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FULL RESEARCH PAPER

Takeaway food, sugar-sweetened beverages and preclinical cardiometabolic phenotypes in children and adults

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Aims To investigate relationships between takeaway food and sugar-sweetened beverage (SSB) consumption with cardiometabolic phenotypes during childhood and mid-adulthood.

Method *Design:* Cross-sectional Child Health CheckPoint within the national population-representative Longitudinal Study of Australian Children. *Participants:* 1838 children (mean age 11.5 years; 49.1% female) and 1846 adults (mean age 43.7 years; 87.6% female). *Exposures:* Self-reported takeaway food and SSB consumption ('frequent': ≥ weekly). *Outcomes:* Functional (pulse wave velocity (PWV), blood pressure (BP)) and structural (carotid intima-media thickness, retinal microvascular calibre) preclinical cardiovascular phenotypes; lipids (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides). *Analysis:* Linear regression (exposure: takeaway or SSB consumption, individually or together) adjusted for age, sex and socio-economic position; and mediation analysis for body mass index (BMI).

Results Associations were small among children (standardized mean difference (SMD) ≤0.15). In adults, associations were stronger with functional, but not structural, cardiovascular phenotypes and lipids, particularly for frequent takeaway food consumption (e.g. PWV (0.20 m/s; 95% confidence interval (CI) 0.03 to 0.37); systolic (3.3 mmHg; 95% CI 1.3 to 5.3) and diastolic BP (1.4 mmHg; 95% CI 0.2 to 2.6); LDL (0.10 mmol/L; 95% CI 0.02 to 0.18); HDL (-0.14 mmol/L; 95% CI -0.19 to -0.10) and triglycerides (0.30 mmol/L; 95% CI 0.12 to 0.48)]. BMI mediated associations between takeaway food consumption and PWV, BP, HDL and TG (proportion of mediation 34% to 75%), while mediation effects were smaller for SSB consumption.

Conclusions Frequent takeaway food consumption in adults was associated with adverse blood lipids and vascular function (mainly via BMI). Lack of strong associations in children highlights opportunities for prevention.

Keywords Takeaway foods • Sugar-sweetened beverages • Cardiometabolic phenotypes • Cardiovascular • Plasma lipids • Blood pressure • Arterial stiffness • Arterial structure • Children • Adults

Introduction

Suboptimal diet is a modifiable proximal determinant for cardiovascular disease, which globally is the leading cause of mortality and loss of disability-adjusted life years.[1] Atherosclerotic changes to arteries begin in childhood and track into adulthood, when cardiovascular disease occurs.[2] The importance of primordial and primary prevention

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in early life to reduce later cardiovascular disease risk is increasingly recognised.[2,3]

Diet is a major intervention target, particularly energy-dense takeaway foods and sugar-sweetened beverages (SSB).[4,5] Takeaway food consumption is linked with traditional cardiovascular risk factors in children and adults; particularly with obesity - the outcome used in many studies[6,7]- and also with elevated blood pressure and adverse lipid profiles.[6,7]SSB consumption is also associated with adiposity and elevated blood pressure in children and adults,[8–11] but associations with lipid profiles in children are inconsistent.[8,12]

Few studies of takeaway foods and SSB have investigated non-invasive preclinical cardiovascular phenotypes, such as pulse wave velocity, carotid intima-media thickness (cIMT) and retinal microvascular calibre. A recent study among children (mean age 8.6 years, $n = 309$) reported faster pulse wave velocity (0.34 m/s; 95% confidence interval (CI) 0.14 to 0.53) with frequent takeaway food consumption.[13] One study of SSB consumption in children (mean age 12 years, $n = 2353$) reported associations between soft drink (-1.9 µm, p = 0.03) and cordial consumption (-1.8 µm, p = 0.002) and narrower retinal arterioles.[14] Among adults, one study ($n = 1054$) has demonstrated an association between soft drink consumption and 3.5% increased carotid intima-media thickness (95% CI 1.1 to 5.8).[15] However, this study did not include all beverages (e.g. fruit juices), which are usually classified as SSB.[16] Furthermore, several studies of SSB used convenience samples, thus limiting generalisability.[13,14]

Importantly, no studies have analysed both takeaway foods and SSB, which are often consumed together, and none have employed a comprehensive range of cardiometabolic measures within a population-based cohort. Such data could inform cardiovascular disease prevention and public health policy. Therefore, we investigated this in a population-derived cohort of 11–12-year-old children and mid-life adults. We examined whether at least weekly (herein referred to as 'frequent') consumption of takeaway food and SSB, individually or together, was associated with adverse preclinical cardiometabolic phenotypes (i.e. pulse wave velocity, blood pressure, carotid intima-media thickness, retinal microvascular calibre, blood lipids). In addition, we examined the extent to which body mass index (BMI) mediated these associations. We hypothesised that frequent consumption of takeaway foods or SSB is associated with adverse cardiometabolic phenotypes, particularly if consumed together.

Methods

Study design and participants

We used data from the Child Health CheckPoint,[17] a cross-sectional study nested within the B-cohort of the Longitudinal Study of Australian Children (LSAC).[18] In 2004, LSAC participants were sampled from Australia's Medicare healthcare database using postcode-based, two-stage clustered random sampling to achieve a broadly population-representative B-cohort sample aged 0–1 years at baseline ($n = 5107$).[18] By wave 6 (2014), 74% of the original sample had been retained ($n = 3764$). CheckPoint was conducted from February 2015 to March 2016, between LSAC waves 6 and 7.[17] Of the 3513 families invited to participate, 1874 attended a CheckPoint assessment (*Figure 1*). Data were collected from children aged 11–12 years and one parent.[17] The attending parent provided informed consent for their own and their child's participation. Ethics approval was granted by the Royal Children's Hospital Human Research Ethics Committee (HREC33225) and the Australian Institute of Family Studies Ethics Committee (14–26). We included participants if they had provided data on takeaway food or SSB consumption, and at least one outcome measurement.

Procedures

We invited participants to a Main Assessment Centre in major Australian cities for a comprehensive 3.5-hour physical health assessment. This involved children and one parent rotating separately through 17 physical assessment and bio-specimen collection stations.[17] Thus, each parent–child pair underwent the same assessments using the same protocols, staff and equipment on the same day. In regional areas, we invited participants to a Mini Assessment Centre for a 2.5-hour assessment consisting of 15 stations, which excluded retinal photography. Alternatively, a shorter 1.5-hour Home Visit consisted of 9 stations, which excluded carotid intima-media thickness, retinal photography and venepuncture.

