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Antidepressant Use and Recurrent Falls in Community-Dwelling Older Adults: Findings From the Health ABC Study

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Abstract

Background—Few studies have compared the risk of recurrent falls across various antidepressant agents—using detailed dosage and duration data—among community-dwelling older adults, including those who have a history of a fall/fracture.

Objective—To examine the association of antidepressant use with recurrent falls, including among those with a history of falls/fractures, in community-dwelling elders.

Methods—This was a longitudinal analysis of 2948 participants with data collected via interview at year 1 from the Health, Aging and Body Composition study and followed through year 7 (1997-2004). Any antidepressant medication use was self-reported at years 1, 2, 3, 5, and 6 and further categorized as (1) selective serotonin reuptake inhibitors (SSRIs), (2) tricyclic antidepressants, and (3) others. Dosage and duration were examined. The outcome was recurrent falls (≥2) in the ensuing 12-month period following each medication data collection.

Results—Using multivariable generalized estimating equations models, we observed a 48% greater likelihood of recurrent falls in antidepressant users compared with nonusers (adjusted odds

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ratio [AOR] = 1.48; 95% CI = 1.12-1.96). Increased likelihood was also found among those taking SSRIs (AOR = 1.62; 95% CI = 1.15-2.28), with short duration of use (AOR = 1.47; 95% CI = 1.04-2.00), and taking moderate dosages (AOR = 1.59; 95% CI = 1.15-2.18), all compared with no antidepressant use. Stratified analysis revealed an increased likelihood among users with a baseline history of falls/fractures compared with nonusers (AOR = 1.83; 95% CI = 1.28-2.63).

Conclusion—Antidepressant use overall, SSRI use, short duration of use, and moderate dosage were associated with recurrent falls. Those with a history of falls/fractures also had an increased likelihood of recurrent falls.

Keywords

antidepressants; aging; drug-related problems; epidemiology; geriatrics; outcomes research/analysis; pharmacoepidemiology

Introduction

Falls and depressive symptoms are common in older adults and result in significant morbidity.[1] The prevalence of mild depressive symptoms in older adults has been estimated to be 15% for community populations; major clinical depression is less common, with a prevalence of 0.4% to 2%.[1] Several studies have reported associations between depressive symptoms and falls in older adults, and it has been suggested that common pathways for both conditions may explain such associations.[2]

Although many older adults with symptoms of depression are not treated, the pharmacological treatment with antidepressants has also been consistently associated with risk of falls.[2,3] Antidepressant use has been found to be associated with falls or fractures, with risks varying from 1.2- to 6-fold in older adults.[4] However, it is unclear whether the main contributing factor to this risk is the antidepressant or the underlying condition (depressive symptoms), especially among those at highest risk—those with a history of falls and/or fractures. Tricyclic antidepressants (TCAs) are thought to contribute to falls because of their sedative and orthostatic hypotension properties. The exact mechanisms by which selective serotonin reuptake inhibitors (SSRIs) contribute to falls are not known, and the literature is mixed on their relative safety related to falls.[3] Moreover, few studies have controlled for depressive symptoms and examined the risk of various antidepressant classes (including SSRIs) with recurrent falls, which may be more clinically important than single falls.[5-7] Recurrent falls may be a marker for those with an increased risk of physical and cognitive status problems as well as other morbidity and mortality in older adults.[8] In addition, few studies have examined the recurrent fall risk with various types of antidepressants in those with a previous history of a fall/fracture (ie, those at the highest risk of future falls).

The objective of this longitudinal study is to assess the association between antidepressant use and recurrent falls, controlling for depressive symptoms in community-dwelling older adults. This study particularly aims to elucidate any risk in falls among antidepressant users with a history of falls/fractures.

