Figure S1. Blood pressure in intensive and standard treatment groups during trial and cohort phases, stratified by estimated glomerular filtration rate (eGFR).
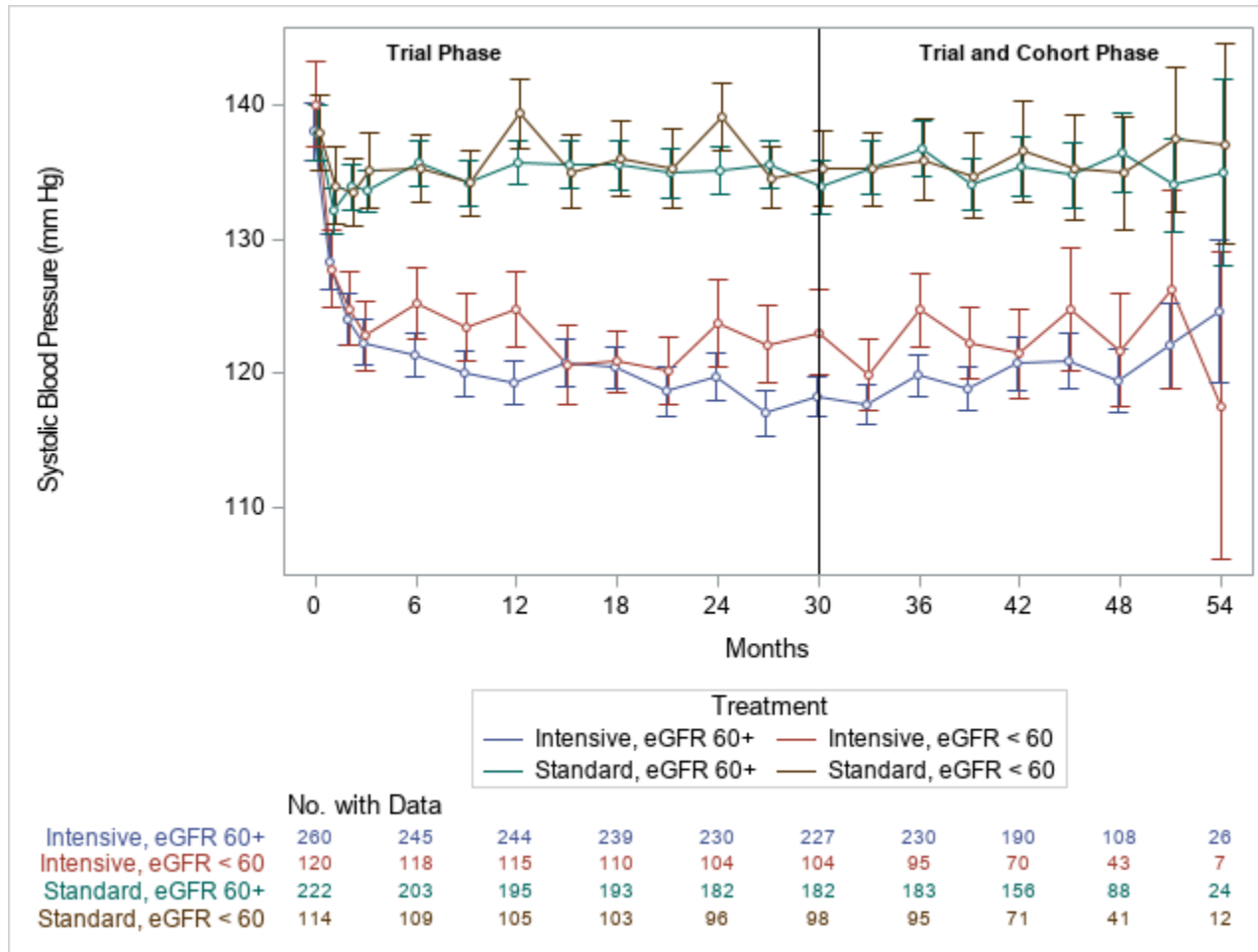

