3D Cohort Study: The Integrated Research Network in Perinatology of Quebec and Eastern Ontario

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Abstract

Background: The 3D Cohort Study (Design, Develop, Discover) was established to help bridge knowledge gaps about the links between various adverse exposures during pregnancy with birth outcomes and later health outcomes in children.

Methods: Pregnant women and their partners were recruited during the first trimester from nine sites in Quebec and followed along with their children through to 2 years of age. Questionnaires were administered during pregnancy and post-delivery to collect information on demographics, mental health and life style, medical history, psychosocial measures, diet, infant growth, and neurodevelopment. Information on the delivery and newborn outcomes were abstracted from medical charts. Biological specimens were collected from mothers during each trimester, fathers (once during the pregnancy), and infants (at delivery and 2 years of age) for storage in a biological specimen bank.

Results: Of the 9864 women screened, 6348 met the eligibility criteria and 2366 women participated in the study (37% of eligible women). Among women in the 3D cohort, 1721 of their partners (1704 biological fathers) agreed to participate (73%). Two thousand two hundred and nineteen participants had a live singleton birth (94%). Prenatal blood and urine samples as well as vaginal secretions were collected for ≥98% of participants, cord blood for 81% of livebirths, and placental tissue for 89% of livebirths.

Conclusions: The 3D Cohort Study combines a rich bank of multiple biological specimens with extensive clinical, life style, and psychosocial data. This data set is a valuable resource for studying the developmental etiology of birth and early childhood neurodevelopmental outcomes.

Keywords: *pregnancy cohort study, biological markers, infant development, adverse birth outcomes.*

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Pregnancy is a foundation period for future health and development. The etiologies of many adverse birth outcomes are poorly understood, and there remain important knowledge gaps concerning the long-term impact of various adverse exposures during pregnancy on later health outcomes in children. Numerous environmental, nutritional, psychosocial, and genetic factors have the potential to impinge on a wide range of biological pathways and thus influence pregnancy and infant outcomes. Environmental, nutritional factors, and psychosocial stress are important potentially modifiable factors that hold promise for developing effective prevention measures, and there appear to be critical windows of vulnerability.[1] Assessing the associations between these exposures and pregnancy and infant health outcomes presents major challenges. Multiple outcomes may arise from a single exposure; different exposures and their interactions may lead to a similar outcome; a given adverse outcome may occur only in genetically susceptible individuals; and dynamic temporal changes in the levels of exposures may produce variable results.[2] To address some of these challenges, we developed a pregnancy and birth cohort of 2366 pregnant women and their partners (n = 1721) recruited in the first trimester in nine Quebec clinical sites (seven sites in Montreal and one each in Sherbrooke and Quebec City; Figure S1) and followed at mid (20–24 weeks) and late (32–35 weeks) gestation and at delivery. Mothers and their children were followed postnatally through 2 years after the birth.

Objectives

The 3D Cohort Study (Design, Develop, Discover) was established to address the intrauterine determinants of important adverse birth outcomes including intrauterine growth restriction (IUGR) and preterm birth (PTB) and to study the links between exposures during pregnancy and patterns of early childhood development. The cohort study was also designed to explore associations between exposure to assisted reproductive technologies (ART) and maternal, fetal, and child health outcomes. Through inclusion of data on nutritional exposures, socio-economic and psychosocial factors, genetic and epigenetic profiles, the study has the potential to contribute to understanding of developmental origins of metabolic and cardiovascular as well as neurodevelopmental risks.

Methods

Study sample

Recruitment

The 3D Cohort Study is structured around a triadic (mother-partner-child) framework. The cohort comprises 2366 women recruited in the first trimester of pregnancy (8–14 weeks) who were planning to deliver in a collaborating hospital in the province of Quebec. Women and their partners were recruited between May 25, 2010 and August 30, 2012 at one of nine study centres during routine first-trimester prenatal visits to study hospitals and infertility clinics. Women were between 18 and 47 years of age at the time of recruitment and able to communicate in French or English. Exclusion criteria included current intravenous drug use, severe illnesses or life threatening conditions, and multiple gestation pregnancies.

Follow-up

Study follow-up was conducted by research nurses, and infant follow-up was carried out by a team consisting of a research nurse and research assistants trained in developmental psychometrics. Following recruitment in the first trimester, participants were seen at mid (20–24 weeks) and late (32–35 weeks) pregnancy, and at delivery. Postnatal visits took place at 3 months, 1 year, and 2 years following the birth.

