Supplementary Online Content

Yano Y, Tanner RM, Sakhuja S, et al. Association of daytime and nighttime blood pressure with cardiovascular disease events among African American individuals. *JAMA Cardiol.* Published online August 14, 2019. doi:10.1001/jamacardio.2019.2845

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplementary methods

Study Population

The JHS is a community-based prospective cohort study designed to identify CVD risk factors among African Americans.[1,2] Between 2000 and 2004, JHS enrolled 5,306 non-institutionalized African Americans aged ≥ 21 years. Four groups were sampled from the Jackson, Mississippi metropolitan residents for enrollment: randomly selected adults, participants enrolled in the Atherosclerosis Risk in Communities (ARIC) study, volunteers, and secondary family members.[1,2]

Data collection

During the in-home interview, trained African-American interviewers administered standardized questionnaires to collect self-reported information on socio-demographics (e.g. age, sex, education, marital status, and socioeconomic status), prior diagnosed co-morbid conditions, parental history of hypertension, and selected health behaviors (e.g. alcohol consumption, current smoking, and physical activity).[2] Education was measured as the highest level of schooling completed and classified into two categories within this study as "less than high school" or "greater than high school". Physical activity over the past 12 months was assessed using the Jackson Heart Study (JHS) Physical Activity Cohort (JPAC) survey, a 30-item validated questionnaire.[3,4] The JPAC has four index scores that correspond to four physical activity domains (active living, work, sport, and home/life). The total physical activity score was calculated as the sum of the four index scores, with work scores set to 0 for participants who reported no paid or volunteer work during the past year. Higher scores represent more daily physical activity. Current smoking was defined by affirmative responses to the questions "Have you smoked more than 400 cigarettes in your lifetime?" and "Do you now smoke cigarettes?" Parental history of hypertension was defined by affirmative responses to the questions "Did your mother ever have (or does she have) high blood pressure or hypertension?" and/or "Did your father ever have (or does he have) high blood pressure or hypertension?"

Participants were asked to bring any medications taken within 2 weeks prior to the baseline examination to the clinic visit and were transcribed verbatim. Medication coding was performed by a pharmacist using the Medispan dictionary and classified into categories according to the Therapeutic Classification System. Antihypertensive medication use was defined by self-report. Participants were asked to avoid caffeine, eating, heavy physical activity, smoking, and alcohol intake for 12 hours prior to the clinic examination. During the clinical examination, weight and height were measured for each participant. Body mass index was calculated as the weight in kilograms divided by height in meters squared (kg/m^2). Fasting blood samples were collected according to standardized procedures[5] and processed at two central laboratories (University of Mississippi Medical Center and the University of Minnesota).[5] Total and high-density lipoprotein (HDL) cholesterol was quantified by an oxidase method. High-sensitivity C-reactive protein (CRP) was calculated using the latex particle immunoturbidimetric assay method.[6] Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[7] Reduced eGFR was defined as <60 ml/min/1.73 m^2. Urinary albumin and creatinine were quantified from a 24-hour urine collection or from a spot urine sample using the

nephalometric immunoassay and enzymatic methods, respectively.[8] Diabetes was defined as a fasting (≥8 hours) serum glucose ≥126 mg/dL or hemoglobin A1c ≥6.5% or use of insulin or oral hypoglycemic medications within 2 weeks prior to the clinic examination.

Clinic BP measurement

Clinic BP was measured two times with 1 minute between measurements using a random-zero sphygmomanometer (Hawksley and Sons Ltd., Lancing, UK) with appropriately sized cuffs placed on the right arm after the participant had been sitting in a quiet room for at least 5 minutes. Clinic BP was defined as the average of these two measurements. The JHS Coordinating Center conducted quality control by monitoring digit preference for each technician and by comparing mean BP measurements within and between trained technicians. A BP comparability substudy was conducted in which BP was measured simultaneously, using a Y connector, by random zero sphygmomanometer and an Omron HEM-907XL device, a semi-automated device. As described in prior analyses of the JHS,[9] the random-zero BP measurements were calibrated to the semi-automated device using robust regression.

ABPM BP measurement

After the Visit 1 examination, participants underwent ABPM for 24 hours using the SpaceLabs model 90207 device (SpaceLabs Healthcare, Snoqualmie, WA) fitted on their non-dominant arm.[10,11] BP readings were obtained every 20 minutes over a 24-hour period. Data were evaluated for quality and processed with Medifacts International's Medicom software (Rockville, MD). SBP < 60 mm Hg and DBP < 30 mm Hg on the ABPM were considered invalid and not included in the calculation of mean daytime and nighttime BP. Among 1,034 JHS participants who completed ABPM at Visit 1, 9.6% did not complete a sleep diary and 1.8% completed the sleep diary but provided insufficient data to determine the times when they were awake and asleep. For these participants, daytime was defined as 10:00-20:00 and nighttime as 00:00-06:00.

