Relationship between TV Watching during Childhood and Adolescence, and Artery Function in Adulthood

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BASIC SCIENCES

ABSTRACT

HAYNES, A., J. MCVEIGH, S. HISSEN, L. LESTER, P. R. EASTWOOD, L. STRAKER, T. A. MORI, L. BEILIN, J. CARSON, and D. J. GREEN. Relationship between TV Watching during Childhood and Adolescence, and Artery Function in Adulthood. *Med. Sci. Sports Exerc.*, Vol. 56, No. 2, pp. 238–248, 2023. **Purpose:** Artery dysfunction is an early, integral stage in atherogenesis that predicts future cardiovascular events. Sedentary behavior, such as TV watching, is highly prevalent and associated with increased risk of developing cardiovascular diseases. This study investigated whether patterns of TV watching throughout childhood and adolescence were associated with artery function in adulthood. **Methods:** TV watching data were collected when participants of the Raine Study were aged 5, 8, 10, 14, 17, and 20 yr. Previous latent class analysis indicated three trajectory groups of TV watching: low TV (<14 h·wk^{-1}), high TV (>14 h·wk^{-1}), and increasing TV (change from low TV to high TV). At age 28 yr, participants were invited to undergo tests of brachial and femoral artery function by flow-mediated dilation (FMD). General linear models examined differences in artery function between TV trajectory groups for men and women. **Results:** Five hundred sixty participants (n = 261 women, n = 299 men) were included in the study. In women, the low TV group had significantly greater femoral artery FMD (10.8 ± 1.6%) than both High TV (9.0 ± 1.3%, P = 0.005) and Increasing TV groups (8.5 ± 1.3%, P < 0.001); these results were maintained following mediation analysis, including contemporaneous risk factors. There were no significant differences in femoral artery FMD between TV trajectory groups in men (P = 0.955). **Conclusions:** This study suggests that TV watching behaviors during childhood and adolescence may have legacy impacts on artery function at age 28 yr, particularly in women. This may increase the risk of atherosclerotic vascular pathologies in later life. **Key Words:** FLOW-MEDIATED DILATION, SEDENTARY BEHAVIOR, PHYSICAL ACTIVITY, CARDIOVASCULAR

Many noncommunicable diseases manifest late in life and are associated with atherosclerosis (1). Heart and cerebrovascular disease are leading causes of death in the United States (2), European Union (3), and Australia (4), whereas other conditions, such as peripheral artery disease (5), carotid stenosis (6), renovascular disease (7), and vascular dementia (8) are important causes of global mortality and morbidity. Atherosclerosis is a disease that begins in childhood and has a decade-long occult incubation phase before symptoms and disease manifest clinically (9). The initiation and progression of atherosclerosis is also highly modifiable, being influenced by lifestyle and behavioral risk factors (10). Awareness of behaviors in early life that may contribute to atherogenic development may help target primary prevention strategies.

Sedentary behavior (SB), such as prolonged sitting during TV watching and other screen time, is highly prevalent in Westernized societies and is associated with negative health outcomes, including cardiovascular diseases (CVD) and all-cause mortality (11). In adults, cross-sectional data indicate that TV watching is associated with increased incidence of cardiovascular risk factors, such as hypertension, obesity, and type 2 diabetes (12). In children and adolescents, high levels of TV and/or screen time are associated with greater adiposity and risk of cardiometabolic disease (13). Indeed, we recently provided

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evidence to suggest that TV watching behaviors during childhood and adolescence may have negative impacts on bone health and cardiorespiratory fitness in adulthood, which was maintained when adjusted for physical activity (PA) levels (14,15). It has been recommended that recreational screen time be limited to less than 3 $h \cdot d^{-1}$ in adults (16) and less than 2 $h \cdot d^{-1}$ in children and adolescents (17,18). Contemporary guidelines integrate PA, SB, and sleep across the 24-$h \cdot d^{-1}$ period (16–18), an approach supported by meta-analyses which indicate that engaging in higher levels of PA can attenuate negative impacts of SB (11,19). Nonetheless, typical periods of sedentary screen time may currently exceed 3.8 $h \cdot d^{-1}$ in children and 5 $h \cdot d^{-1}$ in adolescents (20,21).

It is difficult to directly assess atherosclerotic burden without using invasive (i.e., angiography) or expensive imaging approaches involving radiation exposure (22). Such measurements are unfeasible or contraindicated in apparently healthy younger individuals. An alternative approach is to assess flow-mediated dilation (FMD) of conduit arteries in response to physiological shear stress (i.e., increased frictional drag force on the artery wall). This high-resolution ultrasound technique predicts future cardiovascular events (23), in part because it reflects vascular health and nitric oxide (NO) bioavailability in the artery wall (24). Atherogenesis and CVD progression are linked to the combination of decreased NO-mediated endothelial function and the presence of low-grade inflammation (25). Flow-mediated dilation therefore provides a noninvasive measure of artery function and health *in vivo*. This study used historical TV watching and PA data, measured throughout childhood and adolescence in a cohort study, to determine whether these behaviors were associated with artery function and health in adulthood.

METHODS

Participants were Gen2 of the Raine Study, whose pregnant mothers were recruited between May 1989 and November 1991. The 2868 babies entered into the study subsequently attended follow-ups throughout childhood and adolescence. When participants were approximately 28 yr of age (between March 2018 and December 2019), 1997 participants were contacted (in order of birth oldest–youngest) with an invitation to attend a follow-up appointment. Participants accepting the invitation attended the laboratory to have a variety of physiological and anthropometric tests measured (detailed below). Based on the sample size in this study, the *post hoc* power calculation indicated that we were able to detect a difference in FMD between trajectory groups with 96% power. This indicates that our sample size was sufficient to test our hypotheses.

Written Informed Consent. This study conformed to the Declaration of Helsinki and was approved by The University of Western Australia Human Research Ethics Committee. Written, informed consent was obtained at all time-points before the 28-yr recall. This was obtained from the parents until the children reached 17 yr and were able to provide their own consent.

