Online-Only Data Supplement

Association of Total Medication Burden with Intensive and Standard Blood Pressure Control and Clinical Outcomes

A Secondary Analysis of the Systolic Blood Pressure Intervention Trial (SPRINT)

Short title: Derington et al medication burden in SPRINT

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Supplementary Methods

Definition of Medication Burden

The definition of "polypharmacy" is highly variable; one recent review cited over 138 definitions of polypharmacy in the current literature.[1] Polypharmacy may be defined using numerical counts, ordinal terms (i.e., "minor," "moderate," "major," "excessive," "severe"), or duration of therapy (using terms such as "chronic" or "persistent," or numerical thresholds).[1] Numerical cutoffs of at least 2, 3, 4, 5, 6, 7, and 9 medications have been used.[2-34] Moreover, the inclusion of over-the-counter medications, vitamins, and herbal supplements in the definition of polypharmacy is not well-described. Several studies have found that up to 87% of adults take at least one over-the-counter or herbal/dietary supplement;[35–39] however, documentation and inclusion of these items in medication reconciliation is inconsistent, comprising 68-76.6% of medication reconciliation omissions.[40,41] Furthermore, the inclusion of as-needed medications and non-oral formulations (e.g., creams, inhalers, nasal sprays) in the definition of polypharmacy is not well-elucidated in current literature, which often broadly describe exposures as "concurrently-prescribed medications."

We have selected five or more medications as the cutoff for polypharmacy given that the majority of the polypharmacy literature also uses this threshold. Our study reinforces the need for standardized processes to collect medication use data, including nonprescription products and compounds used as-needed, even within the randomized clinical trial setting.

Medication data standardization and cleaning

All data on medication lists were recorded at the study visits as unstructured, free-text strings (e.g., "atorvastatin 20 mg daily"). Three pharmacists (C.G.D., A.P.B., J.B.K.) manually reviewed, cleaned, and categorized all free-text medication names and dosages strings into structured data fields (i.e., separate fields for drug name, class, and dose).

Outcomes measurement

Blood Pressure Control

BP was measured three times per visit using an automated device (Omron-HEM-907 XL) by trained clinical staff every month for the first three months, then every three months thereafter.[42,43] For each measurement, participants were in the seated position; had rested quietly for five minutes in a chair with back support, legs uncrossed; and had waited one minute between readings. The mean of the three BP measurements was recorded as the BP for the study visit. A participant was considered to have "controlled" hypertension if their SBP was less than their randomized treatment goal at the study visit. Although clinician investigators were encouraged to use medications with strong

CVD event data, blood pressure medication regimens were initiated, modified, or discontinued based on investigator decisions.[42]

Serious Adverse Events

SAEs were defined in SPRINT as events that were fatal or life-threatening, resulted in clinically significant or persistent disability, required or prolonged a hospitalization, or judged by the investigator to represent clinically significant harm to the participant that might require medical or surgical intervention to prevent one of the other events listed above.[42,44] Participants were queried for SAEs at quarterly clinic visits or reported SAEs in between clinic visits to study coordinators.[42]

Patient-Reported Outcomes

Medication adherence and treatment satisfaction were measured concurrently at the baseline, 12-month, and 48-month visits.[42] Scores for the MMAS-8 range from zero to eight, with a score of less than six representing “low” adherence, a score between six and less than eight representing “medium” adherence, and a score of eight representing “high” adherence.[45,46] The modified TSQM prompted the participant to qualify their satisfaction with both BP care and BP treatment using a Likert scale of “very satisfied,” “satisfied,” “neutral,” “dissatisfied,” and “very dissatisfied.”[42,47]

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Supplementary Tables

Table S1: Count of Medications at Baseline and Follow-Up Visits by Treatment Group and Number of Baseline Medications

Time of Medication Assessment	Intensive treatment		Standard treatment	
	No. of baseline medications		No. of baseline medications	
	< 5	≥ 5	< 5	≥ 5
Baseline	**(N = 2,793)**	**(N = 1,885)**	**(N = 2,800)**	**(N = 1,883)**
Total medications	3 [2, 4]	6 [5, 8]	3 [2, 4]	6 [5, 8]
Antihypertensives	2 [1, 2]	3 [2, 3]	1 [1, 2]	3 [2, 3]
Non-antihypertensives	1 [0, 2]	4 [3, 5]	1 [0, 2]	4 [3, 5]
1 Year Follow Up	**(N = 2,550)**	**(N = 1,725)**	**(N = 2,560)**	**(N = 1,703)**
Total medications	4 [3, 5]	6 [5, 8]	3 [2, 4]	6 [4, 7]
Antihypertensives	3 [2, 3]	3 [2, 4]	1 [1, 2]	2 [1, 3]
Non-antihypertensives	1 [0, 2]	3 [2, 5]	1 [0, 2]	3 [2, 5]
2 Year Follow Up	**(N = 2,450)**	**(N = 1,645)**	**(N = 2,447)**	**(N = 1,603)**
Total medications	4 [3, 5]	6 [5, 8]	3 [2, 4]	6 [4, 7]
Antihypertensives	3 [2, 3]	3 [2, 4]	2 [1, 2]	2 [1, 3]
Non-antihypertensives	1 [0, 2]	3 [2, 5]	1 [0, 2]	3 [2, 5]
3 Year Follow Up	**(N = 2,160)**	**(N = 1,436)**	**(N = 2,148)**	**(N = 1,389)**
Total medications	4 [3, 5]	6 [5, 8]	3 [2, 4]	6 [4, 8]
Antihypertensives	3 [2, 3]	3 [2, 4]	2 [1, 2]	2 [1, 3]
Non-antihypertensives	1 [0, 2]	3 [2, 5]	1 [0, 2]	3 [2, 5]
4 Year Follow Up	**(N = 818)**	**(N = 596)**	**(N = 800)**	**(N = 558)**
Total medications	4 [3, 5]	6 [5, 8]	3 [2, 4]	6 [4, 8]
Antihypertensives	3 [2, 3]	3 [2, 4]	2 [1, 2]	2 [1, 3]
Non-antihypertensives	1 [0, 2]	3 [2, 5]	1 [0, 2]	3 [2, 5]

All values are medians and interquartile ranges.

CI=confidence interval, CVD=cardiovascular disease, HR=hazard ratio, RR=risk ratio, SAE=serious adverse event, SBP=systolic blood pressure, SD=standard deviation

*P-value for treatment randomization×medication burden status

Table S2: Blood Pressure Outcomes at 48 months, According to Treatment Group and Number of Baseline Medications

Outcomes	Intensive treatment			Standard treatment			p-value interaction†
	No. of baseline medications		p-value or Risk Ratio* (95% CI)	No. of baseline medications		p-value or Risk Ratio* (95% CI)	
	< 5 (*n* = 429)	≥ 5 (*n* = 337)		< 5 (*n* = 406)	≥ 5 (*n* = 297)		
SBP, mmHg	119.3 ± 13.3	122.0 ± 14.8	0.08	136.0 ± 13.0	137.5 ± 14.5	0.29	0.31
SBP change, mmHg	-19.5 ± 18.7	-16.7 ± 18.9	0.08	-3.3 ± 17.6	-2.1 ± 19.4	0.29	0.31
Below randomization goal‡	288 (67.1)	178 (52.8)	0.82 (0.72, 0.94)	262 (64.5)	176 (59.3)	0.96 (0.84, 1.10)	0.06

All values are no. (%) or means ± SD unless noted otherwise

CI = confidence interval, SBP = systolic blood pressure, SD = standard deviation

* Risk ratios were calculated from Poisson regression with robust error and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

† P-value for treatment randomization X medication burden status (defined as ≥ 5 medications at baseline)

‡ Systolic blood pressure goal less than 140 mmHg for intensive arm and less than 120 mmHg for standard arm

