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Blood Pressure Trajectories in Early Adulthood and Subclinical Atherosclerosis in Middle Age

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Abstract

Importance—Single measures of blood pressure (BP) levels are associated with the development of atherosclerosis; however, long-term patterns in BP and their impact on CVD risk are poorly characterized.

Objective—To identify common BP trajectories throughout early adulthood and to determine their association with presence of coronary artery calcification (CAC) during middle age.

Design—We used data from the CARDIA study from baseline in 1985-1986 through 25 years of follow-up (2010-2011).

Setting—Prospective cohort study

Participants—CARDIA participants were Black and White men and women aged 18-30 years at baseline.

Exposures—We examined systolic BP, diastolic BP, and mid-BP [calculated as (SBP+DBP)/2 and an important marker of CHD risk among younger populations] at baseline and years 2, 5, 7, 10, 15, 20, and 25. Latent mixture modeling was used to identify trajectories in SBP, DBP and mid-BP over time.

Main Outcome Measure—Coronary artery calcification greater than or equal to Agatston score of 100 Agatston units at year 25.

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Conflicts of Interest: There were no conflicts of interest reported.

Results—Among 4,681 participants, we identified 5 distinct mid-BP trajectories: Low-Stable (22% [95% CI 19.9-23.7], n=987), Moderate-Stable (42% [40.3-44.3], n=2,085), Moderate-Increasing (12% [10.4-14.0], n=489), Elevated-Stable (19% [17.1-20.0], n=903) and Elevated-Increasing (5% [4.0-5.5], n=217). As compared to the Low-Stable group, trajectories with elevated BP levels had greater odds of having CAC >100. Adjusted odds ratios (95% CI) were 1.44 (0.83-2.49) for Moderate-Stable, 1.86 (0.91-3.82) for Moderate-Increasing, 2.28 (1.24-3.70) for Elevated-Stable, and 3.70 (1.66-8.20) for Elevated-Increasing groups. The adjusted prevalence of CAC ≥ 100 was 5.8% in the Low-Stable group. These ORs represent an absolute increase of 2.7%, 5%, 6.3% and 12.9% for the prevalence of CAC ≥100 for the Moderate-Stable, Moderate-Increasing, Elevated Stable and Elevated Increasing groups respectively as compared to the Low-Stable Group. Associations were not altered after adjustment for baseline and year 25 BP. Findings were similar for trajectories of isolated systolic BP trajectories, but were attenuated for diastolic BP trajectories.

Conclusions and Relevance—BP trajectories throughout young adulthood vary and higher BP trajectories were associated with an increased risk of CAC in middle age. Long-term trajectories in BP may assist in more accurate identification of individuals with subclinical atherosclerosis.

Keywords

blood pressure; calcium; epidemiology; risk factors

Blood pressure (BP) represents a major modifiable risk factor for cardiovascular disease (CVD). Current risk prediction models only take into account BP level at the time of risk prediction, usually in middle or older age, and do not consider the potential impact of BP levels experienced earlier in life or the changes in BP levels over time. Time-averaged and cumulative BP among adults have also been shown to predict CVD risk among several large prospective investigations .[1,2,3,4] For nearly everyone, at least in populations which consume large amounts of salt[5], systolic BP increases with age and these increases during middle age have been associated with CVD risk.[6,7] It was recently demonstrated that changes in BP throughout middle and older age are significantly associated with the lifetime risk for CVD, and the larger the changes the greater the lifetime risk.[8] However, the patterns of BP change may differ among individuals; thus, a life-course perspective when evaluating the effects of BP is essential. Long-term BP trajectory patterns from young adulthood to middle age and their impact on CVD risk remain unknown. Therefore, the aims of this study are (1) to identify subgroups of individuals with similar trajectories in BP from young adulthood through middle age, (2) to characterize those participants and BP trajectories, and (3) to determine the independent association of BP trajectories from young adulthood to middle age with the presence of subclinical CVD as measured by coronary artery calcification (CAC) during middle age. We hypothesized that there exist multiple trajectory patterns within the CARDIA population and that in comparison to a trajectory in which individuals maintain ideal BP levels throughout young adulthood, a portion of the population will experience higher levels of BP and/or faster rates of increase in BP which will be associated with increased subclinical atherosclerosis in year 25.

Methods

The Coronary Artery Risk Development in Young Adults (CARDIA) study is a prospective cohort study designed to investigate the development of cardiovascular risk and disease. In 1985-1986, 5,115 Black and White men and women aged 18-30 years of age were recruited from four urban sites across the United States including Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA). CARDIA participants have been followed for over 25 years with detailed demographic and clinical data, including self-reported anthropometric and laboratory measures, and assessment for subclinical atherosclerosis. Race was determined by self-report at year 0 and verified at year 2. Participant data have been collected across 8 examination cycles including baseline and at years 2, 5, 7, 10, 15, 20, and 25. Retention rates have been high throughout the 25 years of follow-up (90%, 86%, 81%, 77%, 74%, 72% and 72%, respectively). A more thorough description of the study design and conduct has been previously published.[9-11] The study was approved by the institutional review board at all study sites and all participants signed an informed consent. The current analyses include CARDIA participants with BP measures available at 3 or more examinations.

