Supplementary Online Content

The SPRINT MIND Investigators for the SPRINT Research Group. Association of intensive vs standard blood pressure control with cerebral white matter lesions. *JAMA*.

doi:10.1001/jama.2019.10551

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

eMethods. Multiple Imputation and Inverse Probability Weighting to Assess the Influence of Selection Into the Magnetic Resonance Imaging (MRI) Substudy and Missing Follow-up MRI Scans

There are two potential sources of bias that could influence the results of this imaging substudy. The first is a selection bias, as participants were approached and screened for participation in the imaging sub-study subsequent to randomization. The second potential source of bias is missing data due to participants that did not complete the follow-up MRI scan. We conducted sensitivity analyses to attempt to address both of these issues simultaneously using a combination of inverse probability weighting and multiple imputation (MI).[1] The multiple imputation component of these analyses entails the common missing at random assumption conditional on the variables used in the multiple imputation model.[2]

We estimated inverse probability weights for completing the baseline MRI scan, using the 1,267 participants that were screened for participation (**FIGURE 1**). We estimated the weights using logistic regression using the follow-up baseline variables: treatment group, age, sex, race/ethnicity (White, Black, Hispanic, or Other), education (less than high school education, high school graduate, additional training beyond high school but no college degree, college graduate or higher), polypharmacy (<5 medications, 5 to <10 medications, 10 or more medications), smoking status (never, former, or current smoker), history of cardiovascular disease (CVD, Yes vs No), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), HDL cholesterol, serum bicarbonate, estimated glomerular filtration rate (eGFR), log urine albumin to creatinine ratio, Montreal Cognitive Assessment (MoCA) score, Logical Memory (LM) II score, Digit Symbol Coding (DSC) score, physical and mental component summary scores from the VR-12, and a PHQ-9 score ≥ 10 (Yes vs No). Because of a small degree of sporadic missing data amongst these baseline variables, we first imputed

missing values (10 datasets) based on the conditional specification shown in the table below. The base set of predictors for those imputations included the following set of variables with no missing data: age, sex, race/ethnicity, education, history of CVD, smoking status, SBP, DBP, and polypharmacy. For the imputation models, Linear denotes linear regression; PMM, predictive mean matching; and Logistic, logistic regression.

Auxiliary Variable	**No. Missing (%)**	**Imputation Model**	**Predictors**
Body Mass Index (BMI)	6 (0.5)	Linear	Base Set
HDL Cholesterol (HDL)	4 (0.3)	Linear	Base Set + BMI
Serum Bicarbonate (CO2)	2 (0.2)	Linear	Base Set + BMI + HDL
eGFR	8 (0.6)	Linear	Base Set + BMI + HDL + CO2
Log Urine Albumin to Creatinine Ratio (log UACR)	48 (3.8)	Linear	Base Set + BMI + HDL + CO2+ eGFR
MoCA Score (MoCA)	15 (1.2)	PMM	Base Set + BMI + HDL + CO2 + eGFR + log UACR
Logical Memory (LM) form II	16 (1.3)	PMM	Base Set + BMI + HDL + CO2 + eGFR + log UACR + MoCA
Digit Symbol Coding Score (DSC)	18 (1.4)	PMM	Base Set + BMI + HDL + CO2 + eGFR + log UACR + MoCA + LM
VR-12 Physical Component Summary Score (VR-12 PCS)	1 (<0.1)	Linear	Base Set + BMI + HDL + CO2 + eGFR +log UACR + MoCA + LM + DSC
VR-12 Mental Component Summary Score (VR-12 MCS)	1 (<0.1)	Linear	Base Set + BMI + HDL + CO2 + eGFR + log UACR + MoCA + LM + DSC + VR-12 PCS
PHQ-9 Score ≥ 10	2 (0.2)	Logistic	Base Set + BMI + HDL + CO2 + eGFR + log UACR + MoCA + LM + DSC + VR-12 PCS + VR-12 MCS

Within each imputed dataset from the step above, we then imputed follow-up values for transformed white matter lesion volume and total brain volume, separately by treatment group, as a function of: age, sex, race/ethnicity, education, polypharmacy, smoking status, history of CVD, SBP, DBP, BMI, HDL cholesterol, serum bicarbonate, eGFR, log-transformed urine albumin-to-creatinine ratio, scores on the MoCA, LM, and DSC, baseline value of the MRI outcome of interest, whether or not the participant had a primary cardiovascular event after the baseline MRI but prior to their follow-up MRI, intracranial volume (set to baseline intracranial volume), and days since randomization (set to 1452 days). Note that we did not impute follow-up volumes for participants that died prior to the timing of the follow-up MRI scans. We then fit linear mixed models to each imputed dataset, including random effects for participant and MRI facility as well as incorporating the inverse probability weights. The multiple imputation procedure was implemented using *proc mi* and *proc mianalyze* in SAS v9.4 (SAS, Cary, NC).

