Combined Effects of Child and Adult Elevated Blood pressure on Subclinical Atherosclerosis: The International Childhood Cardiovascular Cohort Consortium

Running title: Juhola et al.; Blood pressure and subclinical atherosclerosis

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Abstract:

Background—Elevated blood pressure (BP) levels in childhood have been associated with subsequent atherosclerosis. However, it is uncertain whether this risk is attenuated in individuals who acquire normal BP by adulthood. The present study examined the effect of child and adult BP levels on carotid artery intima-media thickness (cIMT) in adulthood.

Methods and Results—The cohort consisted of 4,210 participants from four prospective studies (mean follow-up 23 years). Childhood elevated BP was defined according to the tables from the National High Blood Pressure Education Program. In adulthood BP was classified as elevated for individuals with systolic BP ≥120mmHg, diastolic BP ≥80mmHg or with self-reported use of antihypertensive medications. cIMT was measured in the left common carotid artery. High IMT was defined as an IMT ≥age-, sex-, race-, and cohort-specific 90th percentile. Individuals with persistently elevated BP and individuals with normal childhood BP, but elevated adult BP had increased risk of high cIMT (RR[95%CI] 1.82[1.47-2.38] and 1.57[1.22-2.02], respectively) when compared to individuals with normal child and adult BP. In contrast, individuals with elevated BP as children but not as adults did not have significantly increased risk (1.24[0.92-1.67]). In addition, these individuals had lower risk of increased cIMT (0.66[0.50-0.88]) when compared to those with persistently elevated BP. The results were consistent when controlling for age, sex, adiposity and when different BP definitions were applied.

Conclusions—Individuals with persistently elevated BP from childhood to adulthood had increased risk of carotid atherosclerosis. This risk was reduced if elevated BP during childhood resolved by adulthood.

Key words: atherosclerosis, blood pressure, epidemiology, hypertension
Introduction

Hypertension is a major modifiable risk factor for atherosclerosis\(^1\). It was estimated that about 50% of stroke and ischemic heart disease worldwide and a total of 7.6 million deaths in 2001 were attributable to high blood pressure (BP)\(^2\). The atherosclerotic process begins in childhood. In autopsy studies, elevated childhood BP has been associated with atherosclerotic lesions\(^3,4\). Childhood BP levels also predict increased occurrence of subclinical atherosclerosis\(^5-9\). Indeed, expert panel guidelines recommend that BP should be measured annually from the age of 3 years\(^10\). Prior reports have shown that based on multivariable models taking into account adult BP levels, childhood BP levels are significantly associated with subclinical atherosclerosis in adulthood\(^7,9\). However, it is not precisely known if the effects of elevated BP during childhood on atherosclerotic markers are permanent or reversible should the individual acquire normal BP levels by adulthood.

Ultrasound measurement of common carotid intima-media thickness (cIMT) serves as an early marker of structural atherosclerosis. High cIMT has been shown to associate with cardiovascular risk factors and the risk of cardiovascular and cerebrovascular events\(^11-13\).

Within an international consortium of cardiovascular risk factor studies initiated in childhood known as the International Childhood Cardiovascular Cohort (i3C) Consortium\(^14\), we examined data for 4,210 individuals from four cohorts to determine the combined effects of child and adult elevated BP on cIMT. The main aim was to test a hypothesis whether a change from elevated BP status in childhood to normal BP in adulthood is associated with an attenuated risk of developing increased cIMT.
Methods

Study Cohorts

Data from four prospective cohort studies conducted in the United States (Bogalusa Heart Study, Muscatine Study), Finland (Cardiovascular Risk in Young Finns Study), and Australia (Childhood Determinants of Adult Health (CDAH) Study) were analyzed. In all cohorts, analyses included participants who had a baseline evaluation during childhood and who also attended a follow-up examination as an adult. In cohorts that conducted several childhood examinations, data from the earliest examination were used. In adulthood, data from the latest available exam were utilized in Bogalusa, Young Finns and CDAH, whereas in Muscatine the first adult study with IMT measures was used to provide as similar follow-up period as possible.

Descriptions of these cohorts, including attrition analyses, have been previously been published. All blood biochemical values were measured from fasting samples. Korotkoff’s first phase was used to define systolic and fifth phase to define diastolic BP. Height and weight were measured during field studies. Smoking habits were assessed with questionnaires in childhood and adulthood (Muscatine only in adulthood). Each study received ethical approval from the appropriate institutional review boards, and obtained informed consent from the study participants or parents.

The Muscatine Study

Study sample

For this analysis, 721 representative individuals who had previously participated in at least one childhood examination between 1970-1981, and in the 1996-99 adult follow-up (aged 33-45 years) when cIMT was measured were included.

Clinic measurements
Baseline BP was measured using standard mercury sphygmomanometers; follow-up measures were obtained using a Hawksley random-zero sphygmomanometer (GelmanHawksley Limited, Sussex, England). All measurements were taken on the right arm, before venipuncture, and after the participant had been seated for five minutes. The mean of three measurements was used for analysis.

**Carotid artery ultrasound**

Carotid ultrasound studies were performed by a single technician using the Biosound Phase 2 ultrasound machine and a 10-MHz transducer (Biosound Esaote Inc., Indianapolis, IN)\(^\text{15}\). A 4.4% random sample underwent repeat carotid ultrasound studies during a second visit, a mean of 107 days later, to assess intra-individual reproducibility. The mean absolute difference for all cIMT segments was 0.06mm\(^\text{15}\).

**The Bogalusa Heart Study**

**Study sample**

For this analysis, 586 individuals who had BP measured in either the 1981-83, 1984-85, or 1987-88 youth surveys (when aged 4-17-years) and BP and cIMT measured in either the 2001-02 or 2003-07 adult surveys (then aged 23-42-years) were included.

**Clinic measurements**

BP measurements at baseline and follow-up were obtained on the right arm, after venipuncture with participants in a relaxed sitting position. Three BP readings were taken by each of two randomly assigned observers for a total of six measurements. The mean of the six replicate readings was used in the analyses. In childhood, those reporting smoking at least one cigarette per week were defined as regular smokers.

