SUPPLEMENTAL MATERIAL

Effects of arterial stiffness and carotid intima-media thickness progression on the risk of overweight/obesity and elevated blood pressure/hypertension: a cross-lagged cohort study

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Detailed Methods

Data Availability Statement

The informed consent obtained from the Avon longitudinal study of parents and children (ALSPAC) participants does not allow the data to be made freely available through any third party maintained public repository. However, data used for this submission can be made available on request to the ALSPAC Executive. The ALSPAC data management plan describes in detail the policy regarding data sharing, which is through a system of managed open access. Full instructions for applying for data access can be found here: http://www.bristol.ac.uk/alspac/researchers/access/.

Study cohort

Data were from the ALSPAC birth cohort, which investigates factors that influence childhood development and growth. Altogether, 14,541 pregnancies from women residing in Avon, southwestern England, UK, who had a total of 14,676 fetuses, were enrolled between April 1, 1991, and December 31, 1992. When the oldest children were approximately 7 years of age, an attempt was made to bolster the initial sample with eligible cases who had failed to join the study originally resulting in 913 additional pregnancies. The total sample size for analyses using any data collected after 7 years of age is 15,454 pregnancies, resulting in 15,589 foetuses. Of these 14,901 were alive at 1 year of age. Regular clinic visits of the children commenced at 7 years of age and are still ongoing. Study data at 24.5 years were collected and managed using REDCap electronic data capture tools.[1] For our analysis, we included participants who had both cfPWV and cIMT measurements at age 17.7 years (Figure S1). The demographic characteristics of excluded participants were similar to those included in this study as described in the supplementary appendix. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics[2-4] was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004).

Anthropometry and body composition

Anthropometry (height and weight) at ages 17.7 and 24.5 years was assessed using standard protocols.[5] At ages 17.7 and 24.5 years, body composition (total fat mass, trunk fat mass, and lean mass) was assessed using a dual-energy Xray absorptiometry (DEXA) scanner as earlier described.[5-7]*(Agbaje AO, Barker AR, Tuomainen T-P, Unpublished data, 2021)*. We calculated body mass index by dividing weight by squared height. Participants at >75th percentile of total fat mass, trunk fat mass or having >24.9 kg/m^2 of body mass index were classified as overweight and obese while those below this cut points were classified as normal weight.[8-10] A high lean mass category included participants having >75th percentile of lean mass while those below this threshold were considered having normal lean mass.[8]

Vascular phenotype

At age 17.7 years, cfPWV was computed from pressure waveforms obtained using the Vicorder device (Skidmore Medical, Bristol, UK), while cIMT was assessed by ultrasound using a linear 12-MHz transducer (Vivid7, GE Medical, Chicago, Illinois) as earlier described.[5,6,9,10] At 24.5 years, cfPWV was measured, five minutes after resting in a semi-prone position, using a Vicorder instrument (Skidmore Medical, Bristol, UK) with two blood pressure (BP) measurement channels and two Velcro pressure sensor cuffs applied over each of the carotid and femoral arteries. The cfPWV measurement was repeated until three readings that were within 0.5 m/sec of each other had been recorded. The right and left common carotid arteries at age 24 years were imaged using an ultrasound machine (CardioHealth Panasonic and a 13.5 MHz linear array broadband transducer (probe; centre frequency 9.0 MHz).[5] Participants were placed in a supine position with the head rotated by 45 degrees from the midpoint. An automated guide line was placed at the bulb (a

longitudinal scan that included the common carotid artery and the carotid bifurcation) with the region-of-interest box and IMT trace lines automatically positioned 1 cm away from the guide line. The scanner automatically saved an image when the region-of-interest box turned green, indicating good image quality. An automated cIMT measurement, recorded from the posterior wall of the artery, was saved after three consecutive cardiac cycles. When interrogating the common carotid, the CardioHealth system calculated and displayed the cIMT that is updated at each detected R-wave of the cardiac cycle. Once the measurement achieved a predefined quality threshold, scanning automatically stopped and a report was generated. Raw data were checked for outliers and cIMT value >1.0 mm was reviewed by a trained research scientist to assess validity. Abnormal values due to measurement error were removed. Participants had between 1 to 3 cIMT measures for each of the right and left carotid arteries. For our analysis, we computed the mean of the average measurement of the right and left common carotid arteries as cIMT.

Cardiometabolic and lifestyle factors

Pulse rate and BP were measured at ages 17 years as previously detailed.[6,7] BP readings at the 24-year clinic visit were taken using an Omron M6 upper arm BP/pulse monitor. Participants were asked to sit and rest for two minutes prior to taking the first seated BP reading. Participants were categorized as normotensive if systolic BP is <120 mm Hg and elevated BP or hypertension when systolic BP is >120 mmHg. Only 6 participants received anti-hypertensive medication at age 17 years. Using standard protocols, blood samples at ages 17.7, and 24.5years were collected, spun, and frozen at –80 °C and a detailed assessment of fasting glucose, insulin, high sensitivity C-reactive protein, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol, and triglycerides, has been reported (coefficient of variation was <5%).[5,6]

Questionnaire to assess smoking behavior were administered at the 17-year[6] and 24-year clinic visits. The participants were asked whether they smoked in the last 30 days, smoked a whole cigarette, smoked every day, their frequency of use, etc. At the 17-year clinic visit, participants were briefly asked about their personal and family (mother, father, and siblings) medical history such as, a history of hypertension, diabetes, high cholesterol, and vascular disease. Physical activity at age 15.5 years was assessed with ActiGraphTM accelerometer worn for 7 days. Moderate to vigorous physical activity cut point was >2296 count per minute.[5] At 24.5 years physical activity was assessed using ActiGraph GT3X+ accelerometer device worn for four consecutive days, ideally starting the day after the clinic visit. Moderate to vigorous physical activity reported in minutes per day was based on a previously established cutoff of >2020 count per minute.[11] Valid days were considered as wear time of at least 500 minutes, after excluding intervals of >60 minutes of zero counts.