Material and Methods

Study Design, Data Source, and Sample

We used data from the Health, Aging and Body Composition (Health ABC) study, a population-based, prospective, longitudinal, observational study of community-dwelling older adults. This study was approved by the University of California San Francisco, University of Pittsburgh, and University of Tennessee Memphis institutional review boards, and informed consent was obtained from each participant prior to data collection. Recruitment and data collection and management processes used for the Health ABC study are described in detail elsewhere.[9] Briefly, Health ABC was established by recruitment of a population-based cohort based on Medicare records. All black, age-eligible persons in selected zip codes and a random sample of whites were sent an information letter. Those who did not indicate unwillingness to participate were called and received a telephone screen for inclusion/exclusion criteria, including functional status. Because enrollment of black persons lagged, recruitment in the selected areas was also instituted through community centers and churches, enrolled cohort members, and private medical practices used by black persons. For this reason, an absolute response rate is difficult to estimate but would be similar to that for Medicare beneficiaries (approximately 55% of those eligible).[10]

The baseline sample included 3075 black and white men and women 70 to 79 years old, who reported no difficulty walking one-fourth of a mile, climbing 10 steps, or performing basic activities of daily living. Participants lived in specified zip codes surrounding Pittsburgh, Pennsylvania, and Memphis, Tennessee.[9] The sample for the current analysis included 2948 older adults at baseline (ie, year 1 of the Health ABC study) with complete medication use and fall data in the ensuing year to establish a temporal association between medication use and fall outcome (ie, year 1 medication data and year 2 fall outcome; year 2 medication data and year 3 fall outcome, etc). The participants (n = 127) at baseline from the overall cohort study who were not included in the current analysis were excluded because of either missing medication data and/or missing fall data. Participants were followed through year 6 for antidepressant medications and year 7 for recurrent falls.

Data Collection and Management

Participants were seen annually during a clinic or home visit, and detailed physiological and self-report questionnaire measurements (including demographics, health behavior/status, medications, and access-to-care factors) were collected.[5] Detailed medication data were collected by trained research personnel in the clinic or at home about products taken in the previous month, whereby participants were instructed to bring all prescription and over-the-counter medications as well as any herbal products for assessment.[11,12] A similar data collection approach was used for telephone interviews if participants could not be seen in person. Studies have shown that medication use information collected by either the “brown bag” or telephone methods is highly accurate and concordant with information about dispensed prescription drugs in claims data.[13,14] For all medications, the interviewer recorded the name, strength, dosage form, and the number of dosage units the respondents said they had used the previous day, week, or month. The medication data were edited and coded using the Iowa Drug Information System (IDIS) Drug Vocabulary and Thesaurus.[11]

IDIS is a hierarchical coding system with 8 character unique codes for specific drug ingredients, and chemical and therapeutic categories. This therapeutic category code allows drugs to be assigned to 1 of 20 major therapeutic classes and 200 subclasses based on an expanded version of the American Hospital Formulary Services format.[15] Medication data were collected at years 1, 2, 3, 5, and 6.

Teleform was used to create scannable forms for direct data entry. Missing and questionable values were highlighted by the software for visual review and online editing. Additional range checks and data cleaning were conducted at the UCSF Coordinating Center. Deidentified SAS permanent data files were created for analysis.

Primary Outcome

The number of falls in which the participant landed on the floor or ground in the previous 12 months was assessed for 5 waves (years 2, 3, 4, 6, and 7). Falls were self-reported by participants. The primary outcome was recurrent falls (≥2) in the ensuing 12 months following report of medication use (further details below). This method of fall recall (in the previous 12 months) has been shown to be highly specific (91%-95%) when compared with that reported using more frequent assessments.[16]

Primary Independent Variable

Antidepressant medications were grouped as follows: (1) SSRIs, (2) TCAs, and (3) others (ie, bupropion, venlafaxine, mirtazapine, trazodone, phenelzine). The primary independent variable of any antidepressant use was defined as the use of any medication contained in these 3 subclasses.

