

Supplementary Online Content

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

eTable 1. Baseline Characteristics for the Full Sample and by Randomized Group for Morbidity Study at the Time of Randomization

Characteristic	Participants, No. (%) (Unless otherwise indicated)				P value ^a
	Full Sample	Chlorthalidone	Amlodipine	Lisinopril	
At the recruitment in ALLHAT					
See previous references ²					
Eligible for further follow-up as of 3/31/2002	22754	10414	6191	6149	
Age, mean (SD), years	68.72 (7.2)	68.74 (7.2)	68.69 (7.2)	68.74 (7.3)	0.914
Age group at trial baseline					
<i>Age <65</i>	7516 (33.0)	3411 (32.8)	2062 (33.3)	2043 (33.2)	0.712
<i>Age ≥65</i>	15238 (67.0)	7003 (67.2)	4129 (66.7)	4106 (66.8)	
Gender					
<i>Male</i>	9982 (43.9)	4570 (43.9)	2649 (42.8)	2763 (44.9)	0.056
<i>Female</i>	12772 (56.1)	5844 (56.1)	3542 (57.2)	3386 (55.1)	
Race/Ethnicity					
<i>Black</i>	8199 (36.0)	3748 (36.0)	2248 (36.3)	2203 (35.8)	0.848
<i>Non-Black</i>	14555 (64.0)	6666 (64.0)	3943 (63.7)	3946 (64.2)	
Hispanic/Latino Ethnicity					
<i>Hispanic</i>	4872 (21.5)	2228 (21.5)	1294 (21.0)	1350 (22.1)	0.352
<i>Non-Hispanic</i>	17756 (78.5)	8129 (78.5)	4864 (79.0)	4763 (77.9)	
Education, mean (SD), years	10.61 (4.2)	10.63 (4.1)	10.61 (4.1)	10.58 (4.3)	0.747
Education level at trial baseline					
<i>High school or less</i>	15560 (74.1)	7088 (73.6)	4255 (74.3)	4217 (74.5)	0.408
<i>More than high school</i>	5448 (25.9)	2538 (26.4)	1469 (25.7)	1441 (25.5)	
Treatment with antihypertensive drugs prior to trial baseline					
<i>Treated</i>	20586 (90.5)	9403 (90.3)	5618 (90.7)	5565 (90.5)	0.639
<i>Untreated</i>	2167 (9.5)	1010 (9.7)	573 (9.3)	584 (9.5)	
Aspirin use at trial baseline	7828 (34.9)	3573 (34.8)	2110 (34.5)	2145 (35.4)	0.575
Women taking estrogen at trial baseline	1987 (15.8)	918 (16.0)	557 (16.0)	512 (15.4)	0.739
Mean Glomerular Filtration Rate (GFR) at trial baseline, mL/min/1.73 m²	76.14 (19.8)	76.03 (19.9)	76.36 (19.7)	76.10 (19.8)	0.582
GFR <60 mL/min/1.73 m² at trial baseline	4377 (20.2)	2019 (20.3)	1185 (20.1)	1173 (20.1)	0.924
HDL cholesterol at trial baseline, mean (SD), mg/dl	47.83 (14.9)	47.79 (15.0)	48.20 (15.0)	47.54 (14.6)	0.050
HDL <35 mg/dl at trial baseline	2373 (10.4)	1083 (10.4)	646 (10.4)	644 (10.5)	0.989
Cigarette smoking at trial baseline					
<i>Never smoker</i>	9701 (42.6)	4421 (42.5)	2682 (43.3)	2598 (42.3)	0.630
<i>Current Smoker</i>	4301 (18.9)	1967 (18.9)	1178 (19.0)	1156 (18.8)	
<i>Former Smoker</i>	8751 (38.5)	4026 (38.7)	2331 (37.7)	2394 (38.9)	
Diabetes classification at trial baseline					
<i>Diabetes</i>	9133 (43.4)	4187 (43.5)	2499 (43.7)	2447 (42.9)	0.694
<i>Non-diabetes</i>	11922 (56.6)	5443 (56.5)	3224 (56.3)	3255 (57.1)	
History of Coronary Heart Disease (CHD) at trial baseline	5743 (25.4)	2685 (26.0)	1511 (24.6)	1547 (25.3)	0.142

Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline	12120 (53.3)	5597 (53.7)	3231 (52.2)	3292 (53.5)	0.133
History of myocardial infarction (MI) or stroke at trial baseline	5231 (23.0)	2424 (23.3)	1433 (23.1)	1374 (22.3)	0.366
History of coronary artery bypass graft (CABG) at trial baseline	2967 (13.0)	1380 (13.3)	746 (12.0)	841 (13.7)	0.019
Other ASCVD at trial baseline	5774 (25.4)	2637 (25.3)	1556 (25.1)	1581 (25.7)	0.750
Major ST segment depression at trial baseline	2394 (10.6)	1117 (10.8)	621 (10.1)	656 (10.8)	0.335
Hard Left ventricular hypertrophy (LVH) by Minnesota code at trial baseline	1016 (5.3)	459 (5.2)	283 (5.4)	274 (5.3)	0.864
Lipid Lowering Trial (LLT) Participants	5542 (24.4)	2569 (24.7)	1516 (24.5)	1457 (23.7)	0.355
BMI, mean (SD), kg/m² at trial baseline	29.64 (6.2)	29.57 (6.2)	29.69 (6.2)	29.69 (6.2)	0.377
Obesity (BMI ≥ 30 kg/m²) at trial baseline	9381 (41.2)	4266 (41.0)	2566 (41.4)	2549 (41.5)	0.759
Baseline blood pressure (BP) reading, mmHg					
<i>Systolic BP, mean (SD)</i>	146.08 (13.1)	146.07 (13.0)	145.90 (13.2)	146.30 (13.1)	0.234
<i>Diastolic BP, mean (SD)</i>	83.45 (9.0)	83.50 (9.0)	83.30 (9.1)	83.51 (9.0)	0.320
Blood pressure change from baseline to the latest BP reading prior to 3/31/2002, mmHg					
<i>Systolic BP, mean (SD)</i>	-9.90 (19.7)	-10.54 (19.3)	-9.97 (19.3)	-8.73 (20.5)	<0.001
<i>Diastolic BP, mean (SD)</i>	-6.49 (11.5)	-6.56 (11.4)	-6.81 (11.4)	-6.06 (11.9)	<0.001

N= number of participants; SD= standard deviation

^a P values represent significance level of the chi-square test of independence between randomized groups for binary and categorical variables, or the one-way analysis of variance (ANOVA) between randomized groups for continuous variables. Statistically significant p values (<0.05) are shown in bold text.

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 2. Adjusted^a Hazard Ratios for All-Cause and CVD Mortality With Follow-up From 2/23/1994^b to 12/31/2017

	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	1.00 (0.96-1.03)	0.928	0.97 (0.89-1.05)	0.434	1.01 (0.94-1.10)	0.751	1.00 (0.86-1.16)	0.995	1.01 (0.85-1.21)	0.904	1.00 (0.91-1.11)	0.950
<i>Lisinopril vs Chlorthalidone</i>	1.01 (0.97-1.04)	0.762	1.06 (0.97-1.15)	0.174	0.97 (0.90-1.06)	0.518	1.19 (1.03-1.37)	0.017	1.03 (0.86-1.22)	0.776	0.95 (0.85-1.05)	0.299
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	2.09 (2.02-2.16)	<0.001	2.24 (2.06-2.43)	<0.001	1.96 (1.82-2.11)	<0.001	2.41 (2.09-2.78)	<0.001	2.96 (2.47-3.54)	<0.001	2.37 (2.14-2.61)	<0.001
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Female</i>	0.78 (0.75-0.80)	<0.001	0.82 (0.76-0.89)	<0.001	0.71 (0.65-0.76)	<0.001	0.87 (0.76-1.00)	0.054	0.89 (0.76-1.05)	0.170	0.78 (0.71-0.86)	<0.001
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Black</i>	0.98 (0.95-1.02)	0.306	0.95 (0.87-1.03)	0.211	0.95 (0.88-1.03)	0.184	0.95 (0.82-1.09)	0.477	0.94 (0.79-1.12)	0.514	1.21 (1.10-1.33)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hispanic</i>	0.79 (0.76-0.83)	<0.001	0.86 (0.77-0.95)	0.004	0.78 (0.71-0.87)	<0.001	0.76 (0.63-0.91)	0.003	0.70 (0.55-0.88)	0.003	0.70 (0.61-0.80)	<0.001
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>High school or less</i>	1.17 (1.13-1.21)	<0.001	1.19 (1.10-1.30)	<0.001	1.22 (1.13-1.32)	<0.001	1.11 (0.97-1.27)	0.145	1.16 (0.98-1.38)	0.078	1.04 (0.94-1.14)	0.467
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Treated</i>	1.10 (1.04-1.16)	<0.001	1.13 (0.99-1.30)	0.061	1.09 (0.97-1.23)	0.163	1.34 (1.06-1.70)	0.014	0.98 (0.75-1.30)	0.902	1.05 (0.91-1.23)	0.493
Aspirin use at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.99 (0.96-1.03)	0.629	1.05 (0.97-1.14)	0.231	0.98 (0.91-1.06)	0.595	1.14 (0.99-1.30)	0.062	0.97 (0.83-1.15)	0.758	1.07 (0.97-1.18)	0.150
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.50 (1.44-1.55)	<0.001	1.60 (1.46-1.74)	<0.001	1.48 (1.37-1.61)	<0.001	1.60 (1.38-1.85)	<0.001	1.72 (1.44-2.04)	<0.001	1.62 (1.46-1.81)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.90 (0.86-0.95)	<0.001	0.86 (0.77-0.97)	0.012	1.01 (0.91-1.11)	0.920	0.70 (0.57-0.87)	0.001	0.83 (0.65-1.05)	0.126	0.84 (0.73-0.97)	0.018
Cigarette smoking at trial baseline												

