

Blood Pressure, Antihypertensive Polypharmacy, Frailty, and Risk for Serious Fall Injuries Among Older Treated Adults With Hypertension

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See Editorial Commentary, pp 253–254

Abstract—Antihypertensive medication and low systolic blood pressure (BP) and diastolic BP have been associated with an increased falls risk in some studies. Many older adults have indicators of frailty, which may increase their risk for falls. We contrasted the association of systolic BP, diastolic BP, number of antihypertensive medication classes taken, and indicators of frailty with risk for serious fall injuries among 5236 REGARDS study (Reasons for Geographic and Racial Difference in Stroke) participants ≥ 65 years taking antihypertensive medication at baseline with Medicare fee-for-service coverage. Systolic BP and diastolic BP were measured, and antihypertensive medication classes being taken assessed through a pill bottle review during a study visit. Indicators of frailty included low body mass index, cognitive impairment, depressive symptoms, exhaustion, impaired mobility, and history of falls. Serious fall injuries were defined as fall-related fractures, brain injuries, or joint dislocations using Medicare claims through December 31, 2014. Over a median of 6.4 years, 802 (15.3%) participants had a serious fall injury. The multivariable-adjusted hazard ratio for a serious fall injury among participants with 1, 2, or ≥ 3 indicators of frailty versus no frailty indicators was 1.18 (95% confidence interval, 0.99–1.40), 1.49 (95% confidence interval, 1.19–1.87), and 2.04 (95% confidence interval, 1.56–2.67), respectively. Systolic BP, diastolic BP, and number of antihypertensive medication classes being taken at baseline were not associated with risk for serious fall injuries after multivariable adjustment. In conclusion, indicators of frailty, but not BP or number of antihypertensive medication classes, were associated with increased risk for serious fall injuries among older adults taking antihypertensive medication. (*Hypertension*. 2017;70:259-266. DOI: 10.1161/HYPERTENSIONAHA.116.09390.) • [Online Data Supplement](#)

Key Words: aged ■ blood pressure ■ falls ■ hypertension ■ polypharmacy

Older adults have a high risk for falls, which often result in a fracture, serious injury, or death.^{1–3} Low blood pressure (BP) and use of antihypertensive medication have been associated with an increased risk for falls among older adults in some, but not all, studies.^{4–6} The recently completed SPRINT (Systolic Blood Pressure Intervention Trial) showed that a systolic BP (SBP) target goal of 120 versus 140 mmHg did not increase the risk for injurious falls, overall or in the pre-specified subgroup of participants ≥ 75 years of age.^{7,8} Some healthcare providers may remain concerned about low BP targets in older adults.

Indicators of frailty, including low body mass index, impaired cognition, depressive symptoms, exhaustion, limited

mobility, and a history of falls, are common among older adults with hypertension and may increase the risk for falls.⁹ The objective of this study was to contrast the association between SBP, diastolic BP (DBP), number of antihypertensive medication classes being taken, and indicators of frailty with risk for serious fall injuries among older adults with hypertension taking antihypertensive medication at baseline. To accomplish this objective, we used data from the REGARDS study (Reasons for Geographic and Racial Difference in Stroke), linked to Medicare claims. Findings from this study may identify subgroups of older adults with hypertension at high risk of falling, with the overall goal of reducing serious fall injuries.

Received March 20, 2017; first decision April 9, 2017; revision accepted May 18, 2017.

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The online-only Data Supplement is available with this article at <http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA.116.09390/-/DC1>.

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Hypertension is available at <http://hyper.ahajournals.org>

DOI: 10.1161/HYPERTENSIONAHA.116.09390

Methods

Study Population

The REGARDS study enrolled a population-based cohort and was designed to evaluate black:white and regional disparities in stroke mortality in the United States.¹⁰ Black adults and residents of the Southeastern region of the United States were oversampled. Twenty-one percent of the sample was randomly selected from the stroke buckle, which includes the coastal plain region of North Carolina, South Carolina, and Georgia. Thirty-five percent was from the stroke belt, which includes the remainder of North Carolina, South Carolina, and Georgia in addition to Alabama, Mississippi, Tennessee, Arkansas, and Louisiana. The remaining 44% was selected from the other 40 contiguous states. Additional details on the design and conduct of the REGARDS study have been published previously.¹⁰ Overall, 30239 participants 45 years of age and older were enrolled between January 1, 2003 and October 31, 2007.¹⁰ The current analysis was restricted to participants 65 years and older (n=14961; Figure S1 in the [online-only Data Supplement](#)). We excluded 3590 participants without Medicare Part A and B coverage on the date of their baseline study visit. Medicare is the US Federal Health Insurance Program for adults 65 years or older and younger adults with disabilities or end-stage renal disease. Medicare Parts A and B provide insurance coverage for inpatient and outpatient care, respectively. Claims are not required to be submitted for Medicare beneficiaries with Part C coverage, also known as Medicare Advantage, potentially resulting in the incomplete ascertainment of serious fall injuries. Therefore, 1843 REGARDS participants with Medicare Part C coverage on the date of their baseline study visit were excluded from the current analysis. We excluded 25 participants who did not have data available on SBP or DBP from their baseline study visit and 4267 participants who were not taking antihypertensive medication at baseline. After these exclusion criteria were applied, data from 5236 participants were available for analysis. The REGARDS study protocol was approved by the Institutional Review Boards at the participating institutions, and all participants provided written informed consent, including for the linkage with Medicare claims.

Data Collection

Trained staff conducted computer-assisted telephone interviews to obtain information on participants' demographics, education, household income, cigarette smoking status, cognitive impairment, depressive symptoms, exhaustion, impaired mobility, history of falls, and self-report of previous physician-diagnosed comorbid conditions, including coronary heart disease and stroke. After the interview, trained technicians conducted an in-home visit that included the measurement of height, weight, and BP; a pill bottle review; the collection of blood and urine samples; and an electrocardiogram. For the pill bottle review, technicians recorded the names of all medications that participants had taken during the 2 weeks preceding the in-home study visit. Medication doses were not recorded. Use of statins, osteoporosis medication, and benzodiazepines was determined based on the pill bottle review.

History of coronary heart disease at baseline was defined by a self-reported history or electrocardiogram evidence of myocardial infarction or a self-reported history of a coronary artery bypass graft or percutaneous coronary intervention. History of stroke was defined on the basis of self-report. Diabetes mellitus was defined by self-report of a previous diagnosis with current use of insulin or oral hypoglycemic agents, or a fasting blood glucose ≥ 126 mg/dL or a nonfasting blood glucose ≥ 200 mg/dL. Urinary albumin was measured using the BN ProSpec Nephelometer from Dade Behring (Marburg, Germany). Urinary creatinine was measured with a rate-blanked Jaffé procedure, using the Modular P analyzer (Roche/Hitachi; Indianapolis, IN). Using urinary creatinine and albumin, we calculated the albumin-to-creatinine ratio (ACR) in milligrams per gram.

Blood Pressure

BP was measured 2 times during the in-home examination by trained health professionals using an aneroid sphygmomanometer following

a standardized protocol. An appropriate sized cuff was selected after measuring each participant's arm circumference. Participants were asked to sit for 5 minutes with both feet on the floor before the first measurement. A 30-second rest occurred between BP measurements. The 2 BP measurements were averaged for the current analyses. Quality control of BP was monitored by central examination of digit preference, and retraining of technicians took place as necessary. Sphygmomanometers were returned to the manufacturer for calibration as needed.

Antihypertensive Medication Classes

Antihypertensive medication use at baseline was determined by self-report and during the pill bottle review. To be categorized as taking antihypertensive medication at baseline, participants had to both self-report taking antihypertensive medication and have ≥ 1 classes of antihypertensive medication identified during the pill bottle review. Antihypertensive medication classes included angiotensin-converting enzyme inhibitors, aldosterone antagonists, α -blockers, angiotensin receptor blockers, β -blockers, calcium channel blockers, central acting α_2 -agonists, thiazide diuretics, potassium-sparing diuretics, loop diuretics, and vasodilators.

