




BMJ Open The Alberta Pregnancy Outcomes and Nutrition (APrON) longitudinal study: cohort profile and key findings from the first three years

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ABSTRACT

Purpose The objectives of the ongoing Canadian longitudinal cohort called the Alberta Pregnancy Outcomes and Nutrition (APrON) study are to: (1) determine the relationship between maternal nutrient intake and status before, during, after pregnancy, and (a) maternal mental health, (b) pregnancy and birth outcomes, and (c) infant/child neurodevelopment and behavior; (2) identify maternal mental health and nutrient predictors of child behaviour; and (3) establish a DNA biobank to explore genomic predictors of children's neurodevelopment and behavior. The purpose of this paper is to describe the participants, measures, and key findings on maternal and paternal mental health, maternal nutrition, and child outcomes to when children are 3 years of age.

Participants Participants included mothers and their children (n=2189) and mothers' partners (usually fathers; n=1325) from whom data were collected during the period from pregnancy to when children were 3 years of age, in Alberta, Canada. More than 88% of families have been retained to take part in completed data collection at 8 years of age.

Findings to date Data comprise: questionnaires completed by pregnant women/mothers and their partners on mothers', fathers' and children's health; dietary interviews; clinical assessments; linkage to hospital obstetrical records; and biological samples such as DNA. Key findings on mental health, nutrition and child outcomes are presented. APrON women who consumed more selenium and omega-3 were less likely to develop symptoms of perinatal depression. Higher prenatal consumption of choline rich foods such as eggs and milk were recommended as was vitamin D supplementation for both mothers and children to meet guidelines. Couples in which both mothers and fathers were affected by perinatal depression reported lower incomes and higher maternal prenatal depressive symptoms and lower support from fathers postnatally and their children presented with the most behavioural problems. Maternal experiences of early adversity predicted increased likelihood of perinatal depression and anxiety and children's behavioural problems.

Future plans The APrON cohort offers a unique opportunity to advance understanding of the developmental origins of health and disease. There is a planned follow-up to collect data at 12 years of age.

Strengths and limitations of this study

- APrON is a large, ongoing longitudinal study designed to understand the early origins of health and disease.
- APrON has collected data to 8 years of age and has planned follow-up at 12 years of age.
- APrON has retained more than 88% of participants at the 8-year data collection.
- A limitation is that the cohort is largely low-risk, limiting generalisability of study findings to higher-risk populations.

WHY WAS THE APRON COHORT SET UP?

The Alberta Pregnancy Outcomes and Nutrition (APrON) study is a longitudinal cohort of pregnant women, their partners, and their children, in Alberta, Canada. Women in our study are biological mothers, and partners typically self-identified as fathers of their children whether biological or not. The APrON study was designed to investigate the effect of nutrient intake and status during pregnancy on maternal mental health and children's neurodevelopment and behaviour by meeting three objectives.^{1 2} First, the APrON team sought to determine the relationship between maternal nutrient intake and status before, during, and after pregnancy, and (a) maternal mental health, (b) pregnancy and birth outcomes, and (c) infant/child neurodevelopment and behaviour. Second, the team sought to identify maternal mental health and nutrient predictors of child behaviour over time. Third, the team sought to establish a DNA biobank to explore genomic predictors of children's neurodevelopment and behaviour. An original grant of \$5 million provided the foundation for the APrON study, which has subsequently



expanded its focus and contributed to over 50 additional projects on the psychobiology of stress, parent-child relationships and attachment, neurotoxicant exposure, genetics, epigenetics, inflammation and immune activity, probiotics, the microbiome, and children's brain development. To date, the APrON study has received over \$15 million in additional funding. This funding enables follow-up of APrON families until children reach 12 years of age to understand the impact of medical, biological and environmental factors on children's development, behaviour and mental health. Data collection for the 5-year and 8-year follow-up questionnaires is completed, with the data currently being cleaned for analysis and the 12-year follow-up to begin in 2022. Papers have been published detailing how women and their partners were recruited^{2,3} and describing the APrON cohort at enrollment during pregnancy^{4,5} and up to 12 months postpartum¹; however, a summary of key findings has not been reported. Thus, drawn mostly from data collected during the period from pregnancy to when children are 3 years of age, the objectives of this paper are to describe the: (1) participants, (2) measures, and (3) key findings on maternal and paternal mental health, maternal nutrition and child outcomes.

WHO IS IN THE APRON COHORT?

Women were recruited into the cohort if they were 16 years of age or older, able to speak and read English, <27 weeks gestation and willing to come for on-site clinic visits at the University of Calgary, in Calgary or University of Alberta, in Edmonton, Alberta. Partners were eligible if they were cohabitating with the participating woman. Participants were excluded if they planned to move out of the region during the clinic visit timeframe of pregnancy to 3 months postpartum. A total of 2189 pregnant women (aged 16–44) and 1325 men (aged 18–52), residing around Calgary or Edmonton, were enrolled in the study between May 2009 and June 2012. To assess the representativeness of the APrON cohort (see [table 1](#)), socio-demographic characteristics of participants at the time of recruitment were compared with characteristics of women with children in Calgary, Alberta and Canada.^{5–7} A greater proportion of women in the cohort (28.0%) were over 34 years old compared with women in Calgary (20.0%), Alberta (16.0%) and Canada (18.0%). More APrON women were married (95%) compared with women in Calgary (73.0%), Alberta (70.0%) and Canada (60.0%). A greater proportion of women had household incomes of \$60 000 or more (77.0%) compared with Calgary (65.0%), Alberta (61.0%) and Canada (58.0%). More APrON women completed post-secondary education (87.0%) compared with women in Calgary (69.0%), Alberta (70.0%) and Canada (72.0%). The proportion of APrON women who were born outside of Canada (22.0%) was similar to the proportions in Calgary (25.0%), Alberta (22.0%) and Canada (20.0%) (see [figure 1](#)).