References

1. Seaman SR, White IR, Copas AJ, Li L. Combining multiple imputation and inverse-probability weighting. *Biometrics*. 2012;68(1):129-137. doi:10.1111/j.1541-0420.2011.01666.x.
2. Little RJ, Rubin DB. *Statistical Analysis with Missing Data*. John Wiley and Sons, Inc.; 2014.

eTABLE 1. Additional Baseline Characteristics of Participants With a Measured White Matter Lesion Volume From the Baseline Magnetic Resonance Imaging Scan, by Treatment Group

Variable	Intensive treatment N=355	Standard treatment N=315
Education, No. (%)		
Less than high school	25 (7.0)	28 (8.9)
High school graduate	56 (15.8)	47 (14.9)
Post high school training	127 (35.8)	112 (35.6)
College graduate or greater	147 (41.4)	128 (40.6)
Polypharmacy, No. (%)		
<5 medications	142 (40.0)	147 (46.7)
5 to <10 medications	154 (43.4)	120 (38.1)
10 or more medications	59 (16.6)	48 (15.2)
Smoking status, No. (%)		
Never smoker	153 (43.1)	148 (47.0)
Former smoker	153 (43.1)	129 (41.0)
Current smoker	49 (13.8)	38 (12.1)
Body Mass Index, mean (SD), kg/m^2	29.7 (5.3)	29.8 (5.4)
HDL cholesterol, mean (SD), mg/dL	53.6 (14.3)	53.5 (14.7)
Serum bicarbonate, mean (SD), mmol/L	26.4 (2.5)	26.5 (2.6)
Log urine albumin to creatinine ratio, mean (SD), log(mg/g)	2.5 (1.2)	2.6 (1.2)
Logical Memory form II, median [IQR][a]	9 [6 to 11]	8 [6 to 11]
Digit Symbol Coding Test, median [IQR][b]	52 [42 to 62]	52 [42 to 62]
VR-12 PCS, mean (SD)[c]	45.3 (10.0)	46.1 (9.2)
VR-12 MCS, mean (SD)[c]	52.7 (9.4)	53.2 (8.9)
PHQ-9 score≥10, No. (%)[d]	21 (5.9)	21 (6.7)

SD denotes standard deviation; HDL, high density lipoprotein; IQR, interquartile range; VR-12 Veterans RAND 12-item health survey; PCS, Physical Component Summary; MCS, Mental Component Summary; PHQ-9, Patient Health Questionnaire 9-item depression scale;

SI conversion factors: To convert HDL cholesterol to mmol/L, multiply by 0.0259.

[a]Subtest of the Wechsler Memory Scale. Scores range from 0 to 14, with higher scores denoting a better performance. [b]Subtest of the Wechsler Memory Scale. Scores range from 0 to 135, with higher scores denoting better performance. [c]Scores on the PCS and MCS of the VR-12 are standardized with a mean of 50 and a standard deviation of 10. Scores range from 0 to 100, with higher scores denoting better physical health and mental health, respectively. [d]Scores on the PHQ-9 range from 0 to 27, with higher scores indicating greater severity of depressive symptoms and with scores of 10 or higher suggesting moderate-to-severe depressive symptoms.

eTABLE 2. Baseline Characteristics of Participants in the MRI Substudy Versus Remaining Trial Participants

Variable	**In MRI Substudy** N=670	**Not in MRI Substudy** N=8688[a]	P Value
Randomized to Intensive treatment, No. (%)	355 (53.0)	4322 (49.7)	0.12
Age, mean (SD), years	67.3 (8.2)	68.0 (9.5)	0.08
Age 75 year or older, No. (%)	150 (22.4)	2486 (28.6)	0.001
Sex, No (%)			0.007
Male			
Female	271 (40.4)	3061 (35.2)	
Race/Ethnicity, No. (%)			<0.001
White	406 (60.6)	4990 (57.4)	
Black	218 (32.5)	2584 (29.7)	
Hispanic[b]	36 (5.4)	948 (10.9)	
Other[c]	10 (1.5)	166 (1.9)	
Education, No. (%)			0.39
Less than high school	53 (7.9)	823 (9.5)	
High school graduate	103 (15.4)	1433 (16.5)	
Post High school training	239 (35.7)	3072 (35.4)	
College graduate or greater	275 (41.0)	3360 (38.7)	
Smoking status, No. (%)			0.94
Never smoker	301 (44.9)	3846 (44.3)	
Former smoker	282 (42.1)	3690 (42.5)	
Current smoker	87 (13.0)	1152 (13.3)	
Polypharmacy, No. (%)			0.32
<5 medications	289 (43.1)	3783 (43.5)	
5 to <10 medications	274 (40.9)	3696 (42.5)	
10 or more medications	107 (16.0)	1209 (13.9)	
Body Mass Index, mean (SD), kg/m^2	29.8 (5.4)	29.9 (5.8)	0.70
History of CVD, No. (%)	93 (13.9)	1784 (20.5)	<0.001
Systolic BP, mean (SD), mm Hg	138.0 (16.6)	139.8 (15.5)	0.004
Systolic BP tertile, No. (%)			<0.001
≤129 mmHg	229 (34.2)	2095 (24.1)	
>129 to <143 mm Hg	207 (30.9)	3174 (36.5)	
≥143 mm Hg	234 (34.9)	3419 (39.4)	
Diastolic BP, mean (SD), mm Hg	77.9 (11.4)	78.1 (12.0)	0.54
Orthostatic hypotension, No. (%)[d]	43 (6.4)	642 (7.4)	0.39
eGFR, mean (SD), ml/min/1.73 m^2 [e]	72.3 (20.6)	71.7 (20.6)	0.50