Missing data and multiple imputations

Eligible sample size varied by predictor and outcome measure, as presented in Tables S2 and S3. Exclusions via listwise deletion of missing values ranged from 15.6 to 63.9 percent for covariates. We restricted study participants to those who had complete outcome variables at age 17 years follow-up (n=3862) and complete predictors and outcome variables at 24 years of age follow-up (n=1799). We conducted a Little's missing completely at random (MCAR) test to ascertain data missingness.[12] Little's MCAR test: Chi-Square = 683.366, Degree of freedom = 409, P-value <0.0001, made us conclude that the variables are not missing completely at random. Regression modeled multiple imputations were conducted using SPSS version 27 (IBM Corp, Armonk, NY, USA). Imputed variables are described in Tables S4 and S5. The observed minimum and maximum values were constraints for the imputation process and 20 cycles of imputation with 10 iterations resulted in 20 imputed data sets. The multiple imputation module in SPSS pooled the results from these imputed data. In line with previous evidence (3), the percentage of missing values would be sufficiently addressed with 20 imputations: the variable with the highest missing value (63.9%, moderate to vigorous physical activity) had an estimate that was 98% efficient after 20 imputations

(computed using Rubin's formula).[12] The distributions of imputed covariates had the same pattern as in the observed data as evidenced in the histogram normality plot. Variable distributions after imputation (mean, SD, and percentages) were similar to the observed data (Table S6). Descriptive characteristics of participants based on overweight/obesity and elevated BP categories are presented in Tables S7-10. Where multiple imputations have been conducted, presenting imputed results is preferred to presenting non-imputed results (pairwise or listwise deletion).[13]

Statistical Analysis

Participant's descriptive characteristics were summarized as means and standard deviation, medians, and interquartile ranges, or frequencies and percentages. We explored sex differences using Independent t-tests, Mann Whitney-U tests, or Chi-square tests for normally distributed, skewed or dichotomous variables, respectively. We assessed the normality of variables by histogram curve, quantile-quantile plot, and Kolmogorov-Smirnov tests. We conducted a logarithmic and reciprocal transformation of skewed variables and confirmed normality prior to further analysis.

We investigated the separate cross-sectional associations of cfPWV and cIMT with binary categories of total fat mass, trunk fat mass, lean mass, body mass index, systolic BP, and diastolic BP at either 17.7 or 24.5 years using logistic regression analyses. The logistic regression outcome variables were defined as participants at >75th percentile of total fat mass, trunk fat mass or having >24.9 kg/m^2 body mass index were overweight and obese. A high lean mass category included participants at >75th percentile. Participants with BP >120/80 mm Hg were grouped as elevated BP and hypertension. All analyses were adjusted for age, sex, low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, systolic BP, and fat mass and/or lean mass depending on the outcome, moderate to vigorous physical activity, smoking status, and family history of hypertension/diabetes/high cholesterol/vascular disease. All covariates were specific to the age analysed i.e covariates at age 17.7 years for analysis at 17.7 years and covariates at 24.5 years for cross-sectional analysis at age 24.5 years.

We investigated the separate longitudinal associations of cfPWV and cIMT at 17.7 years with each of total fat mass, trunk fat mass, lean mass, body mass index, systolic BP, and diastolic BP categories at 24.5 years using binary logistic regression. Univariable analysis was adjusted for sex, while multivariable analysis was adjusted for baseline covariates such as sex, age, low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, fasting blood glucose, heart rate, diastolic or systolic BP, and fat mass and/or lean mass depending on the outcome, moderate to vigorous physical activity at 15.5 years, smoking status and family history of hypertension/diabetes/high cholesterol/vascular disease.

We examined the separate prospective associations of the 7-year progression in cfPWV and cIMT with the longitudinal progression in each of total fat mass, trunk fat mass, lean mass, body mass index, systolic BP, and diastolic BP measured from ages 17.7 through 24.5 years using linear mixed effect models for repeated measures with restricted maximum likelihood estimation. The estimates quantify the effect of the longitudinal progression in the predictors on the longitudinal progression in the outcome variables. We decided a priori to select the model with the least Bayesian information criterion (BIC). The least BIC resulted in a model with gender as a factor and a random intercept modeled on the subject level. We selected a variance component covariance type and determined the effect of the change in predictors on change in outcome variables. All analyses were adjusted for sex, age at 17.7 years, and covariates measured at 17.7 and 24.5 years such as low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, diastolic or systolic BP and fat mass and/or lean mass depending on the outcome, smoking status, family history of

hypertension/diabetes/high cholesterol/vascular disease and moderate to vigorous physical activity at 15.5 and 24.5 years.

Lastly, we used structural equation modeling with autoregressive cross-lagged design to examine the separate temporal associations of cfPWV and cIMT with total fat mass, trunk fat mass, lean mass, body mass index, and BP. The cross-lagged models first tested the separate associations of cfPWV and cIMT at 17.7 years with each of total fat mass, trunk fat mass, lean mass, body mass index, and BP at 24.5 years; and secondly tested the separate associations of total fat mass, trunk fat mass, lean mass, body mass index, and BP at 17.7 years with cfPWV and cIMT at 24.5 years. These models were adjusted for all the baseline covariates listed above, including the time in years between 17.7 and 24.5 years. In the cross-lagged design, the potential association could be: cfPWV and cIMT leading to body composition and BP, body composition and BP leading to cfPWV and cIMT or bidirectional associations of cfPWV and cIMT with body composition and BP. If a path from cfPWV and cIMT at time t-1 (17.7 years) to body composition and BP at time t-2 (24.5 years) reach significant (p-value<0.05), changes in the earlier variables are considered to lead to changes in the later one, and vice versa. A stronger predictive effect is determined by a larger standardized regression coefficient. We concluded that the cross-lagged models had good fit with the following indices: the root-mean-square error of approximation (<0.019, the value <0.05 is considered to indicate a good model-data fit), the normed fit index (>1.000), the relative fit index (>0.966), the incremental fit index (>1.000), the Tucker–Lewis Fit Index (>0.980), the comparative fit index (>1.000), which are considered good fit if values are >0.90.[14]

All covariates were selected based on previous studies.[5-8,15] *(Agbaje AO, Barker AR, Tuomainen T-P, Unpublished data, 2021)* We excluded pubertal status/somatic maturation from the model because all participants had reached adult-like maturity status by 17.7 years of age. We performed collinearity diagnoses and accepted results with a variance inflation factor <5. There were a few statistically significant sex interactions however, we presented both the combined results adjusted for sex and sex-stratified results when there are statistically significant differences. The sex-stratified results are presented in the supplemental results. We also presented cross-sectional analyses result in Table S11. For sensitivity analyses, we examined the quartile categories (high, moderate-high, moderate-low, and low) of cfPWV and cIMT progression with the increase in body composition and BP and presented the result in Table S12. The lowest category being the reference. We considered differences and associations with a 2-sided p-value <0.05 as statistically significant and made conclusions based on effect estimates, their confidence intervals or standard errors. Analyses involving 40% of a sample of 10,000 ALSPAC children at 0.8 statistical power, 0.05 alpha, and 2-sided p-value would show a minimum detectable effect size of 0.049 standard deviations if they had relevant exposure for a normally distributed quantitative variable.[16] All statistical analyses were performed using SPSS statistics software, Version 27.0 (IBM Corp, Armonk, NY, USA) and structural equation modeling was conducted using IBM AMOS version 27.0.

