International Journal of Epidemiology, 2024, **53(6)**, dyae162
https://doi.org/10.1093/ije/dyae162
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Cohort Profile Update: Project Viva Offspring

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Keywords: Cohort, child, adolescent, obesity, asthma, neurodevelopment, cardiometabolic health, behavioural health, respiratory health, allergy.

Key Features

- Project Viva, a pre-birth cohort of 2128 mother-child pairs, was initiated in 1999–2002 in Massachusetts, USA, to examine the extent to which exposures and experiences during pregnancy and the perinatal period affect health outcomes over a lifetime among women and their children.
- This cohort profile update describes offspring follow-up through late adolescence. We will refer to the offspring as the main 'participant'. Two decades of continual follow-up enable us to evaluate participant's outcome trajectories and health conditions that progress or emerge as they transition through key paediatric stages of the life course.
- New measures include behavioural health, gender identity and sexual orientation, polycystic ovary syndrome among females, collection of deciduous teeth, activity and sleep measured by Fitbits, 24-h dietary recalls, biomarkers of cardiometabolic health, COVID-19 pandemic impact and multiple environmental chemicals and contextual factors based on residential addresses.
- A total of 911 participants had some data collected at the Mid-Teen Visit (2017–21; median age 17.5 years) or Age 19 Questionnaire (2019–22; median age 19.5 years) or a 2020, 2021 or 2022 Questionnaire.
- Investigators interested in learning more about how to obtain Project Viva data can contact Project Viva Principal Investigators Emily Oken or Marie-France Hivert at project_viva@hphci.harvard.edu or can get more information at https://www.projectviva.org.

The original cohort

We launched Project Viva to investigate how exposures and experiences during the perinatal period might influence short- and long-term health outcomes. From April 1999–July 2002, research assistants recruited women during their initial prenatal visits (median 9.9 weeks' gestation) across eight obstetric offices in a multispecialty group practice located in Eastern Massachusetts, USA.[1,2] Eligibility criteria included having a singleton pregnancy, enrolling before 22 weeks' gestation, planning to deliver at one of two designated study hospitals and being able to complete questionnaires in English. Out of 2670 pregnancies recruited, 329 were later deemed ineligible due to reasons such as relocating from the study area, having a multiple gestation or experiencing a miscarriage or stillbirth. This left 2341 eligible pregnancies, with 2128 women still participating at the time of delivery and having given birth to live infants (Figure 1). These 2128 children form the Project Viva offspring cohort, which we will refer to as 'participants' in this cohort profile update.

Received: 30 April 2024. **Editorial Decision:** 14 October 2024. **Accepted:** 18 November 2024