Measures

Dietary assessment

We asked child and adult participants to self-report dietary intake via a modified version of the National Secondary Students' Diet and Activity food frequency questionnaire.[19] This food frequency questionnaire was designed to monitor Australian secondary students' diet (questions included in CheckPoint), but also physical activity and food marketing exposure (questions not included in CheckPoint). The validity of these short dietary questions compared with 24-hour recall has been previously shown to be reasonable in the 1995 National Nutrition Survey.[19] We assessed takeaway food consumption by asking participants 'How often do you have meals or snacks such as burgers, pizza, chicken or chips from places like McDonalds, Hungry Jacks/Burger King, Pizza Hut, KFC, Red Rooster or local takeaway food places?'. We assessed SSB consumption via three questions encompassing soft drink, cordial or sports drink, fruit juice and energy drink consumption, and included references for portion sizes. SSB were selected in accordance with typical definitions of SSB which include non-diet soft drinks, cordials, fruit juices and energy drinks.[16] For statistical analysis, based on the distribution of the responses (and similar to previous research[6,7]) takeaway food and SSB consumption responses were transformed into binary variables: consumption either less than once per week or at least once per week.

Cardiometabolic phenotypes

Cardiometabolic phenotypes include both functional and structural cardiovascular phenotypes as well as blood lipid profiles.

We assessed vascular function by measuring systolic and diastolic blood pressure and PWV using the SphygmoCor XCEL.[20] With participants resting supine for several minutes, we measured blood pressure (mmHg) at the brachial artery 2–3 times and used the mean values of at least two valid measurements in our analyses. We also used tonometry to measure right carotid-femoral pulse wave velocity (m/s) 2–3 times. Faster pulse wave velocity reflects increased vascular stiffness.

We assessed macrovascular structure by measuring right-sided carotid intima-media thickness with standardised vascular ultrasound.[21] With participants lying supine, we used B-mode ultrasound to capture images of the right common carotid artery wall, and also used a modified 3-lead ECG concurrently to detect cardiac rhythm. We calculated maximum values with semi-automatic edge-detection software (Carotid Analyzer™, Medical Imaging Applications, Coralville, IA, USA). We assessed microvascular structure by measuring central retinal arteriolar and venular equivalents from retinal photography using the Integrative Vessel Analysis (IVAN, University of Wisconsin, Wisconsin, USA) software.[22] We selected right eye images preferentially,

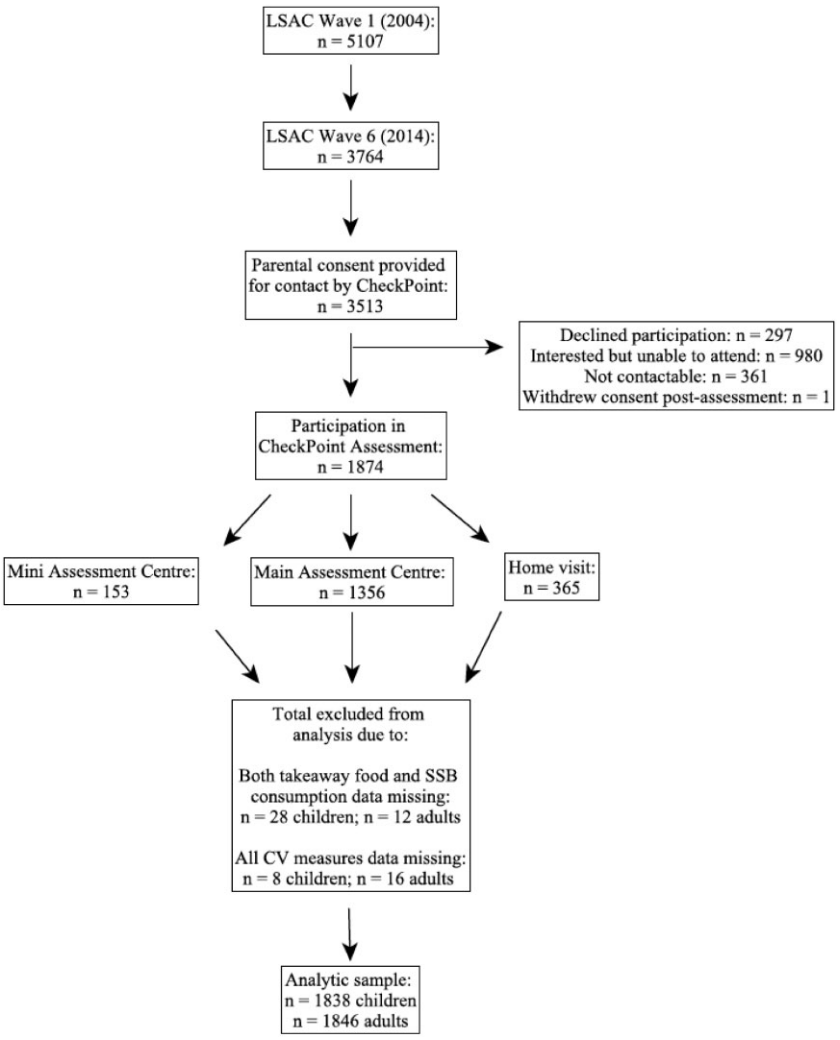

Figure 1 Participant flow from LSAC B-cohort through to CheckPoint. CV, cardiovascular; LSAC, Longitudinal Study of Australian Children; SSB, sugar-sweetened beverage.

and experienced graders then graded the images and calculated average retinal vessel calibre using the Big-Six (revised Knudston–Parr) formula, which combines measurements of the six largest arterioles or venules. Wider central retinal venular equivalent and narrower central retinal arteriolar equivalent represent worse phenotypes and are associated with cardiovascular disease risk in adults.[23]

We obtained peripheral venous blood from semi-fasted (mean fast time: 4.2 hours for children, 3.3 hours for adults) participants using a single venepuncture.[24] We used the 2017-version algorithm of the Nightingale NMR metabolomics platform (Helsinki, Finland) to quantify routine lipids and lipoproteins; total cholesterol, low-density lipoproteins, high-density lipoproteins and triglycerides.

Reproducibility data for cardiometabolic phenotypic measures have been detailed elsewhere.[17,20–22,24]

Confounders and other variables

We identified *a priori* confounders (*Table 1*) on the basis of reported associations with both the exposure and outcome variables.[28–30] They included age, sex, socio-economic position (SEP), energy expenditure and pubertal status. SEP is a composite of three parameters from LSAC Wave 6 data: household income, parents' highest level of education attainment and parents' occupational status. In a single-parent household, an unweighted average of three values was used, and in dual-parent households an average of five values.[25] An SEP value of greater than 0 indicates socio-economic advantage. We calculated children's pubertal status based on a self-reported 5-item sex-specific questionnaire, assessing sexual characteristics.[26] Among children, we also determined their total daily energy expenditure as a product of their physical activity level and their basal metabolic rate[31] and further calculated their BMI z-score based on US Centers for Disease Control and Prevention reference data.[17] We categorised BMI into underweight, normal weight, overweight, or obese using reference cut-points for children and adults.[17]

Table 1 provides additional details on all exposure and outcome measures and describes these other variables of interest in greater detail.