Secondary Independent Variables

To evaluate the possibility of a dose-response relationship, using a previously published approach, the daily dose for regularly scheduled antidepressant medications was calculated for current users for each agent by multiplying the number of dosage units taken the previous day by the strength of the medication reported at the interview.[17] The daily dose was then converted to a standardized daily dose (SDD) by dividing it by the minimum effective geriatric dose per day as noted in a standard reference.[18] Thus, a person taking 1.0 standardized antidepressant drug unit would have taken the minimum recommended effective daily dose for 1 agent. The standardized daily dose was summated for all antidepressants, regardless of class, taken daily. For purposes of analyses, antidepressant dosages were categorized as <1, 1 to 2, and ≥2 summated standardized daily doses. To examine the impact of duration, long-term use was operationally defined as ≥2 years and short-term use as <2 years.[17] Duration of use was measured at each medication use assessment and was transcribed by trained research personnel through interviewing the participant.

Covariates

To address potential confounding, we controlled for several demographic, health status/behavior, and access-to-care factors.[1,17] Demographic factors included age, sex, race, site,

education (less than a high school education, high school graduate, and postsecondary education), and marital status (never married, married, previously married).

Health behavior factors included smoking status and alcohol use. Health status factors included self-reported pulmonary disease, arthritis, urinary problems, cerebrovascular disease, peripheral artery disease, benign prostatic hyperplasia, coronary heart disease, congestive heart disease, diabetes, vision (excellent/good sight, fair sight, and poor to completely blind), body mass index (underweight/normal, <24.9 kg/m^2; overweight, 25.0-29.9 kg/m^2; and obese, ≥30 kg/m^2), self-reported hypertension, and cognitive impairment (The Modified Mini-Mental State Test score <80).[19] Self-rated global health was dichotomized as excellent/very good/good versus fair/poor. We created a time-varying dichotomous variable for exposure to any other central nervous system (CNS) drugs shown to increase the risk of falls (ie, benzodiazepine receptor agonists, anti-psychotics, and opioid receptor agonists).[17] A continuous time-varying variable was created for the total number of prescription medications (excluding other CNS medications that increase falls and antidepressant drugs) per participant. Access-to-care factors included dichotomous variables for hospitalization in the previous 12 months and having a private physician, prescription insurance, and flu shots in the previous 12 months.[20] In addition, a self-reported history of falls and/or fracture (between the age of 45 years and study baseline) was used as a dichotomous variable for stratification.

Antidepressants may be used for a variety of conditions. Therefore, to control for potential confounding by indication, we created a time-varying dichotomous variable for depressive symptoms (Short Center for Epidemiologic Studies–Depression Scale ≥10).[21] We also included a self-reported variable for history of depression, bodily pain in the past 30 days, sleep problems, and anxiety symptoms.[22] All time-varying variables were assessed at years 1, 2, 3, 5, and 6.

Statistical Analysis

We used appropriate descriptive statistics for summarization and generalized estimating equations (GEE) models for eliciting the main findings.[23,24] First, we assessed the unadjusted association between any antidepressant use and recurrent falls over time. Second, a priori determined covariates based on face validity that may affect recurrent falls were included: site, depressive symptoms, self-reported depression, nonantidepressant drugs that increase the risk of falls, bodily pain, sleep problems, and anxiety symptoms. Finally, additional covariates were selected using a forward stepwise selection approach ($\alpha < 0.15$) applied separately for each of 3 domains of covariates (demographic, health status/behavior, and access to health care). Stepwise detected covariates and those deemed important a priori were included in the final GEE model, which used a binomial distribution and a logit link function. The primary analysis examined any use of antidepressants as the main independent variable of interest. For secondary analyses, each antidepressant subclass was run as a separate model controlling for use of antidepressants in other subclasses. In addition, dose and duration of antidepressant use were evaluated for any association with recurrent falls. We also performed analyses stratified by presence of a history of falls and/or fracture between the age of 45 years and study baseline. We did not find a significant interaction

between having a history of falls/fractures and antidepressant use in the fully adjusted multivariable model ($P = 0.13$); therefore, we performed stratified analyses. Finally, following the same approach described above, we also examined the risk of individual classes of antidepressants in those with a previous history of falls/fractures. All analyses were conducted using SAS software (version 9.3; SAS Institute, Cary, NC) with GENMOD procedure to obtain the main results.