Indicators of Frailty

We studied 6 indicators of frailty using data collected during the telephone interview and in-home study visit. Indicators of frailty included low body mass index, cognitive impairment, depressive symptoms, exhaustion, impaired mobility, and history of falls. Each indicator of frailty is defined in Table 1.

Serious Fall Injuries

We obtained data on serious fall injuries from Medicare claims. REGARDS participants were linked to the Medicare beneficiary summary file and claims data by social security number with confirmation assessed by matching sex and date of birth.¹³ Using a previously published algorithm, we defined serious fall injuries as an Emergency Department or an inpatient claim for fall-related fractures, brain injuries, or joint dislocations.^{6,14} In the absence of a fall-related code, a serious fall injury was defined as an Emergency Department or inpatient claim for any of the above serious injuries without a motor vehicle accident.^{6,14,15} For the analysis of serious fall injuries, each participant was followed from their REGARDS in-home study visit to the first occurrence of a serious fall injury, loss of Medicare fee-for-service Parts A or B coverage, initiation of Part C coverage, death, or until December 31, 2014.

Statistical Analyses

Baseline characteristics and the cumulative incidence and incidence rates of serious fall injuries were calculated by level of SBP (<110, 110–119, 120–129, 130–139, and ≥ 140 mmHg), DBP (<60, 60–69, 70–79, 80–89, and ≥ 90 mmHg), number of classes of antihypertensive medication being taken at baseline, and number of frailty indicators. Cox proportional hazards models were used to calculate the hazard ratio for serious fall injuries associated with levels of SBP with 120 to 129 mmHg as the referent category, levels of DBP with 70 to 79 mmHg as the referent category, number of antihypertensive medication classes at baseline with use of a single class as the referent category, and the number of frailty indicators with 0 indicators as the referent category. The middle categories for SBP and DBP were used as the referent to evaluate the association between low and high BP with risk for serious fall injuries. Initial models included adjustment for age, sex, race, and region of residence (model 1). A subsequent model included additional adjustment for education, household income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, ACR, diabetes mellitus, history of coronary heart disease, and history of stroke (model 2). A third model for the association between SBP, DBP, and number of antihypertensive medication classes with serious fall injuries included adjustment for indicators of frailty (model 3). The third model evaluating the association between indicators of frailty with serious fall injuries included

Table 1. Method of Ascertainment and Definition for Each Indicator of Frailty

Indicator	Method of Ascertainment	Definition
Low BMI	Height and weight were measured using standardized equipment and used to calculate BMI: $\left(\frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}\right)$.	<18.5 kg/m ²
Cognitive impairment	Six-item screener which evaluates global cognitive function. ¹¹	Score of ≤ 4
Depressive symptoms	Four-item Center for Epidemiological Studies Depression Scale (CES-D) which evaluates frequency of feelings of depression, loneliness, sadness, and crying spells. ¹²	Score of ≥ 4
Exhaustion	SF-12 question, how much of the time during the past 4 wk did you have a lot of energy?	Self-report little of the time or none of the time
Impaired mobility	SF-12 question, does your health now limit you in climbing several flights of stairs?	Self-report limited a lot
History of falls	Question, have you experienced a fall within the past year?	Self-report yes

BMI indicates body mass index; and SF-12, short form-12.

adjustment for SBP, DBP, and number of antihypertensive medication classes being taken at baseline (model 3). We used linear and quadratic terms to assess trends across levels of SBP, DBP, number of antihypertensive medication classes being taken at baseline, and number of frailty indicators. We repeated the analysis of the association between SBP, DBP, number of antihypertensive medication classes being taken at baseline, and number of frailty indicators with serious fall injuries among the subgroup of REGARDS participants ≥ 75 years of age ($n=1912$).

The association between SBP, DBP, and number of antihypertensive medication classes being taken at baseline with serious fall injuries may differ by degree of frailty.¹⁶ Therefore, we calculated the hazard ratios for serious fall injuries associated with SBP, DBP, and number of antihypertensive medication classes being taken at baseline for participants with 0, 1, or ≥ 2 indicators of frailty, separately. In a final analysis, we calculated the incidence rates and hazards ratios for serious fall injuries associated with each indicator of frailty, separately. To account for missing data (Table S1), we conducted multiple imputation with chained equations to generate 10 data sets, which were combined for all analyses.¹⁷ Analyses were conducted using STATA/IC 13 (Stata Corporation, College Station, TX).

Results

Participant Characteristics

The mean age of the 5236 participants included in this analysis was 73 years, 53.7% were female, and 39.3% were black. Of the study sample, 55.7% had no indicators of frailty, and 26.6%, 11.8%, and 5.9% had 1, 2, and ≥ 3 indicators of frailty, respectively. Participants with more indicators of frailty were older; more likely to be black; have less than a high school education; an annual household income <\$20 000; be a current smoker; have history of coronary heart disease, stroke, and diabetes mellitus, have a higher ACR; and to be taking benzodiazepines (Table 2). Participant characteristics are presented by level of SBP, DBP, and number of antihypertensive medication classes being taken at baseline in Tables S2 through S4, respectively.

SBP and DBP, Number of Antihypertensive Medications, and Number of Indicators of Frailty

Over a median follow-up of 6.4 years (maximum 11.9 years), 802 (15.3%) participants had a serious fall injury. There were no linear or quadratic trends in the cumulative incidence of serious fall injuries across levels of SBP or number of

classes of antihypertensive medication being taken at baseline (Figure 1). The cumulative incidence of serious fall injuries was increased at both low and high levels of DBP and among participants with more indicators of frailty. After multivariable adjustment, SBP, DBP, and number of antihypertensive medication classes taken at baseline were not associated with risk for serious fall injuries (Figure 2, upper left and lower left; Tables S5 through S7). DBP was not associated with risk for serious fall injuries after multivariable adjustment (Figure 2, upper right; Table S6). The multivariable-adjusted hazard ratio (95% confidence interval [CI]) for serious fall injuries among participants with 1, 2, and ≥ 3 , versus 0, indicators of frailty was 1.18 (0.99–1.40), 1.49 (1.19–1.87), and 2.04 (1.56–2.67), respectively (Figure 2, lower right; Table S8). Results were consistent when the analysis was restricted to participants ≥ 75 years of age (Table S9). SBP, DBP, and number of antihypertensive medication classes being taken at baseline were not associated with serious fall injuries among participants with 0, 1, and ≥ 2 indicators of frailty, analyzed separately (Table S10).

Individual Indicators of Frailty

After each level of adjustment, having cognitive impairment, depressive symptoms, exhaustion, and a history of falls was each associated with an increased risk for serious fall injuries (Table S11). Having a low body mass index and impaired mobility was associated with serious fall injuries after age, sex, race, and region of residence adjustment, but these associations were not statistically significant after additional adjustment.

