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. Incidence of withdrawing consent or being loss to follow-up for SPRINT participants 75 years or older by frailty status and gait speed

	Intensive-treatment		Standard-treatment		Model 1		Model 2	
	N	%/year	N	%/year	HR (95% CI)	p-value	HR (95% CI)	p-value
Overall	62	1.55 (1.21, 1.99)	64	1.62 (1.27, 2.07)	1.02 (0.72, 1.46)	0.902	1.04 (0.73, 1.47)	0.846
Frailty Status								
Fit	2	0.41 (0.10, 1.62)	4	0.69 (0.26, 1.85)	0.74 (0.13, 4.14)	0.734	0.76 (0.13, 4.37)	0.756
Less fit	31	1.43 (1.01, 2.03)	33	1.47 (1.04, 2.06)	1.00 (0.61, 1.65)	0.996	1.02 (0.63, 1.66)	0.933
Frail	26	1.97 (1.34, 2.89)	22	1.98 (1.30, 3.00)	1.10 (0.61, 1.96)	0.756	1.11 (0.64, 1.92)	0.717
Gait Speed								
≥0.8 m/s	37	1.38 (1.00, 1.91)	35	1.29 (0.93, 1.80)	1.10 (0.69, 1.76)	0.694	1.12 (0.70, 1.78)	0.637
<0.8 m/s	20	1.81 (1.17, 2.81)	24	2.20 (1.47, 3.28)	0.87 (0.47, 1.62)	0.667	0.87 (0.48, 1.57)	0.645
Missing	5	2.38 (0.99, 5.71)	5	3.08 (1.28, 7.41)	1.22 (0.33, 4.56)	0.764	1.30 (0.33, 5.23)	0.708

N denotes number of participants withdrawing consent or being lost to follow-up. (%/year) Percentage of participants withdrawing consent or being lost to follow-up per year. (HR) Hazard ratio. (CI) Confidence Interval. Model 1 estimates based on Cox proportional hazards regression, which does not account for the competing risk of death. Model 2 estimates based on Fine and Gray model accounting for the competing risk of death. For the primary CVD outcome, median follow-up time for the intensive-treatment group was 3.16 years (interquartile range: 2.63 to 3.70 years), with 3,938.2 person-years of follow-up. In the standard-treatment group, median follow-up time was 3.12 years (interquartile range: 2.67 to 3.67 years), with 3,841 person-years of follow-up.

eTable 2. Utilization of antihypertensive medication classes for SPRINT participants 75 years or older at the most recent study visit as of 8/20/2015

	Intensive-treatment N=1,314 N (%)	**Standard-treatment N=1,316 N (%)**
Number of agents		
Mean (Standard Deviation)	2.6 (1.2)	1.8 (1.1)
0	47 (3.6)	168 (12.8)
1	156 (11.9)	393 (29.9)
2	399 (30.4)	406 (30.9)
3	409 (31.1)	255 (19.4)
4+	303 (23.1)	94 (7.1)
ACE inhibitors or angiotensin II antagonists	928 (70.6)	687 (52.2)
ACE inhibitors	446 (33.9)	351 (26.7)
Angiotensin II antagonists	483 (36.8)	337 (25.6)
Renin inhibitors	0 (0.0)	0 (0.0)
Diuretics	811 (61.7)	557 (42.3)
Thiazide-type diuretics	597 (45.4)	395 (30.0)
Aldosterone receptor blockers	90 (6.8)	39 (3.0)
Other potassium-sparing diuretics	35 (2.7)	32 (2.4)
Alpha-1 blockers	151 (11.5)	87 (6.6)
Beta blockers	567 (43.2)	441 (33.5)
With intrinsic sympathomimetic activity	0 (0.0)	0 (0.0)
Without intrinsic sympathomimetic activity	567 (43.2)	441 (33.5)
Central alpha-2 agonists or other centrally acting drugs	35 (2.7)	12 (0.9)
Calcium channel blockers	736 (56.0)	458 (34.8)
Dihydropyridines	668 (50.8)	400 (30.4)
Non-dihydropyridines	77 (5.9)	61 (4.6)
Direct vasodilators	112 (8.5)	40 (3.0)