Data and biospecimen collection

Questionnaire data were collected prenatally and postnatally and included maternal sociodemographic characteristics, physical activity, and psychosocial measures. We assessed nutritional exposures using a 3-day maternal food diary completed during the second trimester. Data on the use of prescription drugs, over-the-counter medications, and nutritional supplements were collected through maternal and infant medication logs. Maternal blood, vaginal swabs, and urine samples were collected at each prenatal visit, and prenatal toenail samples were collected between 32 and 35 weeks gestation. Obstetrical ultrasound parameters were collected from examinations performed as part of routine prenatal care. Blood and urine samples were collected from the partners of participating women prenatally (60% of samples

collected at the first trimester visit, 24% at the second trimester, 6% at the third trimester) or within 10 days of the delivery (9%). At delivery cord blood, placenta samples, meconium, and maternal and infant hair samples were also collected.

Questionnaires

Exposures of interest were documented throughout the pregnancy and postnatally using a questionnaire-based approach that included: *Maternal characteristics (collected via interviewer-administered questionnaire):* maternal age, ethnicity, marital status, socio-economic status (education, income, occupation), pre-pregnant weight, inter pregnancy interval, pregnancy and medical history, family medical history, mode of conception (ART procedures), time to conception, paternal ethnicity, age, height, and weight. Measures collected on individual and family medical history are shown in Appendix S1. *Maternal tobacco smoke (interviewer-administered questionnaire):* active and passive smoke exposure. Participants' postal codes were also collected, allowing linkage to geographic data sources with area-level measures of air pollutants, noise levels, and proximity to green spaces. *Nutritional exposures:* Consumption of nutritional supplements was recorded in a medication and nutritional supplement log at each prenatal visit (interviewer administered). A 3-day food record and dietary habits questionnaire was given to participants at the second trimester visit and completed between 20 and 24 weeks gestation. The 3-day food record allows the estimation of consumption of energy, macronutrients (carbohydrates – including fibres; lipids – total and different types of lipids; and proteins), and micronutrients (vitamins and minerals). An infant feeding and nutrition questionnaire was completed by interview at 3 months and 12 months postpartum to assess the initiation, duration and exclusivity of breast feeding and the age of introduction of complementary foods. An infant food diary was also completed over 3 days at 24 months. *Medications:* Maternal exposures to prescription and non-prescription medications were recorded via interviewer-administered questionnaire for the periods before pregnancy (retrospective recall by the mother in the 3 months before pregnancy) as well as during each of the three trimesters (prospective measures). The same was done for the children at 3, 12 and 24 months of age. Detailed information was collected including drug name, indication, dosage, frequency and route of administration, and total duration of use (Appendix S2). *Psychosocial measures* were assessed by self-administered questionnaires both prenatally and postnatally (questionnaires given to participants at study visits and returned by post, or completed by participants directly by Internet). Psychosocial measures assessed included perceived stress,[3] pregnancy-related anxiety,[4] depression,[5] and personality traits including self-esteem,[6] dispositional optimism[7] and attachment.[8] Psychosocial measurements including perceived stress,[3] depression,[5] self-esteem,[6] and marital strain[9] were also assessed on participating maternal partners (Table S2).

Infant follow-up

Follow-up of 3D infants was performed at 3, 12, and 24 months of age and completed in February 2015. Visits were scheduled at the study centres (one centre for each city: Montreal, Quebec, Sherbrooke), and detailed sociodemographic, psychosocial, and nutritional questionnaires were administered to the parent (Table 2). Visits included assessment of child behaviour and temperament, neurodevelopment,[10] sensory profile,[11] language development,[12] and a standardised growth assessment: weight, height, arm length, back and arm skinfold thickness, crown-rump length, and head, arm and waist circumference (Table 4). Information collected on child health problems is detailed in Appendix S3. Blood and urine were collected by a nurse at the 2-year visit.

Sample size and power calculation

The sample size that was initially targeted was $n = 3000$. This sample size would have provided 96% power to detect associations of relative risks of 2.0 or greater with a baseline exposure rate of 20%. For bivariate linear regression analyses, the sample size would have provided 80% power to detect a change in standardized regression coefficient from $\beta = 0.5$ under the null hypothesis to $\beta = 0.543$ under the alternative hypothesis, and 95% power to detect a change in standardized regression coefficient β from 0.5 to 0.555. Due to delays in obtaining ethics approval, recruitment begun later than planned, and it was necessary to terminate recruitment before the target sample size of 3000 participants had been achieved in order to complete postnatal follow-up within the study's funding cycle.