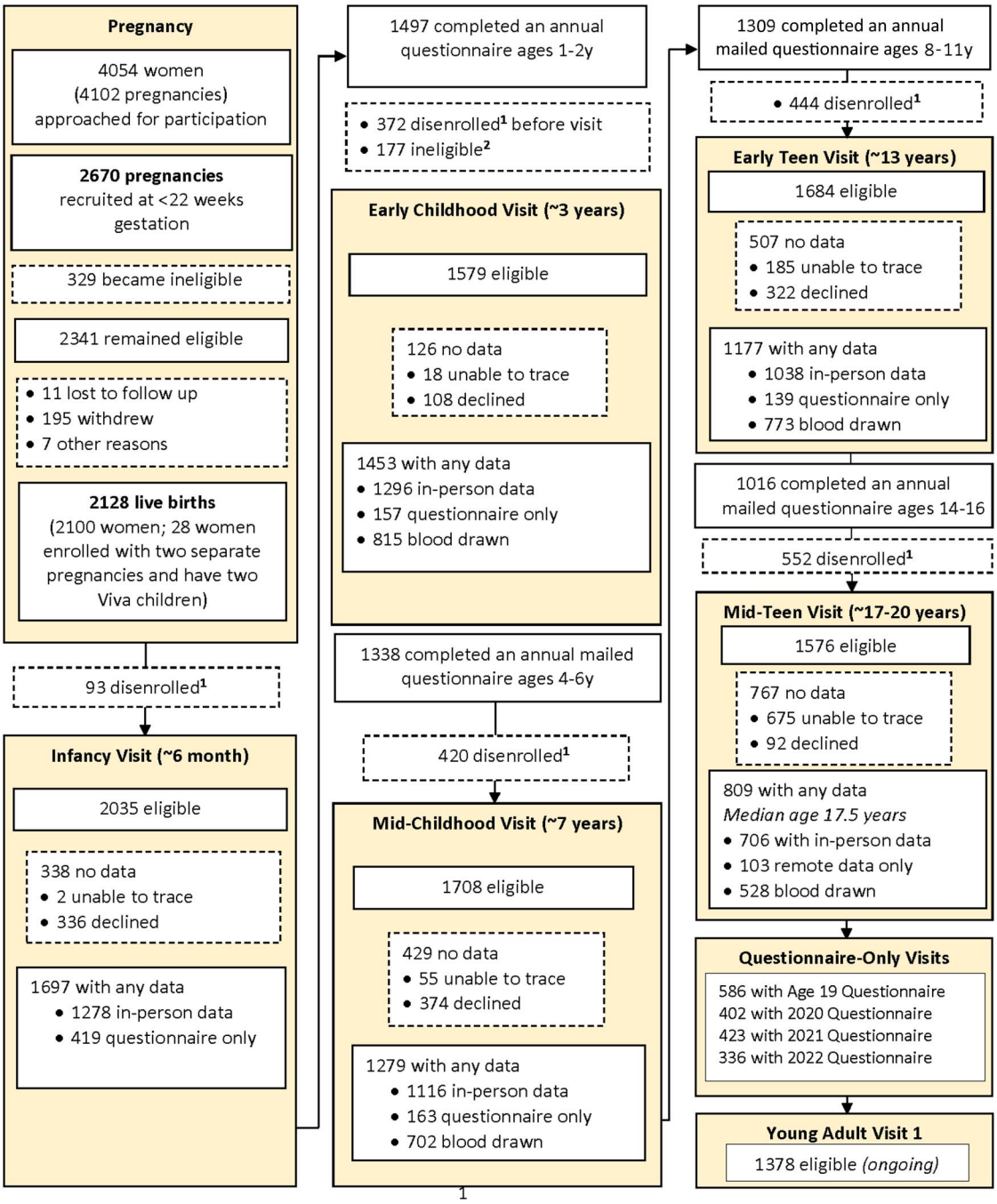

Figure 1. Participant flow from recruitment through mid-late adolescence in Project Viva. [a]Cumulative number disenrolled from birth to visit. [b]Ineligible for visit because no information on diet in pregnancy. We adapted Figure 1 from our original Project Viva cohort profile and our cohort profile update for mothers.[1,2] We sent annual mailed questionnaires to all participants who had not disenrolled in the study at the time of the survey, regardless of their participation in previous study visits

Research assistants conducted in-person visits in mid-pregnancy (median 27.9 weeks' gestation) and at delivery (median 39.7 weeks' gestation). We conducted additional in-person visits with children and their mothers during infancy (median offspring age 6.2 months), early childhood (median 3.3 years), mid-childhood (median 7.7 years) and early adolescence (median 12.9 years), as described in our original cohort profile.[1] Between visits, we administered annual mailed or online questionnaires.

After our original cohort profile, which described follow-up of the cohort through early adolescence,[1] we completed additional research visits with participants. We refer to our main in-person visit as the 'Mid-Teen Visit' (median 17.5 years), conducted from July 2017 through August 2021. We also administered four additional questionnaire-only visits: the Age 19 Questionnaire (administered around the participant's 19th birthday, December 2019–June 2022, median 19.5 years), the Year 2020 Questionnaire (May–September 2020, median 19.2 years), the Year 2021 Questionnaire (February–August 2021, median 19.9 years) and the Year 2022 Questionnaire (January–December 2022, median 21.1 years) (Figure 1). This cohort profile update focuses on

describing visits and findings from Project Viva participants as they transitioned from mid-adolescence to young adulthood. Separately, we recently published a cohort profile update on Project Viva mothers.[2]

What is the reason for the new data collection?

We sought to follow Project Viva participants as they transitioned through key stages of the life course. Adolescence, the next sensitive period of the life course after early childhood, is characterized by multiple physical, physiological, social and developmental changes. Adolescence thus provides opportunities to examine risk trajectories set in motion by pre- and perinatal exposures. Additionally, measures not previously examined, including sexual orientation and gender identity, mental and behavioural health and risk-taking behaviours, are more manifest in adolescence, making this an important period for study.