Variable	In MRI Substudy N=670	Not in MRI Substudy N=8688[a]	P Value
eGFR<60 ml/min/1.73 m^2, No. (%)[e]	184 (27.5)	2461 (28.5)	0.63
Log urine albumin to creatinine ratio, mean (SD), log(mg/g)	2.6 (1.2)	2.6 (1.2)	0.90
HDL cholesterol, mean (SD), mg/dL	53.5 (14.5)	52.8 (14.5)	0.22
Serum bicarbonate, mean (SD), mmol/L	26.5 (2.5)	26.3 (2.6)	0.13
Montreal Cognitive Assessment, median [IQR][f]	24 [21 to 26]	23 [20 to 26]	<0.001
Logical Memory form II, median [IQR][g]	9 [6 to 11]	8 [6 to 11]	0.03
Digit Symbol Coding test, median [IQR][h]	52 [42 to 62]	51 [41 to 61]	0.05
VR-12 PCS, mean (SD)[i]	45.6 (9.6)	44.6 (10.3)	0.01
VR-12 MCS, mean (SD)[i]	52.9 (9.2)	53.2 (9.6)	0.49
PHQ-9 score≥10, No. (%)[j]	42 (6.3)	687 (8.0)	0.14

SD denotes standard deviation; CVD, cardiovascular disease; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; IQR, interquartile range; VR-12 Veterans RAND 12-item health survey; PCS, Physical Component Summary; MCS, Mental Component Summary; PHQ-9, Patient Health Questionnaire 9-item depression scale.

SI conversion factors: To convert HDL cholesterol to mmol/L, multiply by 0.0259.

[a] Excludes 3 participants without a measured white matter lesion volume at baseline, but who completed baseline MRI scan with a measurement of total brain volume that passed quality control. [b] Hispanic race/ethnicity encompasses a self-report of being of Spanish, Hispanic, or Latino origin, independent of any other race/ethnicity designation. [c] Other race/ethnicity includes categories of Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, or other. [d] Defined as a standing systolic BP minus seated systolic BP ≤ -20 mm Hg or a standing diastolic BP minus seated diastolic BP ≤ -10 mm Hg. [e] Based on the 4-variable Modification of Diet in Renal Disease equation. [f]Scores range from 0 to 30, with higher scores denoting better cognitive function. [g]Subtest of the Wechsler Memory Scale. Scores range from 0 to 14, with higher scores denoting a better performance. [h]Subtest of the Wechsler Memory Scale. Scores range from 0 to 135, with higher scores denoting better performance. [i] Scores on the PCS and MCS of the VR-12 are standardized with a mean of 50 and a standard deviation of 10. Scores range from 0 to 100, with higher scores denoting better physical health and mental health, respectively. [j]Scores on the PHQ-9 range from 0 to 27, with higher scores indicating greater severity of depressive symptoms and with scores of 10 or higher suggesting moderate-to-severe depressive symptoms.

eTABLE 3. Baseline Characteristics of Participants in the MRI Substudy With and Without a Follow-up MRI With Measured White Matter Lesion Volume

Variable	**Follow-up MRI** N=449	**No Follow-up MRI** N=221	P Value
Randomized to Intensive treatment, No. (%)	249 (55.5)	106 (48.0)	0.08
Age, mean (SD), years	67.2 (7.8)	67.6 (9.0)	0.48
Age 75 years or older, No. (%)	91 (20.3)	59 (26.7)	0.08
Sex, No. (%)			
Male			
Female	167 (37.2)	104 (47.1)	0.02
Race/Ethnicity, No. (%)			0.10
White	287 (63.9)	119 (53.8)	
Black[a]	134 (29.8)	84 (38.0)	
Hispanic[b]	22 (4.9)	14 (6.3)	
Other	6 (1.3)	4 (1.8)	
Education, No. (%)			0.72
Less than high school	35 (7.8)	18 (8.1)	
High school graduate	66 (14.7)	37 (16.7)	
Post high school training	157 (35.0)	82 (37.1)	
College graduate or greater	191 (42.5)	84 (38.0)	
Smoking status, No. (%)			0.86
Never smoker	205 (45.7)	96 (43.4)	
Former smoker	186 (41.4)	96 (43.4)	
Current smoker	58 (12.9)	29 (13.1)	
Polypharmacy, No. (%)			0.04
<5 medications	204 (45.4)	85 (38.5)	
5 to <10 medications	184 (41.0)	90 (40.7)	
10 or more medications	61 (13.6)	46 (20.8)	
Body Mass Index, mean (SD), kg/m^2	29.5 (5.1)	30.3 (5.7)	0.10
History of CVD, No. (%)	52 (11.6)	41 (18.6)	0.02
Systolic BP, mean (SD), mm Hg	137.0 (16.5)	140.1 (16.8)	0.02
Systolic BP tertile, No. (%)			0.18
≤129 mm Hg	159 (35.4)	70 (31.7)	
>125 to <143 mm Hg	144 (32.1)	63 (28.5)	
≥143 mm Hg	146 (32.5)	88 (39.8)	
Diastolic BP, mean (SD), mm Hg	77.8 (11.4)	78.0 (11.5)	0.81
Orthostatic hypotension, No. (%)[c]	35 (7.8)	8 (3.6)	0.06
eGFR, mean (SD), ml/min/1.73 m^2 [d]	72.4 (19.9)	72.0 (22.1)	0.82
eGFR<60 ml/min/1.73 m^2, No. (%)[d]	121 (26.9)	63 (28.8)	0.69

