



## Cross-sectional associations between Ideal Cardiovascular Health scores and vascular phenotypes in 11- to 12-year-olds and their parents: The Longitudinal Study of Australian Children

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### ABSTRACT

**Background:** Understanding early-life relationships between the Ideal Cardiovascular Health (ICVH) score and vascular phenotypes could inform likely effectiveness and timing of cardiovascular disease prevention strategies. We aimed to describe associations between ICVH scores and vascular phenotypes in 11- to 12-year-old children and their parents.

**Methods and results:** Cross-sectional ICVH scores (range 0–7, higher indicating better health), derived by summing dichotomized metrics for cholesterol, glucose, blood pressure (BP), body mass index (BMI), diet, physical activity and smoking, were constructed for 1235 adults (89% female, mean age 43 years) and 1028 children (48% female, 12 years). The median scores were 4 and 5 for adults and children respectively. Child ICVH scores were associated with parent scores (0.18 higher child score per additional point in parent's score, 95% CI 0.12 to 0.22,  $P < 0.001$ ). Each additional point in the adult ICVH score was associated with slower carotid-femoral pulse wave velocity (PWV,  $-0.32$  m/s, 95% CI  $-0.37$  to  $-0.27$ ), greater carotid elasticity (0.017%/mm Hg, 95% CI 0.014 to 0.020) and reduced carotid intima-media thickness (IMT,  $-7.3$   $\mu$ m, 95% CI  $-12.0$  to  $-2.5$ ). An additional point in the child score was associated with functional phenotypes (PWV  $-0.07$  m/s, 95% CI  $-0.11$  to  $-0.03$ ; carotid elasticity 0.009%/mm Hg, 95% CI 0.004 to 0.015) but not structural phenotypes (IMT  $-1.8$   $\mu$ m, 95% CI  $-5.2$  to 1.5).

**Conclusion:** Few Australian children and even fewer parents have ideal cardiovascular health. Lower ICVH scores were associated with adverse adult vascular phenotypes and adverse child vascular function. Family-based interventions optimizing ICVH metrics may delay onset and progression of subclinical atherosclerosis and later cardiovascular disease.

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### 1. Introduction

In 2010 the American Heart Association (AHA) proposed the concept of Ideal Cardiovascular Health [1]. A 7-point Ideal Cardiovascular Health (ICVH) score (Supplementary Table 1) summarizes an individual's attainment of cardiovascular health metrics and is useful to quantify

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and monitor population trends in cardiovascular disease (CVD) risk factors [1,2]. In adults, ICVH score is inversely associated with all-cause and CVD-related mortality [3], CVD events [4], and other non-communicable diseases including cancer [5] and depression [6]. Importantly, the ICVH score represents a conceptual shift towards primordial prevention [7], as evidenced by the inclusion of child cut-offs for each metric [1].

Few studies have examined the ICVH score in children. Limited evidence suggests that by late adolescence a lower ICVH score is associated with worse vascular outcomes [8]. In 190 US youth with type 1 diabetes, lower ICVH scores were associated with adverse vascular function (increased pulse wave velocity, PWV), but not vascular structure [9–11] (carotid intima-media thickness, IMT), 5 years later [12]. In the Cardiovascular Risk in Young Finns study, worsening ICVH scores over 21 years from childhood to adulthood were associated with increased adult PWV [13]. In another Finnish study of 15- to 19-year-old adolescents, lower ICVH scores were cross-sectionally associated with increased aortic IMT and lower aortic elasticity [14]. Data from earlier in childhood would indicate when associations between ICVH scores and vascular phenotypes become evident. Understanding parent-child relationships in this context would direct family-based interventions.

Here we used national population-derived Australian data to: 1) describe the ICVH score in 11- to 12-year-old children and their parents; 2) examine the relationship between parent and child ICVH scores; and 3) investigate cross-sectional associations of the overall ICVH score with vascular phenotypes among children and their parents. Secondary aims were to explore associations within the individual metrics.

## 2. Methods

### 2.1. Study design and participants

Predominantly cross-sectional data were drawn from the Longitudinal Study of Australian Children (LSAC) [15] and Child Health CheckPoint [16]. Details of the initial two-stage random sampling design (with postcode as primary sampling unit) are outlined elsewhere [17]. Briefly, LSAC recruited a nationally representative sample of 5107 infants (age 0–1 years) [16], and followed them up in biennial 'waves' of data collection up to 2015 (at child age 10–11 years). At the latest visit, families were invited to consent to their contact details being shared with the research team. The child and a parent from consenting families ( $n = 3513$ ) underwent a detailed biophysical assessment (the Child Health CheckPoint) between February 2015 and March 2016 (when all children were aged 11–12 years). In total 1874 families participated [16–18]. The study was approved by the Human Research Ethics Committees of the Royal Children's Hospital (Melbourne, Australia) (33225D) and the Australian Institute of Family Studies (14–26).

### 2.2. Metrics for Ideal Cardiovascular Health score

The study definitions for ICVH score metrics are outlined in Supplementary Table 1 [1]. Metrics drew on largely cross-sectional (Child Health CheckPoint) data with longitudinal data on smoking habits and socioeconomic position (SEP) from LSAC. Definitions for each metric were reproduced from Lloyd-Jones et al. [1], although data limitations required three minor modifications. We used a 4-point ideal dietary score used in previous studies [19] as opposed to the 5-point dietary score outlined by Lloyd-Jones et al. as sodium intake and total energy intake data were not available (Supplementary Table 2). Second, as 11- to 12-year-old children are rarely asked about their own smoking habits, we used parent-reported passive smoking measure ("Including yourself, how many people who live with you smoke inside the house?") in children instead of child-reported smoking habits. Finally, semi-fasted blood was obtained as a traditional >8-hour fast is often not feasible in large population studies and could be dangerous for some individuals. Non-fasting total cholesterol is considered acceptable when assessing CVD risk according to North American and European expert guidelines [20]. For glucose, the GEMCAS study of 28,024 healthy adults has shown that a 3-hour fast equates to a traditional >8-hour fast (difference in mean glucose level <0.10 mmol/L in participants <60 years of age) [21].