TV Watching Trajectories. When participants were aged 5, 8, and 10 yr, parents reported on the length of time their child spent watching TV per day using a six-category question with response options from "none" to "more than 3 h" per day (26). At ages 14, 17, and 20 yr, participants completed their own questionnaire related to TV watching. Data were combined to create overall TV watching categories across all 6 recalls of: i) no $h \cdot wk^{-1}$, ii) less than 7 $h \cdot wk^{-1}$, iii) between 7 and 14 $h \cdot wk^{-1}$, iv) between 14 and 21 $h \cdot wk^{-1}$, and v) more than 21 $h \cdot wk^{-1}$. A comprehensive description of the protocol used to develop these trajectories is available elsewhere (14,27). Using TV watching at 5, 8, 10, 14, 17, and 20 yr, a latent class analysis was conducted using an ordinal logit model including 200 random starts and 100 iterations (LatentGold Version 4.5, Statistical Innovations Inc, Belmont, MA) to estimate trajectories of TV watching. Data from 2411 participants were included in the trajectories and sex was a covariate in the models. A series of models with between one and six trajectories were estimated. Three trajectories were chosen based on a combination of statistical criteria, parsimony, and interpretability. The following were considered: 1) the minimum values of the goodness of fit measures Bayes information criteria, Akaike's information criteria, and the Consistent Akaike's information criteria; 2) consideration of the identification of the model in terms of the proportion of random starts converging on the same solution; 3) bootstrapped *P* value for the log-likelihood difference between models where differences in BIC and AIC were similar; 4) the degree to which the trajectory classes identified captured distinct and potentially meaningful patterns in the data; and 5) the quality of the model in terms of posterior probability diagnostics, namely the entropy R2 value, average posterior probability for each trajectory class, odds of correct classification, and classification error. Only 5% of the study sample had data at one timepoint and were included in the trajectories, with sensitivity analysis being conducted to check trajectories with those missing 1, 2, 3, and 4 timepoints and the model used a best-fit approach. Participants were assigned to the trajectory class for which they had the highest posterior probability of membership. This resulted in three distinct trajectory groups based on levels of TV watching: High TV (>14 $h \cdot wk^{-1}$), Low TV (<14 $h \cdot wk^{-1}$) and Increasing TV (change from low to high TV during adolescence).

PA Trajectories. When participants were aged 8, 10, 14, and 17 yr, parents answered a single question regarding their child's PA levels to derive an ordinal activity score. This question required parents to consider how physically active their child was compared with other children the same age, with four possible answers: less active, equal active, more active, or unable to make a comparison, with children in the latter category being removed from any subsequent analysis. Latent class analysis similar to that performed for TV trajectories (see above) was used to identify trajectories of PA. The development of PA trajectories was conducted before this study and full details can be found elsewhere (28). Participants were included in the trajectories if they had data on at least three

timepoints. This analysis resulted in the identification of three PA trajectory groups: low-activity, mid-activity, and high-activity.

Participant Characteristics—28-yr Follow-Up. Participants arrived at the laboratory in the morning after an overnight fast. Height and body weight were collected and used to calculate body mass index (BMI). For the assessment of resting blood pressure (BP), the participant sat upright in a chair, in a temperature-controlled room for at least 10 min before the commencement of the first BP measurement. An automated BP machine (Carescape V100 Dinamap; General Electric Healthcare) was preset to measure BP and heart rate every 2 min over a 10-min period. The participant was left alone in the room during the six measurements, which were taken at minutes 0, 2, 4, 6, 8, and 10. The average of the measurements taken at 4, 6, and 8 min were used for statistical analysis.

The participant then underwent an artery function assessment (detailed below), after which a fasting venous blood sample was collected for the measurement of plasma glucose and insulin, serum lipids (total cholesterol, high-density lipoprotein [HDL], low density lipoprotein [LDL], and triglycerides), and high sensitivity C-reactive protein (hs-CRP). Fasting glucose and insulin were used to calculate the homeostatic model assessment for insulin resistance (HOMA-IR) for each participant using the formula: glucose*insulin/22.5 (29). During this appointment when participants were approximately age 28 yr, participants were asked to complete the International Physical Activity Questionnaire (IPAQ) short form, to provide contemporary information related to exercise, PA and sedentary behaviors, using a self-report 7-day recall. These data were used to estimate the weekly metabolic equivalent minutes ($METmins \cdot wk^{-1}$) of PA undertaken at different intensities (i.e., walking, moderate PA, vigorous PA, total PA) and total duration spent sitting over the previous 7 days (30). These contemporaneous cardiovascular risk factors were included as mediators in our analyses as they may have an influence on artery function.

Peripheral Artery Functional Assessment: Endothelium-Dependent FMD. The function of the brachial and superficial femoral arteries was measured using the FMD method simultaneously on the left arm and leg respectively, in accordance to well-established guidelines (31). In brief, the participant was positioned on a bed in the supine posture in a quiet, temperature-controlled room for at least 20 min before the assessment. The left arm was extended and positioned at an angle of ~80° from the torso. A rapid inflation/deflation pneumatic cuff (D.E. Hokanson, Bellevue, WA) was positioned on the forearm immediately distal to the olecranon process and a larger cuff was positioned on the left thigh above the knee to provide a forearm and leg ischemia stimulus, respectively. Using two ultrasound systems (T3200; Terason, Burlington, MA), two experienced ultrasonographers used 10 to 15 MHz multifrequency linear array probes to image the brachial artery in the distal one-third of the upper arm and on the left thigh proximal to the leg cuff to image the superficial femoral artery. When both sonographers obtained optimal images, the probe was held stable and the ultrasound parameters were set to optimize the longitudinal, B-mode images of lumen–arterial wall interface. Continuous Doppler velocity assessments were also obtained using the ultrasound and were collected using the lowest possible insonation angle (always <60°). The test commenced with a 1-min baseline recording of brachial and femoral artery diameter and velocity (Camtasia Studio 8, TechSmith, Okemos, MI), after which the recording was paused and both the forearm and thigh cuff were simultaneously inflated to 220 mm Hg for exactly 5 min using a rapid inflation cuff (D.E. Hokanson, Bellevue, WA). Diameter and flow recordings resumed after 4.5 min of cuff inflation (i.e., 30 s before cuff deflation) and continued for 3 min after cuff deflation. Upon deflation of the cuff, shear stress through the artery increases, stimulating NO synthesis, resulting in dilation of the artery.

Posttest analysis of brachial and femoral artery ultrasound scans were performed using custom-designed, semiautomated, edge detection, and wall-tracking software (32). We have shown that this analysis software is largely independent of investigator bias, reduces observer error significantly, and possesses an intraobserver CV of 6.7% (32). This analysis was performed by experienced researchers blinded to the TV trajectory allocation of participants, and it was ensured that all data progressing to the statistical analyses stage was of high quality; scans of insufficient quality were discarded. Primary information gained from this analysis was the baseline artery diameter (D_{base}) before cuff inflation and peak artery diameter (D_{peak}) postcuff deflation. These two variables were used to derive the appropriate allometrically scaled independent variable for the study (see protocol below).