Patient and public involvement

APrON cohort participants were not involved in the development of the initial study design or in the recruitment of participants. However, APrON established a parent advisory committee (PAC) shortly after recruitment ended in 2012. Over time, 70 parents have participated on the PAC, with approximately 10–15 parents taking part in twice yearly meetings to advise the principal and co-investigators on a variety of topics, for example, how to keep participants engaged and interested in APrON research, priorities for future APrON research, and feedback on laymen research summaries posted to APrON's website. APrON has also extensively disseminated knowledge to the public via various modalities including: multiple presentations to various stakeholders, APrON's Newsletter, website (<https://apronstudy.ca/>) and conferences. Held via Zoom due to COVID-19 on 29–30 October 2020, APrON hosted an online conference titled *Celebrating 10 Years: Alberta Pregnancy Outcomes and Nutrition (APrON) Achievements & Evolution*, that attracted over 300 attendees, many who were APrON participants. The APrON cohort PAC members held their own panel session where they spoke to the attendees about their experiences with APrON, why they think the research is important, and how we can continue for years to come.

How often have APrON families been followed up?

Between 2009 and 2012, the initial cohort completed questionnaires and clinical assessments three times during pregnancy, and at 3 months postpartum. Hospital delivery records were also accessed to record birth information. Follow-up questionnaires were provided when children were 6 months, and 1, 2, 3, 5 and 8 years of age (see [figure 2](#)). We plan a 12-year follow-up beginning in 2022.

In total, 2189 women and 1325 men completed at least one questionnaire. Of the women and their children (88.9%) are continuing participants, defined as those who did not become ineligible or were lost to follow-up. Participants who discontinued the study included women who miscarried, had a stillbirth, lost custody of their child or for whom a maternal/child death was reported (n=52, 2.4%); moved out of Calgary or Edmonton before 3 months postpartum (n=43, 2.0%) or withdrew from the study citing loss of interest (n=149, 6.8%). The demographic characteristics of participants who continued in APrON compared with those that discontinued are provided in [table 2](#).

Continuing participants were more likely to be older, married and to have higher education and household incomes (all p's <0.05). The proportion of continuing participants born in Canada was similar to discontinuing participants. When mothers were lost to follow-up, so too were fathers and children.

WHAT HAS THE APRON STUDY MEASURED?

Expectant women and later mothers were asked to complete questionnaires three times during pregnancy

Table 1 Participant intake characteristics (n=3514)

Category	Maternal (n/%)	Paternal (n/%)
<i>Demographics</i>		
Age (years)		
16–24	100 (4.6)	19 (1.4)
25–29	481 (22.0)	216 (15.4)
30–34	980 (44.8%)	493 (35.2)
35–39	512 (23.4)	329 (23.5)
≥40	105 (4.8)	162 (11.6)
Missing age information	11 (0.5)	181 (12.9)
Marital status		
Married/common-law	2035 (93.0)	1275 (91.1)
Single/divorced/separated	97 (4.4)	27 (1.9)
Missing marital information	57 (2.6)	98 (7.0)
Education		
Less than a high school diploma	59 (2.7)	31 (2.2)
Completed high school diploma	202 (9.2)	147 (10.5)
Completed trade, technical	404 (18.5)	376 (26.9)
Completed university or more	1442 (66.8)	746 (53.3)
Missing education information	83 (3.7)	100 (7.1)
Ethnicity		
White	1693 (77.3)	1082 (77.3)
Non-white	485 (22.2)	206 (14.7)
Missing ethnic information	11 (0.5)	112 (8.0)
Mothers' report on total household income		
<\$40 000	190 (8.7)	–
\$40 000–\$69 999	279 (12.7)	–
\$70 000–\$99 999	464 (21.2)	–
>\$100 000	1146 (52.3)	–
Missing household income information	110 (5.0)	–
Born in Canada		
Yes	1618 (73.9)	1024 (73.1)
No	481 (22.0)	277 (19.8)
Missing country of birth	90 (4.1)	99 (7.1)
Gravidity		
Multigravida	1107 (51.6)	n/a
Primigravida	996 (46.4)	n/a
Missing gravidity information	42 (2.0)	n/a
Parity		
0	1222 (55.8)	n/a
1	732 (33.4)	n/a
2	181 (8.3)	n/a
≥3	37 (1.7)	n/a
Missing parity information	17 (0.8)	n/a

(<14, 14–26 and 27–40 weeks gestation; number of scales administered was 37) and seven times postnatally (3 and 6 months, 1, 2, 3, 5 and 8 years; number

of scales administered was 77). Their partners (usually self-reported fathers) were asked to complete questionnaires at 14–26 weeks gestational age (number of scales

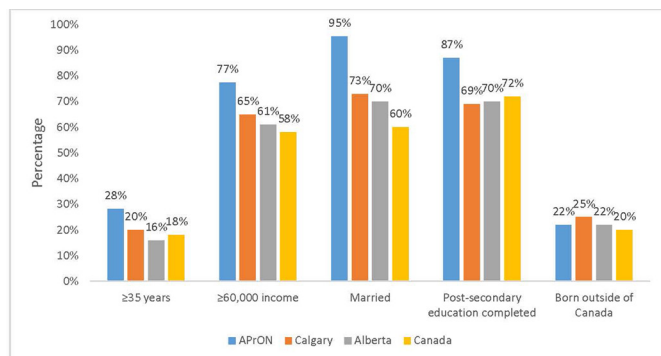


Figure 1 Sociodemographic characteristics of women in APrON, Calgary, Alberta and Canada.