Ethical considerations and governance

The research protocol, questionnaires, consent forms, and recruitment posters and pamphlets were reviewed and approved by human studies research ethics committees, including the research ethics committee at the coordinating centre at Sainte-Justine's Hospital in Montreal, as well as academic and hospital ethics committees at all participating study sites. Participants could partially (data and biospecimens retained) or completely (all data and biospecimens destroyed) withdraw from the study at any time.

The 3D Cohort Study's governance structure includes an executive committee, scientific committee, and external advisory committee, which have five key functions: (i) Intelligence gathering; (ii) Formulating mission and vision, goals and objectives; (iii) Resourcing and implementation; (iv) Promoting collaborative relationships; and (v) Controlling and monitoring the achievement of policy goals.

Results

A total of 9864 women were approached at early (<14 weeks) prenatal clinics, 6348 were eligible and 2456 agreed to participate (39%) (Figure S2). Forty-seven women were later determined to be ineligible and 43 withdrew completely from the study, asking that all their data and biospecimens be destroyed. The most common reasons for ineligibility were: not being within the gestational age window (25% of ineligible women), not planning to deliver in a participating facility (23%), planning to deposit cord blood in another biobank (16%), evidence of fetal demise (16%), participation in another research project (6%), not speaking or understanding French or English (6%), and multifetal pregnancy (6%). Other reasons each accounting for fewer than 1% of ineligible women were age less than 18 years, cancer, cardiovascular disease, connective tissue disease, epilepsy, HIV, illicit drug use, severe haemoglobinopathy, severe pulmonary disease, and severe renal disease. Of the 43 complete withdrawals, 33 participants reported a specific reason for withdrawing from the study: 18 participants cited lack of interest in continuing in the study, eight cited lack of time for the study, and seven reported being convinced by their partner to withdraw from the study. Demographic characteristics concerning women who declined to participate were not documented.

The mean gestational age at recruitment was 11.6 ± 1.8 weeks. Table 1 shows the characteristics of the study sample, along with similar descriptions for Canadian births overall, the Canadian Health Measures Survey (CHMS), and overall births in the province of Quebec. The baseline sociodemographic questionnaires were well-responded to in the 3D Study, with the highest refusal or 'don't know' responses for family income (5.0%). Our study sample is on average both older and of lower parity than Canadian and Quebec births overall. The study also has a higher percentage of mothers born outside of Canada (35%). Compared to Canadian births overall, Quebec births, and the CHMS, the 3D Study sample was substantially more likely to have a university degree (more than 60% of participants), and more than 90% of participants were married or living with a partner. Finally, the household income level was relatively high, with more than half the study sample reporting annual household income of greater than $80 000. 14.6% of participants had a before taxes household income below Statistics Canada's before-tax low-income cut-off for their family size,[13] similar to the 2010 national norm of 13.7%.

Table 2 shows additional demographic and health measures assessed, as well as self-reported psychosocial measurements. The prenatal food diary was completed by 1550 women (66%). Prenatal self-administered questionnaires containing psychosocial measurements were completed by 1866 participants (79%) at visit 1, 1725 (73%) at visit 2, and 1598 (68%) at visit 3. Ultrasound assessments were conducted on 2032 women in the first trimester before 14 weeks, 2256 in the second trimester between 14 and 28 weeks, and 1833 in the third trimester between 28 and 37 weeks. One thousand seven hundred and twenty one participants' partners (1704 biological fathers) agreed to participate (73%), and 2219 participants had a live singleton birth (94%).

Biological specimens collected are listed in Table 3. Maternal blood samples were collected for at least one prenatal visit from 2343 participants (99%) [all three prenatal visits: 1870 participants (79%)], urine samples for at least one prenatal visit from 2351 (99%) [all three prenatal visits: 1923 participants (81%)], vaginal secretions for at least one prenatal visit 2320 (98%) [both first- and second-trimester prenatal visits: 1949 participants (82%)], hair samples for 1956 (83%), cord blood for 1787 (81% of livebirths), placental tissue for 1978 (89%), infant urine or blood

Table 1. Comparison of 3D Study participants with data on Canadian births (2010) and female participants in the biomonitoring component of the Canadian Health Measures Survey (CHMS) Cycle 1, (2007–09)[25–27]