Blood pressure was measured at each of the 8 CARDIA exam cycles. At each exam, trained technicians used either a random zero sphygmomanometer (Y0-Y20) or OmROn sphygmomanometer (Y20-Y25) to measure participants' blood pressure. Resting systolic and diastolic blood pressure was measured three times at 1-minute intervals. We used the average of the second and third blood pressure measurements. In our main analysis we examined trajectories in systolic blood pressure and mid-BP, defined as the mean of the systolic and diastolic BP measurements. In addition to SBP, Mid-BP was chosen a priori because it has been shown to have the greatest predictive utility for CVD compared with other single measures of BP (systolic blood pressure [SBP] or diastolic blood pressure [DBP], pulse pressure or mean arterial pressure).[12,13] In addition, mid-BP allowed us to take into account the effects of both systolic and diastolic blood pressure jointly. This is of particular importance among this younger CARDIA population, as diastolic blood pressure has been shown to play a larger role in CHD risk among the young to middle age adults.[14-17] Separate trajectories in systolic and diastolic blood pressures were also examined.

Subclinical coronary atherosclerosis was quantified using coronary artery calcification (CAC) measured at the year 25 examination. Calcified coronary artery plaque measurement was done with an electrocardiographically gated multidector computed tomography (CT) scanner with a standard phantom for calibration using a standardized protocol[18] with published accuracy, comparability and reproducibility.[19,20] Briefly, scans were obtained and image analysts blinded to participant characteristics calculated a total coronary artery calcium score using a modified Agatston method,[21] with select overreading by a physician expert in cardiovascular imaging. Our outcome in this study was the presence of CAC greater than or equal to Agatston score of 100 Agatston units. CAC ≥ 100 has been identified as a marker of risk for high risk of coronary events[22] and has been used often in previous consensus statements.[23,24] In addition, we examined CAC >0 in sensitivity analyses.

Statistical Analyses

Blood pressure trajectories were modeled among all 4,681 CARDIA participants with BP measured at 3 or more exams. Only 3,442 participants with CAC data available at year 25 were included in the models examining the association between blood pressure and CAC >100. We used latent class models to identify subgroups within the CARDIA cohort that share a similar underlying trajectory in BP. These models were fit using SAS Proc Traj.[25-27] See statistical appendix for more details on the trajectory modeling process. In order to estimate the association of trajectory group on subclinical atherosclerosis, trajectory group membership was included as an independent variable in a logistic regression model examining predictors of the presence of CAC Agatston score ≥ 100 at Exam Year 25. The adjusted model included baseline age, race, sex, highest level of education, antihypertensive medication use at each exam, mg/dL of total cholesterol per year, cumulative number of years with diabetes, cumulative number of years as a current smoker, and BMI at both baseline and Y25. As in other studies, in order to account for the uncertainty in BP trajectory group assignment the posterior probability of group membership we generated 20 multiple imputations of trajectory membership using the posterior probabilities.[28] We then fit the logistic regression model for each of the 20 data sets and combined our results across the multiple imputations. Model calibration was examined using the Hosmer-Lemeshow goodness-of fit chi-square statistic. We compared the predictive utility of trajectory group as compared to other longitudinal BP measures (single baseline BP measurements, multiple BP measurements [baseline and Y25] and cumulative BP [mm Hg × years]) using the logistic C-statistic and the discrimination (D statistic)[29]of the models for each of these BP measures individually and jointly. The D-statistic represents the difference in the average of event probabilities between the groups which experience the event and those who do not. The Wilcoxon test was used to detect significant location shifts and differences in the distributions of the predicted event probabilities. In order to quantify how the model reclassifies individuals with the addition of trajectory group, we calculated the Integrated Discrimination Improvement (IDI) index by calculating the difference in the D-statistics (discrimination slopes) between the models including only baseline BP or year 25 BP and those including trajectory group. All analyses were completed in SAS version 9.3. P-values < 0.05 were considered statistically significant.