Table S3: SPRINT CVD Events, According to Treatment Group and Number of Baseline Medications							
Composite CVD event outcome*	Intensive treatment			Standard treatment			p-value interaction‡
	No. of baseline medications		Hazard Ratio†	No. of baseline medications		Hazard Ratio†	
	<5	≥5	(95% CI)	<5	≥5	(95% CI)	
All participants	**(*n* = 2,630)**	**(*n* = 1,781)**		**(*n* = 2,609)**	**(*n* = 1,770)**		
Primary Analysis	98 (3.8)	136 (7.7)	1.32 (0.98, 1.78)	138 (5.4)	170 (9.7)	1.47 (1.13, 1.92)	0.53
Sensitivity Analyses							
Including OTCs in baseline medication count	62 (3.3)	172 (6.9)	1.26 (0.90, 1.75)	86 (4.6)	222 (9.1)	1.56 (1.17, 2.08)	0.80
Excluding blood pressure medications from the baseline medication count	175 (4.7)	59 (9.0)	1.33 (0.96, 1.84)	243 (6.7)	65 (9.6)	1.17 (0.87, 1.59)	0.18
Stratified by quartile of number of comorbidities							
Q1, 0-3 comorbidities	35 (2.7)	17 (4.6)	1.55 (0.79, 3.04)	53 (4.1)	32 (8.8)	2.52 (1.51, 4.20)	0.55
Q2, 4 comorbidities	12 (3.1)	14 (5.7)	1.22 (0.51, 2.88)	23 (6.3)	18 (7.2)	1.09 (0.52, 2.31)	0.38
Q3, 5-6 comorbidities	28 (5.0)	31 (6.8)	1.32 (0.75, 2.33)	28 (5.4)	34 (7.4)	1.37 (0.78, 2.41)	0.69
Q4, 7-27 comorbidities	23 (6.4)	74 (10.5)	1.46 (0.87, 2.44)	34 (8.9)	86 (12.6)	1.30 (0.84, 2.01)	0.43

Data are number of patients (% per year)

* The composite CVD event outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardio-vascular causes.

† Hazard ratios were calculated from Cox proportional hazards regression and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

‡ P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

Table S4: Serious Adverse Events in SPRINT, According to Treatment Group and Number of Baseline Medications

Serious adverse event*	Intensive treatment: No. of baseline medications <5 (*n* = 2,630)	Intensive treatment: No. of baseline medications ≥5 (*n* = 1,781)	Hazard Ratio† (95% CI)	Standard treatment: No. of baseline medications <5 (*n* = 2,609)	Standard treatment: No. of baseline medications ≥5 (*n* = 1,770)	Hazard Ratio† (95% CI)	p-value interaction
Any serious adverse event	831 (31.9)	872 (49.3)	1.32 (1.18, 1.47)	786 (30.5)	853 (48.4)	1.35 (1.21, 1.51)	0.59
Serious adverse event only							
Hypotension	32 (1.2)	65 (3.7)	2.15 (1.31, 3.51)	16 (0.6)	38 (2.2)	2.74 (1.38, 5.43)	0.70
Syncope	46 (1.8)	45 (2.6)	1.08 (0.67, 1.75)	26 (1.0)	42 (2.4)	1.70 (0.96, 2.99)	0.16
Bradycardia	28 (1.1)	48 (2.7)	1.43 (0.84, 2.43)	23 (0.9)	41 (2.3)	2.16 (1.19, 3.91)	0.94
Electrolyte Abnormality	56 (2.2)	78 (4.4)	1.51 (1.02, 2.25)	44 (1.7)	55 (3.1)	1.54 (0.97, 2.47)	0.40
Injurious fall	42 (1.6)	53 (3.0)	1.20 (0.76, 1.90)	44 (1.7)	52 (3.0)	1.30 (0.81, 2.09)	0.77
Acute kidney injury or failure	78 (3.0)	106 (6.0)	1.34 (0.95, 1.87)	41 (1.6)	70 (4.0)	1.45 (0.92, 2.29)	0.51
Emergency department visit or serious adverse event							
Hypotension	52 (2.0)	87 (4.9)	1.99 (1.34, 2.98)	23 (0.9)	51 (2.9)	2.76 (1.56, 4.88)	0.36
Syncope	75 (2.9)	64 (3.6)	1.02 (0.70, 1.51)	41 (1.6)	54 (3.1)	1.45 (0.90, 2.33)	0.13
Bradycardia	34 (1.3)	56 (3.2)	1.51 (0.93, 2.46)	29 (1.1)	43 (2.5)	1.67 (0.96, 2.90)	0.71
Electrolyte Abnormality	74 (2.8)	90 (5.1)	1.39 (0.97, 1.99)	54 (2.1)	65 (3.7)	1.46 (0.96, 2.24)	0.66
Injurious fall	143 (5.5)	171 (9.7)	1.31 (1.01, 1.68)	156 (6.1)	140 (8.0)	1.00 (0.76, 1.30)	0.05
Acute kidney injury or failure	82 (3.1)	110 (6.2)	1.38 (0.99, 1.93)	46 (1.8)	70 (4.0)	1.29 (0.83, 2.00)	0.82
Monitored clinical events							
Adverse laboratory measure							
Serum sodium <130 mmol/liter	88 (3.4)	88 (5.0)	1.64 (1.16, 2.32)	44 (1.7)	53 (3.0)	1.89 (1.19, 3.02)	0.79
Serum sodium >150 mmol/liter	3 (0.1)	3 (0.2)	1.68 (0.27, 10.27)	0	0	NA	NA
Serum potassium <3.0 mmol/liter	68 (2.6)	42 (2.4)	1.25 (0.80, 1.97)	47 (1.8)	25 (1.4)	1.03 (0.59, 1.79)	0.61
Serum potassium >5.5 mmol/liter	82 (3.1)	89 (5.0)	1.37 (0.97, 1.94)	83 (3.2)	75 (4.3)	1.09 (0.75, 1.58)	0.21
Orthostatic hypotension							
Alone	383 (14.7)	354 (20.1)	1.18 (1.00, 1.40)	431 (16.8)	369 (21.1)	1.11 (0.95, 1.31)	0.39
With dizziness	22 (0.8)	38 (2.2)	1.82 (1.00, 3.30)	31 (1.2)	36 (2.1)	1.34 (0.76, 2.36)	0.24

Data are number of patients (% per year)

* Serious adverse events were defined per the main SPRINT paper and the protocol.[42,44]

† Adjusted hazard ratios were calculated from Cox proportional hazards regression.

Table S5: Patient-Reported Adherence at 12 months, According to Treatment Group and Number of Baseline Medications

Instrument Responses	Intensive treatment		p-value	Standard treatment		p-value	p-value interaction*
	No. of baseline medications			No. of baseline medications			
	< 5	≥ 5		< 5	≥ 5		
	(*n* = 2,607)	(*n* = 1,775)		(*n* = 2,587)	(*n* = 1,762)		
MMAS-8 response at 12-month visit † ‡ §							
High, score of 8	43.7 (44.0)	44.1 (43.7)	0.84	38.2 (38.0)	44.0 (44.5)	<.001	<0.001
Medium, score of 6 to <8	33.1 (33.1)	34.3 (34.3)	0.46	31.6 (31.7)	31.6 (31.5)	0.89	0.62
Low, score of <6	13.0 (12.8)	11.3 (11.5)	0.25	11.1 (11.1)	9.4 (9.4)	0.12	0.75
Missing data	10.1 (10.0)	10.4 (10.5)	0.66	19.1 (19.4)	15.0 (14.6)	<.001	0.03
Change from baseline to 12-month visit † ‡							
Reduction in score	17.1 (17.4)	21.2 (20.7)	0.02	15.5 (16.2)	17.9 (16.9)	0.57	0.39
No change in score	27.3 (28.4)	33.6 (31.9)	0.03	25.0 (25.6)	33.5 (32.5)	<.001	0.20
Improvement in score	34.0 (34.4)	33.4 (32.8)	0.31	31.9 (32.2)	32.4 (32.0)	0.91	0.65
Missing data	21.6 (19.4)	11.8 (14.2)	<.001	27.5 (25.8)	16.1 (17.9)	<.001	0.34

MMAS-8 = Morisky Medication Adherence Scale, 8-item

All values are no. (%) or means ± SD unless noted otherwise

* P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

† Includes all participants alive at 12-month visit, excluding participants who reported no antihypertensive medication use.

‡ Percent unadjusted and (percent adjusted for the baseline characteristics age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, treatment satisfaction and depression.)

