatal conditions may have important consequences for health and disease in later life:[9]

4) to investigate early-life conditions, and ethnic disparities therein, and the extent to which these conditions explain children's health in later life.

(Figure 1 here)

The pregnancy and early-life conditions and outcomes of interest in the ABCD study are broadly defined into the research areas shown in Figure 1. The main maternal and environmental risk factors concern nutrition and metabolism, psychosocial stress, substance abuse, medical conditions, and air pollution. The main outcome parameters concern birth outcomes and infant growth and, when the children are older, obesity and metabolic syndrome, cognitive development, psychosocial health, and nutrition. More information is available on our website: www.abcd-study.nl.

Results of the study will be used to improve prenatal care and to develop culture-specific intervention strategies to promote the health of all children from the earliest age possible.

(Table 1 here)

Who is in the sample?

Between January 2003 and March 2004, all pregnant women living in Amsterdam were asked to participate in the ABCD study during their first prenatal visit to an obstetric care provider (general practitioner, midwife, or gynecologist).Altogether, 12 373 women were approached – by estimate, ≥ 99% of the target population. According to Dutch law, all pregnant women, including illegal immigrants and asylumseekers, are entitled to receive prenatal care, which is free of charge if costs are a problem. For all of the women approached, the care provider

completed a registration form which included personal data such as name, address, and date of birth. Based on this information, a questionnaire covering sociodemographic characteristics, obstetric history, lifestyles, and psychosocial conditions was sent to the pregnant women within two weeks, to be filled out at home and returned to the Public Health Service by prepaid mail. A reminder was sent two weeks later. The questionnaire included an informed consent sheet the women could use to grant permission for follow-up of their infants at the age of 3 months and every 5 years thereafter, and for the perusal of their medical files. In addition, women were invited to participate in the ABCD biomarker study. For this, an extra blood sample (10 ml EDTA and 9 ml serum) was taken during routine blood collection for screening purposes following the first antenatal check-up.

Of the 12 373 women approached, 8266 women filled out the pregnancy questionnaire (response rate: 67%). Of this group, 7050 women granted permission for follow-up (85%) and 7043 women granted permission for perusal of her and her child's medical files (85%). A total of 4389 women (53%) participated in the biomarker study. To enhance participation among foreign-born women, two supportive measures were taken: (1) A Turkish, Arabic, or English translation was provided to women born in Turkey, Morocco, or other non-Dutch-speaking countries, and (2) the possibility of completing the questionnaire orally was offered to women who were illiterate or had reading difficulties. Although the participation rates among foreign-born women (42% to 64%) were still lower than the participation rate among Dutch-born women (77%), they were comparable with response rates observed in other population-based multi-ethnic studies in the Netherlands.[10,11,12]

To investigate the degree of selection bias resulting from this ethnic nonresponse, we conducted a nonresponse analysis by probabilistic medical record linkage with the Netherlands Perinatal Registry; results indicated that selection bias was minimal.[13] Table 1 shows the sociodemographic characteristics of the participants according to country of birth.

The questionnaire focused primarily on the mother, however paternal information was available for country of birth (58.0% Dutch, 6.5% Surinamese, 4.6% Turkish, 8.5% Moroccan, 13.1% other non-Western, 6.8% other Western, and 2.5% unknown), employment status (81.2% employed) and height (mean 180.9 cm, SD 11.5).

Approval of the study was obtained from the Central Committee on Research Involving Human Subjects in the Netherlands, the medical ethics review committees of the participating hospitals, and the Registration Committee of the Municipality of Amsterdam.

(Figure 2 here)

(Figure 3 here)

How often have they been followed-up and what is attrition like?