Statistical analysis

Regression models were analysed using Stata/IC version 15.1, using survey weights (described elsewhere[17]) and survey statistical methods to

Table 1 Exposure and outcome measures, confounders and other variables

Measure	Materials	Additional information
Exposures		
Takeaway food and sugar-sweetened beverage (SSB) consumption	National Secondary Students' Diet and Activity survey (NaSSDA): self-reported questionnaire administered via iPad.	Both children and parents completed an identical 26-item food frequency questionnaire (FFQ) to capture diet quality. The FFQ was a modified version of NaSSDA[19] (originally developed by the Australian Cancer Council and Heart Foundation), with three additional questions adapted from the International Study of Childhood Obesity. We assessed takeaway food consumption with one question: 'How often do you have meals or snacks such as burgers, pizza, chicken or chips from places like McDonalds, Hungry Jacks/Burger King, Pizza Hut, KFC, Red Rooster or local takeaway food places?'. Response options included *never, less than once a week, about 1–2 times a week, about 3–4 times a week, about 5–6 times a week, about once a day, or 2 or more times a day*. We assessed SSB consumption via three questions addressing weekly consumption of fruit juices; soft drinks (like Coke, lemonade), cordials or sports drinks (like Gatorade); and energy drinks (like Redbull, V) respectively. Response options ranged from *don't drink*, up to *5 or more cups a day*. We also provided portion sizes for the SSB questions. For statistical analysis, takeaway food and SSB consumption responses were transformed into binary exposure variables: consumption either *less than once per week* or *at least once per week*.
Outcomes (direction to further details are available in previous publications[17])		
Systolic/diastolic blood pressure (SBP/DBP)	SphygmoCor XCEL (AtCor Medical, West Ryde, AUS).	A measure of *vascular function*. SBP and DBP (mmHg) were measured at the brachial artery using an appropriate sized cuff on the arm and with the participant in supine position. This was done 2–3 times after laying supine for 7 min. Measurements were performed using the SphygmoCor system and readings were averaged to derive a mean value.[20] Higher values indicate worse blood pressure.
Pulse wave velocity (PWV)	SphygmoCor XCEL (AtCor Medical, West Ryde, AUS).	A measure of arterial stiffness and *vascular function*. With participants resting in supine position, PWV was measured by detecting the time taken for an arterial waveform to propagate from the carotid artery (detected via a hand-held tonometer) to the femoral artery (detected simultaneously via a thigh cuff). Distance travelled by the waveform was measured with a tape from the right carotid pulse to the suprasternal notch and then to the right femoral pulse. PWV was then calculated in metres/second (m/s). Waveforms were captured over 10 s, 2–3 times.[20] Higher values indicate quicker PWV and therefore greater arterial stiffness.
Carotid intima-media thickness (Carotid IMT)	Portable ultrasound (GE Health Vivid *i* BT06 with 10 MHz linear array probe, Little Chalfont, UK) with ECG and Carotid Analyzer (Medical Imaging Applications, Coralville, IA, USA).	A measure of *macrovascular* structure. With participants resting supine and head turned 45° to the left, trained technicians used ultrasound to capture images of the carotid artery wall. Once vessel near and far walls were clearly visualised, a minimum of three longitudinal loops of 5-10 cardiac cycles were taken. Modified 3-lead ECG was also used to concurrently detect cardiac rhythm. cIMT was measured using the Carotid Analyzer, approximately 10 mm from the carotid bulb, and maximum values were calculated.[21] Higher values indicate greater large vessel thickness.

Continued

Table I Continued

Measure	Materials	Additional information
Central retinal arteriolar and venular equivalent (CRAE/CRVE)	Retinal camera (Canon CR-DGi, Tokyo, Japan), fitted with a digital SLR camera (Canon EOS 60D, Tokyo, Japan).	A measure of *microvascular* structure. In a darkened room, without mydriasis, two digital photographs were taken of each eye (one focusing on the disc, one focusing on the macula). Right eye images were preferentially selected for scoring, and images were graded by experienced graders. CRAE and CRVE were calculated using the Big-Six (revised Knudston-Parr) formula, which combines measurements of the six largest arterioles or venules.[22] Lower CRAE (narrowed arterioles) and higher CRVE (widened venules) values both reflect poorer retinal calibre.
Blood lipids (TC, LDL, HDL, TG)	S-Monovette vacutainers: 2.7 mL K3 EDTA, 9 mL K3 EDTA, 7.5 mL Lithium Heparin liquid, 9 mL serum gel with clotting activator, Sarstedt, Australia.	Approximately 28 mL of blood was collected from semi-fasted participants by a phlebotomist, using a single venepuncture. Tubes were collected, transported and stored appropriately. Nightingale NMR metabolomics platform (Helsinki, Finland) was used for quantification of routine lipids and lipoproteins.[24] Higher TC, LDL and TG and lower HDL indicate adverse lipid levels, which could increase risk of atherosclerosis.
Confounders and other variables		
Socioeconomic position (SEP)	Parent-reported questionnaire.	SEP was calculated using three parameters from LSAC wave 6 data: combined household income, parents' highest level of education and parents' occupational status.[25] In a single-parent household an unweighted average was calculated over the 3 values, and in a dual-parent household was calculated over 5 values. Values were standardised to mean = 0 and SD = 1, with values greater than 0 indicating better socio-economic positioning.
Pubertal status (children only)	Pubertal development scale.	A 5-item, self-reported sex-specific questionnaire comprising of questions about growth spurts, body hair growth and skin changes; breast development and age of onset of menarche (females); facial hair growth and voice changes (males).[26] Higher scores reflect a later pubertal stage.
Daily energy expenditure (children only)	Total daily energy expenditure.	Total daily energy expenditure was calculated by multiplying children's physical activity level by their basal metabolic rate (kJ/d). Physical activity level was the average daily rate of energy expenditure (MET.min/d) derived from a validated time-use diary[30] using the Ridley compendium.[27] Basal metabolic rate was calculated with Mifflin-St Jeor equations: male = (10*weight) + (6.25*height) - (5*age) + 5; female = (10*weight) + (6.25*height) - (5*age) - 161.
Body mass index (BMI)	Height: Portable rigid stadiometer (Invicta IP0955, Leicester, UK). Weight: 4-limb segmental (InBody230, Biospace, Seoul, Korea) or 2-limb (Tanita BC-351, Kewdale, Australia) body composition scales.	BMI was calculated by combining height and weight. Standing height was measured 2–3 times without shoes or socks, and an average value was calculated. Weight was measured once wearing light clothing, without shoes or socks, using bioelectrical impedance scales. BMI was calculated from measured height and weight values where BMI equals weight (kg)/height $(m)^2$. A BMI z-score for children was calculated according to the US Centers for Disease Control and Prevention reference values using the Stata 'zanthro' function. BMI status was calculated according to International Obesity Task Force 6-level cut-offs for children and World Health Organisation cut-offs for adults.

