

Exposure to parental smoking in childhood or adolescence is associated with increased carotid intima-media thickness in young adults: evidence from the Cardiovascular Risk in Young Finns study and the Childhood Determinants of Adult Health Study

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Aim

Recent evidence suggests that the exposure of children to their parents' smoking adversely effects endothelial function in adulthood. We investigated whether the association was also present with carotid intima-media thickness (IMT) up to 25 years later.

Methods and results

The study comprised participants from the Cardiovascular Risk in Young Finns Study (YFS, $n = 2401$) and the Childhood Determinants of Adult Health (CDAH, $n = 1375$) study. Exposure to parental smoking (none, one, or both) was assessed at baseline by questionnaire. B-mode ultrasound of the carotid artery determined IMT in adulthood. Linear regression on a pooled dataset accounting for the hierarchical data and potential confounders including age, sex, parental education, participant smoking, education, and adult cardiovascular risk factors was conducted. Carotid IMT in adulthood was greater in those exposed to both parents smoking than in those whose parents did not smoke [adjusted marginal means: $0.647 \text{ mm} \pm 0.022$ (mean \pm SE) vs. $0.632 \text{ mm} \pm 0.021$, $P = 0.004$]. Having both parents smoke was associated with vascular age 3.3 years greater at follow-up than having neither parent smoke. The effect was independent of participant smoking at baseline and follow-up and other confounders and was uniform across categories of age, sex, adult smoking status, and cohort.

Conclusions

These results show the pervasive effect of exposure to parental smoking on children's vascular health up to 25 years later. There must be continued efforts to reduce smoking among adults to protect young people and to reduce the burden of cardiovascular disease across the population.

Keywords

Cardiovascular diseases • Children • Epidemiology • Risk factors • Passive smoking

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Introduction

The prevalence of smoking has been decreasing across much of the developed world, resulting in a reduced burden of smoking-related cardiovascular disease. Despite the decreasing prevalence, those most likely to smoke are aged in their 20–40 s,¹ the period typically corresponding with the beginning of parenthood. Several cross-sectional studies in children and adolescents have shown that exposure to passive smoke, of which parental smoking is the greatest source, affects vascular health. This includes impaired endothelial dysfunction,^{2,3} arterial stiffness,⁴ and greater arterial intima-media thickness (IMT).^{3,5} In the first prospective study of its kind using data from the Childhood Determinants of Adult Health (CDAH) study and the Cardiovascular Risk in Young Finns Study (YFS), we recently demonstrated that exposure to parental smoking in childhood or adolescence was associated with lower brachial artery flow-mediated dilatation (FMD) in adulthood independent of own smoking status and traditional cardiovascular risk factors such as blood pressure and lipids at baseline and follow-up.⁶ Our study, therefore, suggested that exposure to parental smoking earlier in life resulted in potentially irreversible changes to endothelial function. Whether or not the effect extends to adult measures of vascular structure, in this case carotid IMT, plausibly reflecting different pathophysiological mechanisms, remains untested and is important to investigate. As such, the aim of this study was to assess the role of exposure to parental smoking in childhood or adolescence on carotid IMT in adulthood in two independent cohorts followed for up to 25 years.

Methods

Cardiovascular Risk in Young Finns Study

Participants

The YFS, conducted in Finland, has been described elsewhere.⁷ Analyses of exposure to parental smoking at baseline (1980) and adult carotid IMT in 2001 or 2007 included 2401 participants (72% eligible) aged 3, 6, 9, 12, 15, or 18 years old at baseline. The analyses of the association between cumulative exposure to parental smoking from 1980 to 1983 and adult carotid IMT in 2001 or 2007 included 2041 individuals.