Results

The CARDIA cohort enrolled 5,115 individuals. Trajectories in mid-blood pressure were examined among 4,681 CARDIA participants with three or more BP measurements. Of these, 3,442 participants had CAC available at year 25. Five discrete trajectories in mid-BP from young adulthood to middle age were identified (Figure 1): 21.8%, 95% CI: 19.9%-23.7% (n=987) of participants maintained low BP throughout follow-up (we refer to these participants as the, “Low-Stable group.”), 42.3%, 95% CI: 40.3%-44.3% (n=2,085) of participants experienced moderate BP levels (Moderate-Stable group), 12.2%, 95% CI: 10.4%-14.0% (n=489) started at moderate levels and experienced a rapid increase in BP starting at an average age of 35 years (Moderate-Increasing group), 19.0%, 95% CI: 17.1%-20.0% (n=903) had relatively elevated BP levels throughout (Elevated-Stable group), and 4.8%, 95% CI: 4.0%-5.5% (n=217) had high BP levels (Elevated-Increasing group).

In general trajectory groups tracked with BP at age 25 and experienced small, steady increases in systolic and diastolic BP, as well as the proportion of participants on antihypertensive medications, however; two groups (the Moderated-Increasing and Elevated-Increasing groups) experienced large and more rapid increases in blood pressure over time (Table 1). The Moderated-Increasing and Elevated-Increasing groups experienced the largest increases in systolic BP (mean increases were 30.2 mm Hg and 21.2 mm Hg, respectively) and diastolic BP (20.9 mm Hg and 11.5 mm Hg, respectively).

Individuals in the Low-Stable group were the most likely to be female, white, more highly educated and more likely to have fewer concurrent cardiovascular risk factors (Table 2). African Americans were more likely to experience rapid increases in BP, with the Moderate-Increasing group having the largest proportion of African American women and the Elevated-Increasing group having the largest proportion of African American men. In addition, these rapid increases in BP were associated with higher rates of smoking and occurred alongside increases in BMI (avg BMI increased by 7.4-7.6 among Increasing and High groups but only by 4.5-5.7 among the other groups with more stable BP levels).

The prevalence of CAC ≥100 varied from 4.0% in the Low-Stable BP trajectory group up to 25.4% in the Elevated-Increasing BP trajectory group. Within each trajectory group, individuals on antihypertensive medications had a higher prevalence of CAC as compared to individuals within the same trajectory group but not on antihypertensive medications. Even among groups that started at similar baseline BP levels, for example the Moderate-Stable and Moderate-Increasing groups, participants who experienced steeper increases in BP had a higher prevalence of CAC >100, 7.9% vs 10.1%, respectively (p for trend was <0.0001). In comparison to individuals in the Low-Stable group, those in trajectory groups with patterns of higher mid-BP had increasingly greater odds of having CAC ≥ 100. Adjustment for individual demographic characteristics and education only slightly attenuated the odds ratios. Additional adjustment for other cardiovascular risk factors and blood pressure medication resulted in larger attenuations of the odds ratios for the higher risk groups especially the Elevated-Stable and Elevated-Increasing groups. Elevated BP trajectory groups were independently associated with CAC≥100 at year 25 (Table 3) even after adjustment for demographic characteristics, other CV risk factors, and anti-hypertensive medication in model 1. Adjusted odds ratios (95% CI) were 1.44 (0.83-2.49) for Moderate-Stable, 1.86 (0.91-3.82) for Moderate-Increasing, 2.28 (1.24-4.18) for Elevated-Stable, and 3.70 (1.66-8.20) for Elevated-Increasing groups. The adjusted prevalence of CAC ≥ 100 was 5.8% in the Low-Stable group. These ORs represent an absolute increase of 2.7%, 5%, 6.3% and 12.9% for the prevalence of CAC ≥100 for the Moderate-Stable, Moderate-Increasing, Elevated Stable and Elevated Increasing groups respectively as compared to the Low-Stable Group. Findings were similar for the outcome of CAC > 0 (eTable 1). In sensitivity analyses, the BP trajectory patterns were similar and their association with CAC ≥100 was essentially unchanged when restricted to individuals who were not on BP medication at any time during follow-up (n=3507).

Odds ratios for CAC for different trajectory groups was not significantly altered even with additional adjustment for baseline systolic and diastolic blood pressure (model 2) or year 25 systolic and diastolic blood pressure (model 3). All models fit the data well with Hosmer-

Lemeshow chi-square statistics with a p-value >0.05. The average predicted probability of having CAC ≥ 100 under the adjusted model including trajectory group for the group of CARDIA participants with CAC ≥ 100 was 25.3% as compared to those who did not have CAC ≥ 100, predicted probability of 8.1%. The discrimination of the model and its ability to correctly identify individuals with CAC ≥ 100 was similar as compared to models with either baseline or year 25 BP alone. The C-statistic for the unadjusted model was 0.66 which increased to 0.84 in models 1, 2 and 3. Similarly, the D-statistic for the adjusted model of trajectory groups was only slightly higher (0.172) as compared to models of baseline BP and Y25 BP (D-statistic 0.167 and 0.169, respectively; p-value <0.001); however, the IDI was only 0.5 and 0.3, respectively.

