SUPPLEMENTAL TABLE 1: Characteristics of ALLHAT participants included and excluded from the analysis - mean (sd) unless otherwise noted.

Characteristic	Included (n=21,245)	Excluded (n=12,112)	p-value
Age, years	66.6 (7.4)	67.3 (8.2)	<0.001
Men, n (%)	11612 (54.7)	6107 (50.4)	<0.001
Non-Hispanic White, n (%)	10854 (51.1)	4851 (40.1)	<0.001
Non-Hispanic Black, n (%)	6537 (30.8)	4071 (33.6)	<0.001
Hispanic White, n (%)	2283 (10.8)	1873 (15.5)	<0.001
Hispanic Black, n (%)	464 (2.2)	626 (5.2)	<0.001
Education status, years	11.2 (3.9)	10.5 (4.1)	<0.001
Current smoking, n (%)	4437 (20.9)	2866 (23.7)	<0.001
BMI, kg/m^2	29.8 (6.1)	29.5 (6.3)	<0.001
Diabetes (type 2 at baseline), n (%)	7455 (35.1)	4608 (38.0)	<0.001
Total cholesterol, mg/dL	215.5 (42.3)	217.2 (45.5)	0.001
Low HDL-cholesterol (<35mg/dl), n (%)	2713 (12.8)	1164 (9.6)	<0.001
History of MI or stroke, n (%)	4652 (21.9)	3085 (25.5)	<0.001
History of revascularization, n (%)	2761 (13.0)	1549 (12.8)	0.59
History of atrial fibrillation, n (%)	186 (0.9)	148 (1.4)	<0.001
History of other ASCVD, n (%)	5009 (23.6)	2892 (23.9)	0.54
Major ST depression or T wave inversion, n (%)	2126 (10.1)	1294 (10.8)	0.07
LVH by electrocardiogram, n (%)	3465 (16.3)	2009 (16.6)	0.51
Use of antihypertensive medication prior to baseline, n (%)	19351 (91.1)	10738 (88.7)	<0.001
eGFR, ml/min/1.73 m^2	74.3 (17.1)	72.9 (19.0)	<0.001
Aspirin use at baseline, n (%)	7920 (37.3)	4032 (33.3)	<0.001
Statin use at any visit during follow up (6-28m), n (%)	7546 (35.5)	2375 (19.6)	<0.001
Mean SBP at baseline, mm Hg	145.6 (15.6)	147.4 (15.6)	<0.001
Mean DBP at baseline, mm Hg	83.7 (10.0)	84.5 (10.2)	<0.001
Pulse pressure at baseline, mm Hg	61.9 (14.2)	62.9 (14.2)	<0.001
Mean SBP during follow up (6-28m), mm Hg	137.4 (11.4)	140.1 (14.8)	<0.001
Mean DBP during follow up (6-28m), mm Hg	78.8 (7.1)	80.0 (9.0)	<0.001
Maximum number of antihypertensive meds at any visit (6-28m)	1.7 (0.9)	1.6 (0.9)	<0.001
Low adherence at any visit, n (%)	3078 (14.5)	1367 (11.3)	<0.001
Changes in medication classes, n (%)	10043 (47.3)	4876 (40.3)	<0.001
Randomization group			
Chlorthalidone, n (%)	9895 (46.6)	5360 (44.3)	<0.001
Amlodipine, n (%)	5793 (27.3)	3255 (26.9)	
Lisinopril, n (%)	5557 (26.2)	3497 (28.9)	

BMI – body mass index, ASCVD – atherosclerotic vascular disease; LVH – left ventricular hypertrophy; eGFR – estimated glomerular filtration rate; SBP – systolic blood pressure; DBP – diastolic blood pressure.

Excluded participants: <5 BP measures, event prior to 28 month visit (REND, USRDS, CHD, CHF, STROKE), Canadian clinical sites, missing baseline creatinine measure (both BL and 1-3 month).

SUPPLEMENTAL TABLE 2: Hazard ratios* for combined renal endpoint associated with the highest versus lowest quintile of standard deviation of systolic blood pressure across ALLHAT follow-up visits conducted 6 to 28 months following baseline in selected sub-groups