Measurements

Parents reported current regular parental smoking in 1980. Categories were 'none', 'one parent', or 'two parents'. Cumulative exposure to parental smoking was determined by combining the parental smoking variables from 1980 and 1983. This generated a score ranging from 0 (no exposure to parental smoking) to 4 (exposure to both parents smoking at both time points). At baseline and follow-up, height and weight were measured, with body mass index (BMI, kg/m²) calculated from weight/(height)². A physical activity score was calculated from the duration, intensity, and frequency of physical activity at baseline and follow-up.⁸ Parents reported their own total years of schooling, current occupation, and family income in 1980. Participants aged 12–18 years in 1980 reported their own smoking status during the collection of physical measures without parents present, with children aged <12 years assumed to be non-smokers. At follow-up, questionnaires gathered data on participants' total years of schooling, current smoking status and pack-years of smoking, physical activity, and alcohol consumption. Cardiovascular risk factors were also assessed at follow-up. Blood pressure

was measured using a random-zero sphygmomanometer. Serum cholesterol and triglyceride concentrations were assessed enzymatically. HDL-cholesterol was analysed after precipitation of very LDL and LDL-cholesterol with dextran sulphate 500 000. LDL-cholesterol was estimated using the Friedewald equation.⁹ Fasting plasma glucose was determined enzymatically. High-sensitivity serum C-reactive protein was measured turbidimetrically on an automated analyser. Non-smokers reported passive smoke exposure in hours per day in the home, workplace, and elsewhere.

Carotid artery ultrasound studies

B-mode ultrasound studies of the left carotid artery were performed with a 13.0 MHz linear-array transducer at follow-up in 2001 and 2007, as described previously.¹⁰ No less than four measurements of the far wall were taken ~10 mm proximal to the bifurcation to derive maximum carotid IMT. The intra-individual reproducibility of ultrasound measurements was assessed in a sample of 57 subjects that were re-examined 3 months after the initial ultrasound study. The average absolute difference and standard deviation (SD) between measurements was 0.05 ± 0.04 mm. The associated coefficient of variation was 6.4%. Readers were blind to the exposure status of participants.

Childhood Determinants of Adult Health Study

Participants

The CDAH study, which is conducted in Australia, has been described in detail elsewhere.¹¹ The current study includes 1375 individuals (23% eligible) aged 9–15 years in 1985 (baseline) who also underwent carotid ultrasound studies in 2004–06 (follow-up, age range: 26–36 years).

Measurements

At baseline, participants completed questionnaires in small groups with a study data collector. Parental smoking was reported as 'none', 'one', or 'two' parents smoking. An additional question that asked how many people smoked in the home was used to estimate the effects of the dose of passive smoke exposure in the home on adult carotid IMT. Participants reported their own smoking status, with ≥ 1 cigarette per week classified as current smoking. Physical activity (minutes per week) was determined from questions on duration and frequency of active commuting, school physical education, school sport, and non-organized physical activity in the past week. Height and weight were measured at baseline and follow-up, with BMI calculated at both time points. Serum total cholesterol and triglycerides were determined according to the Lipid Clinics Program, and HDL-cholesterol was analysed following precipitation of apolipoprotein-B containing lipoproteins with heparin-manganese. LDL-cholesterol concentration was calculated using the Friedewald formula.⁹ Fasting plasma glucose was measured enzymatically. Blood pressure was measured at follow-up using a digital automatic monitor. Serum C-reactive protein at follow-up was determined using an automated analyser and a highly sensitive turbidimetric immunoassay kit. Questionnaires at follow-up assessed the highest level of education, physical activity (International Physical Activity Questionnaire),¹² alcohol consumption, and current smoking status and pack-years of smoking. Participants retrospectively reported parental education and occupation grade when they were aged 12.

Carotid artery ultrasound studies

B-mode ultrasound studies of the carotid artery were performed using the portable Acuson Cypress ultrasound machine with a 7.0-MHz linear-array transducer. This machine has been validated and a single technician performed all scans using the imaging protocols described by the YFS.¹³

Several 3- to 5-s real-time images were recorded that included the beginning of the carotid bulb and ~30 mm of the common carotid artery. The two highest quality end-diastolic images were selected for measurement. Maximum carotid IMT was determined by taking six measurements of the common carotid far wall ~10 mm before the border of the carotid bulb. The measurements of IMT were made by three readers that were blind to exposure status of participants. Linear regression methods were used to estimate the minor differences in means between the three readers. The IMT measurements were calibrated to eliminate the minor differences (<1.2%) in means between the readers. Intra-rater reproducibility was assessed in a random sample of 30 participants. The average absolute difference and SD between IMT measurements was 0.02 ± 0.04 mm, with the coefficient of variation being 5.9%.