Allometric Scaling of FMD. Traditionally, the results of the FMD test are presented as the relative increase in artery diameter from D_{base} to D_{peak} (i.e., $FMD\% = D_{peak} - D_{base} / D_{base} \times 100$) (23,33). However, it has been suggested that FMD can be overestimated in individuals with a small baseline diameter and underestimated in individuals with a larger baseline diameter (34). Therefore, we used an established allometric scaling approach to account for inter-individual differences in baseline diameter in our study analyses. The protocol for this procedure has been discussed in detail elsewhere (34–36). In brief, using Microsoft Excel 360 (Microsoft Corp., Redmond, WA), D_{base} and D_{peak} were logarithmically transformed and referred to as $\log D_{base}$ and $\log D_{peak}$ respectively, after which the difference in the log transformed diameters were calculated, providing a logged difference in artery diameter ($\log D_{diff}$). As recommended for cross-sectional study designs such as this (36), general linear model analysis of covariance (ANCOVA) tests were performed, with $\log D_{diff}$ as the independent variable and $\log D_{base}$ included as a covariate, see *Statistical Analyses* below for further detail. Estimates of $\log D_{diff}$ derived from ANCOVA model adjusted for $\log D_{base}$ were antilogged to derive an adjusted mean FMD% for each TV trajectory group (36).

Endothelium-Independent NO-Mediated Arterial Dilator Function. After a 10-min rest after the FMD procedure in the supine position, images of the brachial and femoral arteries were simultaneously obtained by the two sonographers. A 1-min baseline recording of resting arterial diameters and blood velocity were collected. Subsequently, a single sublingual

dose of glyceryl trinitrate (GTN; 400 μg Nitrolingual-spray) was administered to assess the dilation capacity of the brachial and femoral arteries independent of the endothelium. Exactly 3 min after GTN administration, the recording of the arteries resumed for a further 5 min. The recording from this test was analyzed using the same software and protocols as per the FMD test described above.

Statistical Analyses. For femoral and brachial FMD and GTN tests, general linear model (GLM) ANCOVA tests were performed in SPSS (Version 27; IBM Corp., Armonk, NY), with $\log D_{diff}$ as the dependent variable and $\log D_{base}$ included as a covariate (34–36). TV trajectory membership was the independent variable in analyses, and to balance the importance of correctly classifying individuals in each class, analyses were weighted to the probability of membership for the assigned TV watching group. Because of the likelihood that there would be inherent differences in FMD between male and female participants (37), in addition to differences in the proportion of male and female participants in each TV trajectory class (14), statistical tests were performed separately for male and female participants. These initial analyses were conducted without the inclusion or adjustment of other variables (with the exception of $\log D_{base}$).

To determine whether the impact of TV trajectories on artery function outcome variables at age 28 yr were affected by contemporaneous cardiovascular risk factors, we developed a separate statistical model using a directed acyclic graph (DAG) approach (38). This DAG included 7 established CVD risk factors that were measured during the vascular assessment visit at age 28 yr, that we hypothesized to be mediators in the causal pathway between TV watching in childhood and adolescence and FMD in adulthood (see Supplemental Figure, Supplemental Digital Content, DAG showing potential links between TV trajectory group membership in childhood and adolescence, and adult artery function by FMD via mediators collected contemporaneously with FMD, http://links.lww.com/MSS/C918). These variables were BMI, systolic BP, resting heart rate, HOMA-IR, fasting LDL cholesterol, SB (minutes sitting per week), and PA ($METmin \cdot wk^{-1}$). Initially, the DAG model underwent a statistical assessment using the Baron and Kenny mediation approach (39). This preliminary analysis aimed to establish the connection between longitudinal TV group trajectories and artery function outcomes, separately by sex. Given the multicategorical nature of the independent variable, we integrated the Hayes approach into our workflow (40). This involved using GLM to assess the relationships between the linear outcome and mediators in the context of a categorical exposure. The mediation analysis was then finalized using Stata 18's causal-inference suite (StataCorp, 2023, College Station, TX), which uses a potential-outcome framework to disentangle the estimated total effect into its direct and indirect components, elucidating the relationships among the outcome, exposure, and mediator. The statistical approach described above was then repeated, replacing TV trajectory with PA trajectory as the independent (exposure) variable.

To test for cross-sectional differences in the characteristics of participants at age 28 yr between each of the TV trajectory groups, one-way ANOVA tests or nonparametric equivalent where necessary (Kruskal-Wallis H tests) were performed. These tested for differences in age, height, body weight, BMI, fasting blood tests, resting BP, resting heart rate, hs-CRP, PA, and time spent sitting at age 28 yr. Appropriate *post hoc* tests were used (i.e., either Bonferroni or Games-Howell for parametric tests, or Mann-Whitney U for nonparametric tests) to determine which groups differed significantly. A χ^2 test was conducted to determine whether sex was associated with TV trajectory class membership. Statistical significance was set at $P < 0.05$.

RESULTS

A summary of the participants included in each stage of this study can be seen in Figure 1. Participant characteristics for each TV trajectory are summarized in Table 1. TV trajectories for men and women can be seen in Figure 2.

In women, high TV trajectory membership was associated with greater BMI than increasing TV ($P = 0.033$) and low TV ($P = 0.027$) at age 28 yr. There were no statistical differences between TV trajectory groups for age ($P = 0.774$), height ($P = 0.338$), weight ($P = 0.231$), systolic BP ($P = 0.056$), diastolic BP ($P = 0.935$), resting heart rate ($P = 0.282$), HOMA-IR ($P = 0.381$), total cholesterol ($P = 0.900$), triglycerides ($P = 0.921$), LDL cholesterol ($P = 0.953$), HDL cholesterol ($P = 0.914$), hs-CRP ($P = 0.265$), walking ($P = 0.076$), moderate PA ($P = 0.123$), vigorous PA ($P = 0.226$), total PA ($P = 0.296$), or minutes sitting per week ($P = 0.579$).