Overall patterns were similar when we examined the trajectories of systolic and diastolic blood pressure separately (Figure 2A and AB and eTables 2-6). Five discrete trajectory groups were identified for long-term patterns in systolic BP: 24.6%, 95% CI: 22.5%-26.8% (n=1113) of participants maintained low SBP throughout follow-up (we refer to these participants as the, “Low-Stable group.”), 44.1%, 95% CI: 42.1%-46.1% (n=2,167) of participants experienced moderate SBP levels (Moderate-Stable group), 9.8%, 95% CI: 7.9%-10.7% (n=363) started at moderate levels and experienced a rapid increase in SBP starting at an average age of 35 years (Moderate-Increasing group), 18.8%, 95% CI: 16.6%-21.0% (n=884) had relatively elevated SBP levels throughout (Elevated-Stable group), and 3.3%, 95% CI: 2.6%-4.0% (n=154) had high SBP levels (Elevated-Increasing group). SBP trajectory groups had increasing prevalence of CAC ≥ 100 with increasing SBP trajectory group ranging from e Figure 3. After adjustment for demographic, long-term CV risk factors and BP medication, these SBP trajectory groups were significantly associated with the prevalence of CAC >100; ORs were 1.56 (0.96-2.53) for the Moderate-Stable group, 1.71 (0.82-3.54) for the Moderate-Increasing group, 2.16 (1.23-3.83) for the Elevated-Stable Group, and 5.24 for the Elevated-Increasing group as compared to the Low-Stable group (Table 3). The adjusted prevalence of CAC ≥ 100 at year 25 was 6.4% among the Low-Stable group and increased by 2.5%, 3.3%, 5.9%, and 14.3% for the Moderate-Stable, Moderate-Increasing, Elevated-Stable and Elevated-Increasing groups.

Five discrete trajectory groups were identified for long-term patterns in diastolic BP: 22.5%, 95% CI: 20.5%-24.6% (n=1024) of participants maintained low DBP throughout follow-up (Low-Stable group), 42.6%, 95% CI: 40.4%-44.8% (n=2,108) of participants experienced moderate DBP levels (Moderate-Stable group), 11.4% 95% CI: 9.6%-13.2% (n=448) started at moderate levels and experienced a rapid increase in DBP starting at an average age of 35 years (Moderate-Increasing group), 19.2%, 95% CI: 17.2%-21.2% (n=909) had relatively elevated DBP levels throughout (Elevated-Stable group), and 4.4%, 95% CI: 3.6%-5.1% (n=192) had high DBP levels (Elevated-Increasing group). The adjusted associations (Table 3) for diastolic blood pressure trajectory groups were less strongly associated with CAC≥100. Systolic and diastolic trajectory groups were moderately to highly correlated with mid-BP trajectory groups (Pearson correlation coefficient of 0.83 for DBP and 0.63 for SBP); but only moderately correlated with each other with a correlation coefficient of 0.5.

Discussion

In this study we found that there were heterogeneous trajectories in mid-BP over 25 years from young adulthood to middle age. We identified five unique trajectories in mid-BP and systolic BP that were significantly associated with the presence of subclinical atherosclerosis later in middle age. CARDIA participants who exhibited elevated BP levels throughout and those that experienced increases in BP levels over time had the greatest odds of having CAC ≥ 100. Importantly, the majority of these participants had BP levels within the range of prehypertension. While not significant, even individuals in the Moderate-Stable group who on average maintained BP levels within recommended clinical ranges, but were not in the group exhibiting the lowest levels of BP (Low-Stable group), tended to have almost twice the odds of having CAC≥100. Membership in a trajectory group with elevated BP represented an independent predictor of CAC beyond either baseline blood pressure in young adulthood or year 25 blood pressure during middle age and may help to identify individuals with prevalent levels of CAC that have been shown to be associated with increased CVD risk.

Over 33% of US adults have hypertension[30]; however, much of our understanding of BP levels comes from cross-sectional data. Many longitudinal studies that have examined changes in BP over time often only had fewer than 5 years of follow-up and focused mainly on elderly individuals. BP levels in mid-life have been shown to predict stroke risk[31] and cardiovascular mortality over 25 years later[32], and may be more strongly associated with CHD mortality than BP levels measured at a time closer in proximity to the time of event .[33]Additionally, although BP lowering due to pharmacological treatment may be achieved quickly, measures of cardiovascular function (e.g. left ventricular hypertrophy, increased LV mass, and degree of carotid stenosis) tend tends to remain abnormal after exposure to long-term periods of elevated BP.[34-37]