	3D Cohort Study participants (2010–12)	Canadian births, 2010	CHMS (2007–09) women 20–39 years of age[a] (95% confidence interval)	Quebec births, 2010
Parity (%): Number of previous viable pregnancies				
0	54.2%	43.3%	49.7% (41.5, 57.9)	44.4%
1	32.8%	35.3%	16.7% (12.8, 20.6)	35.8%
2	10.0%	13.8%	25.0% (17.2, 32.7)	13.6%
3+	3.0%	7.5%	8.6% (5.2, 12.1)[b]	6.1%
Maternal age (%) (years)				
<20[c]	0.4%	3.9%		2.7%
20–24	6.9%	14.6%		13.7%
25–29	31.8%	30.3%		33.5%
30–34	38.9%	32.3%		33.6%
35+	22.0%	18.9%		16.4%
Mean age (years) (SD)	31.0 (4.7)	29.6	29.9 (29.0, 30.8)	30.0
Gestational age (weeks)				
Mean (SD)	39.2 (2.2)			
Median	39.6			
Preterm birth (%): <37 weeks	6.7%	7.8%		7.2%
Birthweight (g)				
Mean (SD)	3332 (583)	3358		
Median	3370	3386		
Low birthweight (<2500 g) (%)	5.1%	6.2%		5.7%
Mother born in Canada (%)	65.1%	72.9%	77.8% (67.6, 88.1)	78.3%
Infant gender (%)				
Male	50.2%	51.3%		51.2%
Female	49.8%	48.7%		48.8%
Maternal education (%)		[d]	Highest level of education in household	
High school or less	9.5%	26.8%	10.7% (4.6, 16.8)[b]	36.5%
Some college	1.5%		7.9% (3.3, 12.6)[b]	
College diploma	26.7%	37.0%	38.9% (30.0, 47.9)	24.7%
University degree	62.3%	35.1%	42.4% (28.4, 56.5)	38.8%
Marital status of mother (%)				
Married	94.5%[e]	60.4%	58.7% (51.4, 66.1)	36.9%
Divorced	0.6%	0.9%	1.4% (0.7, 2.1)[b]	1.2%
Separated	0.5%	0.4%	2.1% (0.6, 3.5)[b]	0.3%
Single	4.2%	27.5%	37.8% (30.5, 45.0)	59.1%
Other/Unknown	0.3%	10.9%	[f]	2.5%
Fetal death (≥20 weeks) (% of total births)	0.8%	0.7%		
Smoking status (%)		During last 3 months of pregnancy[d]:		During last 3 months of pregnancy[d]:
Never	65.9%	89.5% did not smoke	59.9% (52.7, 67.0)	89.1% did not smoke
Former	19.8%		19.3% (15.4, 23.1)	
Current smoker	14.3%	10.5%	20.8% (16.2, 25.5)	10.9%
Body mass index (kg/m^2)				
Underweight (<18.50)	6.0%		5.3% (2.1, 8.6)[b]	
Normal (18.50–24.99)	63.3%		50.4% (39.8, 60.9)	
Overweight (25.00–29.99)	18.4%		23.3% (16.2, 30.5)	
Obese (>29.99)	12.3%		20.9% (15.6, 26.3)	

Table 1. *Continued*

	3D Cohort Study participants (2010–12)	Canadian births, 2010	CHMS (2007–09) women 20–39 years of age[a] (95% confidence interval)	Quebec births, 2010
Household income from all sources[g]				
<$20 000	5.6%		10.7% (5.4, 16.0)[b]	
$20 000–30 000	5.2%		5.0% (2.7, 7.3)[b]	
$30 001–40 000	6.1%		9.0% (4.0, 13.9)[b]	
$40 001–50 000	6.0%		9.3% (5.0, 13.6)[b]	
$50 001–60 000	7.0%		9.8% (6.6. 13.0)	
$60 001–80 000	17.2%		18.2% (14.5, 21.8)	
$80 001–100 000	18.9%		9.6% (4.3, 14.9)[b]	
>$100 000	29.1%		20.6% (16.1, 25.1)	
No response	5.0%		7.8% (3.7, 12.0)[b]	

[a]Estimates weighted for the CHMS complex survey design.
[b]High sampling variability associated with these estimates. Results should be interpreted with caution.
[c]Lowest age category defined as 18 to <20 for 3D and under 20 years for Canadian births and Quebec births.
[d]Source: Reference[27], 2006–07.
[e]Married category includes domestic partnerships for 3D Study.
[f]Estimates of unacceptable quality and suppressed by Statistics Canada.
[g]$1 difference in categories between 3D and Statistics Canada.

for 1010 (46% of livebirths), paternal blood for 1570 (92% of participating biological fathers) and paternal urine for 1660 (97%). Protocol deviations in specimen handling were reported for 5% of total maternal/ paternal blood samples taken, 20% of cord blood samples, 3% of maternal/paternal urine samples, and 10% of vaginal secretions. The majority of protocol deviations (82% for urine samples and >90% for all other samples) were due to delays in freezing (greater than 30 min for vaginal secretions or greater than 2 h for all other samples). We have begun a process of micro-aliquoting of the biological specimens.