No. with Data									
Intensive, eGFR 60+	260	245	244	239	230	227	230	190	108	26
Intensive, eGFR < 60	120	118	115	110	104	104	95	70	43	7
Standard, eGFR 60+	222	203	195	193	182	182	183	156	88	24
Standard, eGFR < 60	114	109	105	103	96	98	95	71	41	12

Figure S2. Blood pressure in intensive and standard treatment groups during trial and cohort phases, stratified by urine albumin to creatinine ratio (ACR).
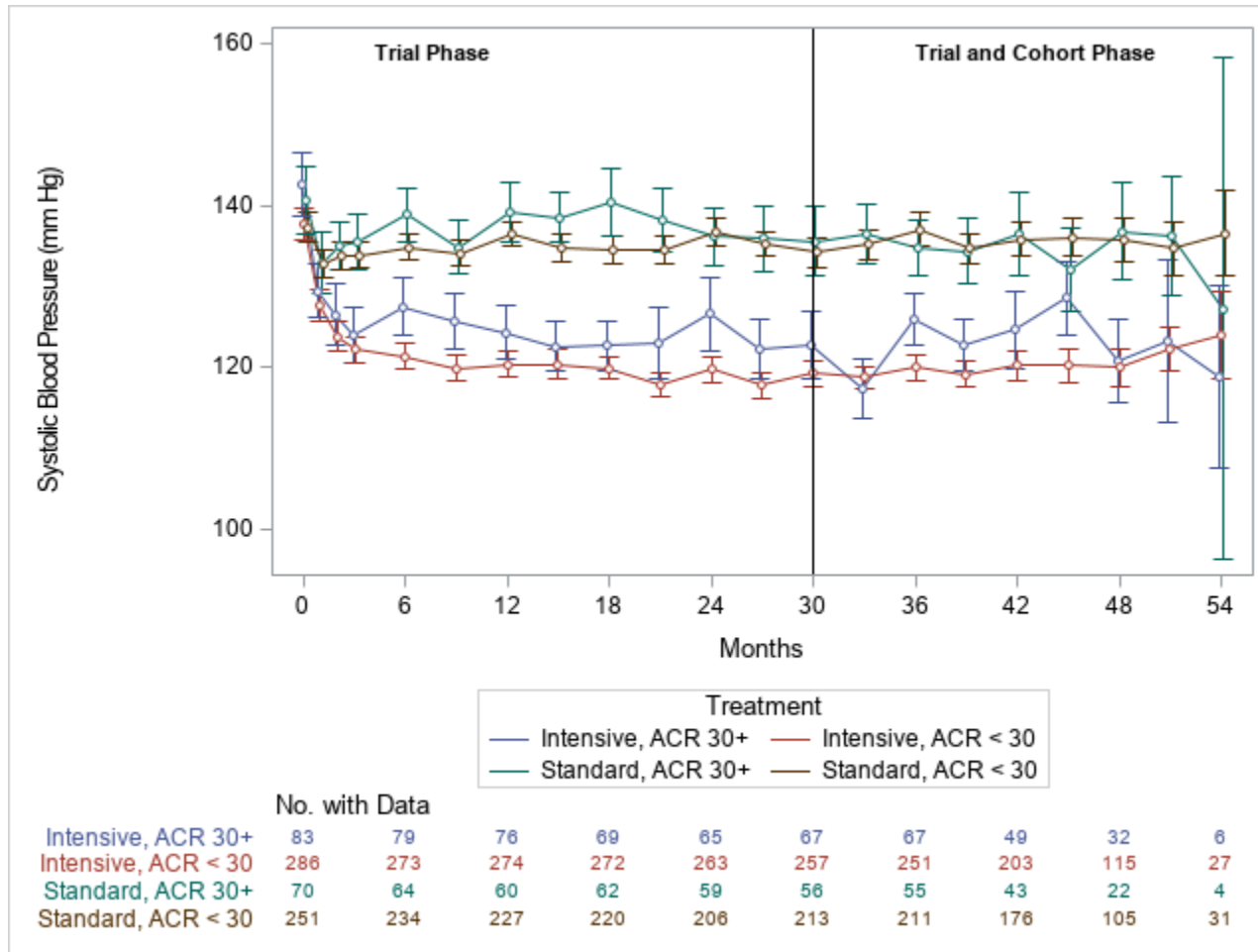