	Lowest quintile of sd SBP	Highest quintile of sd SBP	Interaction p-value
All participants (n=21,245)	HR=1.00 (ref)	HR =2.05 (1.25-3.36), p=0.004	NA
Mean SBP < 130 mmHg from month 6-28 (n=5,207)	HR=1.00 (ref)	HR =3.41 (0.71-16.2), p=0.12	0.22
Mean SBP = 130-139.9 mmHg from month 6-28 (n=8,069)	HR=1.00 (ref)	HR =1.31 (0.56-3.05), p=0.53	
Mean SBP >= 140 mmHg from month 6-28 (n=7,969)	HR=1.00 (ref)	HR =2.88 (1.15-7.20), p=0.024	
Chlorthalidone group (n=9,895)	HR=1.00 (ref)	HR =3.78 (1.64-8.74), p=0.002	0.29
Amlodipine group (n=5,793)	HR=1.00 (ref)	HR =1.00 (0.43-2.32), p=0.99	
Lisinopril group (n=5,557)	HR=1.00 (ref)	HR =1.52 (0.55-4.20), p=0.42	
eGFR at baseline >=90 ml/min/1.73 m^2 (n=4,121)	HR=1.00 (ref)	HR =1.54 (0.43-5.54), p=0.51	0.39
eGFR at baseline =60-89 ml/min/1.73 m^2 (n=12,839)	HR=1.00 (ref)	HR =3.60 (1.60-8.11), p=0.002	
eGFR at baseline < 60 ml/min/1.73 m^2 (n=4,285)	HR=1.00 (ref)	HR =1.37 (0.65-2.88), p=0.41	
Type 2 diabetes at baseline (n=7,455)	HR=1.00 (ref)	HR =2.03 (1.09-3.78), p=0.026	0.64
Non-diabetic at baseline (n=13,790)	HR=1.00 (ref)	HR =1.74 (0.75-4.03), p=0.19	

* We used interval censored regression models to calculate hazard ratios

These hazard ratios are adjusted for the following baseline values: age, gender, race/ethnicity, region of residence, randomization assignment, education, smoking status, body mass index, estimated glomerular filtration rate (eGFR), diabetes, total cholesterol, history of MI or stroke, history of coronary revascularization, history of atrial fibrillation, history of other atherosclerotic cardiovascular disease, major ST depression or T wave inversion, left ventricular hypertrophy, low HDL cholesterol, aspirin use, use of blood pressure medications prior to study randomization; and the following values measured during the VVV of BP assessment period (i.e., month 6 through 28 of follow-up): statin use, mean SBP, mean pulse pressure, medication adherence, antihypertensive medication classes being taken, changes in antihypertensive medication classes being taken, and the number of visits (5, 6, or 7) used to calculate VVV.

SUPPLEMENTAL TABLE 3: Association of VVV of SBP versus mean SBP (both modeled in quintiles, each adjusted for the other) with renal outcomes

A. Hazard ratio for 50% decline in eGFR or ESRD through month 72 (297 events)	Q1	Q2	Q3	Q4	Q5	p-trend
For VVV of SBP (95% CI)	1 (ref)	1.27 (0.74-2.19)	1.69 (1.02-2.81)	1.42 (0.85-2.38)	1.97 (1.20-3.26)	0.007
For mean SBP (95% CI)	1 (ref)	1.28 (0.71-2.34)	1.77 (1.01-3.09)	2.02 (1.17-3.48)	3.55 (2.09-6.05)	<0.001
B. Hazard ratio for ESRD only through month 72 (161 events)						
For VVV of SBP (95% CI)	1 (ref)	1.20 (0.52-2.79)	1.82 (0.84-3.98)	1.61 (0.74-3.50)	1.99 (0.93-4.26)	0.06
For mean SBP (95% CI)	1 (ref)	1.58 (0.66-3.80)	1.44 (0.60-3.46)	2.33 (1.03-5.24)	3.20 (1.44-7.14)	<0.001
C. Hazard ratio for 50% decline in eGFR only (173 events)						
For VVV of SBP (95% CI)	1 (ref)	1.24 (0.63-2.43)	1.78 (0.96-3.30)	1.43 (0.76-2.72)	2.15 (1.15-4.00)	0.01
For mean SBP (95% CI)	1 (ref)	0.92 (0.43-1.96)	1.90 (1.00-3.62)	1.65 (0.86-3.18)	3.18 (1.68-6.03)	<0.001

eGFR = estimated Glomerular Filtration Rate; ESRD = End Stage Renal Disease; CI = Confidence Interval ; SBP – systolic blood pressure; SD = Standard Deviation; VVV = visit to visit variability

* We used interval censored regression models to calculate hazard ratios in Panels A and C, We used Cox proportional hazard models in Panel B

Hazard ratios adjusted for age, gender, race/ethnicity, region of residence, randomization assignment, education, smoking status, body mass index, diabetes, total cholesterol, history of MI or stroke, history of coronary revascularization, history of atrial fibrillation, history of other atherosclerotic cardiovascular disease, major ST depression or T wave inversion, left ventricular hypertrophy, low HDL cholesterol, and eGFR at baseline, statin use during follow-up, use of blood pressure medications and aspirin prior to study randomization, the number of visits (5, 6, or 7) used to calculate VVV and mean SBP, and medication adherence, non-randomized antihypertensive medication classes taken, and changes in antihypertensive medication classes during months 6 through 28 of follow-up.