Figure 2 shows the structure of the ABCD study. Of the 8266 respondents, 7863 women gave birth to viable singleton infants and 132 women gave birth to viable multiples. The remaining mothers either experienced a miscarriage or fetal death (n=92) or were lost-to-follow-up (n=179) with no registered birth and no information on miscarriage or fetal death available from the care provider. By law, all children born in Amsterdam after 24 weeks' gestation (either stillborn or liveborn) must be registered at the municipality's registry office, after which a 'mutation report' is sent to the Public Health Service's YHC department. Between the 4th and 7th day after delivery, YHC nurses visit the liveborn infants and their parents to obtain a blood sample to screen for congenital metabolic disorders. At this time they also record the date of delivery, infant sex, birth weight, and gestational age (based on ultrasound or, if unavailable (< 10%), on the timing of the last menstrual period) as provided by the obstetric care provider.

Three months after giving birth, the mothers who gave permission for follow-up (6735 mothers of singletons, 119 mothers of multiples) received a questionnaire concerning the course of their pregnancy and delivery, the baby's health, development, and growth, and the mother's lifestyle during and after pregnancy (phase II). Again, the questionnaire was available in multiple languages to increase the response in specific ethnic groups. A total of 5218 mothers (5131 mothers of singletons, 87 mothers of multiples) filled out this questionnaire (response rate: 76%). Compared with the initial sample, this group was older, more highly educated, of lower parity, and more often of Dutch origin. However, we found no effect of attrition bias in our first follow-up study, which investigated the association of maternal stress and emotional problems with infant crying.[14]

After the 3-month questionnaire, follow-up measurements were planned for singleton infants only. Until the children are 4 years old, specially trained YHC nurses conduct an average of 14 standardized routine measurements to monitor their growth and feeding patterns. Of the 6735 women who gave birth to liveborn singleton infants, 6575 women gave permission to collect growth data. Data collection is ongoing, and so far, growth data (including feeding type and duration) of 5273 ABCD children have been digitized.

At the current stage, 6161 of the 6735 mothers who gave permission for follow-up are being approached for the 5-year follow-up measurement of their child (phase III, 2008-2010). Attrition in this follow-up number is due to withdrawal, infant or maternal death, and loss-to-follow-up as a result of an unknown address or emigration. Details of the phase III follow-up are given below ('What has been measured?'). In short, mothers receive two questionnaires about the child's health, development, and behavior, with one of them to be filled out by the child's teacher. In addition, the children are invited to participate in the ABCD health check, which takes place at school. Efforts to enhance participation among all women and children, regardless of ethnicity and education, include the use of translated questionnaires, an

information leaflet, and a specially developed cartoon that explains the health check measurements to the children (Figure 3). Also, women from ethnic minority groups who do not respond within a month are approached by phone by trained students who explain the study in the women's own language. Data collection is ongoing, and preliminary results show a response rate of 66% for the general questionnaire (n=4060 out of the 6161 mothers approached) and a response rate of 58% for the teacher questionnaire. Of the participating mothers, 94% gave permission for the health check. Further follow-up measurements will take place every five years (in 2013 at age 10, in 2018 at age 15, etc) until adulthood.

(Table 2 here)

What has been measured?

Table 2 provides an overview of the measurements in the three subsequent phases of the study (details are available from the authors upon request). In phase I, the maternal micronutrient status (including vitamins A, D, B_{12}, folate, iron, Zn, Mg, Ca, and n-3 and n-6 fatty acids), metabolic function (including cholesterol, triglycerides, and thyroid hormone levels), and cortisol levels were measured in blood samples collected at a median of 13 weeks' gestation (interquartile range (IQR): 12-14 weeks). The pregnancy questionnaire was filled out at an average of 16 weeks' gestation (IQR: 14-18 weeks) and included ethnicity-related and sociodemographic variables, lifestyle, psychosocial conditions, and obstetric/medical information. Whenever possible, validated questionnaires were included, such as the CES-D questionnaire for depression[15] and the Job Content Questionnaire for job strain.[16] Furthermore, residential information was used to model individual exposure to traffic-related air pollution (in collaboration with the Institute of Risk Assessment Sciences at Utrecht University). Information on birth outcomes was obtained from YHC, as mentioned

previously. Supplementary information concerning complications during pregnancy and neonatal outcomes was obtained by probabilistic medical record linkage with the Netherlands Perinatal Registry.[13]