CVD events and all-cause mortality

The primary outcome was cardiovascular disease (CVD) events. All-cause mortality was examined as a secondary outcome. Adjudication procedures for these outcomes have been described previously.[12] Briefly, living participants or their proxies were contacted annually via telephone to assess potential CVD events and vital status. Hospital discharge lists with specific diagnosis criteria were also obtained from the Jackson, Mississippi tri-county area hospitals. Death certificates were requested from the Mississippi State Department of Health for JHS participants as needed. When a CVD-related hospitalization or a death was identified, medical records were retrieved and abstracted. Trained clinicians adjudicated events following published guidelines using the information available about the circumstance surrounding an event.[12] For the current analysis, definite or probable CVD events (i.e., coronary heart disease [CHD], nonfatal myocardial infarction or acute CHD death or stroke defined as non-carotid embolic or thrombotic brain infarction, brain hemorrhage or subarachnoid hemorrhage) were available through December 2014, and all-cause mortality were available through December 2016.

References

1. Wilson DK, Kliewer W, Teasley N, Plybon L, Sica DA. Violence exposure, catecholamine excretion, and blood pressure nondipping status in African American male versus female adolescents. Psychosom Med. 2002;64:906-915.
2. Taylor HA, Jr., Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, Nelson C, Wyatt SB. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. Ethn Dis. 2005;15:S6-4-17.
3. Dubbert PM, Carithers T, Ainsworth BE, Taylor HA, Jr., Wilson G, Wyatt SB. Physical activity assessment methods in the Jackson Heart Study. Ethn Dis. 2005;15:S6-56-61.
4. Smitherman TA, Dubbert PM, Grothe KB, Sung JH, Kendzor DE, Reis JP, Ainsworth BE, Newton RL Jr, Lesniak KT, Taylor HA Jr. Validation of the Jackson Heart Study Physical Activity Survey in African Americans. J Phys Act Health. 2009;6 Suppl 1:S124-132.
5. Carpenter MA, Crow R, Steffes M, Rock W, Heilbraun J, Evans G, Skelton T, Jensen R, Sarpong D. Laboratory, reading center, and coordinating center data management methods in the Jackson Heart Study. Am J Med Sci. 2004;328:131-144.
6. Fox ER, Benjamin EJ, Sarpong DF, Rotimi CN, Wilson JG, Steffes MW, Chen G, Adeyemo A, Taylor JK, Samdarshi TE, Taylor HA Jr. Epidemiology, heritability, and genetic linkage of C-reactive protein in African Americans (from the Jackson Heart Study). Am J Cardiol. 2008;102:835-841.
7. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-612.
8. Flessner MF, Wyatt SB, Akylbekova EL, Coady S, Fulop T, Lee F, Taylor HA, Crook E. Prevalence and awareness of CKD among African Americans: the Jackson Heart Study. Am J Kidney Dis. 2009;53:238-247.
9. Abdalla M, Booth JN 3rd, Seals SR, Spruill TM, Viera AJ, Diaz KM, Sims M, Muntner P, Shimbo D. Masked Hypertension and Incident Clinic Hypertension Among Blacks in the Jackson Heart Study. Hypertension. 2016;68:220-226.
10. Ravenell J, Shimbo D, Booth JN 3rd, et al. Thresholds for Ambulatory Blood Pressure Among African Americans in the Jackson Heart Study. Circulation. 2017;135 (25):2470-2480.
11. Booth JN 3rd, Diaz KM, Seals SR, et al. Masked Hypertension and Cardiovascular Disease Events in a Prospective Cohort of Blacks: The Jackson Heart Study. Hypertension. 2016;68 (2):501-510.
12. Keku E, Rosamond W, Taylor HA Jr, Garrison R, Wyatt SB, Richard M, Jenkins B, Reeves L, Sarpong D. Cardiovascular disease event classification in the Jackson Heart Study: methods and procedures. Ethn Dis. 2005;15(4 Suppl 6):S6-62-70.