#### 2.2.1. Cholesterol, glucose, and blood pressure

Semi-fasting (median 4.2 h after last caloric intake) peripheral blood was collected and processed within 4 h of collection at an on-site laboratory, with serum aliquots frozen at  $-80^{\circ}\text{C}$  for batch analysis. High-throughput proton nuclear magnetic resonance metabolomics (Nightingale Ltd., Vantaa, Finland) quantified serum metabolic biomarkers including glucose and total cholesterol [22].

Supine brachial blood pressure was measured after a 7-minute rest up to 3 times using the SphygmoCor XCEL (AtCor Medical Pty Ltd., West Ryde, NSW, Australia) and the mean values used in adult analysis. Mean values were converted to age-sex-height percentiles in children [23].

#### 2.2.2. Body mass index, diet, physical activity, and smoking

Participant's height was measured without shoes and in light clothing, to the nearest 0.1 cm, in duplicate. A third measurement was taken if the difference of the first 2 measurements was >0.5 cm. The mean of all measurements was used in analyses. An InBody230 bioelectrical impedance analysis scale (Biospace Co. Ltd., Seoul, South Korea) measured weight to the nearest 0.1 kg. BMI was calculated by dividing the weight (kg) by the height squared ( $\text{m}^2$ ). For children, US Centers for Disease Control growth reference charts provided age- and sex-specific BMI z-scores and percentiles [24].

A self-administered, modified National Secondary Students' Diet and Activity (NaSSDA) [25] 25-item food frequency diary at CheckPoint assessed dietary patterns in both children and adults. The NaSSDA, where possible, used pre-existing validated measures [26], shown to have reasonable validity when compared to 24-hour diet recall in adults [27]. A 4-point ideal dietary score was created from participants' responses to 4 questions about approximate intake for vegetable and fruit, fish, wholegrains (bread), and sweetened beverage intake. We subsequently matched approximate intake of the abovementioned available items to Australian dietary guidelines [28] for each category (Supplementary Table 2). We were unable to quantify sodium or total caloric intake. We categorized ideal, intermediate and poor diet scores, using a similar approach to studies reporting incomplete diet scores [19].

Adults self-reported physical activity levels in the LSAC wave 6 questionnaire (approximate 1 year prior to CheckPoint) by response to the question: "About how many days each week do you do at least 30 minutes of moderate or vigorous physical activity (like walking briskly, riding a bike, gardening, tennis, swimming, running, etc.?)". Physical activity was categorized as ideal if adults reported 5 or more days with 30-minute sessions of moderate to vigorous physical activity (MVPA) [1].

In children, physical activity was quantified using the Multimedia Activity Recall for Children and Adolescents (MARCA), a computerized recall time diary [29]. A trained interviewer elicited activities over the immediate 24-hour period prior to assessment, detailed into 5-minute intervals. This occurred at both the child's biophysical assessment and up to 3 times afterwards by follow-up telephone calls, including on at least 1 weekday and 1 weekend-day. Children chose from a list of 259 activities, each associated with an energy expenditure metabolic equivalent (MET). The average 'daily MVPA minutes', derived from the sum of reported minutes spent in activities requiring at least 3 METs [30] gave a measure of the physical activity. MARCA has excellent test-retest reliability (intra-class coefficients = 0.88–0.94) [29] and convergent validity with pedometer for physical activity level ( $\rho = 0.54$ ), and is superior to other self-report instruments for children [31].

Adult smoking was a measure of current smoking, while child smoking was a measure of passive smoke exposure. In adults, the smoking metric was determined by their answer to the question "Are you currently smoking?" in the LSAC wave 6 questionnaire. In children, parent-reported questionnaire quantified the number of smokers at home, including parents and older siblings, at each LSAC wave. Those children with ideal health metric had never been exposed to smoking at home.

#### 2.2.3. The Ideal Cardiovascular Health score

We dichotomized each of the 7 metrics into ideal versus not ideal (poor and intermediate combined, see Supplementary Table 1) and then summed the number of metrics for which the participant met the ideal criterion to calculate an ICVH score. A higher score indicated better cardiovascular health.

## 2.3. Vascular phenotypes

### 2.3.1. Carotid-femoral pulse wave velocity

Carotid-femoral pulse wave velocity (PWV) was determined using the SphygmoCor XCEL (AtCor Medical, Australia) [32]. After a 7-minute rest, assessors obtained velocity (distance/time) measurements 1–3 times while participants lay supine. Further analyses used the single or mean measurement where available. Simultaneously recorded carotid waveform, using tonometric applanation and femoral waveform using a cuff placed around the upper thigh inflated to subdiastolic pressure, provided the time component of PWV. Distance was measured with a tape measure from the carotid pulse to the suprasternal notch to right femoral pulse (estimated by the crease between thigh and torso when the knee was bent to  $90^{\circ}$ ) to top of the thigh cuff.

### 2.3.2. Carotid elasticity and intima-media thickness

Carotid elasticity and intima-media thickness (IMT) were measured as previously described [18]. Trained ultrasound technicians acquired real-time B mode ultrasound carotid artery images using standardized protocols. Participants lay supine with their head turned  $45^{\circ}$  to the left to expose the right side of neck. A 10 MHz linear array probe (Vivid-I, GE Healthcare, Chicago, IL, USA) obtained cine-loops of the right common carotid artery, in triplicate. Modified 3-lead electrocardiogram (ECG) captured cardiac cycle information concurrently. All images were transferred to digital storage for archiving and analysis at a core facility in Melbourne.