Statistical analysis

Comparisons of characteristics by the parental smoking group were examined using χ^2 tests or one-way ANOVA. The association between exposure to parental smoking in earlier life and adult continuous maximum carotid IMT was examined using linear regression adjusted for the anticipated hierarchical structure of the data in the pooled analyses using the 'xtmixed' command in Stata. We additionally present cohort-specific analyses using standard linear regression in Supplementary material online.

Models were adjusted for confounders in accordance with purposeful model building procedures.¹⁴ The following were considered from baseline: age, sex, parental education, physical activity, BMI, and participant smoking. From follow-up, the potential confounders were participant education, participant smoking, physical activity, BMI, and alcohol consumption. We also considered biological cardiovascular risk factors in adulthood as covariates, hypothesizing that these might mediate the association between parental smoking and carotid IMT in adulthood. These included systolic and diastolic blood pressure, HDL- and LDL-cholesterol, triglycerides, glucose, and C-reactive protein. For pooled analyses, covariates were transformed to z-scores or re-categorized to reflect similar constructs when necessary and a variable indicating source cohort was also included in models. Models are presented adjusted for age and sex (model 1); model 1 plus childhood covariates (model 2); model 2 plus adult covariates (model 3) and model 3 plus adult cardiovascular risk factors (model 4). Once final models were determined, effect modification between confounders and exposures was tested using product terms in both cohort-specific and pooled analyses. Analyses were repeated for cumulative exposure to parental smoking in 1980 and 1983 in the YFS and total number of smokers in the home in 1985 in CDAH (see 'Measurements' for details).

We extrapolated our findings by calculating the 'vascular age' of those exposed to parental smoking.¹⁵ This involved estimating the mean difference in carotid IMT per year of age using linear regression. We then divided the mean differences in carotid IMT for each category of parental smoking by the mean difference per year of age.

Sensitivity analyses were conducted to determine whether adjusting for alternative measures of covariates that were available in a reduced sample would have altered the results. These included baseline socio-economic status, biomedical cardiovascular risk factors, and smoking level and follow-up measures of pack-years of smoking or passive smoke exposure (non-smokers in YFS only). These results are presented in Supplementary material online. Statistical significance was set at a *P*-value of ≤ 0.05 . Both studies were approved by local ethics committees.

Results

The characteristics of the samples are shown in Table 1. In the CDAH Study, those who completed follow-up were less likely to have been

smoking, living in a low socio-economic status postcode, overweight, or obese or have parents that smoked in childhood. In the YFS, those who completed follow-up were more often female, non-smokers, had parents with higher education levels, and non-smoking parents.

Exposure to both parents smoking earlier in life was associated with greater carotid IMT in adulthood in pooled (Table 2) and cohort-specific analyses (Supplementary material online). Having one parent who smoked was not associated with carotid IMT in adulthood in the pooled analyses. The association between carotid IMT and both parents smoking was robust to adjustment for confounding factors from both childhood and adulthood. Furthermore, in a model adjusted for adult biological cardiovascular risk factors that were possible mediators, the association between both parents smoking and higher carotid IMT remained significant. Analyses were re-run with the category for one parent smoking separated according to the sex of the parent who smoked (data not shown). *Post hoc* Wald tests indicated no significant difference between the coefficients for mother or father in any model in pooled or cohort-specific analyses. There was no evidence that adult smoking status was an effect modifier of the association between parental smoking in childhood and adult carotid IMT.

Interactions between parental smoking and all other variables in the final models were tested (model 4). There were no significant interactions in the pooled cohort or the CDAH study. In the YFS, the effect of parental smoking on carotid IMT appeared to be modified by parental education level ($P = 0.032$, see Supplementary material online). Stratified analyses in Supplementary material online, Table S1 show that carotid IMT was significantly increased when either one or two parents smoked in those with parents of higher education, while in those with parents with lower education, the association with carotid IMT was not significant. To assess the robustness of this finding, we also examined whether other markers of parental socio-economic status (e.g. parental occupation or family income) also modified the association between parental smoking and adult carotid IMT. We found no evidence of significant interactions with these other markers.