Results

At baseline, the mean age was 73.6 years, 51.6% were women, and 40.8% were black (Table 1). In addition, 5.7% had evidence of serious depressive symptoms, and 37.0% had a history of falls/fractures. Baseline characteristics of antidepressant users versus nonusers are shown in Table 1. The groups were found to have several differences. For example, antidepressant users were more likely to have urinary problems, sleep problems, anxiety symptoms, a hospitalization in the previous 12 months, and use of other CNS medications that can increase fall risk. Comparing participants enrolled at years 1 and 6 (n = 2344) with those enrolled at year 1 but not year 6 (n = 604) on select variables from the first wave of data (years 1/2), participants who remained enrolled throughout the entire study were more likely to be female (54.1% vs 42.0%) and white (62.6% vs 46.0%), have excellent/very good/good self-rated health (86.5% vs 75.5%), and have fewer recurrent falls (7.3% vs 11.4%) than those who dropped out.

Table 2 shows the prevalence of antidepressant use over time. At year 1, 5.8% reported antidepressant use. By year 6, the prevalence of antidepressant use increased to 9.8%, with SSRIs remaining the most common category used (6.6%). Moreover, 55.3% were short-term users, and 57.1% of users took 1 to 2 SDDs.

By year 2, 8% of participants reported having ≥2 falls in the previous year (Table 3). This rate remained somewhat stable over the next 4 waves (7.5%-10.4%). Table 4 shows the results of the bivariate and multivariable GEE analyses, controlling for demographic, health status/behavior (including depressive symptoms and self-reported depression), and access-to-care variables. Bivariate analysis showed statistically significant associations for every model except high- and low-dose antidepressant use. Using multivariable GEE models, a 48% increase in likelihood of recurrent falls in antidepressant users (adjusted odds ratio [AOR] = 1.48; 95% CI = 1.12-1.96) was observed. Additional variables in the primary model (ie, any antidepressant use) with statistically significant associations with recurrent falls were as follows: depressive symptoms ($P = 0.001$), anxiety ($P = 0.04$), pulmonary disease ($P = 0.001$), arthritis ($P = 0.02$), cerebrovascular disease ($P < 0.001$), diabetes ($P < 0.001$), vision problems ($P = 0.05$), and other drugs that increase risk of falls ($P = 0.03$). Similar results were found among those taking SSRIs (AOR = 1.62; 95% CI = 1.15-2.28), with short duration of use (AOR = 1.47; 95% CI = 1.04-2.00), and those taking moderate dosages (AOR = 1.59; 95% CI = 1.15-2.18). Among those with a history of falls/fracture at baseline, we found an 83% increase in likelihood of recurrent falls in antidepressant users (AOR = 1.83; 95% CI = 1.28-2.63), but no increased risk was found in those without a history of falls/fracture (Table 5).

Discussion

This study presents some of the first data to longitudinally assess the association of antidepressant use—measured via detailed dosage and duration data—with recurrent falls in community-dwelling older adults. We found a statistically significant association between any antidepressant use and recurrent falls after adjusting for important potential confounders. We also found an increase in risk among those taking SSRIs, those with short duration of use, and those taking moderate doses. In addition, stratifying the sample by a history of falls/fracture revealed a significant association among those with a history of falls/fracture (but not in those without a history of falls/fracture), highlighting the importance of measuring and improving drug-disease interactions in older adults.[3,25]

These findings are consistent with previous literature, which has shown SSRIs to be associated with falls in older adults.[3] Potential proposed mechanisms include impaired level of alertness and neuromuscular function, sedation, insomnia, and confusion. However, the exact mechanisms are not clear. Short duration of use may be an indicator for a recent start of an antidepressant. Moreover, because anti-depressants are used for various health conditions across a wide range of dosages (eg, low-dose TCA for pain), moderate dose may indicate average use for the treatment of mild to moderate depression. However, we were unable to assess indication for antidepressant use in this analysis.