eTable 1. Number and percentage of participants included in the current analysis with missing data for variables (n=1,034)	
Variable	**N (%) missing**
Age	0 (0%)
Gender	0 (0%)
BMI	1 (0.1%)
Diabetes	8 (0.8%)
Less than high school education	4 (0.4%)
Current smoking	7 (0.7%)
History of stroke	0 (0%)
History of MI	0 (0%)
Statin use	11 (1.1%)
Total cholesterol	78 (7.6%)
HDL-cholesterol	79 (7.6%)
CRP > 3 mg/L	11 (1.1%)
eGFR < 60 ml/min/1.73m^2	12 (1.2%)
Albumin-to-creatinine ratio ≥ 30 mg/g	220 (21.3%)
Antihypertensive medication use	24 (2.3%)
Clinic SBP	0 (0%)
Clinic DBP	0 (0%)
Daytime SBP	0 (0%)
Daytime DBP	0 (0%)
Nighttime SBP	0 (0%)
Nighttime DBP	0 (0%)
BMI=body mass index; MI=myocardial infarction; HDL=high-density lipoprotein; CRP=c-reactive protein; eGFR=estimated glomerular filtration rate; SBP=systolic blood pressure; DBP=diastolic blood pressure.	

eTable 2. Characteristics of JHS participants who were included in the current study and those who were not included			
	Included (n=1,034)	**Not included (n=4,272)**	**P value**
Age, years	58.9 (10.9)	53.9 (13.1)	<0.001
Men, %	32.6	37.5	0.003
BMI, kg/m^2	31.2 (6.4)	31.9 (7.4)	0.003
Diabetes, %	26.7	23.0	0.011
Less than high school education, %	18.4	18.4	0.958
Current smoking, %	9.9	14.0	0.001
History of stroke, %	3.9	4.5	0.345
History of MI, %	4.6	5.7	0.194
Statin use, %	15.7	13.2	0.037
Total cholesterol, mg/dL	201.5 (39.6)	198.8 (40.2)	0.060
HDL-cholesterol, mg/dL	54.0 (15.0)	51.2 (14.5)	<0.001
CRP > 3 mg/L, %	47.4	45.8	0.351
eGFR < 60 ml/min/1.73 m^2, %	10.3	8.9	0.175
Albumin-to-creatinine ratio ≥ 30 mg/g, %	10.4	13.3	0.036
Antihypertensive medication use, %	56.4	48.0	<0.001
Data are expressed as means (standard deviation) or percentage. P values were calculated by unpaired t-test or chi-square test. BMI=body mass index; MI=myocardial infarction; HDL=high-density lipoprotein; CRP=c-reactive protein; eGFR=estimated glomerular filtration rate.			

eTable 3. Hazard ratios for cardiovascular disease events and all-cause mortality for daytime SBP and nighttime SBP		
Cardiovascular disease events (n=113)	**HR (95% CI) per 1 SD higher daytime SBP**	**HR (95% CI) per 1 SD higher nighttime SBP**
Model 1	1.76 (1.48, 2.10)	1.81 (1.54, 2.13)
Model 2	1.57 (1.30, 1.89)	1.57 (1.32, 1.86)
Model 3	1.47 (1.22, 1.77)	1.44 (1.20, 1.72)
Model 4	1.53 (1.24, 1.88)	1.48 (1.22, 1.80)
Model 5	1.30 (0.97, 1.73)	1.25 (0.95, 1.65)
All-cause mortality (n=194)	**HR (95% CI) per 1 SD higher daytime SBP**	**HR (95% CI) per 1 SD higher nighttime SBP**
Model 1	1.47 (1.29, 1.67)	1.64 (1.45, 1.86)
Model 2	1.25 (1.08, 1.44)	1.33 (1.16, 1.53)
Model 3	1.21 (1.05, 1.40)	1.29 (1.12, 1.49)
Model 4	1.13 (0.97, 1.33)	1.24 (1.06, 1.45)
Model 5	0.95 (0.76, 1.19)	1.28 (1.03, 1.60)

Adjusted hazard ratios (95% confidence intervals) associated with a one-SD higher daytime SBP and nighttime SBP levels are shown. The one-SD increment of daytime SBP and nighttime SBP are 13.5 mm Hg and 15.5 mm Hg, respectively. Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. Model 5 includes adjustment for the composite risk score, clinic SBP, clinic DBP, daytime SBP, and nighttime SBP. CVD=cardiovascular disease; HR=hazard ratio; SD=standard deviation; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.