Supplemental results

Results

Study population and characteristics

Altogether 14,901 children in the ALSPAC birth cohort were alive at 1 year of age, of whom 5217 adolescents participated in the 17.7-year follow-up clinic visit while 4026 young adults participated in the 24.5-year follow-up clinic visit (Figure S1). Only 3862 participants who had complete cfPWV and cIMT measurements at age 17.7 years were included in the study. At the 24.5-year follow-up clinic visit, 1799 participants had complete measurements for total fat mass, trunk fat mass, lean mass, systolic and diastolic BP, cfPWV, and cIMT. The female participants consistently had higher total fat mass and trunk fat mass, lower lean mass at ages 17.7 and 24.5-years follow-up when compared to the males. However, the significant sex difference in body mass index, low-density lipoprotein cholesterol, and smoking status between sexes at age 17.7 years was attenuated 7 years later. Female participants consistently had lower systolic BP, cfPWV, and cIMT but higher heart rates at ages 17.7 and 24.5-year follow-ups in contrast to the males. The prevalence of overweight/obesity at 17.7 and 24.5 years was 20% and 38% respectively. The prevalence of elevated systolic BP/hypertension at 17.7 and 24.5 years was 26% and 33%, respectively. Other characteristics of our study participants are shown in Table 1 and in Tables S7-S10

Cross-sectional associations of cfPWV and cIMT with fat mass, lean mass, and blood pressure at age 17.7 years

Increased cfPWV was associated with reduced risk for overweight and obesity. cfPWV was directly associated with high lean mass, measured as >75th percentile, elevated systolic and diastolic BP, and hypertension, measured as >120/80 mmHg (Table S11).

cIMT was associated with reduced risk of overweight and obesity measured as >75th percentile of total fat mass and trunk fat mass, and >24.9 kg/m^2 body mass index, but an increased risk for high lean mass, measured as >75th percentile, and elevated systolic BP and hypertension at 17.7 years of age. cIMT was not associated with elevated diastolic BP and hypertension (Table S11).

Cross-sectional associations of cfPWV and cIMT with fat mass, lean mass, and blood pressure at age 24.5 years

At age 24.5 years, cfPWV was associated with decreased risk for overweight and obesity measured >24.9 kg/m^2 body mass index, and higher risk for high lean mass, measured as >75th percentile, and elevated diastolic BP and hypertension, measured as >80 mmHg (Table S11).

cIMT at age 24.5 years was associated with increased risk for high lean mass, measured as >75th percentile, and elevated systolic BP and hypertension at 24.5 years of age. cIMT was not associated with diastolic hypertension and obesity assessed via total fat mass, trunk fat mass, or body mass index (Table S11).

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Results

Table S1 Characteristics of participants excluded from the study

Variables	**Included participants**		**Excluded participants**			
	Mean (SD)	**n**	**Mean/SD**	**n**	***P* for difference**	**Cohen's D**
Age (years)	17.72 (0.32)	3862	18.12 (0.61)	1349	**<0.0001**	0.82
Anthropometry and body composition						
Body height (m)	1.71 (0.09)	3806	1.71 (0.10)	1259	**0.007**	0
*Weight (kg)	64.40 (142.6)	3811	66.30 (119.3)	1253	**<0.0001**	0.25
*Body mass index (kg/m^2)	21.78 (52.1)	3806	22.69 (46.9)	1253	**<0.0001**	0.32
Lean mass (kg)	45.53 (9.88)	3757	45.72 (10.47)	1090	0.584	NA
*Total fat mass (kg)	16.01 (80.8)	3757	17.70 (71.3)	1090	**<0.0001**	0.29
*Trunk fat mass (kg)	7.88 (45.5)	3757	8.87 (40.6)	1090	**<0.0001**	0.29
Metabolic profile						
Total cholesterol (mmol/L)	3.75 (0.68)	2586	3.77 (0.70)	699	0.422	NA
HDL (mmol/L)	1.27 (0.30)	2586	1.27 (0.30)	699	0.911	NA
LDL (mmol/L)	2.10 (0.61)	2586	2.11 (0.61)	699	0.740	NA
*Triglyceride (mmol/L)	0.75 (3.47)	2586	0.77 (3.89)	699	0.065	0.10
*C-reactive protein (mg/L)	0.54 (1.01)	2586	0.61 (0.40)	699	**0.039**	0.06
*Insulin (mU/L)	6.67 (89.1)	2543	6.94 (193.6)	688	**0.001**	0.19
Glucose (mmol/L)	5.04 (0.62)	2586	5.04 (0.46)	699	0.770	NA
Vascular measure						
Pulse rate (beats/mins)	65 (10)	3854	66 (10)	809	0.197	NA
Systolic BP (mm Hg)	114 (10)	3854	114 (11)	809	0.694	NA
Diastolic BP (mm Hg)	64 (6)	3854	66 (7)	809	**<0.0001**	0.31
*Carotid IMT (mm)	0.47 (0.35)	3861	0.48 (0.27)	815	0.807	NA
*Carotid-femoral PWV (m/s)	5.70 (7.68)	3857	5.62 (3.54)	26	0.389	NA
Lifestyle factors						
Smoking status (n, %)	911 (27.2)	3344	268 (31.4)	853	**0.017**	NA
Family history of HDCV (n, %)	1162 (30.1)	3857	289 (31.2)	927	0.533	NA

The values are means (standard deviations) and *median (range/interquartile range) except for maturation status and social economic status in percentage. Differences between participants were tested using Student's t-test for normally distributed continuous variables, Mann–Whitney U test for skewed continuous variables, and Chi-square test for dichotomous variable. A 2-sided P-value <0.05 is considered statistically significant and is bolded. Cohen's D effect size was calculated for statistically significant differences: 0.2 = low, 0.5 = moderate, 0.8 = large effect.

HDCV, hypertension/diabetes/high cholesterol/vascular disease; IMT, intima media thickness; NA, not applicable; PWV, pulse wave velocity; Smoking status, participants had smoked cigarette in the past 30 days.

Table S2 Missing data at 24.5 years of age

Variable	n (valid sample size)	Eligible sample size	% Missing
Age	1799	1799	0
Sex	1799	1799	0
Anthropometry and body composition			
Height (m)	1799	1799	0
Weight (kg)	1799	1799	0
Body mass index	1799	1799	0
Lean mass (kg)	1799	1799	0
Lean mass indexed for squared height (kg/m^2)	1799	1799	0
Total fat mass (kg)	1799	1799	0
Total fat mass indexed for squared height (kg/m^2)	1799	1799	0
Trunk fat mass (kg)	1799	1799	0
Trunk fat mass indexed for squared height (kg/m^2)	1799	1799	0
Metabolic profile			
Low-density lipoprotein (mmol/L)	1490	1799	17.2
Glucose (mmol/L)	1491	1799	17.1
C-reactive protein (mg/L)	1352	1799	24.8
Vascular measure			
Systolic blood pressure (mm Hg)	1799	1799	0
Diastolic blood pressure (mm Hg)	1799	1799	0
Carotid-femoral pulse wave velocity (m/s)	1799	1799	0
Carotid intima-media thickness (mm)	1799	1799	0
Lifestyle factors			
Moderate to vigorous physical activity (mins/day)	649	1799	63.9
Smoking status	1779	1799	1.1
Family history of H-C-D-V	1519	1799	15.6