A total of 278 participants used assisted reproductive technologies for the study pregnancy. Of these, 203 women used ovarian stimulation, 89 intrauterine insemination, 133 *in vitro* fertilization, and seven *in vitro* oocyte maturation.

Infant follow-up has been completed to 2-years of age, with 1732 3-month visits completed, 1617 1-year visits, and 1622 visits at 2 years of age (Figure S2). Child health and developmental measures are detailed in Table 4.

Comment

In the light of its breadth and quality of data collected, the 3D Study has the potential to yield major advances in diverse areas of perinatal research. While several other existing birth cohorts approach or exceed the size of the 3D Study,[2,14–17] the combination of extensive maternal psychosocial measures, serial collection of biological specimens, and measurement of child developmental outcomes sets the 3D Study apart in terms of the research questions that can be addressed.

The 3D cohort includes one of the largest and most comprehensive biological specimen banks of any Canadian birth cohort. Specimens have been aliquoted into several separate samples for analysis, and we have begun a process of micro-aliquoting samples such that specimens will be thawed and re-frozen (−80°C) a maximum of once. The biobank includes whole blood, plasma, and blood cells from maternal, partner, and cord blood. The extensive biobank and high participation rates in this component of the study make the 3D cohort an ideal resource for emerging bio-specimens analysis techniques such as measurement of cortisol levels in hair samples,[18] epigenetic measurements,[19] and -omics technologies.[20,21] Biomarker analyses currently planned or underway include measurement of cotinine, corticotropin-releasing hormone (CRH), vitamin D, fatty acids, and markers of inflammation, oxidative stress, and metabolic dysfunction. Concurrent examination of a broad range

Table 2. Maternal demographic, health, and self-reported psychosocial measurements assessed in the 3D Cohort Study

	Recruitment (8–14 weeks)	Second trimester (20–24 weeks)	Third trimester (32–35 weeks)	Delivery/ Immediately postpartum	3 months postpartum	1 year	2 years
Medical history	X						
Vaccination	X	X	X				
Family medical history	X						
Self-reported pregnancy complications	X	X	X				
Infertility, time to pregnancy	X						
Use of assisted reproductive technologies or ovulation inducing drugs for study pregnancy	X						
Medication, nutrition supplements	X	X	X	X			
Smoking[a]	X	X	X		X	X	X
Alcohol consumption	X	X	X			X	X
Coffee, tea, energy drinks	X	X	X				
Illicit drug use	X	X	X			X	X
Employment status	X				X	X	X
Neighbourhood and financial support						X	
Self-reported environmental exposures[b]	X		X	X	X		
Sociodemographic characteristics	X				X		X
Anthropometric measurements	X	X	X				
3-day food diary		X					
Ultrasound assessment	Up to 14 weeks	14–28 weeks	28–37 weeks				
Pregnancy chart review				X			
Physical activity[28]	X	X	X				
Pittsburgh Sleep Quality Index[29]	X	X	X				
Perceived Stress Scale[3]	X	X	X		X	X	X
Pregnancy anxiety measure[4]	X	X	X				
Quality Marriage Index[30]	X	X	X		X	X	X
Marital strain scale[9]					X	X	X
Center for Epidemiological Studies Depression Scale[5]	X	X	X		X	X	X
Job stress or control scale[31]	X						
Food insecurity	X	X	X	X		X	X
Prenatal Life Events Scale[32]		X[c]					X[c]
Life Orientation Test[7]		X					
Self-esteem scale[6]		X			X		
General Attachment Measure[8]		X					
Anxiety disorders screening instrument		X					
Childhood, adolescence, and adulthood					X		