The questionnaire filled out by mothers in phase II concerned the course of their pregnancy and delivery, their physical and psychosocial health, and the development and health of their child. The questionnaire was filled out at the average infant age of 13 weeks (IQR: 12-13 weeks). Follow-up data from YHC included infant nutrition (ie, duration of breast-feeding and/or bottle-feeding; time of introduction of solid foods), and infant and child weight, length/height, and head circumference at an average of 8 time points in the first 14 months, and 6 time points between the ages of 14 months and 4 years.

In the current phase (phase III), participating mothers are sent a questionnaire approximately two weeks after their ABCD child's 5th birthday. In addition to items about the child's health, development, and behavior, this general questionnaire contains items about family sociodemographics, maternal lifestyle and psychosocial conditions, and family history of medical conditions. The questionnaire is accompanied by a questionnaire about the child's performance, behavior, and CITO (Central Institute for Test Development) index for elementary education, to be filled out by the child's teacher. In both questionnaires, validated questions and scales were used wherever possible (eg, the Strengths and Difficulties Questionnaire for behavior).[17]

The general questionnaire includes an informed consent sheet for granting permission for the child's participation in the ABCD health check. Two weeks before the health check, mothers are notified by letter and receive an additional self-administered food frequency questionnaire (FFQ). The FFQ was developed by TNO Food (Zeist, the Netherlands). It consists of 71 food items for which the frequency of consumption and portion size are to be reported. A validation study comparing the FFQ with the gold standard of doubly labeled

water showed that the questionnaire is a valid instrument for estimating mean energy intake in a group of 4- to 6-year-old children and for ranking subjects according to their energy intake; the Pearson correlation coefficient between energy intake and energy expenditure was 0.62.[18]

For children living in Amsterdam, the health check is held at the child's primary school. Children and parents who have moved outside of Amsterdam and children enrolled in small schools with no space available for the health check are invited to a central location during the weekend and holidays. The health check itself consists of a fasting capillary blood sample for assessing glycaemic control and lipid profile (glucose, C-peptide, total cholesterol, HDL, LDL, triglycerides) as well as fatty acid profile; physical measurements; and a cognitive test battery. The physical measurements include anthropometric measurements (height, weight, waist and hip circumference), body composition measures (fat mass and fat-free mass) by bioelectrical impedance analysis, blood pressure in supine and sitting positions, and cardiovascular function measures (heart rate, heart rate variability, and pre-ejection period) in supine and sitting positions using the VU Ambulatory Monitoring System.[19] Cognitive function is examined using four tasks from the Amsterdam Neuropsychological Tasks (ANT) program. These tasks estimate sensory-motor speed, visuomotor skills, and response selection.[20]

What has it found ?

A full list of publications is available on our website (www.abcd-study.nl). The main findings to date are summarized below. Data collection for phase III is ongoing, and papers are in preparation.

Risk factor-outcome associations

Factors found to be related to adverse pregnancy outcomes (stillbirth or miscarriage, low birth weight, or preterm birth) include having high levels of thyroid-stimulating hormone,[21] folate depletion,[22] an adverse fatty acid profile,[23] smoking, overweight/obesity, high blood pressure and a low educational level,[24,25] living in a poor neighborhood,[26] and having work-related stress.[27] Maternal stress and mood disorders, including work-related stress as well as pregnancy-related anxiety or depression, were associated with continuing to smoke during pregnancy[28] and an increased risk of having an excessive crying infant.[14] No association was found between maternal stress and mood disorders and preeclampsia or gestational hypertension, nor between maternal physical activity and these outcomes.[29,30] Maternal pre-pregnancy BMI was associated with infant BMI at age 14 months.[31]