administered was 16) and two times postnatally (3 months and 5 years; number of scales administered was 14). Questionnaires administered during pregnancy measured previous and current mental and physical health status, nutritional, medication and supplement intake, lifestyle choices, healthcare services used, social support, attitudes towards breast feeding and sociodemographic variables. The follow-up postpartum questionnaires collected information about labour and delivery, postpartum medical problems, maternal and paternal mental health and stress, nutrition, medication and supplement intake, lifestyle choices, food security, parenting, experiences in close relationships, adverse childhood experiences, and sociodemographics (see figure 2). Measures were selected based on several synergistic priorities. First, the APrON team had to judge measures to be reliable and valid indicators of the constructs of interest. Second, measures had to minimise burden to participants in terms of time and difficulty to complete, for example, measures with fewer items and more accessible language were valued most. Finally, an APrON team member had to express an interest in using the measure. Full details and documentation of all APrON measures are available on request.

Clinic visits were undertaken to gather maternal anthropometric measurements during pregnancy and at 3 months postpartum. These measures included height, pre-pregnancy and current weight, highest weight during pregnancy, circumference measurements (i.e., mid-upper arm, waist, hip, thigh) and skinfold thickness (i.e., biceps, triceps, subscapular, suprailiac, thigh). Each measurement was taken three times and averages were reported for analyses. Paternal height and weight were collected during the prenatal period. As an objective of APrON was to establish a biobank for future research on genetics, epigenetics,¹ nutrient exposures and neurotoxicants, biosamples were also collected from mothers, their partners and infants during clinic visits. Midstream random urine samples (10mL) were collected from expectant mothers at 14–26 weeks gestation and 3 months postpartum. A breast milk sample was collected from breastfeeding mothers to determine fatty acid composition. Maternal non-fasting venous blood samples were collected from mothers at <14, 14–26 and 27–40 weeks gestation, and at 3 months postpartum. Maternal blood collection provided whole blood, plasma and serum, which were used for DNA, RNA, cytokines, haematocrit, haemoglobin measures, thyroid hormones and measures of heavy metals (eg, mercury, lead) and perfluorinated chemical exposure. Buccal cell samples were also collected at 14–26 weeks gestation from partners for DNA extraction and future genetic and epigenetic studies. From infants, buccal and/or blood samples were collected at 3 months of age for DNA extraction. Purified DNA is available at the Gene Expression Omnibus data repository (<https://www.ncbi.nlm.nih.gov/geo/>). A detailed list of data collected up to 8 years of age on the full sample is provided in table 3 for mothers, table 4 for fathers and table 5 for children.

Numerous substudies, employing portions of the APrON sample, have utilized the originally collected biosamples in related research; for example, the Neurotoxicant

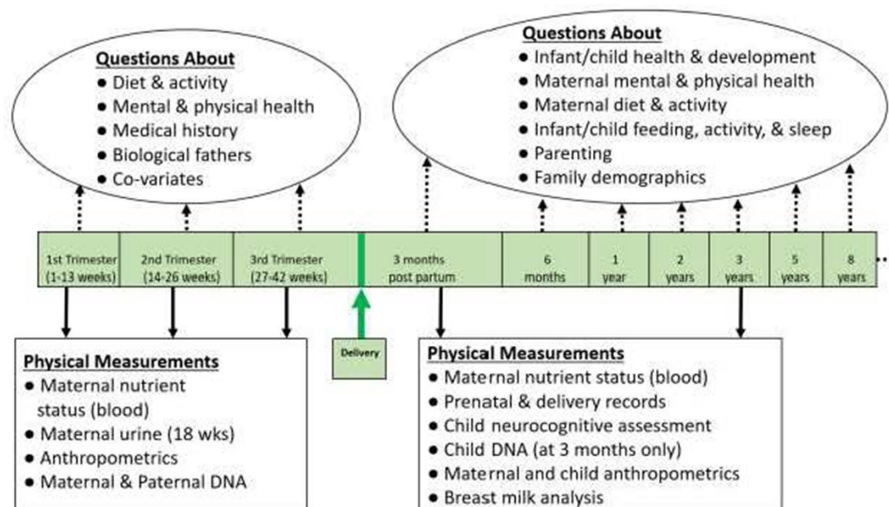


Figure 2 Data collection to 8 years of child age.

Table 2 Comparison of demographic characteristics of continuing and discontinued participants