Medication information missing for three participants in each treatment group, therefore percentages denote frequency of participants out of total sample list in each column.

eTable 3. Serious adverse events, conditions of interest, and monitored clinical measures by treatment group in SPRINT participants 75 years or older

	Intensive-treatment		Standard-treatment			
	N	N with event (%)	N	N with event (%)	HR (95% CI)	p-value
Serious Adverse Events[1]	1,317	637 (48.4)	1,319	637 (48.3)	0.99 (0.89, 1.11)	0.895
By Frailty Status						
Fit	159	50 (31.4)	190	66 (34.7)	0.84 (0.53, 1.31)	0.439
Less Fit	711	333 (46.8)	745	341 (45.8)	0.97 (0.83, 1.14)	0.714
Frail	440	251 (57.0)	375	227 (60.5)	1.02 (0.84, 1.24)	0.844
By Gait Speed						
≥0.8 m/s	880	419 (47.6)	893	412 (46.1)	1.03 (0.89, 1.18)	0.716
<0.8 m/s	371	187 (50.4)	369	195 (52.8)	1.00 (0.80, 1.25)	0.988
Missing	66	31 (47.0)	57	30 (52.6)	0.79 (0.42, 1.50)	0.469
Conditions of Interest[2] **(SAE only)**	1,317	214 (16.2)	1,319	190 (14.4)	1.18 (0.97, 1.44)	0.106
By Frailty Status						
Fit	159	11 (6.9)	190	15 (7.9)	0.60 (0.24, 1.45)	0.262
Less Fit	711	103 (14.5)	745	102 (13.7)	1.03 (0.77, 1.38)	0.832
Frail	440	100 (22.7)	375	71 (18.9)	1.41 (1.01, 1.96)	0.042
By Gait Speed						
≥0.8 m/s	880	133 (15.1)	893	127 (14.2)	1.14 (0.88, 1.47)	0.318
<0.8 m/s	371	66 (17.8)	369	58 (15.7)	1.27 (0.86, 1.90)	0.229
Missing	66	15 (22.7)	57	5 (8.8)	2.83 (0.98, 10.23)	0.055
Individual Conditions of Interest (SAE only)						
Hypotension	1,317	32 (2.4)	1,319	19 (1.4)	1.71 (0.97, 3.09)	0.066
Syncope	1,317	39 (3.0)	1,319	32 (2.4)	1.23 (0.76, 2.00)	0.401