In men, being in the high TV trajectory group was associated with greater BMI than increasing TV ($P = 0.022$), but not Low TV ($P = 0.110$) at age 28 yr. There were no statistical differences between TV trajectory groups for age ($P = 0.297$), height ($P = 0.445$), weight ($P = 0.094$), systolic BP ($P = 0.371$), diastolic BP ($P = 0.400$), resting heart rate ($P = 0.256$), HOMA-IR ($P = 0.086$), total cholesterol ($P = 0.348$), triglycerides ($P = 0.298$), LDL ($P = 0.106$), HDL ($P = 0.319$), hs-CRP ($P = 0.188$), walking ($P = 0.105$), moderate PA ($P = 0.659$), vigorous PA ($P = 0.812$), total PA ($P = 0.228$), and minutes sitting per week ($P = 0.301$).

Sex was significantly associated with TV trajectory class membership ($P = 0.001$), with the percentage of participants in each TV trajectory class being: high TV (42.5% female, 57.5% male), increasing TV (43.3% female, 56.7% male), and low TV (62.9% female, 37.1% male).

Femoral Artery—Endothelium-Dependent Vasodilator Function. In women, the low TV trajectory group had significantly greater femoral FMD than both the high TV ($P = 0.005$) and increasing TV trajectories ($P = 0.001$, see Fig. 3 panel A). There was no significant difference in femoral artery FMD between the High TV and Increasing TV trajectories ($P = 0.494$).

Regressions to determine whether there may be a link between TV watching trajectory and potential mediators indicated that, three variables had significant associations with TV trajectory. These were as follows: BMI and high TV ($P = 0.004$), systolic BP and high TV ($P = 0.031$), resting HR and both high TV ($P = 0.016$), and increasing TV ($P = 0.014$). Associations

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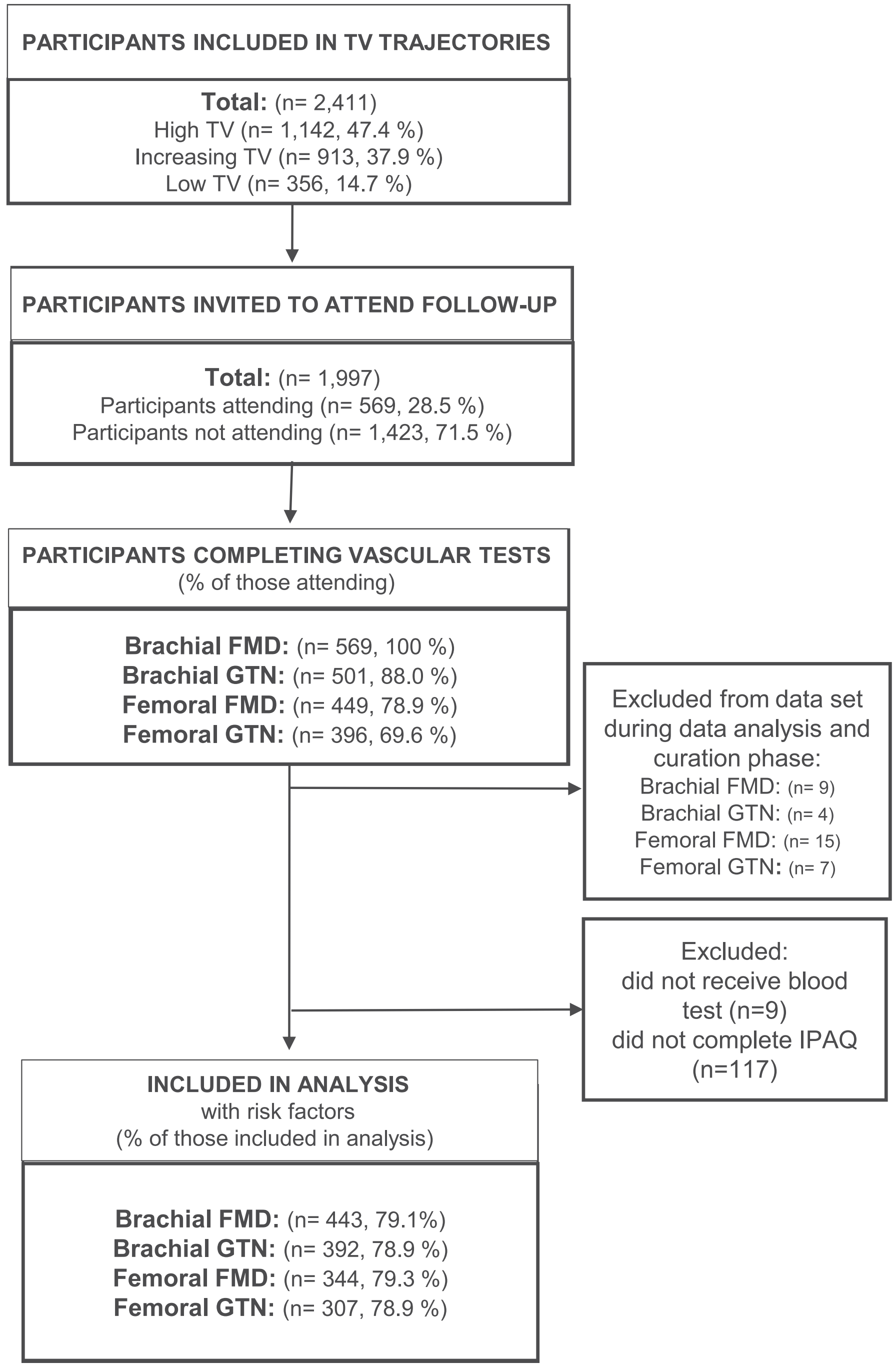
PARTICIPANTS INCLUDED IN TV TRAJECTORIES
Total: (n= 2,411)
High TV (n= 1,142, 47.4 %)
Increasing TV (n= 913, 37.9 %)
Low TV (n= 356, 14.7 %)
PARTICIPANTS INVITED TO ATTEND FOLLOW-UP
Total: (n= 1,997)
Participants attending (n= 569, 28.5 %)
Participants not attending (n= 1,423, 71.5 %)
PARTICIPANTS COMPLETING VASCULAR TESTS
(% of those attending)
Brachial FMD: (n= 569, 100 %)
Brachial GTN: (n= 501, 88.0 %)
Femoral FMD: (n= 449, 78.9 %)
Femoral GTN: (n= 396, 69.6 %)
Excluded from data set during data analysis and curation phase:
Brachial FMD: (n= 9)
Brachial GTN: (n= 4)
Femoral FMD: (n= 15)
Femoral GTN: (n= 7)
Excluded:
did not receive blood test (n=9)
did not complete IPAQ (n=117)
INCLUDED IN ANALYSIS
with risk factors
(% of those included in analysis)
Brachial FMD: (n= 443, 79.1%)
Brachial GTN: (n= 392, 78.9 %)
Femoral FMD: (n= 344, 79.3 %)
Femoral GTN: (n= 307, 78.9 %)

FIGURE 1—Diagram detailing the number of participants included at each part of the study, commencing with participants included in TV trajectory analysis.

between TV watching and fasting LDL, minutes sitting per week, PA and HOMA-IR were not significant (all $P > 0.050$), so these variables were not included in the final mediation analysis. Results of mediation pathways from TV watching to femoral artery FMD via BMI, systolic BP, and resting HR indicated that there were no significant mediation effects of either BMI, systolic BP, or resting HR at age 28 yr on femoral artery function (all $P > 0.050$), see Table 2 for indirect effects. Furthermore, femoral artery function in the low TV group remained greater than both the high TV and increasing TV trajectory groups in all three of these mediation pathways (see Table 2 for direct effects).