Characteristic	Continuing participants	Discontinuing participants			P value
	n (%)	Become ineligible, n (%)	Lost to follow-up, n (%)	Dropped out, n (%)	
Maternal age					
16–24	71 (3.6)	8 (18.6)	15 (34.8)	6 (4.1)	<0.001
25–29	424 (16.2)	7 (16.2)	7 (16.2)	43 (29.2)	
30–34	899 (46.2)	15 (34.8)	14 (32.5)	51 (34.7)	
35–39	454 (23.3)	9 (20.9)	7 (16.2)	41 (27.9)	
≥40	95 (4.8)	4 (9.3)	0 (0.0)	6 (4.1)	
Marital status					
Single	72 (3.8)	12 (24.5)	8 (21.1)	5 (3.8)	0.007
Married	1838 (96.2)	37 (75.5)	30 (78.9)	128 (96.2)	
Maternal education					
Less than a high school diploma	41 (2.2)	6 (16.2)	8 (20.5)	4 (3.01)	<0.001
Completed high school diploma	164 (8.6)	9 (24.3)	9 (23.1)	20 (15.0)	
Completed trade, technical diploma	362 (19.1)	5 (13.5)	10 (25.6)	26 (19.5)	
Completed university or more	1329 (70.1)	17 (45.9)	12 (30.6)	83 (62.4)	
Household income					
<\$40 000	151 (8.1)	12 (30.8)	19 (54.3)	8 (6.15)	<0.001
\$40 000–\$60 000	252 (13.4)	6 (15.4)	5 (14.3)	16 (12.31)	
\$70 000–\$99 999	428 (22.8)	7 (17.9)	4 (11.4)	24 (18.46)	
≥\$100 000	1042 (55.6)	14 (35.9)	7 (20.0)	82 (63.08)	
Born in Canada					
No	425 (22.5)	13 (32.5)	14 (37.8)	28 (21.2)	0.186
Yes	1463 (77.5)	27 (67.5)	23 (62.2)	104 (78.8)	

Assessing the null hypothesis that there is no difference in distributions between those participants who continued and those who did not continue in the study; χ^2 test.

Study (n=546) that examined maternal exposure to endocrine hormone disrupting chemicals (i.e., bisphenol A and phthalates) on child outcomes^{8–13} and the Parenting Research on Mental Illness, Stress and Epi/genetics (PROMISE; n=276) Study of gene-by-environment interactions.^{14–18 19–26} Another substudy, called the Fetal Programming Study^{19–27} (n=276) collected additional data such as maternal and infant saliva for cortisol assessment, infant heart rate variability, and parent-infant interactions via videotaped observations.

WHAT HAS APRON FOUND?

A complete list of publications from APRON can be found at <http://www.apronstudy.ca>. Key findings from the full sample on maternal and paternal mental health, maternal nutrition and child outcomes have been summarised in [box 1](#).

MENTAL HEALTH OUTCOMES

Drawn from the full APRON cohort, three key papers^{28–30} reported on perinatal depression and anxiety symptom prevalence and risk factors and specifically, the impact of

adverse childhood experiences on outcomes. Many more papers report on parental mental health in substudies. See APRONstudy.ca for details.

Predictors of depression

Maternal prenatal depression is known to have negative impacts on pregnancy and maternal postnatal mental health and neonatal outcomes,^{31 32} and the psychosocial predictors of maternal postpartum depression are well known.^{33 34} However, less well known is whether mothers and fathers in partnered, cohabitating couples (e.g., married, common-law) share common predictors and experiences of depressive symptoms in the perinatal period. Further, whether maternal prenatal nutrition impacts postpartum depressive symptoms is less well studied. Thus, using APRON data, Leung and colleagues³⁰ reported on the prevalence of depressive symptoms in couples. For partnered mothers' depressive symptoms, using the recommended Edinburgh Depression Scale (EDS) cut-off score of ≥ 10 ,³⁵ findings revealed that 15.2% and 11.18% of mothers had significant symptoms prenatally and at 3 months postpartum, respectively. For fathers in couples, the cut-off of EDS ≥ 9 was used as

Table 3 Maternal variables and biological samples collected via questionnaires and clinic visits

Variables	<14 weeks	14–26 weeks	27–40 weeks	3 months postpartum	6 months postpartum	1 year	2 years	3 years	5 years	8 years
Sociodemographics										
Household income	X								X	X
Education	X									
Marital status	X								X	X
Age	X									
Primary language	X									
Born in Canada	X									
Family background		X	X	X	X	X	X	X	X	X
Family history		X								
Health and lifestyle										
General health				SF-8	SF-8	SF-8	SF-8	SF-8		
Current medical conditions and medications	X	X	X	X	X	X	X	X		
Substance use	X	X	X	X	X	X	X	X	X	X
Parenting									X	X
Pregnancy history										
Pre-pregnancy physical activity	X	X	X	X	X	X	X	X		
Physical activity	GLTE	GLTE	GLTE	GLTE	GLTE	GLTE	GLTE	GLTE	GLTE	GLTE
Dental care	X	X	X							
Dietary changes since pregnancy	X									
Food security		CCHSC	CCHSC							
Nutrition counselling information										
Diet history pre-pregnancy		FFQ								
Nausea and vomiting										
	PUQUE	PUQUE	PUQUE							
*Breastfeeding information			X	X	X	X	X	X		
24-hour recall of foods consumed	X	X	X	X	X	X	X	X		
Psychosocial health										
Depression										
Stress	EDS	EDS	EDS	EDS	EDS	EDS	EDS	EDS	CESD	CESD
Social support	SLEQ	SLEQ	SLEQ	SLEQ	SLEQ	SLEQ	SLEQ	SLEQ, PSS	SLEQ, PSS	SLEQ, PSS, SSI
Attachment	SSQ	SSQ	SSQ	SSQ	SSQ	SSQ	SSQ	SSQ	SSQ, SSI, ECR	SSQ, SSI, ECR

Continued

Table 3 Continued

Variables	<14 weeks	14–26 weeks	27–40 weeks	3 months postpartum	6 months postpartum	1 year	2 years	3 years	5 years	8 years
DSM-IV Axis I disorders		PDSQ		PDSQ						
Anxiety	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	SCL-90-R	STAI
Adverse childhood events						X				
History of mental health	X	X	X			X	X	X		
Anthropometrics (BMI/height/weight)	X	X	X	X						
Personality traits										
Personality traits										TIP1
Biological specimens										
Urine	X	X	X	X						
Venous blood		X		X						
*Breast milk				X						

X refers to investigator-developed measures.