Ethnic disparities

In the above-mentioned pregnancy outcomes, large differences were observed between ethnic groups. Particularly among women from Surinamese, Antillean, and Ghanaian background, low birth weights and preterm births were more prevalent.[24,25] Ethnic disparities were also observed in the start of prenatal care (ie, the timing of the first visit to a care provider),[32] use of folic acid supplements,[33] maternal thyroid function,[34] and the previously mentioned risk factors.[24,25,27,35] The observed disparities in birth weight and preterm birth were explained in part by these risk factors and their accumulation.[24,25]

What are the main strengths and weaknesses of the study?

The study's main strengths relate to its unique design and mode of operation. It was implemented during routine care, which allowed for detailed measurement in early pregnancy and, currently, for detailed follow-up of children's growth and development. Collecting maternal blood samples in conjunction with routine blood collection for screening purposes

made it possible to use biomarkers to measure nutritional status in early pregnancy. Biochemical analyses generally allow for a more objective measure of dietary intake[36,37] and have the advantage of not suffering from culture-specific bias, a desirable feature for our multiethnic cohort. A drawback of this design relates to the potential changes in exposure occurring in late pregnancy, which we did not measure. However, our choice to focus on early pregnancy was based on existing evidence that the trajectory of human development is set at this stage.[38] In addition, changes are most likely to be attenuations (eg, women with the most stressful working conditions going on leave earlier).[39]

The response rate of the study (initial participation, phase I) was 67%, which is lower than, for example, large population-based pregnancy cohorts in the UK, such as the Southampton Women's Survey (75%)[40] and ALSPAC (85%)[41] but higher than, for example, the Generation R study in Rotterdam, the Netherlands (61%).[42] Particularly in an era where response rates to large epidemiological studies are decreasing,[43] our response rate may be considered adequate. Supportive measures were taken to enhance enrolment of ethnic minority women in particular (translated questionnaires and completing them orally with trained female interviewers). As mentioned earlier, although selective participation could not be prevented, this resulted in a minimal degree of selection bias.[13] Even though the current response rate is 66% (phase III, preliminary results), we need to make even more of an effort to include all ethnic minority groups in the cohort. Ideally, the study would once more provide female trained interviewers who can help the ethnic minority women with the questionnaires in their own language. However, the costs to do so are substantial, and in the Netherlands funding agencies are not yet prepared to finance longitudinal studies at the level that is necessary. So far, the study has continued with a minimum of funds, thanks to a small group of dedicated researchers and technical support staff. In this context, the help of the

obstetric care providers, YHC, and currently also the primary schools has been indispensable to the data collection.

Because the study has been a collaborative effort between the Public Health Service and the university medical centers from the very start, it integrates both clinical and public health relevance. This is an important strength in terms of the study's contribution to health care and prevention. Results of the study are disseminated to health care workers, obstetric care providers, pediatricians, and policymakers on a regular basis, and have, for instance, led to a special prenatal educational program for pregnant Turkish women that focuses on smoking and psychosocial health.[44]

Can I get hold of the data?

Where can I find out more?

The ABCD study welcomes collaboration and the interest of colleagues. A set of guidelines for researchers interested in using data for research purposes is available at www.abcd-study.nl. In brief, we request a short research proposal that should include information on the background, research questions and methods, a plan for publication, timetable, and budget. Approval of a proposal depends upon the topic and the quality of the proposal. If topics are already the subject of research in progress, then access may be refused or subject to constraints. Collaborations are established through a formal contract, which includes mutual obligations (data delivery, rules for publication and presentation, contribution to the ABCD infrastructure, etc).

For more information, please see our website or contact one of the principal investigators at abcd@ggd.amsterdam.nl.