The findings from this current study provide a unique insight into long-term patterns of BP change and highlight the fact that within the CARDIA population there are heterogeneous patterns in BP trajectories. Latent class modeling, as used in these current analyses, has allowed identification of different patterns of BP change as separate trajectory groups, thus providing a more realistic understanding of lifetime trends in BP compared with population mean levels. Among CARDIA participants, Pletcher and colleagues previously demonstrated that cumulative years of prehypertension prior to age 35 was associated with prevalent coronary calcium in middle-age.[4] This current study extends those findings to demonstrate that not only is cumulative prehypertension important, but that certain populations such as African Americans and smokers are more likely to experience rapid increases in blood pressure during middle age placing them at higher risk. Consistent with our long-term findings, recent data from the UK have also demonstrated important heterogeneity in short-term BP trajectories in mid-life.[38] Our findings further suggest that these trajectory groups provide important additional information regarding the presence of significant levels of subclinical atherosclerosis, which has been shown to be a strong indicator of future cardiovascular risk.[22] This understanding of the effect of *change* or *timing of change* in BP on subclinical atherosclerosis may be important for risk stratification in the future.

The strengths and limitations of this investigation are worth note. This study applied innovative statistical methods to examine patterns BP in a large, well-characterized cohort of Black and White Americans. The longitudinal nature of CARDIA and phenotyping at each of the 8 exams provides detailed long-term patterns of blood pressure. Although CARDIA is a racially and geographically diverse cohort, the trajectory groups identified may not be generalizable to other populations. Not all CARDIA participants had blood pressure information available at all exam periods. However, missing BP is unlikely to have altered our findings as the mean number of BP measurements was 7 and did not differ by trajectory group. In sensitivity analyses, BP was imputed at each exam for all surviving CARDIA participants. Using these imputed BPs trajectory group assignment was consistent and did not result in any changes in the association between trajectory group and CAC. In addition, CARDIA participants were aged 18 to 30 years at baseline, thus we have no information on BP patterns prior to their entry into CARDIA. Coronary artery calcification at year 25 was missing for 28% of CARDIA participants. Participants who did not attend more recent exams were more likely to be African American, lower SES and have a greater burden of CV risk factors; nevertheless, these subgroups are well-represented in CARDIA attendees and by adjusting for these risk factors CAC is assumed to be missing at random and thus are results are unlikely to be biased.

Although BP has been a well-known risk factor for CVD for decades, these findings suggest that an individual's long-term patterns of change in BP starting in early adulthood may provide additional information about their risk for the development of coronary calcium. In particular, prehypertension at a young age followed by chronic exposure to blood pressure levels in the prehypertension range or higher was strongly associated with CAC > 100. Additional research is needed to examine the utility of specific BP trajectories in risk prediction for clinical CVD events and to explore the impact of lifestyle modification, treatment, and timing of intervention on lifetime trajectories in BP and outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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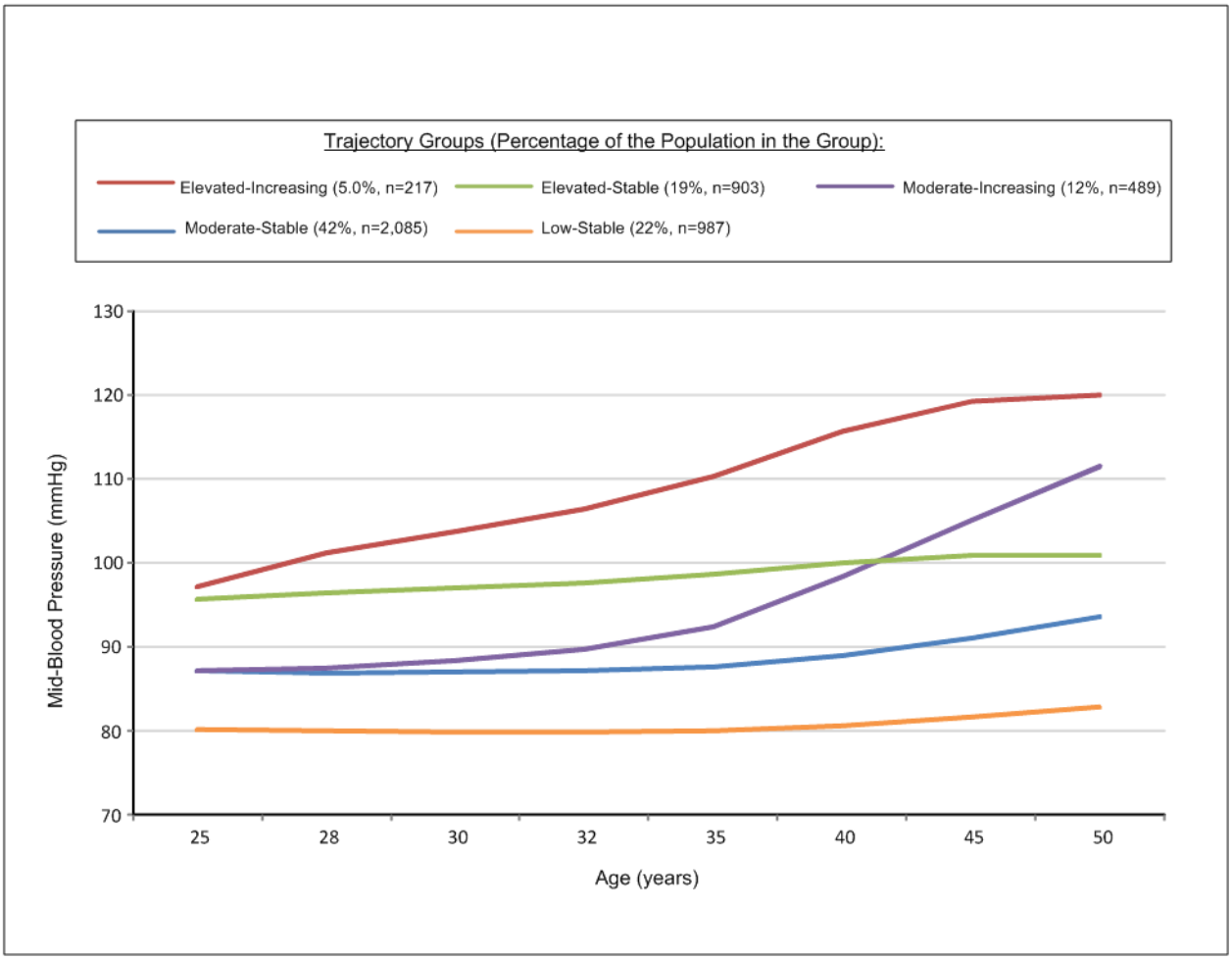