*Breastfeeding mothers only.

ACEs, Adverse Childhood Experiences Questionnaire; CCHSC, Canadian Community Health Survey Cycle 2.2, modified; CES-D, Centre for Epidemiologic Studies Depression Scale; ECR, Experiences in Close Relationship Scale; EDS, Edinburgh Depression Scale; FFQ, Food Frequency Questionnaire, adapted from the Canadian version of the Diet History Questionnaire; GLTE, Godin Leisure-Time Exercise Questionnaire; OECD, Organization for Economic Cooperation and Development Guidelines on Measuring Subjective Wellbeing; PDSQ, Psychiatric Diagnostic Screening Questionnaire; PSS, Perceived Stress; PUQE, Pregnancy-Unique Quantification of Emesis and Nausea Questionnaire; SCL-90-R, Symptom Checklist-90-Revised; SF-8, Short Form Health Survey-8; SLEQ, Stressful Life Events Questionnaire; SSI, Social Support Index; SSQ, Social Support Questionnaire; STAI, State-Trait Anxiety Inventory; TIP1, Ten-Item Personality Inventory.

**Table 4** Paternal variables and biological specimens collected via questionnaires and clinic visits

Variables	<14 weeks gestation	14–26 weeks	27–40 weeks	3 months postpartum	5 years postpartum
Sociodemographics					
Household income			X		
Education			X		
Marital status			X		
Age			X		
Primary language			X		
Born in Canada			X		
Family background			X		X
Family history			X		
Health and lifestyle					
General health		X	X		
Current medical conditions and medications		X	X	X	
Substance use		X	X	X	X
Physical activity anthropometrics (BMI/height/weight)		GLTE	GLTE	GLTE	GLTE
		X	X	X	
Psychosocial health					
Depression		EDS	EDS	EDS	EDS
Social support		SSQ	SSQ	SSQ	SSQ
Stress			SLEQ		SLEQ
Anxiety					SCL-90-R
Biological specimens					
Buccal cell swab			X		
DNA from blood			X		

X refers to investigator-developed measures.

BMI, body mass index; EDS, Edinburgh Depression Scale; GLTE, Godin Leisure-Time Exercise Questionnaire; SLEQ, Stressful Life Events Questionnaire; SSQ, Social Support Questionnaire.

per recommendations³⁶ revealing that 14.0% and 12.1% of fathers had significant symptoms prenatally and at 3 months postpartum, respectively. These rates are consistent with other large samples.^{37,38} Further, 2.3% of couples experienced perinatal depressive symptoms in both mothers and fathers, 78.5% of couples did not experience depressive symptoms in either partner, 9.5% of couples experienced depressive symptoms in mothers only and 9.8% of couples experienced depressive symptoms in fathers only. Leung and colleagues³⁰ also determined the predictors of depression at 3 months postpartum from second trimester data. Risk factors for maternal postpartum depressive symptoms included low household income, high prenatal depressive symptoms, low postnatal support from fathers and high stressful life events. Risk factors for paternal postpartum depressive symptoms included low household income, prenatal depressive symptoms, postpartum stressful life events and smoking. For couples in which both partners were depressed, risk factors included low income, high maternal depressive

symptoms and low prenatal social support from fathers. Postpartum social support was found to be a protective factor associated with decreased risk of maternal and paternal postpartum depressive symptoms.

Additionally, Leung and colleagues²⁸ examined nutritional predictors of maternal postpartum depression, focusing on APrON mothers' reports of their multivitamin and mineral intake in each trimester of pregnancy. Almost all women (99%) took some type of micronutrient supplement during the prenatal period, with the most commonly consumed being vitamins B6, B9 (folate), B12 and E, with more than 90% of mothers consuming above recommended dietary allowances. With respect to predictors of postpartum depression, findings revealed that mothers who experienced postpartum depressive symptoms (EDS ≥ 10) were statistically less likely to take the supplemental micronutrients selenium and omega-3, compared with mothers who reported no postpartum depressive symptoms (EDS < 10). Selenium intake above the recommended dietary allowance appeared to be

Table 5 Child variables and biological specimens collected in questionnaires and clinic visits

Variables	3 months	6 months	1 year	2 years	3 years	5 years	8 years
Health and development		X	X	X	X	X	X
Occupation	X	X	X	X	X	X	
Childcare	X	X	X	X	X	X	
Vaccines						X	
Child food and liquid intake	X	X	X	X	X	X	
Children's eating and drinking behaviours						X	X
Children's activities						X	X
Children's injuries						X	
Community							X
Children's education							X
General infant behaviours							
Infant Behavior Questionnaire (IBQ)	X	X	X	X			
Scales of Independent Behaviors (SIB-R)	X	X	X	X	X	X	
Fussing and crying	X	X	X	X			
Sleeping		X	X	X	X	X	X
Early Childhood Behavior Questionnaire (ECBQ)				X			
Children's Behavior Questionnaire (CBQ)					X		
Child Behaviour Checklist Ages 1.5–5 (CBCL)				X	X		
Behaviour Rating Inventory of Executive Function—Preschool (BRIEF-P)				X	X		
Ages and Stages Questionnaire—Third Edition (ASQ-3)						X	
Children's Communication Checklist—Second Edition (CCC-Q)						X	
Behaviour Assessment System for Children—Second Edition (BASC-2)						X	X
Media use							
Quantitative Checklist for Autism in Toddlers				X	X		
Temper Tantrum Scale—past 2 weeks				X	X		
Temper Tantrum Scale—past 6 months				X	X		
Parenting						X	X
Biological specimens							
Buccal cells	X						
Venous blood	X						

protective, and other research suggests that this micro-nutrient has a role in normal brain function and in the pathway between dopamine and the pathophysiology of depression.³⁹ The supplement taken the least was omega-3; however, 68.5% of women with low depressive symptoms (EDS <10) did not take omega-3, versus 78.0% of women with high depressive symptoms (EDS ≥10), a finding consistent with other research.⁴⁰ The mean intakes of other nutrients were more likely to be higher in women with low depressive symptoms than those with high symptoms, although not statistically significant. The authors conclude with a call for more study into the value of selenium and omega-3 in the prevention of postpartum depression.