	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Current smoker</i>	1.69 (1.62-1.77)	<0.001	1.31 (1.18-1.46)	<0.001	1.49 (1.35-1.65)	<0.001	1.11 (0.93-1.34)	0.248	1.19 (0.94-1.50)	0.142	1.48 (1.31-1.68)	<0.001
<i>Former Smoker</i>	1.11 (1.07-1.15)	<0.001	1.04 (0.96-1.13)	0.313	1.12 (1.04-1.22)	0.004	0.95 (0.82-1.10)	0.479	0.98 (0.83-1.17)	0.853	1.07 (0.96-1.18)	0.206
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Diabetes</i>	1.53 (1.48-1.58)	<0.001	1.65 (1.53-1.78)	<0.001	1.69 (1.57-1.81)	<0.001	1.45 (1.26-1.65)	<0.001	1.76 (1.50-2.06)	<0.001	1.28 (1.17-1.41)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.96 (0.92-1.01)	0.085	0.91 (0.82-1.01)	0.088	1.08 (0.98-1.19)	0.122	0.85 (0.71-1.02)	0.080	1.03 (0.83-1.28)	0.791	0.88 (0.77-1.01)	0.062
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.09 (1.03-1.16)	0.002	1.23 (1.08-1.40)	0.002	1.14 (1.01-1.29)	0.030	1.04 (0.83-1.31)	0.734	1.50 (1.14-1.97)	0.004	1.15 (0.97-1.35)	0.103
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.28 (1.22-1.34)	<0.001	1.43 (1.28-1.59)	<0.001	1.49 (1.35-1.64)	<0.001	1.54 (1.27-1.87)	<0.001	1.04 (0.83-1.30)	0.736	1.30 (1.13-1.50)	<0.001
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.11 (1.05-1.17)	<0.001	1.20 (1.07-1.35)	0.002	1.41 (1.28-1.57)	<0.001	0.97 (0.78-1.19)	0.748	1.20 (0.94-1.54)	0.141	1.03 (0.88-1.20)	0.732
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.15 (1.09-1.20)	<0.001	1.13 (1.02-1.26)	0.020	1.19 (1.09-1.31)	<0.001	1.31 (1.08-1.57)	0.005	0.90 (0.72-1.13)	0.363	1.06 (0.92-1.21)	0.433
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.97 (0.92-1.03)	0.335	0.95 (0.84-1.09)	0.479	0.98 (0.87-1.10)	0.704	0.95 (0.76-1.19)	0.660	0.89 (0.68-1.17)	0.412	0.91 (0.77-1.07)	0.247
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hard LVH</i>	1.33 (1.25-1.42)	<0.001	1.68 (1.46-1.92)	<0.001	1.53 (1.34-1.75)	<0.001	1.73 (1.37-2.18)	<0.001	1.89 (1.44-2.49)	<0.001	1.63 (1.38-1.93)	<0.001
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.93 (0.90-0.97)	<0.001	0.95 (0.88-1.03)	0.238	0.98 (0.91-1.06)	0.605	0.99 (0.86-1.14)	0.863	0.85 (0.71-1.02)	0.077	1.01 (0.92-1.11)	0.844
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.96 (0.93-0.99)	0.008	0.99 (0.92-1.06)	0.753	0.99 (0.93-1.06)	0.862	0.86 (0.76-0.98)	0.025	1.15 (0.99-1.34)	0.064	0.98 (0.89-1.07)	0.599
Baseline blood pressure reading, per 10 mmHg												
<i>Systolic BP</i>	1.11 (1.09-1.12)	<0.001	1.12 (1.08-1.15)	<0.001	1.15 (1.11-1.18)	<0.001	1.13 (1.07-1.20)	<0.001	1.10 (1.03-1.17)	0.005	1.11 (1.07-1.16)	<0.001

	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Diastolic BP</i>	0.88 (0.86-0.90)	<0.001	0.90 (0.86-0.94)	<0.001	0.87 (0.84-0.91)	<0.001	0.99 (0.91-1.07)	0.759	0.78 (0.71-0.86)	<0.001	0.95 (0.90-1.01)	0.079

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

^a Adjusted for each covariate shown in that column. Covariates not included in multivariable analysis are indicated with dashes.

^b First randomization date in the Mortality cohort.

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 3. Adjusted^a Hazard Ratios for Morbidity With Follow-up From 3/10/1994^b to 12/31/2017

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	1.01 (0.96-1.06)	0.628	0.99 (0.92-1.06)	0.795	1.02 (0.97-1.09)	0.426	1.04 (0.96-1.12)	0.389	0.99 (0.92-1.07)	0.842	1.05 (0.90-1.22)	0.535
<i>Lisinopril vs Chlorthalidone</i>	1.04 (0.99-1.09)	0.157	0.98 (0.91-1.05)	0.508	1.03 (0.97-1.09)	0.412	1.11 (1.03-1.20)	0.008	1.02 (0.94-1.10)	0.632	1.12 (0.97-1.30)	0.117
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	1.76 (1.67-1.84)	<0.001	1.66 (1.55-1.78)	<0.001	1.84 (1.74-1.95)	<0.001	1.77 (1.63-1.91)	<0.001	1.63 (1.51-1.76)	<0.001	1.02 (0.89-1.17)	0.807
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Female</i>	0.91 (0.87-0.96)	<0.001	0.80 (0.75-0.86)	<0.001	0.96 (0.91-1.02)	0.151	0.94 (0.88-1.01)	0.117	0.69 (0.64-0.74)	<0.001	0.63 (0.55-0.73)	<0.001
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Black</i>	0.97 (0.93-1.02)	0.265	0.90 (0.84-0.97)	0.006	0.99 (0.93-1.04)	0.630	1.03 (0.95-1.11)	0.481	1.05 (0.97-1.13)	0.214	1.92 (1.67-2.21)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hispanic</i>	0.72 (0.68-0.77)	<0.001	0.80 (0.73-0.87)	<0.001	0.63 (0.59-0.68)	<0.001	0.76 (0.69-0.84)	<0.001	0.63 (0.56-0.69)	<0.001	1.02 (0.85-1.22)	0.836
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>High school or less</i>	1.19 (1.13-1.25)	<0.001	1.20 (1.12-1.29)	<0.001	1.19 (1.12-1.26)	<0.001	1.14 (1.06-1.23)	<0.001	1.12 (1.04-1.21)	0.003	1.06 (0.92-1.23)	0.407
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Treated</i>	1.27 (1.17-1.38)	<0.001	1.09 (0.97-1.21)	0.132	1.23 (1.12-1.35)	<0.001	1.36 (1.19-1.54)	<0.001	1.08 (0.96-1.22)	0.184	1.29 (1.02-1.63)	0.031
Aspirin use at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.06 (1.01-1.11)	0.018	1.05 (0.98-1.12)	0.151	1.02 (0.96-1.08)	0.490	1.15 (1.07-1.23)	<0.001	0.91 (0.84-0.98)	0.013	0.90 (0.78-1.04)	0.141
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.42 (1.34-1.49)	<0.001	1.42 (1.32-1.53)	<0.001	1.55 (1.46-1.65)	<0.001	1.31 (1.21-1.42)	<0.001	1.19 (1.09-1.29)	<0.001	5.30 (4.66-6.04)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.96 (0.90-1.03)	0.260	1.09 (0.99-1.19)	0.078	0.94 (0.87-1.02)	0.160	0.89 (0.80-0.99)	0.040	1.05 (0.95-1.16)	0.354	1.01 (0.82-1.25)	0.920
Cigarette smoking at trial baseline												