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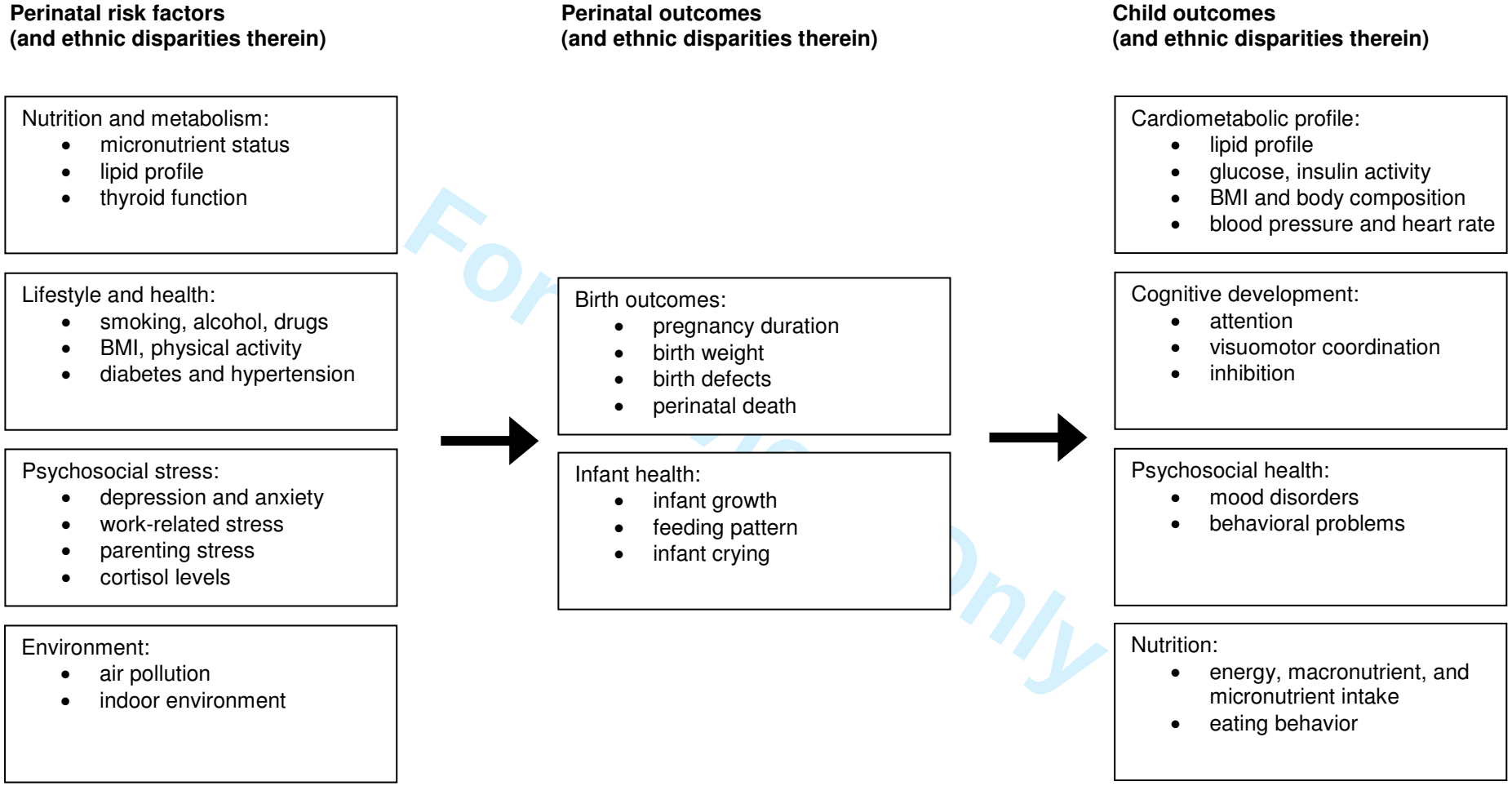