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Table S6: Patient-Reported Adherence at 48 months, According to Treatment Group and Number of Baseline Medications

Instrument Responses	Intensive treatment		p-value	Standard treatment		p-value	p-value interaction*
	No. of baseline medications			No. of baseline medications			
	< 5 (*n* = 2,607)	≥ 5 (*n* = 1,775)		< 5 (*n* = 2,587)	≥ 5 (*n* = 1,762)		
MMAS-8 response at 48-month visit † ‡							
High, score of 8	8.5 (8.3)	8.8 (9.1)	0.48	7.4 (7.3)	7.7 (7.9)	0.52	0.88
Medium, score of 6 to <8	5.9 (6.1)	7.2 (6.9)	0.36	4.4 (4.6)	6.1 (5.7)	0.17	0.38
Low, score of <6	1.8 (1.8)	2.6 (2.7)	0.08	2.1 (2.1)	2.0 (2.1)	0.95	0.13
Missing data	83.8 (83.8)	81.4 (81.4)	0.08	86.1 (86.0)	84.2 (84.3)	0.16	0.67
Change from baseline to 48-month visit † ‡							
Reduction in score	3.5 (3.5)	4.6 (4.5)	0.16	2.9 (2.9)	3.5 (3.4)	0.45	0.74
No change in score	4.6 (4.7)	7.0 (6.6)	0.03	4.1 (4.3)	5.6 (5.2)	0.21	0.53
Improvement in score	6.6 (6.6)	6.9 (6.9)	0.70	5.6 (5.7)	6.4 (6.3)	0.43	0.69
Missing data	85.4 (85.2)	81.6 (81.8)	0.01	87.4 (87.1)	84.4 (84.9)	0.07	0.47

MMAS-8 = Morisky Medication Adherence Scale, 8-item

All values are no. (%) or means ± SD unless noted otherwise

* P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

† Includes all participants alive at 48-month visit, excluding participants who reported no antihypertensive medication use.

‡ Percent unadjusted and (percent adjusted for the baseline characteristics age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, treatment satisfaction and depression.)

Table S7: Patient-Reported Treatment Satisfaction at 12-months, According to Treatment Group and Number of Baseline Medications							
Instrument Responses*	**Intensive treatment**		**p-value**	**Standard treatment**		**p-value**	**p-value interaction†**
	No. of baseline medications			**No. of baseline medications**			
	< 5 (*n* = 2,630)	**≥ 5 (*n* = 1,781)**		**< 5 (*n* = 2,609)**	**≥ 5 (*n* = 1,770)**		
Response at 12-month visit							
Level of satisfaction with blood pressure care ‡§							
Satisfied/Very satisfied	88.4 (88.6)	87.8 (87.6)	0.38	88.3 (87.9)	86.3 (86.8)	0.34	0.35
Neutral	1.7 (1.8)	2.0 (1.8)	0.93	1.7 (1.7)	2.1 (2.2)	0.28	0.78
Dissatisfied/Very dissatisfied	0.7 (0.6)	0.9 (1.0)	0.26	0.9 (0.8)	1.1 (1.3)	0.17	0.93
Missing data	9.2 (8.9)	9.3 (9.7)	0.45	9.2 (9.6)	10.5 (9.7)	0.91	0.43
Level of satisfaction with medications received for blood pressure § ||							
Satisfied/Very satisfied	84.8 (85.2)	84.6 (84.0)	0.34	75.5 (76.0)	79.1 (78.3)	0.12	0.02
Neutral	4.0 (3.8)	3.8 (4.0)	0.79	3.9 (4.0)	4.9 (4.7)	0.33	0.19
Dissatisfied/Very dissatisfied	1.0 (1.0)	1.1 (1.1)	0.79	1.2 (1.2)	1.1 (1.1)	0.84	0.66
Missing data	10.2 (9.9)	10.5 (11.0)	0.33	19.4 (18.8)	14.9 (15.6)	0.02	0.01
Change from baseline to 12-month visit							
Satisfaction with blood pressure care ‡§							
Decline in satisfaction	1.7 (1.8)	1.7 (1.6)	0.59	1.8 (1.8)	2.8 (3.0)	0.03	0.17
No change in satisfaction	75.3 (76.6)	77.9 (76.0)	0.71	74.9 (75.2)	76.7 (76.3)	0.45	0.72
Improvement in satisfaction	13.0 (12.1)	10.7 (12.2)	0.95	13.3 (12.8)	9.7 (10.3)	0.03	0.24
Missing data	10.0 (9.5)	9.6 (10.3)	0.50	9.9 (10.2)	10.8 (10.4)	0.87	0.39
Satisfaction with medications received for blood pressure § ||							
Decline in satisfaction	2.1 (2.2)	2.8 (2.5)	0.59	3.1 (3.2)	4.1 (3.8)	0.40	NA
No change in satisfaction	59.5 (63.6)	67.7 (61.8)	0.23	52.9 (56.1)	64.6 (59.6)	0.03	0.03
Improvement in satisfaction	15.9 (16.1)	17.1 (16.8)	0.56	15.7 (16.0)	14.9 (14.4)	0.18	NA
Missing data	22.5 (18.2)	12.4 (19.2)	0.49	28.3 (24.5)	16.5 (21.5)	0.05	0.43

All values are no. (%) or means ± SD unless noted otherwise

* For each instrument, the appropriate scale was used unless noted otherwise

† P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

‡ Includes all participants alive at 12-month visit

§ Percent unadjusted and (percent adjusted for the baseline characteristics age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 and depression.)

|| Includes all participants alive at 12-month visit, excluding participants who reported no antihypertensive medication use.

Table S8: Patient-Reported Treatment Satisfaction at 48-months, According to Treatment Group and Number of Baseline Medications							
Instrument Responses*	**Intensive treatment**		**p-value**	**Standard treatment**		**p-value**	**p-value interaction†**
	No. of baseline medications			**No. of baseline medications**			
	< 5	**≥ 5**		**< 5**	**≥ 5**		
	(*n* = 2,630)	**(*n* = 1,781)**		**(*n* = 2,609)**	**(*n* = 1,770)**		
Response at 48-month visit							
Level of satisfaction with blood pressure care ‡§							
Satisfied/Very satisfied	15.9 (16.0)	18.5 (18.4)	0.07	15.7 (15.9)	16.7 (16.5)	0.63	0.31
Neutral	0.3 (0.3)	0.2 (0.2)	0.58	0.1 (0.1)	0.2 (0.3)	0.45	NA
Dissatisfied/Very dissatisfied	0.3 (.)	0.3 (.)	NA	0.0 (.)	0.0 (.)	NA	NA
Missing data	83.5 (83.4)	81.0 (81.1)	0.09	84.1 (84.1)	83.2 (83.3)	0.54	0.28
Level of satisfaction with medications received for blood pressure § ||							
Satisfied/Very satisfied	15.2 (15.3)	17.5 (17.3)	0.12	13.5 (13.8)	15.4 (14.9)	0.32	0.96
Neutral	0.6 (0.8)	0.9 (0.7)	0.90	0.3 (0.3)	0.3 (0.7)	0.29	NA
Dissatisfied/Very dissatisfied	0.3 (.)	0.3 (.)	NA	0.0 (.)	0.1 (.)	NA	NA
Missing data	83.8 (83.7)	81.3 (81.5)	0.12	86.2 (86.0)	84.2 (84.4)	0.19	0.63
Change from baseline to 48-month visit							
Satisfaction with blood pressure care ‡§							
Decline in satisfaction	0.4 (0.5)	0.3 (0.3)	0.22	0.1 (0.1)	0.1 (0.2)	0.30	NA
No change in satisfaction	14.4 (14.7)	17.1 (16.7)	0.13	14.2 (14.5)	14.9 (14.4)	0.96	0.20
Improvement in satisfaction	1.5 (1.3)	1.6 (1.9)	0.24	1.5 (1.3)	1.9 (2.2)	0.09	0.51
Missing data	83.6 (83.5)	81.0 (81.2)	0.09	84.3 (84.1)	83.2 (83.4)	0.55	0.30
Satisfaction with medications received for blood pressure § ||							
Decline in satisfaction	0.5 (0.7)	0.9 (0.7)	0.96	0.1 (0.1)	0.3 (0.7)	0.34	NA
No change in satisfaction	11.5 (12.1)	14.5 (13.5)	0.22	10.4 (11.0)	13.1 (12.1)	0.32	0.92
Improvement in satisfaction	2.5 (2.5)	3.1 (3.1)	0.30	2.0 (2.1)	2.3 (2.1)	0.90	NA
Missing data	85.5 (84.8)	81.5 (82.5)	0.09	87.5 (86.9)	84.4 (85.3)	0.21	0.46

All values are no. (%) or means ± SD unless noted otherwise

* For each instrument, the appropriate scale was used unless noted otherwise

† P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

‡ Includes all participants alive at 12-month visit

§ Percent unadjusted and (percent adjusted for the baseline characteristics age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 and depression.)

|| Includes all participants alive at 12-month visit, excluding participants who reported no antihypertensive medication use.