Figure S3. Effect of intensive versus standard BP treatment on change in cerebral blood flow (Panel A), white matter lesion volume (Panel B), and total brain volume (Panel C) expressed as z-scores, by baseline estimated glomerular filtration rate and urine albumin to creatinine ratio.
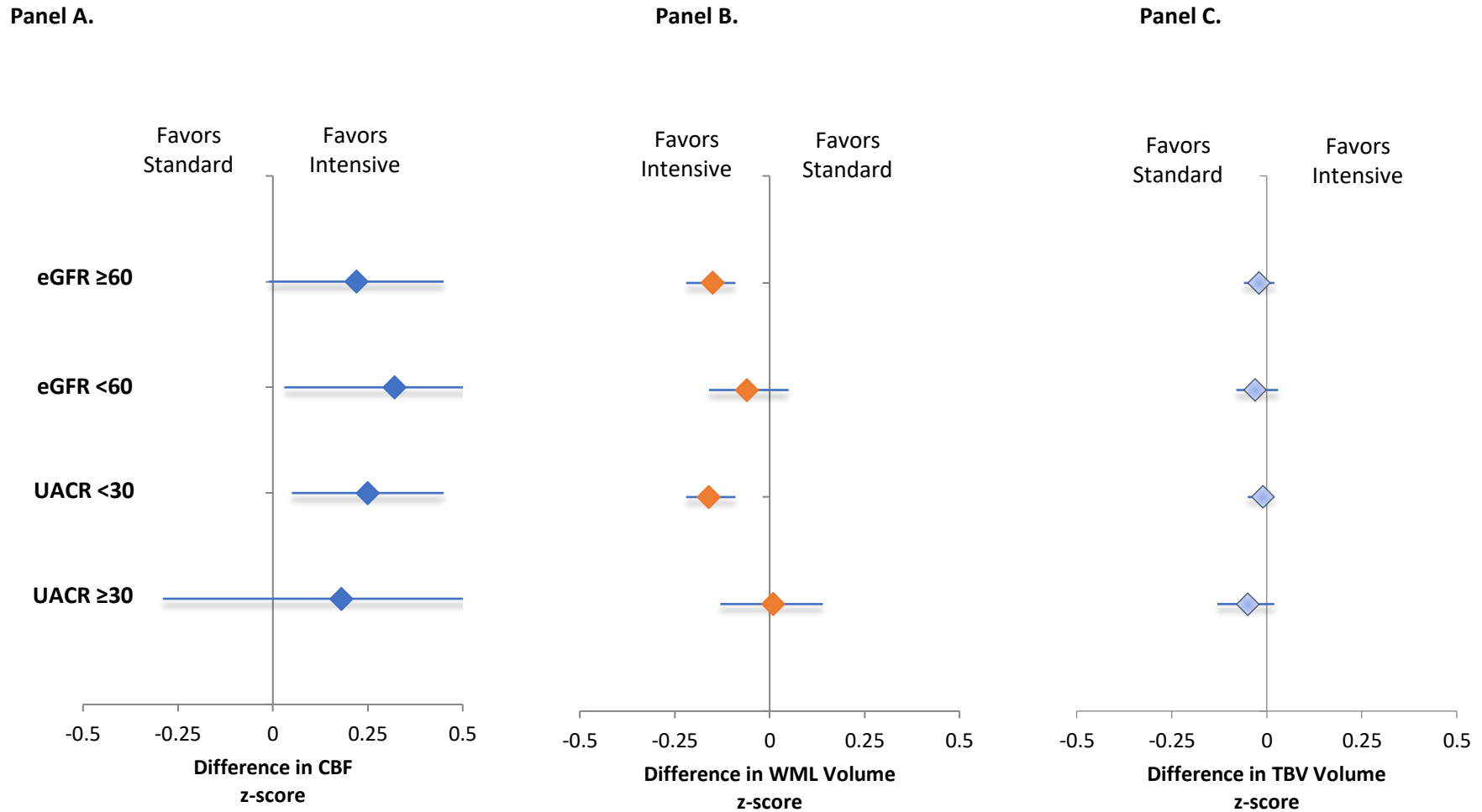
Table S1. Cerebral blood flow at follow-up, with and without correction for hematocrit, by baseline estimated glomerular filtration rate (eGFR) and urine albumin to creatinine ratio (UACR).