Discussion

In this study of older adults with hypertension taking antihypertensive medication at baseline, SBP, DBP, and the number of antihypertensive medications being taken were not associated with an increased risk for serious fall injuries after multivariable adjustment. In contrast, having ≥ 2 indicators of frailty was associated with a substantially increased risk for serious fall injuries. When indicators of frailty were investigated separately, having cognitive impairment, depressive symptoms, exhaustion, and a history of falls was each associated with

Table 2. Characteristics of REGARDS (Reasons for Geographic and Racial Difference in Stroke)-Medicare-Linked Study Participants ≥ 65 Years of Age, Taking Antihypertensive Medication at Baseline by Number of Indicators of Frailty

Characteristic	No. of Indicators of Frailty			
	0 (n=2919)	1 (n=1391)	2 (n=618)	≥ 3 (n=308)
Age, y (SD)	72.2 (5.4)	73.4 (5.9)	74.4 (6.4)	74.0 (6.4)
Women	48.7	57.5	64.9	61.7
Black	35.0	43.7	46.5	46.1
Less than a high school education	13.0	20.4	26.1	31.8
Household income, <\$20 000	20.0	32.3	41.4	48.6
Region of residence				
Stroke belt	34.2	36.0	39.4	38.1
Stroke buckle	23.3	21.9	23.0	25.4
Nonbelt	42.5	42.1	37.6	36.6
Current smoker	7.3	10.3	11.4	12.0
Mean SBP, mm Hg	132.2 (16.3)	133.3 (18.8)	133.4 (18.2)	134.1 (19.1)
Mean DBP, mm Hg	76.0 (9.5)	75.8 (9.6)	75.8 (10.1)	75.2 (10.8)
Classes of antihypertensive medications	2 (1–3)	2 (1–3)	2 (2–3)	2 (2–3)
Coronary heart disease	26.2	31.2	33.8	44.5
Stroke	6.6	12.1	19.7	29.5
Diabetes mellitus	25.1	30.2	39.1	45.5
ACR, mg/g	12.6 (12.0–13.2)	15.4 (14.2–16.7)	19.6 (17.2–22.3)	19.2 (16.1–22.9)
Osteoporosis medication use	8.1	9.3	9.1	7.6
Benzodiazepine use	5.5	7.3	12.1	14.2
Statin use	45.3	45.5	43.6	46.1
Indicators of frailty				
Low BMI	0.0	1.9	1.9	2.7
Cognitive impairment	0.0	21.6	26.0	38.4
Depressive symptoms	0.0	11.2	29.3	60.4
Exhaustion	0.0	19.2	55.7	82.3
Impaired mobility	0.0	34.7	60.6	82.9
History of falls	0.0	11.6	26.5	52.4

Numbers in this table are percentage or mean (SD) except for ACR, which is the geometric mean (95% confidence interval), and number of antihypertensive medications is the median (interquartile range). ACR indicates urine albumin-to-creatinine ratio; BMI, body mass index; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

an increased risk for serious fall injuries. These data suggest that interventions to reduce risk for serious fall injuries among older adults taking antihypertensive medication may be directed toward those with multiple indicators of frailty.

The association between BP and risk for falls among older adults has been evaluated previously.⁴ Among 3544 community-dwelling Austrian adults ≥ 60 years of age, there were lower odds for falls among women with SBP ≥ 140 compared with <140 mm Hg (odds ratio, 0.71; 95% CI, 0.51–0.99) and with DBP ≥ 90 compared with <90 mm Hg (odds ratio, 0.62; 95% CI, 0.43–0.89). In addition, SBP <120 mm Hg compared with 120 to 139 mm Hg and DBP <80 mm Hg compared with 80 to 89 mm Hg were associated with a higher odds for falls

among men (odds ratio, 2.46; 95% CI, 1.10–5.54 and 1.77; 95% CI, 1.02–3.07, respectively). This study was limited by its retrospective design as participants were asked to self-report falls in the previous 3 months, and BP was measured after the falls occurred. The current study used a prospective study design and indicates that low SBP is not associated with an increased risk for serious fall injuries. Both low and high DBP levels were associated with a higher risk for serious fall injuries in crude analyses and after adjustment for age, sex, race, and region of residence. However, this association was no longer present after multivariable adjustment. These findings are consistent with a previous study we conducted on the association between SBP and falls among older adults.¹⁸

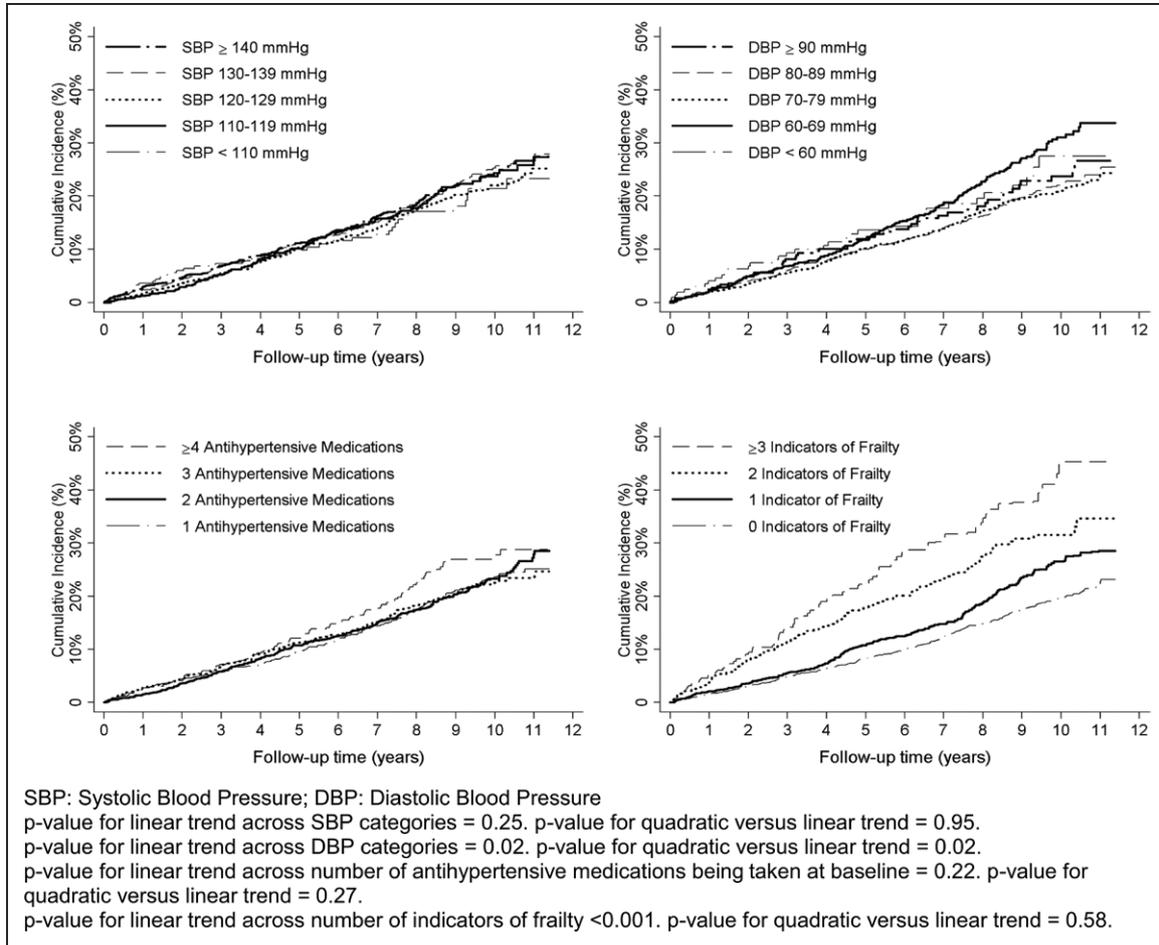


Figure 1. Cumulative incidence of serious fall injuries by level of systolic blood pressure (SBP; upper left), diastolic blood pressure (DBP; upper right), number of antihypertensive medications classes being taken at baseline (bottom left), and number of indicators of frailty (bottom right).

Previous studies have reported conflicting results on the association between antihypertensive medication use and risk for falls or fall-related injuries.^{5,6,15,19–21} A meta-analysis of 22 studies that evaluated the association between several drug classes with falls in adults ≥ 60 years of age reported a pooled odds ratio of 1.24 (95% CI, 1.01–1.50) for those taking versus not taking antihypertensive medication.⁵ However, the risk for falls by the number of antihypertensive medication classes that people were taking was not reported. In a retrospective cohort study of US adults >70 years of age with health insurance through Medicare, the number of antihypertensive medication classes being taken was not associated with risk for falls and related injuries.⁶ In the HYVET (Hypertension in the Very Elderly Trial), being randomized to antihypertensive medication compared with placebo was associated with a lower fracture rate (hazard ratio, 0.58; 95% CI, 0.33–1.00).²⁰ Consistent with several of the aforementioned studies, the current study suggests that taking more classes of antihypertensive medication is not associated with increased risk for a serious fall injury.