There were no differences in femoral artery FMD between PA trajectory groups (low-activity 10.3 ± 3.5%, mid-activity 9.1 ± 3.2%, High-Activity 9.2 ± 3.3%, $P = 0.542$). Therefore, mediation analyses were not conducted.

In men, there were no significant differences in femoral artery FMD between TV trajectory groups ($P = 0.955$, see Fig. 3 panel B). Therefore, mediation analyses were not conducted.

There were no differences in femoral artery FMD between PA trajectory groups (low-activity 5.9 ± 2.5%, mid-activity 6.3 ± 2.3%, High-Activity 5.7 ± 3.2%, $P = 0.322$). Therefore, mediation analyses were not conducted.

TABLE 1. Descriptive characteristics of participants within TV trajectory classes who had artery function assessed at 28 yr.

	Female Participants			Male Participants		
	High TV (Reference Group)	Increasing TV	Low TV	High TV (Reference Group)	Increasing TV	Low TV
n (%)	108 (41.4)	87 (33.3)	66 (25.3)	146 (48.8)	114 (38.1)	39 (13.0)
Age (y)	28.2 ± 0.5	28.2 ± 0.4	28.2 ± 0.4	28.2 ± 0.5	28.2 ± 0.5	28.3 ± 0.5
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.8 ± 0.1	1.8 ± 0.1	1.8 ± 0.1
Weight (kg)	75.1 ± 20.0	71.0 ± 16.7	69.8 ± 14.3	86.1 ± 16.0	81.9 ± 11.9	82.9 ± 16.7
BMI (kg·m^2)	24.8 (6.8)	23.4 (4.6)*	22.6 (7.1)*	25.7 (4.9)	24.5 (4.9)*	24.1 (4.6)
Brachial BD (mm)	3.2 ± 0.4	3.1 ± 0.3	3.2 ± 0.3	4.2 ± 0.4	4.1 ± 0.4	4.0 ± 0.5
Brachial PD (mm)	3.4 ± 0.3	3.4 ± 0.3	3.4 ± 0.3	4.4 ± 0.5	4.4 ± 0.4	4.3 ± 0.5
Femoral BD (mm)	4.9 ± 0.5	5.0 ± 0.5	5.1 ± 0.6	6.1 ± 0.7	6.0 ± 0.6	6.2 ± 0.6
Femoral PD (mm)	5.4 ± 0.5	5.4 ± 0.5	5.6 ± 0.5	6.5 ± 0.6	6.4 ± 0.6	6.5 ± 0.6
Glucose (mmol·L^{-1})	4.5 ± 0.7	4.5 ± 0.5	4.4 ± 0.3	4.7 ± 0.4	4.7 ± 0.3	4.7 ± 0.3
Insulin (mIU·L^{-1})	5.0 (4.25)	6.0 (4.0)	5.0 (5.0)	6.0 (4.0)	5.0 (3.0)	5.0 (4.0)
HOMA-IR	1.1 (0.9)	1.1 (0.8)	1.1 (0.9)	1.2 (0.8)	1.1 (0.7)	1.0 (0.9)
Cholesterol (mmol·L^{-1})	4.8 ± 0.8	4.8 ± 0.8	4.8 ± 0.9	4.8 ± 0.9	4.7 ± 0.9	4.9 ± 1.0
LDL (mmol·L^{-1})	2.7 ± 0.7	2.7 ± 0.8	2.8 ± 0.7	3.0 ± 0.8	2.9 ± 0.8	3.2 ± 0.9
HDL (mmol·L^{-1})	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.3
Triglycerides	0.9 ± 0.6	0.9 ± 0.5	0.9 ± 0.6	1.1 ± 0.5	1.0 ± 0.4	1.0 ± 0.5
Systolic BP (mm Hg)	112 ± 10	110 ± 7	109 ± 8	120 ± 9	118 ± 7	119 ± 11
Diastolic BP (mm Hg)	68 ± 7	69 ± 6	69 ± 6	71 ± 7	70 ± 6	70 ± 7
Resting HR (bpm)	69 ± 9	69 ± 9	67 ± 10	66 ± 8	64 ± 9	64 ± 8
hs-CRP (mg·L^{-1})	1.4 (4.2)	1.0 (2.6)	1.1 (2.8)	0.9 (1.3)	0.7 (14.6)	0.8 (1.7)
Walk (METmin·wk^{-1})	495 (1254)	693 (1151)	644 (1188)	792 (1766)	495 (1155)	462 (1089)
Mod. (METmin wk^{-1})	0 (480)	340 (945)	100 (720)	480 (1440)	330 (1440)	120 (1200)
Vig. (METmin·wk^{-1})	0 (960)	380 (1440)	480 (1440)	960 (2640)	960 (1920)	1080 (2400)
Total PA (METmin·wk^{-1})	1290 (2784)	1773 (3105)	1902 (2551)	2955 (4383)	2445 (3875)	2061 (4138)
Sitting per week (min)	720 (540)	780 (360)	720 (405)	675 (555)	720 (510)	600 (450)

Data are mean ± SD or median (IQR).
*Significant ($P < 0.05$) difference to high TV.
Brachial BD and femoral BD, baseline diameter from FMD test; brachial PD and femoral PD, peak diameter from FMD test; Mod., moderate intensity physical activity; Vig., vigorous physical activity; total PA, composite of walk, moderate, and vigorous PA; sitting per week, time spent sitting at age 28 yr.

Brachial Artery—Endothelium-Dependent Vasodilator Function. In women and men, there were no significant differences in brachial artery FMD between TV trajectory groups ($P = 0.313$, see Fig. 3 panel C and $P = 0.763$, Figure 3 panel D), respectively. Therefore, mediation analyses were not conducted.