Associations with adverse childhood experiences

Adverse childhood experiences are defined as a set of exposures to personal abuse, neglect and household dysfunction prior 18 years of age that includes physical, sexual and emotional abuse, domestic violence, and parental mental illness, substance use and incarceration.⁴¹ A graded relationship has been repeatedly observed between the number of adversities experienced in childhood and later increased risk for poor health, including depression^{42 43}; however, whether such adversities affect perinatal mood more broadly including anxiety was less studied. Felitti and colleagues⁴¹ classic measure of adverse childhood experiences was administered to APrON mothers, revealing that while 55% reported

Box 1 Key findings

Mental health outcomes

- ▶ In partnered couples, both mothers and fathers had depressive symptoms in 2.3% of couples. Low household income and prenatal maternal depression were associated with a higher probability of depressive symptoms in both partners. In 78.5% of couples, neither father nor mother experienced depressive symptoms. Postnatal social support was found to be a protective factor associated with decreased risk of maternal and paternal postpartum depressive symptoms. Risk factors for maternal postpartum depression symptoms included low household income, and prenatal symptoms of depression. For paternal postpartum depression symptoms, risk factors included low household income, prenatal depression symptoms, postpartum stressful life events, and smoking.
- ▶ Women with higher postpartum depression symptoms were less likely to take micronutrients (eg, vitamins B6, B9, B12 and E; essential fatty acids; selenium) compared to those with fewer symptoms; however, only selenium and omega-3 were significantly different between symptomatically depressed and non-depressed groups, with non-depressed mothers consuming higher amounts.
- ▶ 13% of mothers had a score of three or more adverse childhood experiences. Maternal exposure to early adversities predicted higher reported symptoms of perinatal depression and anxiety.

Nutrition outcomes

- ▶ Approximately 70% of women who entered pregnancy with a body mass index (BMI) $>25\text{kg/m}^2$ were likely to exceed gestational weight gain guidelines in the beginning of the second trimester. Women with excessive weight gain also gained higher amounts of body fat and retained higher amounts of fat compared with women who gained within the guidelines. Women who consumed a healthy diet pattern prior to pregnancy were less likely to develop complications such as gestational hypertension.
- ▶ The median vitamin D intake from diet and supplements was 600 IU/day during pregnancy, which was not enough to achieve a target plasma circulation 25(OH)D concentration. A significant relationship between maternal reported dietary vitamin D intake and plasma 25(OH)D and 3-epi-25(OH)D3 concentration were identified.
- ▶ Only 23% of mothers met the adequate intake (AI) recommendations for choline; the number was even lower (10%) in the postpartum period. Consuming eggs and milk during pregnancy increased mothers' likelihood of meeting choline AI recommendations.

Child outcomes

- ▶ Infants with higher birth weights and at 3 months of age had mothers with a higher pre-pregnancy BMI. Gestational weight gain above recommendations was associated with higher infant weight at birth and 3 months of age as well as more rapid postnatal growth.
- ▶ Infants' vitamin D status increases in direct proportion to mothers' vitamin D intake. Given many mothers were found to be below recommended AI for vitamin D, both infants and breastfeeding mothers require vitamin D supplementation.
- ▶ Maternal experiences of early adversity associate with maternal symptoms of anxiety and depression during the perinatal period as well as externalising behavioural problems in their 2-year old children. Boys demonstrate greater vulnerability to the indirect effects of maternal adversity via both depression and anxiety.
- ▶ Both mothers' perinatal depressive symptoms and mothers' and fathers' co-occurring perinatal depressive symptoms predicted more problematic emotionally reactive, withdrawn, and total internalising behaviours in their 2–3-year old children. Children's aggression,

Continued

Box 1 Continued

attention problems and total externalising behaviours were only predicted by mothers' perinatal depressive symptoms.

no early adverse childhood experiences, nearly 32% reported one or two adversities and 13% reported three or more. Employing data from each trimester of pregnancy and 3, 6 and 12 months postpartum, more reported early adversities predicted higher reported symptoms of prenatal and postnatal depression and anxiety.²⁹ Routine screening for maternal childhood adversities may facilitate early identification and preventative interventions for perinatal mood disorders including depression and anxiety; however, this has been recently debated.⁴³ In sum, the identified risks and protective factors provide opportunities for prevention of perinatal depression and anxiety.