	Intensive-treatment		Standard-treatment			
	N	N with event (%)	N	N with event (%)	HR (95% CI)	p-value
Bradycardia	1,317	38 (2.9)	1,319	40 (3.0)	0.89 (0.57, 1.40)	0.610
Electrolyte Abnormality	1,317	53 (4.0)	1,319	36 (2.7)	1.51 (0.99, 2.33)	0.058
Injurious Fall[3]	1,317	65 (4.9)	1,319	73 (5.5)	0.91 (0.65, 1.29)	0.605
Acute Kidney Injury or Acute Renal Failure[4]	1,317	72 (5.5)	1,319	53 (4.0)	1.41 (0.98, 2.04)	0.061
Conditions of Interest[2] (ER Visit or SAE)	1,317	313 (23.8)	1,319	305 (23.1)	1.05 (0.89, 1.23)	0.589
By Frailty Status						
Fit	159	22 (13.8)	190	27 (14.2)	0.75 (0.39, 1.39)	0.356
Less Fit	711	155 (21.8)	745	165 (22.1)	0.97 (0.77, 1.22)	0.788
Frail	440	136 (30.9)	375	110 (29.3)	1.17 (0.89, 1.54)	0.254
By Gait Speed						
≥0.8 m/s	880	202 (23.0)	893	205 (23.0)	1.02 (0.83, 1.24)	0.877
<0.8 m/s	371	91 (24.5)	369	93 (25.2)	1.03 (0.75, 1.42)	0.865
Missing	66	20 (30.3)	57	7 (12.3)	2.98 (1.16, 9.19)	0.022
Individual Conditions of Interest (ER Visit or SAE)						
Hypotension	1,317	44 (3.3)	1,319	27 (2.0)	1.66 (1.03, 2.73)	0.039
Syncope	1,317	57 (4.3)	1,319	43 (3.3)	1.28 (0.85, 1.92)	0.240
Bradycardia	1,317	47 (3.6)	1,319	44 (3.3)	1.01 (0.67, 1.54)	0.961
Electrolyte Abnormality	1,317	60 (4.6)	1,319	43 (3.3)	1.44 (0.97, 2.16)	0.067
Injurious Fall[3]	1,317	153 (11.6)	1,319	186 (14.1)	0.80 (0.64, 0.99)	0.040
Acute Kidney Injury or Acute Renal Failure[4]	1,317	73 (5.5)	1,319	55 (4.2)	1.39 (0.97, 1.99)	0.072
Monitored Clinical Events						
Laboratory Measures[5]						
Sodium<130 mmol/L	1,317	69 (5.2)	1,319	45 (3.4)	1.56 (1.07, 2.30)	0.02

	Intensive-treatment		Standard-treatment			
	N	N with event (%)	N	N with event (%)	HR (95% CI)	p-value
Sodium>150 mmol/L	1,317	1 (0.1)	1,319	0 (0.0)	-	-
Potassium<3 mmol/L	1,317	17 (1.3)	1,319	11 (0.8)	1.50 (0.69, 3.37)	0.303
Potassium>5.5 mmol/L	1,317	69 (5.2)	1,319	65 (4.9)	1.01 (0.71, 1.42)	0.972
Signs and Symptoms						
Orthostatic hypotension[6]	1,317	277 (21.0)	1,319	288 (21.8)	0.90 (0.76, 1.07)	0.241
Orthostatic hypotension with dizziness	1,317	25 (1.9)	1,319	17 (1.3)	1.44 (0.77, 2.73)	0.252