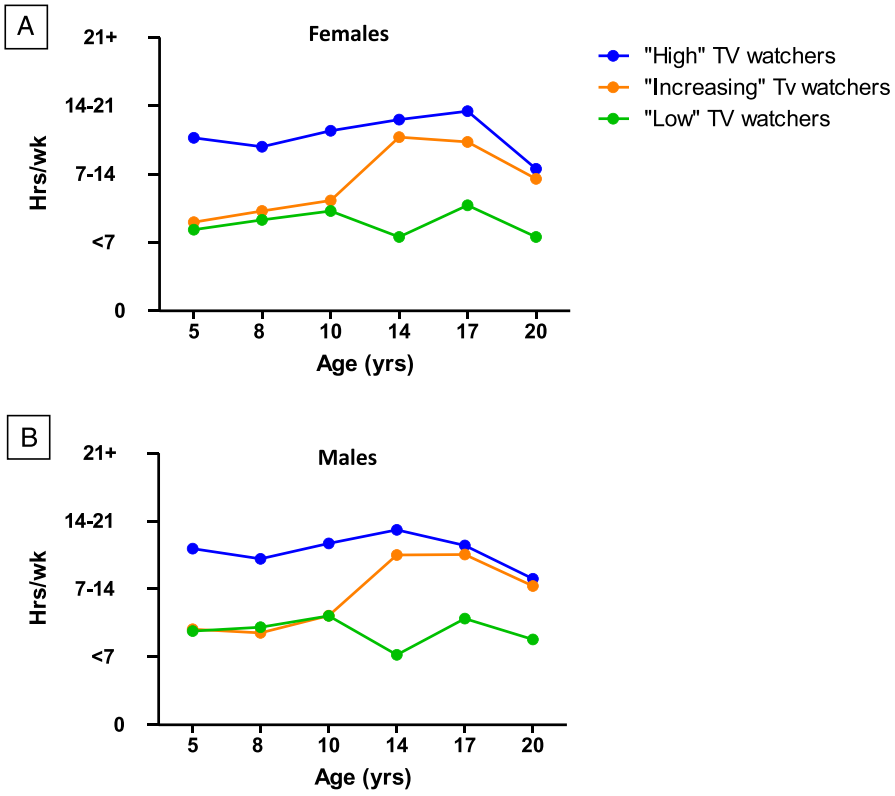

FIGURE 2—Trajectories of TV watching derived from mean television watching hours per week using latent classes analysis based on 15 yr of TV watching data in females (panel A) and males (panel B).

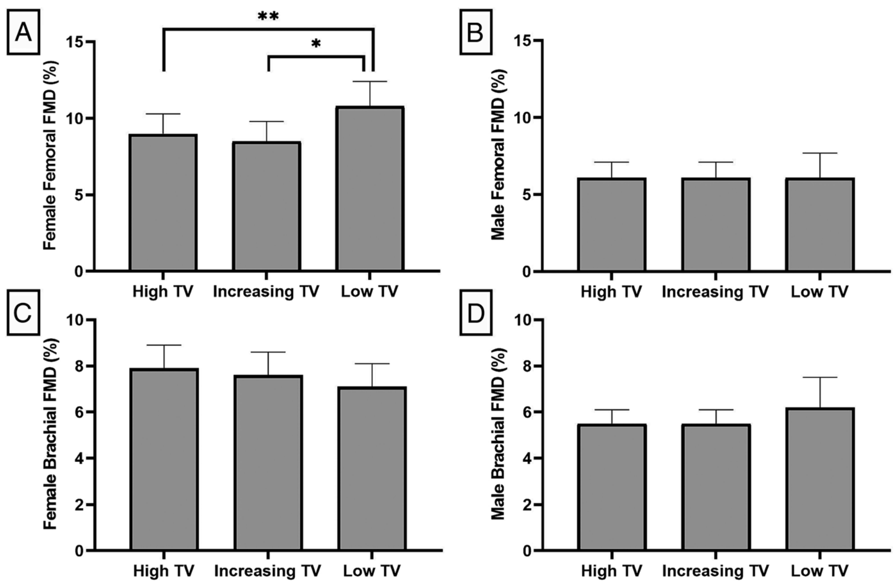

FIGURE 3—Femoral FMD (FMD %) results in female (panel A) and male (panel B); and brachial flow mediated dilation (FMD %) results in female (panel C) and male (panel D) for each TV trajectory group. Data are mean ± SD. *Significance at $P < 0.010$.

There were no differences in brachial artery FMD between PA trajectory groups in either women (low-activity, 8.7 ± 1.6%; mid-activity, 7.8 ± 3.7%; high-activity, 7.1 ± 2.0%; $P = 0.096$) or men (low-activity 6.1 ± 2.3%, mid-activity 5.4 ± 2.6%, high-activity 5.7 ± 1.7%, $P = 0.485$). Therefore, mediation analyses were not conducted.

Femoral Artery—Endothelium-Independent Vasodilator Function. In women and men, there were no significant differences in the dilation of the femoral artery after GTN administration ($P = 0.419$, see Fig. 4 panel A and $P = 0.692$, see Figure 4 panel B), respectively. Therefore, mediation analyses were not conducted.

There were no differences in femoral artery dilation after GTN administration between PA trajectory groups in either women (low-activity, 13.0 ± 3.9%; mid-activity, 14.9 ± 4.2%; high-activity, 16.0 ± 3.9%; $P = 0.101$) or men (low-activity, 10.0 ± 4.1%; mid-activity, 10.7 ± 3.5%; high-activity, 10.5 ± 4.0%; $P = 0.743$). Therefore, mediation analyses were not conducted.

Brachial Artery—Endothelium-Independent Vasodilator Function. In women and men, there were no significant differences in the dilation of the brachial artery after GTN administration ($P = 0.665$, see Fig. 4 panel C and $P = 0.283$, see Figure 4 panel D), respectively. Therefore, mediation analyses were not conducted.

There were no differences in brachial artery dilation after GTN administration between PA trajectory groups in either women (low-activity, 19.8 ± 5.4%; mid-activity, 21.5 ± 5.0%; high-activity, 21.0 ± 4.8%; $P = 0.396$) or men (low-activity, 17.7 ± 4.6%; mid-activity, 17.9 ± 4.0%; high-activity, 18.4 ± 4.3%; $P = 0.769$). Therefore, mediation analyses were not conducted.