In SPRINT, intensive treatment of SBP with a target goal of <120 mmHg lowered the risk for cardiovascular events and mortality compared with the standard target goal of <140 mmHg.⁷ There was no difference in the risk for injurious falls

between the intensive and standard treatment groups. Also, in an a priori specified subgroup analysis of SPRINT participants ≥ 75 years of age, those randomly assigned to the intensive versus standard treatment group did not have an increased risk for falls (hazard ratio, 0.91; 95% CI, 0.65–1.29).⁸ Findings from the current study support the results of SPRINT in a general population sample of older adults with hypertension. A separate analysis of SPRINT data reported frailty, as measured by a 36-item index, to be associated with self-reported falls (hazard ratio, 1.72; 95% CI, 1.55–1.91) and injurious falls (hazard ratio, 1.75; 95% CI, 1.35–2.28).²² The association between individual indicators of frailty and falls was not reported.

In a systematic review and meta-analysis of 74 studies on risk factors for falls, several indicators of frailty were associated with an increased risk for falls in older adults.²³ Cognitive impairment (odds ratio, 1.36; 95% CI, 1.12–1.65), depression (odds ratio, 1.63; 95% CI, 1.36–1.94), and history of falls (odds ratio, 2.77; 95% CI, 2.37–3.25) were each associated with a higher odds of falls. Low body mass index was not associated with falls risk (odds ratio, 1.17; 95% CI, 0.93–1.46). The associations of exhaustion and impaired mobility, as defined in the current study, with falls risk were not reported. Other mobility factors, including having gait problems or vision impairment, which can limit mobility, were associated with an increased

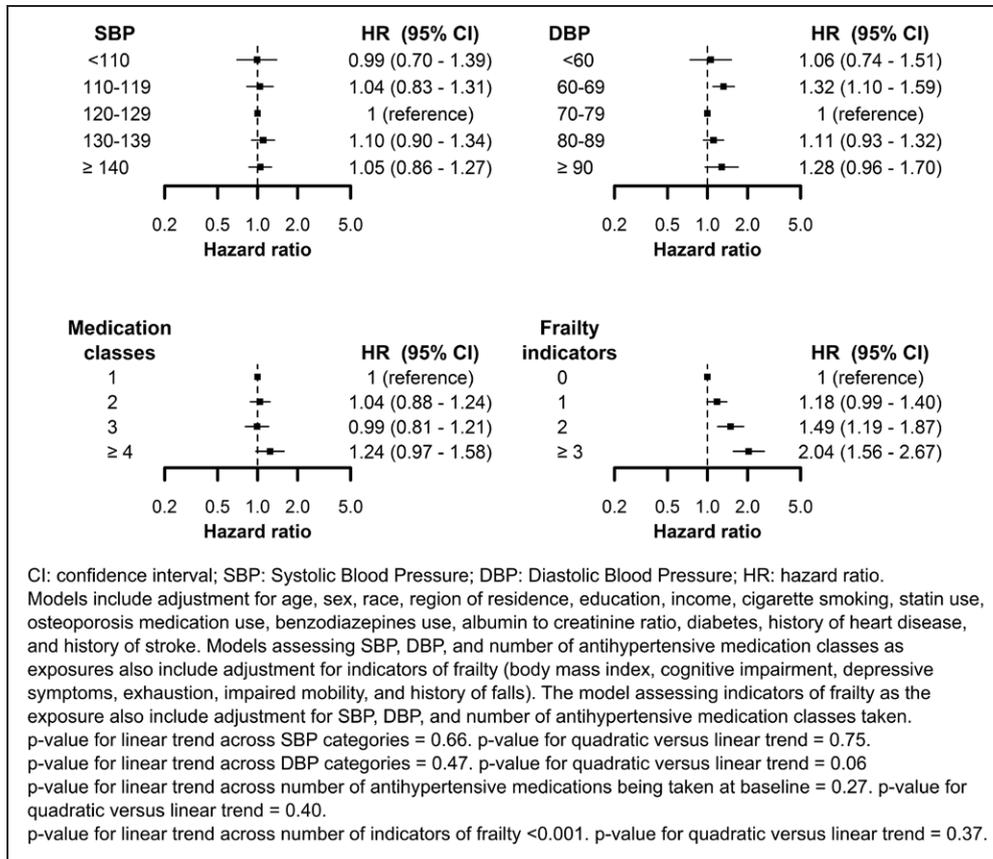


Figure 2. Hazard ratios (HRs) for serious fall injuries associated with systolic blood pressure (SBP; **upper left**), diastolic blood pressure (DBP; **upper right**), number of antihypertensive medications classes being taken at baseline (**lower left**), and numbers of indicators of frailty (**lower right**).

odds for falls. Findings from the current study were consistent with the results of this meta-analysis. Fall risk assessment for older adults with multiple indicators of frailty may identify those with a high risk for serious fall injuries.

The current study suggests that cognitive impairment, depressive symptoms, exhaustion, and a history of falls may be predisposing factors for serious fall injuries in older adults who are taking antihypertensive medication. In addition, several other potential mechanisms may increase the risk for serious fall injuries in this population. For example, postural hypotension is common in older adults and may lead to balance and gait impairments that result in a fall or fall-related injury.^{24,25} Incorporating a multifactorial fall prevention strategy which may include a combination of behavioral and physical modifications into the management and care of older adults taking antihypertensive medication may prevent falls and fall-related injuries.²⁶

The effect of low BP and antihypertensive treatment on falls risk in older adults has been a long-held concern of clinicians.^{27–29} Initiating and titrating antihypertensive medication often triggers healthcare providers to think about their patients' falls risk. Combined with the results from SPRINT, the current study suggests that BP can be intensively lowered to reduce cardiovascular and mortality risk without increasing the risk for falls.⁷ However, serious fall injuries are common among older patients taking antihypertensive medication.

Conducting frailty assessments when antihypertensive treatment is initiated or titrated among older adults may be a practical approach to identify high-risk individuals.

The current study has several strengths, including a large population-based sample of US adults. BP was measured following a standardized protocol; antihypertensive medication classes were identified through a pill bottle review by trained staff; and indicators of frailty were identified by standardized questionnaires and examination measurements. Data on serious fall injuries over a maximum of 11.9 years of follow-up were available through Medicare claims. The REGARDS population with Medicare coverage has been shown to have a high degree of representation of all US adults ≥ 65 years of age with Medicare fee-for-service coverage.¹³ Despite these strengths, the findings from this study should be interpreted within the context of known and potential limitations. Findings may not be generalizable to older adults residing in nursing homes because the REGARDS study only enrolled community-dwelling adults. BP was measured, and information on antihypertensive medication use was obtained during a single visit at baseline and was not available during follow-up, resulting in potential misclassification and preventing the examination of the initiation and intensification of antihypertensive medication on risk for serious fall injuries. A recent study reported a short-term, but not long-term, increased risk for serious fall injuries after initiation and intensification of antihypertensive medication.²⁷

Aneroid sphygmomanometers were used to measure BP. These devices are susceptible to calibration issues. Device calibration was monitored by staff and returned to the manufacturer when they needed to be recalibrated. The questionnaire on cognitive impairment was not implemented in the REGARDS study until December 2003, which resulted in a substantial percentage of missing data for cognition. In addition, we relied on a claims-based algorithm for ascertainment of serious fall injuries and were not able to identify falls that did not result in an emergency room visit or hospitalization.⁶ Information was not available on other risk factors for falls, including low standing BP, visual or hearing impairment, and environmental hazards. Other indicators of frailty, such as weight loss, gait speed, and grip strength, were not available.³⁰

Perspectives

In this study of community-dwelling adults ≥ 65 years of age taking antihypertensive medication at baseline, those with ≥ 2 indicators of frailty had an increased risk for serious fall injuries. In contrast, SBP, DBP, and taking more classes of antihypertensive medication at baseline were not independently associated with risk for serious fall injuries. These data support the safety of intensively lowering BP to reduce cardiovascular and mortality risk without increasing the risk for serious fall injuries among older adults taking antihypertensive medication. Assessment of frailty should be considered to identify older adults taking antihypertensive medication who may have a high falls risk.