Variable	**Follow-up MRI** N=449	**No Follow-up MRI** N=221	P Value
Log urine albumin to creatinine ratio, mean (SD), log(mg/g)	2.5 (1.1)	2.8 (1.4)	0.004
HDL cholesterol, mean (SD), mg/dL	53.8 (15.2)	53.1 (12.9)	0.57
Serum bicarbonate, mean (SD), mmol/L	26.5 (2.4)	26.3 (2.7)	0.23
Montreal Cognitive Assessment, median [IQR][e]	24 [21.25 to 27]	23 [20 to 26]	0.01
Logical Memory form II, median [IQR][f]	9 [6 to 11]	9 [6 to 11]	0.16
Digit Symbol Coding test, median [IQR][g]	53 [43 to 63]	48 [39 to 58]	<0.001
VR-12 PCS, mean (SD)[h]	46.5 (9.4)	43.9 (9.9)	0.001
VR-12 MCS, mean (SD)[h]	53.2 (8.7)	52.4 (10.2)	0.33
PHQ-9 score≥10, No. (%)[i]	23 (5.1)	19 (8.6)	0.12
Intracranial volume, mean (SD), cm^3	1390.7 (144.3)	1362.3 (150.9)	0.02
Total brain volume, mean (SD), cm^3	1142.8 (111.8)	1114.6 (117.2)	0.003
WML volume, median [IQR], cm^3	3.1 [1.6 to 6.1]	3.5 [1.5 to 6.3]	0.24
Transformed WML volume, mean (SD), asinh(cm^3)	2.0 (1.0)	2.1 (1.0)	0.20

SD denotes standard deviation; CVD, cardiovascular disease; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; IQR, interquartile range; VR-12 Veterans RAND 12-item health survey; PCS, Physical Component Summary; MCS, Mental Component Summary; PHQ-9, Patient Health Questionnaire 9-item depression scale; WML, white matter lesion; asinh, inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$.

SI conversion factors: To convert HDL cholesterol to mmol/L, multiply by 0.0259.

[a] Hispanic race/ethnicity encompasses a self-report of being of Spanish, Hispanic, or Latino origin, independent of any other race/ethnicity designation. [b] Other race/ethnicity includes categories of Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, or other. [c] Defined as a standing systolic BP minus seated systolic BP ≤ -20 mm Hg or a standing diastolic BP minus seated diastolic BP ≤ -10 mm Hg. [d] Based on the 4-variable Modification of Diet in Renal Disease equation. [e] Scores range from 0 to 30, with higher scores denoting better cognitive function. [f]Subtest of the Wechsler Memory Scale. Scores range from 0 to 14, with higher scores denoting a better performance. [g]Subtest of the Wechsler Memory Scale. Scores range from 0 to 135, with higher scores denoting better performance. [h] Scores on the PCS and MCS of the VR-12 are standardized with a mean of 50 and a standard deviation of 10. Scores range from 0 to 100, with higher scores denoting better physical health and mental health, respectively. [i]Scores on the PHQ-9 range from 0 to 27, with higher scores indicating greater severity of depressive symptoms and with scores of 10 or higher suggesting moderate-to-severe depressive symptoms.

eTABLE 4. Changes in Small Vessel Ischemic Disease Lesion Volume by Treatment Group

	Intensive Treatment			Standard Treatment				
Outcome	Baseline (95% CI) No.	Follow-up (95% CI) No.	Change (95% CI)	Baseline (95% CI) No.	Follow-up (95% CI) No.	Change (95% CI)	Difference in Change (95% CI)	P Value
Transformed SVID Volume, asinh(cm^3)	2.19 (2.04, 2.34) 355	2.32 (2.17, 2.47) 249	0.12 (0.08, 0.16)	2.16 (2.00, 2.31) 315	2.42 (2.26, 2.57) 200	0.26 (0.21, 0.30)	-0.14 (-0.20, -0.07)	<0.001
SVID Volume, cm^3 (RLMM)	5.42 (4.81, 6.03) 355	6.34 (5.72, 6.97) 249	0.92 (0.67, 1.16)	5.21 (4.56, 5.86) 315	6.74 (6.07, 7.41) 200	1.53 (1.26, 1.79)	-0.61 (-0.97, -0.25)	-