Table S9. Hazard ratios for SPRINT outcomes by treatment arm among those with high and low medication burden at baseline.							
	Medication Burden Status at Baseline						
	Low medication burden (< 5 medications)			High medication burden (≥ 5 medications)			
Outcome	**Intensive Treatment (*n* = 2,630)**	**Standard Treatment (*n* = 2,608)**	**Hazard Ratio* (95% CI)**	**Intensive Treatment (*n* = 1,781)**	**Standard Treatment (*n* = 1,771)**	**Hazard Ratio* (95% CI)**	**p-value interaction†**
Primary Outcome ‡	98 (3.8)	138 (5.4)	0.67 (0.52, 0.87)	136 (7.7)	170 (9.7)	0.76 (0.61, 0.96)	0.53
All-Cause Mortality	72 (2.7)	87 (3.4)	0.82 (0.60, 1.13)	85 (4.8)	117 (6.6)	0.71 (0.54, 0.95)	0.57
Any serious adverse event §	831 (31.7)	786 (30.3)	1.05 (0.95, 1.15)	872 (49.1)	853 (48.3)	1.00 (0.91, 1.10)	0.56

CI= Confidence interval.

Numbers are counts and annual rates.

* Hazard ratios were calculated from Cox proportional hazards regression and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

† P-value for treatment randomization X medication burden

‡ The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.

§ A serious adverse event was defined as an event that was fatal or life-threatening, that resulted in clinically significant or persistent disability, that required or prolonged a hospitalization, or that was judged by the investigator to represent a clinically significant hazard or harm to the participant that might require medical or surgical intervention to prevent one of the other events listed above.

Table S10: Blood Pressure and Clinical Outcomes by Treatment Group and Number of Baseline Medications, using 3 antihypertensive medications or more as threshold

Outcomes	Intensive treatment			Standard treatment			p-value interaction*
	No. of baseline antihypertensive medications		p-value or RR/HR (95% CI)	No. of baseline antihypertensive medications		p-value or RR/HR (95% CI)	
	< 3	≥ 3		< 3	≥ 3		
Participants with SBP value at 12 months	**(n = 2,775)**	**(n = 1,204)**		**(n = 2,739)**	**(n = 1,189)**		
SBP, mmHg	120.8 ± 13.3	122.7 ± 14.3	0.002	135.8 ± 12.9	137.1 ± 15.1	0.06	0.10
SBP change, mmHg	-19.3 ± 18.4	-15.4 ± 18.7	0.002	-4.1 ± 17.8	-2.5 ± 19.6	0.06	0.10
Below randomization goal	1590 (57.3)	626 (52.0)	0.93 (0.87, 0.99)	1808 (66.0)	717 (60.3)	0.94 (0.89, 0.99)	0.56
All Participants	**(n = 3,059)**	**(n = 1,323)**		**(n = 3,017)**	**(n = 1,332)**		
CVD Events†	143 (4.7)	89 (6.8)	1.02 (0.77, 1.35)	168 (5.6)	138 (10.5)	1.62 (1.26, 2.07)	0.22
Any SAE‡	1125 (37.1)	563 (42.7)	0.99 (0.89, 1.11)	1010 (33.9)	615 (46.5)	1.24 (1.11, 1.38)	0.003

All values are no. (%) or means ± SD unless noted otherwise

CI=confidence interval, CVD=cardiovascular disease, HR=hazard ratio, RR=risk ratio, SAE=serious adverse event, SBP=systolic blood pressure, SD=standard deviation

*P-value for treatment randomization×medication burden status

†Composite of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.

‡Defined per main SPRINT paper.[42,44]

Table S11: Blood Pressure and Clinical Outcomes by Treatment Group and Number of Baseline Medications, using 4 antihypertensive medications or more as threshold

Outcomes	Intensive treatment			Standard treatment			p-value interaction*
	No. of baseline antihypertensive medications		p-value or RR/HR (95% CI)	No. of baseline antihypertensive medications		p-value or RR/HR (95% CI)	
	< 4	≥ 4		< 4	≥ 4		
Participants with SBP value at 12 months	**(n = 3,671)**	**(n = 308)**		**(n = 3,624)**	**(n = 304)**		
SBP, mmHg	121.1 ± 13.4	124.7 ± 15.8	<.001	136.0 ± 13.2	138.4 ± 17.1	0.01	0.13
SBP change, mmHg	-18.5 ± 18.4	-13.5 ± 20.1	<.001	-3.8 ± 18.1	-1.7 ± 21.2	0.01	0.13
Below randomization goal	2068 (56.3)	148 (48.1)	0.88 (0.78, 0.99)	2361 (65.1)	164 (53.9)	0.86 (0.77, 0.95)	0.96
All Participants	**(n = 4,044)**	**(n = 338)**		**(n = 4,005)**	**(n = 344)**		
CVD Events†	208 (5.2)	24 (7.1)	1.00 (0.64, 1.55)	272 (6.9)	34 (9.9)	1.15 (0.79, 1.67)	0.92
Any SAE‡	1536 (38.3)	152 (45.2)	1.08 (0.91, 1.28)	1449 (36.6)	176 (51.3)	1.26 (1.07, 1.48)	0.15

All values are no. (%) or means ± SD unless noted otherwise

CI=confidence interval, CVD=cardiovascular disease, HR=hazard ratio, RR=risk ratio, SAE=serious adverse event, SBP=systolic blood pressure, SD=standard deviation

*P-value for treatment randomization×medication burden status

†Composite of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.

‡Defined per main SPRINT paper.[42,44]

Table S12: Blood Pressure Outcomes at 12 and 48 months, According to Treatment Group and Number of Baseline Medications, excluding blood pressure medications and including OTCs in baseline medication count

Outcomes	Intensive treatment			Standard treatment			p-value interaction†
	No. of baseline medications		p-value or Risk Ratio*	No. of baseline medications		p-value or Risk Ratio*	
	< 5	≥ 5	(95% CI)	< 5	≥ 5	(95% CI)	
Excluding blood pressure medications							
12 months, n	3,380	599		3,328	600		
SBP, mmHg	121.2 ± 13.5	122.5 ± 14.1	0.13	136.4 ± 13.5	135.3 ± 14.1	0.26	<0.001
Below randomization goal‡	1906 (56.4)	310 (51.8)	0.96 (0.88, 1.04)	2137 (64.2)	388 (64.7)	1.00 (0.93, 1.07)	0.14
SBP change, mmHg	-18.6 ± 18.6	-15.3 ± 18.2	0.13	-3.7 ± 18.3	-2.8 ± 18.6	0.26	<0.001
48 months, n	655	111		584	119		
SBP, mmHg	120.4 ± 14.3	121.1 ± 12.6	0.84	136.3 ± 13.3	138.3 ± 15.2	0.07	0.51
Below randomization goal‡	407 (62.1)	59 (53.2)	0.94 (0.77, 1.14)	367 (62.8)	71 (59.7)	0.94 (0.79, 1.11)	0.56
SBP change, mmHg	-18.3 ± 19.1	-18.3 ± 17.0	0.84	-3.4 ± 18.3	0.0 ± 18.8	0.07	0.51
Including OTCs							
12 months, n	1,696	2,283		1,718	2,210		
SBP, mmHg	120.4 ± 13.0	122.1 ± 14.0	0.02	136.5 ± 12.7	136.0 ± 14.2	0.41	<.001
Below randomization goal‡	1013 (59.7)	1203 (52.7)	0.91 (0.86, 0.97)	1109 (64.6)	1416 (64.1)	0.99 (0.94, 1.05)	0.003
SBP change, mmHg	-20.7 ± 18.6	-16.2 ± 18.3	0.02	-4.7 ± 17.4	-2.8 ± 19.0	0.41	<.001
48 months, n	299	467		295	408		
SBP, mmHg	118.8 ± 13.1	121.6 ± 14.5	0.02	136.5 ± 12.9	136.7 ± 14.1	0.93	0.06
Below randomization goal‡	204 (68.2)	262 (56.1)	0.85 (0.74, 0.96)	189 (64.1)	249 (61.0)	1.00 (0.87, 1.14)	0.06
SBP change, mmHg	-20.5 ± 17.9	-16.9 ± 19.2	0.02	-3.9 ± 17.3	-2.1 ± 19.1	0.93	0.06

