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Intensive blood pressure control, gait speed, and mobility limitation: The Systolic Blood Pressure Intervention Trial

Michelle C. Odden, PhD¹, Carmen A. Peralta, MD², Dan R. Berlowitz, MD³, Karen C. Johnson, MD, MPH⁴, Jeffrey Whittle, MD⁵, Dalane W. Kitzman, MD⁶, Srinivasan Beddhu, MD⁷, John W. Nord, MD⁷, Vasilios Papademetriou, MD⁸, Jeff D. Williamson, MD⁹, and Nicholas M. Pajewski, PhD¹⁰ for the SPRINT Research Group

¹School of Biological and Population Health Sciences, Oregon State University, Corvallis, OR

²Department of Medicine, University of California San Francisco, San Francisco, CA

³Bedford Veterans Affairs Hospital, Bedford, MA; School of Public Health, Boston University, Boston, MA

⁴Department of Preventive Medicine, University of Tennessee Health Science Center, Memphis, TN

⁵Department of Medicine, Medical College of Wisconsin; and Primary Care Division, Clement J. Zablocki Veterans Affairs Medical Center, Milwaukee, WI

⁶Department of Internal Medicine, Section on Cardiology, Wake Forest School of Medicine, Winston-Salem, NC

⁷Veterans Affairs Salt Lake City Healthcare System, Salt Lake City, UT; Department of Medicine, University of Utah School of Medicine, Salt Lake City, UT

⁸Georgetown University; VA Medical Center, Washington, D.C

⁹Department of Internal Medicine, Section on Geriatric Medicine, Wake Forest School of Medicine, Winston-Salem, NC

¹⁰Department of Biostatistical Sciences, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC

Abstract

Importance—Intensive blood pressure (BP) control confers benefit on cardiovascular morbidity and mortality; whether it affects physical function outcomes is unknown.

Correspondence to: Nicholas M. Pajewski, Ph.D., Department of Biostatistical Sciences, Division of Public Health Sciences, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27106, (336) 713-1396, npajewsk@wakehealth.edu.

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Conflicts of Interest: Dr. Peralta is a Consultant for Cricket Health, Inc. and Vital Labs, Inc. All remaining authors have no conflicts of interest to disclose.

Objective—To examine the effect of intensive blood pressure (BP) control on changes in gait speed and mobility status.

Design, Setting, and Participants—Randomized, controlled trial of hypertensive individuals aged 75 years or older without a history of diabetes or stroke, who participated in the Systolic Blood Pressure Intervention Trial (SPRINT).

Interventions—Participants were randomized to a systolic BP target of <120 mmHg (intensive-treatment, N=1,317) versus <140 mmHg (standard-treatment, N=1,319).

Main Outcomes and Measures—Gait speed was measured using a 4 meter walk test. Self-reported information concerning mobility was obtained from items on the Veterans Rand 12 Item Health Survey (VR-12) and the EQ-5D. Mobility limitation was defined as a gait speed <0.6 m/s (1.34 mph) or self-reported limitations in walking and climbing stairs.

Results—Among 2,636 participants (mean age 79.9 years; 37.9% women), median follow-up was 3 years. There was no difference in mean gait speed decline between the intensive-treatment and standard-treatment groups (mean difference = 0.000 m/s per year, 95% CI: -0.005 to 0.005, $p=0.876$). There was no evidence of any treatment group differences in subgroups defined by age, sex, race/ethnicity, baseline BP, chronic kidney disease, or a history of cardiovascular disease. There was a modest interaction by VR-12 Physical Component Summary Score, although the effect did not reach statistical significance in either subgroup: mean differences of 0.004 m/s per year (95% CI: -0.002 to 0.010) and -0.008 m/s per year (95% CI: -0.016 to 0.001) among those with scores ≥ 40 and <40, respectively ($p=0.027$ for interaction). Multi-state models, allowing for the competing risk of death, demonstrated no effect of intensive treatment on transitions to mobility limitation (hazard ratio: 1.06, 95% CI: 0.92 to 1.22).

Conclusions and Relevance—Among adults age 75 years or older in SPRINT, treating to a systolic BP target <120 mm Hg, compared with a target of <140 mm Hg, had no effect on changes in gait speed, and was not associated with changes in mobility limitation.