What are the new areas of research?

Data collection through late adolescence was largely supported by two large grants from the US National Institutes of Health. The first set of aims, funded by the US National Institute of Child Health and Human Development, focused on characterizing trajectories of body composition and components of the metabolic syndrome through late adolescence. We have used metabolomic profiling in plasma from mid-childhood, early adolescence and late adolescence to refine characterization of adiposity measures and risk of dysglycaemia, and to identify potentially modifiable determinants of growth trajectory milestones linked to future risk of excess adiposity and cardiometabolic risk.[3] Using the extensive dietary data collected via repeated administration of the ASA24, an automated 24-h recall, we have examined dietary intake and practices in adolescence. A second set of aims, supported by the Environmental influences on Child Health Outcomes programme,[4] allowed us to investigate what early life environmental exposures, singly and as mixtures, influence the separate and co-evolution of obesity and asthma as well as related factors including physical activity and sleep.

Additional ancillary grants have leveraged the longitudinal extant data and samples available within Project Viva to examine associations of prenatal exposures with adolescent outcomes. We have used geocoded residential address data to characterize publicly available metrics that represent aspects of neighbourhood disadvantage (Area Deprivation Index, Social Vulnerability Index) and the Childhood Opportunity Index, as well as natural and built environments, to examine the extent to which these neighbourhood metrics explain disparities in child outcomes including cognition, obesity, asthma and cardiometabolic health.[5] We have also compared adolescent outcomes including onset of puberty and biomarkers of cardiometabolic risk, among children born by caesarean delivery and those born vaginally.[6] Other work is focused on estimating the prevalence of ideal cardiovascular health (CVH) in the cohort, characterizing trajectories of CVH from early childhood to mid-adolescence, and identifying prenatal correlates of these CVH trajectories as well as novel protein biomarkers underlying improvement, decline or maintenance of CVH from childhood to adolescence.

We have also examined childhood exposures in relation to adolescent health outcomes, including environmental chemicals such as per- and polyfluorinated substances (PFAS), metals and phthalates, in relation to body composition and bone health across adolescence.[7,8] Another series of analyses examines the hypothesis that exposure to airborne particulate matter and traffic-related air pollution over the life course would be associated with a unique epigenomic signature, and this signature will identify children and adolescents at increased risk for anxiety and depression symptoms. An additional study aims to characterize the neurodevelopmental toll of prenatal and postnatal metals and provide novel biomarkers of exposure and neurodevelopment.[9] We are also working to characterize the prospective associations of childhood exposures to PFAS and metals with vaccine-induced immunity.

In addition to these funded aims, we have a long history of welcoming unfunded repository analyses that examine a range of research questions of interest to students and collaborators.

Who is in the cohort?

At the beginning of the Mid-Teen Visit, 1576 participants were eligible for the visit. Out of these, 809 (51%) had data from the Mid-Teen Visit at a median age of 17.5 years. For the questionnaire-only visits, data availability was as follows: 586 out of 1273 (46%) provided data at Age 19, 402 out of 1204 (33%) at Year 2020, 423 out of 1202 (35%) at Year 2021 and 336 out of 1201 (28%) at Year 2022. In total, 911 adolescents had data from either the Mid-Teen Visit or one of the four questionnaires (Figure 1).

We analysed characteristics of all Project Viva offspring who were enrolled at birth and compared those who did and did not participate in the Mid-Teen Visit as adolescents. Adolescents who completed the Mid-Teen Visit were more likely to have mothers who were older (32.6 vs 31.4 years), more frequently had mothers with a college degree (74% v 59%) and were more likely to come from households with incomes above USD 70 000 per year (65% vs 59%). Other characteristics did not show notable differences (Supplementary Table S1, available as Supplementary data at *IJE* online).[1,2]

What has been measured?