All values are no. (%) or means ± SD unless noted otherwise

CI = confidence interval, OTC = over-the-counter; SBP = systolic blood pressure, SD = standard deviation

* Risk ratios were calculated from Poisson regression with robust error and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

† P-value for treatment randomization X medication burden status (defined as ≥ 5 medications at baseline)

‡ Systolic blood pressure goal less than 140 mmHg for intensive arm and less than 120 mmHg for standard arm

Table S13: Blood Pressure Outcomes at 12 months, According to Treatment Group, Number of Baseline Medications, and Number of Comorbidities							
Outcomes	**Intensive treatment**			**Standard treatment**			
	No. of baseline medications		**p-value or Risk Ratio***	**No. of baseline medications**		**p-value or Risk Ratio***	**p-value interaction†**
	< 5	**≥ 5**	**(95% CI)**	**< 5**	**≥ 5**	**(95% CI)**	
	(*n* = 2,502)	**(*n* = 1,703)**		**(*n* = 2,513)**	**(*n* = 1,674)**		
Mean ± SD SBP, mmHg							
Q1, 0-3 comorbidities	120.3 ± 12.9	121.5 ± 14.1	0.28	136.3 ± 12.1	136.4 ± 12.7	0.62	0.29
Q2, 4 comorbidities	120.9 ± 12.6	122.6 ± 14.3	0.10	135.4 ± 13.6	137.0 ± 15.6	0.20	0.98
Q3, 5-6 comorbidities	120.6 ± 13.3	122.0 ± 13.9	0.12	137.3 ± 12.7	136.0 ± 13.7	0.17	0.03
Q4, 7-27 comorbidities	121.3 ± 13.9	123.4 ± 14.7	0.01	135.4 ± 14.2	135.9 ± 16.1	0.36	0.24
Below randomization goal‡							
Q1, 0-3 comorbidities	725 (60.6)	190 (57.1)	0.97 (0.87, 1.09)	788 (65.9)	198 (61.1)	0.91 (0.82, 1.01)	0.85
Q2, 4 comorbidities	185 (54.7)	108 (48.0)	0.88 (0.74, 1.05)	227 (66.2)	138 (60.5)	0.92 (0.80, 1.05)	0.75
Q3, 5-6 comorbidities	283 (57.3)	218 (53.3)	0.92 (0.81, 1.04)	296 (61.3)	271 (65.9)	1.09 (0.98, 1.21)	0.10
Q4, 7-27 comorbidities	188 (55.5)	319 (49.5)	0.87 (0.77, 0.99)	213 (64.2)	394 (64.4)	0.99 (0.90, 1.10)	0.12
Mean ± SD SBP change, mmHg							
Q1, 0-3 comorbidities	-20.6 ± 19.2	-15.0 ± 17.7	0.28	-4.9 ± 17.1	-2.0 ± 18.3	0.62	0.29
Q2, 4 comorbidities	-18.9 ± 17.8	-15.5 ± 17.8	0.10	-5.2 ± 19.3	-1.2 ± 18.6	0.20	0.98
Q3, 5-6 comorbidities	-19.8 ± 18.1	-16.8 ± 18.3	0.12	-2.7 ± 17.4	-2.6 ± 19.4	0.17	0.03
Q4, 7-27 comorbidities	-19.8 ± 17.7	-14.3 ± 18.4	0.01	-4.6 ± 18.3	-2.7 ± 19.9	0.36	0.24

CI = confidence interval, SBP = systolic blood pressure, SD = standard deviation

* Risk ratios were calculated from Poisson regression with robust error and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

† P-value for treatment randomization X medication burden status (defined as ≥ 5 medications at baseline)

‡ Systolic blood pressure goal less than 140 mmHg for intensive arm and less than 120 mmHg for standard arm

Table S14: Blood Pressure Outcomes at 48 months, According to Treatment Group, Number of Baseline Medications, and Number of Comorbidities							
Outcomes	**Intensive treatment**			**Standard treatment**			
	No. of baseline medications		**p-value or Risk Ratio***	**No. of baseline medications**		**p-value or Risk Ratio***	**p-value interaction†**
	< 5 (*n* = 442)	**≥ 5 (*n* = 347)**	**(95% CI)**	**< 5 (*n* = 440)**	**≥ 5 (*n* = 308)**	**(95% CI)**	
Mean ± SD SBP, mmHg							
Q1, 0-3 comorbidities	118.7 ± 11.9	121.8 ± 15.7	0.09	136.2 ± 12.0	137.5 ± 10.9	0.19	0.63
Q2, 4 comorbidities	117.4 ± 14.6	121.5 ± 13.0	0.19	136.2 ± 13.2	137.5 ± 12.6	0.86	0.16
Q3, 5-6 comorbidities	121.2 ± 14.7	120.6 ± 13.1	0.44	135.1 ± 15.1	137.7 ± 13.9	0.33	0.45
Q4, 7-27 comorbidities	120.9 ± 14.5	123.2 ± 16.1	0.30	135.9 ± 13.5	137.3 ± 17.3	0.69	0.72
Below randomization goal‡							
Q1, 0-3 comorbidities	159 (69.4)	44 (52.4)	0.77 (0.61, 0.98)	148 (67.6)	39 (54.2)	0.81 (0.62, 1.05)	0.92
Q2, 4 comorbidities	42 (70.0)	23 (50.0)	NA	32 (64.0)	27 (67.5)	NA	0.04
Q3, 5-6 comorbidities	52 (63.4)	50 (58.8)	0.95 (0.73, 1.23)	44 (57.9)	40 (56.3)	0.97 (0.69, 1.38)	0.63
Q4, 7-27 comorbidities	35 (60.3)	61 (50.0)	0.79 (0.57, 1.10)	38 (62.3)	70 (61.4)	NA	0.52
Mean ± SD SBP change, mmHg							
Q1, 0-3 comorbidities	-20.1 ± 18.4	-14.7 ± 20.9	0.09	-3.9 ± 16.6	-0.3 ± 16.5	0.19	0.63
Q2, 4 comorbidities	-20.4 ± 18.6	-19.2 ± 18.1	0.19	-1.3 ± 17.4	-3.2 ± 17.4	0.86	0.16
Q3, 5-6 comorbidities	-18.9 ± 18.1	-17.3 ± 16.7	0.44	-3.0 ± 19.3	-2.7 ± 21.1	0.33	0.45
Q4, 7-27 comorbidities	-17.5 ± 20.7	-16.9 ± 19.3	0.30	-3.4 ± 19.1	-2.5 ± 20.8	0.69	0.72

CI = confidence interval, SBP = systolic blood pressure, SD = standard deviation

* Risk ratios were calculated from Poisson regression with robust error and adjusted for baseline age, sex, race or ethnic group, SBP, DBP, eGFR, urine albumin-to-creatinine ratio, blood glucose, total cholesterol, HDL cholesterol, statin use, aspirin use, smoking status, body mass index, metabolic syndrome, FRS, number of comorbidities, atrial fibrillation/flutter, myocardial infarction, heart failure, peripheral vascular disease, MMAS-8 score, treatment satisfaction score, and depression.