eTable 4. Hazard ratios for cardiovascular disease events and all-cause mortality associated with daytime DBP and nighttime DBP		
CVD events (n=113)	**HR (95%CI) per 1 SD higher daytime DBP**	**HR (95%CI) per 1 SD higher nighttime DBP**
Model 1	1.18 (0.98, 1.42)	1.40 (1.16, 1.70)
Model 2	1.32 (1.09, 1.61)	1.40 (1.15, 1.71)
Model 3	1.16 (0.97, 1.40)	1.21 (0.99, 1.47)
Model 4	1.25 (1.02, 1.51)	1.30 (1.06, 1.59)
Model 5	1.09 (0.82, 1.45)	1.21 (0.90, 1.63)
All-cause mortality (n=194)		
Model 1	0.91 (0.79, 1.05)	1.19 (1.02, 1.38)
Model 2	1.03 (0.88, 1.20)	1.17 (1.00, 1.36)
Model 3	0.92 (0.80, 1.07)	1.02 (0.87, 1.19)
Model 4	0.95 (0.81, 1.10)	1.06 (0.90, 1.24)
Model 5	0.82 (0.65, 1.02)	1.24 (0.98, 1.58)

Adjusted hazard ratios (95% confidence intervals) associated with a one standard deviation higher daytime DBP and nighttime DBP levels are shown. The one standard deviation increment of daytime DBP and nighttime DBP are 9.3 mm Hg and 9.5 mm Hg, respectively. Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. Model 5 includes adjustment for the composite risk score, clinic SBP, clinic DBP, daytime SBP, and nighttime SBP. CVD=cardiovascular disease; HR=hazard ratio; SD=standard deviation; SBP=systolic blood pressure; DBP=diastolic blood pressure; CI=confidence interval.

eTable 5. Hazard ratios for cardiovascular disease events by tertile of daytime SBP and nighttime SBP								
	Daytime SBP				**Nighttime SBP**			
	1st tertile (n=344)	**2nd tertile (n=350)**	**3rd tertile (n=340)**		**1st tertile (n=340)**	**2nd tertile (n=352)**	**3rd tertile (n=340)**	
SBP range, mm Hg	<122.5	122.5 – 134.3	>134.3		<113.2	113.2 – 126.4	>126.4	
Number of events	19	32	62		17	37	59	
Rate (95% CI)	4.6 (2.9, 7.2)	7.9 (5.6, 11.2)	17.2 (13.4, 22.0)		4.2 (2.6, 6.7)	9.0 (6.6 ,12.5)	16.3 (12.6, 21.0)	
	HR (95% CI)			**P-trend**	**HR (95% CI)**			**P-trend**
Model 1	1 (ref)	1.74 (0.98, 3.06)	3.76 (2.25, 6.29)	<0.001	1 (ref)	2.18 (1.23, 3.87)	3.92 (2.29, 6.73)	<0.001
Model 2	1 (ref)	1.46 (0.83, 2.58)	2.63 (1.56, 4.44)	<0.001	1 (ref)	1.77 (0.99, 3.15)	2.59 (1.49, 4.52)	<0.001
Model 3	1 (ref)	1.48 (0.83, 2.61)	2.57 (1.51, 4.37)	<0.001	1 (ref)	1.85 (1.04, 3.29)	2.51 (1.43, 4.42)	0.001
Model 4	1 (ref)	1.50 (0.84, 2.68)	2.71 (1.53, 4.80)	<0.001	1 (ref)	1.85 (1.03, 3.33)	2.54 (1.40, 4.61)	0.002

The rate is per 1,000 person years. Adjusted HRs (95% CIs) associated with tertiles of daytime SBP and nighttime SBP are shown.
Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use.
Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP.
CVD=cardiovascular disease; HR=hazard ratio; SBP=systolic blood pressure; DBP=diastolic blood pressure; CI=confidence interval.