Tables 1 and 2 summarize the data that we collected from participants at the Mid-Teen Visit and the latest four questionnaire-only visits. During in-person visits, we measured blood pressure using an automated cuff (Omron HEM-907XL), collected anthropometric measures (height, weight, waist and hip circumferences, middle-upper arm circumference and subscapular and triceps skinfold thicknesses) and bioimpedance and dual X-ray absorptiometry (DXA, Hologic model Discovery A, Bedford, MA) measures of body composition, and obtained fasting blood and cardiometabolic risk markers. We also collected hair and urine samples and previously shed deciduous teeth, if available. We assessed physical activity and sleep using the Fitbit Charge 2. We collected multiple measures of airways health and atopy, including pre-and post-bronchodilator spirometry and exhaled nitric oxide (only prior to the onset of COVID-19) and questionnaire measures of allergic rhinitis, eczema, asthma and

Table 1. Selected characteristics of Project Viva participants at the Mid-Teen Visit (2017–21), overall and by sex

Characteristics	Overall $n = 809$	Female 423 (52%)	Male 386 (48%)
Age at Mid-Teen Visit, years, median (IQR) ($n = 809$)	17.5 (17.2–18.2)	17.5 (17.2–18.2)	17.5 (17.2–18.0)
Race and ethnicity ($n = 809$)			
Hispanic	10%	10%	11%
Non-Hispanic White	65%	66%	63%
Non-Hispanic Black	14%	13%	15%
Non-Hispanic Asian	3%	3%	2%
>1 race, or other	8%	7%	9%
PCOS diagnosis or phenotype[a] ($n = 417$)		13%	
Depression diagnosis ($n = 775$)	11%	13%	10%
Anxiety diagnosis ($n = 775$)	17%	20%	13%
Asthma diagnosis ($n = 795$)	28%	26%	30%
Asthma status ($n = 785$)			
Never asthma	73%	74%	72%
Current asthma	12%	13%	12%
Ever asthma, but not current	14%	13%	16%
Ever tried cigarette smoking ($n = 795$)	14%	12%	16%
Ever tried vaping ($n = 792$)	39%	37%	41%
Ever tried marijuana ($n = 794$)	43%	43%	44%
Ever tried drinking alcohol ($n = 793$)	71%	72%	70%
BMI percentile category ($n = 697$)			
<5th	3%	3%	2%
5–<85th	72%	72%	71%
85–<95th	13%	15%	12%
≥95th	13%	11%	15%
		Mean (SD)	
Self-reported sleep duration, hours/day ($n = 793$)	7.0 (1.0)	7.0 (1.0)	7.0 (1.0)
Self-reported light-moderate physical activity, min/day ($n = 786$)	40.8 (43.9)	40.0 (43.3)	41.7 (44.4)
Self-reported vigorous physical activity, min/day ($n = 786$)	43.6 (49.5)	37.8 (46.7)	50.0 (51.7)
Healthy Eating Index total score (0–100 range), points ($n = 755$)	50.0 (12.8)	51.9 (13.2)	47.7 (11.8)
Fast food, times/week ($n = 797$)	1.0 (1.4)	1.0 (1.4)	1.0 (1.4)
