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Short-term Risk of Serious Fall Injuries in Older Adults Initiating and Intensifying Treatment with Antihypertensive Medication

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Abstract

Background—Antihypertensive medication use has been associated with an increased risk of falls in some but not all studies. Few data are available on the short-term risk of falls following antihypertensive medication initiation and intensification.

Methods and Results—We examined the association between initiating and intensifying antihypertensive medication and serious fall injuries in a case-crossover study of 90,127 Medicare beneficiaries who were ≥65 years old and had a serious fall injury between July 1, 2007 and December 31, 2012, based on emergency department and inpatient claims. Antihypertensive medication initiation was defined by a prescription fill with no fills in the prior year. Intensification was defined by the addition of a new antihypertensive class, and, separately, titration by the addition of a new class or increase in dosage of a current class. Exposures were ascertained for the 15 days before the fall (case period) and six 15-day earlier periods (control periods). Overall, 272, 1508, and 3113 Medicare beneficiaries initiated, added a new class of antihypertensive medication or titrated therapy, respectively, within 15 days of their serious fall injury. The odds for a serious fall injury was increased during the 15 days following antihypertensive medication initiation [odds ratio, OR, 1.36 (95% CI 1.19, 1.55)], adding a new class [OR 1.16 (95% CI 1.10, 1.23)], and titration [OR 1.13 (95% CI 1.08, 1.18)]. These associations were attenuated beyond 15 days.

Conclusions—Antihypertensive medication initiation and intensification was associated with a short-term, but not long-term, increased risk of serious fall injuries among older adults.

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Keywords

antihypertensive agent; elderly; geriatrics; falls

The benefit of antihypertensive medication on cardiovascular disease (CVD) risk reduction has been demonstrated among older adults in randomized controlled trials.[1–3] However, there may be unintended harm associated with antihypertensive medication use in older adults.[4–7] Older adults are susceptible to adverse side effects associated with antihypertensive medication use including postural hypotension, balance and gait impairment, dizziness, and electrolyte disturbances,[8–10] which may increase the risk of serious fall injuries. Clinicians often weigh the CVD risk-reduction benefits of antihypertensive medications against their potential for inducing fall injuries among older adults.

Some, but not all, studies suggest that antihypertensive medication use in older adults is associated with an increased risk for falls or injuries related to falls including fractures.[4–7,11,12] As most studies have examined prevalent users of antihypertensive medication, the relevance of these findings to clinical decision-making regarding antihypertensive medication initiation or intensification is limited. Also, few data are available on the short-term vs. long-term risk for falls after initiation or intensification of antihypertensive medication.[7] Determining whether antihypertensive medication initiation or intensification is associated with an increased risk for serious fall injuries, and identifying a hazard period associated with increased risk have important implications given the large number of older adults initiating and titrating antihypertensive medication[13] and the availability of preventive strategies to reduce falls risk.[14] We determined whether antihypertensive medication initiation is associated with a short-term increased risk for a serious fall injury among older US adults, and whether the risk for a serious fall injury is similarly increased after antihypertensive medication intensification. We also examined the long-term fall injury risk following antihypertensive medication initiation and intensification.

Methods

We conducted two types of analyses using a national 5% random sample of Medicare beneficiaries from 2006 through 2012. The first analysis was a retrospective cohort study, which was used to estimate the absolute risk for serious fall injuries among beneficiaries initiating, adding a new antihypertensive medication class or titrating antihypertensive medication. The second analysis was a case-crossover study of Medicare beneficiaries who experienced a serious fall injury. The case-crossover study was used to determine if initiating, adding a new class or titrating antihypertensive medication were associated with an increased risk for serious fall injuries. Data used for the current analyses include claims from Medicare fee-for-service Parts A (inpatient), B (outpatient) and D (prescription drug). Institutional review boards at the University of Alabama at Birmingham and the Center for Medicare and Medicaid Services approved this analysis.