Figure 1 Main research areas of the ABCD study

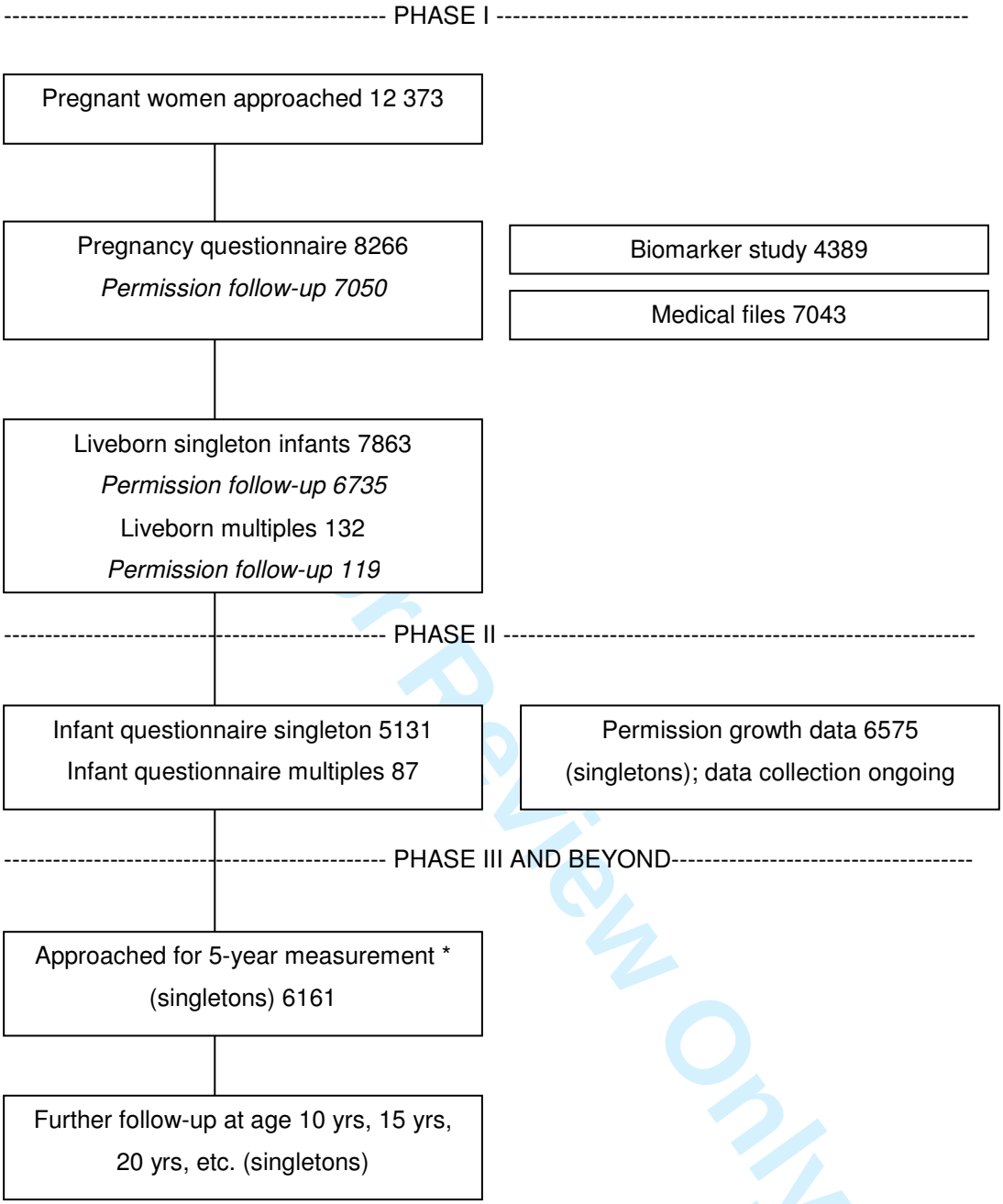

Figure 2 Structure of the ABCD study

* attrition at this stage due to withdrawal, infant or maternal death, and unknown address or emigration

Figure 3 Information for participants: a specially developed cartoon (in Dutch) that explains the measurements to the 5-year-old children. Reprinted with the permission of Floor de Goede/ComicHouse.nl.

