Supplemental Online Content

Rao S, Segar MW, Bress AP, et al. Association of genetic West African ancestry, blood pressure response to therapy, and cardiovascular risk among self-reported Black individuals in the Systolic Blood Pressure Reduction Intervention Trial (SPRINT). *JAMA Cardiol*. Published online November 13, 2020. doi:10.1001/jamacardio.2020.6566

eFigure 4. Adjusted Cornell Voltage over time by treatment group and ancestry tertile.

eFigure 5. Cumulative incidence curves of the primary composite outcome (MI, ACS, stroke, HF and CV death) among intensive vs. standard BP control arms across West African ancestry tertiles with associated hazard ratio.

eFigure 6. Continuous association (solid black line) and 95% confidence interval (dashed red lines) between African ancestry and risk of all-cause mortality using restricted cubic splines.

e-References.

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

eMethods

Design of the SPRINT Study

SPRINT was a randomized, open-label, multicenter clinical trial among 9,361 participants without a prior history of diabetes or stroke enrolled from 2010-2012.[1] Participants were adults aged 50 years or older with systolic BP (SBP) between 130 and 180 mm Hg depending on the number of antihypertensive medication being taken, as well as elevated cardiovascular risk, defined by age of 75 years or older, prior diagnosis of clinical or subclinical CVD, chronic kidney disease (CKD), or 10-year Framingham risk score (FRS) of 15% or greater. Patients were randomized to intensive BP (goal SBP <120 mmHg) or to standard treatment (goal SBP <140 mmHg). Treatment algorithms were provided by study coordinators to guide dose titrations and encouraged the use of drug classes with evidence for cardiovascular risk reduction. An average of 3 BP measurements was required for making dose adjustments. All antihypertensive agent classes were available to providers, and medications were provided free of cost to participants. The trial was stopped short at three years due to the superiority of intensive treatment compared to standard.

Clinical Covariates and Laboratory Assessment

Age, sex, and education level were self-reported. Race was self-reported by participants as Black (or African American), White, Native American, Native Hawaiian, Asian/ Pacific Islander, or other. Participants were assessed at pre-specified monthly visits for the first three months, then every three months thereafter.[2] BP was recorded as the average of 3 readings obtained after 5 minutes of quiet rest in a seated position using an automated system. Serum and urine laboratory markers were obtained at each office visit and estimated at a core laboratory at the University of Minnesota. The 4-variable Modification of Diet in Renal Disease (MDRD)

equation was used to estimate the glomerular filtration rate (GFR).[3] Serum and urine creatinine were measured using an enzymatic procedure, and urine albumin was measured using a nephelometric method as previously described.[4] Left ventricular hypertrophy (LVH) was defined by Cornell Voltage criteria and assessed by 12-lead electrocardiogram at baseline, 24-month and 48-month visits. The number of antihypertensive agents required to reach target blood pressure was collected at baseline, 12-month, 24-month, and 48-month visits. Finally, the 10-year Framingham risk score (FRS) for cardiovascular disease (CVD) risk was calculated for each participant as previously described.[5]

eTable 1. Estimates of linear mixed effect models of blood pressure over time by 5% increase in continuous measures of African ancestry. Models were adjusted for ancestry, age, sex, education level, eGFR, history of cardiovascular disease, trial site, and APOL1 risk count.

Group	Time period	Estimate (95% CI)	Overall *P*-value
Standard treatment arm			
SBP	Acute (≤6 mo)	-0.27 (-1.27, 0.73)	0.60
SBP	Chronic (>6 mo)	0.06 (-0.05, 0.17)	0.28
DBP	Acute (≤6 mo)	-0.35 (-0.93, 0.22)	0.23
DBP	Chronic (>6 mo)	0.004 (-0.06, 0.07)	0.90
Intensive treatment arm			
SBP	Acute (≤6 mo)	-0.17 (-1.16, 0.83)	0.74
SBP	Chronic (>6 mo)	-0.05 (-0.16, 0.05)	0.31
DBP	Acute (≤6 mo)	0.18 (-0.41, 0.78)	0.55
DBP	Chronic (>6 mo)	-0.008 (-0.07, 0.05)	0.81

Abbreviations:
DBP, diastolic blood pressure; SBP, systolic blood pressure

eTable 2. Sensitivity analysis of slopes of linear mixed models of systolic blood pressure and eGFR over time by African ancestry categories stratified by APOL1 risk count. Models were adjusted for ancestry, age, sex, education level, eGFR, history of cardiovascular disease, and trial site.