H-D-C-V, hypertension/diabetes/high cholesterol/vascular disease

Table S3 Missing data at 17.7 years of age

Variable	n (valid sample size)	Eligible sample size	% Missing
Age	3862	3862	0
Sex	3862	3862	0
Anthropometry and body composition			
Height (m)	3806	3862	1.5
Weight (kg)	3811	3862	1.3
Body mass index	3806	3862	1.5
Lean mass (kg)	3756	3862	2.8
Lean mass indexed for squared height (kg/m^2)	3737	3862	3.3
Total fat mass (kg)	3756	3862	2.8
Total fat mass indexed for squared height (kg/m^2)	3737	3862	3.3
Trunk fat mass (kg)	3756	3862	2.8
Trunk fat mass indexed for squared height (kg/m^2)	3737	3862	3.3
Metabolic profile			
Low-density lipoprotein (mmol/L)	2587	3862	33.0
Glucose (mmol/L)	2587	3862	33.0
C-reactive protein (mg/L)	2587	3862	33.0
Vascular measure			
Systolic blood pressure (mm Hg)	3856	3862	0.2
Diastolic blood pressure (mm Hg)	3856	3862	0.2
Carotid-femoral pulse wave velocity (m/s)	3862	3862	0
Carotid intima-media thickness (mm)	3862	3862	0
Lifestyle factors			
Smoking status	3344	3862	27.2
Family history of H-C-D-V	3859	3862	0.1

H-D-C-V, hypertension/diabetes/high cholesterol/vascular disease

Table S4 Variables used in multivariable multiple imputation model at 24.5 years

Variable	Missing values imputed in this variable	Imputed values			
		Minimum	Maximum	Rounding	(n) imputed
Age (years)	NA, no missing			Integer	
Sex	NA, no missing				
Anthropometry and body composition					
Height (m)	NA, no missing				
Weight (kg)	NA, no missing				
Body mass index (kg/m^2)	NA, no missing				
Lean mass (kg)	NA, no missing				
Lean mass indexed for squared height (kg/m^2)	NA, no missing				
Total fat mass (kg)	NA, no missing				
Total fat mass indexed for squared height (kg/m^2)	NA, no missing				
Trunk fat mass (kg)	NA, no missing				
Trunk fat mass indexed for squared height (kg/m^2)	NA, no missing				
Metabolic profile					
Low-density lipoprotein (mmol/L)	Yes	0.15	5.73		309
Glucose (mmol/L)	Yes	3.59	22.15		308
C-reactive protein (μg/ml)	Yes	0.10	164.42		447
Vascular measure					
Systolic blood pressure (mm Hg)	NA, no missing				
Diastolic blood pressure (mm Hg)	NA, no missing				
Carotid-femoral pulse wave velocity (m/s)	NA, no missing				
Carotid intima media thickness (mm)	NA, no missing				
Lifestyle factors					
Moderate to vigorous physical activity	Yes	3.17	181.06		1150
Smoking status	Yes	0	1		20
Family history of H-D-C-V	Yes	1	2		280

H-D-C-V, hypertension/diabetes/high cholesterol/vascular disease; NA, not applicable

Table S5 Variables used in multivariable multiple imputation model at 17.7 years

Variable	Missing values imputed in this variable	Imputed values			
		Minimum	Maximum	Rounding	(n) imputed
Age (years)	NA, no missing	16.25	19.92	Integer	0
Sex	NA, no missing				0
Anthropometry and body composition					
Height (m)	Yes	1.47	2.08		57
Weight (kg)	Yes	21.40	144.0		52
Body mass index (kg/m^2)	Yes	9.36	41.49		57
Lean mass (kg)	Yes	23.72	74.81		107
Lean mass indexed for squared height (kg/m^2)	Yes	7.27	21.87		126
Total fat mass (kg)	Yes	1.68	65.56		107
Total fat mass indexed for squared height (kg/m^2)	Yes	0.51	20.77		126
Trunk fat mass (kg)	Yes	0.96	38.01		107
Trunk fat mass indexed for squared height (kg/m^2)	Yes	0.30	11.62		126
Metabolic profile					
Low-density lipoprotein (mmol/L)	Yes	0.23	5.10		1276
Glucose (mmol/L)	Yes	3.44	8.66		1276
C-reactive protein (µg/ml)	Yes	0.20	86.47		1276
Vascular measure					
Systolic blood pressure (mmnHg)	Yes	82.5	152.0		7
Diastolic blood pressure (mm Hg)	Yes	42.3	104.0		7
Carotid-femoral pulse wave velocity (m/s)	NA, no missing	4.27	11.46		0
Carotid intima media thickness (mm)	NA, no missing	0.35	0.63		0
Lifestyle factors					
Smoking status	Yes	1	2		518
Family history of H-D-CV	Yes	1	2		4

H-D-CV, hypertension/diabetes/high cholesterol/vascular disease; NA, not applicable

Table S6 Characteristics of cohort participants at age 24.5 years (imputed data)

Variable	Observed data set Mean/SD	Imputed data set Mean/SD
Age	24.32 (0.63)	NA
Sex, male (n,%)	684 (38)	NA
Anthropometry and body composition		
Height (m)	1.72 (0.09)	NA
Weight (kg)		NA
[a]Body mass index (kg/m^2)	24.62 (4.68)	NA
[a]Lean mass (kg)	47.21 (9.79)	NA
[a]Lean mass indexed for squared height (kg/m^2)	15.91 (2.17)	NA
[a]Total fat mass (kg)	22.91 (10.16)	NA
[a]Total fat mass indexed for squared height (kg/m^2)	7.88 (3.61)	NA
[a]Trunk fat mass (kg)	10.99 (5.86)	NA
[a]Trunk fat mass indexed for squared height (kg/m^2)	3.77 (2.04)	NA
Metabolic profile		
Low-density lipoprotein (mmol/L)	2.38 (0.74)	2.40 (0.74)
Glucose (mmol/L)	5.33 (0.70)	5.32 (0.70)
[a]C-reactive (mg/L)	2.19 (6.00)	2.79 (5.83)
Vascular measure		
Systolic blood pressure (mm Hg)	115 (11)	NA
Diastolic blood pressure (mm Hg)	67 (8)	NA
[a]Carotid-femoral pulse wave velocity (m/s)	6.27 (1.08)	NA
[a]Carotid intima media thickness (mm)	0.46 (0.05)	NA
Lifestyle factors		
Moderate to vigorous physical activity	49.60 (29.9)	52.0 (29.1)
Smoked cigarette in the last 30 days, Yes, (n,%)	455 (25.6)	20 (1.1)
Family history of H-C-D-V, Yes, (n,%)	473 (31.1)	559 (31.1)

