

## **SUPPLEMENTARY MATERIALS**

### **Blood Pressure Levels in Young Adulthood and Midlife Stroke Incidence in a Diverse Cohort**

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Table S1. Adaptation of 2017 ACC/AHA Blood Pressure Classification in Adults\*

<b>BP Category</b>	<b>SBP</b>		<b>DBP</b>		<b>Antihypertensive Treatment</b>
Normal	< 120 mm Hg	and	< 80 mm Hg	and	No
Elevated	120-129 mm Hg	and	< 80 mm Hg	and	No
Hypertension					
Stage 1	130-139 mm Hg	or	80-89 mm Hg	and	No
Stage 2	≥ 140 mm Hg	or	≥ 90 mm Hg	or	Yes

\*Individuals with SBP and DBP in 2 categories were designated to the higher BP category. At any exam, 3 BP readings were taken at 1-minute intervals after the participant had been sitting in a quiet room for 5 minutes, with the first discarded and the 2<sup>nd</sup> and 3<sup>rd</sup> averaged.

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S2. Approaches to Blood Pressure Classification\*

Classification	Data Source (CARDIA Cycles)	Data Used for Classification	Mobility Between BP Categories	Time Scale
Baseline groups	Y0, Y2, Y5	Highest reading	No	Time-on-study
T-D groups, cumulative method	Y0, Y2, Y5, Y7, Y10, Y15, Y20, Y25, Y30	Highest reading <sup>†</sup>	Upward	Time-on-study
T-D groups, dynamic method	Y0, Y2, Y5, Y7, Y10, Y15, Y20, Y25, Y30	Last reading <sup>†</sup>	Upward/downward	Time-on-study
Age 30, cumulative method	Y0, Y2, Y5, Y7, Y10	Highest reading <sup>‡</sup>	No	Age
Age 30, dynamic method	Y0, Y2, Y5, Y7, Y10	Last reading <sup>‡</sup>	No	Age
Age 40, cumulative method	Y0, Y2, Y5, Y7, Y10, Y15, Y20	Highest reading <sup>‡</sup>	No	Age
Age 40, dynamic method	Y0, Y2, Y5, Y7, Y10, Y15, Y20	Last reading <sup>‡</sup>	No	Age

\*See Table S1 for definition of the blood pressure categories; <sup>†</sup>Prior to the start of each follow-up interval (as defined by CARDIA examination date); <sup>‡</sup>Prior to attaining the specified age.

BP, blood pressure; CARDIA, Coronary Artery Risk Development in Young Adults; T-D, time-dependent.

**BP classification schemes:**

Baseline groups- Using the highest BP measured from the first 3 examinations (Y0, Y2 and Y5). The decision to aggregate these examinations was supported by the fact that no stroke events occurred during this time range.

Time-dependent (T-D) groups, cumulative approach- Using the highest BP measured up to each follow-up interval. Examinations at Y5, Y7, Y10, Y15, Y20, Y25, and Y30 denoted the start dates of follow-up intervals. BP classification could be updated when new exposure data were obtained as follow-up continued. This approach allowed participants to remain in the same BP group or to progress into a more severe group throughout the follow-up.

T-D groups, dynamic approach- Using the last BP measured before each follow-up interval. Examinations at Y5, Y7, Y10, Y15, Y20, Y25, and Y30 denoted the start date of follow-up interval. BP classification could be updated when new exposure data were obtained as follow-up continued. This approach allowed participants to regress to a less severe BP group, remain in the same group, or progress to a more severe group throughout the follow-up.

Age-specific groups, cumulative approach- Using the highest BP measured from the first examination to the examination closest to, but not after, attaining the age of 30 or 40 years, as appropriate (which marked the start of follow-up).

Age-specific groups, dynamic approach- Using the last examination before attaining the age of 30 or 40 years, as appropriate (which marked the start of follow-up).

Table S3. Characteristics of Participants in the CARDIA Study by Ethnic Group According to 2017 ACC/AHA Guideline for Blood Pressure Classification