eTable 6. Hazard ratios for cardiovascular disease events by tertile of daytime DBP and nighttime DBP								
	Daytime DBP				**Nighttime DBP**			
	1st tertile (n=346)	**2nd tertile (n=353)**	**3rd tertile (n=335)**		**1st tertile (n=348)**	**2nd tertile (n=343)**	**3rd tertile (n=343)**	
DBP range, mm Hg	<73.4	73.4 – 81.3	>81.3		<63.9	63.9 – 72.1	>72.1	
Number of events	79	53	62		56	66	72	
Rate (95% CI)	9.9 (7.2, 13.5)	5.8 (3.9, 8.6)	13.6 (10.3, 17.9)		7.9 (5.6, 11.2)	7.0 (4.8, 10.2)	14.2 (10.8, 18.5)	
	HR (95% CI)			**P-trend**	**HR (95% CI)**			**P-trend**
Model 1	1 (ref)	0.58 (0.35, 0.97)	1.37 (0.90, 2.08)	0.117	1 (ref)	0.89 (0.53, 1.47)	1.79 (1.16, 2.78)	0.006
Model 2	1 (ref)	0.72 (0.43, 1.21)	1.79 (1.14, 2.80)	0.010	1 (ref)	0.88 (0.53, 1.46)	1.72 (1.09, 2.73)	0.014
Model 3	1 (ref)	0.58 (0.35, 0.97)	1.35 (0.89, 2.07)	0.134	1 (ref)	0.8 (0.52, 1.46)	1.42 (0.90, 2.24)	0.103
Model 4	1 (ref)	0.65 (0.39, 1.10)	1.59 (1.00, 2.51)	0.041	1 (ref)	0.93 (0.56, 1.56)	1.63 (1.01, 2.64)	0.039

The rate is per 1,000 person years. Adjusted HRs (95% CIs) associated with tertiles of daytime DBP and nighttime DBP are shown.
Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; SBP=systolic blood pressure; DBP=diastolic blood pressure; CI=confidence interval.

eTable 7. Heterogeneity in the association between each BP measure and outcome by antihypertensive medication use with the inclusion of multiplicative interaction terms		
	Cardiovascular disease events (n=113)	**All-cause mortality (n=194)**
Daytime SBP × Antihypertensive medication use	p=0.105	p=0.464
Nighttime SBP × Antihypertensive medication use	p=0.032	p=0.298
Heterogeneity in the association between daytime SBP or nighttime SBP and each outcome by antihypertensive medication use was evaluated with the inclusion of multiplicative interaction terms (i.e., daytime SBP × antihypertensive medication use, nighttime SBP × antihypertensive medication use, high daytime BP × antihypertensive medication use, or high nighttime BP × antihypertensive medication use). P values for each multiplicative interaction term were shown. All analyses also include adjustment for clinic SBP, clinic DBP, and a composite risk score (consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin), antihypertensive medication use, and each BP measure. CVD=cardiovascular disease; HR=hazard ratio; SD=standard deviation; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.		

eTable 8. Hazard ratios for cardiovascular disease events for daytime SBP and nighttime SBP among participants taking and not taking antihypertensive medication		
	Not taking antihypertensive medication (n=440)	**Taking antihypertensive medication (n=570)**
Cardiovascular disease events (n=75)	**HR (95%CI) per 1 SD higher daytime SBP**	**HR (95%CI) per 1 SD higher daytime SBP**
Model 1	2.11 (1.54 , 2.90)	1.45 (1.16, 1.81)
Model 2	1.70 (1.22, 2.38)	1.38 (1.09, 1.73)
Model 3	1.72 (1.20, 2.46)	1.25 (0.99, 1.58)
Model 4	1.52 (1.02, 2.27)	1.36 (1.06, 1.74)
	Not taking antihypertensive medication	**Taking antihypertensive medication**
Cardiovascular disease events (n=33)	**HR (95%CI) per 1 SD higher nighttime SBP**	**HR (95%CI) per 1 SD higher nighttime SBP**
Model 1	2.19 (1.58, 3.03)	1.51 (1.22, 1.86)
Model 2	1.79 (1.26, 2.54)	1.38 (1.11, 1.73)
Model 3	1.83 (1.29, 2.60)	1.25 (0.99, 1.58)
Model 4	1.68 (1.13, 2.50)	1.36 (1.07, 1.72)

Adjusted HRs (95% CIs) associated with a one-SD increase of daytime SBP and nighttime SBP levels are shown. The one-SD increment of daytime SBP and nighttime SBP are 13.5 mm Hg and 15.5 mm Hg, respectively. Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; SD=standard deviation; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.