Trial Registration—clinicaltrials.gov Identifier: NCT01206062

Introduction

Results from The Systolic Blood Pressure Intervention Trial (SPRINT) indicate that targeting a systolic blood pressure (BP) <120 mmHg confers benefits on cardiovascular morbidity and mortality in hypertensive adults aged ≥ 50 years free of diabetes and stroke.¹ This benefit was apparent in adults 75 years or older and, in exploratory analyses, also among persons with frailty or slow gait speed.² A critical direction for SPRINT is to evaluate the balance between this benefit and other health consequences of intensive BP control.³ This is especially true for adults 75 years of age or older, where it has been estimated that 5.8 million adults in this age range would meet the SPRINT eligibility criteria.⁴ Physical functioning during the course of the trial has yet to be reported.

Gait speed is a well-established physical function measure predictive of adverse health outcomes and mortality.^{5,6} Decline in gait speed may be an early harbinger of decline in physical function, the development of disability, and loss of independence.⁷ Observational evidence suggests a faster rate of gait speed decline among older adults with high BP.⁸ In

contrast, some evidence suggests that among very old adults, lower systolic BP is associated with greater limitations on activities of daily living and greater probability of worsening disability.⁹ There have been no large-scale randomized controlled trials of BP control that have reported on gait speed as an outcome.

Here we compare the trajectory of gait speed decline and incident mobility limitation in the intensive-treatment and standard-treatment groups in SPRINT, within the subgroup of participants 75 years or older at the time of randomization. The findings of this study will help inform our understanding of the effect of intensive BP control on the net balance of health outcomes in older adults with hypertension.

Methods

Population

The design, eligibility, and baseline characteristics of SPRINT have been described previously.¹⁰ Of 9,361 participants randomized to an intensive SBP target of <120 mm Hg or a standard target of <140 mm Hg, 2,636 were 75 years or older. The characteristics of participants in this subgroup by treatment group have been previously described.² The only statistically significant treatment group differences at baseline were a higher frequency of aspirin use (62.3% versus 58.0%) and higher prevalence of frailty, as assessed by a 37-item frailty index,¹¹ (33.4% versus 28.4%) in the intensive-treatment group.

Study Measurements

Demographic, clinical, and laboratory data were collected at baseline. Race/ethnicity was collected by self-report. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters, squared. Estimated glomerular filtration rate (eGFR) was calculated by the 4-variable Modification in Diet in Renal Disease (MDRD) equation.¹² Physical and mental health-related quality of life were assessed using the Veterans RAND 12 item Health Survey (VR-12).¹³ The VR-12 is summarized via a Physical and Mental Component Summary Score (PCS and MCS respectively); for each a score of 50 represents the U.S. population mean, 10 points represent one standard deviation, and higher scores denote better quality of life (QOL).¹⁴

Gait speed measurements

Gait speed was measured at the time of randomization and annually thereafter via a timed 4-meter walk performed twice at the participant's usual pace from a standing start. The use of a walking assistive device was permitted if typically used by the participant to walk short distances. The faster of the two gait speeds in meters/second (m/s) was used in this analysis. Gait speeds slower than 0.20 m/s and faster than 2.0 m/s were set to missing (n=22).

Self-reported mobility

We considered two self-reported questions concerning mobility from QOL instruments administered at baseline and then annually thereafter. From the VR-12,¹³ we considered the question, "Does your health now limit you in climbing several flights of stairs?", with responses of "Yes, Limited A Lot", "Yes, Limited A Little", or "No, Not Limited At All".

We also considered the mobility question from the EQ-5D,¹⁵ with responses of “I have no problems in walking about”, “I have some problems in walking about”, or “I am confined to bed”. Mobility limitation was defined as A) having a gait speed below 0.6 m/s¹⁶ OR B) reporting a lot of difficulty climbing stairs, AND C) reporting some difficulty walking about or being confined to bed [A or (B and C)]. As a secondary approach, we examined models that defined mobility limitation based solely on gait speed (<0.6 m/s). Because gait speed based on a 4 meter walk test entails measurement error, we required that any changes in gait speed were 0.127 m/s (the 95% confidence limit for an estimated minimal detectable change¹⁷) in order to define a transition between mobility status for models defining mobility limitation based solely on gait speed. For example, if a participant's gait speed at baseline was 0.650 m/s, their gait speed would need to decrease to <0.523 m/s at a subsequent visit in order to be classified as having developed a mobility limitation.