Retrospective Cohort Study

Medicare beneficiaries who initiated antihypertensive medication between January 1, 2007 and December 31, 2011 were included in the retrospective cohort used to estimate the absolute risk for serious fall injuries in the 15 days following initiation, adding a new class and titration of treatment (Supplemental Figure 1). Initiation was defined by a Medicare Part D claim for antihypertensive medication with 365 continuous days of Medicare fee-for-service coverage (Parts A, B, and D but not C) prior to the fill with no claims for antihypertensive medication. Medicare beneficiaries enrolled in a managed care program (Part C) during this time period were not included as this is a capitated program and claims for these individuals are not complete. The date of the antihypertensive medication fill is provided with the claim. All medication classes filled within the 7 days following the date of initiation were included as part of the initiation regimen.[15] We restricted the sample to beneficiaries with hypertension, defined by one or more outpatient physician evaluation and management claims with International Classification of Diseases, 9th Revision (ICD-9) diagnoses of 401.x (malignant, benign or unspecified essential hypertension) during the 365 days prior to each beneficiary's first fill. We included Medicare beneficiaries with age ≥ 65 years old and < 110 years old at the start of the look-back period (365 days prior to the first antihypertensive medication fill), and having continuous residence in the US during the look-back period, to provide information for the general population of older US adults. Adding a new class of antihypertensive medication was defined by a Medicare Part D claim for a class of antihypertensive medication other than those filled upon initiation. Titration was defined by adding a new class of antihypertensive medication or an increase in the dosage of the medication class filled upon initiation. Adding a new antihypertensive medication class and titration were studied in the 365 days following initiation. Therefore, for these analyses, follow-up occurred through December 31, 2012.

Case-crossover Study

The case-crossover study design is useful for investigating the transient effect of an exposure.[16–18] Using this study design, only individuals who experience an outcome are analyzed and each case serves as their own control. Medicare beneficiaries who experienced a serious fall injury event between July 1, 2007 and December 31, 2012 formed the base population for these analyses (Supplemental Figure 2). We used International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) and current procedure terminology (CPT) codes to identify these events. Serious fall injuries were defined as emergency department and inpatient claims with a fall-related E code (8800–8889) and an injury code for nonpathological skull, facial, cervical, clavicle, humeral, forearm, pelvic, hip, fibula, tibia, or ankle fractures (80000–80619, 8070–8072, 8080–8089, 81000–81419, 8180–8251, or 8270–8291), brain injury (85200–85239), or dislocation of the hip, knee, shoulder, or jaw (8300–8321, 83500–83513, or 83630–83660).[6] In the absence of a fall-related E code, an emergency department or inpatient claim with any of these codes was considered a serious fall injury as long as there was no motor vehicle accident E code (8100–8199).[6] We required all beneficiaries to have at least 560 days of continuous Medicare fee-for-service coverage preceding the date of their serious fall injury. As described below, the 560-day interval includes the 195-day period (days 0–194) between the index date and the start of the earliest control period, and a 365-day period (days 195–559)

prior to the earliest control period, which was used for assessing antihypertensive medication use and clinical characteristics. We restricted the population to Medicare beneficiaries with age ≥ 65 years old and < 110 years old 560 days prior to their fall injury, and having continuous residence in the US during the 560 days prior to their fall injury. For each beneficiary, we included the first occurrence of a serious fall injury meeting the above criteria. The date of the serious fall injury diagnosis was assigned as the index date.

The primary exposure was the initiation of antihypertensive medication. The case period was defined as the 15 days prior to and including the index date (days 0–14) and we selected six 15-day control periods (30 to 44, 60 to 74, 90 to 104, 120 to 134, 150 to 164, and 180 to 194 days prior to the index date). A schematic of this study design is presented in Figure 1. For the case period and each control period, initiation of antihypertensive medication was defined by a claim in Medicare Part D for an angiotensin converting enzyme (ACE)-inhibitor, aldosterone antagonist, angiotensin receptor blocker (ARB), alpha blocker, beta blocker, calcium channel blocker, central acting agent, diuretic (thiazide-type, loop or potassium sparing), renin inhibitor, or vasodilator with no claims for any of these medication classes during the 365 days prior to the first antihypertensive medication fill. These drugs were identified using National Drug Codes (NDC).

The risk for serious fall injuries associated with two secondary exposures representing antihypertensive medication intensification was examined: (1) addition of a new class of antihypertensive medication, and alternatively (2) antihypertensive medication titration. Addition of a new class of antihypertensive medication was defined as a fill for a class of antihypertensive medication within the case period or, separately, the control periods with no fills for that drug class during the preceding 365 days. Medication titration was defined as the addition of a new class of antihypertensive medication or an increase in the dosage of a medication class during the case or control periods.

Characteristics of Medicare Beneficiaries

Age, race/ethnicity, sex, region of residence, and calendar month of the fall were obtained from the Medicare beneficiary summary file. Using previously published algorithms,[19–25] we identified a history of diabetes, coronary heart disease, heart failure, stroke, chronic kidney disease, syncope, osteoporosis, depression, or dementia. Additionally, based on Part D claims and NDCs, the number of different generic medications, besides antihypertensive medications, that each beneficiary filled was determined. The Charlson score, a measure of overall co-morbidity, was calculated.[26] Additionally, a skilled nursing facility stay and any hospitalizations was identified in Medicare claims. These characteristics were identified at the time of at initiation of antihypertensive medication for the retrospective cohort study; and on the 365 days prior to the index date for the case-crossover study.