Characteristics*	Black Participants					White Participants				
	Overall (n=2,614)	Baseline Blood Pressure Groups <sup>†</sup>				Overall (n=2,465)	Baseline Blood Pressure Groups <sup>†</sup>			
		Normal (n=1,598)	Elevated (n=281)	Stage 1 HTN (n=535)	Stage 2 HTN (n=200)		Normal (n=1,733)	Elevated (n=235)	Stage 1 HTN (n=399)	Stage 2 HTN (n=98)
Age, y	29.2±3.8	28.9±3.8	28.4±3.8	29.9±3.7	31.2±3.4	30.4±3.4	30.2±3.4	30.1±3.4	30.5±3.4	31.5±2.8
Female, n (%)	1,472 (56.3)	1,073 (67.1)	87 (31.0)	218 (40.7)	94 (47.0)	1,306 (53.0)	1,117 (64.5)	52 (22.1)	112 (28.1)	25 (25.5)
Education, y	13.4±2.6	13.5±2.9	13.3±1.9	13.4±2.0	13.2±2.3	15.1±2.5	15.2±2.5	14.9±2.5	15.1±2.7	14.7±2.5
BMI, kg/m <sup>2</sup>	26.2±6.0	25.3±5.3	26.2±5.4	27.4±6.7	29.5±7.8	24.2±4.2	23.5±3.7	25.5±4.1	25.9±4.8	27.8±6.3
Smoking, n (%)										
Current	924 (35.4)	570 (35.7)	112 (39.9)	165 (30.8)	77 (38.5)	609 (24.7)	444 (25.6)	60 (25.6)	82 (20.6)	23 (23.7)
Past	230 (8.8)	137 (8.6)	27 (9.6)	55 (10.3)	11 (5.5)	476 (19.3)	338 (19.5)	48 (20.4)	75 (18.8)	15 (15.5)
Never	1,459 (55.8)	890 (55.7)	142 (50.5)	315 (58.9)	112 (56.0)	1,379 (56.0)	951 (54.9)	127 (54.0)	242 (60.7)	59 (60.8)
Total cholesterol, mg/dL	177.0±32.0	175.0±31.3	176.8±31.9	180.6±32.1	183.4±35.9	177.4±30.0	175.0±28.7	179.8±28.5	181.9±32.1	196.1±37.8
LDL cholesterol, mg/dL	129.0±32.8	126.5±32.5	128.7±33.5	133.4±31.7	137.0±35.1	131.8±30.3	128.9±28.5	136.0±29.0	137.6±33.3	150.7±38.3
HDL cholesterol, mg/dL	54.5±12.5	55.1±12.2	54.3±13.2	54.0±12.9	51.4±12.4	51.9±12.5	53.5±12.4	48.6±11.1)	48.7±12.7	46.0±10.4
SBP, mm Hg	110.3±9.9	104.9±6.2	117.2±4.5	116.9±7.5	126.9±10.2	107.3±9.6	103.0±6.5	116.1±4.4	116.4±7.1	125.9±10.4
DBP, mm Hg	69.1±8.6	65.0±5.9	68.4±5.8	76.0±5.2	84.0±8.9	67.7±7.8	64.6±5.8	68.8±5.0	76.4±4.6	84.0±8.0
Fasting glucose, mg/dL	82.2±19.4	80.7±15.7	83.8±17.2	84.3±25.1	86.8±27.8	83.0±12.4	82.0±11.5	84.8±9.2	84.8±12.3	90.0±25.1
Physical activity, units <sup>‡</sup>	372.5±269.9	354.0±261.7	449.1±290.3	397.9±277.7	344.0±260.1	421.1±239.0	411.3±234.5	495.5±263.3	420.5±234.7	417.0±245.0
Excessive alcohol use, n (%)	321 (12.3)	144 (9.0)	51 (18.1)	85 (15.9)	41 (20.5)	395 (14.3)	222 (12.8)	38 (16.2)	73 (18.3)	19 (19.6)
eGFR, mL/min/1.73 m <sup>2</sup>	131.8±22.5	132.2±22.2	134.8±24.3	129.9±22.6	128.7±21.1	111.9±18.6	111.1±18.6	113.2±18.5	114.1±17.6	112.4±20.9
No. of clinic visits <sup>§</sup>	2.7±0.6	2.6±0.6	2.7±0.6	2.8±0.5	2.9±0.4	2.9±0.4	2.8±0.4	2.9±0.4	2.9±0.4	2.9±0.4

BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HTN, hypertension; LDL, low-density lipoprotein; SBP, systolic blood pressure.

Data are presented as mean (SD) unless otherwise specified.

\*Based on cumulative data obtained during CARDIA clinic visits taken place at Y0, Y2 and Y5; the latter defined the follow-up start date for the main analysis. Average values are presented for BMI, total cholesterol, LDL cholesterol, HDL cholesterol, SBP, DBP, and physical activity (last available information for the other variables presented).

<sup>†</sup>Classification based on the highest blood pressure measured during CARDIA Y0, Y2 and Y5 clinic visits.

<sup>‡</sup>As assessed with the CARDIA Physical Activity History questionnaire.

<sup>§</sup>Number of clinic visits from Y0 (first CARDIA examination) to Y5 (after which follow-up began).