TABLE 2. Estimated causal effects and their 95% confidence interval of potential mediators between longitudinal TV group trajectories and femoral artery FMD in females.

Mediator	Effect	High TV[a]	Increasing TV[a]
BMI	Indirect	1.001 (0.998–1.004)	1.000 (0.998–1.002)
	Direct	0.982 (0.970–0.994)*	0.979 (0.967–0.991)*
	Total	0.983 (0.971–0.995)*	0.979 (0.967–0.991)*
Systolic BP	Indirect	1.001 (0.998–1.004)	0.999 (0.996–1.003)
	Direct	0.982 (0.970–0.994)*	0.980 (0.967–0.992)*
	Total	0.983 (0.972–0.995)*	0.979 (0.967–0.991)*
Resting HR	Indirect	1.001 (0.997–1.004)	0.999 (0.995–1.003)
	Direct	0.982 (0.970–0.995)*	0.980 (0.967–0.992)*
	Total	0.983 (0.971–0.995)*	0.979 (0.967–0.991)*

* $P < 0.005$.
[a] Versus low TV trajectory (reference) group.

DISCUSSION

In this study, we investigated whether patterns of TV watching throughout childhood and adolescence had an impact on artery function in adulthood. Our data suggest that, in women, consistently watching less than 14 h of TV per week between the ages of 5 and 20 yr was associated with enhanced femoral artery function compared with watching more than 14 h of TV per week. There was no evidence to suggest that this relationship also applied to the male participants in this cohort, in whom artery function was similar between TV trajectory groups.

Previous research has indicated that in participants approximately 50 yr of age, watching more than 4 $h \cdot d^{-1}$ of TV was associated with 46% greater risk of all-cause mortality and 80% higher risk of CVD mortality compared with watching less than 2 $h \cdot d^{-1}$, after ~6.6 yr follow-up (41). There is also cross-sectional data suggesting in middle- and older-aged adults that TV watching was positively associated with carotid intima-media thickness (42). The cutoff for membership in the low TV watching trajectory in our study was consistently watching less than 2 $h \cdot d^{-1}$ throughout childhood and adolescence, which corresponds to the current recommended threshold for

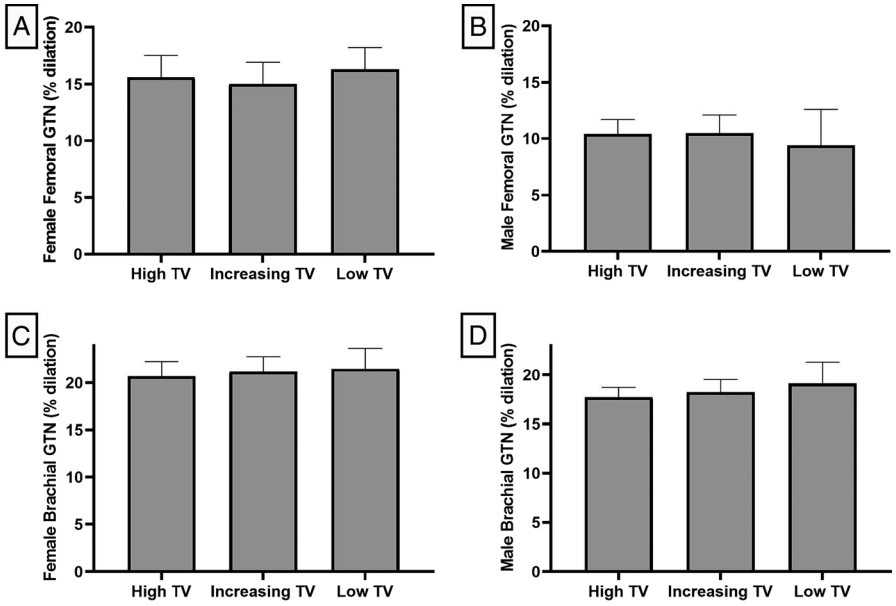

FIGURE 4—Dilation of the femoral artery (GTN % dilation) results in female (panel A) and male (panel B); and brachial artery dilation (GTN % dilation) results in female (panel C) and male (panel D) for each TV trajectory group. Data are mean ± SD.

viewing time in international 24-h activity guidelines for children and adolescents (17). Detection of artery dysfunction and its antecedent causes provides an opportunity for early intervention and prevention of CVD related events, morbidity and mortality. It is currently unclear whether SB in childhood and adolescence predisposes individuals to the earliest stages of atherosclerosis, such as impaired endothelial or vascular smooth muscle function. As the participants in this study were aged 28 yr, our findings in relation to TV watching and femoral FMD in women may reflect the early development of occult CVD. Notably, this relationship was not found in the male participants in our cohort.

Others have reported that the relationship between TV viewing and cardiovascular risk factors may be sex specific (43,44). For example, the relationship between TV viewing time and cardiovascular risk factors including percent body fat, waist circumference, fasting glucose and triglycerides were found to be stronger in female adults compared with male adults (43,44). In women, time spent watching TV was found to be positively correlated with time spent in other sedentary behaviors and negatively correlated with leisure time PA; but no such associations were found in men (45). Men in this study did appear to be more active overall at age 28 yr in each TV trajectory group compared with women, most noticeably in the high TV group. It is possible that the greater PA levels in the high TV groups in men at age 28 yr could be at least in part responsible for the sex-differences we observed. Importantly, there was no evidence to suggest that differences in femoral FMD between TV trajectory groups in women occurred due to mediation effects via the contemporaneous risk factors included in the analyses.

There were no differences in adult artery function between PA trajectories in our cohort. Although it remains unclear whether sedentary behavior and PA have independent or inter-related effects on cardiovascular risk, it has been suggested in other studies that PA participation diminishes the negative effects of SB (11,19). Our data add novelty in that they are longitudinal and derived from TV watching across the early years of life. Nonetheless, it is important to acknowledge that our PA trajectory data were based on questionnaires and surveys collected across childhood and adolescence in the 1990s and 2000s, preceding the contemporary accelerometry era of PA assessment. Our data, therefore, lack the level of discrimination we would prefer when assessing the developmental impacts of PA on adult artery function. Regardless, our study indicates that TV watching in childhood and adolescence is associated with negative impacts on artery function in adulthood, and this supports current screen-time based guidelines for children and adolescents (17,18).