Sugary beverages, servings/day ($n = 797$)	0.7 (0.8)	0.5 (0.6)	0.9 (1.0)
Fitbit sleep, hours/day ($n = 588$)	7.9 (0.9)	8.0 (0.9)	7.8 (0.9)
Fitbit sedentary, min/day ($n = 610$)	593.0 (96.5)	590.6 (89.1)	595.7 (105)
Fitbit light physical activity, min/day ($n = 610$)	240.6 (64.3)	249.0 (61.3)	230.6 (66.4)
Fitbit moderate physical activity, min/day ($n = 610$)	23.8 (19.7)	17.9 (14.4)	30.8 (22.6)
Fitbit vigorous physical activity, min/day ($n = 610$)	20.9 (20.0)	14.8 (15.5)	28.2 (22.3)
PROMIS Meaning and Purpose T-score ($n = 786$)	44.8 (9.4)	45.2 (9.4)	44.4 (9.4)
PROMIS Psychological Stress Experiences T-score ($n = 787$)	58.2 (8.0)	59.7 (7.9)	56.5 (7.8)
PROMIS Depressive Symptoms T-score ($n = 791$)	48.0 (10.3)	49.4 (10.3)	46.5 (10.1)
Social Responsiveness Scale (SRS-2) T-score ($n = 759$)	47.0 (7.8)	47.0 (7.3)	47.0 (8.3)
Self-reported health (1 = poor to 5 = excellent)			
General health ($n = 796$)	3.6 (0.9)	3.5 (0.9)	3.7 (0.9)
Quality of life ($n = 794$)	3.9 (0.9)	3.9 (0.9)	4.0 (0.9)
Physical health ($n = 793$)	3.5 (1.0)	3.3 (1.0)	3.6 (1.0)
Mental health, including mood/ability to think ($n = 794$)	3.4 (1.1)	3.2 (1.0)	3.6 (1.1)
Life's Essential 8, overall score[b] ($n = 467$)	75.5 (10.2)	76.5 (10.2)	74.5 (10.1)
Systolic blood pressure, mmHg ($n = 701$)	111.2 (10.0)	106.6 (8.0)	116.3 (9.4)
Diastolic blood pressure, mmHg ($n = 701$)	65.0 (7.9)	65.1 (7.3)	64.9 (8.5)
Anthropometry and body composition metrics (by DXA)			
BMI, kg/m^2 ($n = 700$)	24.0 (5.2)	23.9 (5.4)	24.0 (4.9)
BMI z, units ($n = 697$)	0.39 (1.05)	0.40 (0.98)	0.38 (1.11)
Waist circumference, cm ($n = 701$)	81.6 (12.8)	79.8 (12.7)	83.6 (12.7)
DXA total percentage fat ($n = 563$)	28.3 (8.7)	33.1 (6.6)	22.7 (7.3)
DXA lean fat mass, kg ($n = 563$)	50.2 (10.8)	43.4 (6.9)	58.0 (8.9)
DXA truncal fat mass, kg ($n = 563$)	8.6 (5.4)	9.4 (5.3)	7.7 (5.2)
DXA fat mass, kg ($n = 563$)	20.5 (10.3)	22.6 (9.9)	18.2 (10.1)
Blood assays			
HbA1c, percent ($n = 517$)	5.1 (0.3)	5.1 (0.3)	5.1 (0.3)
Fasting insulin, uU/ml ($n = 501$)	12.1 (8.2)	12.4 (7.5)	11.8 (8.9)
Fasting glucose, mg/dL ($n = 496$)	84.5 (6.7)	83.1 (6.1)	86.0 (7.0)
Triglycerides, mg/dL ($n = 521$)	69.0 (29.4)	66.4 (26.3)	71.8 (32.2)
HOMA-IR, units ($n = 490$)	2.5 (1.9)	2.5 (1.7)	2.5 (2.1)
Total cholesterol, mg/dL ($n = 522$)	154.6 (30.3)	161.5 (29.5)	147.1 (29.5)
HDL, mg/dL ($n = 522$)	55.2 (12.6)	59.3 (12.6)	50.8 (10.9)
Non-HDL cholesterol, mg/dL ($n = 522$)	99.4 (27.5)	102.2 (26.2)	96.4 (28.5)
hsCRP, mg/L ($n = 521$)	1.5 (3.3)	1.7 (3.1)	1.4 (3.5)