[a]Prenatal smoking measurements include maternal exposure to first-hand, second-hand, and third-hand smoke; postnatal measurements include maternal exposure to first-hand and second-hand smoke, and exposure of child to second-hand smoke.
[b]Self-reported environmental exposures include use of hair products, nail care products, makeup, skincare products, sunscreen, and fragrances.
[c]Prenatal life events scale administered at second-trimester visit with reference to the timeframe since the beginning of the pregnancy, and at 2-year postnatal visit with reference to the timeframe since the delivery.

of psychosocial measures will enable validation of these exposures with related biomarkers. The study includes extensive psychosocial data and biological specimens collected from mothers' partners. With more than 1700 partners participating, the 3D cohort is a major resource for studying emerging research

Table 3. Biological specimens collected in the 3D Cohort Study

	Recruitment (8–14 weeks)	Second trimester (20–24 weeks)	Third trimester (32–35 weeks)	Delivery/48 h postpartum	2 years
Mother					
Urine	X	X	X		
Blood	X	X	X	X	
Vaginal secretions	X	X			
Nails			X		
Hair				X	
Partner					
Urine	X				
Blood	X				
Child					
Cord blood				X	
Umbilical cord				X	
Placenta samples				X	
Meconium				X	
Hair				X	
Urine					X
Blood					X

The 3-month and 1-year postnatal visits did not include biological specimens collection.

Table 4. Child health and developmental measurements assessed in the 3D Cohort Study

	3 months postpartum	1 year	2 years
Vaccination	X		
Health problems	X	X	X
Special education services			X
Injuries			X
Hospitalization	X	X	X
Medication, nutrition supplements	X	X	X
Breast feeding and nutrition	X	X	Nutrition items, food frequency questionnaire, 3-day food diary
Mother–baby relationship[33]	X	X	X
Father–baby relationship[33]	X	X	X
Visual testing	X		
Teller acuity cards	X		
Auditory testing	X		
Electrophysiological testing	X		X
Anthropomorphic measurements	X	X	X
Sleep pattern		X	
Maternal-reported environmental exposures		X	X
Child care		X	X
Language exposure			X
General child behaviour		X	
Infant Characteristics Questionnaire (ICQ)[34]			X
Bayley Scales of Infant and Toddler Development (BSID-III)[10]			X
Bayley Adaptive Behaviour Questionnaire (ABAS-II)[10]			X
Sensory Profile 2[11]			X
MacArthur Communicative Development Inventories (CDI)[12]			X
Modified Checklist of Autism in Toddlers (M-CHAT)[35]			X

topics on issues such as paternal psychosocial exposures[22] and family based genetic studies.[23]

As mentioned above, the final sample size was lower than the initial goal of 3000 because of administrative delays, thus the study power was somewhat reduced compared to that of the target sample size. The participation rate of 37% is consistent with participation rates of several large pregnancy cohorts.[24] As in other pregnancy cohort studies,[15] 3D Study participants tended to be older and of higher socio-economic status than the overall Canadian[25] and Quebec[26] populations giving birth in 2010. Response rates for psychosocial measures collected from self-administered questionnaires (68–79%) were somewhat modest. Participation in postnatal follow-up (1622 (73% of livebirths) at 24 months of age) was also relatively moderate. Those who responded to self-administered questionnaires and who participated in postnatal follow-up visits tended to be older, of lower parity, had higher household incomes and education levels, and were less likely to smoke. Combined with the relatively high socio-economic status of the study population, these differential response rates are likely to limit generalizability of results from this cohort, particularly in psychosocial and developmental domains. In addition, the cohort was recruited from urban clinical centres in three of the four largest metropolitan areas in the province, and generalizability to rural populations may also be limited.

In summary, principal strengths of the 3D Cohort Study include the rich biological specimen collection, availability of numerous medical and psychosocial measures collected from mothers, fathers, and children, as well as child neurodevelopmental assessment. Contingent on funding of longer term follow-up, the study has the potential to make important contributions to understanding of developmental origins of metabolic and cardiovascular risks. Challenges include limits to generalizability and administrative coordination required to maintain postnatal follow-up and to support the biobank.

Acknowledgements

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1. Map of 3D Cohort Study sites.
Figure S2. 3D Cohort Study recruitment, follow-up, and data collection.
Table S1. Demographic, environmental, and health measurements assessed on maternal partners in the 3D Cohort Study.
Table S2. Self-reported psychosocial measurements assessed on maternal partners in the 3D Cohort Study.
Appendix S1. Measures collected on individual and family medical history.
Appendix S2. Template for maternal and infant medication and nutritional supplement logs.
Appendix S3. Information collected on child health problems.