Statistical Analysis

For the retrospective cohort study, we calculated the percentage of Medicare beneficiaries experiencing a serious fall injury within 15 days after antihypertensive medication initiation. Among Medicare beneficiaries who initiated antihypertensive medication, characteristics at the time of initiation were calculated for those who experienced and did not experience a

serious fall injury within 15 days. We then calculated the percentage of Medicare beneficiaries experiencing a serious fall injury within 15 days after adding a new antihypertensive medication class and medication titration.

For the case-crossover study, the characteristics of all Medicare beneficiaries who experienced a serious fall injury and those who experienced a serious fall injury within 15 days following initiation of antihypertensive medication were calculated. The distribution of classes of antihypertensive medication that were initiated in the 15-day case period and the six control periods were calculated for the overall sample and among Medicare beneficiaries with one or more diagnoses of hypertension. As some drugs, classified as antihypertensive medication, may be prescribed for indications other than hypertension, sensitivity analyses were conducted in which the definitions of initiation, addition of a new antihypertensive medication class, and antihypertensive medication titration also required having one or more diagnoses of hypertension (International Classification of Diseases, 9th Revision [ICD-9] diagnoses of 401.xx) in the 365 days prior to the case or control period. Further, as being hospitalized could result in an increased risk for falls and may be associated with initiation of antihypertensive medication, sensitivity analyses were conducted after excluding beneficiaries who were hospitalized in the 365 days prior to their serious fall injury. The odds ratio and 95% confidence interval (95% CI) for a serious fall injury associated with initiation of antihypertensive medication in the case period (0–14 days prior to the fall) were calculated using conditional logistic regression accounting for each beneficiary having six control periods (Table 1). Analyses were repeated using one (60 to 74 days prior to the fall) instead of six control periods. Cumulative mortality through 90 days after having a serious fall injury was determined. To assess the longer-term effects of initiating antihypertensive medication on risk for serious fall injuries, we calculated odds ratios (95% CI) using three alternate case and multiple control periods for each case period prior to the index date (i.e. date of the serious fall injury) (Table 1). Analyses were also repeated using one control period for each of the 3 case periods.

In exploratory analyses, odds ratios (95% CI) for a serious fall injury were also calculated within pre-specified subgroups defined by demographics and the presence of medical co-morbidities, which are associated with an increased risk of falls.[27,28] Some studies have suggested that specific classes of antihypertensive medication are associated with a higher risk of falls or fractures.[4,29] Further, the majority of older US adults on antihypertensive medication are taking 2 or more classes.[6] Therefore, pre-specified analyses were also conducted for subgroups defined by antihypertensive medication class and also the number of antihypertensive medication classes. Differences across subgroups were calculated using multiplicative interaction terms.

The case-crossover analyses were repeated to assess the association between adding a new class of antihypertensive medication and antihypertensive medication titration and the odds ratios for serious fall injuries. Analyses were conducted using SAS Version 9.3 (SAS Institute, Cary, NC).

Results

Risk for Serious Fall Injuries in the Retrospective Cohort Study

Between January 1, 2007 and December 31, 2011, 65,210 Medicare beneficiaries who met the inclusion criteria initiated antihypertensive medication. Of this population, 186 (0.29%) Medicare beneficiaries had a serious fall injury within 15 days following treatment initiation. Beneficiaries who initiated antihypertensive medication and had a serious fall injury within 15 days were older; less likely to be male; more likely to have a history of coronary heart disease, heart failure, stroke, syncope, osteoporosis, depression, and dementia; and were taking more medication classes, have a higher Charlson comorbidity index, and be hospitalized or in a skilled nursing facility in the prior year (Supplemental Table 1). Within 365 days following antihypertensive medication initiation, 23,315 and 30,143 beneficiaries added a class of antihypertensive medication and titrated their antihypertensive medication, respectively. A serious fall injury occurred within 15 days after adding a new class of antihypertensive medication for 0.27% (n=64) of beneficiaries and within 15 days after titration for 0.29% (n=88) of beneficiaries.

Short-term Risk of Serious Fall Injuries Associated with Antihypertensive Medication in the Case-crossover Study

Table 2 shows the characteristics of the 90,127 Medicare beneficiaries who had a serious fall injury between January 1, 2007 and December 31, 2012 and of the subset of 272 individuals who initiated antihypertensive medication in the 15 days prior to their fall. Of those initiating antihypertensive medication, 30.9%, 34.6%, and 34.6% were aged 65 to 74, 75 to 84, and ≥ 85 years, respectively; 28.3% were male; and 89.7% were white.