(continued)

Table 1. (continued)

Characteristics	Overall $n = 809$	Female 423 (52%)	Male 386 (48%)
Leptin, ng/mL ($n = 522$)	15.5 (18.2)	23.7 (20.4)	6.8 (9.8)
Adiponectin, ug/mL ($n = 522$)	6.6 (3.3)	7.7 (3.5)	5.5 (2.7)
Adiponectin/leptin ratio ($n = 522$)	1.8 (2.9)	0.7 (1.1)	3.0 (3.6)

Numbers vary depending on questionnaire, in-person measurements and blood assays. Percentages may not add up to 100% due to rounding.
BMI, body mass index; DXA, dual X-ray absorptiometry; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein; PCOS, polycystic ovary syndrome; PROMIS, Patient-Reported Outcomes Measurement Information System.
[a] Among females, we defined PCOS phenotype as self-reported doctor diagnosis, or ovulatory dysfunction plus evidence of clinical and/or biochemical hyperandrogenism in mid-late adolescence.
[b] We calculated Life's Essential 8 score (possible range 0–100 points, higher = healthier), that includes eight components of cardiovascular health: diet, physical activity, smoking status, sleep duration, BMI, blood pressure, blood lipids and glycaemia.

Table 2. Data elements collected during the Mid-Teen Visit and Questionnaire-Only Visits (Age 19 and Years 2020–22) among participants of Project Viva, a longitudinal pre-birth cohort started in 1999

	Mid-teen visit (809 participants with any data; median age 17.5 years)	Questionnaire-only visits[a] (up to four questionnaires)
Questionnaire		
Home and neighbourhood environment	X	X
Gender identity and sexual orientation	X	X
Sexual behaviour		X[b]
Drugs, alcohol and smoking	X	X
Body image	X	X
Dietary patterns and behaviours	X	X
Physical activity and inactivity	X	X
Sleep duration and quality	X[c]	X[c,d]
Medical history	X	
General health	X	X[e]
Reproductive health	X	X
Bone health	X	X
Depression and anxiety diagnosis	X	
Depression and anxiety symptoms	X[f]	X[f]
Emotional and behavioural functioning		X[g,h]
Stress/resilience	X[i]	X[j]
Mood	X[k]	X[k]
Social cognition	X[l]	
Discrimination		X[m]
History of adverse childhood experiences		X[n]
COVID-19 experiences		X
Health behaviour measures (remote and/or in-person)		
Fitbit sleep and physical activity	X[o]	
Dietary intake	X[p]	
Research measures (during in-person visits)		
Anthropometry	X	
DXA whole-body scan	X	
Blood pressure	X	
Fasting blood and urine collection	X	
Biomarkers of cardiometabolic health, metabolomics, and hormones	X	
Extracted DNA from blood samples to obtain genotypes	X	
Hair collection	X	
Baby teeth collection	X	
Spirometry	X	
Exhaled nitric oxide	X	

DXA, dual X-ray absorptiometry.
[a] We administered four additional questionnaire-only visits: 586 of 1273 (46%) had any Age 19 data, 402 of 1204 (33%) had any 2020 Questionnaire data, 423 of 1202 (35%) had any 2021 Questionnaire data and 336 of 1201 (28%) had any 2022 Questionnaire data; 669 participants had data from any of the four questionnaires; 911 had data from the Mid-Teen Visit or any of the four questionnaires.
[b] Youth Risk Behavior Survey (YRBS).
[c] PROMIS Pediatric Sleep-Related Impairment Short Form 4a.
[d] PROMIS Sleep Disturbance Scale 4a.
[e] PROMIS Global Health v1.2.
[f] PROMIS Pediatric Depressive Symptoms—Short Form 8a.
[g] PROMIS Support.
[h] Strengths and Difficulties Questionnaire (SDQ).
[i] PROMIS Psychological Stress Experiences.
[j] PROMIS Perceived Stress Scale v1.2.
[k] PROMIS Meaning and Purpose.
[l] Social Responsiveness Scale, Version 2 (SRS-2).
[m] Everyday Discrimination Scale v1.2.
[n] Adverse Childhood Experiences Survey (ACES).
[o] Fitbit Charge 3.
[p] Automated Self-Administered 24-h (ASA24) Dietary Assessment Tool.

food allergy. We assessed diet and analysed dietary intake data using the ASA24 Dietary Assessment Tool, versions 2016, 2018 and 2020, developed by the National Cancer Institute, Bethesda, MD.

We collected data on self-reported clinical diagnosis of polycystic ovary syndrome, depressive and anxiety symptoms, substance use, smoking and vaping, sexual orientation, gender identity, eating behaviors, body image and bullying. We assessed behavioural and psychosocial impacts of the COVID-19 pandemic on annual questionnaires in 2020 and 2021. Our earlier publication[1] provides additional details about the measures collected at prior study visits and questionnaires.

We have linked lifetime geocoded residential address information to multiple measures of neighbourhood environment including social factors such as the Social Vulnerability Index, and markers of air pollution including $PM_{2.5}$ and black carbon, daily from enrolment onwards,[10] and measures of the built and natural environments, including Landsat Normalized Difference Vegetation Index,[11] satellite-based objective indicator of the quantity of green vegetation on the ground, and Google Street View-based measures.

What has it found?

The Project Viva team and collaborators have continued to be highly productive since the publication of the original cohort profile in 2015 [https://www.projectviva.org/publications].[1] We have started to analyse and publish findings from the Mid-Teen Visit, Age 19 questionnaire, and Years 2020–22 Questionnaire data. In this section we summarize some of our notable findings among Project Viva participants, published after our 2015 original cohort profile related to our new research focus.