Group	Time period	Tertile 1 Slope (95% CI)	Tertile 2 Slope (95% CI)	Tertile 3 Slope (95% CI)	Overall *P*-value
APOL1-0					
Standard treatment arm					
SBP	Acute (≤6 mo)	3.13 (-2.96, 9.21)	-1.38 (-8.49, 5.73)	0.55 (-7.74, 8.85)	0.67
SBP	Chronic (>6 mo)	-0.20 (-0.81, 0.41)	0.46 (-0.31, 1.14)	0.21 (-0.53, 0.96)	0.34
eGFR	Acute (≤6 mo)	6.09 (-2.61, 14.80)	1.24 (-8.73, 11.20)	2.95 (-7.88, 13.78)	0.75
eGFR	Chronic (>6 mo)	-0.39 (-1.95, 1.16)	-0.20 (-1.88, 1.47)	1.32 (-0.59, 3.22)	0.39
Intensive treatment arm					
SBP	Acute (≤6 mo)	-14.96 (-21.25, -8.67)	-10.06 (-18.26, -1.86)	-18.96 (-27.87, -10.05)	0.30
SBP	Chronic (>6 mo)	0.10 (-0.52, 0.72)	-0.65 (-1.40, 0.10)	0.08 (-0.71, 0.87)	0.19
eGFR	Acute (≤6 mo)	-3.12 (-12.33, 6.09)	-4.36 (14.52, 5.80)	-6.40 (-17.69, 4.88)	0.91
eGFR	Chronic (>6 mo)	-1.35 (-2.83, 0.14)	-1.14 (-2.87, 0.59)	0.09 (-1.96, 2.14)	0.50
APOL1-1/2					
Standard treatment arm					
SBP	Acute (≤6 mo)	10.35 (4.67, 16.03)	7.89 (2.39, 13.40)	2.78 (-2.98, 8.54)	0.18
SBP	Chronic (>6 mo)	0.20 (-0.38, 0.77)	0.07 (-0.45, 0.60)	0.30 (-0.33, 0.92)	0.85
eGFR	Acute (≤6 mo)	0.47 (-7.36, 8.30)	5.70 (-2.47, 13.87)	4.94 (-2.78, 12.65)	0.60
eGFR	Chronic (>6 mo)	-0.24 (-1.65, 1.16)	-0.31 (-1.73, 1.12)	-1.97 (-3.46, -0.49)	0.19
Intensive treatment arm					
SBP	Acute (≤6 mo)	-10.10 (-16.24, -3.95)	-12.17 (-18.33, -6.01)	-11.81 (-18.03, -5.59)	0.88
SBP	Chronic (>6 mo)	-0.25 (-0.84, 0.35)	-0.63 (-1.25, 0.00)	-0.83 (-1.43, -0.23)	0.33
eGFR	Acute (≤6 mo)	-4.91 (-13.22, 3.39)	-4.54 (-12.46, 3.39)	-4.27 (-12.40, 3.87)	0.99
eGFR	Chronic (>6 mo)	-0.09 (-1.45, 1.27)	-1.02 (-2.40, 0.36)	-1.36 (-2.70, -0.02)	0.39

eTable 3. Slopes of linear mixed models of number of anti-hypertensive medications over time by African ancestry categories. Categorical African ancestry was grouped into tertiles of African admixture. Models were adjusted for ancestry, age, sex, education level, eGFR, history of cardiovascular disease, trial site, and APOL1 risk count.

Group	Time period	Tertile 1 Slope (95% CI)	Tertile 2 Slope (95% CI)	Tertile 3 Slope (95% CI)	Overall *P*-value
Standard treatment arm					
Number of medications	Acute (≤6 mo)	-0.24 (-0.51, 0.03)	-0.08 (-0.36, 0.21)	0.12 (-0.18, 0.43)	0.23
Number of medications	Chronic (>6 mo)	0.04 (0.01, 0.08)	0.02 (-0.02, 0.05)	0.06 (0.02, 0.10)	0.32
Intensive treatment arm					
Number of medications	Acute (≤6 mo)	1.08 (0.80, 1.36)	1.15 (0.86, 1.44)	1.10 (0.81, 1.40)	0.94
Number of medications	Chronic (>6 mo)	0.01 (-0.03, 0.04)	0.07 (0.03, 0.11)	0.04 (0.00, 0.08)	0.07

eTable 4. Differences in medication use by classes over time by African ancestry categories in both the standard and intensive blood pressure treatment arms.