Small Vessel Ischemic Disease (SVID) volume encompasses abnormal lesions in the white matter, gray matter, and basal ganglia. Estimates based on a linear mixed model, adjusting for intracranial volume and days since randomization, with random effects for participant and MRI facility. All estimates computed using the baseline mean intracranial volume 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 indicate increases from baseline. Difference in Change represents intensive treatment group minus standard treatment group. CI denotes confidence interval, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$, and RLMM robust linear mixed model.

eTABLE 5. Sensitivity Analyses for Magnetic Structural Outcomes Based on Inverse Probability Weighting and Multiple Imputation

	Intensive Treatment			Standard Treatment				
Outcome	Baseline (95% CI) No.	Follow-up (95% CI) No.	Change (95% CI)	Baseline (95% CI) No.	Follow-up (95% CI) No.	Change (95% CI)	Difference in Change (95% CI)	P Value
Transformed WML Volume, asinh(cm^3)	1.99 (1.86, 2.13) 355	2.14 (2.00, 2,27) 341	0.14 (0.10, 0.18)	1.97 (1.83, 2.11) 315	2.26 (2.12, 2.39) 304	0.29 (0.24, 0.33)	-0.14 (-0.20, -0.08)	<0.001
Total Brain Volume, cm^3	1134.6 (1125.3, 1143.8) 356	1104.7 (1095.3, 1114.0) 342	-29.9 (-32.4, -27.5)	1134.8 (1125.4, 1144.3) 317	1107.1 (1097.4, 1116.8) 306	-27.7 (-31.0, -24.5)	-2.2 (-6.5, 2.2)	0.33

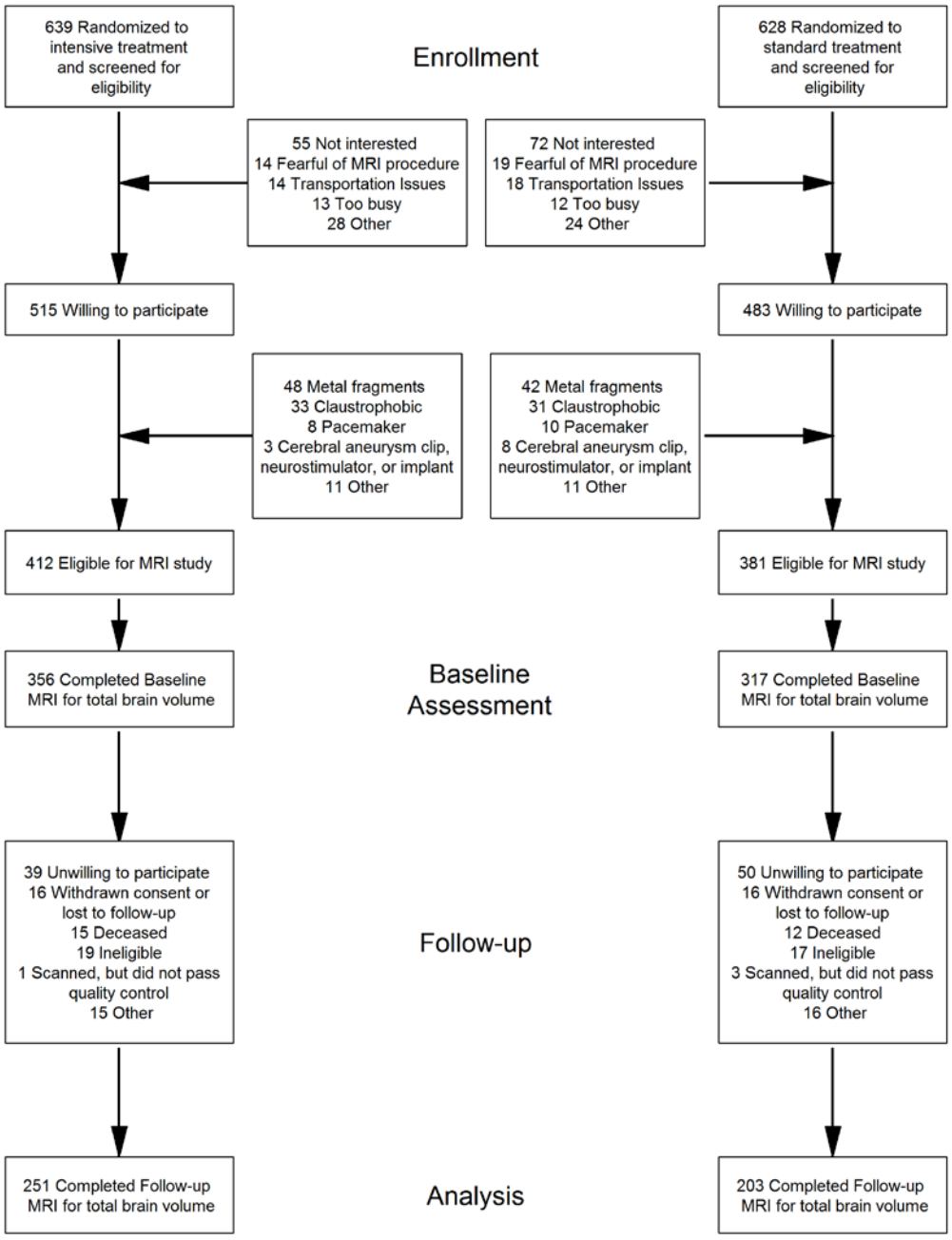
Estimates based on a linear mixed model, adjusting for intracranial volume and days since randomization, with random effects for participant and MRI facility. All estimates computed using the baseline mean intracranial volume of 1382.03 cm^3, with follow-up estimates computed at 1452 days (3.98 years) post-randomization. For change estimates, negative values denote decreases from baseline, while positive values indicate increases from baseline. Difference in Change represents intensive treatment group minus standard treatment group. CI denotes confidence interval, WML white matter lesion, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$.