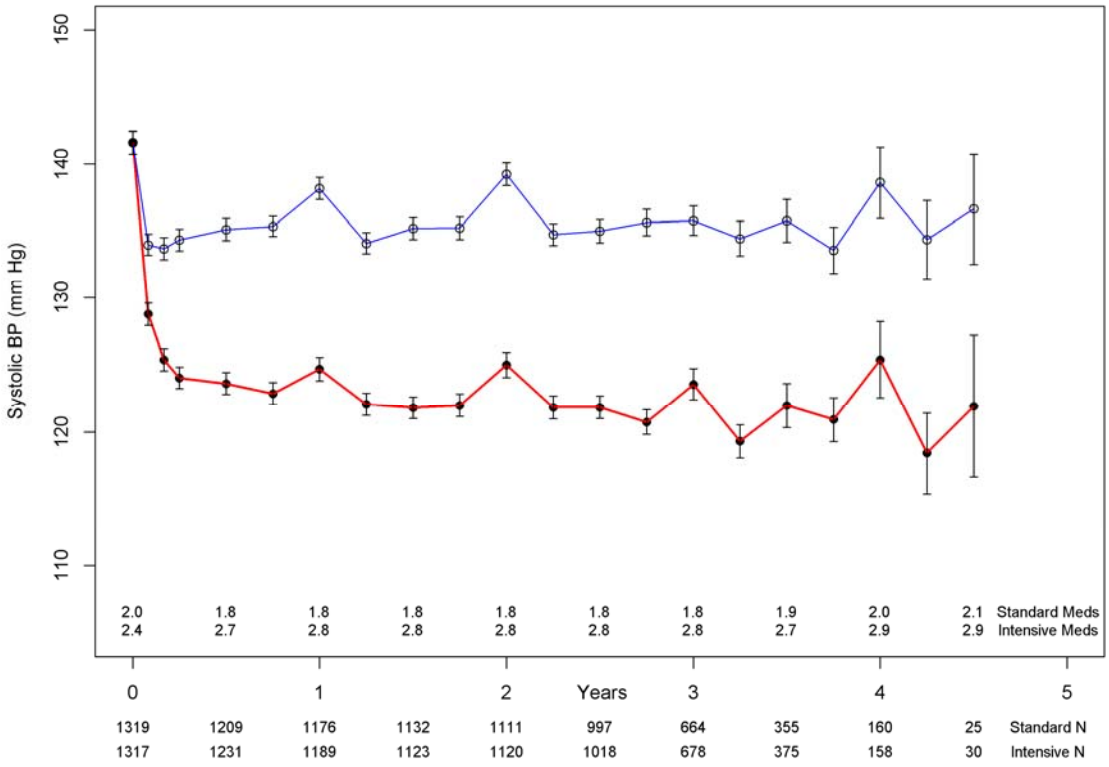
[1]Defined as an event that was fatal or life threatening, resulting in significant or persistent disability, requiring or prolonging a hospitalization, or was an important medical event that the investigator judged to be a significant hazard or harm to the participant that may have required medical or surgical intervention to prevent one of the other events listed above. [2]Conditions of interest include hypotension, syncope, bradycardia, electrolyte abnormalities, injurious falls, or acute kidney injury or acute renal failure.[3]An injurious fall was defined as a fall that resulted in evaluation in an emergency department or resulted in hospitalization. [4]Acute Kidney Injury and Acute Renal Failure were coded if the diagnosis was listed in the hospital discharge summary and was felt to be one of the top 3 reasons for admission or continued hospitalization. A few cases of acute kidney injury were noted in an emergency department if the participant presented for one of the other conditions of interest. [5]Detected on routine or as needed SPRINT labs; routine labs drawn quarterly for first year, then every 6 months; numbers represent the number (%) of participants having 1 or more alert value. [6]Defined as drop in systolic BP ≥20 mmHg or drop in diastolic ≥10 mmHg 1 minute after standing. Standing blood pressures were measured at screening, baseline, 1, 6, and 12 months and yearly thereafter. Participants were asked if they felt dizzy at the time the orthostatic measure was taken.

eTable 4. Serious adverse events (SAE) and conditions of interest (SAE only) by treatment group in SPRINT participants 75 years or older allowing for recurrent events

Serious Adverse Events	**Intensive-treatment**			**Standard-treatment**			
	N	Events	MCC (95% CI)	N	Events	MCC (95% CI)	HR (95% CI)
Overall	1,317	1,222	92.7 (85.6, 100.5)	1,319	1,387	103.6 (92.8, 114.7)	0.93 (0.86, 1.00)
Frailty Status							
Fit	159	77	49.5 (34.0, 69.6)	190	94	51.5 (36.7, 68.3)	0.95 (0.70, 1.28)
Less Fit	711	566	81.0 (72.2, 89.8)	745	729	96.2 (82.6, 112.8)	0.88 (0.79, 0.99)
Frail	440	573	127.2 (110.4, 143.6)	375	558	144.0 (125.3, 165.2)	0.92 (0.82, 1.04)
Gait Speed							
≥0.8 m/s	880	730	83.9 (75.4, 92.1)	893	858	94.3 (83.8, 104.5)	0.91 (0.82, 1.00)
<0.8 m/s	371	408	108.9 (91.9, 127.4)	369	468	125.2 (101.4, 155.9)	0.94 (0.82, 1.08)
Missing	66	84	119.8 (78.7, 166.3)	57	61	110.1 (70.2, 150.8)	0.98 (0.71, 1.37)
Conditions of Interest (SAE Only)	**Intensive-treatment**			**Standard-treatment**			
	N	Events	MCC (95% CI)	N	Events	MCC (95% CI)	HR (95% CI)
Overall	1,317	279	21.1 (18.1, 24.6)	1,319	246	19.4 (16.2, 22.8)	1.12 (0.94, 1.33)
Frailty Status							
Fit	159	13	9.3 (4.1, 15.4)	190	18	9.8 (4.4, 16.1)	0.85 (0.41, 1.72)
Less Fit	711	124	17.7 (14.1, 21.6)	745	124	17.0 (13.4, 21.2)	1.03 (0.80, 1.32)
Frail	440	142	31.4 (24.7, 38.4)	375	100	28.1 (20.8, 35.8)	1.19 (0.92, 1.55)
Gait Speed							
≥0.8 m/s	880	168	19.3 (16.0, 23.1)	893	160	17.9 (14.3, 21.7)	1.07 (0.86, 1.33)
<0.8 m/s	371	88	23.8 (18.1, 30.3)	369	81	24.7 (17.5, 31.9)	1.07 (0.79, 1.45)
Missing	66	23	29.3 (15.1, 47.2)	57	5	8.3 (1.9, 16.4)	2.85 (1.17, 8.50)