Overall, 272, 1,508, and 3,113 Medicare beneficiaries initiated, added a new class of antihypertensive medication, and titrated therapy, respectively, within 15 days prior to their serious fall injury. The short-term odds ratios (95% CI) for a serious fall injury were 1.36 (95% CI 1.19, 1.55) for initiation of antihypertensive medication, 1.16 (95% CI 1.10, 1.23) for adding a new antihypertensive medication class, and 1.13 (95% CI 1.08, 1.18) for antihypertensive medication titration (Table 3). The associations were similar when the definition of antihypertensive medication initiation, addition, and titration required one or more diagnoses of hypertension, and when the population was restricted to Medicare beneficiaries without a recent hospitalization. The associations were similar using one control period (Supplemental Table 2). Among Medicare beneficiaries with a serious fall injury within 15 days following antihypertensive medication initiation, addition of new class, and titration, 14.0%, 15.6 %, and 14.6%, respectively, died within 90 days following the fall.

Antihypertensive Medication Class Initiated in Case vs. Control Periods

Initiation of diuretics, particularly loop diuretics, was more common in the 15-day case period compared to the control periods (Supplemental Table 3). Initiation with other classes of antihypertensive medication was similar in the case and control periods. The percentage of beneficiaries who simultaneously initiated more than one antihypertensive class was higher in the case period (20.2%) compared with the control periods (17.4%). These results

were similar when the definition of antihypertensive medication initiation required one or more diagnoses of hypertension, and when the population was restricted to Medicare beneficiaries without a recent hospitalization

Subgroup Analyses

The association between antihypertensive medication initiation and serious fall injuries did not vary by subgroup (Supplemental Table 4). The short-term odds ratio for a serious fall injury associated with the addition of a new class of antihypertensive medication was stronger for Medicare beneficiaries without a history of diabetes, without heart failure, and who were taking fewer non-antihypertensive medications (Supplemental Table 5). The short-term odds ratio for a serious fall injury associated with the titration of antihypertensive medication was stronger for older Medicare beneficiaries, those without a history of heart failure, and without chronic kidney disease (Supplemental Table 6). The associations of initiation and addition of antihypertensive medication with serious fall injuries did not vary by medication class or the number of classes initiated (Supplemental Table 7) or added (Supplemental Table 8).

Long-term Risk of Serious Fall Injuries

No association was present between initiating antihypertensive medications, and, separately, adding a new class of antihypertensive medication in the 30–44 days, 60–74 days, or 90–104 days prior to a fall, and the risk for a subsequent fall injury (Table 4). The odds ratio for a serious fall injury associated with the titration of antihypertensive medication within 30–44 days, 60–74 days, and 90–104 days prior to the fall was 1.04 (95% CI 1.00, 1.09), 1.05 (95% CI 1.00, 1.09) and 1.04 (95% CI 1.00, 1.09), respectively. The associations were similar in analyses using one instead of six control periods (Supplemental Table 9).

Discussion

Falls risk among elderly individuals is a major public health concern.[30] Falls are often attributed to the interaction of long-term predisposing conditions and short-term precipitating factors.[27,31] The high rate of falls and risk for adverse outcomes following a fall has generated an increasing recognition of the need to identify precipitating factors for falls in older adults.[14] In the current study, the odds for a serious fall injury were increased in the 15 days after antihypertensive medication initiation and intensification. An increased risk for a serious fall injury was no longer present more than 15 days after either initiation or adding a new class, and was attenuated more than 15 days after titration of antihypertensive medication.

Prior studies of the short-term risks following antihypertensive medication initiation have focused on fractures as an outcome rather than the risk of falls or injuries related to falls.[4,5,12,32] For example, Butt et al.[5] showed that hip fracture risk was increased in the 45 days after antihypertensive medication initiation among Ontario residents who were 66 years and older. Initiation of ACE inhibitors and beta blockers were each significantly associated with an increased risk of hip fractures, whereas thiazide diuretics, ARBs, and calcium channel blockers were not. In the current study, an increased odds ratio for a serious fall

injury was present when antihypertensive medication was initiated in a 15-day period prior to the fall, but not beyond 15 days. This association did not vary by the class of antihypertensive medication initiated.