BMI, body mass index; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; DBP, diastolic blood pressure; FFQ, Food Frequency Questionnaire; HDL, high-density lipoprotein; IMT, intima-media thickness; LDL, low-density lipoprotein; LSAC, Longitudinal Study of Australian Children; NaSSDA, National Secondary Students' Diet and Activity survey; PWV, pulse wave velocity; SBP, systolic blood pressure; SEP, socio-economic position; SSB, sugar-sweetened beverage; TC, total cholesterol; TG, triglycerides.

account for multi-level sampling and to adjust for non-response and loss to follow-up over LSAC waves 1–6.[17] All models were adjusted for the potential confounders age, sex, and SEP;[28–30] with further adjustment for children's pubertal status or daily energy expenditure in sensitivity analyses. For main analysis, we performed two separate sets of linear regression analyses to estimate associations of takeaway food or SSB consumption individually with cardiometabolic phenotypes. We calculated adjusted marginal means for outcomes and present regression coefficients, as well as standardised mean differences (SMD). As SMD are calculated by standardising the outcome variable prior to the regression and can be interpreted as a standardised beta, they indicate the change per standard deviation unit and allow comparison of effects across outcomes measured on various scales. We also fitted a third model including an interaction effect between takeaway foods and SSB with cardiometabolic phenotypes. Where there was evidence of association, we ran mediation analysis to estimate the total causal effect of takeaway food and SSB consumption (exposures) on cardiometabolic phenotypes (outcomes) occurring via an intermediate variable ('mediator'; BMI in this case) using the 'mediation' R package (version 3.6.2).[32] This utilises a g-computation approach with linear regression for the outcome and mediator given their antecedent variables as building blocks.

Results

Sample characteristics

In total, 1874 parent–child dyads participated in CheckPoint, of whom 1838 children (mean age 11.5 years) and 1846 adults (mean age 43.7 years) were included in our analytic sample (*Table 2*). There were similar proportions of male and female children, but the majority of adults were female (87.6%). In keeping with Australian national data,[33] 23.0% of children and 61.6% of adults were overweight or obese. Takeaway food consumption was reported at least weekly for 31.7% and 18.0% of children and adults respectively, and SSB consumption at least weekly for 59.6% of children and 34.2% of adults. Although this takeaway consumption frequency is comparable to other national data, rates of SSB consumption are higher than previous nationally representative data that exclude fruit juice.[4,5] Supplementary analysis also shows that those consuming takeaway foods or SSB at least weekly were more likely to be overweight or obese and of lower SEP (Supplementary material online, *Table S1*).

Associations of takeaway food and/or sugar-sweetened beverage consumption with cardiometabolic phenotypes

Children

There was little evidence of associations between frequent takeaway food or SSB consumption and cardiometabolic phenotypes (*Table 3*, *Figure 2*). The largest effects included higher triglyceride levels with frequent consumption of takeaway food (0.06 mmol/L; 95% CI -0.03 to 0.15; SMD 0.11) or with SSB (0.08 mmol/L; 95% CI 0.01 to 0.15; SMD 0.15) and 0.6 mmHg higher diastolic blood pressure (95% CI -0.1 to 1.3; SMD 0.11) associated with frequent SSB consumption. A similar effect size (SMD) was obtained for the association between takeaway food consumption and central retinal arteriolar equivalent, but this effect was in the opposite direction to that hypothesised. All patterns remained similar on adjustment for daily energy expenditure and puberty (Supplementary material online, Tables S2 and S3).

Adults

Frequent takeaway food consumption was associated with worse vascular function and blood lipid levels. SMD for frequent SSB consumption with functional phenotypes and lipids were similar, although smaller in magnitude. For example, with frequent consumption of takeaway foods and SSB, respectively, pulse wave velocity was greater by 0.20 m/s (95% CI 0.03 to 0.37; SMD 0.18) and 0.10 m/s (95% CI: -0.05 to 0.24; SMD 0.09), systolic blood pressure by 3.3 mmHg (95% CI 1.3 to 5.3; SMD 0.26) and 1.5 mmHg (95% CI 0.0 to 2.9; SMD 0.12), and high-density lipoprotein was lower by 0.14 mmol/L (95% CI: -0.19 to -0.10; SMD -0.40) and 0.09 mmol/L (95% CI -0.14 to -0.05; SMD -0.26). Relationships for structural macro- and micro-vascular phenotypes (i.e. carotid intima-media thickness, central retinal arteriolar and venular equivalents) were close to 0 and uncertain, albeit in the hypothesised direction. Nonetheless they too were stronger for frequent consumption of takeaway foods (SMDs 0.08 to 0.12) compared to SSB (SMDs 0.01 to 0.04).

Mediation via body mass index

Among adults, the proportion of associations between takeaway food consumption and cardiometabolic functional phenotypes mediated by BMI ranged from 62% (95% CI: 0.40 to 1.16) to 75% (95% CI: 0.53 to 1.18) (Supplementary material online, *Table S4*). In contrast, although BMI did not mediate associations between SSB consumption and systolic or diastolic blood pressure, it mediated a small proportion of the association with pulse wave velocity (indirect effect via BMI 0.06, 95% CI 0.01 to 0.10; proportion of mediation 36%, 95% CI 0.10 to 1.01). For lipids, only the associations between adults' takeaway food consumption and high-density lipoprotein and triglyceride, but not total cholesterol or low-density lipoprotein, were mediated by BMI (proportion of mediation ranging from 34% (95% CI 0.24 to 0.51) to 48% (95% CI 0.33 to 0.70)). Although the total effects of adult's SSB consumption and high-density lipoprotein and triglyceride were similar to takeaway food consumption, less effect was mediated by BMI (proportion of mediation 17%; 95% CI 0.03 to 0.33).

Interaction effects between consumption of both takeaway foods and sugar-sweetened beverage and cardiometabolic phenotypes

There was no evidence that frequent consumption of both takeaway foods and SSB interacted to differentially affect cardiometabolic phenotypes among children or adults.

Discussion

Principal findings

Among children, there was little evidence of associations between takeaway food or SSB consumption and cardiometabolic phenotypes. Evidence of association, by contrast, were more apparent in adults. In particular, compared to SSB consumption, frequent (at least weekly) takeaway food consumption was more strongly associated with adult functional vascular phenotypes and blood lipid profiles. This pattern (larger effects for takeaway foods compared to SSB) was also evident for structural vascular phenotypes, but magnitude of effects were