Kidney marker	Cerebral blood flow, in mL/100 g/min	
	Uncorrected	Corrected for hematocrit
	Mean (SD)	
eGFR ≥ 60 ml/min/1.73m^2	37.82 (10.21)	37.19 (10.69)
eGFR < 60 ml/min/1.73m^2	37.82 (10.31)	37.08 (10.82)
UACR < 30 mg/g	38.36 (10.22)	37.46 (10.78)
UACR ≥ 30 mg/g	35.54 (10.05)	35.86 (10.44)

Table S3. Baseline characteristics of trial participants by MRI data completeness

Characteristic	Follow up MRI (n=492)	No Follow up MRI (n=223)	p-value
Age	68.0 (8.4)	67.8 (9.1)	0.8
Female Sex	179 (36.4%)	104 (46.6%)	0.01
Race			0.04
White	323 (65.7%)	122 (54.7%)	
Black	138 (28.1%)	83 (37.2%)	
Hispanic	22 (4.5%)	14 (6.3%)	
Other	9 (1.8%)	4 (1.8%)	
Education			0.3
< high school	36 (7.3%)	17 (7.6%)	
High school diploma	68 (13.8%)	35 (15.7%)	
Post high school	166 (33.7%)	87 (39.0%)	
College degree	222 (45.1%)	84 (37.7%)	
Smoking			0.6
Never	230 (46.8%)	95 (42.6%)	
Former	205 (41.7%)	99 (44.4%)	
Current	57 (11.6%)	29 (13.0%)	
Alcohol			0.02
Non-drinker	180 (38.8%)	107 (51.4%)	
Light Drinker	116 (25.0%)	46 (22.1%)	
Moderate Drinker	108 (23.3%)	33 (15.9%)	
Heavy Drinker	60 (12.9%)	22 (10.6%)	
History of CVD	59 (12.0%)	43 (19.3%)	0.01
ACE Inhibitor/ARB	290 (58.9%)	124 (55.6%)	0.4
Systolic BP, mm Hg	137.5 (16.2)	140.0 (16.8)	0.05
Diastolic BP, mm Hg	77.6 (11.4)	77.7 (11.9)	0.9
eGFR, ml/min/1.73m^2	70.3 (20.5)	70.7 (22.5)	0.8
UACR, mg/g	9.7 (5.4, 20.8)	10.7 (6.4, 33.8)	0.04
Hematocrit*	41.4 (4.2)	40.6 (4.0)	0.1

Results are presented as N and (%), or mean (standard deviation).

P-values based on Chi-square or t-test with the exception of urine albumin to creatinine ratio which is based on Wilcoxon rank sum test

* Measured at closeout

Abbreviations: GFR – glomerular filtration rate, CVD – cardiovascular disease, ACE – angiotensin converting enzyme inhibitor, ARB – angiotensin receptor blocker, BP – blood pressure, UACR – urine albumin to creatinine ratio

Table S3. Effect of SPRINT intervention on change in cerebral blood flow, white matter lesion volume, and total brain volume, stratified by baseline eGFR using the Chronic Kidney Disease Epidemiology equation.