NUTRITION OUTCOMES

Gestational weight gain and dietary intake, especially perinatal nutrient intake and status focused on vitamin D and choline were examined in eight key papers.^{44–51}

Gestational weight gain and dietary intake

Gestational weight gain over or below Health Canada's Gestational Weight Gain Guidelines is associated with an increased risk of adverse outcomes for mother and infant.⁵² The APrON cohort was the first to provide evidence that more than half of women gain more than Health Canada's Guidelines, using prospectively collected body weights from across pregnancy.⁴⁴ Since then, several studies have been completed with body weight or body composition in pregnancy or postpartum as a main outcome. Analysis of the APrON data by Jarman and colleagues⁴⁵ provided a clear picture indicating that approximately 70% of women who become pregnant with a body mass index (BMI) $>25\text{kg/m}^2$ are likely to exceed gestational weight gain guidelines, by about 19 weeks gestation. Women with excessive weight gain also gain higher amounts of body fat and retain higher amounts of fat compared with women who gain within the guidelines.⁴⁶ The detailed dietary intake information that was collected showed that women who consumed a healthy diet pattern prior to pregnancy were less likely to develop complications such as gestational hypertension.⁴⁷ An individualised approach to supportive dietary counselling that considers pre-pregnancy BMI in addition to the woman's social and financial context may be key to helping women meet national recommendations for both diet and gestational weight gain in pregnancy.⁵³

Nutrient intake and status

Vitamin D is critical for a healthy pregnancy and the major circulating form of vitamin D is 25-hydroxyvitamin D (25(OH)D); thus, the total serum 25(OH)D level is

Table 6 Response rates for questionnaires

Data collection time point	Targeted participants (n)	Participants responded (n)	Response rate (%)
Mothers <14 weeks gestation	2189	2145	97.9
Mothers at 14–26 weeks gestation			
Mothers at 14–26 weeks gestation and those recruited at <14 weeks gestation	563	475	84.3
Fathers at 14–26 weeks gestation	1325	1315	99.2
Mothers at 27–40 weeks gestation	1838	1830	99.5
Mothers at 3 months postpartum	2051	1811	88.3
Fathers at 3 months postpartum	1287	1150	89.3
Mothers at 6 months postpartum	1727	1523	88.1
Mothers at 1 year postpartum	1747	1305	74.7
Mothers at 2 years postpartum	1809	1299	71.8
Mothers at 3 years postpartum	1648	1282	77.7

currently considered the best indicator of vitamin D supply.⁵⁴ Three studies that included APrON participants examined the role of maternal vitamin D intake during pregnancy.^{48–50} Aghajafari and colleagues⁴⁹ reported that the median vitamin D intake from diet and supplements was 600 International Units (IU)/day during pregnancy, which was not sufficient to achieve a target circulation of 25(OH)D concentration. When the 3-epimer (3-epi-25(OH)D3) was included in the estimation of vitamin D status, the prevalence of vitamin D insufficiency (<75 nmol/L) was lower (33.0%) compared with when it was excluded (38.0%). Vitamin D supplementation (2000 IU/day) was associated with 25(OH)D3 sufficiency.^{48–50} A significant relationship between maternal reported dietary vitamin D intake and plasma 25(OH)D and 3-epi-25(OH)D3 concentration was identified.

Choline intake during pregnancy and lactation is critical to the offspring's brain function.⁵⁵ Lewis and colleagues⁵¹ reported that the mean choline intake in pregnant and lactating women ranged between 340 (SD 148) in the second trimester and 346 (SD 151) mg/day at 3 months postpartum. Only 23% of mothers met the adequate intake (AI) recommendations for choline; the number was even lower (10%) in the postpartum period.⁵¹ Consuming eggs and milk during pregnancy increased mothers' likelihood of meeting choline AI recommendations. These findings contributed to the European Food Safety Authority dietary reference values for choline guidelines.⁵⁶ To conclude, a significant number of women were not meeting recommendations for vitamin D and choline intake during pregnancy and postpartum. Increased consumption of these nutrients may be necessary for pregnant and lactating women to improve the health and development of their infants.

CHILD OUTCOMES

The impacts of maternal and infant nutrient intake, maternal BMI and gestational weight gain, and perinatal depression and maternal adverse childhood

experiences on child outcomes were examined in four key papers.^{29 57–59} Many more papers will emerge as the cohort matures and data become available.

Maternal BMI, gestational weight gain and vitamin D

Subhan and colleagues⁵⁷ described the effects of maternal pre-pregnancy BMI and gestational weight gain on infant anthropometrics at birth and 3 months and infant growth rates between birth and 3 months. Other research shows that children who are heavier at birth have an increased risk of high BMI in childhood, being overweight or obese as adults,^{60 61} a condition linked to increased risk for hypertension, type 2 diabetes and cardiovascular diseases.^{60 62} APrON findings revealed that infants with higher weight at birth and at 3 months of age had mothers with a higher pre-pregnancy BMI. Also gestational weight gain above recommendations was associated with higher infant weight at birth and 3 months of age as well as more rapid postnatal growth. The authors concluded that clinicians and healthcare professionals should encourage women to enter pregnancy with a healthy BMI and adhere to the current gestational weight gain recommendations.

Aghajafari and colleagues⁵⁸ examined the association between APrON mothers' vitamin D intake during breast feeding with their infants' vitamin D status to determine whether infant supplementation was sufficient. Other research reveals that low vitamin D is associated with increased rates of infections, autoimmunity and allergies⁶³ and poor bone health in children.⁶⁴ Using plasma from a subset of breastfed infants, vitamin D status was measured by liquid chromatography–tandem mass spectrometry and mothers' and infants' dietary data were attained from questionnaires. Controlling for race, season, prenatal maternal vitamin D status, infant birth weight and daily infant vitamin D supplementation, infants' vitamin D status increased in direct proportion to mothers' vitamin D intake. Moreover, a quarter of mothers were below recommended AI for vitamin D. The authors concluded that to ensure optimal infant vitamin

D status, both infants and breastfeeding mothers require vitamin D supplementation.