Scarce data are available on the association between antihypertensive medication intensification and the risk of a serious fall injury. In a substudy of 3,099 middle age and older participants with diabetes enrolled in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, Margolis et al.[11] did not find an increased risk for self-reported falls or non-spine fractures between participants randomized to a systolic pressure of less than 120 mmHg, vs. systolic pressure of less than 140 mmHg. It is unclear whether these results are applicable for older adults who undergo antihypertensive medication intensification, as the ACCORD substudy participants were relatively young (mean age 62 years old) and the outcomes were ascertained years after reductions in blood pressure had occurred in the intensive treatment arm. In the current study, there was no long-term increased risk for serious falls injuries associated with antihypertensive medication use, a finding that is consistent with the findings from ACCORD.[11]

The Systolic Blood Pressure Intervention Trial (SPRINT) recently demonstrated that a systolic blood pressure target goal of 120 mmHg (intensive treatment) versus 140 mmHg (conventional treatment) was associated with a lower risk of CVD events and mortality in adults at least 50 years of age with a systolic blood pressure of 130 to 180 mm Hg and high cardiovascular risk, but without diabetes or a prior stroke.[3] The intensive versus conventional treatment goal was associated with a higher risk of hypotension, syncope, electrolyte abnormalities, but not injurious falls, defined as falls that resulted in evaluation in an emergency department or hospitalization. However, when adverse events were classified as possibly or definitely related to intensive treatment, the risk of injurious falls was higher in the intensive vs. conventional treatment arm (0.8% versus 0.5%, p=0.05). The results from the current study indicating a short-term increased risk of serious fall injuries after antihypertensive medication intensification but no increased risk with long-term antihypertensive medication use are consistent with the findings in SPRINT. It was reported that 7.6% or 16.8 million of US adults meet the SPRINT eligibility criteria.[33] Therefore, many older US adults may have their antihypertensive medication intensified to reach a lower systolic blood pressure target, and be susceptible to a short-term increased risk of serious fall injuries.

Some, but not all, studies have reported that antihypertensive medication use in older adults is associated with an increased risk for falls or fall injuries injuries.[4–7,11,12] Tinetti et al.[6] conducted a retrospective cohort study and found that in clinical practice, Medicare beneficiaries older than 70 years of age who were taking antihypertensive medication had a higher risk of a serious fall injury than their counterparts not taking antihypertensive medication. Using a case-crossover study design, which minimizes confounding by having each individual serve as his/her own control, we have extended the results of Tinetti et al.[6] to demonstrate that antihypertensive medication initiation and intensification may be associated with a short-term increased risk of serious fall injuries in older adults.

Using a retrospective cohort study design, we also showed that the risk of a serious fall injury was low within 15 days after initiating antihypertensive medication, adding a new class, and titrating antihypertensive medication. However, the risk for a fall after antihypertensive initiation and intensification is likely to be substantially higher, as serious fall injuries represent only 10% of all falls experienced by older adults.[27,34] Serious fall injuries including fractures, brain injuries, and dislocations are the most adverse consequences of falls in older adults. Nonetheless, falls that do not result in a serious injury are also clinically important as they are associated with functional decline and nursing home placement in older adults.[35,36]

There are several potential mechanisms for the short-term increased risk of serious falls associated with antihypertensive medication initiation and intensification. Older adults are at increased risk for postural hypotension,[37,38] which may result in neurologic effects and consequently balance and gait impairment. In addition, antihypertensive medication-induced electrolyte disturbances may cause neurologic and physical side effects, which may make older adults more susceptible to falls.[9,10,39,40] Multicomponent interventions that include multiple risk factor assessment, physical therapy, and exercise are effective in falls prevention.[14,41] These strategies could be adopted by clinicians in the short-term to prevent falls and fall-related injuries when antihypertensive medication is initiated or intensified in their older patients.

There are several strengths of the current study. Given the longitudinal nature of Medicare claims, we were able to study serious injuries after antihypertensive medication initiation and intensification. Another strength of the study is that Medicare provides data that are highly generalizable to older adults in the US. Some limitations must be noted. The generalizability to younger adults may be limited. Also, as with all claims-based analyses, the results depend on the accuracy of coding of disease states and pharmacy fills. As blood pressure data are not available in Medicare claims, we could not determine whether the associations we report can be explained by changes in blood pressure levels. As there was a lack of information on falls that did not result in a serious injury, we could not determine whether antihypertensive medication initiation or intensification was associated with less serious falls. Another potential limitation is the assumption that clinical characteristics were stable over time in the case-crossover study. Given that the duration between the control periods and the case period was relatively short (195 days or less), it is likely that substantial changes in clinical characteristics did not occur. It was not possible to determine the exact timing between antihypertensive medication initiation and intensification and the occurrence of the serious fall injury using Medicare claims. However, the inability to pinpoint the timing of the outcome and the appropriate time window for the exposure will likely bias results toward the null.[42,43] Therefore, if the exact time course were known, the associations of antihypertensive medication initiation and intensification with the risk of serious fall injuries would be even stronger. Finally, although the case-crossover study demonstrated that antihypertensive medication initiation and intensification are associated with an increased risk of serious fall injuries, caution is warranted when concluding the results indicate causality.