Carotid artery lumen-lumen diameter was automatically measured at least 3 times at end-diastole and end-systole (diastolic and systolic lumen diameter respectively) by Carotid Analyzer (Medical Imaging Applications, Coralville, IA, USA) a semi-automatic

edge detection software program. These values and concomitant brachial blood pressure were used to measure carotid artery elasticity, in the following formula:

$$\frac{(D_s - D_d)}{D_d} \times \frac{P_s - P_d}{P_s} \times 100\%$$

where  $D_d$  is the diastolic diameter;  $D_s$ , the systolic diameter;  $P_s$ , systolic blood pressure; and  $P_d$ , diastolic blood pressure, and expressed as a percentage per mm Hg, by multiplying by 100 [14,33].

One of six raters measured carotid IMT on ultrasound images using semi-automated Carotid Analyzer software. Measurement was made  $\approx 10$  mm proximal to the carotid bulb, over 5–10 mm length. We reported maximum carotid IMT, calculated as the mean of 3–5 still frames, timed at the R-wave by ECG, of the largest thickness measurement in this 5–10 mm window. All images were measured once, but a subset of 105 images were reanalysed four times each, in an incomplete block design, to examine within-observer and between-observer reliability between all six raters. The within-observer and between-observer coefficients of variation were 4.9% and 6.2% respectively [18].

#### 2.4. Age, sex, and family socioeconomic position

We created directed acyclic graphs to help select the a priori covariates that would be mostly likely to confound our analyses; age, sex of the parents and children, family SEP and assessment center attended by the family (Supplementary Fig. 1). We obtained self-reported sex and age at assessment. Family SEP, collected at LSAC wave 6 [34,35] summarized parent-reported combined household income, current or most recent occupation of each parent, and highest educational qualification of each parent. Each component was scaled and an unweighted average was calculated and standardized within the wave to have a mean 0 and standard deviation (SD) of 1.

#### 2.5. Statistical analysis

The primary cross-sectional analyses examined associations of overall ICVH scores with vascular phenotypes, using adjusted linear regression models. We examined whether individual parent scores were associated with child scores using Poisson regression adjusted for parent and child age, sex, family SEP and assessment center. Poisson regression was used as the ICVH score was a typical count variable (integer scores between 0 and 7). Further exploratory analyses examined associations of individual metrics (ideal compared to non-ideal) with vascular phenotypes. We then explored whether individual parent ICVH metrics were associated with their respective child ICVH metrics using logistic regression models. All models included the following covariates: parent and child age and sex, family SEP and assessment center attended, where relevant.

Analyses used survey weights obtained for the assessment center sample [36], taking into account the initial complex multi-level sampling of LSAC, and adjusted for non-response and loss to follow-up over the 6 waves of data collection. We also used multiple imputation with the method of chained equations [37] to examine any biases introduced by data assumed to be missing at random. Variables included in the imputation models were all ICVH metrics and/or the ICVH score, adult and child vascular phenotypes, and covariates (adult and child age, sex, maximum carotid artery lumen diameter, family SEP, postcode, sampling stratum, sampling weight and assessment center). Metric variables were included in models as continuous variables where possible (e.g. BMI value in  $\text{kg}/\text{m}^2$ ), otherwise were included as categorical variables dependent on whether they fulfilled ideal metric criteria (e.g. ideal or non-ideal BMI). Eight models were specified, as detailed in Supplementary Table 3. Twenty imputed datasets were generated for each model. When compared with complete case analyses, multiple imputation did not substantially alter our results or conclusions. We present the complete case data and provide the multiple imputation results in the online supplement.

##### 2.5.1. Sensitivity analysis

We further explored the robustness of our results in sensitivity analyses using the continuous variable of each metric in both complete case and multiple imputation models.

Analyses were performed using Stata 14.2 (StataCorp LP, TX, USA), with *svy* and *mi* chained packages.

## 3. Results

### 3.1. Participants and missing data

The analytical sample contained 1482 of 1874 families who attended CheckPoint (Supplementary Fig. 2). Participants were excluded because they had home visits where carotid ultrasound was not available, or because the attending adult was not a biological parent. The sample characteristics of participants who were excluded were not substantially different to the characteristics of those included (Supplementary Table 4). Within the analytic sample, complete data on all 7 metrics of the ICVH score were available for 1028 (69%) children, 1235 (83%) adults, and 949 (64%) parent-child dyads (Table 1). Missing data were

most prevalent in the blood-derived, blood pressure, and elasticity measures (Supplementary Table 5). Outcomes in those with missing data were not substantially different from those with data (Supplementary Table 6). The main reasons for missingness were refusal of blood sampling or insufficient quantity of blood drawn, or insufficient time in the cardiovascular assessment.

### 3.2. Ideal Cardiovascular Health in children and adults

A perfect ICVH score (i.e. 7/7) was present in 16 adults (1%) and 76 (7%) children, whereas 124 (10%) adults and 406 (39%) children achieved ideal levels in 6 or more metrics. The median ICVH score was lower in adults (4 metrics) than children (5 metrics). After applying survey weights, prevalence estimates were largely unchanged (Supplementary Fig. 3).

Compared to children, the prevalence of ideal values was equivalent or lower in adults for all individual ICVH metrics except smoking (Supplementary Fig. 4). The exception in smoking was likely due to the adult definition related to current smoking. Of the ICVH metrics, the prevalence of ideal scores differed the most between children and adults for physical activity (absolute unit difference 52%), followed by blood pressure (42%). Ideal diet was the metric least likely to be attained both by adults (17%) and children (16%).

### 3.3. Associations between parent and child cardiovascular health metrics

There was a small correlation between adult and child ICVH scores in parent-child dyads (Supplementary Table 7, 0.18 higher child score per additional point in parent's score, 95% CI 0.12 to 0.22,  $P < 0.001$ ). Children whose parent had non-ideal health in any given metric had substantially higher odds for non-ideal health in that metric, for all ICVH metrics except for physical activity and serum glucose (Table 2). Use of multiple imputation models did not substantially alter results (Supplementary Table 8).