MRI measure	Intensive			Standard			Difference in Change (95% CI)	P for interaction
	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)		
Global cerebral blood flow (mL/100 g/min) eGFR ≥60								0.51
eGFR <60	36.87 (33.42, 40.31)	38.37 (34.74, 42.0)	1.58 (-0.16, 3.17)	35.66 (32.21, 39.12)	34.91 (31.29, 38.52)	-0.76 (-2.45, 0.94)	2.26 (-0.11, 4.62)	
	37.13 (33.19, 41.07)	38.2 (34.05, 42.34)	1.07 (-1, 3.14)	37.69 (33.64, 41.73)	35.09 (30.73, 39.46)	-2.59 (-4.96, -0.23)	3.66 (0.53, 6.8)	
WML volume, asinh(cm^3) eGFR ≥60								0.03
	1.89 (1.75, 2.03)	2.01 (1.87, 2.15)	0.12 (0.08, 0.17)	1.84 (1.7, 1.99)	2.13 (1.98, 2.28)	0.28 (0.23, 0.33)	-0.16 (-0.23, -0.09)	
eGFR <60	2.31 (2.13, 2.49)	2.53 (2.35, 2.72)	0.22 (0.15, 0.29)	2.17 (1.98, 2.36)	2.41 (2.21, 2.6)	0.24 (0.16, 0.32)	-0.02 (-0.12, 0.09)	
Total brain volume (cm^3) eGFR ≥60								0.64
	1139.9 (1129.2, 1150.5)	1109.7 (1098.9, 1120.4)	-30.2 (-32.3, -28.2)	1140.2 (1129.4, 1151.0)	1113.0 (1102.1, 1123.9)	-27.2 (-29.4, -24.9)	-3.0 (-6.1, 0.02)	
eGFR <60	1112.1 (1097.7, 1126.4)	1082.7 (1068.2, 1097.2)	-29.4 (-32.5, -26.2)	1108.5 (1093.7, 1123.3)	1083.4 (1068.5, 1098.4)	-25.1 (-28.5, -21.6)	-4.3 (-9.0, 0.3)	

Interaction p-value is testing the difference in change between eGFR groups. Estimates are based on a linear mixed model adjusting for intracranial volume (except in CBF models) and days since randomization, with random effects for participant and MRI facility. All estimates computed using the baseline mean intracranial volume (except in CBF models) of 1382.03 cm^3, with follow-up estimates computed at 1452 days (3.98 years) post-randomization. For change estimates, negative values denote decreases from baseline, while positive values indicating increases from baseline. Difference in change represents intensive treatment group minus standard treatment group.

SE denotes Standard Error, CI confidence interval, WML white matter lesion, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$.

There were N=671, 713, and 716 participants included in the cerebral blood flow, WML volume, and brain volume analyses, respectively.

Abbreviations: eGFR – estimated glomerular filtration rate, MRI – magnetic resonance imaging, SE - standard error, CI - confidence interval, WML - white matter lesion,

Table S4. Effect of SPRINT intervention on change in cerebral blood flow, white matter lesion volume, and total brain volume, including individuals scanned outside of baseline window.

MRI measure	Intensive			Standard			Difference in Change (95% CI)	P for interaction
	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)		
Global cerebral blood flow (mL/100 g/min)								0.47
eGFR ≥60	36.74 (33.53, 39.96)	38.28 (34.87, 41.69)	1.54 (-0.12, 3.2)	35.57 (32.32, 38.82)	34.98 (31.36, 38.24)	-0.77 (-2.51, 0.96)	2.31 (-0.08, 4.7)	
eGFR <60	37.92 (33.84, 42.01)	39.37 (35.07, 43.66)	1.44 (-0.69, 3.58)	39.2 (35.08, 43.32)	36.84 (32.45, 41.23)	-2.36 (-4.63, -0.1)	3.8 (0.7, 6.91)	
WML volume, asinh(cm^3)								0.19
eGFR ≥60	1.88 (1.72, 2.04)	2.01 (1.84, 2.17)	0.13 (0.08, 0.17)	1.87 (1.7, 2.03)	2.14 (1.97, 2.31)	0.27 (0.22, 0.32)	-0.14 (-0.21, -0.07)	
eGFR <60	2.23 (2.05, 2.40)	2.44 (2.26, 2.61)	0.21 (0.14, 0.28)	2.15 (1.97, 2.32)	2.43 (2.25, 2.61)	0.28 (0.21, 0.35)	-0.07 (-0.16, 0.03)	
Total brain volume (cm^3)								0.83
eGFR ≥60	1139.2 (1128.3, 1150.0)	1108.9 (1097.9, 1119.8)	-30.3 (-32.3, -28.2)	1137. 9 (1126.8, 1149.0)	1110.7 (1099.5, 1121.9)	-27.2 (-29.5, -24.9)	-3.1 (-6.2, -0.03)	
eGFR <60	1113.3 (1098.9, 1127.6)	1084.6 (1070.2, 1099.0)	-28.6 (-31.6, -25.7)	1108.2 (1093.7, 1122.6)	1082.0 (1067.5, 1096.6)	-26.1 (-29.2, -23.0)	-2.5 (-6.8, 1.8)	