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Current smoker</i>	1.42 (1.33-1.51)	<0.001	1.50 (1.37-1.64)	<0.001	1.40 (1.30-1.51)	<0.001	1.42 (1.29-1.57)	<0.001	2.08 (1.90-2.28)	<0.001	1.79 (1.49-2.14)	<0.001
<i>Former Smoker</i>	1.09 (1.04-1.15)	<0.001	1.13 (1.05-1.21)	<0.001	1.08 (1.02-1.14)	0.009	1.11 (1.03-1.20)	0.008	1.24 (1.15-1.35)	<0.001	1.23 (1.07-1.43)	0.004
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Diabetes</i>	1.57 (1.50-1.64)	<0.001	1.70 (1.59-1.81)	<0.001	1.69 (1.60-1.79)	<0.001	1.49 (1.38-1.60)	<0.001	1.11 (1.03-1.20)	0.004	3.01 (2.62-3.45)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.97 (0.91-1.03)	0.283	1.08 (0.99-1.18)	0.074	1.06 (0.98-1.14)	0.121	0.84 (0.76-0.93)	<0.001	0.96 (0.87-1.07)	0.464	0.86 (0.71-1.05)	0.147
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.13 (1.05-1.23)	0.002	1.13 (1.01-1.26)	0.030	1.11 (1.01-1.22)	0.025	1.13 (1.00-1.27)	0.050	0.98 (0.87-1.11)	0.772	1.00 (0.79-1.27)	0.996
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.39 (1.30-1.48)	<0.001	1.40 (1.29-1.53)	<0.001	1.36 (1.26-1.46)	<0.001	1.39 (1.25-1.53)	<0.001	1.08 (0.97-1.20)	0.142	1.22 (0.99-1.49)	0.060
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.26 (1.18-1.36)	<0.001	1.41 (1.28-1.55)	<0.001	1.24 (1.14-1.35)	<0.001	1.32 (1.18-1.47)	<0.001	1.05 (0.93-1.18)	0.451	1.36 (1.08-1.71)	0.009
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.12 (1.05-1.19)	<0.001	1.14 (1.05-1.24)	0.003	1.10 (1.03-1.19)	0.008	1.16 (1.05-1.28)	0.003	1.18 (1.06-1.31)	0.002	1.11 (0.90-1.35)	0.329
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.03 (0.95-1.11)	0.433	0.95 (0.85-1.06)	0.358	1.11 (1.02-1.22)	0.018	0.94 (0.83-1.06)	0.336	1.09 (0.96-1.23)	0.176	1.17 (0.93-1.48)	0.188
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hard LVH</i>	1.55 (1.42-1.69)	<0.001	1.46 (1.28-1.65)	<0.001	1.73 (1.57-1.91)	<0.001	1.48 (1.30-1.69)	<0.001	0.99 (0.85-1.16)	0.924	1.35 (1.07-1.72)	0.013
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.94 (0.90-0.99)	0.020	0.94 (0.87-1.01)	0.080	0.94 (0.89-1.00)	0.038	0.95 (0.88-1.02)	0.162	0.93 (0.86-1.00)	0.063	1.00 (0.87-1.15)	0.986
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.09 (1.05-1.14)	<0.001	0.94 (0.88-1.00)	0.054	1.25 (1.19-1.32)	<0.001	0.94 (0.88-1.01)	0.106	1.01 (0.94-1.08)	0.881	1.19 (1.04-1.35)	0.009
Baseline blood pressure reading, per 10 mmHg												
<i>Systolic BP</i>	1.11 (1.09-1.14)	<0.001	1.13 (1.10-1.16)	<0.001	1.12 (1.10-1.15)	<0.001	1.16 (1.13-1.20)	<0.001	1.02 (0.99-1.05)	0.269	1.32 (1.24-1.39)	<0.001

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Diastolic BP</i>	0.89 (0.86-0.91)	<0.001	0.91 (0.88-0.95)	<0.001	0.86 (0.83-0.89)	<0.001	0.91 (0.87-0.95)	<0.001	0.92 (0.88-0.96)	<0.001	0.89 (0.82-0.96)	0.005

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

^a Adjusted for each covariate shown in that column. Covariates not included in multivariable analysis are indicated with dashes.

^b First randomization date in the full Morbidity cohort.

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 4. Adjusted^a Hazard Ratios for Non-CVD Mortality With Follow-up From 2/23/1994^b to 12/31/2017

	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	0.99 (0.95-1.04)	0.722	0.96 (0.88-1.04)	0.334	1.00 (0.81-1.23)	0.995	0.86 (0.67-1.09)	0.219	1.02 (0.96-1.08)	0.590	1.01 (0.74-1.38)	0.940
<i>Lisinopril vs Chlorthalidone</i>	1.01 (0.96-1.06)	0.651	1.05 (0.97-1.14)	0.237	1.18 (0.97-1.44)	0.094	1.08 (0.86-1.35)	0.522	0.97 (0.91-1.03)	0.301	0.97 (0.70-1.33)	0.828
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	2.02 (1.93-2.11)	<0.001	1.73 (1.60-1.87)	<0.001	1.71 (1.42-2.06)	<0.001	1.94 (1.56-2.41)	<0.001	2.25 (2.12-2.38)	<0.001	1.80 (1.33-2.43)	<0.001
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Female</i>	0.78 (0.74-0.81)	<0.001	0.67 (0.62-0.72)	<0.001	0.69 (0.58-0.84)	<0.001	0.49 (0.39-0.62)	<0.001	0.88 (0.83-0.93)	<0.001	1.03 (0.77-1.38)	0.830
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Black</i>	0.94 (0.90-0.99)	0.013	1.08 (1.00-1.17)	0.040	1.32 (1.09-1.60)	0.004	0.73 (0.58-0.93)	0.010	0.85 (0.80-0.91)	<0.001	1.76 (1.32-2.34)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hispanic</i>	0.82 (0.78-0.87)	<0.001	0.62 (0.56-0.70)	<0.001	1.11 (0.88-1.40)	0.362	0.58 (0.43-0.80)	<0.001	0.93 (0.87-1.00)	0.050	1.03 (0.70-1.52)	0.863
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>High school or less</i>	1.20 (1.15-1.26)	<0.001	1.27 (1.18-1.38)	<0.001	1.43 (1.16-1.75)	<0.001	1.22 (0.98-1.52)	0.073	1.14 (1.07-1.21)	<0.001	0.91 (0.68-1.22)	0.535
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Treated</i>	1.10 (1.02-1.18)	0.011	1.02 (0.90-1.15)	0.740	1.30 (0.95-1.78)	0.106	0.92 (0.64-1.31)	0.632	1.14 (1.04-1.26)	0.007	1.27 (0.77-2.11)	0.346
Aspirin use at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.97 (0.92-1.01)	0.124	0.93 (0.86-1.00)	0.057	0.85 (0.70-1.04)	0.111	1.11 (0.89-1.37)	0.362	0.99 (0.93-1.05)	0.681	1.05 (0.79-1.41)	0.718
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.44 (1.37-1.51)	<0.001	1.22 (1.11-1.34)	<0.001	3.85 (3.20-4.62)	<0.001	1.15 (0.88-1.50)	0.313	1.43 (1.34-1.53)	<0.001	1.82 (1.35-2.47)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.90 (0.85-0.96)	0.001	1.04 (0.94-1.15)	0.460	0.91 (0.69-1.20)	0.498	0.68 (0.49-0.95)	0.022	0.84 (0.78-0.92)	<0.001	1.21 (0.81-1.80)	0.352
Cigarette smoking at trial baseline												

	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Current smoker</i>	1.91 (1.81-2.02)	<0.001	2.59 (2.35-2.86)	<0.001	2.01 (1.58-2.56)	<0.001	1.36 (1.03-1.78)	0.030	1.62 (1.50-1.75)	<0.001	1.91 (1.32-2.76)	<0.001
<i>Former Smoker</i>	1.14 (1.09-1.20)	<0.001	1.33 (1.22-1.45)	<0.001	1.25 (1.02-1.53)	0.034	0.77 (0.61-0.97)	0.030	1.09 (1.03-1.16)	0.004	1.30 (0.94-1.80)	0.109
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Diabetes</i>	1.52 (1.45-1.58)	<0.001	1.10 (1.02-1.19)	0.014	2.43 (2.02-2.92)	<0.001	1.35 (1.09-1.68)	0.007	1.75 (1.65-1.85)	<0.001	1.74 (1.32-2.31)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.94 (0.88-1.00)	0.050	0.99 (0.89-1.10)	0.829	0.96 (0.73-1.26)	0.753	0.88 (0.65-1.19)	0.396	0.91 (0.84-0.99)	0.033	1.12 (0.76-1.66)	0.566
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.07 (1.00-1.16)	0.066	0.95 (0.83-1.08)	0.403	1.01 (0.73-1.39)	0.976	1.60 (1.09-2.34)	0.017	1.14 (1.03-1.26)	0.013	0.76 (0.47-1.23)	0.265
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.17 (1.10-1.25)	<0.001	1.15 (1.03-1.29)	0.013	1.28 (0.97-1.70)	0.085	0.80 (0.58-1.11)	0.186	1.20 (1.10-1.31)	<0.001	1.69 (1.12-2.54)	0.012
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.01 (0.94-1.09)	0.755	1.03 (0.91-1.16)	0.688	1.21 (0.88-1.65)	0.243	0.84 (0.59-1.20)	0.344	1.00 (0.91-1.10)	0.991	0.79 (0.50-1.27)	0.333
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.13 (1.06-1.21)	<0.001	1.27 (1.14-1.41)	<0.001	1.06 (0.80-1.40)	0.680	0.90 (0.65-1.24)	0.507	1.09 (1.00-1.19)	0.053	1.51 (1.03-2.23)	0.036
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.97 (0.90-1.05)	0.445	1.06 (0.93-1.21)	0.412	1.29 (0.94-1.76)	0.114	0.76 (0.51-1.14)	0.182	0.91 (0.82-1.02)	0.095	1.67 (1.09-2.56)	0.020
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hard LVH</i>	1.12 (1.02-1.23)	0.016	0.98 (0.83-1.16)	0.793	1.19 (0.84-1.70)	0.327	1.20 (0.75-1.92)	0.441	1.20 (1.06-1.35)	0.004	1.16 (0.69-1.95)	0.572
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.91 (0.87-0.95)	<0.001	0.95 (0.87-1.02)	0.166	0.93 (0.76-1.13)	0.461	0.97 (0.77-1.21)	0.771	0.88 (0.83-0.94)	<0.001	0.71 (0.51-1.00)	0.047
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.94 (0.91-0.98)	0.006	0.93 (0.87-1.00)	0.049	1.08 (0.91-1.29)	0.358	0.88 (0.72-1.08)	0.225	0.95 (0.90-1.00)	0.043	0.83 (0.63-1.10)	0.188
Baseline blood pressure reading, per 10 mmHg												
<i>Systolic BP</i>	1.09 (1.07-1.11)	<0.001	1.04 (1.01-1.07)	0.008	1.26 (1.17-1.36)	<0.001	0.96 (0.88-1.05)	0.349	1.12 (1.09-1.15)	<0.001	1.09 (0.97-1.22)	0.156