eTABLE 6. Association of Change in Structural Magnetic Resonance Imaging Outcomes by Adjudicated Cognitive Status

Outcome	Adjudicated Cognitive Outcome	Baseline (95% CI)	Follow-up (95% CI)	Change (95% CI)	P value
Transformed WML Volume, asinh(cm^3)	No Impairment	1.92 (1.84, 2.01)	2.13 (2.04, 2.21)	0.20 (0.17, 0.24)	-
	Mild Cognitive Impairment	2.61 (2.22, 2.99)	2.86 (2.47, 3.24)	0.25 (0.11, 0.39)	0.52
	Probable Dementia	1.78 (1.06, 2.49)	2.33 (1.62, 3.04)	0.55 (0.31, 0.79)	0.005
	Mild Cognitive Impairment or Probable Dementia	2.42 (2.08, 2.76)	2.75 (2.41, 3.09)	0.33 (0.20, 0.45)	0.06
Total Brain Volume	No Impairment	1143.2 (1135.8, 1150.6)	1114.5 (1107.1, 1121.9)	-28.7 (-30.0, -27.3)	-
	Mild Cognitive Impairment	1137.8 (1120.2, 1155.4)	1106.4 (1088.8, 1124.0)	-31.4 (-37.6, -25.2)	0.40
	Probable Dementia	1119.4 (1088.8, 1150.1)	1069.5 (1039.0, 1100.1)	-49.9 (-60.6, -39.2)	<0.001
	Mild Cognitive Impairment or Probable Dementia	1134.0 (1118.2, 1149.8)	1097.9 (1082.1, 1113.8)	-36.1 (-30.6, -41.5)	0.01

Least Squares estimates based on a linear mixed model, adjusting for intracranial volume, days since randomization, age, and sex, with random effects for participant and MRI facility. Follow-up estimates computed at 1452 days post-randomization. For change estimates, negative values denote decreases from baseline, while positive values indicate increases from baseline. CI denotes confidence interval, WML white matter lesion, asinh inverse hyperbolic sine transformation, $f(x) = \log(x + (x^2 + 1)^{0.5})$. P values denote comparison for difference in change from baseline to follow-up, with the reference group being participants with no cognitive impairment.

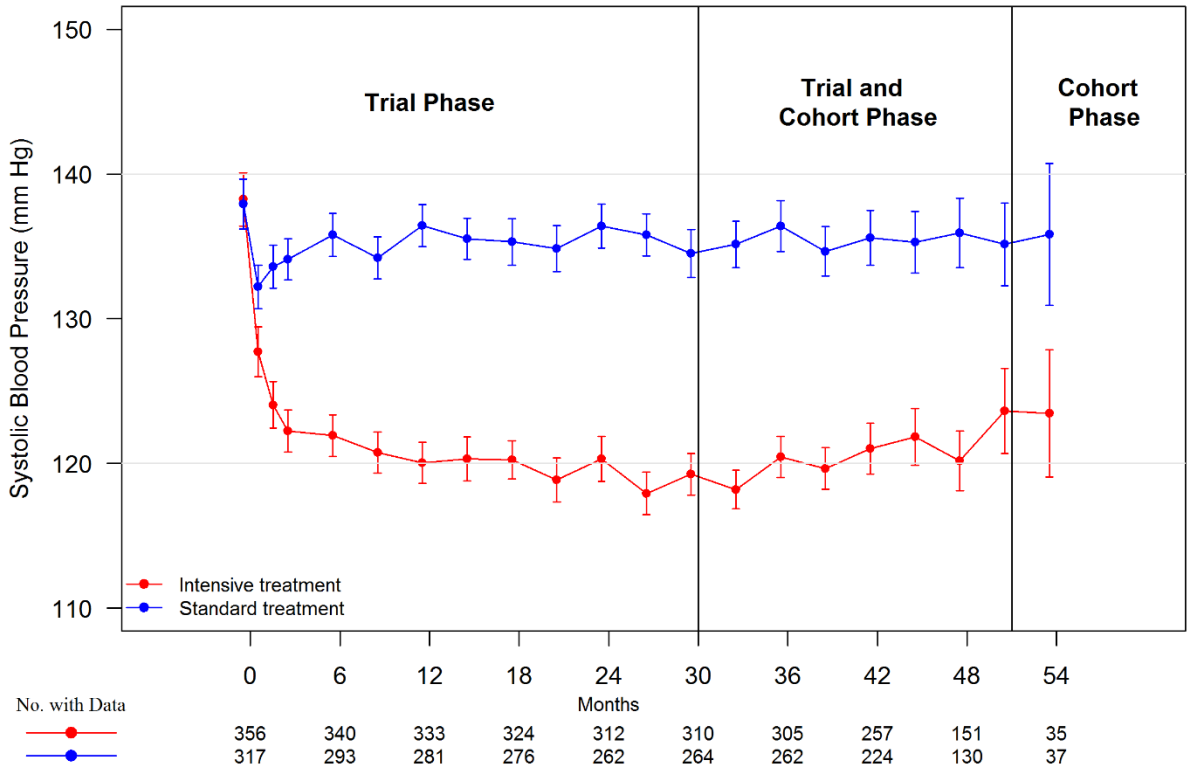
eFIGURE 1. Eligibility, Randomization, and Follow-up for Participants in the MRI Substudy for the Secondary Outcome of Total Brain Volume