Duration of Follow-up

The Director of the National Heart, Lung, and Blood Institute (NHLBI) accepted the Data Safety and Monitoring Board recommendation to stop the SPRINT intervention on August 20th, 2015. In order to maximize the number of follow-up assessments for gait speed, we included study visits through December 1st, 2015. Our analysis includes 527 gait speed assessments during a period where participants were transitioning to having their BP managed by their primary care provider. Comparing BPs in the 103 day period from 8/20/2015 to 12/1/2015 to BPs measured in the 103 days prior to 8/20/2015, the mean systolic BP increased slightly in both treatment groups, from 133.6 to 135.5 mm Hg in the standard-treatment group and from 118.4 to 121.3 mm Hg in the intensive-treatment group. However, the mean systolic BP difference only decreased by approximately 1 mm Hg during this transition period, from 15.2 mm Hg (95% CI: 14.6 to 15.8 mm Hg) to 14.1 mm Hg (95% CI: 13.5 to 14.7 mm Hg).

Statistical Analysis

Linear mixed-effect models, assuming linear decline, were used to compare longitudinal trajectories for gait speed between the treatment groups. The models included nested random effects (participants within clinic site), to address within-subject correlations due to repeated assessments and correlations between participants at the same clinical site. We included a time by randomization group interaction term to test if the change in gait speed differed between the treatment groups. The mixed models were fit using SAS v9.4 (SAS, Cary, NC). We tested for interaction between treatment group and the following subgroups: age (<80 years versus 80 years and older), sex, race (black versus non-black), baseline systolic BP (<140 mmHg, 140-159 mmHg, 160 mmHg), and presence of chronic kidney disease (CKD, eGFR <60 ml/min/1.73m²), history of cardiovascular disease, and VR-12 PCS (<40 versus ≥40).

Sensitivity Analyses—We conducted two sensitivity analyses for the models of change in gait speed. We used multiple imputation techniques to infer missing gait speed measurements, using the same mixed model framework described above. Details about the multiple imputation procedure are described in the Supplementary Material. Second, we

censored gait speed measures at the time of the NHLBI Director decision to stop the SPRINT intervention.

Multi-State Modeling—We examined transitions in mobility status using a multi-state model as shown in Figure 1; this method accounts for the competing risk of death. Mobility limitation was defined based on gait speed and self-reported limitation in walking and climbing stairs, as described above. The model included three states: alive with no mobility-limitation, alive with a mobility-limitation, and death. We conducted a secondary analysis of mobility limitation defined by gait speed alone as described above. The multi-state models were fit using the *mstate* package for the R Statistical Computing Environment.^{18,19}

Results

Among 2,636 randomized participants aged 75 years or older, 2,629 (99.7%) had information on mobility at baseline. (Table 1 and Supplementary Table 1) In defining mobility status at baseline, 2,541 participants had gait speed measured, while mobility status was based solely on self-report in an additional 88 participants. Of these, 464 (17.6%) were classified as having a mobility limitation at baseline, with similar frequencies in the intensive-treatment (N = 233/1,313, 17.8%) and standard-treatment (N=231/1,316, 17.6%) groups. Participants with a mobility limitation were older, and more likely to be female and not white. They had higher BMI and albumin to creatinine ratio, and lower eGFR than participants without a mobility limitation. Participants with a mobility limitation were using more antihypertensive agents and were more likely to use aspirin at baseline.