Figure 1. Trajectories in Mid-Blood Pressure in the Coronary Artery Risk Development in Young Adults (CARDIA) Study

Trajectory classes identified for mid-blood pressure; their pattern by age and the percentage (number) of CARDIA participants in each class.

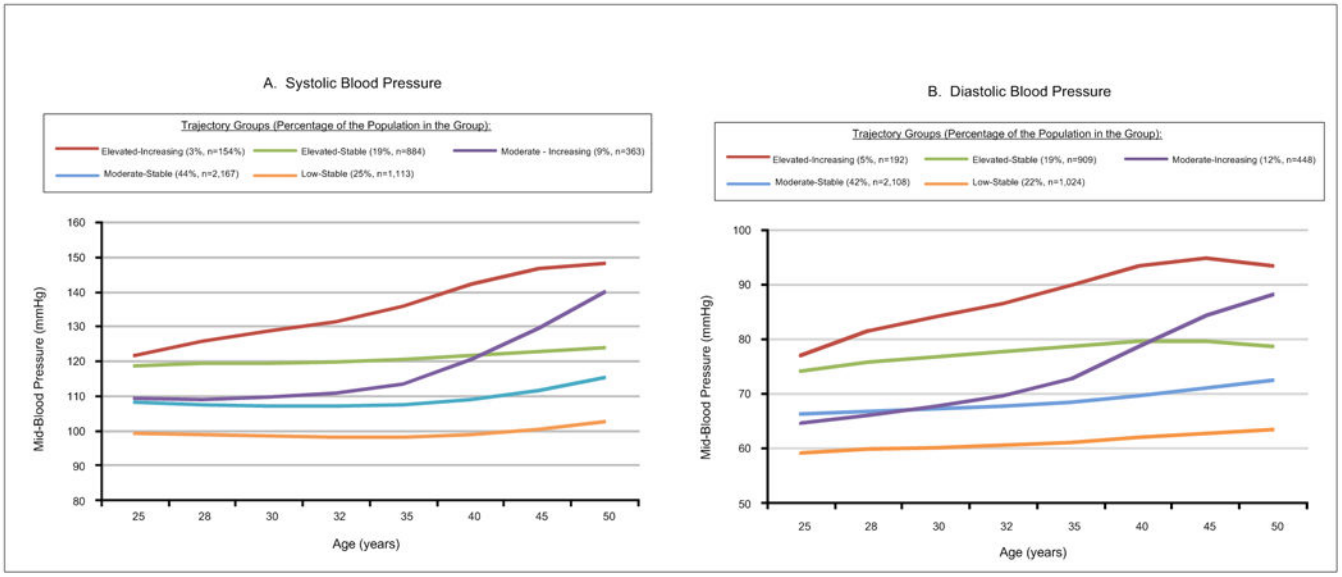

Figure 2. Trajectories in Systolic and Diastolic Blood Pressure in the Coronary Artery Risk Development in Young Adults (CARDIA) Study

Trajectory classes identified for systolic [A] and diastolic [B] blood pressure; their pattern by age and the percentage (number) of CARDIA participants in each class.