Table S4. Association of Baseline Blood Pressure Groups\* with Subsequent Stroke Incidence Using Average Blood Pressure Measurements at Y0, Y2, and Y5 Among CARDIA Participants

Exposure Definition	Blood Pressure Groups				C-Statistic (se)
	Normal BP	Elevated BP	Stage 1 HTN	Stage 2 HTN	
No. of subjects	4,062	291	338	117	-
No. of events	68	4	15	10	-
Incidence rate <sup>†</sup>	64 (50-81)	53 (15-137)	178 (100-293)	361 (173-665)	-
Unadjusted	1 (ref.)	0.85 (0.31-2.27)	2.91 (1.66-5.09)	6.04 (3.11-11.74)	.595 (.025)
Model 1 <sup>‡</sup>	1 (ref.)	0.81 (0.29-2.87)	2.34 (1.30-4.19)	4.05 (2.05-8.00)	.776 (.022)
Model 2 <sup>§</sup>	1 (ref.)	0.79 (0.28-2.21)	2.15 (1.19-3.91)	3.18 (1.52-6.64)	.805 (.022)

Figures represent hazard ratios (95% confidence intervals) for incident stroke associated with BP groups (unless otherwise specified). Classification of the BP groups is based on average BP values at CARDIA Y0, Y2 and Y5 examinations (restricted to participants at  $\geq 2$  examinations). The Harrell concordance index (C-statistic) is provided for each model as a measure of risk discrimination.

BP, blood pressure; CARDIA, Coronary Artery Risk Development in Young Adults; HTN, hypertension.

\*As defined by the 2017 ACC/AHA blood pressure guideline (see Table S1 for definitions).

<sup>†</sup>Incidence density per 100,000 person-years (Fisher's exact 95% confidence intervals).

<sup>‡</sup>Model 1: Adjusted for baseline age, race, sex, study center, and education.

<sup>§</sup>Model 2: Model 1 + smoking, diabetes, LDL cholesterol, HDL cholesterol, BMI, physical activity, and excessive alcohol use (as measured at baseline).

Table S5. Association of 2017 ACC/AHA Blood Pressure Groups at Different Ages with Subsequent Stroke Incidence Among CARDIA Participants

Age at start of follow-up	Blood Pressure Groups (Cumulative Method)				C-Statistic (se)
	Normal BP	Elevated BP	Stage 1 HTN	Stage 2 HTN	
<b>Age 30 Years</b>					
No. of subjects	3,388	540	888	268	-
No. of events	53	11	16	19	-
Incidence rate*	60 (45-78)	80 (40-144)	72 (41-116)	295 (178-461)	-
Unadjusted	1 (ref.)	1.41 (0.73-2.69)	1.26 (0.72-2.21)	5.29 (3.13-8.95)	.604 (.030)
Model 1 <sup>†</sup>	1 (ref.)	1.44 (0.71-2.92)	1.22 (0.68-2.19)	4.46 (2.56-7.77)	.790 (.022)
Model 2 <sup>‡</sup>	1 (ref.)	1.33 (0.66-2.66)	1.15 (0.62-2.12)	3.90 (2.19-6.94)	.807 (.023)
<b>Age 40 Years</b>					
No. of subjects	2,614	448	1,207	708	-
No. of events	24	8	17	42	-
Incidence rate*	56 (36-83)	112 (49-221)	86 (50-138)	382 (275-516)	-
Unadjusted	1 (ref.)	2.07 (0.93-4.60)	1.57 (0.84-2.91)	7.03 (4.26-11.61)	.707 (.029)
Model 1 <sup>†</sup>	1 (ref.)	1.97 (0.87-4.47)	1.46 (0.78-2.74)	5.32 (3.14-9.01)	.810 (.023)
Model 2 <sup>‡</sup>	1 (ref.)	2.03 (0.90-4.55)	1.52 (0.81-2.87)	5.46 (3.22-9.25)	.838 (.022)

Figures represent hazard ratios (95% confidence intervals) for incident stroke associated with BP groups (unless otherwise specified). The Harrell concordance index (C-statistic) is provided for each model as a measure of risk discrimination. BP groups at ages 30 and 40 years were determined according to the highest measurement from first to last examination before attaining that specified ages (cumulative method).