Translations:

(1) Exciting: ABCD measurements at school today. What's going to happen?
(2) A cold spray to numb your finger …
(3) Then a tiny prick you can hardly feel …
(4) Weight ...
(5) Height … and waist
(6) Heart rate
(7) A little balloon around your arm to measure your blood pressure …
(8) And at the end, some tests on the computer and on paper
(9) Done! Heading home with a small gift and your ABCD diploma …

Table 1 Response rates and maternal characteristics in the study population according to country of birth*

	Total	Dutch	Surinamese	Turkish	Moroccan	Other NW	Other W
N	8266	5082	462	343	607	1040	732
Response rates (%)							
biomarker study	53.1	59.0	44.8	41.4	36.7	41.4	53.0
permission medical files	85.2	89.4	77.1	74.3	68.9	80.5	86.7
permission follow-up	85.3	91.3	76.7	70.8	69.9	78.6	88.8
Maternal age (%)							
<25 y	13.8	10.4	17.5	40.8	25.5	17.7	7.5
25-29 y	22.0	18.1	21.0	28.9	35.6	31.8	20.8
30-34 y	40.4	45.8	35.7	19.0	24.2	31.7	41.8
≥35 y	23.8	25.7	25.8	11.4	14.7	18.8	29.9
Maternal education (%)							
<6 y	23.0	11.4	41.8	63.8	59.0	41.6	16.4
6-10 y	37.9	37.6	44.4	29.4	33.3	38.5	42.8
≥11 y	38.1	50.7	11.0	5.8	5.3	17.0	39.9
unknown	1.0	0.3	2.8	0.9	2.5	2.9	1.0
Parity (%)							
0	55.4	60.6	39.4	37.3	40.2	45.5	64.9
1	31.4	31.9	30.7	35.9	27.2	32.6	28.1
≥2	13.2	7.5	29.9	26.8	32.6	21.9	7.0
BMI (%)							
<18.5 kg/m^2	5.0	4.7	6.5	5.0	2.6	5.7	7.2
18.5-24.9 kg/m^2	71.4	77.5	55.0	61.2	51.4	59.8	77.5
25.0-29.9 kg/m^2	17.3	13.6	23.4	22.2	33.3	25.2	11.7
≥30.0 kg/m^2	6.3	4.2	15.2	11.1	12.5	9.3	3.6
unknown	0.04	0.0	0.0	0.6	0.2	0.0	0.0
Smoking (%)							
no	75.5	71.1	73.4	75.2	96.0	87.8	72.8
quit	14.9	17.7	15.2	6.4	1.0	8.8	19.8
yes	9.4	11.2	11.5	17.5	2.5	2.8	7.2
unknown	0.2	0.0	0.0	0.9	0.5	0.7	0.1

* NW: non-Western, W: Western

Table 1 Response rates and maternal characteristics in the study population according to country of birth* (continued)