Acknowledgments

We thank the investigators, staff, and the participants of the REGARDS study (Reasons for Geographic and Racial Difference in Stroke) for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at <http://www.regardsstudy.org>.

Sources of Funding

This research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, and Department of Health and Human Service. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health. Representatives of the funding agency have been involved in the review of the article but not directly involved in the collection, management, analysis, or interpretation of the data. We thank the other investigators, the staff, and the participants of the REGARDS study (Reasons for Geographic and Racial Difference in Stroke) for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at <http://www.regardsstudy.org>. Additional support was provided by grants R01-HL080477 and K24-HL111154 from the National Heart, Lung, and Blood Institute and 15SFRN2390002 from the American Heart Association.

Disclosures

Dr Shimbo is a consultant for Abbott Vascular and Novartis Pharmaceuticals Corporation. The other authors report no conflicts.

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Novelty and Significance

What Is New?

- There are few population-studies that have examined the association between blood pressure and risk for falls among older adults taking antihypertensive medication.
- We contrasted the association between systolic blood pressure, diastolic blood pressure, number of antihypertensive medication classes being taken, and indicators of frailty with the risk for serious fall injuries among older hypertensive individuals taking antihypertensive medication at baseline.

What Is Relevant?

- Blood pressure and the number of antihypertensive medications were not associated with an increased risk for serious fall injuries.

- There was a strong association of multiple indicators of frailty with serious fall injuries among individuals taking antihypertensive medication at baseline.
- There is a need to identify indicators of frailty in individuals taking antihypertensive medication and consider interventions to prevent falls.

Summary

Having ≥ 2 indicators of frailty was associated with an increased risk for serious fall injuries among older adults taking antihypertensive medication at baseline. These results suggest the importance of assessing frailty in older adults taking antihypertensive medication.

Blood Pressure, Antihypertensive Polypharmacy, Frailty, and Risk for Serious Fall Injuries Among Older Treated Adults With Hypertension

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Hypertension. 2017;70:259-266; originally published online June 26, 2017;

doi: 10.1161/HYPERTENSIONAHA.116.09390

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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Data Supplement (unedited) at:

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Supplemental Materials

BLOOD PRESSURE, ANTIHYPERTENSIVE POLYPHARMACY, FRAILITY, AND RISK FOR SERIOUS FALL INJURIES AMONG OLDER TREATED ADULTS WITH HYPERTENSION

Short Title: BP, Frailty, and Risk for Falls

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Table S1. Variables with missing data that were imputed in this analysis.

Table S2. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by systolic blood pressure.

Table S3. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by diastolic blood pressure.

Table S4. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by number of antihypertensive medication classes being taken at baseline.

Table S5. Incidence rates and hazard ratios for serious fall injuries by systolic blood pressure.

Table S6. Incidence rates and hazard ratios for serious fall injuries by diastolic blood pressure.

Table S7. Incidence rates and hazard ratios for serious fall injuries by number of antihypertensive medication classes being taken at baseline.

Table S8. Incidence rates and hazard ratios for serious fall injuries by number of indicators of frailty.

Table S9. Incidence rates and hazard ratios for serious fall injuries by systolic blood pressure, diastolic blood pressure, number of antihypertensive medication classes being taken at baseline and number of indicators of frailty among REGARDS-Medicare linked study participants ≥ 75 years of age taking antihypertensive medication (n=1,912).

Table S10. Hazard ratios for serious fall injuries associated with systolic blood pressure, diastolic blood pressure, and number of antihypertensive medication classes being taken at baseline, stratified by number of indicators of frailty.

Table S11. Hazard ratios for serious fall injuries associated with individual indicators of frailty.

Figure S1. Exclusion Criteria for REGARDS-Medicare Linked Falls Analysis

Table S1. Variables with missing data that were imputed in this analysis.

Variable	Missing n (%)
Less than a High School Education	5 (0.1)
Household Income <\$20,000	707 (13.5)
Current Smoking	15 (0.3)
Coronary Heart Disease	96 (1.8)
Stroke	28 (0.5)
Diabetes	184 (3.5)
Cognitive Impairment	1,199 (22.9)
Depressive symptoms	35 (0.7)
Low body mass index	19 (0.4)
Exhaustion	2 (0.04)
Impaired Mobility	1 (0.02)
History of falls	10 (0.2)
Albumin to Creatinine Ratio	282 (5.4)

Table S2. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by systolic blood pressure.

Characteristic	Systolic Blood Pressure, mmHg				
	<110 (n=286)	110-119 (n=741)	120-129 (n=1,354)	130-139 (n=1,267)	≥ 140 (n=1,588)
Age, years	72.3 (5.6)	73.0 (5.9)	72.6 (5.7)	72.8 (5.6)	73.3 (5.9)
Women	59.8	54.0	55.2	53.2	51.6
Black	38.1	34.3	36.3	39.5	44.2
Less than a high school education	14.7	16.0	15.1	16.8	21.6
Household income < \$20,000	23.3	24.1	25.4	27.4	31.6
Region of residence					
Stroke belt	30.4	36.3	34.9	35.2	36.8
Stroke buckle	30.4	22.3	23.5	23.1	21.5
Non-belt	39.2	41.4	41.6	41.7	41.6
Current smoker	14.4	7.3	8.5	7.8	9.7
Mean SBP, mmHg	103.2 (5.0)	115.1 (3.2)	124.1 (3.1)	134.2 (3.1)	152.5 (12.4)
Mean DBP, mmHg	64.8 (7.1)	70.0 (7.8)	74.1 (7.5)	76.8 (7.7)	81.5 (10.1)
Classes of antihypertensive medications	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-3)
Coronary heart disease	30.4	30.7	28.3	29.3	30.0
Stroke	9.8	11.2	10.8	10.8	11.4
Diabetes	24.8	26.3	26.3	30.6	33.0
ACR, mg/g	9.9 (8.7-11.3)	11.0 (10.1-12.0)	12.0 (11.2-12.9)	13.5 (12.5-14.5)	21.2 (19.6-22.9)
Osteoporosis medication use	12.9	10.9	8.7	8.9	6.2
Benzodiazepine use	7.0	8.2	8.1	6.5	6.9
Statin use	49.7	49.1	46.1	44.4	42.4
Indicators of frailty					
Low BMI	1.0	1.1	0.9	0.6	1.0
Cognitive impairment	8.9	10.8	10.2	11.6	11.8
Depressive symptoms	9.1	9.1	9.1	9.9	11.3

Exhaustion	18.9	16.1	16.2	14.8	18.0
Impaired mobility	18.5	22.5	20.8	20.1	22.4
History of falls	10.8	9.5	9.7	8.5	9.2

Numbers in this table are percentage or mean (standard deviation) except for ACR, which is the geometric mean (95% confidence interval) and number of antihypertensive medications is the median (interquartile range).

ACR: Urine Albumin to Creatinine Ratio; BMI: Body mass index; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure.

Table S3. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by diastolic blood pressure.