**Carotid artery ultrasound**
B-mode ultrasound examinations of the carotid arteries were performed at the 2001-02 and 2003-07 follow-ups using a Toshiba Sonolayer SSH160A ultrasound machine with a 7.5-MHz linear array transducer (Toshiba Medical, Tokyo, Japan). Seventy-five participants underwent repeat ultrasound examinations 10-12 days after their initial visit to determine intra-individual reproducibility. The mean absolute difference and standard deviation (SD) between measurements for all cIMT segments was 0.05±0.03 mm.

The Cardiovascular Risk in Young Finns Study

Study Sample

For this analysis, 2,223 participants who were 6-18 years old at baseline in 1980 and who had BP measured in childhood and cIMT and BP measured in 2001 or 2007 (27-45 years) were included. Participants aged 3 years at baseline were not included because BP measures were collected using an ultrasound device.

Clinic measurements

BP was measured using a standard mercury sphygmomanometer at baseline and using a random zero sphygmomanometer (Hawksley&Sons Ltd, Lancin, UK) at follow-up. All measurements were taken on the right arm, before venipuncture (among adults after venipuncture) and after the participant had been seated for five minutes. Readings to the nearest even number of millimeters of mercury were performed at least three times on each participant. The mean of these three measurements was used in the analyses. Socioeconomic position in childhood was assessed by questionnaires. Baseline pubertal status was assessed by Tanner staging and categorized as not started, on-going or finished. In childhood, those reporting smoking daily or weekly were defined as regular smokers.

Carotid Artery Ultrasound Studies
B-mode ultrasound studies of the left carotid artery were performed at both 2001 and 2007 follow-ups using an Acuson Sequoia 512 ultrasound machine with a 13-MHz linear-array transducer (Siemens Medical Solutions USA Inc., Mountainview, CA). To assess intra-individual reproducibility of ultrasound measurements, 57 participants were re-examined 3 months after their initial visit. The average absolute difference and SD between measurements was 0.05±0.04 mm.

**The Childhood Determinants of Adult Health (CDAH) Study**

**Study sample**

For this analysis, data were included from 680 individuals who had BP measured in the 1985 baseline survey (when aged 9-15 years) and cIMT and BP measured in the 2004-06 adult follow-up survey (27-36-years).

**Clinic measurements**

BP measurements were obtained from the left brachial artery, before venipuncture, using a standard mercury sphygmomanometer at baseline. All measurements were taken after the participant had been seated for five minutes. This procedure was repeated after five minutes, and the mean of the two measurements was used in the analyses. At follow up, BP was measured from the right brachial artery, after venipuncture, using a digital automatic monitor (Omron Corporation, Kyoto, Japan). The mean of the three consecutive measurements separated by a one-minute interval was used in the analyses. Participants retrospectively reported the highest level of education completed by their guardian. Smoking in childhood was assessed using a question: How long have you been smoking regularly?

**Carotid artery ultrasound**

B-mode ultrasound studies of the carotid artery were performed using a portable Acuson Cypress
ultrasound machine with a 7.0-MHz linear-array transducer (Siemens Medical Solutions USA Inc., Mountainview, CA)\textsuperscript{22}. Intra-individual reproducibility for replicate max cIMT measurements was assessed in a random sample of 30 participants. The average absolute difference and SD between measurements was 0.02±0.04 mm.

**Classification of BP levels**

Elevated BP in childhood was defined according to BP tables issued by the National High Blood Pressure Education Program (NHBPEP)\textsuperscript{23} and in adulthood according to the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood pressure\textsuperscript{24}. BP status in youth was classified as normal if systolic and diastolic BP (fifth phase) were <90\textsuperscript{th} percentile for age, sex, and height using the NHBPEP tables, and elevated if systolic or diastolic BP were ≥90\textsuperscript{th} percentile. BP status in adulthood was classified as normal if systolic BP<120mmHg and diastolic BP<80mmHg, and elevated if systolic BP≥120mmHg or diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications.

Four groups based on childhood and adult BP levels were defined for comparison of outcomes: (1) Control group – participants who had a normal BP in childhood and normal BP as an adult; (2) Resolution group – participants who had elevated BP in childhood but not as an adult; (3) Incident group – participants with a normal BP in childhood who had elevated BP as an adult; and (4) Persistent group – participants who had elevated BP in childhood and as an adult.

**Definition and classification of high cIMT in adulthood**

The maximum cIMT measurement from the far wall of the left common carotid artery was chosen since it was the most consistent cIMT measurement across the cohorts\textsuperscript{25}. Additional
analyses performed using average cIMT values (CDAH and Young Finns cohorts) or data from
the left and right carotid arteries (Muscatine and Bogalusa cohorts) gave essentially similar
results (data not shown). In line with our previous reports, percentile points stratified by age, sex,
race (Bogalusa) and cohort were first calculated and those with a maximum cIMT ≥90th
percentile were classified as having high cIMT.20, 25, 26 In individual cohorts, IMT cut-points in
different age-, sex-, and race-groups varied as follows: Muscatine, 0.804-0.927 mm; Bogalusa,
0.796-1.110 mm; YF, 0.672-0.920 mm; CDAH, 0.660-0.825 mm.

Statistical Analyses

Comparisons of characteristics among the cohorts were conducted using chi-square tests or
analysis of variance.

Relative risks (RR) and 95% confidence intervals (CI) were calculated using Poisson
regression with robust standard errors to examine the associations between child-adult BP groups
and adult high cIMT. All analyses were adjusted for length of follow-up, cohort and race (five
cohort/race groups: Muscatine, Bogalusa whites, Bogalusa blacks, Young Finns, and CDAH),
and adult body mass index (BMI, calculated as weight(kg)/[height(m)²]). Those analyses that
were not stratified by age or sex were adjusted for these factors. Both data pooling and random-
effects meta-analysis27, 28 techniques were used. In addition, a linear trend over BP groups was
tested with a regression analysis. Cohort×BP, sex×BP, and age×BP group interaction effects on
high cIMT were tested. There were no significant interaction effects.