	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
<i>Diastolic BP</i>	0.86 (0.84-0.89)	<0.001	0.88 (0.84-0.92)	<0.001	0.89 (0.80-0.99)	0.029	0.84 (0.74-0.96)	0.008	0.86 (0.83-0.89)	<0.001	1.06 (0.89-1.25)	0.520

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

^a Adjusted for each covariate shown in that column. Covariates not included in multivariable analysis are indicated with dashes.

^b First randomization date in the Mortality cohort.

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 5. Hazard Ratios Adjusted^a by Variables Selected Through Penalized Regression for All-Cause and CVD Mortality With Follow-up From 2/23/1994^b to 12/31/2017^c

	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	1.00 (0.96-1.03)	0.827	0.96 (0.88-1.05)	0.388	1.01 (0.94-1.10)	0.763	1.00 (0.86-1.16)	0.968	1.00 (0.84-1.19)	0.990	1.01 (0.91-1.11)	0.914
<i>Lisinopril vs Chlorthalidone</i>	1.00 (0.97-1.04)	0.785	1.06 (0.98-1.16)	0.151	0.97 (0.90-1.05)	0.493	1.19 (1.03-1.37)	0.017	1.02 (0.86-1.21)	0.830	0.95 (0.86-1.05)	0.331
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	2.18 (2.11-2.25)	<0.001	2.35 (2.17-2.55)	<0.001	2.08 (1.93-2.24)	<0.001	2.54 (2.20-2.92)	<0.001	3.05 (2.56-3.63)	<0.001	2.47 (2.24-2.72)	<0.001
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Female</i>	0.79 (0.76-0.82)	<0.001	0.85 (0.78-0.92)	<0.001	0.72 (0.67-0.78)	<0.001	0.90 (0.79-1.03)	0.143	0.90 (0.77-1.05)	0.176	0.80 (0.72-0.88)	<0.001
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Black</i>	0.97 (0.94-1.00)	0.062	0.93 (0.86-1.01)	0.081	0.93 (0.86-1.01)	0.080	0.93 (0.81-1.08)	0.338	-----	-----	1.19 (1.08-1.31)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hispanic</i>	0.79 (0.76-0.83)	<0.001	0.85 (0.76-0.94)	0.002	0.79 (0.71-0.87)	<0.001	0.74 (0.62-0.89)	0.001	0.70 (0.56-0.88)	0.002	0.69 (0.60-0.79)	<0.001
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>High school or less</i>	1.19 (1.15-1.23)	<0.001	1.21 (1.11-1.31)	<0.001	1.24 (1.15-1.34)	<0.001	1.12 (0.97-1.29)	0.111	1.16 (0.98-1.36)	0.083	1.05 (0.96-1.16)	0.302
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	-----	-----	1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Treated</i>	-----	-----	1.02 (0.90-1.16)	0.731	0.97 (0.86-1.09)	0.587	1.20 (0.95-1.51)	0.126	-----	-----	0.96 (0.82-1.11)	0.552
Aspirin use at trial baseline												
<i>No</i>	-----	-----	1.00 (reference)		-----	-----	1.00 (reference)		-----	-----	1.00 (reference)	
<i>Yes</i>	-----	-----	1.06 (0.98-1.14)	0.159	-----	-----	1.14 (0.99-1.30)	0.061	-----	-----	1.08 (0.98-1.18)	0.125
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.50 (1.44-1.55)	<0.001	1.59 (1.46-1.73)	<0.001	1.48 (1.37-1.61)	<0.001	1.60 (1.38-1.85)	<0.001	1.71 (1.44-2.03)	<0.001	1.62 (1.46-1.81)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.89 (0.84-0.93)	<0.001	0.84 (0.75-0.94)	0.002	0.97 (0.88-1.07)	0.582	0.69 (0.55-0.85)	<0.001	0.79 (0.62-1.00)	0.049	0.82 (0.71-0.94)	0.006
	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	

	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Cigarette smoking at trial baseline												
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Current smoker</i>	1.68 (1.61-1.75)	<0.001	1.29 (1.17-1.44)	<0.001	1.46 (1.32-1.61)	<0.001	1.11 (0.92-1.33)	0.261	-----	-----	1.46 (1.29-1.65)	<0.001
<i>Former Smoker</i>	1.11 (1.07-1.15)	<0.001	1.05 (0.96-1.14)	0.299	1.12 (1.04-1.21)	0.004	0.95 (0.83-1.10)	0.517	-----	-----	1.07 (0.96-1.18)	0.219
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Diabetes</i>	1.54 (1.49-1.59)	<0.001	1.65 (1.53-1.78)	<0.001	1.70 (1.59-1.82)	<0.001	1.48 (1.29-1.68)	<0.001	1.64 (1.41-1.91)	<0.001	1.29 (1.18-1.42)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.31 (1.27-1.36)	<0.001	1.52 (1.41-1.65)	<0.001	1.63 (1.51-1.75)	<0.001	1.47 (1.28-1.70)	<0.001	1.26 (1.06-1.49)	0.008	1.33 (1.20-1.47)	<0.001
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Yes</i>	1.12 (1.07-1.17)	<0.001	1.21 (1.09-1.34)	<0.001	1.51 (1.39-1.65)	<0.001	0.91 (0.75-1.09)	0.303	1.39 (1.14-1.70)	<0.001	-----	-----
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.20 (1.16-1.24)	<0.001	1.24 (1.14-1.34)	<0.001	1.30 (1.20-1.40)	<0.001	1.30 (1.13-1.50)	<0.001	1.10 (0.93-1.32)	0.262	1.11 (1.00-1.24)	0.044
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Yes</i>	1.02 (0.97-1.08)	0.345	1.05 (0.94-1.18)	0.365	1.05 (0.94-1.17)	0.390	0.97 (0.79-1.19)	0.775	-----	-----	0.98 (0.85-1.13)	0.758
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hard LVH</i>	1.40 (1.31-1.49)	<0.001	1.75 (1.53-2.01)	<0.001	1.63 (1.42-1.86)	<0.001	1.81 (1.44-2.28)	<0.001	1.96 (1.50-2.55)	<0.001	1.72 (1.46-2.03)	<0.001
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Yes</i>	0.94 (0.91-0.97)	<0.001	0.96 (0.88-1.04)	0.301	0.97 (0.90-1.05)	0.449	-----	-----	0.86 (0.72-1.02)	0.091	-----	-----
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.95 (0.92-0.98)	0.001	0.98 (0.91-1.05)	0.535	0.98 (0.92-1.05)	0.630	0.85 (0.75-0.97)	0.015	1.14 (0.98-1.32)	0.084	0.97 (0.88-1.06)	0.445
Baseline blood pressure reading, per 10 mmHg												
	All-Cause Mortality		CVD Mortality		CHD Mortality		Stroke Mortality		CHF Mortality		Other CVD Mortality	

	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Systolic BP</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Diastolic BP</i>	0.94 (0.92-0.96)	<0.001	0.96 (0.92-1.00)	0.064	0.95 (0.92-0.99)	0.013	1.07 (0.99-1.15)	0.072	0.83 (0.77-0.90)	<0.001	1.02 (0.97-1.07)	0.514

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

^a Adjusted for each covariate shown in that column using LASSO penalty for variable selection (no penalty for the randomization group). Covariates not included in multivariable analysis are indicated with dashes.

^b First randomization date in the Mortality cohort.

^c Correlation between candidate variables was assessed prior to initiation of Least Absolute Shrinkage and Selection Operator (LASSO) regression procedures; variables that demonstrated moderate to high correlation with each other/other candidate variables were subject to preliminary removal. These included ASCVD, history of CHD, and baseline systolic blood pressure reading.