Data regarding TV watching and screen time derived from countries including Canada and the United States have indicated that screen time is high among children and adolescents, with reports of more than 5 $h \cdot d^{-1}$ and 40% to 60% of waking hours being common (13,21). We would expect that the results of our study, which suggests that TV viewing time has negative impacts on artery function in adulthood, would also be applicable to other developed countries. However, it would be beneficial if our study was repeated in other cohorts where similar data on TV watching are available, including other screen use such as videogames and smartphones, the prevalent use of which postdate our study. It is germane that overall screen time has likely increased in children and adolescents in the years after our data were collected (13,21). It is possible that future studies may find more pronounced effects of SB on artery function compared with what we observed.

Cross-sectional data comparing TV watching duration in children aged 7 to 10 yr with inflammatory and endothelial

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cell biomarkers have indicated that C-reactive protein and vascular cellular adhesion molecule 1 rises for every hour of weekly TV viewing time (46). Our group has also provided evidence in overweight and obese adult participants, to indicate that a single uninterrupted 5 h bout of sitting decreased femoral artery function, but this effect was mitigated when participants walked for 10 min each hour (47). This finding supports 24-h movement guidelines which recommend breaking up prolonged sitting with regular movement breaks (16–18). Furthermore, FMD of the popliteal artery was reduced after a 5-day reduction in daily steps from ~10,000 to less than 5,000 steps per day in active individuals, but this reduction in FMD was not found in the brachial artery (48). Collectively, these data suggest that the apparent link between prolonged sitting and FMD in the large arteries of the leg are due to local, as opposed to systemic effects on endothelial function; and that breaking up prolonged sitting with brief bouts of PA counteracts the negative impacts of SB on artery function. As optimal shear rate patterns (i.e., laminar shear stress) are necessary to maintain the integrity and health of the endothelium (49), it is plausible that prolonged impairment of femoral artery shear stress induced by prolonged uninterrupted sitting (particularly with knee flexion) may be a key physiological mechanism contributing to the negative impact of sitting on femoral artery function (50,51). Indeed, acute laboratory experiments have suggested that blood velocity and shear rate in the popliteal artery are markedly reduced when sitting upright in a chair with knees bent, compared with when legs are straight or in a recumbent position (52). This hypothesis is in line with data that indicates that one of the many benefits of exercise is the direct result of episodic increases in shear stress on the vascular endothelium (49). The distinction between femoral and brachial artery results we observed may be of some pathological relevance; the majority (~90%) of peripheral artery disease occurs in lower limb arteries, whereas upper limb artery disease is rare (53). A recent review indicated that the incidence of peripheral artery disease may be higher in women than in men (54), and this may also be relevant to the sex-specific nature of our results.

We measured several traditional risk factors contemporaneously with artery function in participants that attended the 28-yr follow-up. The impact of TV watching on femoral endothelial function in women appears to be independent of any effect of these risk factors at that age. Furthermore, differences between TV trajectories in women were apparent for endothelium-dependent dilation, but not when an exogenous NO donor (GTN) was administered. This suggests that the difference in femoral FMD between TV trajectories in women was likely due to greater endothelial function in the low TV group; and not to greater sensitivity of smooth muscle or generic improvement in artery responsiveness (55). This has pathophysiological implications, since low endothelial shear stress associated with SB is known to be proatherogenic (49,51). There were significant associations between sex and TV class membership, with the most notable difference being the higher proportion of the women in the low TV group. This finding, based on participants who attended the vascular assessment, is also representative of the larger cohort, including 2411 participants (27).

Strengths of this study were that we performed sex-specific analyses and that artery function was measured in all participants at the same age (i.e., ~28 yr). Therefore, our results are less likely to be confounded by the known impact sex and age may have on cardiovascular risk factors or the results of the FMD test (37,55). We also developed a DAG to account for potential mediation effects via a variety of contemporaneous cardiovascular risk factors in our analyses. Our study adopted a statistical approach that adjusted for interindividual differences in baseline artery diameter, which is preferrable in observational datasets of FMD (34,36). Some larger studies have reported FMD to be a significant predictor of cardiovascular events despite not accounting for inter-individual differences in baseline diameter (23,56). However, these studies were composed primarily of older adults (i.e., older than 60 yr) in which clinical end-points can also be measured and there may be greater range in artery function between participants. Our study is unique, due to the comprehensive retrospective data gathered throughout childhood and adolescence; and this study also provides baseline data that may be used in the future when the cohort ages to determine whether artery function at age 28 yr was predictive of future events.

This study has several limitations. The duration of TV watching was reported during childhood and adolescence, and other forms of SB were not included in the questionnaire. However, TV watching has been used as a surrogate for overall SB in other studies, particularly those in which data collection took place before the widespread use of the Internet and devices such as smart phones and tablets (57). Likewise, it would have been beneficial if our study had included detail of how participants spent their 24-h·d^{-1} (17) and future studies should attempt to understand the interplay of SB, PA, sleep and diet on risk factors such as artery function. We were unable to assess the potential influence of factors, such as diet and smoking, due to insufficient data on these habits. For feasibility reasons, the time of the menstrual cycle was not matched for all female participants attending the 28 yr follow-up, and this may influence the FMD results gained (31). The use of oral contraceptive medications was also not controlled for in our study. However, the impact of these shortcomings is somewhat mitigated by our sample size and the virtue of studying ecologically valid populations. It is also a limiting factor that not all participants provided answers to all questions in the IPAQ related to how much time they spent engaged in PA and sitting at age 28 yr, reducing the number of participants when the statistical model included variables derived from the IPAQ. None of the participants in this study had been diagnosed with CVD, although participants were not screened for occult atherosclerosis by modern imaging techniques.

CONCLUSIONS

In conclusion, we provide novel evidence suggesting that regularly watching TV for more than 14 h·wk^{-1} in childhood and/or adolescence is associated with lower endothelium-mediated function of the femoral artery in female participants

compared with watching less than 14 h·wk^{-1}. This impact of TV watching on artery function appears to be independent of the presence of other cardiovascular risk factors at age 28 yr, and PA throughout childhood and adolescence. No relationship between antecedent TV watching and adult artery function was evident in men. Our findings support current 24-h activity guidelines for children and adolescents, which recommend breaking up prolonged sitting time with bouts of PA and limiting daily screen time to less than 2 h. Public health agendas aimed at optimizing artery function and health and decreasing CVD progression and risk in adults, should start in childhood and include limiting screen time, particularly in women. This may be an important finding for the current generation of children and adolescents, since contemporary screen time has increased since the period across which our cohort was studied, when TV watching was the primary source of screen time.

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Conflict of interest: The authors have no conflicts of interest to declare. The results of the present study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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