H-D-C-V, hypertension/diabetes/high cholesterol/vascular disease; NA, Not applicable; [a]skewed variables presented as median and inter quartile range

Table S7 Descriptive characteristics of participants based on body mass index classification of normal weight and overweight and obesity at age 17.7 years

	Male					Female				
Variables	**Normal weight**		**Overweight and obesity**		**P-value**	**Normal weight**		**Overweight and obesity**		**P-value**
	N	Mean (SD)	N	Mean (SD)		N	Mean (SD)	N	Mean (SD)	
Anthropometry										
Height (m)	1390	1.79 (0.07)	303	1.78 (0.07)	0.438	1648	1.66 (0.06)	464	1.65 (0.06)	0.193
*Weight (kg)	1390	66.85 (11.10)	303	87.30 (13.60)	**<0.0001**	1648	57.50 (9.90)	464	75.65 (12.28)	**<0.0001**
Body composition										
*Total fat mass (kg)	1367	8.81 (6.54)	297	25.48 (11.85)	**<0.0001**	1618	17.30 (7.04)	454	32.22 (9.97)	**<0.0001**
*Trunk fat mass (kg)	1367	4.45 (3.44)	297	14.05 (6.74)	**<0.0001**	1618	8.37 (3.87)	454	16.98 (5.98)	**<0.0001**
Lean mass (kg)	1367	54.38 (5.89)	297	57.66 (6.09)	**<0.0001**	1618	37.34 (3.80)	454	40.01 (4.44)	**<0.0001**
*Body mass index (kg/m^2)	1390	20.99 (2.90)	303	27.11 (3.55)	**<0.0001**	1648	21.18 (3.06)	454	27.48 (4.39)	**<0.0001**
Metabolic profile										
Total Cholesterol (mmol/L)	1030	3.51 (0.59)	227	3.77 (0.69)	**<0.0001**	1013	3.93 (0.69)	278	3.97 (0.67)	0.337
High density lipoprotein (mmol/L)	1030	1.21 (0.26)	227	1.07 (0.24)	**<0.0001**	1013	1.38 (0.31)	278	1.23 (0.30)	**<0.0001**
Low density lipoprotein (mmol/L)	1030	1.95 (0.53)	227	2.23 (0.64)	**<0.0001**	1013	2.17 (0.62)	278	2.32 (0.63)	**0.001**
*Triglyceride (mmol/L)	1030	0.72 (0.32)	277	0.91 (0.53)	**<0.0001**	1013	0.75 (0.35)	278	0.81 (0.44)	**0.001**
Glucose (mmol/L)	1030	5.15 (0.75)	227	5.23 (0.38)	0.145	1013	4.89 (0.53)	278	4.98 (0.42)	**0.006**
*Insulin (mU/L)	1013	5.66 (3.49)	226	8.81 (6.17)	**<0.0001**	991	6.91 (3.99)	275	9.40 (5.85)	**<0.0001**
*High sensitivity C-reactive protein (mg/L)	1030	0.39 (0.55)	227	0.77 (1.22)	**<0.0001**	1013	0.60 (1.08)	278	1.10 (2.10)	**<0.0001**
Vascular measures										
Pulse rate (beat/mins)	1388	63 (9)	303	64 (10)	**0.021**	1645	67 (10)	462	69 (10)	**0.008**
Systolic blood pressure (mm Hg)	1388	119 (9)	303	124 (9)	**<0.0001**	1645	109 (7)	462	114 (8)	**<0.0001**
Diastolic blood pressure (mm Hg)	1388	63 (6)	303	66 (7)	**<0.0001**	1645	64 (6)	462	68 (7)	**<0.0001**
*Carotid-femoral PWV (m/s)	1390	5.95 (0.85)	303	6.01 (0.78)	0.853	1648	5.45 (0.74)	464	5.56 (0.73)	**0.006**
*Carotid IMT (mm)	1390	0.48 (0.06)	303	0.48 (0.06)	0.996	1648	0.47 (0.05)	464	0.47 (0.07)	0.346

The values are means (standard deviations) and *median (interquartile range). Differences were tested using Student's t-test for normally distributed continuous variables and Mann–Whitney U test for skewed continuous variables. A 2-sided P-value <0.05 is considered statistically significant. Body mass index was classified as <24.99 as normal weight and >24.99 as overweight and obese

Table S8 Descriptive characteristics of participants based on body mass index classification of normal weight and overweight and obesity at age 24.5 years

	Male					Female				
Variables	**Normal weight**		**Overweight and obesity**		**P-value**	**Normal weight**		**Overweight and obesity**		**P-value**
	N	Mean (SD)	N	Mean (SD)		N	Mean (SD)	N	Mean (SD)	
Anthropometry										
Height (m)	571	1.81 (0.07)	377	1.79 (0.07)	**0.006**	933	1.66 (0.06)	550	1.66 (0.06)	0.131
*Weight (kg)	571	71.70 (11.30)	377	89.0 (13.80)	**<0.0001**	933	60.40 (8.75)	550	79.30 (16.45)	**<0.0001**
Body composition										
*Total fat mass (kg)	554	14.72 (5.66)	371	25.99 (11.51)	**<0.0001**	907	18.49 (5.98)	526	32.71 (12.54)	**<0.0001**
*Trunk fat mass (kg)	554	6.94 (3.44)	371	13.57 (7.26)	**<0.0001**	907	7.94 (3.30)	526	16.06 (7.22)	**<0.0001**
Lean mass (kg)	554	53.93 (6.20)	371	60.77 (6.83)	**<0.0001**	907	39.36 (4.10)	526	44.61 (5.05)	**<0.0001**
*Body mass index (kg/m^2)	571	22.17 (2.65)	377	27.32 (3.63)	**<0.0001**	933	21.88 (2.92)	550	28.54 (5.47)	**<0.0001**
Metabolic profile										
Total Cholesterol (mmol/L)	510	4.19 (0.81)	324	4.60 (0.84)	**<0.0001**	753	4.44 (0.84)	407	4.55 (0.78)	**0.023**
High density lipoprotein (mmol/L)	510	1.49 (0.37)	324	1.28 (0.33)	**<0.0001**	753	1.75 (0.41)	407	1.49 (0.40)	**<0.0001**
Low density lipoprotein (mmol/L)	509	2.29 (0.74)	323	2.74 (0.80)	**<0.0001**	753	2.30 (0.72)	407	2.57 (0.74)	**<0.0001**
*Triglyceride (mmol/L)	509	0.82 (0.42)	324	1.10 (0.75)	**<0.0001**	753	0.76 (0.39)	407	0.93 (0.52)	**<0.0001**
Glucose (mmol/L)	510	5.44 (0.65)	324	5.50 (0.44)	0.138	753	5.14 (0.48)	407	5.36 (0.83)	**<0.0001**
*Insulin (mU/L)	510	6.16 (3.37)	324	9.71 (8.42)	**<0.0001**	753	6.65 (3.74)	407	11.28 (7.70)	**<0.0001**
*High sensitivity C-reactive protein (mg/L)	430	0.49 (0.77)	315	0.95 (1.44)	**<0.0001**	691	0.75 (1.57)	396	1.81 (2.96)	**<0.0001**
Vascular measures										
Pulse rate (beat/mins)	570	63 (9)	376	66 (11)	**<0.0001**	930	68 (10)	548	70 (10)	**<0.0001**
Systolic blood pressure (mm Hg)	570	120 (10)	376	126 (10.2)	**<0.0001**	930	109 (9)	548	116 (9)	**<0.0001**
Diastolic blood pressure (mm Hg)	570	66 (7)	376	70 (8)	**<0.0001**	930	64 (7)	548	70 (8)	**<0.0001**
*Carotid-femoral PWV (m/s)	387	6.53 (1.30)	250	6.40 (1.03)	0.134	635	5.87 (1.03)	368	5.97 (1.0)	**0.004**
*Carotid IMT (mm)	330	0.46 (0.07)	201	0.47 (0.07)	0.159	555	0.45 (0.06)	305	0.45 (0.06)	0.549