### 3.4. Associations of ideal health scores with vascular phenotypes

The adult data strongly supported an association between overall ICVH score and all vascular phenotypes (Fig. 1, Supplementary Table 9). In linear regression analyses using survey weights and adjusted for age, sex, family SEP and assessment center, each additional point in the ICVH score was associated with a more favorable vascular phenotype, e.g. slower PWV ( $-0.32$  m/s, 95% CI  $-0.37$  to  $-0.27$ ,  $P < 0.001$ ), higher arterial elasticity (0.017% per mm Hg, 0.014 to 0.020,  $P < 0.001$ ) and a smaller carotid IMT ( $-7.3$   $\mu\text{m}$ ,  $-12.0$  to  $-2.5$ ,  $P = 0.003$ ). In children, associations between the ICVH score and each of the vascular phenotypes were smaller in absolute magnitude (Fig. 1, Supplementary Table 9). In linear regression models adjusted for age, sex and family SEP, a higher ICVH score was associated with better vascular function (PWV  $-0.07$  m/s per extra ideal health metric,  $-0.11$  to  $-0.03$ ,  $P < 0.001$ ; and carotid elasticity 0.009% per mm Hg, 0.004 to 0.015,  $P = 0.001$ ), but not with vascular structure (carotid IMT  $-1.8$   $\mu\text{m}$ ,  $-5.2$  to 1.5,  $P = 0.28$ ). Sensitivity analyses using continuous variables and multiple imputation models did not substantially alter results (Supplementary Tables 10 and 11).

In exploratory analyses, adult blood pressure and BMI were associated with all vascular outcomes in models adjusted for age, sex, family SEP and assessment center (Table 3). Childhood BMI and blood pressure metrics were associated with child measures of artery stiffness and elasticity, and to a lesser extent, carotid IMT. This was replicated when using multiple imputation, and/or continuous versions of the metric (Supplementary Tables 10 and 11). Overall, the absolute value of associations was smaller in children than adults (Table 3). The correlation between metrics in adults and children is reported in Supplementary Table 12.

**Table 1**

Sample characteristics stratified by ICVH score, where values are expressed as survey-weighted mean (SD) or unweighted n (survey-weighted %).