The mean gait speed at baseline was 0.91 m/s (2.04 mph) with a mean annual change of -0.026 m/s (95% CI: -0.028 to -0.023). The trajectory of gait speed appeared similar among participants in the intensive and standard treatment groups. (Figure 2) There was no difference in mean gait speed decline between participants randomized to intensive-treatment and those randomized to standard-treatment (mean difference= 0.000 m/s per year, 95% CI: -0.005 to 0.005, p-value for difference=0.879). (Table 2) The change in gait speed among intensive-treatment and standard-treatment groups did not differ significantly for subgroups defined by age, sex, race/ethnicity, baseline systolic BP, chronic kidney disease, or history of cardiovascular disease (Table 2). The effect of intensive treatment on change in gait speed was modestly more beneficial among those with higher VR-12 Physical Component Summary Scores, although the effect on change in gait speed did not reach statistical significance in either group: mean differences of 0.004 m/s (95% CI: -0.002 to 0.010) and -0.008 m/s (95% CI: -0.016 to 0.001) among those with scores ≥ 40 and <40 , respectively. The proportion of missing data for gait speed appeared similar between the intensive-treatment and standard-treatment groups and ranged from $<5\%$ at baseline to approximately 20% at 36 and 48 months (Supplementary Table 1). The proportion of missing data over time was greater among those with a mobility limitation at baseline than those without a mobility limitation (Supplementary Table 2). Multiple imputation of missing gait speed measures did not alter the results. The difference in mean gait speed decline per year between the intensive-treatment group and the standard-treatment group was -0.000 (95% CI: -0.005 to 0.005 m/s, p-value =0.983) after imputation. Censoring follow-up at the time of the decision to stop the SPRINT intervention also did not impact the results; the

difference in mean gait speed decline per year was also 0.000 (95% CI: -0.006 to 0.005 m/s, p-value for difference=0.931).

The mean transition rate from no mobility limitation to mobility limitation was 12.5 per 100 person-years. Transitions from no mobility limitation to mobility limitation and vice versa did not differ in the intensive treatment and standard treatment groups. (Table 3) There was no effect of intensive treatment on transitions to mobility limitation (HR: 1.06, 95% CI: 0.91 to 1.22) or on transitions from mobility limitation to no mobility limitation (HR: 0.92, 95% CI: 0.77, 1.10). Participants in the intensive treatment group with no mobility limitation had a lower risk of death than those in the standard treatment group (HR = 0.62, 95% CI: 0.43 to 0.90). Findings were unchanged when we restricted the definition of mobility limitation to only consider clinically relevant changes in gait speed, though the effect of intensive BP control on mortality (from a state of no mobility limitation) was no longer statistically significant.

Discussion

Among adults age 75 years or older in SPRINT, there were no differences in gait speed decline among those in the intensive-treatment versus standard-treatment groups. In both groups, the mean rate gait speed decline was approximately 0.08 m/s (0.18 mph) over 3 years. Additionally, intensive treatment was not associated with changes in mobility limitation compared with standard treatment. These findings were robust to statistical attempts to account for missing data and the competing risk of death. The effect of intensive blood pressure lowering on change in gait speed was consistent across subgroups defined by age, sex, race, systolic BP, history of CKD, history of CVD, although there was modest evidence of a differential effect by physical QOL.

SPRINT is the first large-scale randomized controlled trial of BP control to report results concerning gait speed as an outcome. Our findings are consistent with findings from the Systolic Hypertension in the Elderly Program (SHEP), which found no significant differences in change in function in basic, moderate, or advanced activities of daily living (ADL).²⁰ However, a subsequent paper demonstrated that the presence of missing data may have biased the findings against a benefit of the treatment group.²¹ Additionally, investigators from the SHEP trial found a modest benefit of treatment on self-reported evening walks, considered a leisure time activity in the SHEP questionnaire.²⁰ The ongoing INTensive versus Standard Ambulatory Blood Pressure Lowering to Prevent Functional Decline In The Elderly (INFINITY) trial may provide additional insight regarding the role of ambulatory BP control on mobility outcomes.²²

Observational evidence on the effect of BP on gait speed is mixed, although the majority points towards an association of higher BP and worse gait function among older adults. In the Cardiovascular Health Study, participants with a BP of >140/90 mmHg had a faster rate of decline in gait speed than those without.⁸ In the LIFE-Pilot trial, investigators found that wider pulse pressure was associated with slower gait.²³ A small study of older adults found that adults with hypertension had worse gait function parameters, although not slower gait speed.²⁴ It has been hypothesized that worsening gait and functional performance may be

due to increased white matter hyperintensities among individuals with hypertension. Investigators in the Health, Aging, and Body Composition (Health ABC) study found that white matter hyperintensities among specific regions were associated with slower gait.²⁵ However, some evidence suggests the opposite relationship may exist among the very old. Investigators from the Leiden-85+ study found higher systolic BP was associated with less worsening of ADLs compared with lower BP.⁹ However limitations in ADLs are likely to be downstream of changes in mobility status, so these conflicting findings may be due to the evaluation of the role of BP at differing stages of the disablement process.