Table 2 Characteristics of children and adults in analytic sample

	Characteristics	Child (overall *n* = 1838)		Adult (overall *n* = 1846)	
		n	Mean (SD) or %	*n*	Mean (SD) or %
Demographics	Age (years)	1838	11.5 (0.5)	1846	43.7 (5.2)
	Male	1838	50.9	1846	12.4
	SEP z-score	1832	0.2 (1.0)	1839	0.2 (1.0)
Body composition	**BMI**[a]	1836	0.3 (1.0)	1838	27.8 (6.1)
	BMI status	1836	–	1838	–
	% Underweight	113	6.2	10	0.5
	% Normal weight	1301	70.9	695	37.8
	% Overweight	334	18.2	596	32.4
	% Obese	88	4.8	537	29.2
Pubertal status	% **Pre-pubertal**	163	9.5	–	–
	% **Early/mid-pubertal**	1324	76.8	–	–
	% **Late/post-pubertal**	237	13.8	–	–
Energy expenditure	**Total daily energy expenditure (kJ/d)**	1828	2086.4 (437.3)	–	–
Takeaway food consumption	Never	189	10.3	293	15.9
	Less than weekly	1059	58.0	1218	66.1
	1–2 times per week	499	27.3	308	16.7
	3–4 times per week	72	3.9	22	1.2
	5–6 times per week	5	0.3	1	0.1
	Every day	3	0.2	0	0
	≥1/week ('frequent')	579	31.7	331	18.0
SSB consumption	Never	170	9.3	611	33.1
	Less than weekly	573	31.2	603	32.7
	1–3 cups per week	688	37.4	396	21.5
	4–6 cups per week	221	12.0	122	6.6
	1–2 cups per day	128	7.0	84	4.6
	3–4 cups per day	38	2.1	19	1.0
	5+ cups per day	20	1.1	10	0.5
	≥1/week ('frequent')	1095	59.6	631	34.2
Cardiometabolic phenotypes	**Pulse wave velocity (m/s)**	1780	4.46 (0.57)	1664	6.86 (1.13)
	Systolic blood pressure (mmHg)	1755	108.1 (8.0)	1737	119.4 (12.6)
	Diastolic blood pressure (mmHg)	1755	62.4 (5.7)	1737	73.0 (8.6)
	Carotid intima-media thickness (μm)	1463	581.1 (46.7)	1465	663.0 (96.8)
	Central retinal arteriolar equivalent (μm)	1271	159.1 (11.9)	1262	151.0 (14.0)
	Central retinal venular equivalent (μm)	1271	230.7 (16.5)	1262	218.9 (18.5)
	Total cholesterol (mmol/L)	1161	4.07 (0.65)	1321	4.77 (0.87)
	LDL cholesterol (mmol/L)	1161	1.36 (0.31)	1321	1.66 (0.43)
	HDL cholesterol (mmol/L)	1161	1.41 (0.27)	1321	1.46 (0.36)
	Triglycerides (mmol/L)	1161	1.19 (0.55)	1321	1.49 (0.84)

BMI, body mass index; d, day; HDL, high-density lipoprotein; kj, kilojoules; LDL, low-density lipoprotein; SD, standard deviation; SEP, socio-economic position; SSB, sugar-sweetened beverages.
[a]BMI z-score for children, BMI (kg/m^2) for adults.

Table 3 Adjusted linear regression models examining associations between takeaway food and SSB consumption separately and cardiometabolic phenotypes in children and adults

	Takeaway food ≥ once per week				SSB ≥ once per week			
	Reference[a] Marginal mean (SD)	Regression co-efficient (95% CI)	SMD	*p*-value	Reference[a] Marginal mean (SD)	Regression co-efficient (95% CI)	SMD	*p*-value
Children								
Vascular measures:								
PWV (m/s)	4.47 (0.72)	0.05 (-0.03 to 0.12)	0.08	0.21	4.47 (0.77)	0.02 (-0.05 to 0.09)	0.03	0.58
SBP (mmHg)	108.8 (11.7)	-0.5 (-1.5 to 0.6)	-0.06	0.37	108.2 (11.0)	0.6 (-0.4 to 1.6)	0.07	0.26
DBP (mmHg)	62.7 (8.6)	-0.4 (-1.1 to 0.3)	-0.07	0.29	62.2 (6.2)	0.6 (-0.1 to 1.3)	0.11	0.08
cIMT (μm)	584.1 (65.2)	-2.9 (-10.0 to 4.3)	-0.06	0.43	584.9 (64.5)	-3.0 (-9.36 to 3.41)	-0.06	0.36
CRAE (μm)	158.7 (17.3)	1.6 (-0.0 to 3.2)	0.13	0.05	158.6 (17.8)	1.1 (-0.5 to 2.6)	0.09	0.19
CRVE (μm)	230.7 (23.6)	0.5 (-1.6 to 2.6)	0.03	0.65	230.4 (25.3)	0.7 (-1.5 to 3.0)	0.04	0.51
Blood lipids (mmol/L):								
TC	4.07 (0.98)	-0.02 (-0.11 to 0.08)	-0.02	0.75	4.08 (0.91)	-0.01 (-0.10 to 0.07)	-0.02	0.79
LDL	1.36 (0.50)	-0.02 (-0.06 to 0.03)	-0.06	0.47	1.36 (0.49)	-0.01 (-0.05 to 0.03)	-0.04	0.59
HDL	1.40 (0.37)	0.01 (-0.03 to 0.05)	0.04	0.64	1.41 (0.42)	0.00 (-0.04 to 0.04)	0.00	0.98
TG	1.19 (0.78)	0.06 (-0.03 to 0.15)	0.11	0.22	1.16 (0.68)	0.08 (0.01 to 0.15)	0.15	0.02
ADULTS								
Vascular measures:								
PWV (m/s)	6.81 (1.36)	0.20 (0.03 to 0.37)	0.18	0.02	6.81 (1.39)	0.10 (-0.05 to 0.24)	0.09	0.19
SBP (mmHg)	119.1 (15.4)	3.3 (1.3 to 5.3)	0.26	0.001	119.3 (14.3)	1.5 (0.0 to 2.9)	0.12	0.05
DBP (mmHg)	72.9 (10.6)	1.4 (0.2 to 2.6)	0.16	0.03	72.8 (10.2)	1.0 (0.0 to 2.1)	0.12	0.05
cIMT (μm)	661.0 (117.1)	11.7 (-4.7 to 28.0)	0.12	0.16	663.1 (125.0)	0.9 (-11.5 to 13.2)	0.01	0.89
CRAE (μm)	151.6 (22.7)	-1.2 (-3.5 to 1.1)	-0.09	0.30	151.6 (21.5)	-0.4 (-2.4 to 1.6)	-0.03	0.69
CRVE (μm)	220.3 (31.0)	1.4 (-2.0 to 4.8)	0.08	0.42	220.4 (31.4)	0.7 (-2.1 to 3.4)	0.04	0.64
Blood lipids (mmol/L):								
TC	4.75 (1.37)	0.11 (-0.05 to 0.27)	0.13	0.17	4.73 (1.29)	0.14 (0.00 to 0.28)	0.16	0.05
LDL	1.65 (0.64)	0.10 (0.02 to 0.18)	0.24	0.01	1.63 (0.59)	0.11 (0.04 to 0.18)	0.25	0.002
HDL	1.46 (0.52)	-0.14 (-0.19 to -0.10)	-0.40	0.000	1.46 (0.52)	-0.09 (-0.14 to -0.05)	-0.26	0.000
TG	1.50 (1.37)	0.30 (0.12 to 0.48)	0.36	0.001	1.49 (1.49)	0.18 (0.03 to 0.34)	0.22	0.02

Models and marginal means adjusted for age, sex and socio-economic position.
CI, confidence interval; cIMT, carotid intima-media thickness; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PWV, pulse wave velocity; SBP, systolic blood pressure; SD, standard deviation; SMD, standardised mean difference (change per SD unit); SSB, sugar-sweetened beverage; TC, total cholesterol; TG, triglycerides.
[a]Reference group: participants consuming takeaway foods or SSB less than weekly.
Note: Less favourable cardiometabolic phenotype = Higher pulse wave velocity, blood pressure; Increased cIMT; Narrower retinal arteriolar vessel calibre; Wider retinal venular vessel calibre; Higher TC, LDL, TG; Lower HDL.

smaller. In adults, increased BMI largely, but not completely, mediates the adverse effects associated with takeaway food consumption, and to a lesser extent for SSB. There was little evidence to suggest that frequent consumption of both takeaway foods and SSB had additional effects on associations.