Additional cohort-specific analyses were undertaken to estimate the effect of a greater dose of exposure to passive smoking in the home using relevant variables from both studies (Table 3). In the YFS, 58% of participants ($n = 1175$) were not exposed to parental smoking, whereas 6% ($n = 121$) were exposed to both parents smoking at both time points. Greater exposure to parental smoking over a 3-year period from 1980 to 1983 was associated with a significantly greater carotid IMT in adulthood. The concordance for both parents smoking between follow-ups was very high ($r = 0.80$) with 75% of those with both parents smoking in 1980 also having both parents smoking in 1983. The magnitude of effect remained relatively unchanged in models adjusting for age and sex, baseline sociodemographic and health factors (model 2), follow-up sociodemographic and health factors (model 3), and follow-up cardiovascular risk factors (model 4). In the CDAH study, 53% ($n = 717$) of participants reported no smokers in the family home, whereas 4% ($n = 49$) reported greater than two people smoking in the home. Greater exposure to smokers in the home was associated with greater carotid IMT in adulthood even after adjusting for all relevant confounding factors.

Full details of the sensitivity analyses can be found in Supplementary material online. In brief, adjustment for other markers of baseline

Table 1 Baseline and follow-up characteristics of Young Finns and Childhood Determinants of Adult Health study samples according to exposure to parental smoking in childhood or adolescence

	Young Finns				CDAH			
	Parental smoking			P-value	Parental smoking			P-value
	0	1	2		0	1	2	
<i>n</i>	1288	822	291		807	403	165	
Baseline								
Males (%)	45	46	42	0.439	51	49	43	0.145
Age (years)	10.9 ± 5.1	10.3 ± 4.8	9.4 ± 4.8	<0.001	11.9 ± 2.0	11.9 ± 2.0	12.2 ± 2.0	0.136
Parental school years	11.0 ± 3.8	10.4 ± 3.4	11.1 ± 3.4	<0.001				
Parental education (%) (school/vocational/university)					32/34/33	46/33/22	47/38/15	<0.001
Smoking prevalence (%) ^a	10	12	16	0.129	3	3	7	0.033
BMI ^b	17.9 ± 3.2	17.8 ± 2.9	17.5 ± 2.9	0.053	18.4 ± 2.6	18.7 ± 2.8	18.8 ± 2.7	0.062
Physical activity								
3 and 6 year olds (<i>n</i> = 767)	16.0 ± 2.4	16.1 ± 2.6	16.2 ± 2.5	0.641				
9, 12, 15, and 18 year olds (<i>n</i> = 1522)	9.0 ± 1.9	9.0 ± 1.9	9.3 ± 1.8	0.137				
Total physical activity (min/week)					439 ± 425	459 ± 425	424 ± 376	0.621
Follow-up								
Age (years)	37.9 ± 5.1	37.3 ± 4.8	36.3 ± 4.8	<0.001	32.2 ± 2.1	32.3 ± 2.1	32.6 ± 2.1	0.204
Own school years	15.7 ± 3.5	14.8 ± 3.4	14.3 ± 3.2	<0.001				
Own education (%) (school/vocational/university)					23/30/48	32/31/37	32/42/26	<0.001
Smoking prevalence (%)	16	25	34	<0.001	11	19	19	<0.001
BMI ^b	25.9 ± 4.8	25.9 ± 4.6	25.9 ± 4.7	0.983	25.5 ± 4.7	26.0 ± 4.8	26.1 ± 4.3	0.127
Physical activity score	19.6 ± 21.9	19.7 ± 19.6	17.9 ± 18.3	0.428				
Physical activity (mins/week)					166 ± 198	159 ± 200	149 ± 156	0.613
Alcohol consumption (<i>n</i> = 2289, doses/day)	0.9 ± 1.4	1.0 ± 1.4	1.2 ± 1.8	0.002				
Alcohol consumption (g/day)					10.2 ± 14.6	9.7 ± 12.8	9.4 ± 15.5	0.771
Systolic blood pressure (mmHg)	121 ± 14	120 ± 14	118 ± 14	0.049	119 ± 13	119 ± 13	120 ± 13	0.750
Diastolic blood pressure (mmHg)	75 ± 11	75 ± 12	74 ± 11	0.175	73 ± 10	73 ± 9	74 ± 9	0.663
HDL-cholesterol (mmol/L)	1.34 ± 0.33	1.33 ± 0.32	1.31 ± 0.32	0.429	1.42 ± 0.32	1.42 ± 0.33	1.41 ± 0.31	0.902
LDL-cholesterol (mmol/L)	3.16 ± 0.80	3.07 ± 0.78	3.11 ± 0.82	0.057	2.98 ± 0.83	3.00 ± 0.88	3.03 ± 0.83	0.758
Triglycerides (mmol/L)	1.29 ± 0.66	1.32 ± 0.70	1.39 ± 0.72	0.084	1.04 ± 0.61	1.13 ± 0.75	1.02 ± 0.58	0.056
Glucose (mmol/L)	5.28 ± 0.79	5.30 ± 0.96	5.26 ± 0.77	0.811	5.04 ± 0.50	5.02 ± 0.44	5.00 ± 0.44	0.535
C-reactive protein	1.85 ± 3.48	1.86 ± 4.34	1.94 ± 3.6	0.928	3.00 ± 5.78	3.02 ± 4.76	3.73 ± 10.11	0.135