We found modest evidence of an interaction by physical QOL, such that among those with better physical QOL, intensive BP lowering appeared to be associated with a slower rate of decline in gait speed; whereas among those with worse physical QOL, intensive BP lowering appeared to be associated with faster decline in gait speed. It is possible that those with preserved physical QOL may gain additional benefit from intensive treatment. However, these findings should be interpreted with caution as the effect size was modest and did not reach statistical significance in either group. Further research is needed to determine if there are factors that can differentiate the populations for whom intensive BP treatment may slow or accelerate gait speed decline.

There are several possible explanations for why intensive treatment did not substantially impact gait speed or mobility outcomes in SPRINT participants 75 years or older, or in the majority of subgroups examined. Gait speed incorporates function across multiple domains including cardiorespiratory fitness, musculoskeletal health, vision, balance, and even mood/psychosocial health,^{5,16} so it is possible that the cardiovascular benefit conferred from intensive BP control did not extend to mobility outcomes due to the multifactorial nature of mobility. The heart failure literature presents a similar conundrum in that the optimal therapy can differ for the outcomes of survival and exercise capacity; medications that confer a survival benefit, such as beta-adrenergic blockers, can negatively impact exercise capacity.^{26,27} Additionally, physical functioning is affected by a lifetime of exposures, so it is possible that the intervention was not long enough to significantly impact mobility.

SPRINT participants aged 75 years and older had an average decline in gait speed of approximately 0.08 m/s over 3 years. A pooled analysis of the association of gait speed and survival found a 12% lower risk of mortality per 0.1 m/s increment of gait speed,⁵ indicating that the change observed in SPRINT is clinically relevant. The gait speed decline observed in SPRINT is similar to other populations of older adults. In the Cardiovascular Health Study, a study of community dwelling adults aged 65 years and older at baseline, gait speed declined a median of -0.2 m/s over 9 years,²⁸ or approximately 0.022 m/s per year. In Health ABC, the estimated change in gait speed over 4 years was 0.10 m/s or a decline of 0.025 m/s per year.²⁹ The mean annual decline in gait speed for participants aged 75-79 in the InCHIANTI study was 0.036 m/s per year for women and 0.034 for men.³⁰

Our study has a number of limitations. SPRINT excluded individuals with a history of diabetes or stroke, symptomatic heart failure, or an indication for a specific BP lowering medication, so our findings may not be applicable to populations with these conditions. SPRINT also excluded individuals with orthostatic hypotension or dementia, and did not

enroll elderly persons living in nursing homes. The large majority of SPRINT participants were already treated with BP medication; therefore our results do not address the impact of initiating BP therapy. Additionally, the clinic staff that performed gait speed assessments were not blinded to treatment assignment. There was a modest amount of missing data, although this appeared evenly distributed across treatment groups and the results were unchanged when we used multiple imputation. Furthermore, the results were similar when we used gait speed alone as an outcome, or mobility limitation which included self-reported data. Finally, SPRINT was stopped early owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group, so we are not able to look at the long term effects of intensive BP lowering on gait and mobility outcomes. This may have limited power to detect differences in gait speed or mobility limitation.

In summary, intensive BP lowering was not associated with changes in gait speed or transitions in mobility status among adults 75 years and older in SPRINT. The benefits of intensive BP lowering on cardiovascular prevention and mortality do not appear to impact short-term mobility.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Diagram of multi-state model for mobility limitation

Boxes denote states for multi-state model, arrows depict possible transitions.

Figure 2. Least square means for gait speed by treatment group over the course of follow-up
Circles denote estimated least square mean for gait speed based on linear mixed model, treating time discretely (0, 12, 24, 36, and 48 months). Error bars represent 95% confidence intervals.