† P-value for treatment randomization X medication burden status (defined as ≥ 5 medications at baseline)

‡ Systolic blood pressure goal less than 140 mmHg for intensive arm and less than 120 mmHg for standard arm

Table S15: Serious Adverse Events in SPRINT, According to Treatment Group and Number of Baseline Medications, excluding blood pressure medications from baseline medication count

Serious adverse event*	Intensive treatment			Standard treatment			p-value interaction‡
	No. of baseline medications		Hazard Ratio† (95% CI)	No. of baseline medications		Hazard Ratio† (95% CI)	
	<5 (*n* = 3,747)	≥5 (*n* = 664)		<5 (*n* = 3,697)	≥5 (*n* = 682)		
Any serious adverse event	1330 (35.8)	373 (56.5)	1.42 (1.25, 1.61)	1273 (34.8)	366 (54.0)	1.32 (1.16, 1.50)	0.52
Serious adverse event only							
Hypotension	68 (1.8)	29 (4.4)	1.46 (0.90, 2.36)	31 (0.9)	23 (3.4)	3.04 (1.64, 5.63)	0.17
Syncope	76 (2.0)	15 (2.3)	0.81 (0.44, 1.46)	49 (1.3)	19 (2.8)	1.59 (0.88, 2.86)	0.09
Bradycardia	58 (1.6)	18 (2.7)	0.96 (0.54, 1.70)	51 (1.4)	13 (1.9)	1.11 (0.57, 2.16)	0.65
Electrolyte Abnormality	91 (2.5)	43 (6.5)	2.10 (1.38, 3.17)	77 (2.1)	22 (3.3)	1.37 (0.81, 2.30)	0.05
Injurious fall	73 (2.0)	22 (3.3)	1.17 (0.70, 1.96)	70 (1.9)	26 (3.9)	1.49 (0.91, 2.46)	0.62
Acute kidney injury or failure	129 (3.5)	55 (8.4)	1.82 (1.28, 2.59)	87 (2.4)	24 (3.6)	0.94 (0.58, 1.55)	0.09
Emergency department visit or serious adverse event							
Hypotension	102 (2.7)	37 (5.6)	1.32 (0.87, 2.00)	44 (1.2)	30 (4.5)	3.09 (1.83, 5.23)	0.05
Syncope	118 (3.2)	21 (3.2)	0.79 (0.48, 1.30)	68 (1.9)	27 (4.0)	1.75 (1.06, 2.86)	0.02
Bradycardia	68 (1.8)	22 (3.3)	1.13 (0.67, 1.90)	59 (1.6)	13 (1.9)	0.95 (0.49, 1.81)	0.32
Electrolyte Abnormality	113 (3.0)	51 (7.8)	2.16 (1.48, 3.15)	90 (2.5)	29 (4.3)	1.53 (0.97, 2.43)	0.11
Injurious fall	239 (6.4)	75 (11.4)	1.31 (0.98, 1.74)	228 (6.3)	68 (10.1)	1.35 (1.01, 1.81)	0.67
Acute kidney injury or failure	134 (3.6)	58 (8.8)	1.89 (1.34, 2.67)	92 (2.5)	24 (3.6)	0.91 (0.55, 1.48)	0.05
Monitored clinical events							
Adverse laboratory measure							
Serum sodium <130 mmol/liter	143 (3.9)	33 (5.0)	1.25 (0.82, 1.91)	79 (2.2)	18 (2.7)	1.10 (0.63, 1.92)	0.53
Serum sodium >150 mmol/liter	4 (0.1)	2 (0.3)	3.70 (0.56, 24.54)	0	0	NA	NA
Serum potassium <3.0 mmol/liter	94 (2.5)	16 (2.4)	1.31 (0.73, 2.36)	62 (1.7)	10 (1.5)	1.14 (0.55, 2.36)	0.74
Serum potassium >5.5 mmol/liter	134 (3.6)	37 (5.6)	1.26 (0.84, 1.89)	130 (3.6)	28 (4.2)	1.03 (0.66, 1.60)	0.35
Orthostatic hypotension							
Alone	603 (16.2)	134 (20.4)	1.05 (0.86, 1.29)	640 (17.6)	160 (23.8)	1.22 (1.01, 1.47)	0.40
With dizziness	42 (1.1)	18 (2.7)	1.73 (0.92, 3.26)	46 (1.3)	21 (3.1)	1.70 (0.95, 3.05)	0.94

Data are number of patients (% per year)

* Serious adverse events were defined per the main SPRINT paper and the protocol.[42,44]

† Adjusted hazard ratios were calculated from Cox proportional hazards regression.

‡ P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

Table S16: Serious Adverse Events in SPRINT, According to Treatment Group and Number of Baseline Medications where the event was related to study treatments

Serious adverse event*	Intensive treatment			Standard treatment			p-value interaction‡
	No. of baseline medications		Hazard Ratio† (95% CI)	No. of baseline medications		Hazard Ratio† (95% CI)	
	<5 (n = 2,630)	≥5 (n = 1,781)		<5 (n = 2,609)	≥5 (n = 1,770)		
Any serious adverse event	138 (5.3)	173 (9.8)	1.32 (1.02, 1.71)	75 (2.9)	142 (8.1)	1.93 (1.40, 2.67)	0.03
Serious adverse event only							
Hypotension	22 (0.8)	53 (3.0)	2.80 (1.58, 4.98)	8 (0.3)	19 (1.1)	3.25 (1.20, 8.79)	0.97
Syncope	27 (1.0)	24 (1.4)	1.03 (0.55, 1.93)	11 (0.4)	16 (0.9)	1.98 (0.79, 4.97)	0.35
Bradycardia	14 (0.5)	21 (1.2)	1.37 (0.63, 2.99)	6 (0.2)	19 (1.1)	4.42 (1.52, 12.89)	0.23
Electrolyte Abnormality	33 (1.3)	37 (2.1)	1.26 (0.73, 2.17)	14 (0.5)	25 (1.4)	2.00 (0.95, 4.22)	0.37
Injurious fall	5 (0.2)	11 (0.6)	1.96 (0.59, 6.43)	3 (0.1)	7 (0.4)	3.10 (0.51, 18.69)	0.97
Acute kidney injury or failure	29 (1.1)	52 (2.9)	1.68 (1.00, 2.83)	10 (0.4)	19 (1.1)	1.48 (0.60, 3.64)	0.93
Emergency department visit or serious adverse event							
Hypotension	43 (1.7)	71 (4.0)	2.18 (1.39, 3.39)	13 (0.5)	33 (1.9)	3.63 (1.73, 7.62)	0.26
Syncope	44 (1.7)	35 (2.0)	1.03 (0.62, 1.71)	20 (0.8)	24 (1.4)	1.53 (0.75, 3.11)	0.31
Bradycardia	16 (0.6)	31 (1.8)	1.91 (0.96, 3.79)	7 (0.3)	21 (1.2)	3.69 (1.37, 9.97)	0.46
Electrolyte Abnormality	46 (1.8)	48 (2.7)	1.25 (0.78, 1.99)	24 (0.9)	31 (1.8)	1.47 (0.79, 2.71)	0.71
Injurious fall	12 (0.5)	28 (1.6)	2.47 (1.15, 5.30)	10 (0.4)	14 (0.8)	1.42 (0.56, 3.59)	0.24
Acute kidney injury or failure	33 (1.3)	54 (3.1)	1.69 (1.02, 2.80)	12 (0.5)	19 (1.1)	1.25 (0.54, 2.94)	0.90

Data are number of patients (% per year)

* Serious adverse events were defined per the main SPRINT paper and the protocol.[42,44]

† Adjusted hazard ratios were calculated from Cox proportional hazards regression.