Interaction p-value is testing the difference in change between eGFR groups. Estimates are based on a linear mixed model adjusting for intracranial volume (except in CBF models) and days since randomization, with random effects for participant and MRI facility. All estimates computed using the baseline mean intracranial volume (except in CBF models) of 1382.03 cm^3, with follow-up estimates computed at 1452 days (3.98 years) post-randomization. For change estimates, negative values denote decreases from baseline, while positive values indicating increases from baseline. Difference in change represents intensive treatment group minus standard treatment group.

SE denotes Standard Error, CI confidence interval, WML white matter lesion, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$.

There were N=701, 744, and 747 participants included in the cerebral blood flow, WML volume, and brain volume analyses, respectively.

Abbreviations: eGFR – estimated glomerular filtration rate, MRI – magnetic resonance imaging, SE - standard error, CI - confidence interval, WML - white matter lesion,

Table S5. Effect of SPRINT intervention on change in cerebral blood flow, white matter lesion volume, and total brain volume, stratified by albuminuria, including individuals scanned outside baseline window.

MRI measure	Intensive			Standard			Difference in Change (95% CI)	P for interaction
	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)		
Global cerebral blood flow								0.56
ACR <30	36.73 (33.39, 40.07)	38.65 (35.18, 42.12)	1.92 (0.47, 3.37)	36.8 (33.44, 40.16)	35.72 (32.21, 39.23)	-1.08 (-2.64, 0.47)	3.00 (0.89, 5.12)	
ACR ≥30	39.43 (35.05, 43.81)	38.47 (33.47, 43.48)	-0.95 (-4.42, 2.51)	38.1 (33.67, 42.53)	35.87 (30.85, 40.9)	-2.23 (-5.75, 1.3)	1.27 (-3.66, 6.2)	
Transformed WML Volume, asinh(cm^3)								0.06
ACR <30	1.92 (1.81, 2.03)	2.05 (1.94, 2.16)	0.13 (0.09, 0.17)	1.9 (1.78, 2.01)	2.18 (2.06, 2.3)	0.28 (0.23, 0.33)	-0.15 (-0.21, -0.09)	
ACR ≥30	2.31 (2.08, 2.53)	2.53 (2.3, 2.76)	0.22 (0.14, 0.31)	2.3 (2.06, 2.55)	2.54 (2.29, 2.79)	0.24 (0.15, 0.33)	-0.02 (-0.14, 0.11)	
Total brain volume (cm^3)								0.26
ACR <30	1130.0 (1116.2, 1143.8)	1100.2 (1086.3, 1114.1)	-29.8 (-31.7, -27.9)	1124.9 (1110.9, 1138.8)	1097.1 (1083.1, 1111.0)	-27.9 (-29.9, -25.8)	-1.94 (-4.73, 0.85)	
ACR ≥30	1113.6 (1094.2, 1132.9)	1084.2 (1064.6, 1103.7)	-29.4 (-33.5, -25.3)	1112.0 (1092.2, 1131.8)	1088.2 (1068.2, 1108.1)	-23.8 (-28.2, -19.5)	-5.53 (-11.52, 0.46)	

Interaction p-value is testing the difference in change between UACR groups. Estimates are based on a linear mixed model adjusting for intracranial volume (except in CBF models) and days since randomization, with random effects for participant and MRI facility. All estimates computed using the baseline mean intracranial volume (except in CBF models) of 1382.03 cm^3, with follow-up estimates computed at 1452 days (3.98 years) post-randomization. For change estimates, negative values denote decreases from baseline, while positive values indicating increases from baseline. Difference in change represents intensive treatment group minus standard treatment group.

SE denotes Standard Error, CI confidence interval, WML white matter lesion, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$.

There were N=675, 718, and 721 participants included in the cerebral blood flow, WML volume, and brain volume analyses, respectively.

Abbreviations: eGFR – estimated glomerular filtration rate, MRI – magnetic resonance imaging, SE - standard error, CI - confidence interval, WML - white matter lesion,