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 6. Hazard Ratios Adjusted^a by Variables Selected Through Penalized Regression for Morbidity With Follow-up From 3/10/1994^b to 12/31/2017^c

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	1.01 (0.96-1.06)	0.701	0.99 (0.92-1.06)	0.780	1.02 (0.96-1.08)	0.495	1.03 (0.95-1.12)	0.428	0.99 (0.92-1.07)	0.835	1.05 (0.90-1.22)	0.536
<i>Lisinopril vs Chlorthalidone</i>	1.04 (0.99-1.09)	0.150	0.98 (0.91-1.05)	0.520	1.03 (0.97-1.09)	0.364	1.11 (1.03-1.20)	0.007	1.02 (0.94-1.10)	0.626	1.13 (0.98-1.31)	0.091
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	1.82 (1.74-1.92)	<0.001	1.74 (1.62-1.86)	<0.001	1.92 (1.81-2.03)	<0.001	1.86 (1.72-2.01)	<0.001	1.64 (1.52-1.76)	<0.001	1.10 (0.96-1.26)	0.169
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Female</i>	0.93 (0.89-0.98)	0.004	0.82 (0.77-0.88)	<0.001	0.98 (0.93-1.04)	0.483	0.97 (0.91-1.05)	0.499	0.69 (0.64-0.74)	<0.001	0.67 (0.58-0.77)	<0.001
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Black</i>	0.96 (0.91-1.01)	0.110	0.89 (0.83-0.96)	0.002	0.97 (0.92-1.03)	0.328	1.01 (0.94-1.09)	0.766	1.06 (0.98-1.14)	0.157	1.86 (1.63-2.13)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Hispanic</i>	0.71 (0.67-0.76)	<0.001	0.79 (0.72-0.86)	<0.001	0.62 (0.58-0.67)	<0.001	0.74 (0.67-0.82)	<0.001	0.62 (0.56-0.69)	<0.001	-----	-----
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>High school or less</i>	1.20 (1.14-1.26)	<0.001	1.21 (1.13-1.30)	<0.001	1.20 (1.13-1.27)	<0.001	1.16 (1.07-1.25)	<0.001	1.13 (1.05-1.22)	0.002	1.09 (0.94-1.26)	0.254
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Treated</i>	1.15 (1.07-1.25)	<0.001	0.98 (0.88-1.09)	0.727	1.11 (1.01-1.22)	0.029	1.18 (1.05-1.34)	0.007	1.07 (0.95-1.21)	0.246	-----	-----
Aspirin use at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.06 (1.02-1.12)	0.009	1.06 (0.99-1.13)	0.093	1.03 (0.97-1.09)	0.312	1.15 (1.07-1.23)	<0.001	0.92 (0.85-0.98)	0.017	0.90 (0.78-1.04)	0.165
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.41 (1.34-1.49)	<0.001	1.42 (1.32-1.53)	<0.001	1.55 (1.46-1.64)	<0.001	1.31 (1.21-1.42)	<0.001	1.19 (1.09-1.29)	<0.001	5.25 (4.62-5.97)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.94 (0.87-1.00)	0.066	1.06 (0.97-1.16)	0.217	0.92 (0.85-1.00)	0.045	0.86 (0.77-0.97)	0.010	1.03 (0.93-1.14)	0.599	0.96 (0.78-1.19)	0.704
Cigarette smoking at trial baseline												

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Current smoker</i>	1.40 (1.31-1.49)	<0.001	1.47 (1.34-1.61)	<0.001	1.38 (1.28-1.49)	<0.001	1.41 (1.28-1.55)	<0.001	2.03 (1.86-2.22)	<0.001	1.76 (1.47-2.11)	<0.001
<i>Former Smoker</i>	1.09 (1.04-1.15)	<0.001	1.13 (1.05-1.21)	<0.001	1.08 (1.02-1.15)	0.007	1.11 (1.03-1.20)	0.009	1.24 (1.14-1.34)	<0.001	1.23 (1.06-1.42)	0.005
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Diabetes</i>	1.58 (1.51-1.65)	<0.001	1.70 (1.60-1.82)	<0.001	1.70 (1.61-1.79)	<0.001	1.51 (1.41-1.62)	<0.001	-----	-----	3.17 (2.77-3.63)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Yes</i>	1.46 (1.39-1.53)	<0.001	1.52 (1.42-1.63)	<0.001	1.45 (1.37-1.54)	<0.001	1.38 (1.28-1.50)	<0.001	-----	-----	1.17 (1.00-1.36)	0.051
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Yes</i>	1.29 (1.22-1.38)	<0.001	1.53 (1.41-1.66)	<0.001	1.32 (1.23-1.42)	<0.001	1.26 (1.15-1.39)	<0.001	-----	-----	1.27 (1.04-1.55)	0.017
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.19 (1.14-1.26)	<0.001	1.23 (1.15-1.32)	<0.001	1.19 (1.12-1.26)	<0.001	1.20 (1.11-1.30)	<0.001	1.13 (1.05-1.22)	0.001	1.08 (0.92-1.27)	0.324
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Yes</i>	1.10 (1.03-1.18)	0.006	1.01 (0.91-1.11)	0.873	1.18 (1.09-1.27)	<0.001	1.00 (0.89-1.11)	0.938	-----	-----	1.20 (0.98-1.46)	0.078
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)	
<i>Hard LVH</i>	1.61 (1.48-1.76)	<0.001	1.53 (1.35-1.73)	<0.001	1.81 (1.64-2.00)	<0.001	1.57 (1.37-1.79)	<0.001	-----	-----	1.49 (1.17-1.89)	0.001
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Yes</i>	0.95 (0.90-0.99)	0.025	0.93 (0.87-1.00)	0.050	0.94 (0.88-0.99)	0.024	0.96 (0.89-1.04)	0.293	0.93 (0.86-1.00)	0.044	-----	-----
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.08 (1.04-1.13)	<0.001	0.93 (0.87-0.99)	0.028	1.24 (1.18-1.30)	<0.001	0.93 (0.87-0.99)	0.034	1.02 (0.95-1.09)	0.609	1.15 (1.02-1.31)	0.027
Baseline blood pressure reading, per 10 mmHg												
<i>Systolic BP</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

	CVD Morbidity		CHD Morbidity		CHF Morbidity		Stroke Morbidity		Cancer Morbidity		Kidney Disease Morbidity	
	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value	Adjusted* HR (95% CI)	P value
<i>Diastolic BP</i>	0.95 (0.93-0.98)	<0.001	0.98 (0.95-1.02)	0.411	0.92 (0.90-0.95)	<0.001	1.00 (0.96-1.04)	0.834	0.92 (0.89-0.96)	<0.001	1.06 (0.98-1.14)	0.136

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

^a Adjusted for each covariate shown in that column using LASSO penalty for variable selection (no penalty for the randomization group). Covariates not included in multivariable analysis are indicated with dashes.

^b First randomization date in the full Morbidity cohort

^c Correlation between candidate variables was assessed prior to initiation of Least Absolute Shrinkage and Selection Operator (LASSO) regression procedures; variables that demonstrated moderate to high correlation with each other/other candidate variables were subject to preliminary removal. These included ASCVD, history of CHD, and baseline systolic blood pressure

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

eTable 7. Hazard Ratios Adjusted^a by Variables Selected Through Penalized Regression for Non-CVD Mortality With Follow-up From 2/23/1994^b to 12/31/2017[†]

	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Randomized group												
<i>Amlodipine vs. Chlorthalidone</i>	0.99 (0.94-1.04)	0.617	0.97 (0.90-1.05)	0.490	1.00 (0.82-1.24)	0.966	0.85 (0.67-1.08)	0.187	1.01 (0.95-1.08)	0.650	0.97 (0.72-1.31)	0.845
<i>Lisinopril vs Chlorthalidone</i>	1.01 (0.96-1.06)	0.681	1.06 (0.98-1.14)	0.154	1.18 (0.97-1.44)	0.094	1.08 (0.86-1.35)	0.518	0.97 (0.91-1.03)	0.292	0.95 (0.70-1.29)	0.762
Age group at trial baseline												
<i>Age <65</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Age ≥65</i>	2.09 (2.00-2.18)	<0.001	1.73 (1.61-1.85)	<0.001	1.84 (1.53-2.21)	<0.001	1.92 (1.55-2.37)	<0.001	2.35 (2.22-2.49)	<0.001	1.87 (1.40-2.49)	<0.001
Gender												
<i>Male</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Female</i>	0.79 (0.76-0.82)	<0.001	0.68 (0.63-0.73)	<0.001	0.73 (0.61-0.88)	<0.001	0.49 (0.39-0.61)	<0.001	0.90 (0.85-0.95)	<0.001	-----	-----
Race/Ethnicity												
<i>Non-Black</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Black</i>	0.93 (0.89-0.97)	0.002	1.07 (1.00-1.15)	0.051	1.26 (1.05-1.51)	0.013	0.75 (0.60-0.95)	0.016	0.84 (0.79-0.89)	<0.001	1.65 (1.27-2.15)	<0.001
Hispanic/Latino Ethnicity												
<i>Non-Hispanic</i>	1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)		-----	-----
<i>Hispanic</i>	0.82 (0.77-0.86)	<0.001	0.64 (0.58-0.70)	<0.001	-----	-----	0.61 (0.45-0.83)	0.002	0.93 (0.87-1.00)	0.046	-----	-----
Education level at trial baseline												
<i>More than high school</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>High school or less</i>	1.21 (1.16-1.27)	<0.001	1.26 (1.17-1.36)	<0.001	1.48 (1.21-1.81)	<0.001	1.22 (0.98-1.51)	0.074	1.15 (1.09-1.22)	<0.001	-----	-----
Treatment with antihypertensive drugs prior to trial baseline												
<i>Untreated</i>	-----	-----	1.00 (reference)		-----	-----	-----	-----	-----	-----	-----	-----
<i>Treated</i>	-----	-----	0.97 (0.87-1.09)	0.651	-----	-----	-----	-----	-----	-----	-----	-----
Aspirin use at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	-----	-----
<i>Yes</i>	0.97 (0.93-1.01)	0.181	0.90 (0.84-0.97)	0.006	0.86 (0.71-1.04)	0.113	1.12 (0.92-1.38)	0.255	-----	-----	-----	-----
GFR <60 mL/min/1.73 m² at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.44 (1.36-1.51)	<0.001	1.21 (1.10-1.32)	<0.001	3.83 (3.19-4.59)	<0.001	1.13 (0.87-1.48)	0.352	1.43 (1.34-1.53)	<0.001	1.86 (1.40-2.48)	<0.001
HDL cholesterol <35 mg/dl at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----
<i>Yes</i>	0.89 (0.83-0.94)	<0.001	1.05 (0.95-1.16)	0.343	0.87 (0.66-1.15)	0.329	0.73 (0.54-0.99)	0.046	0.82 (0.76-0.89)	<0.001	-----	-----
	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	