Standard treatment arm				
	Tertile 1	**Tertile 2**	**Tertile 3**	**P-value**
Baseline				
ACE/ARB	270 (60.5)	246 (57.1)	216 (57.0)	0.48
BB	162 (36.3)	133 (30.9)	126 (33.2)	0.23
CCB	224 (50.2)	225 (52.2)	202 (53.3)	0.67
MRA	24 (5.4)	17 (3.9)	19 (5.0)	0.59
Thiazide	253 (56.7)	264 (61.3)	223 (58.9)	0.40
6 Months				
ACE/ARB	231 (56.3)	211 (53.6)	198 (57.4)	0.55
BB	128 (31.2)	105 (26.7)	113 (0.33)	0.16
CCB	182 (44.4)	206 (52.3)	179 (51.9)	0.04
MRA	21 (5.1)	17 (5.4)	21 (6.1)	0.55
Thiazide	200 (48.8)	203 (51.5)	179 (51.9)	0.64
4 Years				
ACE/ARB	76 (62.3)	65 (47.1)	52 (55.9)	0.05
BB	41 (33.6)	36 (26.1)	27 (29.0)	0.41
CCB	59 (48.4)	81 (58.7)	45 (48.4)	0.17
MRA	7 (5.7)	8 (5.8)	4 (4.3)	0.86
Thiazide	49 (40.2)	61 (44.2)	46 (49.5)	0.40
Intensive treatment arm				
Baseline				
ACE/ARB	283 (64.9)	268 (69.4)	263 (67.8)	0.37
BB	175 (40.1)	137 (35.5)	136 (35.1)	0.24
CCB	220 (50.5)	200 (51.8)	208 (53.6)	0.66
MRA	22 (5.0)	14 (3.6)	16 (4.1)	0.59
Thiazide	237 (61.1)	262 (67.9)	237 (61.1)	0.14
6 Months				
ACE/ARB	295 (71.8)	276 (77.8)	275 (75.1)	0.16
BB	188 (45.7)	142 (40.0)	132 (36.1)	0.02
CCB	265 (64.5)	233 (65.6)	241 (65.8)	0.91
MRA	46 (11.2)	28 (7.9)	35 (9.6)	0.30
Thiazide	284 (69.1)	276 (77.7)	260 (71.0)	0.02
4 Years				
ACE/ARB	93 (70.5)	86 (76.1)	94 (80.3)	0.19
BB	67 (50.8)	56 (49.6)	45 (38.5)	0.11
CCB	94 (71.2)	83 (73.4)	93 (79.5)	0.31
MRA	22 (16.7)	16 (14.2)	18 (15.4)	0.86
Thiazide	67 (50.8)	85 (75.2)	73 (62.4)	<0.001

Abbreviations:
ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta blocker; CCB, calcium channel blocker; MRA, mineralocorticoid receptor antagonist

eTable 5. Estimates of linear mixed effect models of kidney function parameters over time by 5% increase in continuous measures of African ancestry. Models were adjusted for ancestry, age, sex, education level, eGFR, history of cardiovascular disease, trial site, and APOL1 risk count.

Group	Time period	Estimate (95% CI)	Overall *P*-value
Standard treatment arm			
eGFR	Acute (≤6 mo)	-0.19 (-0.79, 0.41)	0.53
eGFR	Chronic (>6 mo)	0.10 (-0.009, 0.21)	0.07
BUN	Acute (≤6 mo)	0.09 (-0.17, 0.34)	0.51
BUN	Chronic (>6 mo)	0.002 (-0.05, 0.05)	0.94
UACR	Acute (≤6 mo)	-0.04 (-8.55, 8.47)	0.99
UACR	Chronic (>6 mo)	-0.96 (-3.21, 1.29)	0.40
Intensive treatment arm			
eGFR	Acute (≤6 mo)	-0.02 (-0.65, 0.61)	0.96
eGFR	Chronic (>6 mo)	0.04 (-0.07, 0.15)	0.45
BUN	Acute (≤6 mo)	0.05 (-0.26, 0.37)	0.75
BUN	Chronic (>6 mo)	-0.03 (-0.09, 0.03)	0.30
UACR	Acute (≤6 mo)	3.09 (-12.98, 19.17)	0.71
UACR	Chronic (>6 mo)	-0.81 (-3.27, 1.66)	0.52