Trajectories of growth, adiposity and metabolic risk factors

We have leveraged our multiple outcome measures, particularly of child growth, body composition and cardiometabolic health, to identify predictors of longitudinal metabolic health from childhood into adolescence.[12] For example, we observed that prenatal and mid-childhood PFAS exposures were associated with blood pressure at specific time points between birth and late adolescence, but associations were not consistent across all time points or PFAS types.[13] We also found that higher concentrations of select prenatal PFAS were associated with higher obesity risk and greater adiposity in late adolescence. Prenatal PFAS mixture was also associated with higher obesity risk, body mass index (BMI) and dual energy absorptiometry (DXA) measures in a dose-dependent manner.[14]

We observed that a higher maternal dietary inflammatory index and a lower Mediterranean Diet Score in pregnancy were associated with higher offspring BMI z-score trajectories during distinct growth periods from birth through adolescence.[15] We also found that prenatal exposure to non-nutritive sweeteners was associated with higher BMI z-score and body fat longitudinally throughout childhood, from birth to 18 years, and that the effect became more pronounced with age.[16] We found evidence of programming of offspring systolic blood pressure trajectories by gestational diabetes, hypertensive disorders of pregnancy and formula intake.[17] We identified key characteristics of individual BMI trajectories, including ages and magnitudes of BMI at peak (in infancy) and rebound (in early childhood), and identified multiple perinatal predictors as well as cardiometabolic sequelae associated with these milestones.[18] We explored patterns of change in metabolic biomarker trajectories from childhood through adolescence and identified differences with respect to sex, baseline weight status, pubertal status and race and ethnicity.[19]

Metabolomics

We carried out untargeted metabolomics profiling in fasting plasma collected at the Early Teen and Mid-Teen visits. In one analysis, we found that long-chain fatty acids, branched-chain amino acids (BCAA), acylcarnitines, diacylglycerols and steroid hormones differed by weight status and metabolic phenotype.[20] We also identified sex-specific metabolite profiles that mark the relationship between age and magnitude of the infancy BMI peak, and the childhood BMI rebound with metabolic syndrome score during early adolescence and found evidence that alterations in sex steroid hormone and lipid metabolism were involved in the relationship of early growth with subsequent metabolic risk in males.[3] In another study, we found that the BCAA and androgen hormone metabolite patterns at ages 6–10 years were related to changes in metabolic parameters, including precursors and risk factors of type 2 diabetes, in a sex-specific manner during adolescence.[21]

Place-based measures

We found that more favourable neighbourhood opportunities in mid-childhood, measured using the Child Opportunity Index, a publicly available surveillance tool, predicted better cardiometabolic health from mid-childhood to early adolescence.[5] We did not observe evidence of associations between residential green space from infancy to early adolescence and measures of insulin resistance in early adolescence.[11]

Respiratory and airways health

We identified four longitudinal wheeze phenotypes from infancy to adolescence (never or infrequent wheeze, mid-childhood onset wheeze, early transient wheeze and persistent wheeze).[22] We then determined that proinflammatory diet during pregnancy was associated with wheeze trajectory during early childhood and decrements in small airways calibre in mid-childhood,[23] and characterized a bidirectional relationship between overweight and wheeze trajectories.[24] Using data we collected on epigenomic markers from nasal cells collected at the Early-Teen Visit, we found that the nasal epigenome is a sensitive biomarker of asthma, allergy and airway inflammation.[25]

Other predictors of cardiometabolic health

We also examined associations of adolescent overeating and binge eating behaviour with subsequent cardiometabolic health outcomes. We found that adolescents reporting overeating behaviour had higher later body fat and poorer inflammatory and adipokine profiles than those who did not report overeating, and these associations were only partially explained by higher baseline BMI.[26]

We examined associations of cardiometabolic biomarkers and adiposity in mid-childhood, early adolescence and late adolescence with polycystic ovary syndrome (PCOS) among females in late adolescence. PCOS prevalence was 13%, and

we found differences in adiposity and adipocyte dysfunction among PCOS cases vs non-cases, suggesting a potential contribution of childhood adiposity.[27] In another study, we found that urinary concentrations of select phthalate/replacement metabolites in mid-childhood were associated with changes in body composition, including DXA bone mineral density, through early adolescence.[8]

What are the main strengths and weaknesses?