	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Cigarette smoking at trial baseline												
<i>Never smoker</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Current smoker</i>	1.90 (1.80-2.01)	<0.001	2.58 (2.36-2.82)	<0.001	1.99 (1.57-2.53)	<0.001	1.27 (0.97-1.66)	0.082	1.59 (1.48-1.72)	<0.001	1.87 (1.33-2.63)	<0.001
<i>Former Smoker</i>	1.15 (1.09-1.20)	<0.001	1.32 (1.22-1.44)	<0.001	1.25 (1.02-1.53)	0.033	0.75 (0.60-0.95)	0.015	1.09 (1.03-1.16)	0.004	1.26 (0.94-1.68)	0.126
Diabetes classification at trial baseline												
<i>Non-diabetes</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Diabetes</i>	1.53 (1.47-1.60)	<0.001	1.12 (1.05-1.20)	0.001	2.52 (2.12-3.00)	<0.001	1.25 (1.01-1.53)	0.037	1.77 (1.67-1.87)	<0.001	1.77 (1.36-2.30)	<0.001
History of Coronary Heart Disease (CHD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
Atherosclerotic Cardiovascular Disease (ASCVD) at trial baseline												
<i>No</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Yes</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
History of myocardial infarction (MI) or stroke at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.18 (1.13-1.24)	<0.001	1.15 (1.06-1.24)	<0.001	1.27 (1.03-1.57)	0.024	-----	-----	1.24 (1.16-1.32)	<0.001	1.54 (1.16-2.04)	0.002
History of coronary artery bypass graft (CABG) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.00 (0.94-1.07)	0.922	1.00 (0.90-1.11)	0.989	1.18 (0.90-1.55)	0.224	-----	-----	1.00 (0.92-1.08)	0.967	0.80 (0.54-1.20)	0.284
Other ASCVD at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.17 (1.12-1.23)	<0.001	1.20 (1.11-1.30)	<0.001	-----	-----	1.12 (0.89-1.42)	0.342	1.16 (1.09-1.23)	<0.001	1.31 (0.98-1.76)	0.072
Major ST segment depression at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)	
<i>Yes</i>	1.01 (0.95-1.08)	0.680	1.02 (0.92-1.14)	0.673	1.32 (1.01-1.71)	0.039	-----	-----	0.99 (0.90-1.08)	0.763	1.46 (1.01-2.10)	0.042
LVH by Minnesota code at trial baseline												
<i>No/Soft LVH</i>	1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Hard LVH</i>	1.16 (1.06-1.28)	0.001	-----	-----	1.29 (0.90-1.83)	0.162	1.12 (0.71-1.79)	0.622	1.25 (1.11-1.42)	<0.001	1.16 (0.70-1.92)	0.555
Lipid Lowering Trial (LLT) Participant												
<i>No</i>	1.00 (reference)		1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.91 (0.87-0.95)	<0.001	0.95 (0.88-1.02)	0.162	0.93 (0.77-1.13)	0.478	-----	-----	0.89 (0.84-0.94)	<0.001	0.68 (0.49-0.94)	0.018
Obesity (BMI ≥ 30 kg/m²) at trial baseline												
<i>No</i>	1.00 (reference)		1.00 (reference)		-----	-----	1.00 (reference)		1.00 (reference)		1.00 (reference)	
<i>Yes</i>	0.94 (0.90-0.98)	0.002	0.91 (0.85-0.97)	0.005	-----	-----	0.89 (0.73-1.09)	0.262	0.94 (0.89-0.99)	0.023	0.83 (0.64-1.08)	0.158
Baseline blood pressure reading, per 10 mmHg												
	All Non-CVD Mortality		Cancer Mortality		Kidney Disease Mortality		Mortality Accident/Suicide		Other Non-CVD Mortality		Mortality Unknown Cause	

	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
<i>Systolic BP</i>	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
<i>Diastolic BP</i>	0.91 (0.89-0.93)	<0.001	0.90 (0.87-0.94)	<0.001	-----	-----	0.82 (0.74-0.92)	<0.001	0.92 (0.89-0.94)	<0.001	1.04 (0.91-1.20)	0.557

HR= Hazard ratio; 95% CI= 95% Confidence interval; CHD= coronary heart disease; CVD= cardiovascular disease; ASCVD= Atherosclerotic Cardiovascular Disease; OASCVD= Other ASCVD; HDL= high density lipoprotein; eGFR= estimated glomerular filtration rate; LVH= left ventricular hypertrophy; SBP= systolic blood pressure; DBP= diastolic blood pressure

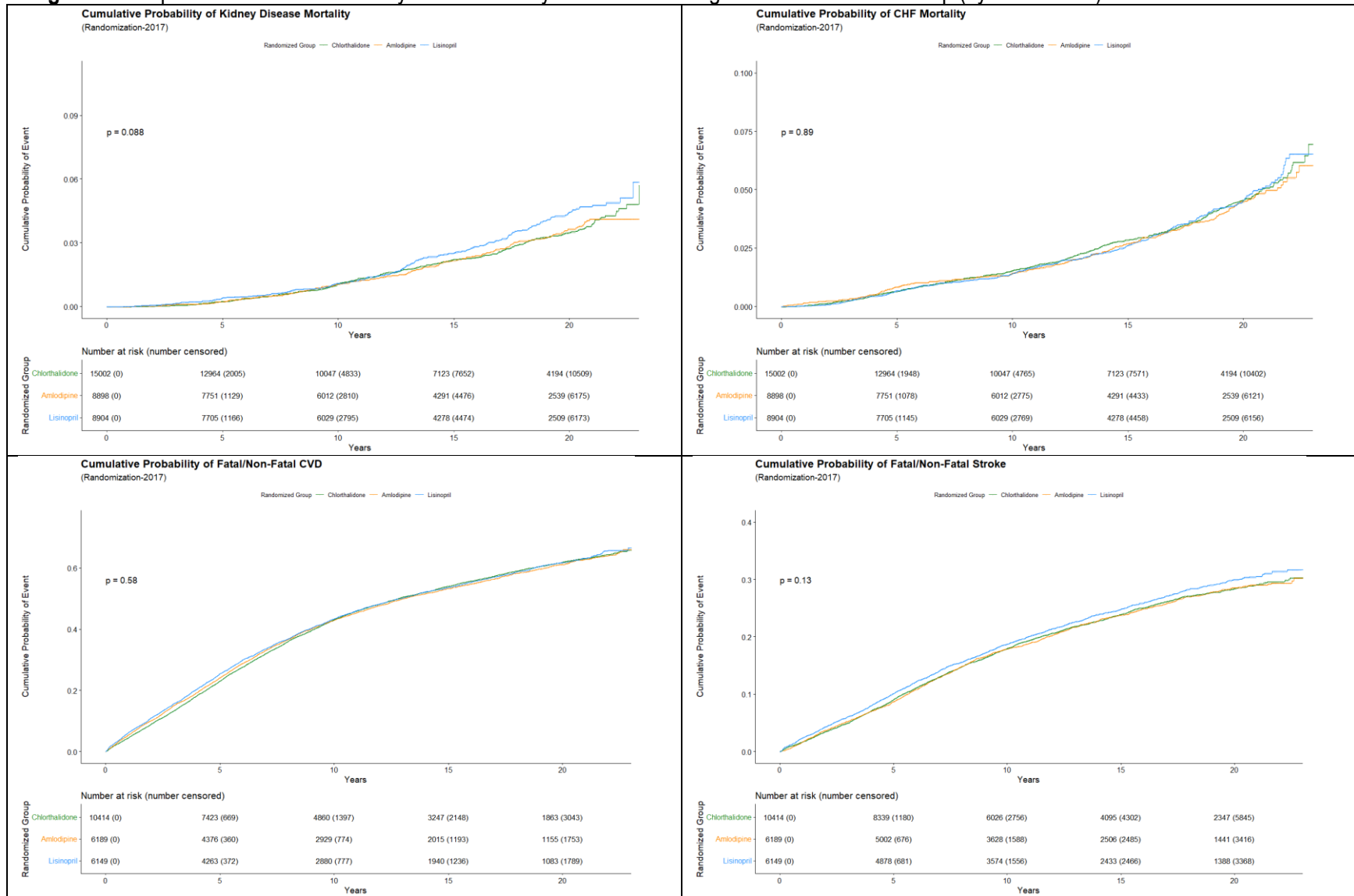
†Correlation between candidate variables was assessed prior to initiation of Least Absolute Shrinkage and Selection Operator (LASSO) regression procedures; variables that demonstrated moderate to high correlation with each other/other candidate variables were subject to preliminary removal. These included ASCVD, history of CHD, and baseline systolic blood pressure reading.