	Total	Dutch	Surinamese	Turkish	Moroccan	Other NW	Other W
Gestational age at blood sampling (start prenatal care) (%)							
<12 weeks	27.9	30.7	21.2	19.2	16.5	24.5	31.1
12-14 weeks	37.5	41.4	28.1	33.2	29.8	29.2	36.6
14-16 weeks	16.7	16.1	21.0	16.6	20.1	16.5	15.3
16-18 weeks	7.7	6.1	10.8	12.2	11.9	10.5	7.4
18-20 weeks	3.2	2.1	7.4	5.0	5.4	4.9	3.1
≥20 weeks	6.6	3.2	11.3	13.1	16.3	14.1	6.1
unknown	0.3	0.4	0.2	0.6	0.0	0.2	0.3
Gestational age at completion pregnancy questionnaire (%)							
<12 weeks	5.1	5.7	3.5	3.2	2.8	4.0	6.7
12-14 weeks	12.6	13.9	7.4	11.4	8.4	11.1	13.4
14-16 weeks	26.2	29.6	19.0	21.6	18.9	19.6	25.3
16-18 weeks	25.2	26.6	23.8	23.6	23.7	21.6	23.8
18-20 weeks	11.9	11.3	15.8	12.8	13.2	10.6	13.3
≥20 weeks	18.8	12.8	30.1	27.1	32.8	32.8	17.5
unknown	0.1	0.1	0.4	0.3	0.2	0.3	0.1

* NW: non-Western, W: Western

Table 2 General overview of data collected in the ABCD study

Data source	Measurements					
	General	Mother			Child	
	Sociodemographic variables	Lifestyle & nutrition	Psychosocial conditions	Health	Lifestyle, nutrition, health	Cognition & behavior
PHASE I						
Pregnancy questionnaire	Country of birth Parental country of birth Ethnic identity Age Education Parity Cohabitant status Work status	Smoking Alcohol Substance abuse Folic acid use Fish consumption Physical activity BMI	Depression Anxiety Parenting stress Work-related stress Fatigue	Obstetric history Medical history and current medical problems Medicine use		
Blood samples		Vitamins & minerals Antioxidants Fatty acids Cholesterol, triglycerides, fructosamine Thyroid hormones Cortisol				
Medical files				Health care during pregnancy Obstetric complications Medical problems	Infant gender Gestational age at delivery Birth weight Apgar score NICU admission Perinatal death	
Birth records					Infant gender Gestational age at delivery Birth weight Perinatal death	

Table 2 continued

	General	Mother			Child	
	Sociodemographic variables	Lifestyle & nutrition	Psychosocial conditions	Health	Lifestyle, nutrition, health	Cognition & behavior
PHASE II						
Infant questionnaire	Work status Residential history	Smoking, alcohol, substance abuse in pregnancy Supplement use in pregnancy, BMI	Nursing style Depression Anxiety Fatigue	Course of pregnancy and delivery Medicine use during pregnancy Family history of asthma and allergies	Hospital admission Respiratory symptoms Feeding type (breast/bottle) and duration Current weight and length	Crying behavior Sleeping behavior
Youth Health Care records					Feeding type and duration Weight Length/height	
PHASE III						
Youth Health Care records					Residential history	
Child questionnaire for parents	Financial situation Family structure Education Age	Smoking, alcohol, substance abuse, BMI	In retrospect: Working conditions during pregnancy Parenting style Depression Anxiety Parental history of psychosocial problems	Parental history of obesity and cardiovascular disease	In retrospect: Birth weight and gestational age at delivery Start and duration of breast-feeding, bottle-feeding, and weaning Weight and height Medical problems Medicine use Physical activity	Mood disorders Behavioral problems (SDQ*) Eating behavior Sleeping behavior

Table 2 continued

	General	Mother			Child	
	Sociodemographic variables	Lifestyle & nutrition	Psychosocial conditions	Health	Lifestyle, nutrition, health	Cognition & behavior
PHASE III						
Child questionnaire for teacher	Grade child is in Hours of school per week					Behavioral problems (SDQ*) School performance (CITO* index)
Health check					Weight and height Waist and hip circumference Body composition Blood pressure Cardiovascular function Blood sample for measures of glycaemic control, lipid profile and fatty acid profile	Cognitive function (ANT*)
Food frequency questionnaire					Average food consumption for calculation of energy, macronutrients, and micronutrients	

*SDQ: Strengths and Difficulties Questionnaire; CITO: Central Institute for Test Development; ANT: Amsterdam Neuropsychological Tasks