In conclusion, the results of the current study indicate that the initiation and intensification of antihypertensive medication are associated with a short-term increased risk of a serious fall injury in older adults. However, the short-term risk of a serious fall injury is low, and there does not appear to be a long-term increased risk for serious fall injuries associated with antihypertensive medication. The short-term risk of serious fall injuries as well as approaches for reducing this risk should be discussed with older patients when initiating or intensifying antihypertensive medication.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is Known

- In older adults, antihypertensive medication use has been associated with an increased risk of falls in some but not all studies.
- Few data are available on the short-term vs. long-term risk for falls after initiation or intensification of antihypertensive medication in older adults.

What the Study Adds

- Using Medicare claims from 2007 through 2012, we found that although the risk of a serious fall injury was low, there was a short-term increased risk of a serious fall injury within a 15-day period after initiation or intensification of antihypertensive medication.
- In contrast, the association between antihypertensive medication initiation or intensification and a serious fall injury was attenuated beyond 15 days.
- The results of this study suggest that antihypertensive medication initiation and intensification was associated with a short-term, but not long-term, increased risk of serious fall injuries among older adults.

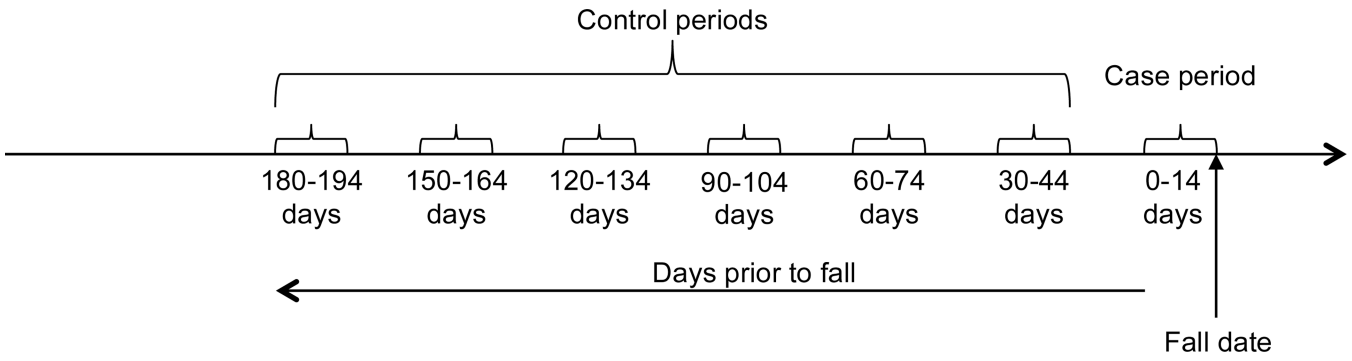

Figure 1.

Schematic of the case-crossover study design. For the case and each 15-day control period, separately, the initiation of antihypertensive medication was defined as a fill within the time period with no antihypertensive medication fills during the 365 days prior to the first antihypertensive medication fill.

Table 1

Case and control periods used in assessing the odds ratio for a serious fall injury associated with initiation, adding a new drug class, and antihypertensive medication titration.

Case period	Control periods (primary analyses)	Control period (secondary analyses)
Analysis of short-term risk for serious fall injuries		
0 to 14 days	Six control periods 30 to 44 days 60 to 74 days 90 to 104 days 120 to 134 days 150 to 164 days 180 to 194 days	One control period 60 to 74 days
Analysis of long-term risk for serious fall injuries		
30 to 44 days	Five control periods 60 to 74 days 90 to 104 days 120 to 134 days 150 to 164 days 180 to 194 days	One control period 90 to 104 days
60 to 74 days	Four control periods 90 to 104 days 120 to 134 days 150 to 164 days 180 to 194 days	One control period 120 to 134 days
90 to 104 days	Three control periods 120 to 134 days 150 to 164 days 180 to 194 days	One control period 150 to 164 days

Table 2

Characteristics of Medicare beneficiaries experiencing a serious fall injury between July 1, 2007 and December 31, 2012, overall and within 15 days following initiation of antihypertensive medication.