Characteristic	By ICVH score						P for trend <sup>b</sup>	Total
	0–2 <sup>a</sup>	3	4	5	6	7		
Adult	n = 196	n = 316	n = 335	n = 264	n = 108	n = 16		n = 1235
Age, years	43.6 (5.2)	44.0 (5.7)	42.7 (5.5)	43.4 (4.9)	43.5 (5.5)	45.1 (3.1)	0.54	43.4 (5.5)
Male	39 (21%)	44 (12%)	35 (9%)	22 (7%)	7 (6%)	1 (3%)	<0.001	148 (11%)
Family socioeconomic position, z-score	−0.32 (1.00)	−0.11 (0.88)	−0.02 (0.96)	0.21 (0.90)	0.46 (0.90)	0.49 (0.57)	<0.001	−0.01 (0.97)
BMI, kg/m <sup>2</sup>	32.8 (5.3)	31.1 (6.1)	27.3 (5.1)	24.5 (4.5)	22.8 (2.1)	23.1 (1.3)	<0.001	28.4 (6.3)
Total cholesterol, mmol/L	5.35 (0.97)	4.91 (0.82)	4.61 (0.83)	4.47 (0.75)	4.36 (0.66)	4.17 (0.59)	<0.001	4.77 (0.89)
Glucose, mmol/L	5.56 (1.87)	4.99 (1.25)	4.80 (0.75)	4.60 (0.57)	4.58 (0.54)	4.64 (0.43)	<0.001	4.93 (1.22)
Blood pressure								
Systolic pressure, mm Hg	131 (10)	126 (11)	119 (13)	112 (8)	111 (7)	113 (4)	<0.001	121 (13)
Diastolic pressure, mm Hg	80 (7)	77 (8)	73 (9)	69 (7)	68 (6)	66 (5)	<0.001	74 (9)
Ideal diet								
Parent diet score	1.4 (0.7)	1.7 (0.8)	1.6 (0.8)	1.9 (0.8)	2.3 (0.8)	3.0 (0.2)	<0.001	1.7 (0.8)
Fruit & vegetables >7 serves per day	1 (1%)	14 (6%)	7 (3%)	12 (5%)	22 (21%)	7 (52%)	<0.001	63 (6%)
Fish ≥2 times per week	90 (41%)	167 (51%)	182 (53%)	161 (59%)	85 (76%)	15 (96%)	<0.001	700 (54%)
Wholegrain bread ≥2 slices per day	36 (20%)	80 (25%)	78 (22%)	90 (37%)	45 (39%)	11 (57%)	<0.001	340 (27%)
Sweetened beverages <4 cups per week	152 (74%)	276 (89%)	296 (86%)	244 (92%)	101 (94%)	16 (100%)	<0.001	1085 (86%)
Est. weekly MVPA							<0.001	
No exercise	28 (16%)	45 (16%)	28 (9%)	15 (5%)	1 (1%)	0 (0%)	–	117 (11%)
<150 min/wk	166 (83%)	233 (70%)	234 (67%)	152 (55%)	31 (25%)	0 (0%)	–	816 (64%)
>150 min/wk	2 (0%)	38 (14%)	73 (24%)	97 (40%)	76 (75%)	16 (100%)	–	302 (25%)
Current smoker	39 (28%)	31 (13%)	22 (8%)	11 (7%)	0 (0%)	0 (0%)	<0.001	103 (12%)
PWV, m/s	7.56 (1.17)	7.39 (1.15)	6.91 (1.13)	6.41 (0.87)	6.22 (0.84)	6.18 (0.74)	<0.001	6.97 (1.19)
Carotid elasticity, %/mm Hg	0.212 (0.048)	0.225 (0.051)	0.260 (0.066)	0.267 (0.059)	0.278 (0.058)	0.285 (0.062)	<0.001	0.247 (0.063)
Carotid IMT, μm	680.3 (97.7)	684.0 (105.1)	660.7 (89.3)	638.6 (81.0)	645.6 (104.1)	666.9 (97.4)	<0.001	664.9 (99.1)
Child	n = 14	n = 61	n = 173	n = 374	n = 330	n = 76		n = 1028
Age, years	11.8 (0.2)	11.8 (0.3)	11.9 (0.4)	11.9 (0.4)	11.9 (0.4)	11.9 (0.4)	0.95	11.9 (0.4)
Male	6 (48%)	27 (50%)	85 (52%)	167 (44%)	150 (46%)	50 (69%)	<0.001	485 (48%)
Family socioeconomic position, z-score	−0.37 (0.87)	−0.38 (0.67)	−0.26 (0.95)	−0.01 (0.88)	0.22 (0.89)	0.69 (0.95)	<0.001	0.02 (0.95)
BMI z-score (CDC)	1.62 (0.32)	1.26 (0.68)	0.57 (1.06)	0.30 (0.91)	−0.03 (0.89)	0.12 (0.62)	<0.001	0.34 (1.00)
Total cholesterol, mmol/L	4.78 (0.58)	4.46 (0.53)	4.27 (0.67)	4.07 (0.67)	3.82 (0.56)	3.77 (0.47)	<0.001	4.06 (0.67)
Glucose, mmol/L	5.16 (1.17)	4.95 (0.52)	4.98 (0.49)	4.90 (0.70)	4.89 (0.87)	4.82 (0.44)	0.06	4.91 (0.70)
Blood pressure								
Systolic BP, age-sex-height percentile	83.1 (16.9)	70.1 (17.3)	60.4 (22.8)	53.2 (22.8)	46.0 (21.3)	53.6 (24.4)	<0.001	54.4 (23.9)
Diastolic BP, age-sex-height percentile	69.0 (18.1)	60.5 (13.6)	53.3 (16.9)	49.5 (16.3)	46.6 (18.9)	48.9 (22.5)	<0.001	50.5 (18.3)
Systolic pressure, mm Hg	125 (13)	114 (7)	111 (8)	108 (7)	106 (7)	108 (7)	<0.001	109 (8)
Diastolic pressure, mm Hg	70 (6)	66 (4)	64 (6)	63 (5)	62 (6)	63 (7)	<0.001	63 (6)
Ideal diet								
Child diet score	1.4 (0.7)	1.4 (0.6)	1.2 (0.7)	1.5 (0.8)	1.7 (1.0)	3.1 (0.4)	<0.001	1.6 (0.9)
Fruit & vegetables >7 serves per day	0 (0%)	6 (8%)	14 (7%)	44 (13%)	62 (19%)	43 (54%)	<0.001	169 (15%)
Fish ≥2 times per week	4 (24%)	22 (43%)	37 (22%)	120 (32%)	134 (40%)	64 (81%)	<0.001	381 (36%)
Wholegrain bread ≥2 slices per day	3 (32%)	14 (24%)	42 (23%)	118 (29%)	125 (34%)	58 (80%)	<0.001	360 (32%)
Sweetened beverages <4 cups per week	12 (87%)	39 (62%)	131 (70%)	290 (76%)	262 (79%)	75 (98%)	<0.001	809 (76%)
Daily MVPA, minutes	64 (52)	67 (49)	101 (78)	121 (73)	144 (75)	149 (65)	<0.001	120 (78)
Ever exposed to smoke at home	11 (78%)	37 (64%)	66 (46%)	80 (25%)	4 (1%)	0 (0%)	<0.001	198 (25%)
PWV, m/s	4.79 (0.75)	4.60 (0.40)	4.54 (0.58)	4.45 (0.56)	4.40 (0.57)	4.38 (0.61)	0.004	4.47 (0.58)
Carotid elasticity, %/mm Hg	0.433 (0.072)	0.461 (0.078)	0.474 (0.089)	0.485 (0.087)	0.491 (0.095)	0.478 (0.084)	0.008	0.482 (0.091)
Carotid IMT, μm	574.8 (38.0)	587.1 (39.0)	586.8 (49.2)	578.5 (46.6)	580.7 (51.8)	573.2 (44.6)	0.21	581.0 (49.1)

ICVH indicates Ideal Cardiovascular Health; BMI, body mass index; CDC, the Centers for Disease Control and Prevention; BP, blood pressure; MVPA, moderate to vigorous physical activity; IMT, intima-media thickness.

<sup>a</sup> Adults and children with 0–2 ideal ICVH metrics were grouped together due to small numbers.

#### 4. Discussion

We report a low prevalence of perfect ICVH scores in this relatively advantaged population of Australian children and adults. Parental and child attainment of individual ICVH metrics were correlated. Lower ICVH scores were associated with adverse structural and functional adult vascular phenotypes. For the first time, we report associations between ICVH and functional phenotypes (PWV and carotid elasticity) in children, and between two specific ICVH metrics (blood pressure and BMI) and adverse vascular phenotypes.

Our adult data are in keeping with previous studies [13,19,38,39], suggesting the associations in children are robust. The reported overall prevalence of an ICVH score of 6 or higher in adults varied from <1% in an African American population [40] to 15% in a large Chinese corporation [41]. Our reported prevalence in adults (8% for a score of 6 or greater) is comparable to scores reported from other national Australian data [19]. Despite our relatively strict definition of ideal

smoking behavior, our Australian children had a higher prevalence of perfect ICVH scores (6%) than previous studies; <1% in US [42] and <2% in European adolescents [43]. This may be partly due to the higher frequency of ideal diet in our cohort than previously reported [42,43]. The absence of one diet parameter (sodium) may overestimate the prevalence of ideal health in the diet metric. In addition, as our sample is younger than those in previous studies, our results may reflect a decrease in ICVH score with age.