Several sensitivity analyses were performed to examine the influence of different child
and adult BP definitions, sex, age and adiposity status on the magnitude of the associations. In
cohorts with relevant available data, pooled analyses were re-run after additional adjustment for
smoking status (Bogalusa, Young Finns, and CDAH), socioeconomic status (Young Finns,
CDAH) and pubertal status (Young Finns) in childhood.

In order to examine the influence of BMI on change in BP status between childhood and adulthood, we present mean (SD) change in BMI (adult minus child) of age-, sex-, cohort-, and race-specific (Bogalusa) z-scores for each BP group (control, resolution, incident, and persistent). Logistic regression analysis was used to examine differences between the control group and the remaining BP groups. The logistic regression models were adjusted for length of follow-up for analyses stratified by cohort and additionally adjusted for cohort in pooled analyses.

Statistical analyses were performed using STATA-10 and SAS 9.1.3. Statistical significance was inferred at a 2-tailed P-value <0.05, without adjustment for multiple comparisons.

Results
Data for 4,210 participants (Table 1) with mean follow-up interval of 23 years were available. 1,632 (39%) participants in childhood and 2,078 (49%) participants in adulthood had elevated BP. Among children with normal or elevated BP, 42% and 60% respectively had elevated BP as adults (Supplemental Table 1). In all cohorts, significant tracking was observed between child and adult BP levels (Supplemental Table 2).

Influence of childhood and adult elevated BP on cIMT

Pooled Analyses
The risk of high cIMT among participants whose elevated BP resolved by adulthood was not significantly different from those in the control group (Table 2). Risks were higher among participants who had elevated BP in adulthood (incident and persistent groups) compared with the control group. Individuals in the resolution group had lower risk of increased cIMT (RR 0.66,
95% CI 0.50-0.88) when compared to those with persistently elevated BP. In linear regression analyses, a significant trend over BP groups was observed in age-stratified, sex-stratified and pooled data (P always <0.05).

**Meta-Analysis**

The meta-analysis results are shown in Figure 1. The results were similar to those observed using pooled analyses. Although there were some between-cohort differences in effects, notably CDAH showing no difference between any of the comparator groups with the control group, heterogeneity was non-significant.

**Sensitivity Analyses**

Sensitivity analyses that used alternate BP status definitions were consistent with the observation that the risk of high cIMT among the resolution group was not significantly different from the risk among the control group (Supplemental Tables 3 and 4). For example, in analyses using more stringent BP cut-offs (≥95th percentile using the NHBPEP tables in childhood and ≥140/90 in adulthood), the RR (95% CI) values in comparisons with control group were 1.22 (0.96-1.54) for resolution group, 1.33 (1.04-1.71) for incident group and 1.94 (1.45-2.61) for persistent group.

Findings were consistent in analyses stratified by age, sex or adiposity status (Table 2, Supplemental Table 5). The results were not altered when analyzed without race-adjustment (data not shown) or using different IMT cut-points (Supplemental Table 6). Data from the Bogalusa, Young Finns, and CDAH cohorts allowed us to determine the independence of the observed effects after accounting for child smoking, SES and puberty. The findings were not altered after inclusion of these variables (data not shown). The analyses were also repeated after exclusion of those individuals using antihypertensive medication (N=254, 6.0% of the whole
cohort) with essentially similar findings.

**Interactions between adiposity and BP status**

To assess the effect of BMI on BP values from childhood to adulthood, change in BMI z-score was calculated and examined across BP groups (Table 3). In pooled analyses, BMI z-score in the resolution group significantly decreased between childhood and adulthood compared to the control group. For the incident and persistent groups, BMI z-score significantly increased between childhood and adulthood. As illustrated in **Supplemental Table 7**, changes in adiposity status from childhood to adulthood paralleled BP status changes.

**Discussion**

The main finding of the pooled analyses from four prospective cohort studies was that among individuals with elevated BP in childhood and normal BP in adulthood the risk of increased cIMT in adulthood was somewhat higher (RR 1.2), but not significantly increased compared to those with persistently normal BP. In contrast, adults with elevated BP, irrespective of their childhood BP status, had significantly increased risk of high cIMT. These results were consistently demonstrated in meta-analysis of the data, in both sexes, and across different age and adiposity groups.

In prior analyses in the Muscatine Study\textsuperscript{15}, the Bogalusa Heart Study\textsuperscript{16} and the Young Finns Study\textsuperscript{7}, childhood BP levels predicted increased adult cIMT. In the Young Finns Study\textsuperscript{7, 9}, analyses using continuous BP data showed that in 12-18 year old individuals the association between childhood BP levels and adult cIMT or coronary calcification remained significant after adjustment for adult BP levels or BP change between childhood and adulthood. In addition, in other cohort studies elevated BP in childhood and adolescence has been linked with
cardiovascular morbidity and premature death.\textsuperscript{30-32} In the present analyses conducted in four cohorts using categorically-defined BP levels, the risk of high cIMT was not significantly increased among adolescents aged 12-18 years with elevated BP only in childhood, even though the risk increase in this age group approached 30\% and was higher than among children aged 4-9 years. These results suggest that the effects of elevated BP in childhood on early atherosclerosis can be mostly reversed if normal BP levels are achieved by adulthood. However, as the lower limit of the 95\% confidence interval was close to 1 in some analyses comparing resolution and control groups, the independent effect of elevated childhood BP cannot be definitely ruled out.

Concerning the reversibility of childhood risk factor effects, we\textsuperscript{20} previously reported that overweight or obese children who become non-obese adults have a mainly similar adult risk profile as those who were never obese. However, childhood adiposity had some residual effect on hypertension risk. Tirosh et al.\textsuperscript{33} observed among a cohort of over 37,000 apparently healthy males that BMI measured at a mean age of 17 years, independent of adult BMI, was associated with later risk of coronary heart disease, but not diabetes.