The values are means (standard deviations) and *median (interquartile range). Differences were tested using Student's t-test for normally distributed continuous variables and Mann–Whitney U test for skewed continuous variables. A 2-sided P-value <0.05 is considered statistically significant. Body mass index was classified as <24.99 as normal weight and >24.99 as overweight and obese.

Table S9 Descriptive characteristics based on systolic blood pressure classification as normotensive or elevated blood pressure and hypertension at age 17.7 years

	Male					Female				
Variables	**Normotensive**		**Elevated blood pressure**		**P-value**	**Normotensive**		**Elevated blood pressure**		**P-value**
	N	Mean (SD)	N	Mean (SD)		N	Mean (SD)	N	Mean (SD)	
Anthropometry										
Height (m)	896	1.78 (0.07)	795	1.80 (0.07)	**<0.0001**	1918	1.65 (0.06)	189	1.66 (0.06)	0.064
*Weight (kg)	899	66.30 (13.80)	795	72.20 (14.30)	**<0.0001**	1920	59.70 (12.70)	189	69.70 (19.60)	**<0.0001**
Body composition										
*Total fat mass (kg)	885	8.94 (8.31)	788	12.05 (11.15)	**<0.0001**	1887	18.97 (9.74)	188	26.55 (16.66)	**<0.0001**
*Trunk fat mass (kg)	885	4.49 (4.36)	788	6.27 (6.31)	**<0.0001**	1887	9.23 (5.24)	188	13.30 (9.26)	**<0.0001**
Lean mass (kg)	885	53.57 (5.75)	788	56.56 (5.99)	**<0.0001**	1887	37.73 (3.96)	188	39.85 (4.96)	**<0.0001**
*Body mass index (kg/m^2)	896	20.83 (3.28)	795	22.48 (4.24)	**<0.0001**	1918	21.81 (4.16)	189	25.28 (7.62)	**<0.0001**
Metabolic profile										
Total Cholesterol (mmol/L)	673	3.52 (0.59)	602	3.60 (0.64)	**0.036**	1194	3.93 (0.69)	114	3.96 (0.64)	**0.654**
High density lipoprotein (mmol/L)	673	1.19 (0.25)	602	1.18 (0.27)	0.907	1194	1.36 (0.32)	114	1.27 (0.30)	**0.007**
Low density lipoprotein (mmol/L)	673	1.98 (0.55)	602	2.01 (0.57)	0.325	1194	2.20 (0.64)	114	2.28 (0.54)	0.171
*Triglyceride (mmol/L)	673	0.71 (0.32)	602	0.78 (0.39)	**<0.0001**	1194	0.75 (0.37)	114	0.85 (0.42)	**0.008**
Glucose (mmol/L)	673	5.15 (0.53)	602	5.19 (0.84)	0.282	1194	4.90 (0.51)	114	4.98 (0.50)	0.143
*Insulin (mU/L)	666	5.72 (3.76)	591	6.43 (4.37)	**<0.0001**	1171	7.26 (4.25)	112	8.32 (7.73)	**<0.0001**
*High sensitivity C-reactive protein (mg/L)	673	0.39 (0.61)	602	0.51 (0.81)	**0.001**	1194	0.65 (1.23)	114	0.86 (1.74)	**0.003**
Vascular measures										
Pulse rate (beat/mins)	908	62 (9)	809	64 (10)	**<0.0001**	1941	67 (10)	197	71 (11)	**<0.0001**
Systolic blood pressure (mm Hg)	908	113 (5)	809	127 (6)	**<0.0001**	1941	109 (6)	197	125 (5)	**<0.0001**
Diastolic blood pressure (mm Hg)	908	61 (5)	809	66 (6)	**<0.0001**	1941	64 (5)	197	73 (7)	**<0.0001**
*Carotid-femoral PWV (m/s)	908	5.87 (0.86)	809	6.07 (0.78)	**<0.0001**	1941	5.44 (0.73)	197	5.83 (0.82)	**<0.0001**
*Carotid IMT (mm)	908	0.48 (0.06)	809	0.48 (0.06)	**0.018**	1941	0.47 (0.06)	197	0.47 (0.07)	0.116

The values are means (standard deviations) and *median (interquartile range). Differences were tested using Student's t-test for normally distributed continuous variables and Mann–Whitney U test for skewed continuous variables. A 2-sided P-value <0.05 is considered statistically significant. Systolic blood pressure was classified as <120 mmHg as normotensive and >120 mmHg as elevated blood pressure and hypertension.