The age-dependence of some associations suggests critical periods when traditional risk factors differentially affect functional and structural vascular phenotypes. In adults, a higher ICVH score was associated with favorable vascular phenotypes: slower PWV, higher carotid elasticity and reduced carotid IMT. At age 11–12 years, a higher ICVH score was associated with better functional measures (PWV and carotid elasticity), but not convincingly with structural measures (carotid IMT). When using multiple imputation, the association with score changed slightly for one of the six outcomes (child's carotid IMT),

**Table 2**  
Odds ratios for a child having a non-ideal ICVH metric (poor or intermediate), given parent category for ICVH metric.

Child metric <sup>a</sup>	Parent metric category <sup>b</sup>	n	% <sup>c</sup>	OR (95% CI)	P value for trend
Cholesterol	Ideal	770	69	1.0	<0.001
	Intermediate	279	25	2.0 (1.4, 3.0)	
	Poor	71	6	3.3 (1.9, 5.7)	
Glucose	Ideal	981	88	1.0	0.09
	Intermediate	108	10	2.0 (0.9, 4.9)	
	Poor	30	3	1.7 (0.5, 6.4)	
Blood pressure	Ideal	743	55	1.0	<0.001
	Intermediate	492	36	2.4 (1.3, 4.5)	
	Poor	116	9	5.9 (2.6, 13.4)	
BMI	Ideal	567	38	1.0	<0.001
	Intermediate	481	33	2.1 (1.4, 3.0)	
	Poor	428	29	3.0 (2.0, 4.7)	
Diet	Ideal	250	18	1.0	<0.001
	Intermediate	634	45	1.8 (1.2, 2.7)	
	Poor	516	37	4.0 (2.4, 6.7)	
Physical activity	Ideal	355	25	1.0	0.22
	Intermediate	946	66	1.2 (0.8, 1.7)	
	Poor	134	9	1.4 (0.8, 2.5)	

ICVH indicates Ideal Cardiovascular Health; SEP, socioeconomic position; BMI, body mass index; OR, odds ratio; CI, confidence interval.

<sup>a</sup> Smoking excluded as non-ideal parental health perfectly predicts non-ideal child health according to definitions.

<sup>b</sup> Metric category definitions found in supplementary online material (Supplementary Table 1).

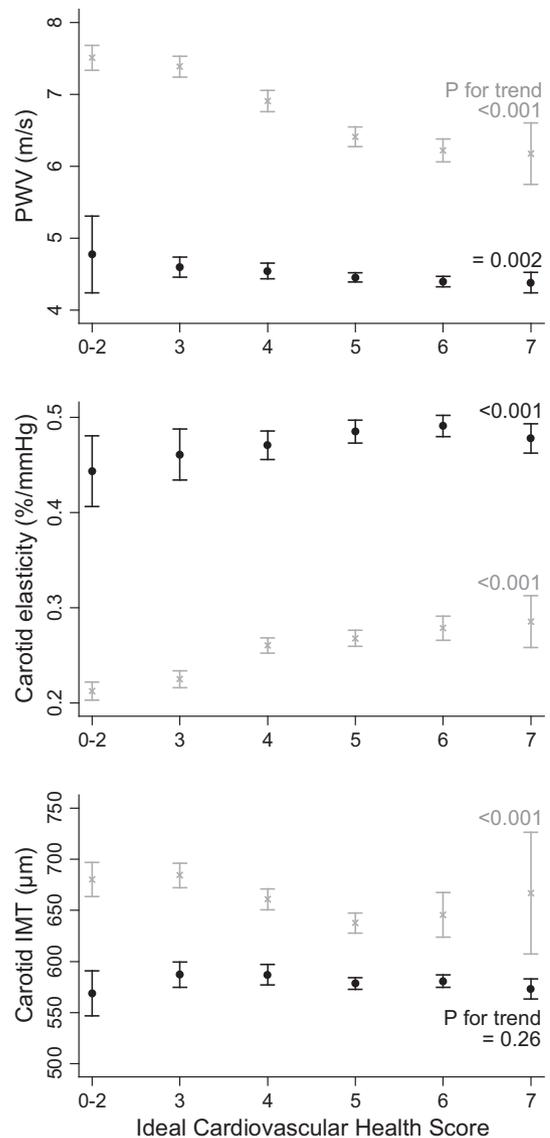
<sup>c</sup> Unweighted n and unweighted % reported here.

from a mean difference in the complete case model of  $-1.8 \mu\text{m}$  ( $P = 0.28$ ) to  $-3.4 \mu\text{m}$  ( $P = 0.07$ ) in the multiple imputation model (Supplementary Table 10), implying that missing data may have biased our complete case analysis. However, given the multiple comparisons, small difference and weak evidence of effect, we think this is most likely a chance finding. Even in multiple imputation analyses, there is lack of strong evidence for an association in children between the ICVH score and vascular structure. Two hypotheses plausibly explain these results: 1) discernible changes to functional vascular phenotype may occur prior to structural phenotype [44], and 2) vascular structural changes in childhood are below the resolution limit of ultrasound measurement ( $\sim 100 \mu\text{m}$ ) [45].

Of the 7 ICVH metrics, non-ideal BMI and blood pressure were robustly associated with both structural and functional vascular phenotypes. High quality meta-analysis of randomized trial evidence shows that a reduction of 5 mm Hg systolic blood pressure in adults leads to a 17% reduction in hazard for major cardiovascular events [46], and observational and Mendelian randomization studies posit a causal role for obesity in CVD events [47] and adverse vascular phenotypes [48]. Our associations between these metrics and vascular phenotypes were independent of other metrics in adjusted models, and were largely invariant to parent or child status, use of continuous measures, and multiple imputation models—consistent with a causal relationship of these risk factors with vascular phenotypes.