Table 1
Baseline characteristics of SPRINT participants 75 years or older by mobility status

Characteristic	No Mobility Limitation N=2,165	Mobility Limitation N=464	p-value
Randomized to intensive-treatment	1,080 (49.9%)	233 (50.2%)	0.938
Age, Years, mean (SD)	79.6 ± 3.8	81.0 ± 4.6	<0.001
Age ≥ 80 years	909 (42.0%)	254 (54.7%)	<0.001
Female sex	770 (35.6%)	226 (48.7%)	<0.001
Race / Ethnicity			<0.001
White	1,676 (77.4%)	284 (61.2%)	
Black	330 (15.2%)	120 (25.9%)	
Hispanic	115 (5.3%)	57 (12.3%)	
Other	44 (2.0%)	3 (0.6%)	
Systolic BP, mmHg, mean (SD)	141.5 ± 15.8	142.5 ± 15.7	0.187
Systolic BP			0.773
<140 mmHg	1,024 (47.3%)	211 (45.5%)	
140 to <160 mmHg	868 (40.1%)	192 (41.4%)	
≥ 160 mmHg	273 (12.6%)	61 (13.1%)	
Diastolic BP, mmHg, mean (SD)	71.3 ± 10.9	70.7 ± 11.0	0.254
Body Mass Index (kg/m ²), mean (SD)	27.5 ± 4.4	29 ± 5.8	<0.001
Serum creatinine, mg/dL, median (IQR)	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)	0.109
eGFR, ml/min/1.73m ² , mean (SD)	63.8 ± 17.7	61.4 ± 20.2	0.012
eGFR<60 ml/min/1.73m ²	927 (43.0%)	233 (50.7%)	0.003
Urine albumin to creatinine ratio (mg/g), median (IQR)	12.4 (7.0 to 29.8)	16.9 (9.6 to 40.3)	<0.001
History of cardiovascular disease (CVD)	525 (24.2%)	121 (26.1%)	0.441
# of antihypertensive medications at baseline, mean (SD)	1.9 ± 1.0	2.1 ± 1.0	<0.001
Statin use at baseline	1,143 (53.2%)	235 (51.3%)	0.485
Aspirin use at baseline	1,326 (61.4%)	259 (55.9%)	0.035
10-year Framingham CVD Risk Score, %, median (IQR)	24.8 (17.0 to 33.0)	23.6 (16.2 to 33.3)	0.335
VR-12 Physical Component Summary Score, mean (SD)	46.2 ± 8.5	34.1 ± 10.6	<0.001
VR-12 Mental Component Summary Score, mean (SD)	55.4 ± 8.0	53.7 ± 10.0	<0.001

Mobility limitation was defined as having a gait speed <0.6 m/s OR (reporting a lot of difficulty climbing stairs AND reporting some difficulty walking about or being confined to bed). eGFR = Estimated glomerular filtration rate based on MDRD study equation. SD = standard deviation, IQR = interquartile range.

Table 2
Linear mixed model estimates of annual change in gait speed by treatment group and for subgroups