Mean SBP and VVV of SBP are calculated from SBP measured at all (5, 6, or 7) available visits during months 6 through 28 of follow up.

Quintiles 1 – 5 of mean SBP (in mmHg) were <128.4, 128.4-134.0, 134.1-139.1, 139.2-145.9, and >145.9, respectively.

Quintiles 1 – 5 of VVV of SBP were <6.6, 6.6-8.8, 8.8-11.1, 11.2-14.6, and > 14.6, respectively

SUPPLEMENTAL TABLE 4: Comparison of the hazard ratios* for a 50% decline in eGFR or ESRD through month 72 post randomization between the highest vs. lowest quintile of VVV of systolic blood pressure (SBP) when measured by standard deviation, average real variability, or peak value. (n=21,245)

	Standard Deviation of SBP	Average Real Variability of SBP	Peak value of SBP
A. Combined endpoint, n=297 (Hazard Ratio, 95% CI)			
Model 1	4.17 (2.73-6.39), p<0.001	2.81 (1.88-4.18), p<0.001	2.53 (1.72-3.72), p<0.001
Model 2	4.23 (2.65-6.78), p<0.001	3.04 (1.96-4.71), p<0.001	2.71 (1.75-4.18), p<0.001
Model 3	2.55 (1.56-4.15), p<0.001	1.86 (1.18-2.92), p=0.007	1.70 (1.09-2.65), p=0.02
Model 4	2.32 (1.42-3.80), p=0.001	1.71 (1.08-2.71), p=0.021	1.50 (0.96-2.36), p=0.08
Model 5	2.05 (1.25-3.36), p=0.004	1.53 (0.97-2.43), p=0.069	1.47 (0.94-2.30), p=0.09
B. End Stage Renal Disease prior to Y6, n=161 (Hazard Ratio, 95% CI)			
Model 1	5.31 (2.85-9.88), p<0.001	3.08 (1.78-5.32), p<0.001	2.26 (1.37-3.72), p=0.001
Model 2	5.49 (2.69-11.2), p<0.001	3.47 (1.87-6.45), p<0.001	2.30 (1.31-4.06), p=0.004
Model 3	3.04 (1.45-6.36), p=0.003	1.96 (1.03-3.73), p=0.039	1.33 (0.74-2.38), p=0.34
Model 4	2.61 (1.24-5.49), p=0.012	1.76 (0.92-3.36), p=0.087	1.14 (0.63-2.06), p=0.67
Model 5	1.98 (0.93-4.21), p=0.077	1.44 (0.74-2.78), p=0.28	1.05 (0.58-1.91), p=0.86
C. 50% decrease in eGFR, n=173 (Hazard Ratio, 95% CI)			
Model 1	3.00 (1.78-5.07), p<0.001	2.46 (1.46-4.14), p=0.001	2.85 (1.69-4.82), p<0.001
Model 2	3.43 (1.92-6.14), p<0.001	2.51 (1.45-4.35), p=0.001	3.17 (1.77-5.67), p<0.001
Model 3	2.29 (1.25-4.20), p=0.007	1.67 (0.95-2.96), p=0.077	2.21 (1.21-4.02), p=0.009
Model 4	2.27 (1.23-4.19), p=0.009	1.67 (0.94-2.98), p=0.082	2.02 (1.10-3.70), p=0.02
Model 5	2.21 (1.19-4.08), p=0.012	1.63 (0.91-2.90), p=0.099	2.00 (1.09-3.67), p=0.02

* We used interval censored regression models to calculate hazard ratios in Panels A and C. We used Cox proportional hazards models to calculate hazard ratios in Panel B.

In each panel, Model 1 includes adjustment for age, gender, race/ethnicity, region of residence and randomization assignment.

Model 2 includes variables in model 1 and education, smoking status, body mass index, diabetes, total cholesterol, history of MI or stroke, history of coronary revascularization, history of atrial fibrillation, history of other atherosclerotic cardiovascular disease, major ST depression or T wave inversion, left ventricular hypertrophy, low HDL cholesterol, aspirin use, statin use, use of blood pressure medications prior to study randomization.

Model 3 includes variables in model 2 and variables measured during the VVV of BP assessment period (i.e., month 6 through 28 of follow-up) mean SBP, mean pulse pressure, and medication adherence

Model 4 includes the variables in model 3 plus the number of visits (5, 6, or 7) used to calculate VVV randomization group, non-randomized antihypertensive medication classes taken, and changes in antihypertensive medication classes during months 6-28.