Our findings suggest that the effects of elevated childhood BP on cIMT are not completely permanent, as those individuals with resolution of increased BP did not have significantly increased adult cIMT. While it might be tempting to interpret these data by downplaying the importance of childhood elevated BP, it is necessary to consider that elevated child BP is the strongest predictor of adult hypertension\textsuperscript{34} and that once elevated BP is established it is difficult to reverse – as was highlighted in our results with only 40\% of youth with elevated BP able to avoid having elevated BP as adults. We observed significant tracking of BP levels within all cohorts, and the risk of elevated adult BP was dependent on childhood BP status. Adiposity status is known to have a substantial effect on both BP levels and accelerated...
atherosclerosis. We previously observed that especially adult BMI levels are associated with elevated BP and increased carotid IMT\textsuperscript{20}. Therefore, we conducted several analyses to take into account the effect of adiposity. First, the main analyses were adjusted for adult BMI levels. Second, analyses were performed separately in normal weight and overweight/obese participants with essentially similar results. These results support the view that the markedly reduced risk for high cIMT among the BP resolution group is independent of adiposity status. However, we found support for weight management by observing the most favorable changes in adiposity levels between childhood and adulthood among the BP resolution group. Clearly maintaining normal BMI and normal BP throughout life is preferred, and maintaining low or optimum risk status throughout life is associated with a very low lifetime risk of CVD\textsuperscript{35}. However, these results suggest that when increased BMI or BP are detected in childhood or adolescence, interventions should be implemented to reduce risk of atherosclerosis development in adulthood, as persistence of these risk factors is associated with increased carotid IMT. These results are limited in that they do not demonstrate the optimum timing (age) of risk factor improvement or whether more aggressive treatment of elevated BP in childhood with medication would be beneficial. Future research should focus on these questions.

Using the NHBPEP tables, there were considerable differences in childhood prevalence of elevated BP. In the Muscatine, Young Finns, and CDAH cohorts (on the order of 33-49\%) prevalence was far higher than what would be expected based on the definition coinciding with the 90th percentile within the NHANES data (on which the NHBPEP tables were based). Population, secular, and/or method differences (e.g., a different number of BP measurements to derive mean values) may have contributed to this disparity. For example, Muscatine, Young Finns, and CDAH participants are predominantly of white European descent whereas NHANES
measured participants of all ethnicities represented in the USA. These findings should be considered while using the tables in the clinical setting. Sensitivity analyses using a definition for elevated childhood BP as diastolic or systolic BP ≥90th percentile according to age-, sex-, height-, and cohort-specific levels (Supplemental Table 3) which provided similar results suggests the validity of our main findings. Although there was no statistically significant heterogeneity among the cohorts, the findings from the CDAH study were somewhat different from others as the risk of high cIMT was not increased in the incident high BP or persistent high BP groups. In line, in our previous analyses concerning the link between childhood obesity and adult cIMT, the association was non-significant and weakest in the CDAH study20. The most likely explanation for this is that carotid imaging in CDAH was performed using a portable ultrasound equipment with lower resolution compared to other studies22.

Potential limitations of our study should be considered. First, as the cohorts were comprised of young adults at follow-up, we were not able to study associations with cardiovascular events. Instead we used cIMT as a surrogate end-point. Our main analyses were performed using a maximal measure of left common carotid artery, the most consistent cIMT measurement across the cohorts25. Ideally average measures of both carotid arteries would have been used in the analyses. Only Bogalusa and Muscatine studies had measures from both the left and right sides. Additional analyses using data from both sides in these cohorts showed essentially similar results compared to the main analyses. Concerning cardiovascular event prediction, Polak et al. 13 have shown that both common and internal carotid IMT measures predict cardiovascular outcomes, but only internal carotid data improves the classification of risk of cardiovascular disease. However, prior reports have shown that BP is more strongly related to the cIMT in the common segment than in other segments36 and the common segment rarely has
any raised plaque\textsuperscript{37}. Second, BP measurements were only taken from a single time-point in childhood and again in adulthood. However, in the Young Finns cohort we have previously shown that concerning the association between childhood BP and adult cIMT, single childhood measurements seem to be nearly as informative as repeated measurements\textsuperscript{7}. Third, although the RRs indicated some residual effect of elevated child BP, the differences between resolution and control groups were not statistically significant among a total cohort of 4,210 participants. Therefore the possibility of limited power in our analyses has to be taken into account while interpreting these findings. Fourth, during the time of baseline examinations the prevalence of overweight or obesity was lower than contemporary children, and given the link between obesity and BP the results might not be completely generalized to today’s children. Finally, as study participants were predominantly Caucasian, the results should be generalized to other ethnicities with caution. The main strength is the opportunity to combine data from four longitudinal cohorts around the world. The pooled analyses allowed comparisons between different BP groups whereas in separate cohorts there would have been insufficient statistical power.

**Conclusions**

Our analyses from four longitudinal childhood cohort studies showed that the effect of elevated BP in childhood on carotid atherosclerosis as assessed by cIMT is markedly reduced if these individuals become normotensive adults.

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**Conflict of Interest Disclosures:** None.

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Table 1. Child and adult characteristics of participants in the four cohorts.