‡ P-value for treatment randomization X medication burden status (defined as > 5 medications at baseline)

Supplementary Figures

Figure S1: Histogram of baseline medication number in SPRINT participants

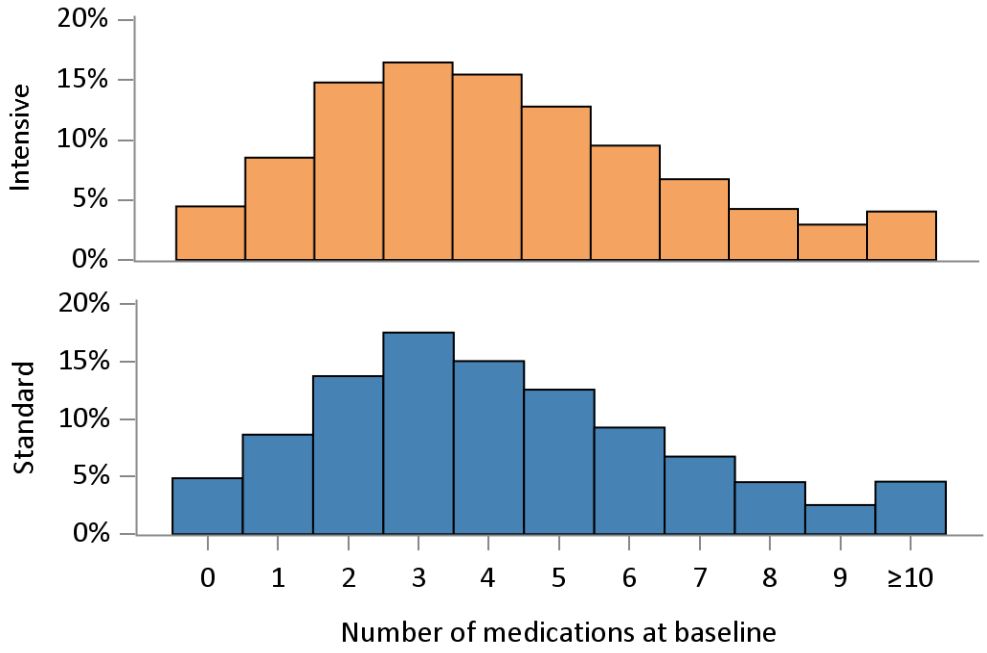


Figure S2: Histogram of baseline number of non-antihypertensive medications in SPRINT participants

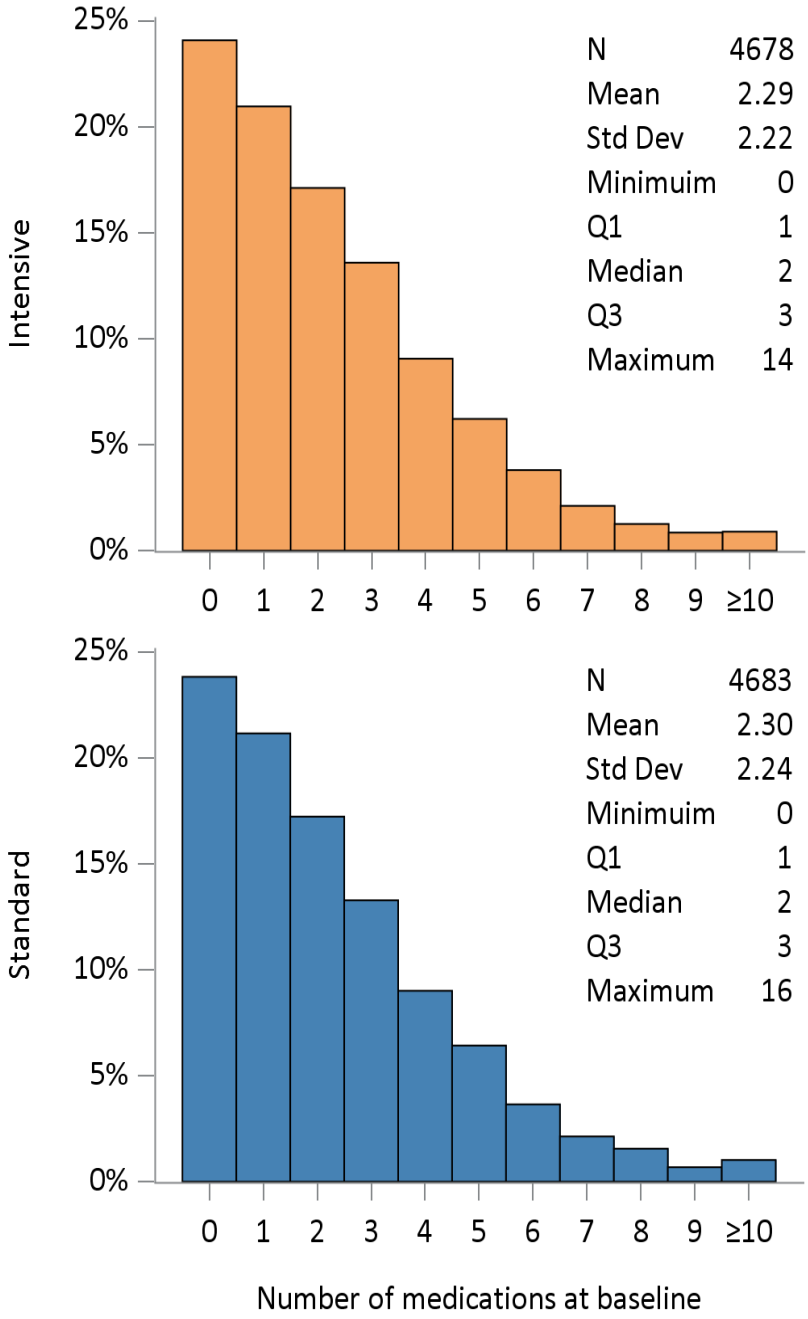


Figure S3: Histogram of baseline number of antihypertensive medications in SPRINT participants