^a12–18 year olds only, *n* = 1204.^bBody mass index: kg/m² calculated from weight/(height)².

Table 2 Carotid intima-media thickness in adulthood according to exposure to parental smoking in childhood or adolescence in the pooled dataset containing data from the Young Finns and Childhood Determinants of Adult Health studies

Parental smoking	n	Adjusted model 1 ^a			Adjusted model 2 ^b			Adjusted model 3 ^c			Adjusted model 4 ^d		
		Mean	SE	P-value	Mean	SE	P-value	Mean	SE	P-value	Mean	SE	P-value
None	1930	0.637	0.002		0.638	0.002		0.637	0.002		0.637	0.002	
Either parent smoked	1112	0.638	0.003	0.729	0.637	0.003	0.910	0.637	0.003	0.967	0.638	0.003	0.921
Both parents smoked	408	0.653	0.004	0.001	0.653	0.004	0.001	0.652	0.005	0.003	0.652	0.005	0.003
P _{trend}				0.005			0.011			0.021			0.017

Values are estimated marginal means of maximum carotid IMT.
^aAdjusted for age, sex, and cohort.
^bAdjusted for age, sex, cohort, parental education, childhood BMI, and childhood smoking.
^cAdjusted for age, sex, cohort, parental education, childhood BMI, childhood smoking, adult education, and adult smoking status.
^dAdjusted for age, sex, cohort, parental education, childhood BMI, childhood smoking, adult education, and adult smoking status, adult systolic blood pressure, adult LDL-cholesterol, adult triglycerides, adult C-reactive protein.

socio-economic status (Supplementary material online, *Tables S2 and 3*), baseline biomedical cardiovascular risk factors (Supplementary material online, *Tables S6 and 7*), baseline smoking level (Supplementary material online, *Tables S4 and 5*), participant pack-years of smoking (Supplementary material online, *Tables S4 and 5*), or passive smoking (Supplementary material online, *Table S8*, YFS only) did not appreciably alter the interpretation of the results.

Discussion

These data demonstrate the pervasive effect of exposure to parental smoking earlier in life on arterial health in adulthood. Adults who had been exposed to both parents smoking in childhood or adolescence had greater carotid IMT in adulthood than those not exposed. The effect was consistent across two independent cohorts, present when alternative measures of exposure were used and was largely independent of cardiovascular risk factors. This adds further evidence that exposure to parental smoking earlier in life has an irreversible effect on arterial health, consistent with our earlier findings regarding brachial artery FMD.⁶

Using the vascular age concept,¹⁵ we determined that the independent effect of exposure to both parents smoking on vascular age was equivalent to being 3.3 (95% CI: 1.31, 4.48) years older in the pooled cohort (YFS: 2.3 years older; CDAH study: 4.6 years older). While this difference appears modest, it is important to consider that it represents the independent effect of a single measure of exposure some 20 years earlier in a group with greater cardiovascular risk. For example, those with both parents smoking were more likely, as adults, to be smokers or overweight than those not exposed to parental smoking. The effect was only present when both parents smoked, suggesting the level of exposure is important. This is supported by the cumulative exposure data in the YFS and total number of smokers in the home in the CDAH study, both of which were significantly associated with greater carotid IMT. Parental smoking showed a high continuation over time, suggesting that exposure in the group with both parents smoking likely remained high, perhaps contributing to the greater effect seen. Others using

retrospective¹⁶ and cross-sectional^{2,3,17} study designs have also shown dose–response effects of passive smoke on arterial health.