Strengths and limitations

The strengths of this study include the large, population-derived sample with cross-generational data using identical measures, allowing us to make inferences about cardiometabolic phenotypes at two points in the life course. Our study is the first to utilise a validated, reproducible and comprehensive suite of measures to assess preclinical cardiometabolic phenotypes in relation to takeaway food and SSB consumption. However, the CheckPoint cohort is not entirely representative of the Australian population or of LSAC itself. Nonetheless, we used survey weights to partly account for this. In addition, although food frequency questionnaires serve as reasonable measures in large-scale studies where objective dietary data are difficult to collect, this self-reported data may be inaccurate due to recall or social desirability bias. Furthermore, missing cardiometabolic data (vascular structure and blood lipids) from home visits, as well as the majority of adult participants being female, reduce the generalisability of our findings. Finally, while it is plausible that observed effects could be causal, confirmation would require consideration of additional potential confounders, longitudinal repeated measurement of both the exposures and

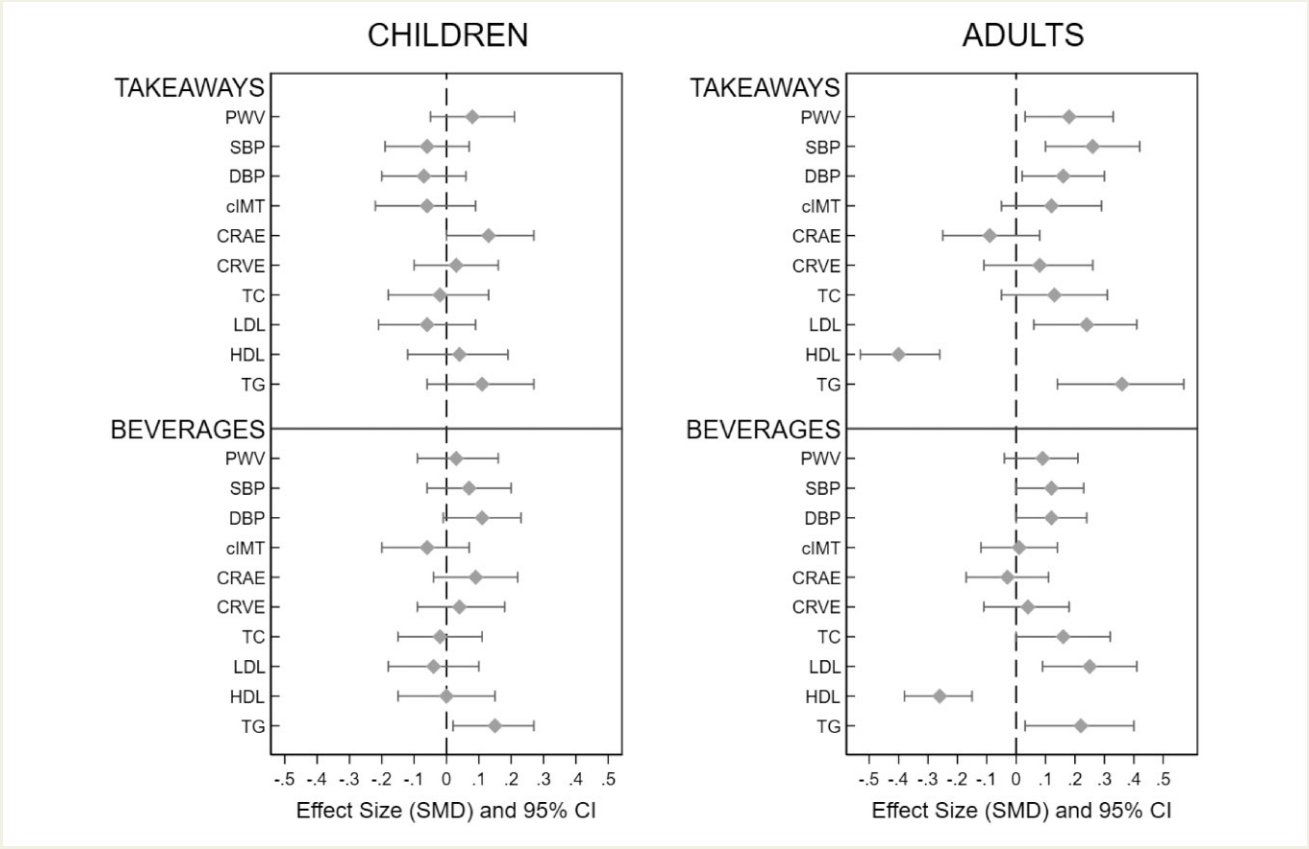

Figure 2 Standardised mean differences for associations between takeaway food and SSB consumption and cardiometabolic phenotypes in children and adults adjusted for age, sex and SEP. Beverages, sugar-sweetened beverages; CI, confidence interval; cIMT, carotid intima-media thickness; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PWV, pulse wave velocity; SBP, systolic blood pressure; SEP, socio-economic position; SMD, standardized mean difference (effect size); SMD, standardized mean difference; SSB, sugar-sweetened beverages; Takeaways, takeaway food; TC, total cholesterol; TG, triglycerides. Models adjusted for age, sex, and socio-economic position. SMD, standardized mean difference (change per SD unit). Note: Less favourable cardiometabolic phenotype = Higher pulse wave velocity, blood pressure; Increased cIMT; Narrower retinal arteriolar vessel calibre; Wider retinal venular vessel calibre; Higher TC, LDL, TG; Lower HDL.

the outcomes, replication in different populations and ideally intervention trials.

Interpretation in relation to previous research

Our findings in children differ from most previous studies reporting associations between takeaway foods or SSB and increased pulse wave velocity or blood pressure, narrower arterioles, or adverse blood lipid profiles.[6,8–10,12,13] Additional research is needed to understand if this may reflect the younger age of the children in our cohort,[8–10,14] inclusion of different covariates and confounders in our models[6,8,13,14] or differences in definitions and measurement of exposure variables (e.g. SSB definitions, food intake measurement tools).[8,9,12]

Our positive associations of takeaway food and SSB consumption with blood pressure and blood lipids in adults align with previous literature,[7,10] including a recent SSB review of 26 studies (median age 44 years).[34] In terms of novel outcome measures, only one previous study demonstrated an association between soft drink consumption and carotid intima-media thickness, however, drawing comparisons is difficult due to its narrower definition of SSB.[15] Finally, to the best of our knowledge, there are no previous studies exploring the mediation effect of BMI on the relationship between takeaway food or SSB consumption and adults' cardiometabolic phenotypes.