<table>
<thead>
<tr>
<th>N (males/females)</th>
<th>Muscatine</th>
<th>Bogalusa</th>
<th>Young Finns</th>
<th>CDAH</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Childhood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>14.6 (1.9)</td>
<td>12.5 (3.4)</td>
<td>12.0 (4.2)</td>
<td>11.9 (2.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age range, y</td>
<td>8-18</td>
<td>4-18</td>
<td>6-18</td>
<td>9-15</td>
<td></td>
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<tr>
<td>Blacks, N(%)</td>
<td>-</td>
<td>209 (35.7)</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Height, cm</td>
<td>163.4 (10.2)</td>
<td>153.3 (17.6)</td>
<td>149.4 (20.2)</td>
<td>151.3 (14.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>116.9 (12.7)</td>
<td>106.9 (10.8)</td>
<td>114.1 (11.3)</td>
<td>109.3 (12.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>68.8 (10.9)</td>
<td>55.9 (11.6)</td>
<td>68.7 (9.6)</td>
<td>66.4 (11.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BP status, N(%)</td>
<td>Normal</td>
<td>Elevated</td>
<td>Normal</td>
<td>Elevated</td>
<td></td>
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<tr>
<td></td>
<td>437 (60.6)</td>
<td>534 (91.1)</td>
<td>1151 (51.8)</td>
<td>456 (67.1)</td>
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<td></td>
<td>284 (39.4)</td>
<td>52 (8.9)</td>
<td>1072 (48.2)</td>
<td>224 (32.9)</td>
<td>&lt;0.001</td>
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<td>BMI, kg/m²</td>
<td>21.4 (3.4)</td>
<td>19.9 (4.3)</td>
<td>18.3 (3.1)</td>
<td>18.6 (2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI status, N(%)</td>
<td>Normal</td>
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<td>Normal</td>
<td>Overweight</td>
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<tr>
<td></td>
<td>573 (79.5)</td>
<td>121 (16.8)</td>
<td>2017 (90.8)</td>
<td>603 (88.7)</td>
<td></td>
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<tr>
<td></td>
<td>27 (3.7)</td>
<td>88 (13.1)</td>
<td>173 (7.8)</td>
<td>62 (9.1)</td>
<td></td>
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<td>Regular smoking, N(%)</td>
<td>-</td>
<td>42 (7.2)</td>
<td>31 (1.4)</td>
<td>15 (2.2)</td>
<td>&lt;0.001</td>
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<td>55 (15.0)</td>
<td>157 (12.5)</td>
<td>71 (10.6)</td>
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<tr>
<td><strong>Adulthood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>38.6 (2.9)</td>
<td>33.9 (3.6)</td>
<td>38.0 (4.8)</td>
<td>31.8 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age range, y</td>
<td>33-46</td>
<td>23-42</td>
<td>27-45</td>
<td>27-36</td>
<td></td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>113.8 (11.8)</td>
<td>115.7 (14.4)</td>
<td>120.8 (14.3)</td>
<td>118.2 (13.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>74.0 (9.7)</td>
<td>77.8 (10.6)</td>
<td>75.7 (11.4)</td>
<td>72.7 (9.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>BP status, N(%)</td>
<td>Normal</td>
<td>Elevated</td>
<td>Normal</td>
<td>Elevated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>450 (62.4)</td>
<td>322 (55.0)</td>
<td>999 (44.9)</td>
<td>361 (53.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>271 (37.6)</td>
<td>264 (45.1)</td>
<td>1224 (55.1)</td>
<td>319 (46.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.2 (5.8)</td>
<td>30.2 (7.9)</td>
<td>26.1 (4.8)</td>
<td>25.8 (4.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI status, N(%)</td>
<td>Normal</td>
<td>Overweight</td>
<td>Normal</td>
<td>Overweight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>235 (32.6)</td>
<td>173 (29.5)</td>
<td>1023 (46.2)</td>
<td>328 (50.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>245 (34.0)</td>
<td>161 (27.5)</td>
<td>795 (35.9)</td>
<td>221 (34.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>241 (33.4)</td>
<td>252 (43.0)</td>
<td>395 (17.9)</td>
<td>102 (15.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cIMT, mm</td>
<td>0.71 (0.15)</td>
<td>0.74 (0.16)</td>
<td>0.67 (0.10)</td>
<td>0.60 (0.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of follow-up, y</td>
<td>24.0 (2.1)</td>
<td>21.4 (1.5)</td>
<td>26.0 (2.2)</td>
<td>19.9 (0.6)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Values are mean (SD) for continuous variables or N(%) for dichotomous variables unless stated otherwise. Abbreviations: BMI, body mass index; BP, blood pressure; CDAH, Childhood Determinants of Adult Health; cIMT, carotid intima-media thickness. In childhood, overweight and obesity were defined using international cut-points. In adulthood, a cut-point of 25 kg/m² was used to define overweight and 30 kg/m² for obesity. Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if systolic BP≥120mmHg, diastolic BP≥80mmHg or if individual self-reported use of antihypertensive medications.

*P-values are for comparisons across cohorts, with the use of linear regression and chi-square tests.
Table 2. Relative risks (RR) and 95% confidence intervals (95%CI) of high cIMT (≥90th percentile) according to blood pressure (BP) group* in childhood and adulthood (age 23-46 years, mean follow-up 23 years).

<table>
<thead>
<tr>
<th>BP group</th>
<th>Participants 4-11 years</th>
<th>Participants 12-18 years</th>
<th>Males</th>
<th>Females</th>
<th>All participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
</tr>
<tr>
<td>Control</td>
<td>35/457 1.00 ref</td>
<td>74/983 1.00 ref</td>
<td>31/471 1.00 ref</td>
<td>78/969 1.00 ref</td>
<td>109/1440 1.00 ref</td>
</tr>
<tr>
<td>Resolution</td>
<td>20/224 1.07 (0.63-1.82)</td>
<td>40/409 1.29 (0.89-1.86)</td>
<td>15/172 1.33 (0.74-2.39)</td>
<td>45/461 1.20 (0.85-1.71)</td>
<td>60/633 1.24 (0.92-1.67)</td>
</tr>
<tr>
<td>Incident</td>
<td>36/294 1.42 (0.89-2.27)</td>
<td>107/765 1.67 (1.24-2.24)</td>
<td>84/645 1.66 (1.11-2.48)</td>
<td>59/414 1.54 (1.10-2.16)</td>
<td>143/1059 1.57 (1.22-2.02)</td>
</tr>
<tr>
<td>Persistent</td>
<td>46/300 1.63 (1.08-2.48)</td>
<td>109/669 1.96 (1.45-2.63)</td>
<td>91/573 1.99 (1.34-2.96)</td>
<td>64/396 1.79 (1.29-2.47)</td>
<td>155/969 1.82 (1.47-2.38)</td>
</tr>
</tbody>
</table>

All analyses adjusted for length of follow-up, cohort, race, and adult BMI. The age-stratified model additionally adjusted for sex; the sex-stratified model additionally adjusted for age; and the ‘All’ model additionally adjusted for both age and sex.

*Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group—normal BP in childhood and normal BP as adults; resolution group—elevated BP in childhood but not as adults; incident group—normal BP in childhood, but elevated BP as adults; and persistent group—elevated BP in childhood and as adults.

Table 3. Change in BMI z-score between childhood (4-18 years) and adulthood (age 23-46 years, mean follow-up 23 years) according to blood pressure (BP) groups.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Control N</th>
<th>mean (SD)</th>
<th>Resolution N</th>
<th>mean (SD)</th>
<th>Incident N</th>
<th>mean (SD)</th>
<th>Persistent N</th>
<th>mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscatine</td>
<td>307</td>
<td>-0.04 (0.74)</td>
<td>146</td>
<td>-0.23 (0.82)*</td>
<td>128</td>
<td>0.30 (1.04)†</td>
<td>137</td>
<td>0.05 (0.97)</td>
</tr>
<tr>
<td>Bogalusa</td>
<td>307</td>
<td>0.06 (0.73)</td>
<td>22</td>
<td>0.18 (0.94)</td>
<td>224</td>
<td>0.04 (0.90)</td>
<td>28</td>
<td>0.01 (1.01)</td>
</tr>
<tr>
<td>Young Finns</td>
<td>635</td>
<td>-0.07 (0.86)</td>
<td>401</td>
<td>-0.21 (0.94)*</td>
<td>513</td>
<td>0.28 (0.91)†</td>
<td>670</td>
<td>0.05 (1.03)*</td>
</tr>
<tr>
<td>CDAD</td>
<td>248</td>
<td>0.09 (0.83)</td>
<td>97</td>
<td>-0.18 (0.86)*</td>
<td>193</td>
<td>0.20 (0.95)</td>
<td>119</td>
<td>0.16 (0.90)</td>
</tr>
<tr>
<td>All</td>
<td>1497</td>
<td>-0.03 (0.81)</td>
<td>666</td>
<td>-0.21 (0.90)†</td>
<td>1058</td>
<td>0.22 (0.93)†</td>
<td>954</td>
<td>0.06 (1.01)*</td>
</tr>
</tbody>
</table>

Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group—normal BP in childhood and normal BP as adults; resolution group—elevated BP in childhood but not as adults; incident group—normal BP in childhood, but elevated BP as adults; and persistent group—elevated BP in childhood and as adults.

*P<0.05 and † P<0.01 for comparisons between control (reference group) and resolution, incident, and persistent groups using logistic regression adjusted for length of follow-up in cohort stratified analyses and additionally for cohort in pooled analyses.
Figure Legend:

Figure 1. Forest plots showing relative risk of high carotid intima media thickness (cIMT) in four cohorts. Data were analyzed from four studies — the Muscatine Study, the Bogalusa Heart Study, the Cardiovascular Risk in Young Finns Study, and the Childhood Determinants of Adult Health (CDAH) Study. In each individual study cohort and in a meta-analysis of all four cohorts, the risk of high cIMT (≥90th percentile for age-, sex-, race-, study-year-, and cohort-specific values) is shown. Child blood pressure (BP) was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. Participants who had a normal blood pressure (BP) in childhood and had normal BP as adults (Control) were compared with participants who had elevated BP in childhood but not as adults (Resolution), participants with a normal BP in childhood who had elevated BP as adults (Incident), and participants who had elevated BP in childhood and as adults (Persistent). The size of each box is proportional to the weight of the cohort in the meta-analysis. The diamonds represent the relative risks estimated from the meta-analysis, with the lateral points indicating the 95% confidence intervals. The P values for heterogeneity among groups were 0.34 for the comparison of Resolution with Control, 0.27 for the comparison of Incident with Control, and 0.15 for the comparison of Persistent with Control, suggesting that there was no dissimilarity among cohorts.
Combined Effects of Child and Adult Elevated Blood pressure on Subclinical Atherosclerosis: 
The International Childhood Cardiovascular Cohort Consortium
Jonna Juhola, Costan G. Magnusson, Gerald S. Berenson, Alison Venn, Trudy L. Burns, Matthew A. Sabin, Sathanur R. Srinivasan, Stephen R. Daniels, Patricia H. Davis, Wei Chen, Mika Kähönen, Leena Taittonen, Elaine M. Urbina, Jorma S. A. Viikari, Terence Dwyer, Olli T. Raitakari and Markus Juonala

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SUPPLEMENTAL MATERIAL

Combined effects of child and adult elevated blood pressure on subclinical atherosclerosis.

The International Childhood Cardiovascular Cohort Consortium

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TABLE OF CONTENTS

Supplementary Table 1. Blood pressure status in adulthood according to childhood blood pressure status. Page 5

Supplemental Table 2. Partial correlation coefficients (r) for tracking of blood pressure (BP) z-scores from childhood to adulthood. Page 7

Supplemental Table 3: Relative risks (RR) and 95% confidence intervals (95%CI) of high carotid IMT (≥90th percentile) according to blood pressure (BP) groups in childhood and adulthood.

In this table child BP was classified as elevated if systolic or diastolic BP were ≥95th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if systolic BP≥140mmHg or diastolic BP≥90mmHg. Page 8

Supplemental Table 4: Relative risks (RR) and 95% confidence intervals (95%CI) of high carotid IMT (≥90th percentile) according to blood pressure (BP) groups in childhood and adulthood.