The association between exposure to parental smoking earlier in life and carotid IMT in adulthood was independent of biomedical risk factors. These findings are consistent with our recent results regarding impaired brachial FMD, which was suggestive of an effect of parental smoking exposure on adult endothelial function.⁶ Conflicting evidence regarding the nature of the relationship between measures of vascular function (i.e. FMD) and structure (i.e. IMT),^{18–20} provided a rationale for examining carotid IMT as a separate outcome. Together, these studies suggest a direct and pervasive effect of exposure to environmental cigarette smoke during this period on both vascular structure and function into adulthood. Importantly, the results were robust to adjustment for a wide range of potential covariates and alternative exposure measures that have not previously been explored. Biologically, environmental cigarette smoke affects several processes related to IMT, including some that are distinct to the process of endothelial dysfunction.²¹ These include the activation of platelets leading to their recruitment, adherence, and migration to the endothelium,²² increased oxidative stress resulting in endothelial dysfunction,²³ greater levels of inflammatory markers such as C-reactive protein and oxidized LDL-cholesterol,²⁴ a weakening of serum antioxidant defence, accelerated lipid peroxidation, and accumulation of LDL-cholesterol in macrophages,²⁵ and reduced levels of HDL-cholesterol, the latter shown in children exposed to maternal smoking.²⁶

The effect of parental smoking appeared stronger in the CDAH study than in the YFS, though an interaction between parental smoking and cohort was not evident in the pooled analyses. Though the same difference was also present in our study of brachial FMD, the differences in IMT measurement between the studies mean we cannot be sure this is a true difference. If the difference in the magnitude of effect were true, the dose of exposure could explain it; however, data on the dose of parental smoking were lacking in both studies. Information on cigarette consumption in both countries from 1980 suggests that per capita consumption of cigarettes in Australia (3279) was double that in Finland (1613).²⁷ Furthermore, serum cotinine levels of Finnish children are much lower than in

Table 3 Difference in carotid intima-media thickness per unit increase in exposure to parental smoking in childhood or adolescence in the Childhood Determinants of Adult Health and Young Finns studies

	<i>n</i>	Adjusted model 1 ^a			Adjusted model 2 ^b			Adjusted model 3 ^c			Adjusted model 4 ^d		
		<i>β</i>	SE	P-value	<i>β</i>	SE	P-value	<i>β</i>	SE	P-value	<i>β</i>	SE	P-value
CDAH													
Number smokers at home (per smoker)	1362	0.007	± 0.003	0.021	0.007	± 0.003	0.013	0.007	± 0.003	0.025	0.007	± 0.003	0.022
YFS													
Cumulative parental smoking exposure (per unit) ^e	2041	0.004	± 0.002	0.034	0.003	± 0.002	0.060	0.003	± 0.002	0.066	0.003	± 0.002	0.083

^aAdjusted for age and sex.
^bAdjusted for age, sex, and parental education.
^cAdjusted for age, sex, parental education, adult education, and adult smoking status.
^dAdjusted for age, sex, parental education, adult education, adult smoking status, adult BMI, adult LDL-cholesterol, and C-reactive protein.
^eRange: 0 (no parents smoked at either time point) to 4 (both parents smoked at both time points).

other countries.²⁸ Therefore, exposure to parental smoking might have been less in Finland, which could account for the weaker effect on adult carotid IMT in that cohort, if the differences are real.