Characteristic	Diastolic Blood Pressure, mmHg				
	<60 (n=206)	60-69 (n=1,004)	70-79 (n=2,044)	80-89 (n=1,599)	≥ 90 (n=383)
Age, years	74.8 (6.2)	73.6 (6.0)	72.9 (5.7)	72.3 (5.7)	71.9 (5.5)
Women	62.1	57.0	54.0	50.6	52.2
Black	39.3	35.2	36.5	42.3	52.7
Less than a high school education	19.4	18.2	16.3	17.1	24.0
Household income < \$20,000	32.9	27.7	26.5	26.0	35.2
Region of residence					
Stroke belt	35.9	37.0	34.5	36.5	32.6
Stroke buckle	23.3	23.6	25.0	20.2	22.2
Non-belt	40.8	39.4	40.4	43.3	45.2
Current smoker	10.2	9.8	8.7	8.1	9.9
Mean SBP, mmHg	119.4 (17.7)	123.3 (14.1)	130.6 (13.9)	138.0 (14.9)	154.5 (17.2)
Mean DBP, mmHg	55.7 (4.1)	64.6 (3.2)	74.5 (3.2)	82.9 (2.8)	94.6 (5.8)
Classes of antihypertensive medications	2 (2-3)	2 (2-3)	2 (1-3)	2 (1-3)	2 (1-3)
Coronary heart disease	33.2	34.1	29.8	26.6	26.4
Stroke	12.1	11.5	10.6	10.9	11.4
Diabetes	39.0	33.1	28.6	26.9	28.1
ACR, mg/g	14.4 (11.8-17.7)	12.9 (11.9-14.1)	13.4 (12.7-14.2)	15.1 (14.1-16.2)	21.3 (18.1-25.1)
Osteoporosis medication use	12.6	9.2	9.6	7.2	4.7
Benzodiazepine use	7.8	7.8	7.8	5.8	9.1
Statin use	50.5	50.5	44.5	43.8	37.9
Indicators of frailty					
Low BMI	2.9	1.5	0.7	0.6	0.3
Cognitive impairment	12.3	9.9	11.2	11.1	12.3
Depressive symptoms	13.1	10.0	9.3	10.0	11.6

Exhaustion	27.2	16.9	16.3	15.3	15.7
Impaired mobility	27.2	22.8	19.6	21.6	20.9
History of falls	8.7	9.8	9.7	8.8	7.8

Numbers in this table are percentage or mean (standard deviation) except for ACR, which is the geometric mean (95% confidence interval) and number of antihypertensive medications is the median (interquartile range).

ACR: Urine Albumin to Creatinine Ratio; BMI: Body mass index; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure.

Table S4. Characteristics of REasons for Geographic And Racial Difference in Stroke (REGARDS)-Medicare linked study participants ≥ 65 years of age, taking antihypertensive medication by number of antihypertensive medication classes being taken at baseline.

Characteristic	Number of Antihypertensive Medication Classes at Baseline			
	1 (n = 1,471)	2 (n = 1,977)	3 (n = 1,216)	≥ 4 (n = 572)
Age, years	72.8 (5.8)	72.8 (5.8)	73.3 (5.8)	72.5 (5.6)
Women	54.1	53.7	53.8	52.6
Black	32.7	38.9	41.9	52.3
Less than a high school education	15.9	17.3	17.7	22.7
Household income < \$20,000	26.0	26.6	28.6	31.7
Region of residence				
Stroke belt	35.4	36.2	34.4	36.2
Stroke buckle	23.7	22.3	24.5	20.8
Non-belt	41.0	41.6	41.1	43.0
Current smoker	9.4	8.8	8.6	8.0
Mean SBP, mmHg	132.5 (16.6)	132.3 (16.3)	133.7 (17.6)	133.2 (17.7)
Mean DBP, mmHg	76.9 (9.1)	75.9 (9.6)	75.5 (10.0)	74.1 (10.3)
Classes of antihypertensive medications	-	-	-	-
Coronary heart disease	22.6	28.1	33.9	42.4
Stroke	8.7	10.5	12.0	16.3
Diabetes	21.1	28.5	33.4	44.2
ACR, mg/g	12.2 (11.5-13.0)	13.4 (12.7-14.3)	15.8 (14.6-17.2)	22.1 (19.2-25.4)
Osteoporosis medication use	9.5	9.2	7.2	6.8
Benzodiazepine use	5.4	7.8	8.0	8.6
Statin use	37.8	44.3	51.8	53.1
Indicators of frailty				
Low BMI	1.1	0.8	1.1	0.3
Cognitive impairment	11.1	11.0	9.7	14.0
Depressive symptoms	8.9	10.2	10.8	10.1
Exhaustion	14.0	15.4	18.3	22.7
Impaired mobility	16.8	21.4	24.0	26.0

History of falls	8.3	8.9	10.8	9.8
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Numbers in this table are percentage or mean (standard deviation) except for ACR, which is the geometric mean (95% confidence interval) and number of antihypertensive medications is the median (interquartile range).

ACR: Urine Albumin to Creatinine Ratio; BMI: Body mass index; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure.

Table S5. Incidence rates and hazard ratios for serious fall injuries by systolic blood pressure.

Outcome	Systolic Blood Pressure, mmHg					p-trend	
	<110 (n =286)	110-119 (n = 741)	120-129 (n = 1,354)	130-139 (n = 1,267)	≥ 140 (n = 1,588)	linear	quadratic
Incidence rate* (95% CI)	23.4 (16.2-30.7)	25.3 (20.7-29.9)	23.7 (20.4-27.0)	26.6 (22.9-30.2)	26.7 (23.3-30.1)	0.25	0.95
	Hazard ratio (95% CI)						
Model 1	1.02 (0.73-1.44)	1.04 (0.83-1.31)	1 (ref)	1.12 (0.92-1.36)	1.15 (0.95-1.39)	0.17	0.78
Model 2	1.01 (0.72-1.43)	1.03 (0.82-1.30)	1 (ref)	1.07 (0.88-1.31)	1.04 (0.86-1.26)	0.78	0.90
Model 3	0.99 (0.70-1.39)	1.04 (0.83-1.31)	1 (ref)	1.10 (0.90-1.34)	1.05 (0.86-1.27)	0.66	0.75

CI – confidence interval

* Incidence per 1,000 person-years.

Model 1 includes adjustment for age, sex, race, and region of residence.

Model 2 includes variables in Model 1 and education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Model 3 includes variables in Models 1 and 2 and indicators of frailty (low body mass index, depressive symptoms, cognitive impairment, impaired mobility, exhaustion, and history of falls).

Linear p-trend represents the p-value for a linear trend across the systolic blood pressure categories.

Quadratic p-trend represents the p-value for a deviation from linearity across the systolic blood pressure categories.

Table S6. Incidence rates and hazard ratios for serious fall injuries by diastolic blood pressure.

Outcome	Diastolic Blood Pressure, mmHg					p-trend	
	<60 (n = 206)	60-69 (n = 1,004)	70-79 (n = 2,044)	80-89 (n = 1,599)	≥ 90 (n = 383)	linear	quadratic
Incidence rate* (95% CI)	29.5 (19.8-39.3)	32.1 (27.5-36.7)	23.0 (20.3-25.6)	24.0 (20.9-27.0)	26.8 (19.9-33.8)	0.02	0.02
	Hazard ratio (95% CI)						
Model 1	1.13 (0.79-1.61)	1.32 (1.10-1.59)	1 (ref)	1.12 (0.94-1.33)	1.36 (1.03-1.82)	0.53	0.01
Model 2	1.07 (0.75-1.53)	1.32 (1.10-1.59)	1 (ref)	1.11 (0.93-1.32)	1.26 (0.95-1.68)	0.43	0.06
Model 3	1.06 (0.74-1.51)	1.32 (1.10-1.59)	1 (ref)	1.11 (0.93-1.32)	1.28 (0.96-1.70)	0.47	0.06

CI – confidence interval

* Incidence per 1,000 person-years.

Model 1 includes adjustment for age, sex, race, and region of residence.

Model 2 includes variables in Model 1 and education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Model 3 includes variables in Models 1 and 2 and indicators of frailty (low body mass index, depressive symptoms, cognitive impairment, impaired mobility, exhaustion, and history of falls).

Linear p-trend represents the p-value for a linear trend across the diastolic blood pressure categories.

Quadratic p-trend represents the p-value for a deviation from linearity across the diastolic blood pressure categories.

Table S7. Incidence rates and hazard ratios for serious fall injuries by number of antihypertensive medication classes being taken at baseline.