Model 5 includes all the variables in model 4 and baseline eGFR

SUPPLEMENTAL TABLE 5: Association of quintile of Standard Deviation of Diastolic Blood Pressure with 50% decline in eGFR or ESRD through month 72 post randomization (n=21,245) (Using interval censored regression models in Panel A and C, and Cox proportional hazards models in Panel B)

A. ESRD through month 72 or 50% decrease in eGFR between month 24 and month 48 or month 72 or both (n=297)						
Quintiles	Q1 (<4.19 mm Hg)	Q2 (4.19-5.40 mm Hg)	Q3 (5.41-6.71 mm Hg)	Q4 (6.72-8.37 mm Hg)	Q5 (>8.37 mm Hg)	p-trend
Participants, n	4237	4258	4252	4242	4256	NA
Cases, n (%)	33 (0.8%)	48 (1.1%)	64 (1.5%)	60 (1.4%)	92 (2.2%)	<0.001
Hazard ratio (95% CI)						
Model 1	1.00 (ref)	1.43 (0.92-2.23)	1.90 (1.25-2.89)	1.75 (1.14-2.68)	2.60 (1.74-3.88)	<0.001
Model 2	1.00 (ref)	1.40 (0.88-2.24)	1.85 (1.19-2.87)	1.57 (1.00-2.48)	2.47 (1.61-3.78)	<0.001
Model 3	1.00 (ref)	1.33 (0.83-2.12)	1.67 (1.07-2.60)	1.31 (0.83-2.07)	1.74 (1.12-2.68)	0.03
Model 4	1.00 (ref)	1.29 (0.81-2.06)	1.59 (1.02-2.47)	1.21 (0.77-1.92)	1.59 (1.03-2.47)	0.09
Model 5	1.00 (ref)	1.31 (0.82-2.09)	1.53 (0.98-2.39)	1.17 (0.74-1.86)	1.48 (0.95-2.30)	0.21
B. End Stage Renal Disease through month 72 (n=161)						
Cases, n (%)	14	24	37	29	57	<0.001
Hazard ratio (95% CI)						
Model 1	1.00 (ref)	1.67 (0.87-3.24)	2.58 (1.39-4.78)	1.98 (1.05-3.76)	3.70 (2.05-6.67)	<0.001
Model 2	1.00 (ref)	1.73 (0.85-3.52)	2.70 (1.40-5.23)	1.68 (0.82-3.42)	3.70 (1.95-7.04)	<0.001
Model 3	1.00 (ref)	1.65 (0.81-3.36)	2.42 (1.25-4.68)	1.40 (0.68-2.86)	2.49 (1.30-4.79)	0.029
Model 4	1.00 (ref)	1.61 (0.79-3.29)	2.22 (1.15-4.32)	1.26 (0.61-2.59)	2.20 (1.14-4.24)	0.06
Model 5	1.00 (ref)	1.77 (0.86-3.64)	2.14 (1.09-4.21)	1.18 (0.56-2.45)	1.87 (0.96-3.63)	0.30
C. 50% decrease in eGFR 50% decrease in eGFR between month 24 and month 48 or month 72 or both (n=173)						
Cases, n (%)	24 (0.6%)	29 (0.7%)	35 (0.8%)	41 (1.0%)	44 (1.0%)	0.005
Hazard ratio (95% CI)						
Model 1	1.00 (ref)	1.20 (0.70-2.06)	1.43 (0.85-2.41)	1.62 (0.97-2.68)	1.67 (1.01-2.76)	0.03
Model 2	1.00 (ref)	1.17 (0.66-2.07)	1.36 (0.79-2.36)	1.60 (0.95-2.72)	1.64 (0.97-2.78)	0.04
Model 3	1.00 (ref)	1.11 (0.63-1.95)	1.25 (0.72-2.17)	1.36 (0.80-2.31)	1.23 (0.71-2.10)	0.42
Model 4	1.00 (ref)	1.10 (0.62-1.94)	1.22 (0.71-2.12)	1.32 (0.77-2.25)	1.20 (0.69-2.07)	0.48
Model 5	1.00 (ref)	1.09 (0.62-1.93)	1.22 (0.70-2.11)	1.30 (0.76-2.23)	1.18 (0.68-2.03)	0.53

p-y – person years; SD – standard deviation

Model 1 includes adjustment for age, gender, race/ethnicity, region of residence and randomization assignment.

Model 2 includes variables in model 1 and education, smoking status, body mass index, diabetes, total cholesterol, history of MI or stroke, history of coronary revascularization, history of atrial fibrillation, history of other atherosclerotic cardiovascular disease, major ST depression or T wave

inversion, left ventricular hypertrophy, low HDL cholesterol, aspirin use, statin use, use of blood pressure medications prior to study randomization.
Model 3 includes variables in model 2 and variables measured during the VVV of BP assessment period (i.e., month 6 through 28 of follow-up), mean DBP, mean pulse pressure, and medication adherence.
Model 4 includes variables in model 3 and randomization group, non-randomized antihypertensive medication classes taken, the number of visits (5, 6, or 7) used to calculate VVV and changes in antihypertensive medication classes during months 6-28.
Model 5 includes all the variables in model 4 and baseline eGFR.