Clinical implications

The small or null associations in children, yet larger associations among adults, suggest that adverse cardiometabolic phenotypes manifest later in life with cumulative and prolonged risk factor exposure. Alternatively, other mitigating behaviours in children, such as higher physical activity levels and/or 'healthier' takeaway food or SSB consumption (e.g. fruit juice vs. soda), may also explain these stage-of-life effects.

Among adults, our findings for vascular function and blood lipids may influence both individual and public health. Previous literature suggests that 1 m/s faster pulse wave velocity in adults (mean age 50–87 years) is associated with 12% and 13% increased risk of cardiovascular events and mortality, respectively,[35] and that 5 mmHg lower

systolic blood pressure leads to a 17% risk reduction for major cardiovascular events.[36] Therefore, similar small increments to those observed in our study (e.g. 0.20 m/s faster pulse wave velocity and 3.3 mmHg higher systolic blood pressure with takeaway food consumption) may predispose adults to increased cardiovascular risk with ongoing frequent takeaway food and, to a lesser extent, SSB consumption. Furthermore, the observed 0.30 mmol/L increase in triglyceride levels associated with frequent takeaway food consumption in adults, when considered with an adjusted marginal mean of 1.50 mmol/L, is close to criteria for dyslipidaemia (triglycerides ≥2 mmol/L).[37] We are less confident in clinical inferences for the associations with vascular structure in adults due to small effects and wide confidence intervals. However, patterns in adults fit with the proposed evolution of preclinical cardiovascular phenotypes, where functional changes generally precede structural changes.[38]

In line with recent UK Biobank analysis ($n = 132\,479$) reporting stronger associations between BMI and energy consumption from fat (vs. sugar),[39] the magnitude of effects among adults (takeaway foods > SSB) in our sample suggests that sodium and fat may be stronger drivers of increased BMI and cardiometabolic risk than sugar intake. Further research is needed to address this specific question.

Finally, we highlight a greater proportion of associations between takeaway food consumption and cardiometabolic phenotypes mediated via BMI, than for SSB consumption. This suggests that takeaway foods drive adverse cardiometabolic phenotypes via changes in BMI. This is consistent with another study among adults ($n = 3294$) which showed that high salt consumption is associated with increased blood pressure in adults, but that this effect is largely driven by obesity.[40] On the other hand, SSB effects may operate via other mechanisms. For instance, high SSB consumption may increase cardiometabolic risk by increasing glycaemic load and contributing to inflammation and cellular dysfunction.[41]

The lack of an interaction effect in our study reflects that there is no magnified effect associated with consuming both takeaway food and SSB together; i.e. a greater effect when consumed together than the effect of each consumed alone, multiplied together. This suggests that the constituents of takeaway food and SSB might not interact to amplify inflammatory changes and contribute to cardiometabolic phenotypes.

Public health and policy implications

Further longitudinal research exploring these relationships at various ages will inform the causal nature of associations between takeaway food and SSB consumption and cardiometabolic phenotypes, the impact of elevated BMI, and critical time points for targeting intervention. Health initiatives should promote awareness around the poor nutritional content of takeaway foods and SSB from an early age to reduce cumulative risk factor exposure and modify nutritional behaviours.[3] Patterns in our data suggest that policies targeting takeaway food consumption, over SSB consumption, may be more effective and pragmatic.

Conclusion

In adults, largely mediated by increased BMI, frequent takeaway food consumption was associated with worse vascular function and blood lipid profiles. To a lesser extent, the same was true for SSB consumption - possibly through alternative mechanisms. We could not, however, demonstrate these associations in childhood. Together, the findings highlight childhood as a window of opportunity for targeted prevention of adult cardiovascular disease.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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References

1. GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2019;**393**:1958–1972.
2. D'Ascenzi F, Sciaccaluga C, Cameli M, Cecere A, Ciccone MM, Di Francesco S, Ganau A, Imbalzano E, Liga R, Palermo P, Palmiero P, Parati G, Pedrinelli R, Scicchitano P, Zito A, Mattioli AV. When should cardiovascular prevention begin? The importance of antenatal, perinatal and primordial prevention. *Eur J Prev Cardiol* 2019;**0**:2047487319893832.
3. Magnussen CG, Niinikoski H, Juonala M, Kivimäki M, Rönnemaa T, Viikari JSA, Simell O, Raitakari OT. When and how to start prevention of atherosclerosis? Lessons from the Cardiovascular Risk in the Young Finns Study and the Special Turku Coronary Risk Factor Intervention Project. *Pediatr Nephrol* 2012;**27**:1441–1452.
4. Rangan AM, Randall D, Hector DJ, Gill TP, Webb KL. Consumption of 'extra' foods by Australian children: types, quantities and contribution to energy and nutrient intakes. *Eur J Clin Nutr* 2008;**62**:356–364.
5. Rangan AM, Schindeler S, Hector DJ, Gill TP, Webb KL. Consumption of 'extra' foods by Australian adults: types, quantities and contribution to energy and nutrient intakes. *Eur J Clin Nutr* 2009;**63**:865–871.
6. Donin AS, Nightingale CM, Owen CG, Rudnicka AR, Cook DG, Whincup PH. Takeaway meal consumption and risk markers for coronary heart disease, type 2