Outcome	Number of Antihypertensive Medication Classes at baseline				p-trend	
	1 (n = 1,471)	2 (n = 1,977)	3 (n = 1,216)	≥4 (n = 572)	linear	quadratic
Incidence rate* (95% CI)	24.8 (21.6-28.0)	25.0 (22.2-27.9)	24.8 (21.1-28.5)	30.4 (24.4-36.5)	0.22	0.27
	Hazard ratio (95% CI)					
Model 1	1 (ref)	1.07 (0.90-1.27)	1.06 (0.87-1.29)	1.42 (1.12-1.81)	0.02	0.23
Model 2	1 (ref)	1.03 (0.87-1.23)	1.00 (0.82-1.22)	1.22 (0.95-1.56)	0.27	0.40
Model 3	1 (ref)	1.04 (0.88-1.24)	0.99 (0.81-1.21)	1.24 (0.97-1.58)	0.27	0.40

CI – confidence interval

* Incidence per 1,000 person-years.

Model 1 includes adjustment for age, sex, race, and region of residence.

Model 2 includes variables in Model 1 and education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Model 3 includes variables in Models 1 and 2 and indicators of frailty (low body mass index, depressive symptoms, cognitive impairment, impaired mobility, exhaustion, and history of falls).

Linear p-trend represents the p-value for a linear trend across the number of antihypertensive medication classes being taken at baseline categories.

Quadratic p-trend represents the p-value for a deviation from linearity across the number of antihypertensive medication classes being taken at baseline categories.

Table S8. Incidence rates and hazard ratios for serious fall injuries by number of indicators of frailty.

Outcome	Number of indicators of frailty				p-trend	
	0 (n = 2,919)	1 (n = 1,391)	2 (n = 618)	≥3 (n = 308)	linear	quadratic
Incidence rate* (95% CI)	20.8 (18.7-22.8)	26.6 (22.9-30.2)	39.5 (32.0-46.9)	53.2 (40.9-65.4)	<0.001	0.58
	Hazard ratio (95% CI)					
Model 1	1 (ref)	1.26 (1.06-1.50)	1.71 (1.38-2.13)	2.47 (1.92-3.18)	<0.001	0.40
Model 2	1 (ref)	1.18 (0.99-1.41)	1.49 (1.19-1.87)	2.05 (1.56-2.68)	<0.001	0.37
Model 3	1 (ref)	1.18 (0.99-1.40)	1.49 (1.19-1.87)	2.04 (1.56-2.67)	<0.001	0.37

CI – confidence interval

* Incidence per 1,000 person-years.

Model 1 includes adjustment for age, sex, race, and region of residence.

Model 2 includes variables in Model 1 and education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Model 3 includes variables in Models 1 and 2, systolic blood pressure, diastolic blood pressure, and number of antihypertensive medication classes being taken at baseline.

Linear p-trend represents the p-value for a linear trend across the number of indicators of frailty categories.

Quadratic p-trend represents the p-value for a deviation from linearity across the number of indicators of frailty categories.

Table S9. Incidence rates and hazard ratios for serious fall injuries by systolic blood pressure, diastolic blood pressure, number of antihypertensive medication classes being taken at baseline and number of indicators of frailty among REGARDS-Medicare linked study participants ≥ 75 years of age taking antihypertensive medication (n=1,912).

Outcome	Systolic Blood Pressure, mmHg					p-trend	
	<110 (n =94)	110-119 (n = 266)	120-129 (n = 467)	130-139 (n = 463)	≥ 140 (n = 622)	linear	quadratic
Incidence rate* (95% CI)	34.4 (18.0-50.7)	37.1 (27.3-46.8)	37.4 (30.0-44.8)	37.6 (30.2-45.0)	38.4 (31.6-45.2)	0.70	0.87
	Hazard ratio (95% CI)						
Model 1	0.93 (0.56-1.56)	0.96 (0.69-1.34)	1 (ref)	1.03 (0.78-1.36)	1.06 (0.81-1.38)	0.49	0.89
Model 2	0.90 (0.54-1.52)	0.99 (0.71-1.38)	1 (ref)	0.98 (0.74-1.30)	1.00 (0.76-1.31)	0.82	0.85
Model 3	0.88 (0.52-1.49)	0.99 (0.71-1.38)	1 (ref)	0.99 (0.74-1.31)	1.00 (0.76-1.31)	0.84	0.77
	Diastolic Blood Pressure, mmHg						
	<60 (n = 101)	60-69 (n = 433)	70-79 (n = 739)	80-89 (n = 521)	≥ 90 (n = 118)	linear	quadratic
Incidence rate* (95% CI)	47.5 (28.9-66.1)	42.8 (34.5-51.0)	34.6 (28.8-40.4)	34.9 (28.1-41.7)	40.7 (24.1-57.4)	0.14	0.16
	Hazard ratio (95% CI)						
Model 1	1.30 (0.85-2.00)	1.22 (0.94-1.57)	1 (ref)	1.02 (0.79-1.31)	1.30 (0.83-2.02)	0.29	0.12
Model 2	1.25 (0.81-1.93)	1.22 (0.95-1.59)	1 (ref)	1.01 (0.78-1.31)	1.21 (0.77-1.90)	0.25	0.23
Model 3	1.22 (0.79-1.89)	1.22 (0.94-1.58)	1 (ref)	1.00 (0.77-1.29)	1.17 (0.74-1.85)	0.23	0.31
	Number of Antihypertensive Medication Classes at Baseline						
	1 (n = 533)	2 (n = 705)	3 (n = 471)	≥ 4 (n = 203)	linear	quadratic	

Incidence rate* (95% CI)	36.7 (30.0-43.4)	37.9 (31.7-44.1)	34.4 (27.0-41.7)	46.6 (33.2-60.1)	0.49	0.36
	Hazard ratio (95% CI)					
Model 1	1 (ref)	1.08 (0.85-1.38)	1.00 (0.75-1.33)	1.45 (1.03-2.05)	0.16	0.33
Model 2	1 (ref)	1.06 (0.83-1.36)	0.98 (0.74-1.31)	1.38 (0.96-1.97)	0.27	0.35
Model 3	1 (ref)	1.08 (0.85-1.39)	0.99 (0.74-1.31)	1.43 (1.00-2.05)	0.23	0.36
	Number of indicators of frailty					
	0 (n =927)	1 (n = 563)	2 (n = 289)	≥3 (n = 133)	linear	quadratic
Incidence rate* (95% CI)	31.7 (27.0-36.5)	37.3 (30.0-44.7)	49.6 (36.9-62.2)	67.5 (45.3-89.7)	<0.001	0.50
	Hazard ratio (95% CI)					
Model 1	1 (ref)	1.24 (0.96-1.60)	1.52 (1.12-2.06)	2.18 (1.50-3.16)	<0.001	0.62
Model 2	1 (ref)	1.17 (0.90-1.52)	1.39 (1.01-1.90)	1.94 (1.32-2.85)	<0.001	0.54
Model 3	1 (ref)	1.17 (0.90-1.52)	1.40 (1.02-1.93)	1.94 (1.32-2.84)	<0.001	0.53

CI – confidence interval

* Incidence per 1,000 person-years.

Model 1 includes adjustment for age, sex, race, and region of residence.

Model 2 includes variables in Model 1 and education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Model 3 includes variables in Models 1 and 2 and indicators of frailty (low body mass index, depressive symptoms, cognitive impairment, impaired mobility, exhaustion, and history of falls).

Table S10. Hazard ratios for serious fall injuries associated with systolic blood pressure, diastolic blood pressure, and number of antihypertensive medication classes being taken at baseline, stratified by number of indicators of frailty.