Subgroup	N	Intensive-treatment Annual Change in Gait Speed, m/s (95% CI)	Standard-treatment Annual Change in Gait Speed, m/s (95% CI)	Intensive - Standard Difference (95% CI)	p-value	Interaction p-value
Overall	2,614	-0.026 (-0.029, -0.022)	-0.026 (-0.029, -0.022)	0.000 (-0.005, 0.005)	0.879	
Age						0.290
<80 years	1,461	-0.023 (-0.028, -0.019)	-0.021 (-0.026, -0.017)	-0.002 (-0.008, 0.005)	0.574	
80 years	1,153	-0.029 (-0.035, -0.024)	-0.033 (-0.038, -0.028)	0.004 (-0.004, 0.011)	0.356	
Sex						0.206
Male	1,627	-0.025 (-0.029, -0.020)	-0.028 (-0.032, -0.023)	0.003 (-0.004, 0.009)	0.373	
Female	987	-0.027 (-0.032, -0.021)	-0.023 (-0.028, -0.018)	-0.004 (-0.011, 0.004)	0.358	
Race / Ethnicity						0.906
Nonblack	2,153	-0.027 (-0.030, -0.023)	-0.027 (-0.031, -0.023)	0.000 (-0.005, 0.006)	0.865	
Black	461	-0.021 (-0.029, -0.013)	-0.021 (-0.029, -0.012)	0.000 (-0.012, 0.011)	0.957	
Systolic BP						0.435
<140 mmHg	1,227	-0.024 (-0.029, -0.013)	-0.024 (-0.029, -0.019)	-0.000 (-0.007, 0.007)	0.973	
140 to <160 mmHg	1,056	-0.025 (-0.031, -0.019)	-0.028 (-0.034, -0.023)	0.003 (-0.005, 0.011)	0.436	
160 mmHg	331	-0.033 (-0.043, -0.024)	-0.026 (-0.035, -0.017)	-0.007 (-0.020, 0.006)	0.269	
Previous CKD						0.523
No	1,446	-0.023 (-0.027, -0.018)	-0.025 (-0.030, -0.020)	0.002 (-0.004, 0.009)	0.525	
Yes	1,156	-0.029 (-0.034, -0.024)	-0.028 (-0.033, -0.023)	-0.001 (-0.009, 0.006)	0.771	
Previous CVD						0.089
No	1,972	-0.026 (-0.031, -0.022)	-0.024 (-0.028, -0.020)	-0.002 (-0.008, 0.004)	0.500	
Yes	642	-0.023 (-0.029, -0.017)	-0.031 (-0.038, -0.024)	0.008 (-0.001, 0.017)	0.089	
VR-12 PCS						0.027
PCS 40	1,769	-0.023 (-0.027, -0.018)	-0.027 (-0.031, -0.022)	0.004 (-0.002, 0.010)	0.171	
PCS<40	835	-0.032 (-0.038, -0.026)	-0.024 (-0.030, -0.018)	-0.008 (-0.016, 0.001)	0.073	

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N denotes number of participants with at least one assessment of gait speed (at baseline or during the course of follow-up). BP = Blood Pressure. CKD = Chronic Kidney Disease. CVD=Cardiovascular Disease. PCS = Physical Component Summary Score. For the treatment group differences, negative values indicate a faster rate of decline in gait speed for the intensive-treatment group.

Table 3
Effect of intensive-treatment versus standard-treatment on transition probabilities for multi-state model of mobility limitation accounting for the competing risk of death

Based on Gait Speed And Self-Report		Intensive-treatment		Standard-treatment		Hazard Ratio (95% CI)	p-value
Transition		N	Rate	N	Rate		
No Mobility Limitation → Mobility Limitation		366	12.83	357	12.20	1.06 (0.91, 1.22)	0.456
No Mobility Limitation → Death		46	1.61	74	2.53	0.62 (0.43, 0.90)	0.013
Mobility Limitation → No Mobility Limitation		238	32.04	238	34.66	0.92 (0.77, 1.10)	0.378
Mobility Limitation → Death		35	4.71	44	6.41	0.82 (0.52, 1.28)	0.382
Based on Gait Speed Only		Intensive-treatment		Standard-treatment		Hazard Ratio (95% CI)	p-value
Transition		N	Rate	N	Rate		
No Mobility Limitation → Mobility Limitation		176	5.86	170	5.49	1.09 (0.88, 1.35)	0.419
No Mobility Limitation → Death		62	2.06	85	2.74	0.74 (0.54, 1.04)	0.079
Mobility Limitation → No Mobility Limitation		82	22.93	80	26.39	0.86 (0.63, 1.17)	0.328
Mobility Limitation → Death		15	4.19	25	8.25	0.56 (0.29, 1.07)	0.078

N = Number of times each transition was observed. Rate = Rate of each transition per 100 person-years of follow-up. For Gait Speed and Self-Report model, mobility limitation was defined as having a gait speed <0.6 m/s OR reporting a lot of difficulty climbing stairs AND reporting some difficulty walking about or being confined to bed. For Gait Speed Only model, mobility limitation was based solely on gait speed (<0.6 m/s), requiring that any changes in gait speed were 0.127 m/s in order to define a transition between the two mobility states (See Methods).