To our knowledge this is the first study to examine adult and child associations with the breadth of exposures summarized in the ICVH score. Previous research has examined intergenerational transmission of individual metrics such as dietary patterns [49] and body weight [50]. Our exploratory analysis suggests opportunities for family-based behavioral interventions aimed at both children and their parents across a number of metrics, some of which are modestly correlated (Supplementary Table 12).

Some limitations warrant consideration. We are unable to comment on the long-term consequences of adverse vascular phenotypes in our cohort as data are primarily cross-sectional. We aimed to address substantial missing data (>5% of the total sample for some variables; Supplementary Table 5) with multiple imputation models and survey weighting. Despite this, the adult sample is not generalizable to the



**Fig. 1.** Ideal Cardiovascular Health score associations with vascular phenotypes – PWV, carotid elasticity and carotid IMT – in adults (gray) and children (black). Those with scores 0–2 are grouped together due to small numbers. P value for trends are derived from linear regression models using survey weights and complete cases, adjusted for age, sex, SEP and assessment center, modelling the ICVH score as a categorical variable with 6 categories, from 1 (0–2 group) up to 6 (7 group). Symbol color indicates adult (gray) and child (black) models. Crosses (x) and dots (●) represent point estimates, and vertical bars the 95% confidence interval for a predicted outcome, given the ICVH score. PWV indicates pulse wave velocity; IMT, intima-media thickness; ICVH, Ideal Cardiovascular Health; SEP, socioeconomic position.

general adult population, as it mainly comprised mothers, under-represented socioeconomically disadvantaged families, and survey weights were centered around the child as the base unit. Replication in other populations and settings is warranted.

Physical activity, diet and smoking data were self- or parent-reported, which have well-described limitations [2,51]. Balancing precise measurement with the logistics of a multi-domain population study is difficult. For example, in the physical activity metric, precision could be improved with accelerometry data, but this would put the score out of reach of busy clinicians. Measuring cotinine levels could capture complete smoking exposure more precisely [2], for small additional cost to existing blood analyses. At time of writing, we are not aware of any highly accurate dietary measures that could feasibly be used in large-scale, multi-domain population studies. Steinberger et al.

**Table 3**

The survey-weighted mean values (SD) and per metric difference for PWV, carotid elasticity, and IMT in those who fulfil ideal criteria compared to those who do not fulfil criteria, for a) the ICVH score overall (6 or higher), and b) a given ICVH metric (definitions from Supplementary Table 1).

Outcome and metric	Adults			P	Children			P
	Mean (SD) <sup>a</sup>		Adjusted difference (95% CI) <sup>b</sup> (ideal - non-ideal)		Mean (SD) <sup>a</sup>		Adjusted difference (95% CI) <sup>b</sup> (ideal - non-ideal)	
	Ideal	Non-ideal			Ideal	Non-ideal		
PWV, m/s			N = 1149			N = 1019		
ICVH score	6.22 (0.83)	7.05 (1.16)	-0.32 (-0.37, -0.27)	<0.001	4.39 (0.58)	4.50 (0.56)	-0.07 (-0.11, -0.03)	0.002
Total cholesterol	6.86 (1.15)	7.25 (1.19)	-0.08 (-0.22, 0.06)	0.28	4.45 (0.57)	4.47 (0.54)	-0.03 (-0.12, 0.05)	0.43
Glucose	6.93 (1.16)	7.33 (1.21)	-0.17 (-0.39, 0.04)	0.12	4.47 (0.57)	4.39 (0.55)	0.05 (-0.10, 0.20)	0.54
Blood pressure	6.47 (0.88)	7.57 (1.17)	-0.83 (-0.98, -0.67)	<0.001	4.46 (0.56)	4.83 (0.63)	-0.35 (-0.56, -0.14)	0.001
BMI	6.53 (1.00)	7.25 (1.17)	-0.44 (-0.57, -0.31)	<0.001	4.42 (0.57)	4.67 (0.53)	-0.27 (-0.36, -0.18)	<0.001
Diet	6.81 (1.15)	7.00 (1.16)	-0.08 (-0.25, 0.09)	0.37	4.41 (0.56)	4.49 (0.58)	-0.06 (-0.14, 0.02)	0.16
Physical activity	6.82 (1.20)	7.01 (1.15)	-0.13 (-0.28, 0.03)	0.11	4.49 (0.57)	4.46 (0.58)	0.06 (-0.03, 0.16)	0.19
Smoking	6.99 (1.21)	6.83 (0.85)	0.22 (-0.03, 0.47)	0.09	4.48 (0.60)	4.48 (0.49)	0.06 (-0.03, 0.16)	0.19
Carotid elasticity, %/mm Hg			N = 1028			N = 974		
ICVH score	0.279 (0.059)	0.244 (0.061)	0.017 (0.014, 0.020)	<0.001	0.489 (0.094)	0.479 (0.087)	0.009 (0.004, 0.015)	0.001
Total cholesterol	0.251 (0.063)	0.233 (0.058)	0.002 (-0.005, 0.010)	0.56	0.482 (0.086)	0.485 (0.097)	-0.004 (-0.017, 0.010)	0.61
Glucose	0.249 (0.061)	0.216 (0.061)	0.024 (0.013, 0.035)	<0.001	0.483 (0.091)	0.483 (0.068)	0.010 (-0.012, 0.032)	0.37
Blood pressure	0.272 (0.064)	0.216 (0.051)	0.036 (0.028, 0.044)	<0.001	0.483 (0.089)	0.417 (0.085)	0.050 (0.023, 0.077)	<0.001
BMI	0.268 (0.065)	0.234 (0.061)	0.026 (0.017, 0.035)	<0.001	0.486 (0.093)	0.458 (0.080)	0.030 (0.013, 0.047)	<0.001
Diet	0.253 (0.065)	0.247 (0.065)	0.003 (-0.008, 0.014)	0.62	0.489 (0.102)	0.476 (0.088)	0.009 (-0.007, 0.026)	0.27
Physical activity	0.254 (0.062)	0.247 (0.065)	0.005 (-0.004, 0.014)	0.28	0.479 (0.090)	0.478 (0.090)	-0.003 (-0.018, 0.013)	0.74
Smoking	0.248 (0.066)	0.244 (0.052)	0.006 (-0.009, 0.022)	0.43	0.479 (0.095)	0.478 (0.075)	0.002 (-0.016, 0.019)	0.86
Carotid IMT, $\mu$ m			N = 1211			N = 1016		
ICVH score	648.8 (103.5)	666.5 (96.6)	-7.3 (-12.0, -2.5)	0.003	579.5 (51.0)	581.8 (46.5)	-1.8 (-5.2, 1.5)	0.28
Total cholesterol	664.7 (98.1)	669.5 (97.4)	10.6 (-2.0, 23.3)	0.10	582.2 (49.9)	580.2 (43.5)	-5.0 (-11.8, 1.9)	0.15
Glucose	661.4 (94.0)	699.7 (117.4)	-20.4 (-41.6, 0.8)	0.06	580.8 (47.3)	591.6 (57.4)	-5.3 (-22.3, 11.8)	0.54
Blood pressure	643.5 (82.4)	683.4 (104.6)	-22.7 (-33.5, -11.9)	<0.001	581.7 (50.1)	591.9 (43.5)	0.8 (-11.4, 12.9)	0.90
BMI	644.3 (91.7)	674.2 (97.5)	-19.9 (-31.8, -8.0)	0.001	579.5 (49.0)	593.0 (49.7)	-6.9 (-15.6, 1.7)	0.12
Diet	660.3 (99.7)	664.4 (96.7)	-4.8 (-19.1, 9.5)	0.51	583.0 (44.9)	583.0 (50.5)	7.7 (0.0, 15.4)	0.05
Physical activity	666.6 (100.2)	660.4 (94.3)	12.4 (0.0, 24.8)	0.05	583.4 (48.6)	582.6 (53.0)	0.4 (-9.5, 10.3)	0.93
Smoking	663.6 (99.6)	662.0 (76.3)	2.9 (-16.3, 22.1)	0.77	581.5 (51.7)	587.8 (43.3)	-2.4 (-11.2, 6.5)	0.60