In this table child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile according to age-, sex-, height-, and cohort-specific levels. Adult BP was classified as elevated if systolic BP≥120mmHg or diastolic BP≥80mmHg. Page 10

Supplemental Table 5: Relative risks (RR) and 95% confidence intervals (95%CI) of high carotid IMT (≥90th percentile) according to blood pressure (BP) group in childhood and adulthood and adult BMI status. Page 12

Supplemental Table 6: Relative risks (RR) and 95% confidence intervals (95%CI) of high carotid IMT according to blood pressure (BP) group in childhood and adulthood. These analyses were performed using cut-points of 75th or 50th percentile to define high carotid IMT. Page 13

Supplemental Table 7: Child and adult blood pressure (BP) status according to child and adult adiposity status groups. Page 14
Supplemental Table 1. Blood pressure status in adulthood (age 23-46 years) according to childhood (age 4-18 years) blood pressure status

<table>
<thead>
<tr>
<th>Cohort</th>
<th>BP status in childhood</th>
<th>BP status in adulthood</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>Elevated</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Muscatine</td>
<td>Normal</td>
<td>307 (70.3)</td>
<td>130 (29.8)</td>
<td>437</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated</td>
<td>143 (50.4)</td>
<td>141 (49.7)</td>
<td>284</td>
<td></td>
</tr>
<tr>
<td>Bogalusa</td>
<td>Normal</td>
<td>301 (56.4)</td>
<td>233 (43.6)</td>
<td>534</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated</td>
<td>21 (40.4)</td>
<td>31 (59.6)</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Young Finns</td>
<td>Normal</td>
<td>618 (53.7)</td>
<td>533 (46.3)</td>
<td>1151</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated</td>
<td>381 (35.5)</td>
<td>691 (64.5)</td>
<td>1072</td>
<td></td>
</tr>
<tr>
<td>CDAH</td>
<td>Normal</td>
<td>260 (57.0)</td>
<td>196 (43.0)</td>
<td>456</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated</td>
<td>101 (45.1)</td>
<td>123 (54.9)</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>Normal</td>
<td>1486 (57.6)</td>
<td>1092 (42.4)</td>
<td>2578</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated</td>
<td>646 (39.6)</td>
<td>986 (60.4)</td>
<td>1632</td>
<td></td>
</tr>
</tbody>
</table>

% values mean row %.

Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP ≥120mmHg or Diastolic BP ≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications.

Altogether in childhood BP was elevated in 39.4% of individuals in Muscatine, 8.9% in Bogalusa, 48.2% in Young Finns and 32.9% in CDAH study. In adulthood respective values were 37.6% in Muscatine, 45.1% in Bogalusa, 55.1% in Young Finns and 46.9% in CDAH study.
Mean follow-up intervals were 24.0 years in Muscatine, 21.4 years in Bogalusa, 26.0 years in Young Finns and 19.9 years in CDAH study.
Table 2. Partial correlation coefficients ($r$) for tracking of blood pressure (BP) z-scores from childhood (age 4-18 years) to adulthood (age 23-46 years,*

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$ (N)</td>
<td>$r$ (N)</td>
</tr>
<tr>
<td>Muscatine</td>
<td>0.26 (718)</td>
<td>0.23 (718)</td>
</tr>
<tr>
<td>Bogalusa</td>
<td>0.33 (583)</td>
<td>0.21 (583)</td>
</tr>
<tr>
<td>Young Finns</td>
<td>0.34 (2223)</td>
<td>0.24 (2222)</td>
</tr>
<tr>
<td>CDAH</td>
<td>0.31 (680)</td>
<td>0.17 (680)</td>
</tr>
<tr>
<td>All</td>
<td>0.32 (4204)</td>
<td>0.22 (4203)</td>
</tr>
</tbody>
</table>

*All models adjusted for length of follow-up. All $P$-values <0.001. Z-scores are age-, sex-, race- (Bogalusa), and cohort-specific.
Supplemental Table 3. Relative risks (RR) and 95% confidence intervals (95%CI) of high left common carotid IMT (≥90th percentile) according to blood pressure (BP) groups* in childhood (age 4-18 years) and adulthood (age 23-46 years, mean follow-up 23 years). Compared to Table 2 this analysis was performed with more stringent BP cut-points (≥95th percentile using the NHBPEP tables in childhood and ≥140/90 in adulthood).

<table>
<thead>
<tr>
<th>Child – adult BP group</th>
<th>Participants 4-11 years</th>
<th>Participants 12-18 years</th>
<th>Males</th>
<th>Females</th>
<th>All participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>RR (95%CI)</td>
<td>n/N</td>
<td>RR (95%CI)</td>
<td>n/N</td>
</tr>
<tr>
<td>Control</td>
<td>82/844</td>
<td>1.00 ref</td>
<td>188/1945</td>
<td>1.00 ref</td>
<td>119/1194</td>
</tr>
<tr>
<td>Resolution</td>
<td>27/262</td>
<td>0.96 (0.65-1.46)</td>
<td>49/371</td>
<td>1.31 (0.98-1.76)</td>
<td>33/261</td>
</tr>
<tr>
<td>Incident</td>
<td>11/101</td>
<td>0.88 (0.47-1.62)</td>
<td>66/388</td>
<td>1.50 (1.14-1.98)</td>
<td>43/290</td>
</tr>
<tr>
<td>Persistent</td>
<td>17/68</td>
<td>1.82 (1.12-2.95)</td>
<td>27/122</td>
<td>1.92 (1.32-2.79)</td>
<td>26/116</td>
</tr>
</tbody>
</table>

All analyses adjusted for length of follow-up, cohort, race, and adult BMI. The age-stratified model additionally adjusted for sex; the sex-stratified model additionally adjusted for age; and the ‘All’ model additionally adjusted for both age and sex.

*Child BP was classified as elevated if systolic or diastolic BP were ≥95th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥140mmHg or Diastolic BP≥90mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group – normal BP in childhood and normal BP as adults; resolution
group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.
Supplemental Table 4. Relative risks (RR) and 95% confidence intervals (95%CI) of high left common carotid IMT (≥90th percentile) according to blood pressure (BP) group* in childhood (age 4-18 years) and adulthood (age 23-46 years, mean follow-up 23 years). Compared to Table 2 this analysis was performed with cohort specific BP cut-points (≥90th percentile according to age, sex, height and cohort) in childhood.