Abbreviations:
BUN, blood urea nitrogen; CI, confidence interval; UACR, urine microalbumin/creatinine ratio

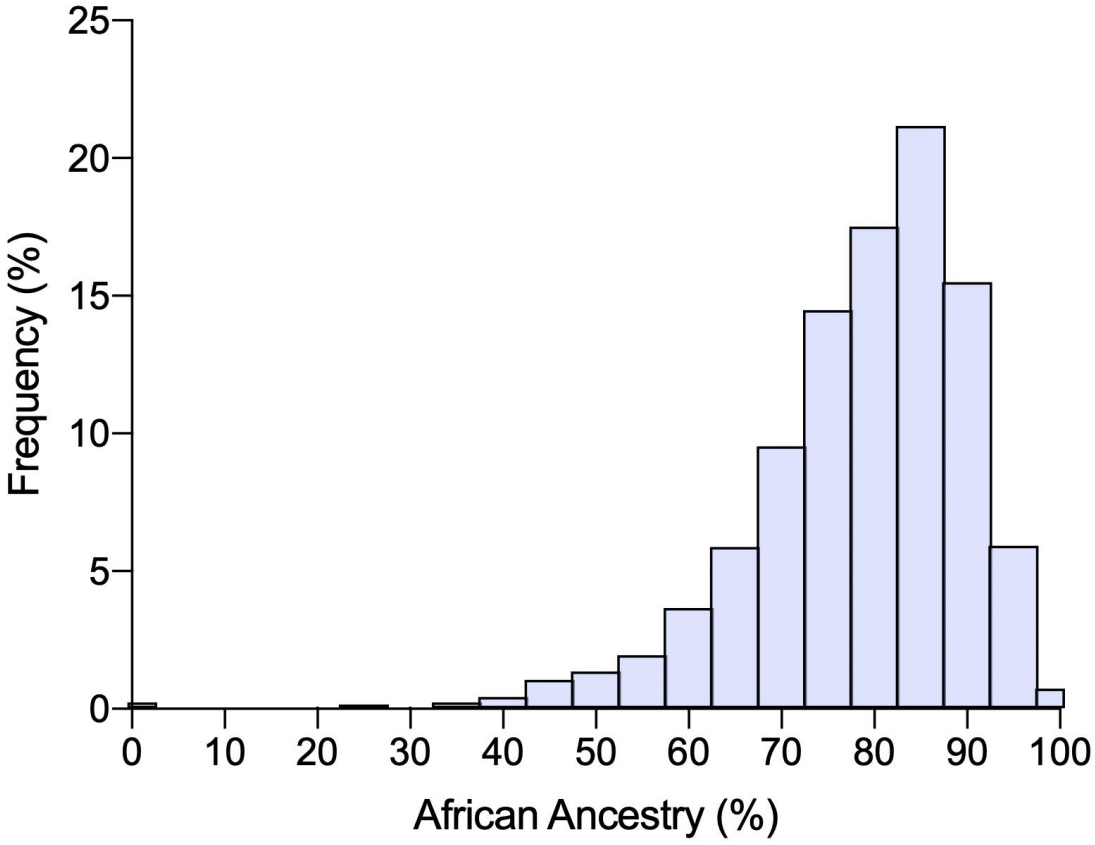
eTable 6. Estimates of linear mixed effect models of Cornell Voltage over time by tertiles of African ancestry and 5% increase in continuous measures of African ancestry. Models were adjusted for ancestry, age, sex, intensive treatment arm, education level, eGFR, history of cardiovascular disease, trial site, and APOL1 risk count.

	Estimate (95% CI)	**Global p-value**
Standard arm		
Tertile 1	-17.6 (-46.2, 11.0)	0.86
Tertile 2	-5.70 (-36.9, 25.5)	
Tertile 3	-16.5 (-48.7, 15.7)	
Continuous (per 5% increase)	-2.64 (-7.04, 1.75)	0.24
Intensive arm		
Tertile 1	-56.9 (-87.5, -26.3)	0.69
Tertile 2	-60.5 (-91.5, -29.6)	
Tertile 3	-75.2 (-105.2, -45.2)	
Continuous (per 5% increase)	-2.48 (-6.77, 1.80)	0.26