Table S10 Descriptive characteristics based on systolic blood pressure classification as normotensive or elevated blood pressure and hypertension at age 24.5 years

	Male					Female				
Variables	**Normotensive**		**Elevated blood pressure**		**P-value**	**Normotensive**		**Elevated blood pressure**		**P-value**
	N	Mean (SD)	N	Mean (SD)		N	Mean (SD)	N	Mean (SD)	
Anthropometry										
Height (m)	421	1.79 (0.07)	526	1.81 (0.07)	**0.007**	1212	1.66 (0.06)	267	1.67 (0.06)	**0.023**
*Weight (kg)	421	73.10 (16.60)	525	80.80 (15.85)	**<0.0001**	1213	63.50 (14.65)	266	74.25 (22.60)	**<0.0001**
Body composition										
*Total fat mass (kg)	411	15.65 (9.35)	515	19.70 (10.91)	**<0.0001**	1178	21.15 (10.43)	255	28.46 (16.85)	**<0.0001**
*Trunk fat mass (kg)	411	7.40 (5.33)	515	9.97 (6.71)	**<0.0001**	1178	9.41 (5.85)	255	13.12 (9.42)	**<0.0001**
Lean mass (kg)	411	54.90 (7.10)	515	58.12 (7.12)	**<0.0001**	1178	40.78 (4.88)	255	43.72 (5.56)	**<0.0001**
*Body mass index (kg/m^2)	421	22.75 (4.43)	525	24.74 (4.78)	**<0.0001**	1212	23.02 (4.82)	266	26.95 (7.90)	**<0.0001**
Metabolic profile										
Total Cholesterol (mmol/L)	375	4.30 (0.84)	464	4.38 (0.85)	0.149	975	4.46 (0.83)	194	4.57 (0.75)	0.073
High density lipoprotein (mmol/L)	375	1.45 (0.36)	464	1.37 (0.37)	**0.001**	975	1.68 (0.42)	194	1.54 (0.44)	**<0.0001**
Low density lipoprotein (mmol/L)	374	2.41 (0.79)	463	2.50 (0.79)	0.073	975	2.37 (0.74)	194	2.56 (0.73)	**0.001**
*Triglyceride (mmol/L)	374	0.82 (0.48)	464	0.94 (0.58)	**0.001**	975	0.79 (0.43)	194	0.93 (0.54)	**<0.0001**
Glucose (mmol/L)	375	5.47 (0.71)	464	5.46 (0.46)	0.684	975	5.21 (0.59)	194	5.28 (0.81)	0.188
*Insulin (mU/L)	375	6.35 (4.46)	464	7.52 (5.59)	**<0.0001**	975	7.35 (5.02)	194	10.07 (7.80)	**<0.0001**
*High sensitivity C-reactive protein (mg/L)	322	0.61 (0.95)	428	0.68 (1.24)	**0.014**	907	0.92 (1.90)	188	1.40 (3.25)	**<0.0001**
Vascular measures										
Pulse rate (beat/mins)	424	63 (10)	528	65 (11)	0.122	1226	68 (10)	269	72 (10)	**<0.0001**
Systolic blood pressure (mm Hg)	424	114 (5)	528	130 (8)	**<0.0001**	1226	108 (7)	269	126 (5)	**<0.0001**
Diastolic blood pressure (mm Hg)	424	63 (6)	528	70 (8)	**<0.0001**	1226	65 (6)	269	75 (8)	**<0.0001**
*Carotid-femoral PWV (m/s)	296	6.36 (1.17)	344	6.53 (1.18)	**0.019**	837	5.90 (1.0)	175	6.15 (1.12)	**<0.0001**
*Carotid IMT (mm)	253	0.45 (0.06)	279	0.47 (0.06)	**<0.0001**	720	0.45 (0.06)	146	0.46 (0.06)	**0.012**

The values are means (standard deviations) and *median (interquartile range). Differences were tested using Student's t-test for normally distributed continuous variables and Mann–Whitney U test for skewed continuous variables. A 2-sided P-value <0.05 is considered statistically significant. Systolic blood pressure was classified as <120 mmHg as normotensive and >120 mmHg as elevated blood pressure and hypertension.

Table S11 Cross-sectional associations of carotid-femoral pulse wave velocity and carotid intima-media thickness with increased fat mass, lean mass, and blood pressure at age 17.7 and 24.5 years respectively

3862 participants	***17.7 years of age***											
	Total fat mass (kg)		**Trunk fat mass (kg)**		**Lean mass (kg)**		**Body mass index (kg/m^2)**		**Systolic blood pressure (mm Hg)**		**Diastolic blood pressure (mm Hg)**	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Carotid-femoral pulse wave velocity	0.824 (0.704 – 0.964)	**0.016**	0.819 (0.702 – 0.956)	**0.012**	0.969 (0.820 – 1.146)	0.716	0.811 (0.689 – 0.954)	**0.012**	1.543 (1.344 – 1.772)	**<0.0001**	1.890 (1.268 – 2.819)	**0.002**
Carotid intima-media thickness	0.040 (0.005 – 0.342)	**0.003**	0.034 (0.004 – 0.322)	**0.003**	0.009 (0.001 – 0.103)	**<0.0001**	0.049 (0.005 – 0.476)	**0.009**	13.687 (1.641 – 114.15)	**0.016**	198.23 (0.083 – 472161.3)	0.182
1799 participants	***24.5 years of age***											
Carotid-femoral pulse wave velocity	0.976 (0.843 – 1.130)	0.744	0.912 (0.787 – 1.057)	0.221	0.755 (0.634 – 0.899)	**0.002**	0.844 (0.739 – 0.965)	**0.013**	1.089 (0.962 -1.234)	0.177	1.300 (1.046 – 1.617)	**0.018**
Carotid intima-media thickness	0.117 (0.004 – 3.111)	0.200	0.108 (0.004 – 2.767)	0.179	0.008 (<0.0001 – 0.272)	**0.007**	0.125 (0.006 – 2.721)	0.185	248.58 (15.092 – 4094.15)	**<0.0001**	0.126 (<0.0001 – 34.283)	0.469

Multivariable analysis was adjusted for age, sex, low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, systolic blood pressure and fat mass and/or lean mass depending on the outcome, moderate to vigorous physical activity, smoking status and family history of hypertension/diabetes/high cholesterol/vascular disease. All covariates were specific to the age analysed i.e covariates at age 17.7 years for cross-sectional analysis at 17.7 years. OR, odds ratio from multivariable logistic regression; CI, confidence interval. Multiple imputations were used to account for missing cases. Participants at >75th percentile of total and trunk fat mass or having >24.9 kg/m^2 body mass index were classified as overweight and obese, while others were grouped as having normal weight. Lean mass was reciprocally transformed prior to analysis. A high lean mass category included participants at >75th percentile and others were grouped as having moderate lean mass. Participants with blood pressure >120/80 mm Hg were classified as having elevated blood pressure and hypertension while others had normal blood pressure according to the American Heart Association guideline.