diabetes and obesity in children aged 9-10 years: a cross-sectional study. *Arch Dis Child* 2018;**103**:431–436.
7. Duffey KJ, Gordon-Larsen P, Steffen LM, Jacobs DR, Popkin BM. Regular consumption from fast food establishments relative to other restaurants is differentially associated with metabolic outcomes in young adults. *J Nutr* 2009;**139**:2113–2118.
8. Ambrosini GL, Oddy WH, Huang RC, Mori TA, Beilin LJ, Jebb SA. Prospective associations between sugar-sweetened beverage intakes and cardiometabolic risk factors in adolescents. *Am J Clin Nutr* 2013;**98**:327–334.
9. Nguyen S, Choi HK, Lustig RH, Hsu C-Y. Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents. *J Pediatr* 2009;**154**:807–813.
10. Malik AH, Akram Y, Shetty S, Malik SS, Yanchou Njike V. Impact of sugar-sweetened beverages on blood pressure. *Am J Cardiol* 2014;**113**:1574–1580.
11. Yi S-Y, Steffen LM, Terry JG, Jacobs DR, Duprez D, Steffen BT, Zhou X, Shikany JM, Harnack L, Carr JJ. Added sugar intake is associated with pericardial adipose tissue volume. *Eur J Prev Cardiol* 2020;2047487320931303.
12. Seferidi P, Millett C, Laverty AA. Sweetened beverage intake in association to energy and sugar consumption and cardiometabolic markers in children. *Pediatr Obes* 2018;**13**:195–203.
13. Giontella A, Bonafini S, Tagetti A, Bresadola I, Minuz P, Gaudino R, Cavarzere P, Ramaroli DA, Marcon D, Branz L, Nicolussi Principe L, Antoniazzi F, Maffeis C, Fava C. Relation between dietary habits, physical activity, and anthropometric and vascular parameters in children attending the primary school in the Verona South district. *Nutrients* 2019;**11**:1070.
14. Gopinath B, Flood VM, Wang JJ, Smith W, Rochtchina E, Louie JC, Wong TY, Brand-Miller J, Mitchell P. Carbohydrate nutrition is associated with changes in the retinal vascular structure and branching pattern in children. *Am J Clin Nutr* 2012;**95**:1215–1222.
15. Arvizu M, Monge A, Thamez M, Ortiz-Panozo E, Yunes E, Catzín-Kuhlmann A, Cantu-Brito C, López-Ridaura R, Lajous M. Abstract P322: soda consumption is associated with carotid intima-media thickness among middle-aged Mexican women. *Circulation* 2015;**131(suppl_1)**:AP322-AP.
16. Cancer Council Victoria. Rethink Sugary Drink - Key messages and definitions, 2016. http://www.rethinksugarydrink.org.au/for-professionals/key-messages.html (5 August 2019).
17. Clifford SA, Davies S, Wake M. Child Health CheckPoint: cohort summary and methodology of a physical health and biospecimen module for the Longitudinal Study of Australian Children. *BMJ Open* 2019;**9**:3–22.
18. Soloff CL, Johnstone R. *Sample Design, LSAC Technical Paper No. 1*. Melbourne: Australian Institute of Family Studies; 2005.
19. Rutishauser IW, Abraham B, Allsopp R. *Evaluation of Short Dietary Questions from the 1995 National Nutrition Survey*. Australian Food and Nutrition Monitoring Unit; Australia, 2001.
20. Kahn FK, Wake M, Lycett K, Clifford S, Burgner DP, Goldsmith G, Grobler AC, Lange K, Cheung M. Vascular function and stiffness: population epidemiology and concordance in Australian children aged 11-12 years and their parents. *BMJ Open* 2019;**9**:34–43.
21. Liu RS, Dunn S, Grobler AC, Lange K, Becker D, Goldsmith G, Carlin JB, Juonala M, Wake M, Burgner DP. Carotid artery intima-media thickness, distensibility and elasticity: population epidemiology and concordance in Australian children aged 11-12 years old and their parents. *BMJ Open* 2019;**9**:23–33.
22. Dascalu J, Liu M, Lycett K, Grobler AC, He M, Burgner DP, Wong TY, Wake M. Retinal microvasculature: population epidemiology and concordance in Australian children aged 11-12 years and their parents. *BMJ Open* 2019;**9**:44–52.
23. Drobnjak D, Munch IC, Glümer C, Faerch K, Kessel L, Larsen M, Veiby NCBB. Retinal vessel diameters and their relationship with cardiovascular risk and all-cause mortality in the Inter99 Eye Study: a 15-year follow-up. *J Ophthal* 2016;**2016**:1–8.
24. Ellul S, Wake M, Clifford SA, Lange K, Würtz P, Juonala M, Dwyer T, Carlin JB, Burgner DP, Saffery R. Metabolomics: population epidemiology and concordance in Australian children aged 11–12 years and their parents. *BMJ Open* 2019;**9**:106–117.
25. Blakemore TS. Measuring family socio-economic position. *Aust Soc Policy* 2009;**8**:121–168.
26. Petersen AC, Crockett L, Richards M, Boxer A. A self-report measure of pubertal status: reliability, validity, and initial norms. *J Youth Adolesc* 1988;**17**:117–133.
27. Ridley K, Ainsworth BE, Olds TS. Development of a compendium of energy expenditures for youth. *Int J Behav Nutr Phy* 2008;**5**:45.
28. Liu RS, Mensah FK, Carlin J, Edwards B, Ranganathan S, Cheung M, Dwyer T, Saffery R, Magnussen CG, Juonala M, Wake M, Burgner DP. Socioeconomic position is associated with carotid intima-media thickness in mid-childhood: the Longitudinal Study of Australian Children. *J Am Heart Assoc* 2017;**6**:e005925.
29. Magnussen CG, Smith KJ, Juonala M. What the long term cohort studies that began in childhood have taught us about the origins of coronary heart disease. *Curr Cardiovasc Risk Rep* 2014;**8**:373.
30. Gasser CE, Mensah FK, Kerr JA, Wake M. Early life socioeconomic determinants of dietary score and pattern trajectories across six waves of the Longitudinal Study of Australian Children. *J Epidemiol Community Health* 2017;**71**:1152–1160.
31. Foley LS, Maddison R, Rush E, Olds TS, Ridley K, Jiang Y. Doubly labeled water validation of a computerized use-of-time recall in active young people. *Metab Clin Exp* 2013;**62**:163–169.
32. Tingley D, Yamamoto T, Hirose K, Keele L, Imai K. Mediation: R package for causal mediation analysis. *J Stat Softw* 2014;**59**:38.
33. Australian Bureau of Statistics. National Health Survey: First Results, 2014-15. 2015. https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4364.0.55.0012014-15?OpenDocument (28 September 2019).
34. Liu Q, Ayoub-Charette S, Khan TA, Au-Yeung F, Blanco Mejia S, de Souza RJ, Wolever TMS, Leiter LA, Kendall CWC, Sievenpiper JL. Important food sources of fructose-containing sugars and incident hypertension: a systematic review and dose-response meta-analysis of prospective cohort studies. *J Am Heart Assoc* 2019;**8**:e010977.
35. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;**55**:1318–1327.
36. Ninomiya T, Perkovic V, Turnbull F, Neal B, Barzi F, Cass A, Baigent C, Chalmers J, Li N, Woodward M, MacMahon S. Blood pressure lowering and major cardiovascular events in people with and without chronic kidney disease: meta-analysis of randomised controlled trials. *BMJ* 2013;**347**:f5680.
37. Australian Institute of Health and Welfare. Risk factors to health - abnormal blood lipids (dyslipidaemia) 2018. https://www.aihw.gov.au/reports/biomedical-risk-factors/risk-factors-to-health/contents/abnormal-blood-lipids-dyslipidaemia (27 March 2019).
38. Koivistoinen T, Virtanen M, Hutri-Kähönen N, Lehtimäki T, Jula A, Juonala M, Moilanen L, Aatola H, Hyttinen J, Viikari JSA, Raitakari OT, Kähönen M. Arterial pulse wave velocity in relation to carotid intima-media thickness, brachial flow-mediated dilation and carotid artery distensibility: the Cardiovascular Risk in Young Finns Study and the Health 2000 Survey. *Atherosclerosis* 2012;**220**:387–393.
39. Anderson JJ, Celis-Morales CA, Mackay DF, Iliodromiti S, Lyall DM, Sattar N, Gill J, Pell JP. Adiposity among 132 479 UK Biobank participants; contribution of sugar intake vs other macronutrients. *Int J Epidemiol* 2017;**46**:492–501.
40. Thuesen BH, Toft U, Buhelt LP, Linneberg A, Friedrich N, Nauck M, Wallaschofski H, Jørgensen T. Estimated daily salt intake in relation to blood pressure and blood lipids: the role of obesity. *Eur J Prev Cardiol* 2015;**22**:1567–1574.
41. Malik VS, Popkin BM, Bray GA, Després J-P, Hu FB. Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. *Circulation* 2010;**121**:1356–1364.