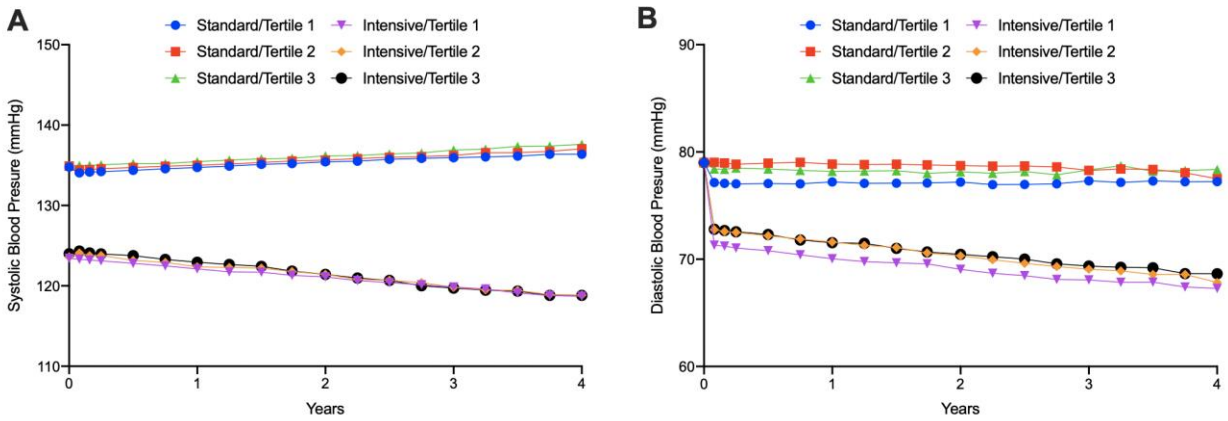
eTable 7. Adjusted association between continuous measures of African ancestry (per 5% increase) and risk of adverse clinical outcomes as assessed by Cox proportional hazard models. Primary composite outcome is a composite of myocardial infarction (MI), non-MI acute coronary syndrome, stroke, acute decompensated heart failure, or cardiovascular death**.** Model 1 is unadjusted. Model 2 was adjusted for age, sex, treatment arm, smoking status, education level, estimated glomerular filtration rate, APOL1 count, and trial site. Model 3 was adjusted for age, sex, treatment arm, education level, systolic blood pressure, smoking status, estimated glomerular filtration rate, total cholesterol, high-density lipoprotein cholesterol, APOL1 count, and trial site.

Outcome	**Model 1 (unadjusted)**		**Model 2**		**Model 3**	
	HR (95% CI)	**P-value**	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Primary composite outcome	0.92 (0.86, 0.99)	0.03	0.92 (0.85, 0.99)	0.02	0.92 (0.85, 0.99)	0.02
All-cause mortality	1.02 (0.93, 1.12)	0.63	1.05 (0.95, 1.15)	0.36	1.05 (0.95, 1.15)	0.36

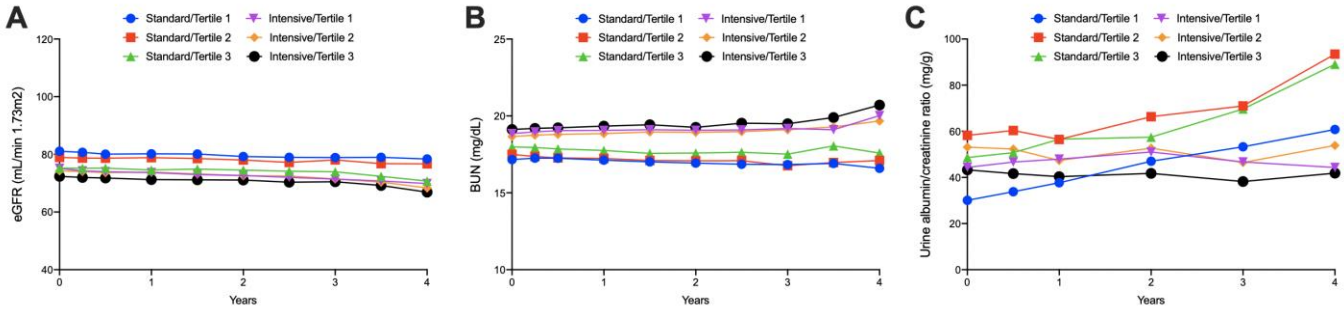
eFigure 1. Histogram of the percentage of African ancestry in self-reported Black SPRINT participants (n=2,466) in the current analysis.