Other reasons for unwillingness to participate include: participant could not lie flat for extended period of time (N=7), participant reported metal in body prior to formal screening (N=8), participant concerns about stent or other cardiac device (N=8), concerns about body size (N=2), other reasons (N=7), and unknown reason (N=22).

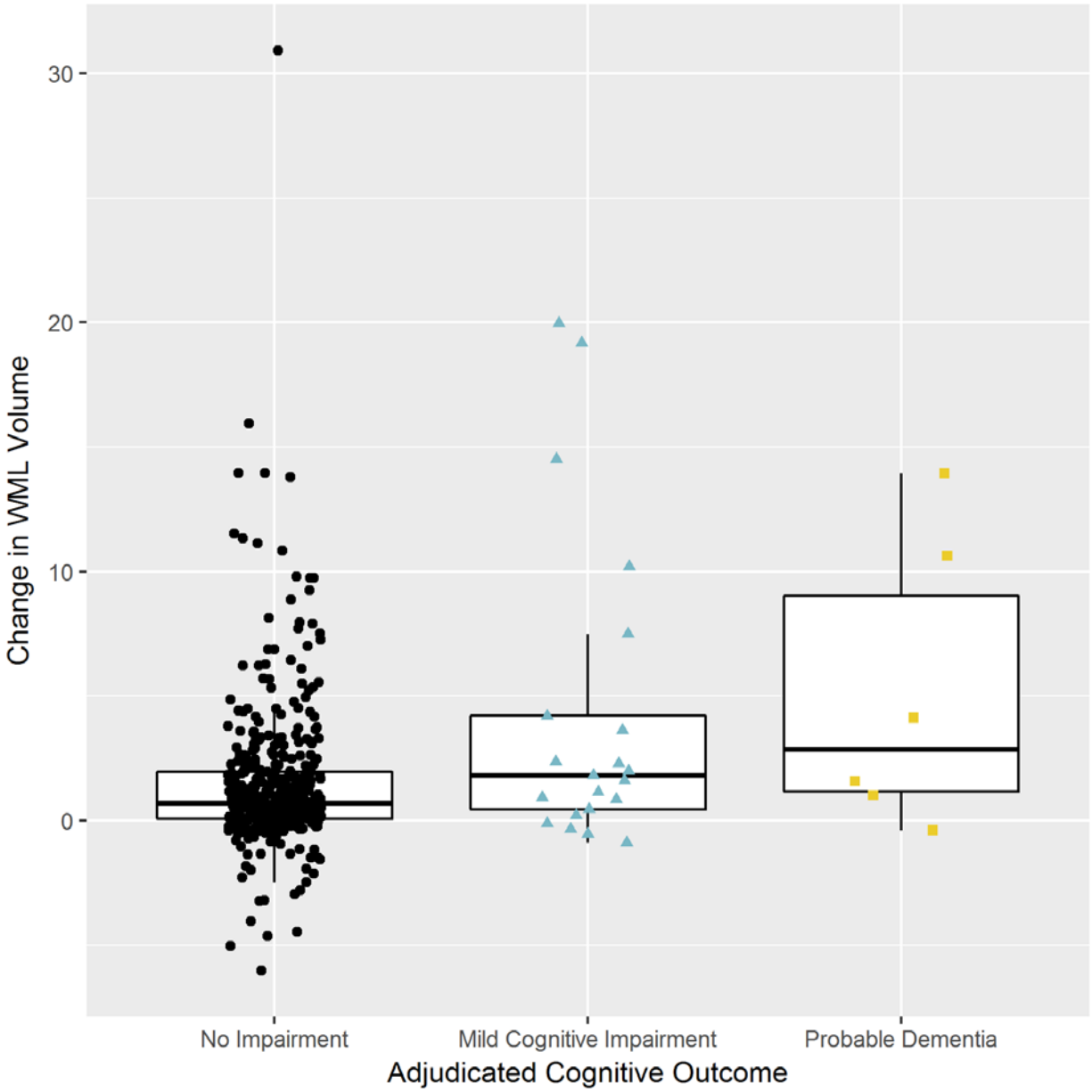
Other reasons for ineligibility include: participant concerns about stent or other cardiac device (N=8), use of pain pump (N=2), prolonged hospitalization (N=2), participant declined consent (N=2), participant too large for MRI scanner (N=1), and other reasons (N=7).