Table 1

Average Systolic and Diastolic Blood Pressure and Percentage on Medication at Each Study Exam by Mid-BP Trajectory Group: The Coronary Artery Risk Development in Young Adults Study

	Low-Stable Group N=987	Moderate-Stable Group N=2,085	Moderate-Increasing Group N=489	Elevated-Stable Group N=903	Elevated-Increasing Group N=217
Average SBP, mm Hg (SD)					
Year 0	100.5 (7.3)	109.0 (7.9)	111.3 (8.5)	120.4 (8.8)	125.0 (12.0)
Year 2	98.0 (7.0)	106.4 (7.8)	109.2 (8.1)	117.5 (8.5)	123.6 (12.3)
Year 5	96.9 (6.6)	105.9 (7.5)	109.7 (8.3)	117.8 (8.6)	129.7 (14.7)
Year 7	97.3 (7.1)	106.4 (7.3)	111.9 (9.3)	118.9 (8.8)	134.5 (16.7)
Year 10	97.8 (6.5)	107.7 (7.5)	115.3 (10.4)	120.4 (9.3)	135.3 (18.5)
Year 15	99.1 (6.9)	109.9 (8.2)	124.2 (13.4)	122.7 (11.7)	144.4 (18.5)
Year 20	101.8 (7.4)	113.3 (8.9)	132.4 (15.0)	122.4 (10.5)	142.1 (16.2)
Year 25	104.2 (8.5)	118.0 (10.4)	141.5 (14.4)	122.6 (10.4)	146.2 (18.8)
Average DBP, mm Hg, (SD)					
Year 0	61.7 (7.7)	67.6 (7.6)	68.5 (8.9)	75.8 (8.3)	80.3 (11.2)
Year 2	60.1 (7.3)	66.4 (7.4)	67.4 (8.2)	75.0 (8.6)	80.1 (11.1)
Year 5	60.5 (6.9)	67.9 (7.2)	70.2 (8.3)	77.5 (7.8)	86.3 (12.2)
Year 7	60.5 (6.9)	67.6 (6.8)	71.2 (9.0)	77.4 (8.5)	88.0 (12.2)
Year 10	63.0 (6.4)	70.7 (6.9)	76.6 (8.7)	80.5 (7.9)	90.4 (11.6)
Year 15	64.1 (7.0)	72.3 (7.4)	81.7 (10.7)	81.7 (9.3)	96.1 (13.8)
Year 20	61.4 (6.5)	70.6 (7.3)	84.8 (9.3)	77.3 (8.4)	91.3 (11.0)
Year 25	63.8 (6.9)	74.1 (7.7)	89.4 (8.6)	77.3 (7.9)	91.8 (12.2)
Participants on Medication No. (%)					
Year 0	1 (0.1)	6 (0.3)	3 (0.6)	13 (1.4)	13 (6.0)
Year 2	1 (0.1)	3 (0.1)	2 (0.4)	18 (2.0)	14 (6.5)
Year 5	0 (0.0)	2 (0.1)	5 (1.0)	32 (3.5)	31 (14.3)
Year 7	1 (0.1)	2 (0.1)	6 (1.2)	39 (4.3)	33 (15.2)
Year 10	0 (0.0)	11 (0.5)	12 (2.5)	64 (7.1)	48 (22.1)
Year 15	4 (0.4)	48 (2.3)	35 (7.2)	142 (15.7)	63 (29.0)

	Low-Stable Group N=987	Moderate-Stable Group N=2,085	Moderate-Increasing Group N=489	Elevated-Stable Group N=903	Elevated-Increasing Group N=217
Year 20	14 (1.4)	164 (7.9)	110 (22.5)	238 (26.4)	91 (41.9)
Year 25	31 (3.1)	286 (13.7)	185 (37.8)	323 (35.8)	110 (50.7)

Table 2

Demographic Characteristics and Risk Factors of Participants by Mid-BP Trajectory Group: The Coronary Artery Risk Development in Young Adults Study