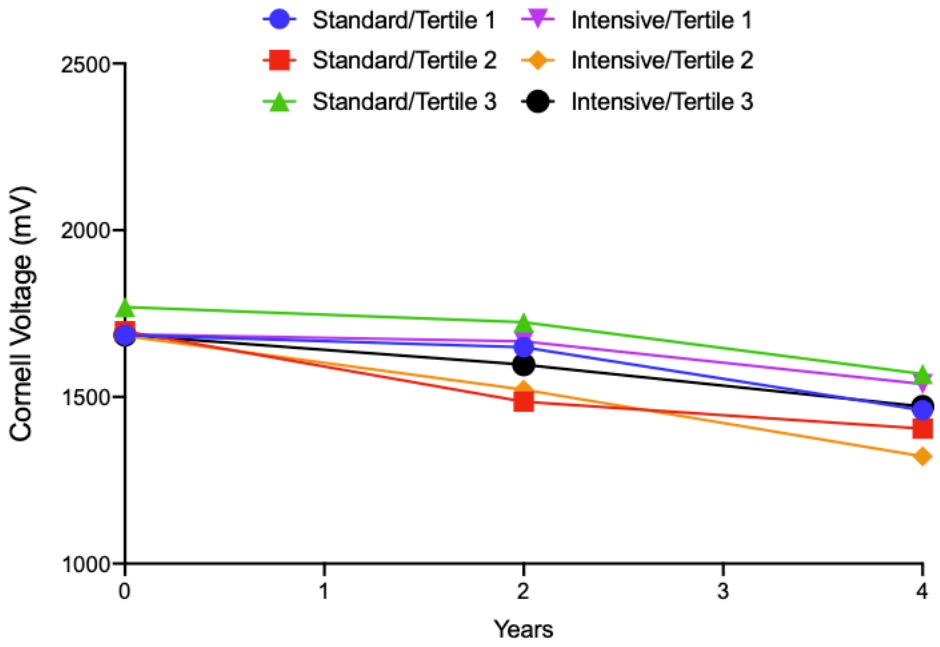
eFigure 2. Adjusted A) systolic blood pressure and B) diastolic blood pressure over time by treatment group and ancestry tertile. Model was adjusted for age, sex, smoking status, education level, estimated glomerular filtration rate, APOL1 count, and trial site.



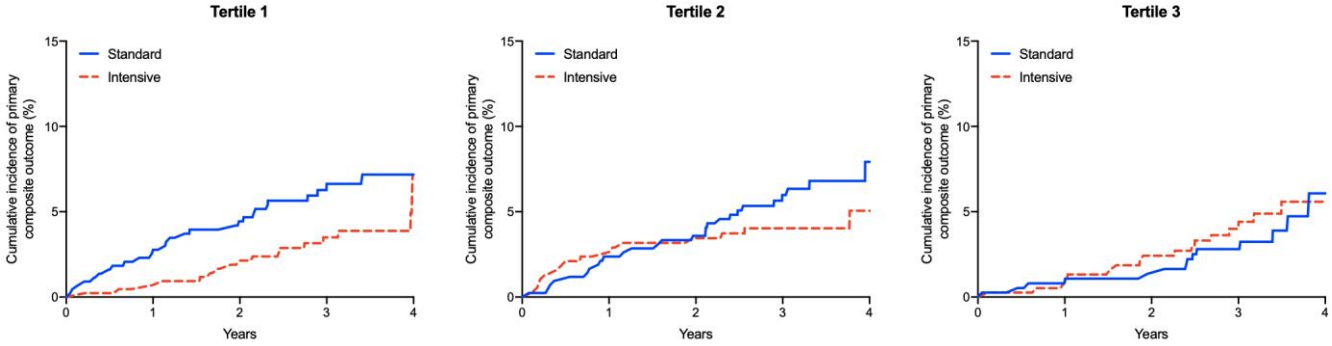
eFigure 3. Adjusted A) estimated glomerular filtration rate (eGFR), B) blood urea nitrogen (BUN), and C) urine microalbumin/creatinine ratio over time by treatment group and ancestry tertile. Model was adjusted for age, sex, smoking status, education level, estimated glomerular filtration rate, APOL1 count, and trial site.



eFigure 4. Adjusted Cornell Voltage over time by treatment group and ancestry tertile. Model was adjusted for age, sex, smoking status, education level, estimated glomerular filtration rate, APOL1 count, and trial site.