eTable 9. Changes in discrimination for cardiovascular disease events and all-cause mortality for daytime and nighttime BP				
	Cardiovascular disease events (n=113)		**All-cause mortality (n=194)**	
	C statistic (95% CI)	Change (mean; 95%CI) in C statistic from base model	C statistic (95% CI)	Change (mean; 95%CI) in C statistic from base model
Base model	0.763 (0.721, 0.798)	0 (ref)	0.779 (0.746, 0.808)	0 (ref)
Model 1: Base model + daytime SBP	0.775 (0.736, 0.811)	0.011 (0.0004, 0.030)	0.779 (0.748, 0.808)	0.000 (-0.002, 0.003)
Model 2: Base model + daytime DBP	0.770 (0.728, 0.804)	0.0057 (-0.0004, 0.020)	0.780 (0.750, 0.809)	0.001 (-0.001, 0.007)
Model 3: Base model + nighttime SBP	0.780 (0.738, 0.810)	0.0123 (0.0003, 0.031)	0.780 (0.748, 0.809)	0.0005 (-0.001, 0.006)
Model 4: Base model + nighttime DBP	0.770 (0.731, 0.805)	0.0072 (-0.0003, 0.023)	0.780 (0.747, 0.809)	0.00000 (-0.001, 0.004)
Harrell's C was used to calculate C statistics for each outcome. The differences in C statistics and 95% CIs for each outcome after each BP measure was added to base models are shown. Base model includes adjustment for a composite risk score (consisting age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, statin and antihypertensive medication use), clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.				

eTable 10. Hazard ratios for cardiovascular disease events and all-cause mortality for high daytime BP and high nighttime BP defined in the 2017 ACC/AHA High BP guidelines				
	High daytime BP		**High nighttime BP**	
	No (n=465)	**Yes (n=569)**	**No (n=199)**	**Yes (n=835)**
Cardiovascular disease				
Number of events	34	79	9	104
Rate (95% CI)	6.2 (4.4, 8.6)	12.6 (10.1, 15.7)	3.8 (2.0, 7.2)	11.1 (9.1, 13.4)
		HR (95% CI)		**HR (95% CI)**
Model 1	1 (ref)	2.05 (1.37, 3.06)	1 (ref)	2.94 (1.49, 5.81)
Model 2	1 (ref)	1.78 (1.19, 2.67)	1 (ref)	2.12 (1.07, 4.22)
Model 3	1 (ref)	1.64 (1.08, 2.47)	1 (ref)	2.07 (1.03, 4.13)
Model 4	1 (ref)	1.65 (1.07, 2.54)	1 (ref)	2.02 (1.00, 4.09)
All-cause mortality				
Number of events	72	122	20	174
Incidence rate (95% CI)	11.0 (8.7 – 13.8)	15.7 (13.1 – 18.7)	7.0 (4.5 – 10.9)	15.1 (13.0 – 17.5)
		HR (95% CI)		
Model 1	1 (ref)	1.45 (1.08, 1.93)	1 (ref)	2.18 (1.37, 3.46)
Model 2	1 (ref)	1.20 (0.89, 1.61)	1 (ref)	1.34 (0.84, 2.14)
Model 3	1 (ref)	1.08 (0.80, 1.46)	1 (ref)	1.41 (0.88, 2.27)
Model 4	1 (ref)	1.01 (0.75, 1.38)	1 (ref)	1.30 (0.80, 2.10)

The rate is per 1,000 person years. Adjusted hazard ratios (95% confidence intervals) associated with high daytime BP and high nighttime BP are shown. Following the 2017 ACC/AHA guideline, high daytime BP was defined as mean daytime SBP ≥130 mm Hg or DBP ≥ 80 mm Hg. High nighttime BP was defined as mean nighttime SBP ≥110 mm Hg or DBP ≥ 65 mm Hg. Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. ACC=American College of Cardiology; AHA= American Heart Association; CVD=cardiovascular disease; HR=hazard ratio; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.

eTable 11. Hazard ratios for cardiovascular disease events and all-cause mortality for dipping status in two categories (see footnote)		
	Dipping (n=283)	**Non-dipping (n=751)**
Cardiovascular disease		
Number of events	23	90
Rate (95% CI)	7.0 (4.6, 10.5)	10.6 (8.6, 13.0)
	HR (95% CI)	
Model 1	1 (ref)	1.52 (0.96, 2.40)
Model 2	1 (ref)	1.25 (0.79, 1.99)
Model 3	1 (ref)	1.27 (0.79, 2.02)
Model 4	1 (ref)	1.26 (0.79, 2.01)
All-cause mortality		
Number of events	34	160
Rate (95% CI)	8.5 (6.0, 11.8)	15.5 (13.3, 18.1)
	HR (95% CI)	
Model 1	1 (ref)	1.86 (1.29, 2.70)
Model 2	1 (ref)	1.44 (0.99, 2.09)
Model 3	1 (ref)	1.56 (1.06, 2.28)
Model 4	1 (ref)	1.54 (1.05, 2.24)