Characteristic	All beneficiaries (N=90,127)	Beneficiaries who initiated antihypertensive medication in case period (N=272)
Age on fall date		
<75 years	23,392 (26.0%)	84 (30.9%)
75 –84years	35,209 (39.1%)	94 (34.6%)
≥ 85 years	31,526 (35.0%)	94 (34.6%)
Male sex	21,499 (23.9%)	77 (28.3%)
Race/ethnicity		
White	80,567 (89.4%)	244 (89.7%)
African American	4,341 (4.8%)	12 (4.4%)
Other	5,219 (5.8%)	16 (5.9%)
Region		
Northeast	17,999 (20.0%)	47 (17.3%)
Midwest	22,968 (25.5%)	69 (25.4%)
South	34,673 (38.5%)	110 (40.4%)
West	14,487 (16.1%)	46 (16.9%)
Calendar month of fall		
January	7,190 (8.0%)	22 (8.1%)
February	6,538 (7.3%)	23 (8.5%)
March	6,854 (7.6%)	15 (5.5%)
April	6,721 (7.5%)	24 (8.8%)
May	6,860 (7.6%)	19 (7.0%)
June	6,737 (7.5%)	21 (7.7%)
July	7,560 (8.4%)	27 (9.9%)
August	7,966 (8.8%)	21 (7.7%)
September	7,964 (8.8%)	23 (8.5%)
October	8,237 (9.1%)	23 (8.5%)
November	8,212 (9.1%)	24 (8.8%)
December	9,288 (10.3%)	30 (11.0%)
History of Diabetes	24,027 (26.7%)	54 (19.9%)
History of CHD	24,028 (26.7%)	66 (24.3%)
History of heart failure	14,231 (15.8%)	36 (13.2%)
History of stroke	2,365 (2.6%)	12 (4.4%)
History of CKD	18,413 (20.4%)	47 (17.3%)
History of syncope	9,542 (10.6%)	33 (12.1%)
History of osteoporosis	18,591 (20.6%)	61 (22.4%)
History of depression	17,515 (19.4%)	70 (25.7%)

Characteristic	All beneficiaries (N=90,127)	Beneficiaries who initiated antihypertensive medication in case period (N=272)
History of dementia	17,905 (19.9%)	68 (25.0%)
Number of medication classes		
0 – 5	18,085 (20.1%)	75 (27.6%)
6 – 10	28,888 (32.1%)	90 (33.1%)
>10	43,154 (47.9%)	107 (39.3%)
Charlson comorbidity index		
0	65,840 (73.1%)	167 (61.4%)
1–3	11,945 (13.3%)	61 (22.4%)
≥ 4	12,342 (13.7%)	44 (16.2%)
Any hospitalization in the prior year	29,916 (33.2%)	126 (46.3%)
Skilled nursing facility stay in the prior year	11,307 (12.5%)	54 (19.9%)

Data are expressed as number (percentage).

CHD = coronary heart disease, CKD = chronic kidney disease

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Table 3

Short-term odds ratios for a serious fall injury associated with initiation, adding a new drug class, and antihypertensive medication titration.

	Overall (N=90,127 serious fall injuries)			Prior hypertension diagnosis* (N=90,127 serious fall injuries)			No recent hospitalization† (N=60,211 serious fall injuries)		
	Case period N(%‡)	Control periods N(%§)	OR (95% CI)	Case period N(%‡)	Control periods N(%§)	OR (95% CI)	Case period N(%‡)	Control periods N(%§)	OR (95% CI)
Initiation	272 (0.30)	1,201 (0.22)	1.36 (1.19, 1.55)	159 (0.18)	701 (0.13)	1.36 (1.15, 1.62)	146 (0.24)	635 (0.18)	1.38 (1.15, 1.65)
Addition of new class	1,508 (1.67)	7,820 (1.45)	1.16 (1.10, 1.23)	1,276 (1.42)	6,664 (1.23)	1.15 (1.09, 1.23)	687 (1.14)	3,450 (0.95)	1.20 (1.10, 1.30)
Titration	3,113 (3.45)	16,714 (3.09)	1.13 (1.08, 1.18)	2,696 (2.99)	14,542 (2.69)	1.12 (1.08, 1.17)	1,432 (2.38)	7,662 (2.12)	1.13 (1.07, 1.20)

Initiation, adding a new drug class, or antihypertensive medication titration during the case period (within 15 days prior to fall) was compared with initiation of antihypertensive medication during six control periods (30–44, 60–74, 90–104, 120–134, 150–164, and 180–194 days prior to the fall).

*For the prior hypertension diagnosis, definitions of initiation, addition of a new antihypertensive medication class, and antihypertensive medication titration additionally required having one or more diagnoses of hypertension (International Classification of Diseases, 9th Revision [ICD-9] diagnoses of 401.xx) in the 365 days prior to the case or control period.

†Beneficiaries who were hospitalized within 365 days prior to their serious fall injury were excluded.

‡Calculated as 100 times (number of serious fall injuries in case period divided by total number of serious fall injuries).

§Calculated as 100 times (total number of serious fall injuries across the control periods divided by the product of six control periods times total number of serious fall injuries)

Table 4

Short-term and long-term odds ratios for a serious fall injury associated with initiation, addition of new class, and titration of antihypertensive medication.