	Low-Stable Group N=987	Moderate-Stable Group N=2,085	Moderate-Increasing Group N=489	Elevated-Stable Group N=903	Elevated-Increasing Group N=217	p-value
Demographic Characteristics						
Age at Baseline (SD)	25.1(3.7)	24.9 (3.6)	24.9 (3.7)	24.9 (3.6)	25.1 (3.6)	0.57
Female, %	78.8	55.1	60.1	29.7	38.2	<0.001
Race, %						<0.001
Black	29.4	49.3	69.9	56.8	79.3	
White	70.6	50.7	30.1	43.2	20.7	
Education, %						
High School or Less	34.5	42.6	44.2	47.6	61.3	<0.001
Some College	15.7	19.9	26.4	24.0	21.2	<0.001
College Graduate	24.4	19.9	17.6	16.1	9.2	<0.001
Graduate School	25.4	17.6	11.9	12.3	8.3	<0.001
Cardiovascular Risk Factors, %						
Current Smoker at Y0	29.0	29.4	31.8	27.7	37.5	0.055
Current Smoker at Y25	12.8	16.6	22.9	16.8	28.2	<0.001
Total Cholesterol at Y0 (SD)	173.3 (32.0)	176.0 (32.1)	178.4 (33.9)	181.7 (35.5)	183.7 (36.3)	<0.001
Total Cholesterol at Y25 (SD)*	194.2 (34.4)	192.8 (36.4)	194.8 (38.0)	186.4 (38.7)	196.4 (42.4)	0.0112
Diabetes at Y0	0.3	0.5	0.8	1.0	1.8	0.048
Diabetes at Y25	5.2	12.1	17.7	23.4	35.9	<0.001
Avg. BMI at Y0 (SD)	22.4 (3.5)	24.2 (4.6)	25.6 (5.3)	26.2 (5.9)	27.6 (6.6)	<0.001
Avg. BMI at Y25 (SD)	26.9 (5.7)	29.9 (6.6)	33.2 (7.6)	31.8 (7.8)	35.0 (8.9)	<0.001
Mean Coronary Artery Calcification Score, (SD)	16.9 (91.0)	32.4 (159.4)	44.4 (172.1)	87.2 (288.9)	190.5 (638.8)	<0.0001

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Table 3

Adjusted Odds Ratios and 95% Confidence Intervals of the Association of Blood Pressure Trajectory Groups with Coronary Artery Atherosclerosis ≥ 100

	No. of Participants with CAC ≥ 100 at Year 25 (%)	Unadjusted	Model 1	Model 2	Model 3
Mid-BP Trajectory Group					
Low-Stable	28 (4.0%)	1.00	1.00	1.00	1.00
Moderate-Stable	109 (7.9%)	**1.94 (1.18-3.20)**	1.44 (0.83-2.49)	1.56 (0.88-2.78)	1.53 (0.84-2.79)
Moderate-Increasing	38 (10.1%)	**2.57 (1.44-4.59)**	1.86 (0.91-3.82)	2.11 (0.98-4.53)	2.07 (0.76-5.62)
Elevated-Stable	102 (17.4%)	**4.79 (2.92-7.85)**	**2.28 (1.24-4.18)**	**2.77 (1.34-5.74)**	**2.48 (1.24-4.98)**
Elevated-Increasing	32 (25.4%)	**8.02 (4.50-14.29)**	**3.70 (1.66-8.20)**	**4.87 (1.34-12.63)**	**4.12 (1.45-11.71)**
SBP Trajectory Group					
Low-Stable	33 (4.2%)	1.00	1.00	1.00	1.00
Moderate-Stable	**117 (8.2%)**	**2.22 (1.44-3.41)**	1.56 (96-2.53)	1.67 (1.00-2.77)	1.54 (0.92-2.58)
Moderate-Increasing	**25 (9.1%)**	**2.36(1.33-4.18)**	1.71 (0.82-3.54)	1.90 (0.88-4.10)	1.53 (0.56-4.22)
Elevated-Stable	**107 (18.5%)**	**4.78 (3.07-7.45)**	**2.16 (1.23-3.83)**	**2.50 (1.25-4.98)**	**2.11 (1.12-3.99)**
Elevated-Increasing	**27 (30.3%)**	**10.91 (5.89-20.21)**	**5.24 (2.21-12.44)**	**6.44 (2.37-17.53)**	**4.78 (1.67-13.68)**
DBP Trajectory Group					
Low-Stable	33 (4.7%)	1.00	1.00	1.00	1.00
Moderate-Stable	**118 (8.3%)**	**1.87 (1.22-2.86)**	1.48 (0.89-2.47)	1.55 (0.90-2.65)	1.57 (0.91-2.71)
Moderate-Increasing	**38 (11.3%)**	**2.47 (1.46-4.17)**	1.77 (0.88-3.57)	1.87 (0.89-3.93)	1.97 (0.77-5.03)
Elevated-Stable	**97 (16.2%)**	**3.92 (2.54-6.04)**	**1.93 (1.11-3.36)**	**2.16 (**1.12-4.16)	2.09 (1.13-3.89)
Elevated-Increasing	**23 (21.1%)**	**5.49 (3.00-10.07)**	1.98 (0.86-4.54)	2.28 (0.87-6.00)	2.20 (0.81-6.01)

Model 1 = age, race, sex, highest level of education, antihypertensive medication use at each exam, mg/dL of total cholesterol per year, cumulative number of years with diabetes, cumulative number of years as a current smoker, and BMI at both baseline and Y25

Model 2 = Model 1 + baseline systolic and diastolic blood pressure

Model 3 = Model 1 + year 25 systolic and diastolic blood pressure