The rate is per 1,000 person years. Adjusted hazard ratios (95% confidence intervals) associated with non-dipping are shown. Dipping status included: non-dipping BP status (nighttime-to-daytime SBP ratio >0.90); and dipping BP status (nighttime-to-daytime SBP ratio ≤0.90).
Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use.
Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.

eTable 12. Hazard ratios for cardiovascular disease events and all-cause mortality for dipping status in three categories (see footnote)			
	Dipping (n=283)	**Non-dipping (n=587)**	**Reverse dipping (n=164)**
Cardiovascular disease			
Number of events	23	68	22
Rate (95% CI)	7.0 (4.6, 10.5)	10.2 (8.1, 13.0)	11.8 (7.8, 18.0)
	HR (95% CI)		
Model 1	1 (ref)	1.47 (0.92, 2.36)	1.70 (0.95 – 3.05)
Model 2	1 (ref)	1.28 (0.80, 2.06)	1.17 (0.65 – 2.13)
Model 3	1 (ref)	1.35 (0.84, 2.17)	1.02 (0.55 – 1.90)
Model 4	1 (ref)	1.34 (0.83, 2.16)	1.02 (0.55 – 1.89)
All-cause mortality			
Number of events	34	113	47
Rate (95% CI)	8.5 (6.0, 11.8)	14.0 (11.6, 16.8)	21.1 (15.8, 28.0)
	HR (95% CI)		
Model 1	1 (ref)	1.68 (1.14, 2.46)	2.54 (1.64, 3.95)
Model 2	1 (ref)	1.40 (0.95, 2.06)	1.55 (0.99, 2.44)
Model 3	1 (ref)	1.61 (1.09, 2.38)	1.42 (0.88, 2.27)
Model 4	1 (ref)	1.57 (1.07, 2.32)	1.44 (0.90, 2.29)

The rate is per 1,000 person years. Adjusted hazard ratios (95% confidence intervals) associated with non-dipping and reverse dipping are shown. *Dipping status included: non-dipping BP status (nighttime-to-daytime SBP ratio >0.90 to ≤1.00); reverse dipping BP status (nighttime-to-daytime SBP ratio >1.00); and dipping BP status (nighttime-to-daytime SBP ratio ≤0.90). Model 1 is unadjusted. Model 2 includes adjustment for age and sex. Model 3 includes adjustment for a composite risk score consisting of age, sex, body mass index, diabetes, education, smoking status, history of stroke, history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use. Model 4 includes adjustment for the composite risk score, clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; CI=confidence interval; SBP=systolic blood pressure; DBP=diastolic blood pressure.

eTable 13. Hazard ratios for cardiovascular disease events and all-cause mortality for daytime SBP and nighttime SBP among participants without a history of myocardial infarction and stroke (n=952)		
	Cardiovascular disease events (n=95)	**All-cause mortality (n=168)**
Per 1 SD higher daytime SBP	1.42 (1.13, 1.80)	1.11 (0.94, 1.32)
Per 1 SD higher daytime DBP	1.26 (1.02, 1.55)	0.94 (0.80, 1.10)
Per 1 SD higher nighttime SBP	1.37 (1.10, 1.72)	1.23 (1.03, 1.46)
Per 1 SD higher nighttime DBP	1.29 (1.03, 1.62)	1.03 (0.87, 1.22)
High daytime BP, No High daytime BP, Yes	1 (ref) 2.26 (1.45, 3.51)	1 (ref) 1.29 (0.93, 1.79)
High nighttime BP, No High nighttime BP, Yes	1 (ref) 1.76 (1.07, 2.92)	1 (ref) 0.97 (0.67, 1.39)
Adjusted hazard ratios (95% confidence intervals) associated with a one-SD higher daytime SBP and nighttime SBP levels are shown. The one-SD increment of daytime SBP and nighttime SBP are 13.5 mm Hg and 15.5 mm Hg, respectively. High daytime BP was defined as daytime SBP ≥135 mm Hg or DBP ≥ 85 mm Hg. High nighttime BP was defined as nighttime SBP ≥120 mm Hg or DBP ≥ 70 mm Hg. All analyses include adjustment for a composite risk score (consisting of age, sex, body mass index, diabetes, education, smoking status, total cholesterol, high-density lipoprotein cholesterol, C-reactive protein, estimated glomerular filtration rate < 60 ml/min/1.73m^2, and statin and antihypertensive medication use), clinic SBP and clinic DBP. CVD=cardiovascular disease; HR=hazard ratio; SD=standard deviation; CI=confidence interval; SBP=systolic blood pressure.		