eFIGURE 2. Mean Systolic Blood Pressure by Treatment Group for Participants in the MRI Substudy



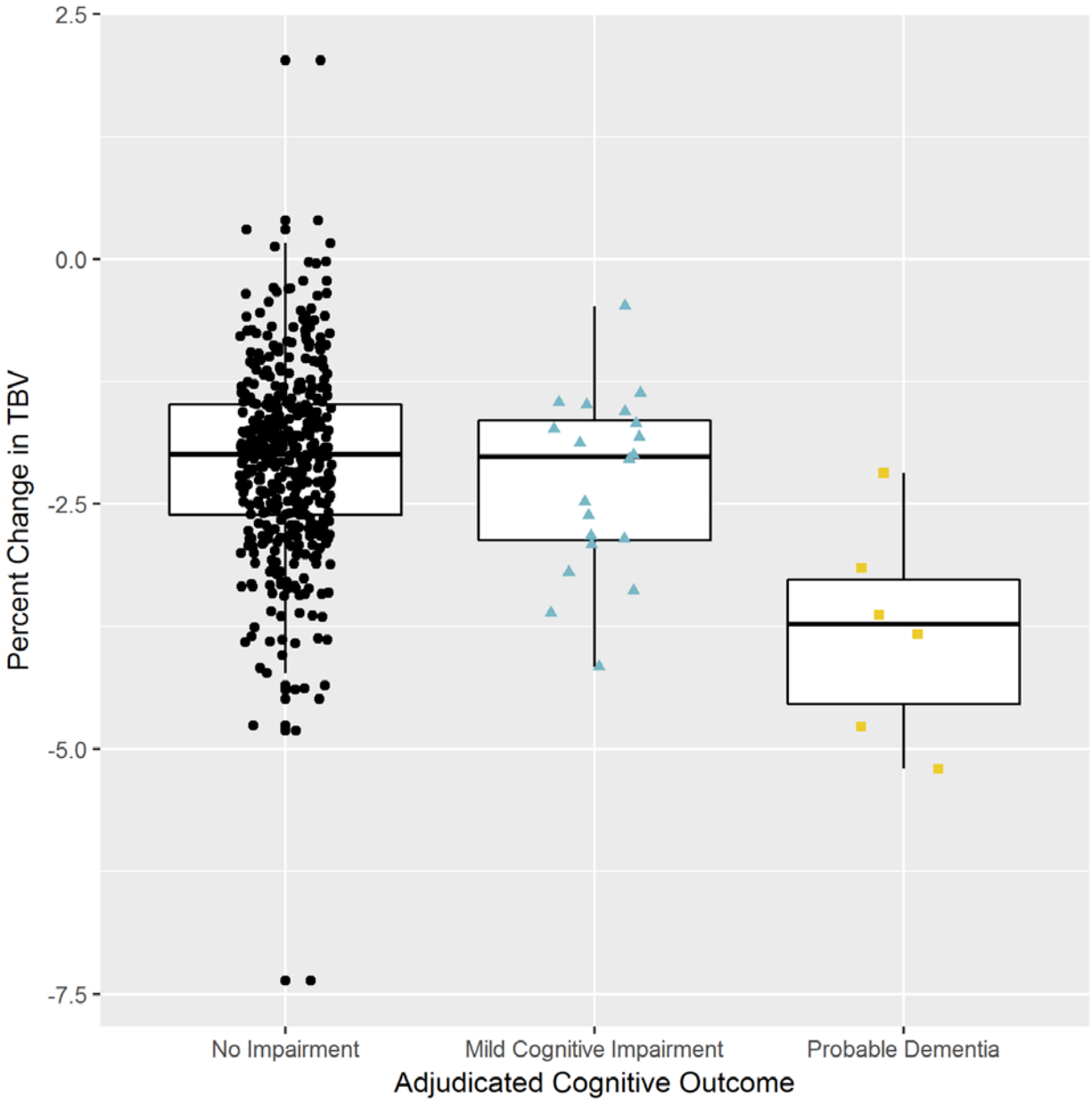
The systolic blood pressure (SBP) target was <120 mmHg in the Intensive treatment group, and <140 mmHg in the Standard treatment group. Trial phase includes follow-up through the decision to stop the trial intervention on 8/20/2015, while cohort phase denotes visits that occurred after that date. Points indicate least square means with error bars denoting 95% Confidence Intervals.

eFIGURE 3. Association Between Change in White Matter Lesion Volume and Adjudicated Cognitive Status



Change in White Matter Lesion (WML) volume denotes follow-up minus baseline, in cm^3.

eFIGURE 4. Association Between Change in Total Brain Volume and Adjudicated Cognitive Status



Percent change in Total Brain Volume (TBV) denotes 100 X [($TBV_{Follow\text{-}up}$ / $ICV_{Follow\text{-}up}$) – ($TBV_{Baseline}$ / $ICV_{Baseline}$)], where ICV represents intracranial volume.