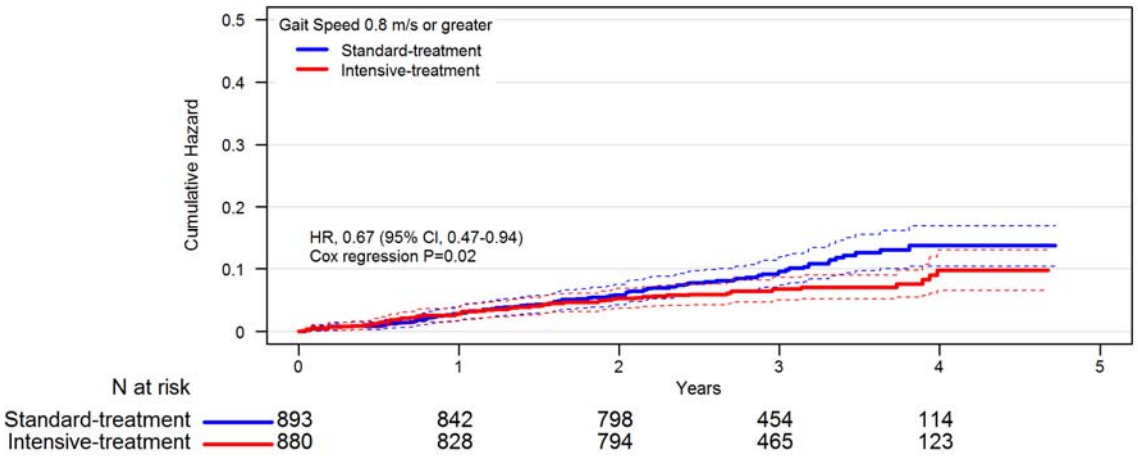
(CI) Confidence Interval. (MCC) Mean Cumulative Count estimate at 3.14 years per 100 individuals. (HR) Hazard Ratio based on Prentice, Williams, and Peterson recurrent events model, allowing for recurrent SAEs and conditions of interest. Conditions of interest include hypotension, syncope, bradycardia, electrolyte abnormalities, injurious falls, or acute kidney injury or acute renal failure.