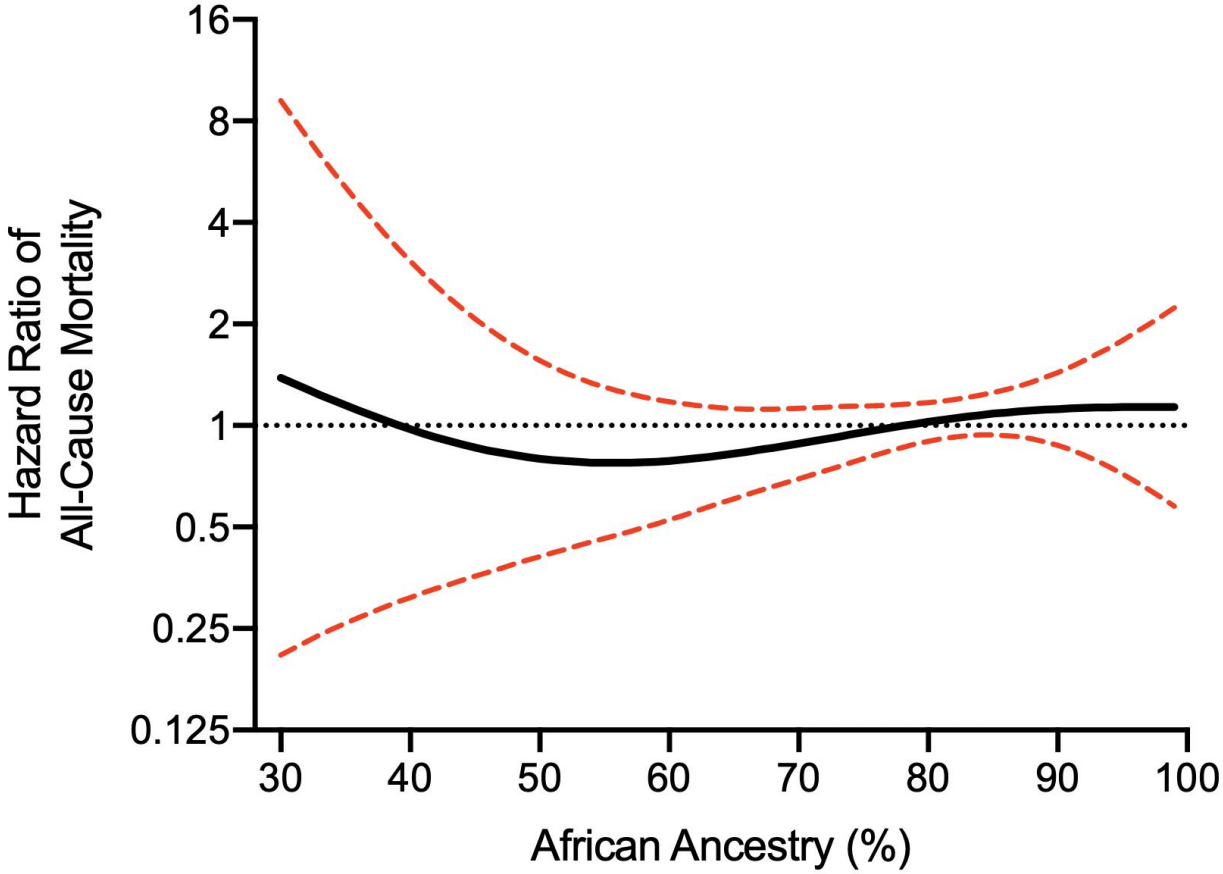


eFigure 5. Cumulative incidence curves of the primary composite outcome (MI, ACS, stroke, HF and CV death) among intensive vs. standard BP control arms across West African ancestry tertiles with associated hazard ratio. Adjusted Cox proportional hazard models were constructed using Model 3 adjustments.



	Tertile 1		Tertile 2		Tertile 3		
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	P-interaction
Unadjusted	0.63 (0.35, 1.13)	0.12	0.67 (0.36, 1.25)	0.21	1.19 (0.59, 2.41)	0.63	0.35
Adjusted	0.59 (0.32, 1.07)	0.08	0.67 (0.36, 1.26)	0.21	1.18 (0.57, 2.43)	0.66	0.22

eFigure 6. Continuous association (solid black line) and 95% confidence interval (dashed red lines) between African ancestry and risk of all-cause mortality using restricted cubic splines. The model was adjusted for model 3 adjustments.



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