Table S12 Longitudinal progression of quartile categories of arterial stiffness and carotid intima-media thickness in relation to the increase in fat mass, lean mass, and blood pressure from age 17.7 through 24.5 years

	Total fat mass (kg)		**Trunk fat mass (kg)**		**Lean mass (kg)**		**Body mass index (kg/m^2)**		**Systolic blood pressure (mm Hg)**		**Diastolic blood pressure (mm Hg)**	
Carotid-femoral pulse wave velocity	*Effect estimate* (95% CI)	p-value	*Effect estimate* (95% CI)	p-value	*Effect estimate* (95% CI)	p-value	*Effect estimate* (95% CI)	p-value	*Effect estimate* (95% CI)	p-value	*Effect estimate* (95% CI)	p-value
High	-0.050 (-0.075 – -0.024)	**<0.0001**	-0.058 (-0.087 – -0.029)	**<0.0001**	0.008 (0.001 – 0.015)	**0.026**	-0.014 (-0.022 – -0.007)	**<0.0001**	4.104 (2.852 – 5.356)	**<0.0001**	2.581 (1.765 – 3.396)	**<0.0001**
Moderate high	-0.014 (-0.039 – 0.011)	0.281	-0.020 (-0.048 – 0.008)	0.155	0.004 (-0.003 – 0.011)	0.260	-0.006 (-0.014 – 0.001)	0.088	2.447 (1.245 – 3.688)	**<0.0001**	1.880 (1.091 – 2.669)	**<0.0001**
Moderate low	-0.001 (-0.025 – 0.023)	0.938	-0.008 (-0.034 – 0.019)	0.571	0.003 (-0.003 – 0.010)	0.314	-0.002 (-0.009 – 0.005)	0.495	1.996 (0.812 – 3.180)	**0.001**	1.194 (0.432 – 1.956)	**0.002**
Low	Reference		Reference		Reference		Reference		Reference		Reference	
Carotid intima-media thickness												
High	-0.002 (-0.028 – 0.024)	0.893	-0.004 (-0.033 – 0.025)	0.785	0.008 (0.001 – 0.015)	**0.020**	-0.001 (-0.008 – 0.007)	0.907	1.426 (0.186 – 2.665)	**0.024**	-0.659 (-1.462 – 0.144)	0.108
Moderate high	-0.003 (-0.028 – 0.022)	0.829	-0.005 (-0.033 – 0.022)	0.703	0.002 (-0.005 – 0.008)	0.637	-0.001 (-0.008 – 0.006)	0.726	-0.072 (-1.269 – 1,125)	0.906	0.055 (-0.719 – 0.829)	0.889
Moderate low	-0.001 (-0.023 – 0.026)	0.912	-0.0001 (-0.027 – 0.027)	0.996	0.002 (-0.005 – 0.009)	0.562	-0.002 (-0.009 – 0.005)	0.654	-0.389 (-1.575 – 0.796)	0.520	0.023 (-0.747 – 0.792)	0.954
Low	Reference		Reference		Reference		Reference		Reference		Reference	

Multivariable analysis was adjusted for sex, age at 17.7 years, and covariates at 17.7 and 24.5 years such as low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, diastolic or systolic blood pressure and fat mass and/or lean mass depending on the outcome, moderate to vigorous physical activity at 15.5 years, smoking status, and family history of hypertension/diabetes/high cholesterol/vascular disease. Skewed variables were logarithmically transformed before analyses. Effect estimate was from linear mixed-model analyses for repeated measures. CI, confidence interval. P-value <0.05 was considered statistically significant.

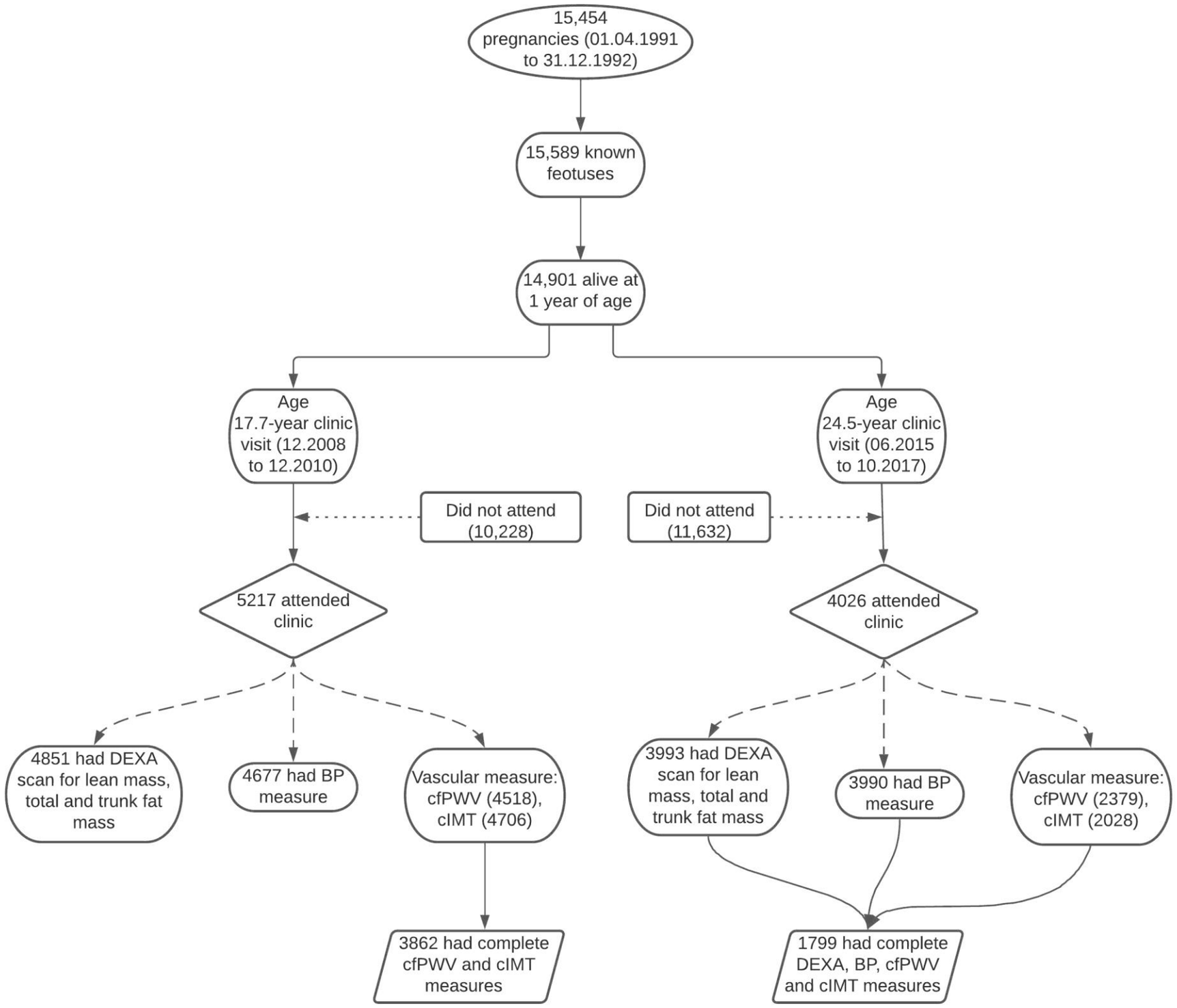

Figure S1 Flowchart of study participants
DEXA, Dual-energy Xray Absorptiometry; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; cIMT, carotid intima-media thickness. Participants that had complete predictor and or outcome of interest were included in the analyses