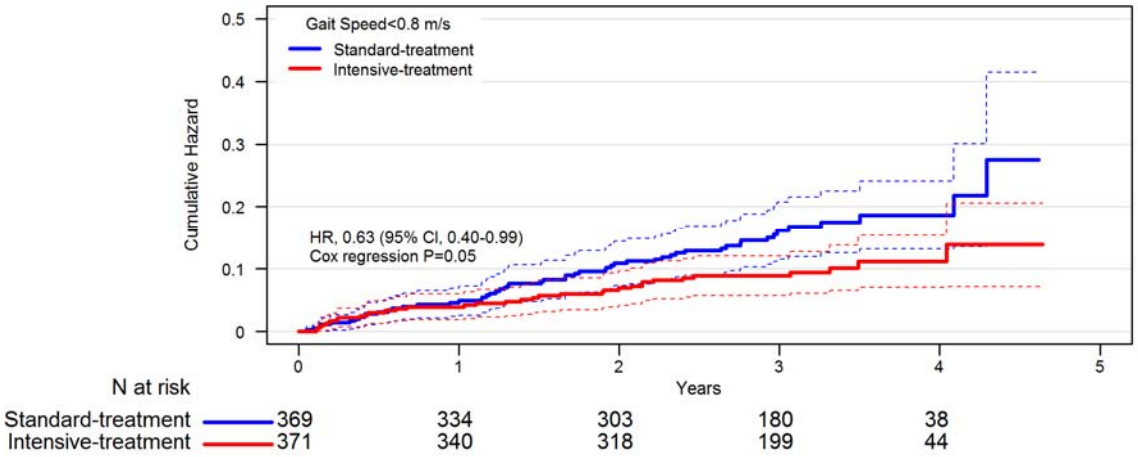
eFigure 1. Mean systolic blood pressures (BP) over time by treatment group in SPRINT participants 75 years or older

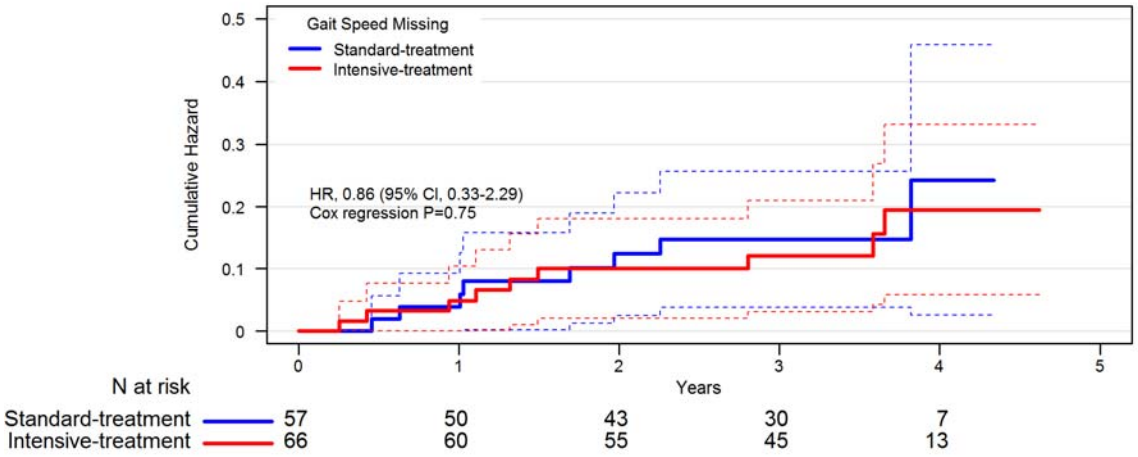


Open circles denote mean systolic BP in standard-treatment group, while numbers in Standard Meds row denote mean number of antihypertensive medications at 6 month intervals in standard-treatment group. Solid circles denote mean systolic BP in intensive-treatment group, while numbers in Intensive Meds row denote mean number of antihypertensive medications at 6 month intervals in intensive-treatment group. Error bars represent 95% confidence intervals.

eFigure 2. Kaplan-Meier curves for the primary cardiovascular disease outcome by gait speed







Cardiovascular disease (CVD) primary outcome includes non-fatal myocardial infarction (MI), acute coronary syndrome not resulting in MI, non-fatal stroke, non-fatal acute decompensated heart failure, and CVD death. Dashed lines denote 95% point-wise confidence intervals.