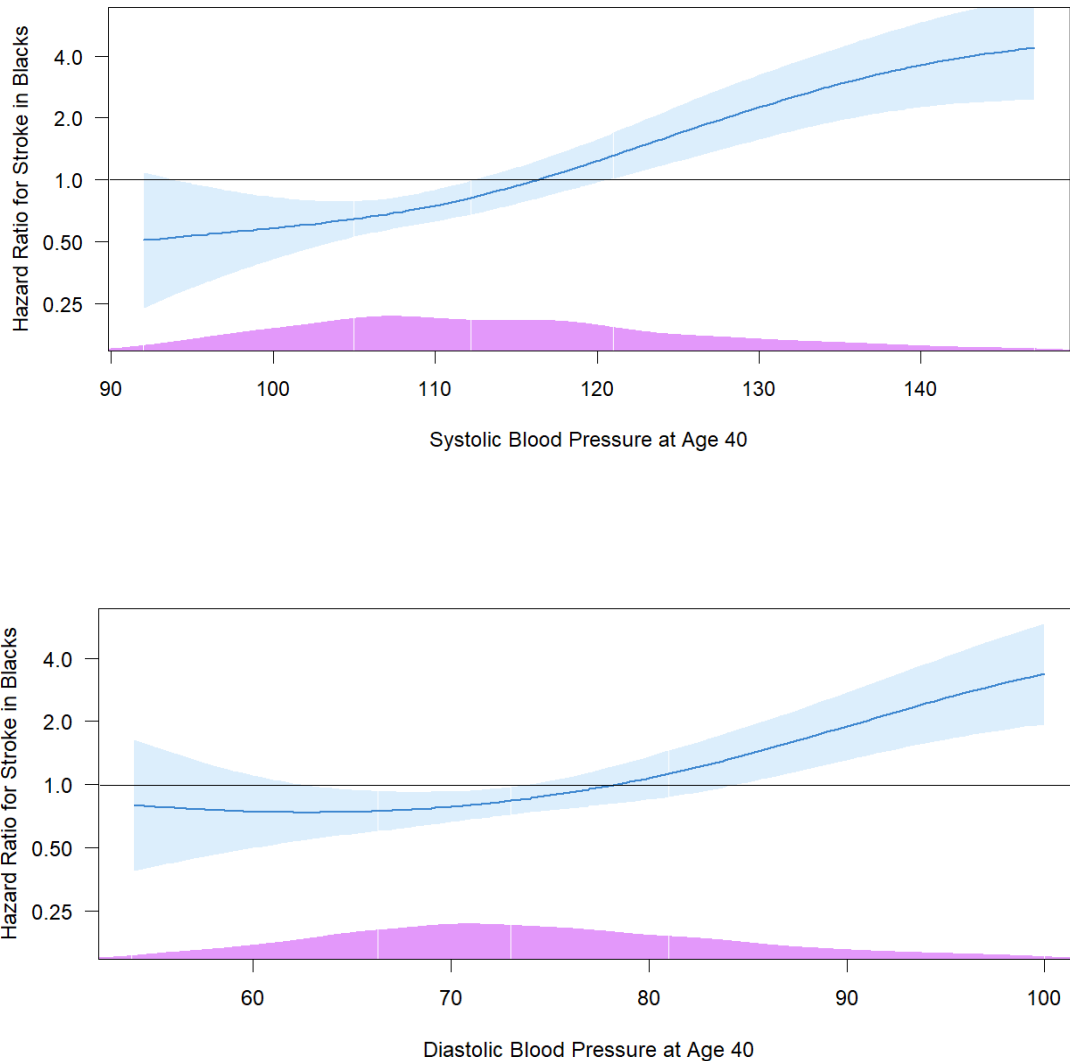
BP, blood pressure; CARDIA, Coronary Artery Risk Development in Young Adults; HTN, hypertension.

\*Incidence density per 100,000 person-years (Fisher's exact 95% confidence intervals).

<sup>†</sup>Model 1: Adjusted for race, sex, study center, and education.

<sup>‡</sup>Model 2: Model 1 + smoking, diabetes, LDL cholesterol, HDL cholesterol, BMI, physical activity, and excessive alcohol use (as measured at/last before ages 30 or 40 years, as appropriate).

Figure S1.



Spline-based hazard ratios (95% confidence intervals) for stroke incidence associated with systolic blood pressure (upper panel) and diastolic blood pressure (lower panel), in mm Hg, as measured at age 40 years or last before among black participants only. The curves are based on multivariable Cox models adjusted for covariates assessed at age 40 years or last before, including sex, study center, education, antihypertensive medications, smoking, diabetes, LDL cholesterol, HDL cholesterol, BMI, physical activity, and excessive alcohol use. The reference points are 117 and 78 mm Hg (65th percentile) for systolic and diastolic blood pressure, respectively. The histograms at the bottom (purple) show the distribution of blood pressure in the sample. The highest and lowest 2.5% of blood pressure values have been winsorized for visualization purposes.