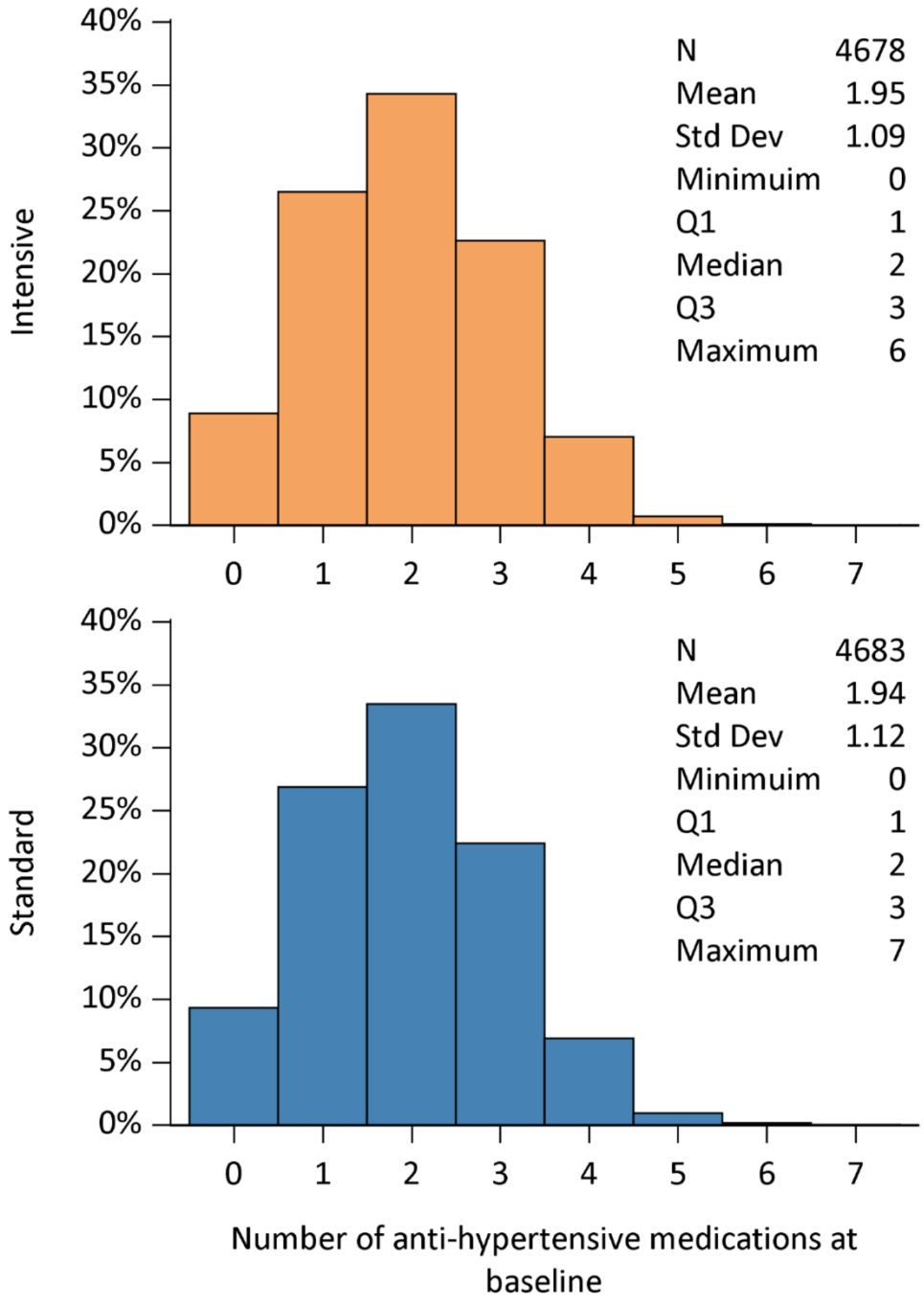
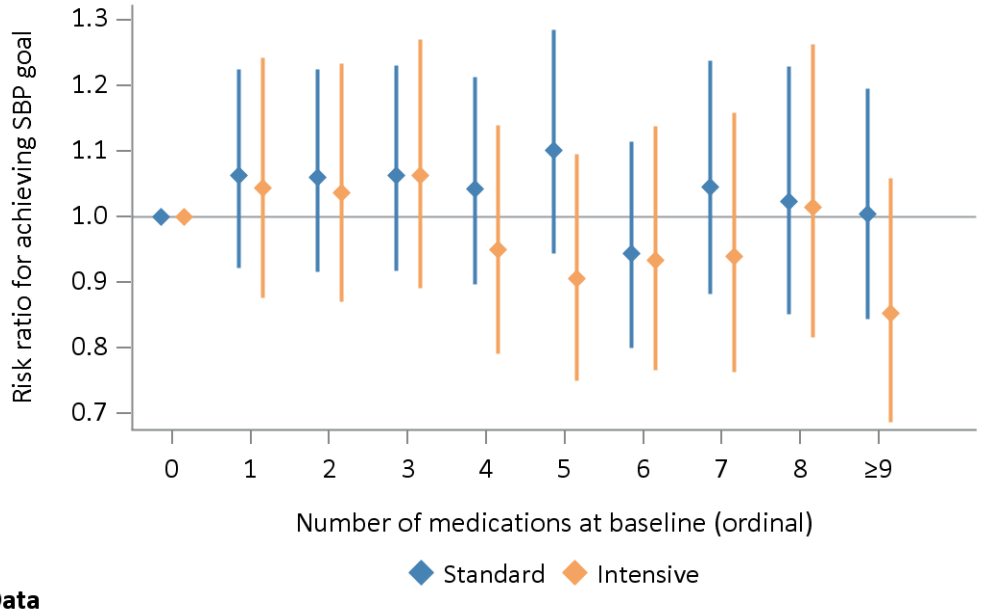
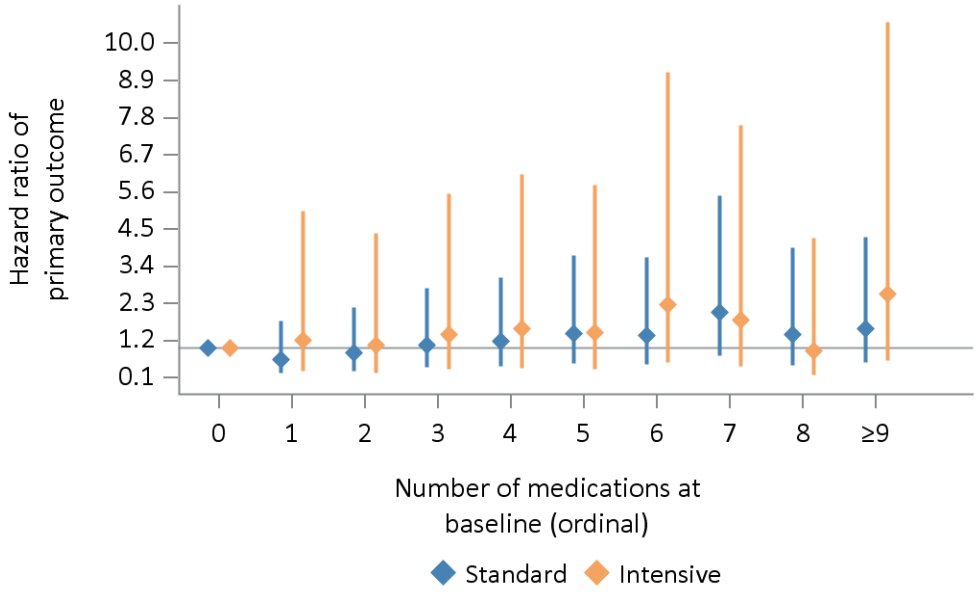


Figure S4: Relative risk ratios and 95% confidence intervals for achieving SBP goals, by randomization group and medication burden



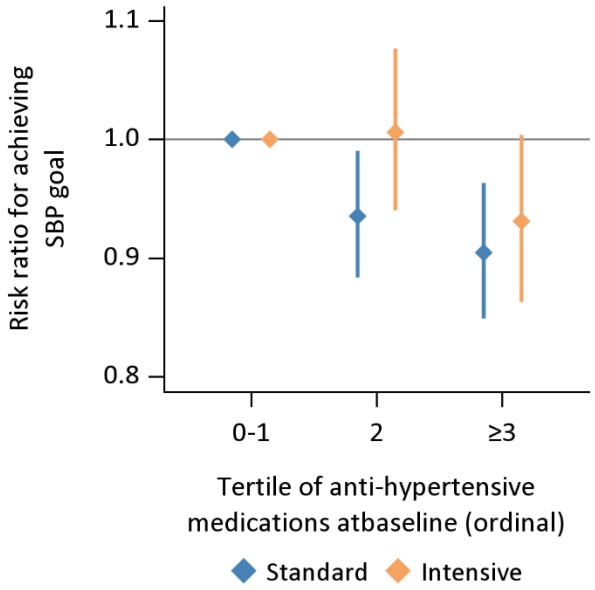
No. with Data										
Standard treatment	228	405	643	820	704	588	434	316	212	333
Intensive treatment	209	399	692	770	723	598	446	315	199	327

Figure S5: Hazard ratios and 95% confidence intervals for SPRINT CVD event outcome by randomization group and medication burden.



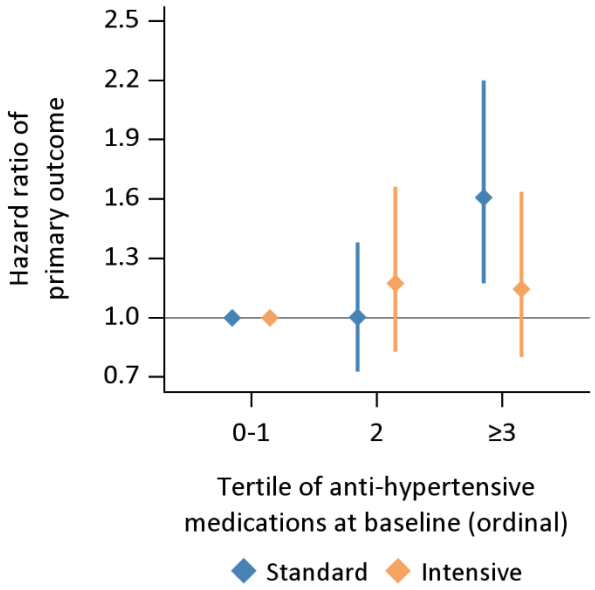
No. with Data										
Standard treatment	228	405	643	820	704	588	434	316	212	333
Intensive treatment	209	399	692	770	723	598	446	315	199	327

Figure S6: Adjusted risk ratios and 95% confidence intervals for achieving SBP goal at 12 months by tertile of baseline antihypertensive medication number and treatment group



No. with Data			
Standard treatment	1694	1567	1422
Intensive treatment	1654	1603	1421

Figure S7: Adjusted hazard ratios and 95% confidence intervals for experiencing CVD event, by tertile of baseline antihypertensive medication number and treatment group



No. with Data			
Standard treatment	1694	1567	1422
Intensive treatment	1654	1603	1421