eFigure 1

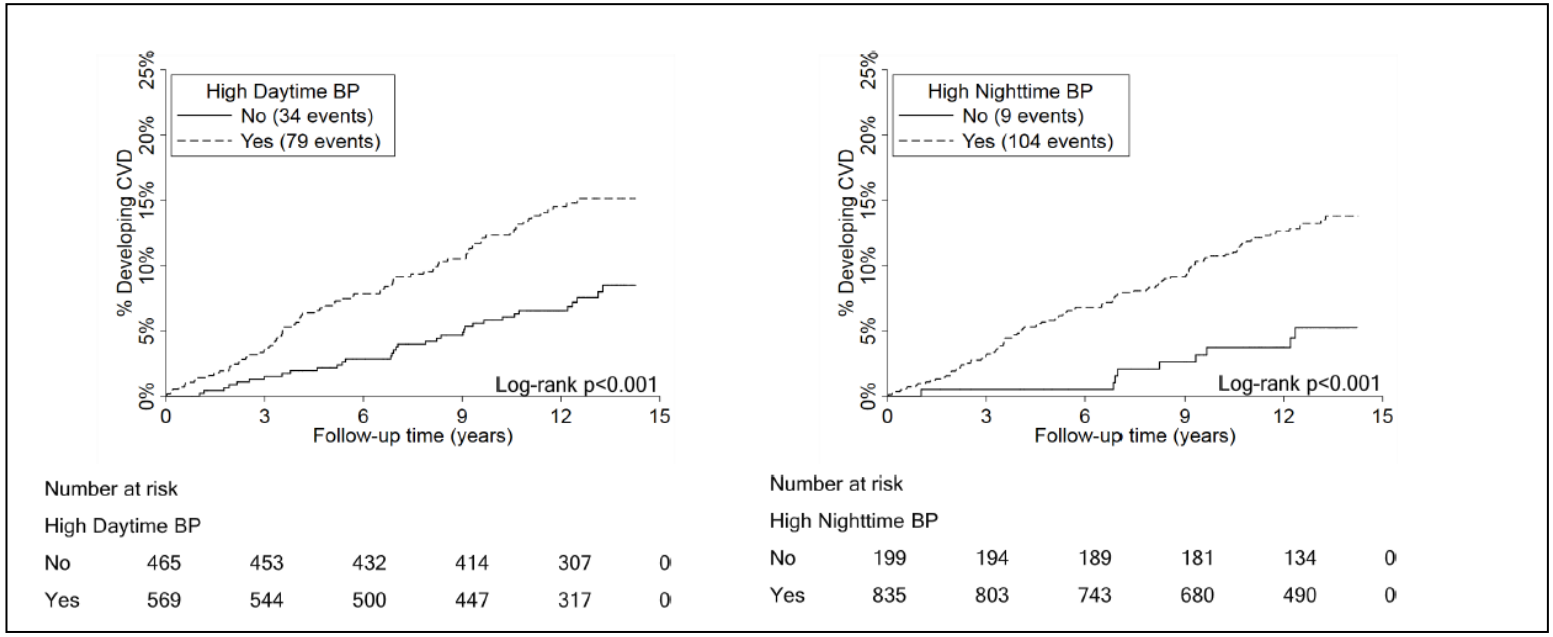
High Daytime BP
No (34 events)
Yes (79 events)
% Developing CVD
0%
5%
10%
15%
20%
25%
Log-rank p<0.001
0
3
6
9
12
15
Follow-up time (years)
Number at risk
High Daytime BP
No 465 453 432 414 307 0
Yes 569 544 500 447 317 0
High Nighttime BP
No (9 events)
Yes (104 events)
% Developing CVD
0%
5%
10%
15%
20%
25%
Log-rank p<0.001
0
3
6
9
12
15
Follow-up time (years)
Number at risk
High Nighttime BP
No 199 194 189 181 134 0
Yes 835 803 743 680 490 0

Figure legends

eFigure 1. Cumulative rate of CVD events by high nighttime BP status and high daytime BP status defined in the 2017 ACC/AHA BP guidelines

The cumulative probability of CVD events for participants with and without high nighttime BP (left panel) and high daytime BP (right panel) were calculated using the Kaplan-Meier method. High daytime BP was defined as daytime SBP ≥130 mm Hg or DBP ≥ 80 mm Hg. High nighttime BP was defined as nighttime SBP ≥110 mm Hg or DBP ≥ 65 mm Hg. Log-rank tests were used to calculate P values.