^a Adjusted for each covariate shown in that column using LASSO penalty for variable selection (no penalty for the randomization group). Covariates not included in multivariable analysis are indicated with dashes.

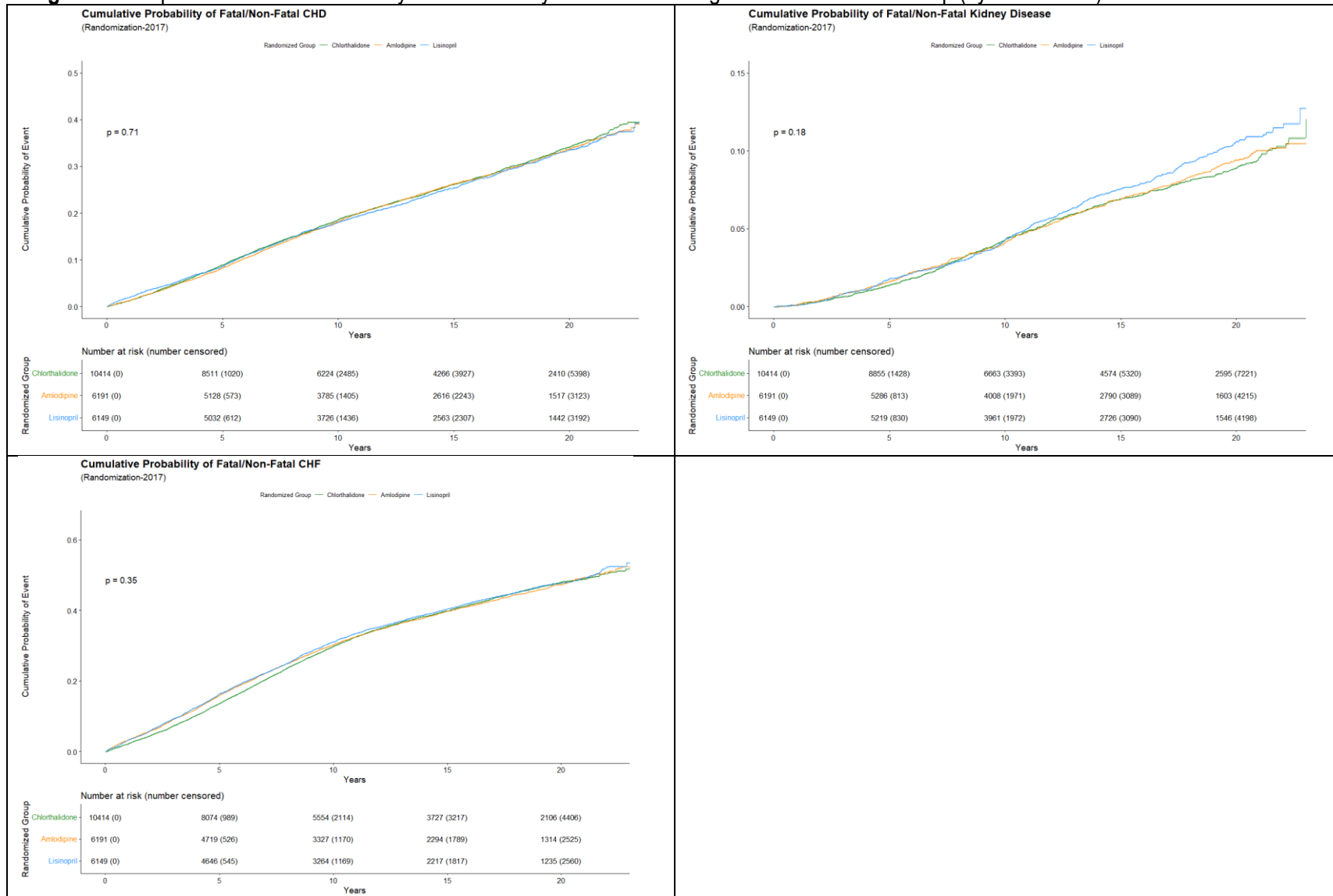
^b First randomization date in the Mortality cohort

Conversion factors: 1 mL/min/1.73m² = 0.0167 mL/s/m²; 1 mg/dl = 0.0259 mmol/L; 1 mmHg = 0.133 kPa

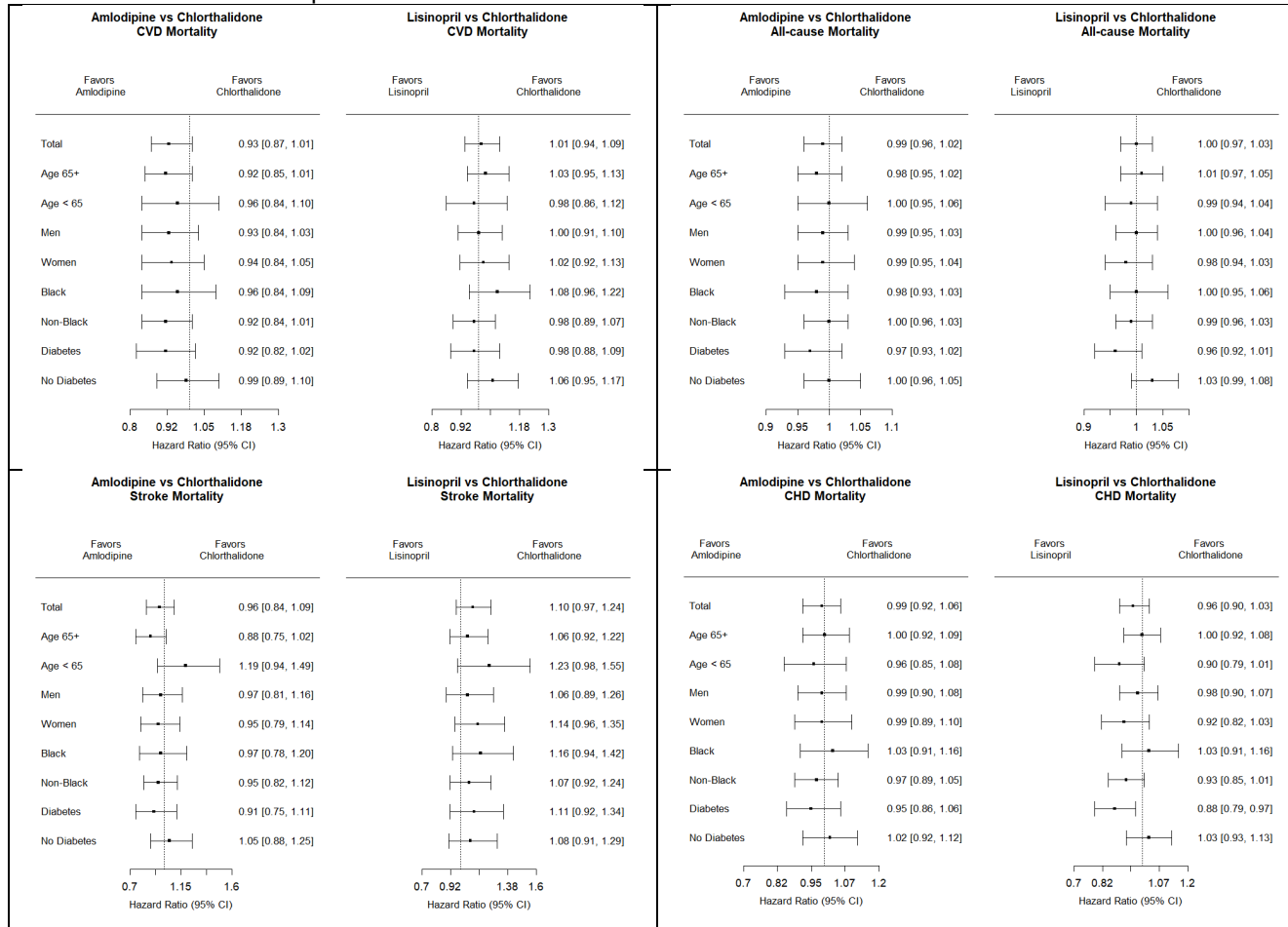
eFigure 1A. Kaplan-Meier Plots of Primary and Secondary Outcomes Through the Extended Follow-up (by 12/31/2017)



eFigure 1B. Kaplan-Meier Plots of Primary and Secondary Outcomes Through the Extended Follow-up (by 12/31/2017)