		Overall (N=90,127 serious fall injuries)			Prior hypertension diagnosis* (N=90,127 serious fall injuries)			No recent hospitalization† (N=60,211 serious fall injuries)		
	Case period days	Case period N(%‡)	Control periods N(%§)	OR (95% CI)	Case period N(%‡)	Control periods N(%§)	OR (95% CI)	Case period N(%‡)	Control periods N(%§)	OR (95% CI)
Initiation										
	0–14 days‖	272 (0.30)	1,201 (0.22)	1.36 (1.19, 1.55)	159 (0.18)	701 (0.13)	1.36 (1.15, 1.62)	146 (0.24)	635 (0.18)	1.38 (1.15, 1.65)
	30–44 days#	201 (0.22)	1,000 (0.22)	1.01 (0.86, 1.17)	133 (0.15)	568 (0.13)	1.17 (0.97, 1.41)	100 (0.17)	535 (0.18)	0.93 (0.75, 1.16)
	60–74 days**	195 (0.22)	805 (0.22)	0.97 (0.83, 1.13)	116 (0.13)	452 (0.13)	1.03 (0.84, 1.26)	111 (0.18)	424 (0.18)	1.05 (0.85, 1.29)
	90–104 days††	201 (0.22)	604 (0.22)	1.00 (0.85, 1.17)	116 (0.13)	336 (0.12)	1.04 (0.84, 1.28)	102 (0.17)	322 (0.18)	0.95 (0.76, 1.19)
Addition of new class										
	0–14 days‖	1,508 (1.67)	7,820 (1.45)	1.16 (1.10, 1.23)	1,276 (1.42)	6,664 (1.23)	1.15 (1.09, 1.23)	687 (1.14)	3,450 (0.95)	1.20 (1.10, 1.30)
	30–44 days#	1,361 (1.51)	6,459 (1.43)	1.05 (0.99, 1.12)	1,160 (1.29)	5,504 (1.22)	1.06 (0.99, 1.13)	577 (0.96)	2,873 (0.95)	1.00 (0.92, 1.1)
	60–74 days**	1346 (1.49)	5,113 (1.42)	1.05 (0.99, 1.12)	1,146 (1.27)	4,358 (1.21)	1.05 (0.99, 1.12)	595 (0.99)	2,278 (0.95)	1.05 (0.95, 1.15)
	90–104 days††	1,290 (1.43)	3,823 (1.41)	1.01 (0.95, 1.08)	1,105 (1.23)	3,253 (1.20)	1.02 (0.95, 1.09)	567 (0.94)	1,711 (0.95)	0.99 (0.90, 1.09)
Titration										
	0–14 days‖	3,113 (3.45)	16,714 (3.09)	1.13 (1.08, 1.18)	2,696 (2.99)	14,542 (2.69)	1.12 (1.08, 1.17)	1,432 (2.38)	7,662 (2.12)	1.13 (1.07, 1.20)
	30–44 days#	2,874 (3.19)	13,840 (3.07)	1.04 (1.00, 1.09)	2,510 (2.78)	12,032 (2.67)	1.05 (1.00, 1.10)	1,275 (2.12)	6,387 (2.12)	1.00 (0.94, 1.06)
	60–74 days**	2,865 (3.18)	10,975 (3.04)	1.05 (1.00, 1.09)	2,511 (2.79)	9,521 (2.64)	1.06 (1.01, 1.11)	1,302 (2.16)	5,085 (2.11)	1.03 (0.96, 1.09)
	90–104 days††	2,820 (3.13)	8,155 (3.02)	1.04 (1.00, 1.09)	2,434 (2.70)	7,087 (2.62)	1.03 (0.98, 1.08)	1,280 (2.13)	3,805 (2.11)	1.01 (0.95, 1.08)

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[*] For the prior hypertension diagnosis, definitions of initiation, addition of a new antihypertensive medication class, and antihypertensive medication titration additionally required having one or more diagnoses of hypertension (International Classification of Diseases, 9th Revision [ICD-9] diagnoses of 401.xx) in the 365 days prior to the case or control period.

[†] Beneficiaries who were hospitalized within 365 days prior to their serious fall injury were excluded.

[‡] Calculated as 100 times (number of serious fall injuries in case period divided by total number of serious fall injuries).

[§] Calculated as 100 times (total number of serious fall injuries across the control periods divided by the product of number of control periods times total number of serious fall injuries)

[//] Six control periods: 30–44, 60–74, 90–104, 120–134, 150–164, and 180–194 days prior to the fall.

[#] Five control periods: 60–74, 90–104, 120–134, 150–164, and 180–194 days prior to the fall.

[**] Four control periods: 90–104, 120–134, 150–164, and 180–194 days prior to the fall.

[††] Three control periods: 120–134, 150–164, and 180–194 days prior to the fall.