Indicators of frailty	Systolic Blood Pressure, mmHg					p-trend	
	<110 (n = 286)	110-119 (n = 741)	120-129 (n = 1,354)	130-139 (n = 1,267)	≥ 140 (n = 1,588)	linear	quadratic
	Hazard ratio (95% CI)						
0	0.91 (0.56-1.48)	0.92 (0.66-1.28)	1 (ref)	0.97 (0.74-1.28)	1.01 (0.77-1.33)	0.57	0.86
1	1.24 (0.60-2.55)	1.68 (1.07-2.63)	1 (ref)	1.16 (0.76-1.75)	1.37 (0.92-2.03)	0.85	0.18
≥ 2	0.99 (0.51-1.94)	0.73 (0.45-1.19)	1 (ref)	1.22 (0.82-1.82)	0.77 (0.51-1.16)	0.69	0.09
	Diastolic Blood Pressure, mmHg						
	<60 (n = 206)	60-69 (n = 1,004)	70-79 (n = 2,044)	80-89 (n = 1,599)	≥ 90 (n = 383)		
	Hazard ratio (95% CI)						
0	1.26 (0.73-2.15)	1.44 (1.11-1.88)	1 (ref)	1.15 (0.90-1.47)	1.11 (0.72-1.71)	0.13	0.18
1	0.70 (0.32-1.54)	1.16 (0.79-1.71)	1 (ref)	0.93 (0.66-1.32)	1.43 (0.83-2.46)	0.76	0.50
≥ 2	1.10 (0.59-2.05)	1.28 (0.86-1.90)	1 (ref)	1.18 (0.82-1.69)	1.39 (0.78-2.47)	0.92	0.30
	Number of Antihypertensive Medication Classes at Baseline						
	1 (n = 1,471)	2 (n = 1,977)	3 (n = 1,216)	≥ 4 (n = 572)			
	Hazard ratio (95% CI)						
0	1 (ref)	1.01 (0.79-1.28)	0.82 (0.61-1.10)	1.26 (0.89-1.79)	0.88	0.19	
1	1 (ref)	0.90 (0.63-1.30)	1.11 (0.75-1.64)	1.06 (0.66-1.72)	0.58	0.68	

≥ 2	1 (ref)	1.26 (0.86-1.87)	1.28 (0.84-1.94)	1.36 (0.83-2.23)	0.21	0.52
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Indicators of frailty include low body mass index, cognitive impairment, depressive symptoms, exhaustion, impaired mobility, and history of falls (defined in **Table 1**).

CI – confidence interval

Hazard ratios are adjusted for age, sex, race, region of residence, education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, and history of stroke.

Table S11. Hazard ratios for serious fall injuries associated with individual indicators of frailty.

Indicator of frailty	Total participants	Injury falls (%)	Hazard ratio (95% CI)		
			Model 1	Model 2	Model 3
Body Mass Index, kg/m²					
≥18.5	5,190	791 (15.2)	1 (ref)	1 (ref)	1 (ref)
<18.5	46	11 (23.9)	1.44 (0.79-2.62)	1.20 (0.66-2.20)	1.20 (0.65-2.20)
Cognitive Impairment					
No	4,663	702 (15.1)	1 (ref)	1 (ref)	1 (ref)
Yes	573	100 (17.5)	1.46 (1.14-1.87)	1.38 (1.07-1.77)	1.38 (1.07-1.77)
Depressive Symptoms					
No	4,714	700 (14.8)	1 (ref)	1 (ref)	1 (ref)
Yes	522	102 (19.5)	1.51 (1.22-1.86)	1.35 (1.09-1.68)	1.35 (1.09-1.68)
Exhaustion					
No	4,372	633 (14.5)	1 (ref)	1 (ref)	1 (ref)
Yes	864	169 (19.6)	1.51 (1.27-1.79)	1.33 (1.11-1.58)	1.32 (1.11-1.57)
Impaired Mobility					
No	4,124	616 (14.9)	1 (ref)	1 (ref)	1 (ref)
Yes	1,112	186 (16.7)	1.24 (1.05-1.46)	1.09 (0.92-1.30)	1.09 (0.92-1.29)
History of Falls					
No	4,750	676 (14.2)	1 (ref)	1 (ref)	1 (ref)
Yes	486	126 (25.9)	2.19 (1.81-2.65)	1.96 (1.61-2.38)	1.97 (1.62-2.40)

CI – confidence interval

Hazard ratios adjust for age, sex, race, region of residence, education, income, cigarette smoking, statin use, osteoporosis medication use, benzodiazepine use, albumin to creatinine ratio, diabetes, history of heart disease, history of stroke, systolic blood pressure, diastolic blood pressure, and number of antihypertensive medication classes being taken at baseline.

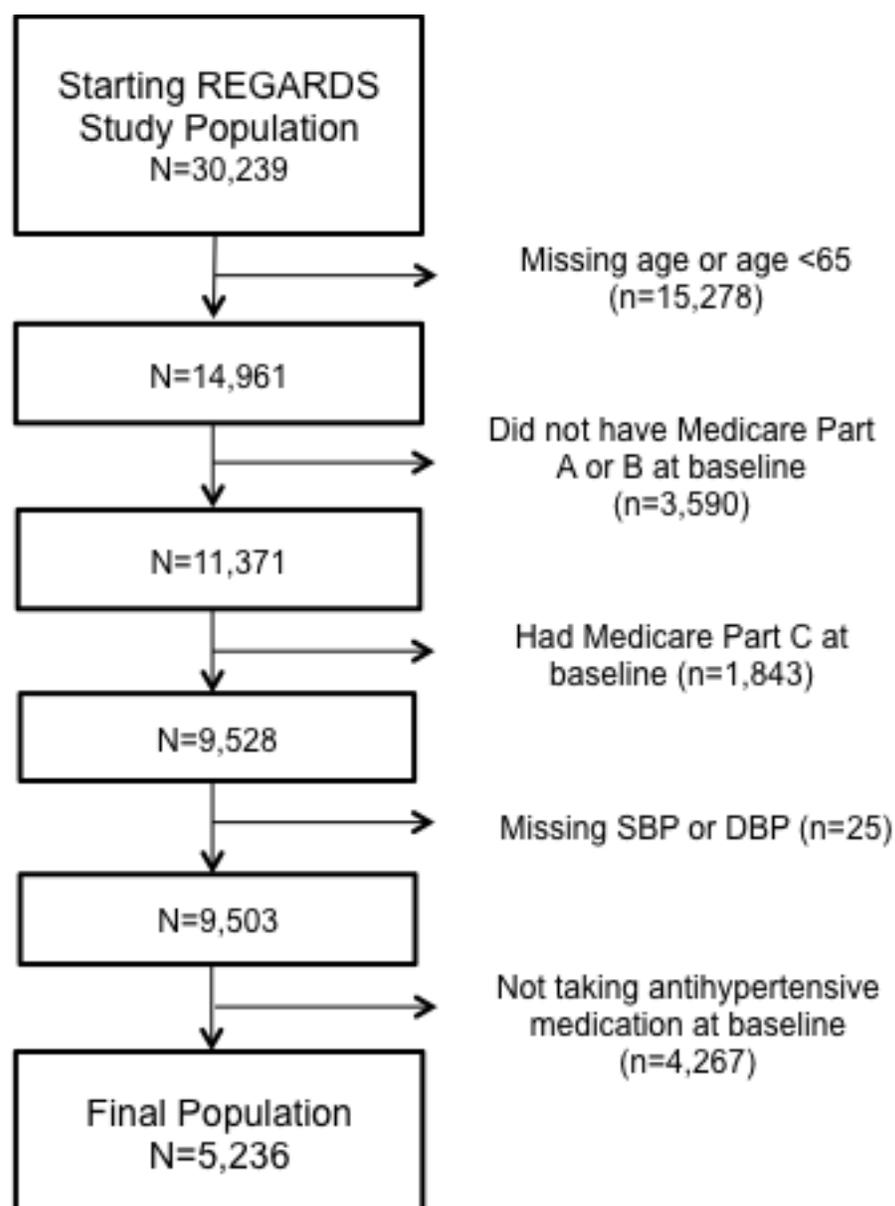


Figure S1. Exclusion Criteria for REGARDS-Medicare Linked Falls Analysis