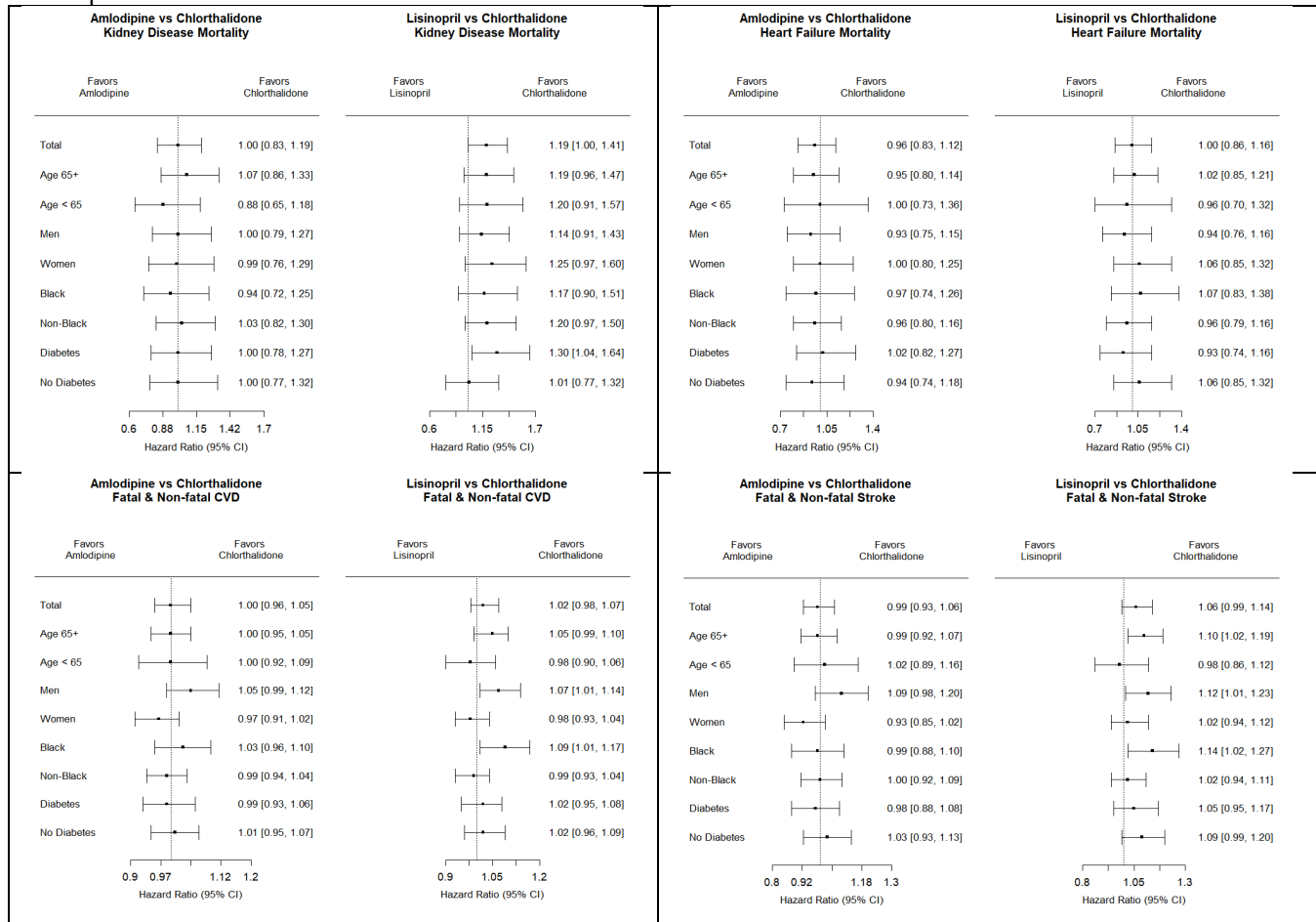


eFigure 2A. Unadjusted Hazard Ratios (95% CI) and Forest Plots of Overall and Subgroup Analyses of Mortality and Morbidity Outcomes Through the Extended Follow-up (by 12/31/2017) – Amlodipine vs. Chlorthalidone and Lisinopril vs. Chlorthalidone^a



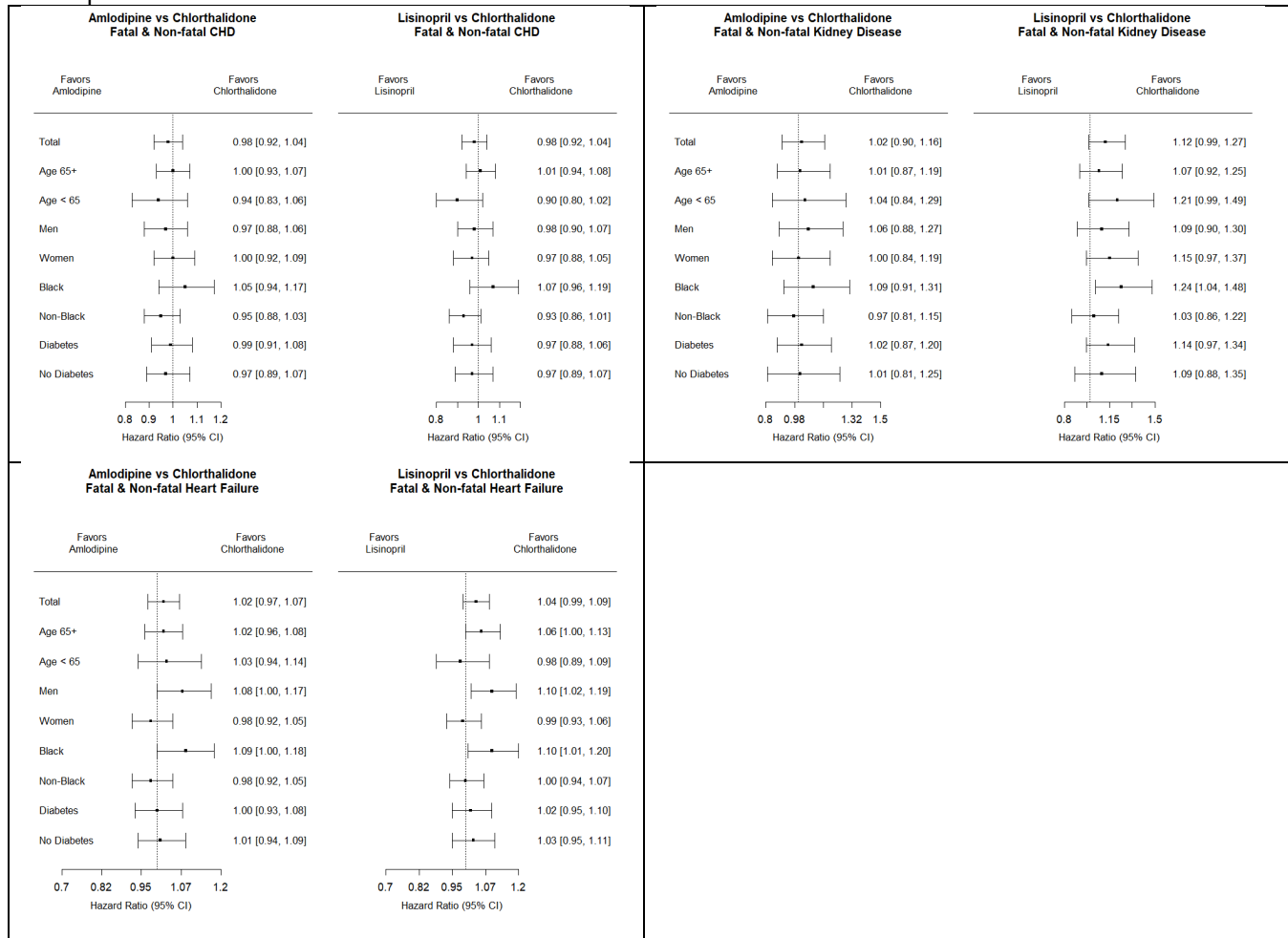
^a Significant interactions were detected between lisinopril/chlorthalidone × diabetes status for all-cause mortality (p=0.024) and for CHD mortality (p=0.027). Significant interaction was detected for amlodipine/chlorthalidone × age 65+ for stroke mortality (p=0.033).

eFigure 2B. Unadjusted Hazard Ratios (95% CI) and Forest Plots of Overall and Subgroup Analyses of Mortality and Morbidity Outcomes Through the Extended Follow-up (by 12/31/2017) – Amlodipine vs. Chlorthalidone and Lisinopril vs. Chlorthalidone^a



^a Significant interactions were detected between Lisinopril/Chlorthalidone × female/male for fatal and non-fatal CVD (p=0.043), between Lisinopril/Chlorthalidone × Black/non-Black for fatal and nonfatal CVD (p=0.031), and between amlodipine/chlorthalidone × male/female for fatal and non-fatal stroke (p=0.027).

eFigure 2C. Unadjusted Hazard Ratios (95% CI) and Forest Plots of Overall and Subgroup Analyses of Mortality and Morbidity Outcomes Through the Extended Follow-up (by 12/31/2017) – Amlodipine vs. Chlorthalidone and Lisinopril vs. Chlorthalidone^a



^a Significant interactions were detected between Lisinopril/Chlorthalidone × Black/non-Black for fatal and non-fatal CHD (p=0.042) and between Lisinopril/Chlorthalidone × female/male for fatal and non-fatal heart failure (p=0.046).