Perinatal depression and adverse childhood experiences

Two studies addressed impacts of perinatal depression and adverse childhood experiences on children's behaviour. It is well established that children's internalising behavioural problems (e.g., emotional reactivity, anxiety, depression, somatic complaints and social withdrawal) and externalising behavioural problems (i.e., inattention, hyperactivity and aggression) predict adult mental health problems.^{65–67} As indicated above, adverse childhood experiences increased risk for poor health over the lifespan^{68–70}; however, intergenerational impacts have also been noted^{71–72} with an incomplete understanding of the mechanism of transmission from one generation to the next.²⁹ In examining intergenerational impacts, Letourneau and colleagues²⁹ found that APrON mothers' experiences of early adversity were associated with maternal symptoms of anxiety and depression during the perinatal period (discussed earlier) as well as externalising behavioural problems in their 2-year old children. Indirect associations were observed between maternal adverse childhood experiences and children's internalising and externalising problems via maternal anxiety and depression. Sex differences were also observed with boys demonstrating greater vulnerability to the indirect effects of maternal adversity via both depression and anxiety. The authors concluded that interventions may be targeted to women who have multiple adverse childhood experiences as well as mental health problems to prevent behavioural problems in their children. Letourneau and colleagues⁵⁹ further examined perinatal depression in mothers, as well as fathers or both parents and how symptoms in one or both parents predict children's behavioural problems. Other research has shown that fathers may buffer the impacts of maternal depression on children's outcomes and thus this protective factor is likely undermined when fathers are depressed as well as mothers.^{32–73} Mothers' and fathers' depressive symptoms were measured during pregnancy and 3 months postpartum, and children's behaviour was measured at 24 and 36 months of age. Results revealed that both mothers' perinatal depressive symptoms and mothers' and fathers' co-occurring perinatal depressive symptoms predicted more problematic emotionally reactive, withdrawn and total internalising behaviours. In contrast, children's aggression, attention problems and total externalising behaviours were only predicted by mothers' perinatal depressive symptoms. The authors urge healthcare providers to consider the whole family, including fathers, when treating maternal symptoms of depression, aligned with review recommendations to also consider fathers.^{32–74}

WHAT ARE THE MAIN STRENGTHS AND WEAKNESSES?

The major strengths of APrON are recruitment and retention of the large community-based cohort during

pregnancy, postpartum and early childhood. The APrON study used a detailed array of standardised validated psychological and physiological measures and biospecimens. The prospective data collection and follow-up enabled investigation of a wide range of maternal and paternal health outcomes. The APrON team has been successful in continuously engaging participants, as evidenced by high response rates over the years (see [table 6](#)).

The high response rates over time may be due to the recruitment of a relatively low-risk sample as sociodemographic characteristics are skewed toward a high percentage of well-educated, higher income, married participants. Consequently, generalisability of findings to those with different sociodemographic backgrounds should be made with caution. Further, the study likely included participants with healthier lifestyle behaviours or with more positive attitudes towards research, because such characteristics are associated with higher socioeconomic status.⁷⁵ Selective attrition bias is likely operating in the cohort, which may lead to underestimation of the effect of parental mental health and lifestyle choices on children's development. While attrition has been relatively low over time, differences in the sociodemographic characteristics of the continuing participants compared with discontinuing participants should be considered when interpreting the findings. There were also fewer fathers than mothers in the sample; thus, most developmental and behavioural outcomes are based on maternal reports.

WHERE CAN I FIND OUT MORE ABOUT APRON RESEARCH?

Information about the APrON study is available at www.apronstudy.ca. APrON data are available through

Profile in a nutshell

- ▶ The APrON study is a longitudinal cohort of mothers, fathers and their children investigating mental health, nutrition, and child development outcomes.
- ▶ A total of 2189 women (aged 16–44) and 1325 fathers (aged 18–52), residing around Calgary or Edmonton, Alberta, enrolled and completed at least one questionnaire between May 2009 and June 2012. The majority were married, educated, had annual household incomes >\$70 000 and were born in Canada.
- ▶ Mothers completed questionnaires and clinic visits spanning pregnancy to 8 years postpartum and provided access to their medical records as well as blood and urine samples.
- ▶ The APrON dataset includes comprehensive maternal and child sociodemographic data, maternal nutrition and psychological data from pregnancy to 8 years postpartum, and infant and child neurodevelopmental and behavioural data to 8 years of age. Maternal, paternal and infant biosamples for genetics were also collected. Five-year and 8-year data collection is complete and 12-year data collection will start in 2022.

Requests for data and collaboration are welcomed, contact Dr. Nicole Letourneau at nicole.letourneau@ucalgary.ca

Secondary Evidence to Generate Evidence (<https://policywise.com/sage/>). For more information, contact Principal Investigator, Dr. Nicole Letourneau at Nicole.Letourneau@ucalgary.ca. Collaboration or data access inquiries will be considered by the APrON Study team.

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Contributors NL conceived of the idea for the paper, oversaw all aspects of the APrON cohort, including the collection, cleaning and analysis of data for reviewed studies, and wrote major sections of the paper, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. FA contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. RCB wrote a key section of the paper, contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. AD contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. DD contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. CF contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. GG contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. BK contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. BL contributed to the collection, cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. HN contributed to the cleaning and analysis of data for reviewed studies, critically reviewed the drafts, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work. APrON Study Cohort Participants volunteered time and energy to share their individual and family's experiences with us to help improve the long-term health outcomes for future newborns, mother, fathers and families. NL is the author who is responsible for the overall content as the guarantor.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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Data availability statement Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. Data can be collected at the Secondary Analysis to General Evidence (SAGE) data repository or by contacting Dr Nicole Letourneau (the principal investigator for the APrON Study).

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