As previously outlined,[1] Project Viva's primary strength lies in its use of standardized procedures for in-person collection of exposure and outcome data by highly trained staff, which helps minimize measurement bias. This includes anthropometric measurements that have been validated against gold-standard measures like DXA. Another key advantage is the extensive breadth of data we have gathered, which allows for the use of analytical models to control for both baseline and time-varying confounders.[28] The study's over two decades of continual follow-up provide valuable insights into phenotype trajectories from birth through adolescence, revealing the progression of health and disease during this period.

However, there are some limitations. Loss to follow-up can lead to a smaller sample size and reduced statistical power for analysing rare exposures or outcomes, and may introduce selection bias. We have employed advanced modern causal inference methods and analytical techniques to address these biases in several analyses.[24,29] Additionally, the generalizability of our findings may be limited since all Project Viva mothers lived in Eastern Massachusetts, had health insurance and health care at enrolment and many were college-educated. Most participants identified as non-Hispanic White (Table 1), although the proportions of racial and ethnic minorities initially enrolled were higher compared with the overall population of Massachusetts as reported in the 2000 US census.[30]

Challenges of long-term follow-up

Early in the cohort study, we followed up 'linked' mother-child pairs together. In-person and questionnaire-only visits now focus on offspring as separate study participants. Participants at these ages are more independent than younger children and decide for themselves whether and to what extent to continue their participation, particularly after they turn 18 years and are solely responsible for providing consent. To motivate ongoing follow-up, we have applied multiple strategies for tracking and staying in contact with our participants and use age-appropriate incentives for participation. As older adolescents and young adults are busy, we have also tried to offer maximum flexibility in visit timing, length, location, frequency and type.

Can I get hold of the data? Where can I find out more?

We recognize that Project Viva provides a unique data resource, and we have a long track record of sharing data with investigators throughout the world. Please see [https://www.projectviva.org] and [https://vivaroadmap.net] for information and resources related to data collection.

We have a formal protocol that details procedures for individual investigators seeking to use Project Viva data [https://www.projectviva.org]. For more information, investigators can also contact Project Viva Principal Investigators (Drs Oken or Hivert) at [project_viva@hphci.harvard.edu]. We recently launched a new web-based research portal to support data sharing, the Research Operations and Data Management Platform or Viva ROADMaP [vivaroadmap.net]. Through this portal, investigators can access information and documentation related to the data, propose analytical plans, schedule presentations, submit dataset requests, update the status of their ongoing and completed projects and record and submit work products including meeting abstracts and published papers.

Ethics approval

At each visit, we obtained written informed consent from the mothers, and beginning in mid-childhood, verbal assent from the child through age 18 years, after which we obtain written informed consent from offspring themselves. The Harvard Pilgrim Health Care Institutional Review Board approved all study protocols in line with ethical standards established by the Declaration of Helsinki.

Data availability

See 'Can I get hold of the data?' above.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

S.R.S. wrote the article. E.O. and M.F.H. are the principal investigators of Project Viva and designed the study. E.O. drafted sections of the text. I.A., K.S., J.Y., A.F., W.P., J.C., A.C., D.G., M.Z., P.J., R.W. and K.K. are co-investigators of Project Viva and have led grants and conducted research related to Project Viva adolescents. All authors have contributed to and reviewed the article for submission. S.R.S. and M.F.H. had primary responsibility for final content.

Use of artificial intelligence (AI) tools

We did not use AI in collecting and/or analysing data, in producing images or graphical elements, or in the writing of the paper.

Funding

Project Viva and its team of co-investigators have been funded by grants from the National Institutes of Health (grant numbers R01 HD034568, UH3 OD023286, R01 ES031065, R24 ES030894, 3R01HD096032-04S1, R01 ES024765, R01ES031259, P42ES004705, K23DK13132).

Acknowledgements

We appreciate the Project Viva mothers, children and families for their ongoing participation and are grateful to the dozens of Project Viva staff, past and present, who collected such high-quality data. We are indebted to the vision of Matthew W Gillman, the founding PI of Project Viva.

Conflict of interest

None declared.

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