Parental education modified the effect of parental smoking on carotid IMT in the YFS. Children of parents with less education had greater mean carotid IMT than those with more parental education, but the effect of parental smoking on carotid IMT was only evident in those with greater parental education. The same interaction was not present between parental smoking and other markers of parental socio-economic status, nor in the CDAH study, so its importance is unclear. If the association is true, we hypothesize that the lower burden of cardiovascular risk factors in those from higher SES backgrounds makes the effect of parental smoking more apparent, a result consistent with our previous findings on brachial FMD.⁶

Reducing young people’s exposure to tobacco smoke is a public health priority. Legislation can reduce passive smoke exposure, with restriction of smoking in public places reducing hospitalizations for cardiovascular and respiratory disease.²⁹ Home smoking bans specifically benefit young people and data from the USA suggest such bans have increased from ~50% in the mid-1990s to 85% in 2006–07, suggesting that exposure to passive smoke at home is declining.³⁰ Unfortunately, these reductions have largely occurred in higher socio-economic groups, meaning socio-economic inequalities in passive smoke exposure remain. Banning smoking in cars where young people are present, which is enforceable and targeting an environment where exposure is high,³¹ could reduce these inequalities. Such legislation already exists in Australia, Canada, and USA.³² Our results support adoption of all measures that protect young people from passive smoke.

Study strengths and limitations

The strengths of this study are the two independent cohorts, follow-up over >20 years and the similarity of carotid imaging protocols between the studies. Furthermore, the availability of carotid IMT measurements from a much larger sample of CDAH participants than the subset with FMD measurements (*n* = 1375 vs. *n* = 104) helped to overcome previous study limitations associated with a small sample size in this cohort and allowed examination of different exposure categories and covariates with much greater precision. A limitation is that IMT measurements were performed manually rather than with automatic edge detection largely because the technology was not widely available or well accepted when the measurements were undertaken. Although studies have shown that manual and automatic IMT measures have similar reproducibility and associations with cardiovascular risk factors,^{33,34} this has likely contributed to variation in our data. In support of our data, the test–re-test coefficients of variation for both cohorts (YFS 6.4%¹⁰ and CDAH 5.9%, see ‘Methods’) among a subsample of participants in each cohort are similar to those reported in the literature for both manual and automated IMT measures.³⁴ It is perhaps of more importance to this study that the imaging and measurement protocols were similar across cohorts and that readers were blinded to the exposure status of participants, meaning that any error in IMT measurements was likely non-differential. The ultrasound transducer in the CDAH study (7 mHz) had a lower frequency than that used in the YFS (13 mHz). The lower resolution of the CDAH images may have increased measurement variability in these data. However, we do

not believe this has greatly affected our results as the dispersion of the IMT measurements (calculated as SD/mean) in the CDAH study (male: 0.1639; female: 0.1379), was very similar to those of the YFS where the higher frequency transducer was used (male: 0.1606; female: 0.1376).¹⁰ These limitations in IMT measurement will have contributed to variation in the reproducibility of IMT measures and it is possible the true level of IMT and the difference in IMT between exposure groups differs to that shown here. As such, the results should be interpreted with caution.

Other limitations include the lack of information on smoking dose and that parental smoking was gathered from parents in the YFS and from children or adolescents in the CDAH study. How this may have influenced results is uncertain, but there is high concordance between parents' and children's reports of parental smoking.³⁵ While the measurement of serum cotinine of participants would be ideal, parental smoking reported by parents or children correlates with children's cotinine levels.^{28,36} Parental smoking may have been under-reported³⁷ and this might mean we have underestimated the association between parental smoking and carotid IMT. Adult exposure to passive smoking was only measured in the YFS. Adjusting for this among non-smokers did not alter the associations seen (Supplementary material online, Table S8). Only 6.5% of Australian adults report passive smoke exposure in the home³⁸ and, in both countries, exposure outside the home is limited because of public smoking bans.³⁹ We therefore believe that adult passive smoke exposure is unlikely to explain these associations. Data on baseline biomedical cardiovascular risk factors were not available for all CDAH study participants and were not included as covariates in the main analyses. Sensitivity analyses (see Supplementary material online) show that it is unlikely these risk factors explain the association. Further, in the main analyses, we controlled for BMI, a major determinant of cardiovascular risk factors, and adjusted for adult biomedical cardiovascular risk factors based on the rationale that they track over time.⁴⁰

Conclusions

This is the first study to prospectively examine the association between exposure to parental smoking and carotid IMT measured in adulthood. In support of our earlier finding in relation to brachial FMD, our data demonstrate the pervasive effect of exposure to parental smoking on arterial health in adulthood. These data reinforce the importance of reducing the population's exposure to environmental cigarette smoke, particularly for young people.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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