<table>
<thead>
<tr>
<th>Child-adult BP group</th>
<th>Participants 4-11 years</th>
<th>Participants 12-18 years</th>
<th>Males</th>
<th>Females</th>
<th>All participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
</tr>
<tr>
<td>Control</td>
<td>47/605 1.00 ref</td>
<td>95/1227 1.00 ref</td>
<td>41/583 1.00 ref</td>
<td>101/1249 1.00 ref</td>
<td>142/1832 1.00 ref</td>
</tr>
<tr>
<td>Resolution</td>
<td>8/76 1.27 (0.62-2.60)</td>
<td>19/165 1.43 (0.90-2.27)</td>
<td>5/60 1.13 (0.48-2.69)</td>
<td>22/181 1.44 (0.93-2.23)</td>
<td>27/241 1.37 (0.93-2.03)</td>
</tr>
<tr>
<td>Incident</td>
<td>59/441 1.55 (1.06-2.26)</td>
<td>157/1118 1.62 (1.25-2.11)</td>
<td>125/950 1.57 (1.12-2.22)</td>
<td>91/609 1.63 (1.23-2.16)</td>
<td>216/1559 1.58 (1.28-1.96)</td>
</tr>
<tr>
<td>Persistent</td>
<td>23/153 1.55 (0.96-2.51)</td>
<td>59/316 2.14 (1.57-2.91)</td>
<td>50/268 2.08 (1.40-3.10)</td>
<td>32/201 1.72 (1.18-2.49)</td>
<td>82/469 1.93 (1.49-2.50)</td>
</tr>
</tbody>
</table>

All analyses adjusted for length of follow-up, cohort, race, and adult BMI. The age-stratified model additionally adjusted for sex; the sex-stratified model additionally adjusted for age; and the ‘All’ model additionally adjusted for both age and sex.

*Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile according to age-, sex-, height-, and cohort-specific levels. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group –normal BP in childhood and normal BP as
adults; resolution group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.
Supplemental Table 5. Relative risks (RR) and 95% confidence intervals (95%CI) of high left common carotid IMT (≥90th percentile) according to blood pressure (BP) group in childhood (age 4-18 years) and adulthood (age 23-46 years, mean follow-up 23 years) and adult BMI status. Compared to Table 2 this analysis was performed stratified by adult adiposity status.

<table>
<thead>
<tr>
<th>Child-adult BP group</th>
<th>Normal weight in adulthood</th>
<th>Overweight/Obese in adulthood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N RR (95%CI)</td>
<td>n/N RR (95%CI)</td>
</tr>
<tr>
<td>Control</td>
<td>51/756 1.00 (ref)</td>
<td>58/679 1.00 (ref)</td>
</tr>
<tr>
<td>Resolution</td>
<td>31/331 1.39 (0.91-2.14)</td>
<td>29/302 1.12 (0.73-1.71)</td>
</tr>
<tr>
<td>Incident</td>
<td>38/329 1.83 (1.21-2.77)</td>
<td>104/725 1.71 (1.26-2.33)</td>
</tr>
<tr>
<td>Persistent</td>
<td>32/298 1.71 (1.11-2.64)</td>
<td>122/667 2.19 (1.61-2.96)</td>
</tr>
</tbody>
</table>

All analyses adjusted for length of follow-up, cohort, age, sex, and race.

Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group – normal BP in childhood and normal BP as adults; resolution group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.

In adulthood, a cut-point of 25 kg/m² was used to define overweight and 30 kg/m² for obesity.
Supplemental Table 6. Relative risks (RR) and 95% confidence intervals (95%CI) of high left common carotid IMT (≥75th percentile cut-point in left and ≥50th percentile cut-point in right) according to blood pressure (BP) group in childhood (age 4-18 years) and adulthood (age 23-46 years, mean follow-up 23 years). Compared to Table 2 this analysis was performed using different definitions for high cIMT.

<table>
<thead>
<tr>
<th>Child-adult BP group</th>
<th>75th percentile cut-point</th>
<th>50th percentile cut-point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>RR (95%CI)</td>
</tr>
<tr>
<td>Control</td>
<td>291/1439</td>
<td>1.00 ref</td>
</tr>
<tr>
<td>Resolution</td>
<td>134/631</td>
<td>1.06 0.88-1.27</td>
</tr>
<tr>
<td>Incident</td>
<td>287/1057</td>
<td>1.26 1.09-1.47</td>
</tr>
<tr>
<td>Persistent</td>
<td>289/969</td>
<td>1.44 1.24-1.67</td>
</tr>
</tbody>
</table>

All analyses adjusted for length of follow-up, cohort, age, sex, and race.

Child BP was classified as elevated if systolic or diastolic BP were ≥90th percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group – normal BP in childhood and normal BP as adults; resolution group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.
Supplemental Table 7. Child (age 4-18 years) and adult (age 23-46 years, mean follow-up 23 years) blood pressure (BP) status according to child and adult adiposity status groups.

<table>
<thead>
<tr>
<th>BP status</th>
<th>Adiposity status</th>
<th>Control</th>
<th>Resolution</th>
<th>Incident</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Normal BMI in childhood and normal BP as adults; resolution group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution</td>
<td>Overweight/obese child, non-obese adult; Incident: normal BMI in childhood, obese adult; Persistent: overweight/obese child, obese adult.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident</td>
<td>Normal BMI in childhood, obese adult; Persistent: overweight/obese child, obese adult.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent</td>
<td>Overweight/obese child, non-obese adult; Incident: normal BMI in childhood, obese adult; Persistent: overweight/obese child, obese adult.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

% values mean row %.

Child BP was classified as elevated if systolic or diastolic BP were ≥90\textsuperscript{th} percentile using the NHBPEP tables for age, sex, and height. Adult BP was classified as elevated if Systolic BP≥120mmHg or Diastolic BP≥80mmHg. In addition, adult BP status was considered elevated among those self-reporting use of antihypertensive medications. BP groups were: control group – normal BP in childhood and normal BP as adults; resolution group – elevated BP in childhood but not as adults; incident group – normal BP in childhood, but elevated BP as adults; and persistent group – elevated BP in childhood and as adults.

Adiposity status defined as follows\textsuperscript{1}: Control: normal BMI in childhood (according to the international cut-points\textsuperscript{2}), non-obese adult (BMI < 30 kg/m\textsuperscript{2}); Resolution: overweight/obese child, non-obese adult; Incident: normal BMI in childhood, obese adult; Persistent: overweight/obese child, obese adult.
References