ICVH indicates Ideal Cardiovascular Health; SD, standard deviation; CI, confidence interval; BMI, body mass index; PWV, pulse wave velocity; IMT, intima-media thickness; SEP, socioeconomic position.

<sup>a</sup> Estimates derived from survey-weighted complete case analyses which were otherwise unadjusted.

<sup>b</sup> Adjusted difference is the estimated difference for a single metric higher ICVH score, or the estimated difference when an individual fulfils criteria for each individual metric. Adjusted models use survey weights and complete cases, and are adjusted for participant age, sex, socioeconomic position, and assessment center. In secondary analyses of individual metrics, models are additionally adjusted for other ICVH metrics. Sample size of the adjusted model listed at the top of each outcome.

have questioned the role of the diet metric in the ICVH score, citing the very low prevalence of ideal health in the diet metric in studies, and unclear additional value in stratifying risk [2]. Other possible confounders not available to these analyses included ethnicity and alcohol use. Finally, blood samples were collected after a semi-fast (median time of 4.2 h) rather than a traditional 8-hour fast as stipulated by the Score definitions. For many large population-based studies 8-hour fasting samples are not feasible. We do not think this would have resulted in misclassification of the glucose metric, since glucose levels are very similar by the end of a 3-hour fast to those following a traditional >8-hour fast. Moreover, prevalence of ideal glucose levels in our semi-fasted sample is comparable to other published studies using fasted samples [14,19].

The size of association between different components of the ICVH score and the vascular phenotypes varies (Table 3), suggesting that contributions of each metric towards the score may not be equal. Weighting each metric to reflect this, however, could undermine the original purpose of the score as a simple tool to easily assess patients' health and set future health goals. While additional research would be required to ascertain appropriate weightings, the current iteration of the ICVH score has been robustly associated with CVD-related mortality [3] and CVD events [4].

Few children and fewer parents have Ideal Cardiovascular Health in high income countries, including Australia. Lower ICVH scores were associated with adverse structural and functional adult vascular phenotypes, and robustly associated with adverse functional but not structural phenotypes in children. Specifically, BMI and blood pressure were strongly associated with vascular phenotypes. Optimizing blood pressure and reducing obesity in childhood could delay onset and progression of subclinical atherosclerosis and may reduce later cardiovascular

disease. Focus on family-wide interventions may have additional benefit for child cardiovascular health.

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### CRediT authorship contribution statement

**Richard S. Liu:** Conceptualization, Investigation, Methodology, Formal analysis, Writing - original draft. **Melissa Wake:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing - review & editing. **Anneke Grobler:** Formal analysis, Writing - review & editing. **Michael Cheung:** Methodology, Writing - review & editing. **Kate Lycett:** Writing - review & editing. **Sarath Ranganathan:** Writing - review & editing. **Ben Edwards:** Writing - review & editing. **Terence Dwyer:** Writing - review & editing. **Peter Azzopardi:** Writing - review & editing. **Markus Juonala:** Conceptualization, Supervision, Writing - review & editing. **David P. Burgner:** Conceptualization, Funding acquisition, Supervision, Writing - review & editing.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2018.11.020>.

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