A previous study by Ensrud et al[5] of community-dwelling older women (mean age approximately 77 years) found that antidepressant use overall was associated with a 54% increased likelihood of frequent falling. It is important to note that the study by Ensrud et al and our study, both controlled for potential confounding by indication by including a measure of depressive symptoms as well as other important variables such as health status. Also similar to our findings, Ensrud et al found that SSRI use was associated with a 3.5 times increase in likelihood of falling frequently. Taken together, these findings suggest that the preferential use of SSRIs (over TCAs) is unlikely to decrease the fall risk in older adults taking antidepressants. However, in contrast to our findings, they found that the risk of falling among antidepressant users was similar in women with and without a fall in the previous year. Our results validate the inclusion of a drug-disease interaction between antidepressant use and those with a history of falls/fracture for the recently updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[3]

Moreover, previous studies have been limited in their ability to assess dose and duration effects. Using current state-of-the-art methods for calculating antidepressant dosage, we found a significant association between moderate doses (SDD 1-2) and recurrent falls. It is not entirely clear why moderate, but not high or low, antidepressant doses were found to increase the likelihood of recurrent falls. Assessing the mean (SD) SDD values for each of the 3 antidepressant subclasses reveals the following: SSRI, 1.74 (0.94); TCA, 3.45 (2.63); and Other, 2.49 (1.98). Given our result showing SSRI use to be significantly associated with recurrent falls and the fact that the mean SDD value falls within the moderate dosage category, this individual subclass could be driving the dose-response modeling. We also found a significant association between short duration of use (<2 years) and recurrent falls, but not long duration of use. This long duration group may represent antidepressant users

who tolerated the early adverse effects (eg, falls) of the drugs, thus biasing our findings toward the null. However, it is important to note that the point estimates (ie, AOR) for short and long duration were similar in magnitude, with overlapping CIs.

Our findings have several clinical implications. First, it is important to recognize that current decisions about anti-depressant selection in older adults are driven by drug adverse effect profiles. When an antidepressant is prescribed, the clinician needs to estimate the risk of falls consequent on prescribing or continuing it and to estimate the relative risks of falls with different classes of drug.[2,25] However, comparative effectiveness research is needed to determine these risks among antidepressants, including the newer agents, to reach the market. If an antidepressant is needed, its use should be restricted to the lowest effective possible dose, and the need for continuation should be reassessed on a regular basis. In addition, older adults taking antidepressant medications in addition to other medications that can increase the risk of falling should be closely monitored.[26] Yet clinicians need to balance the risk of untreated or undertreated depression—as seen in our results showing a significant association between depressive symptoms and recurrent falls—with the risk of antidepressant use for falls.

There are important potential limitations to our study. First, the main outcome of recurrent falls was retrospectively collected via self-report. However, it is a highly specific method compared with self-reporting of falls via diary.[16] Second, medication data were collected at fixed annual assessments, preventing documenting the exact date in which antidepressants were initiated, changed, or discontinued. Third, it is possible that there is residual confounding, including physical function. Fourth, our analyses for higher doses and other antidepressants that included serotonin norepinephrine reuptake inhibitors (SNRIs) may have been underpowered because of small numbers. This later point is important because a published case-control study of primary care patients aged 60+ years from the United Kingdom found a nearly 2-fold increased risk of falls in those taking SNRIs.[27] Whether similar increased risk is seen with different serotonergic antidepressants (eg, mirtazapine, trazodone) or bupropion is not known at this time. Fifth, we were unable to assess dynamic patterns (ie, switching) of antidepressant use in this cohort. Sixth, the indication for antidepressant use (a field that is not routinely collected for prescription drugs) was unknown. In addition, power may have been an issue for some exposure groups with low numbers of participants, such as the <1 SDD group. Moreover, we were unable to assess medication adherence in the observational cohort study, and participants who may have dropped out of the study could have led to attrition bias. Finally, our analysis focused on older, well-functioning, community-dwelling black and white men and women from the Memphis and Pittsburgh areas, and the generalizability to older adults in other regions, of poorer health status, or different care settings is unknown.

Conclusion

In conclusion, antidepressant use overall, SSRI use, short duration of use, and moderate dosage were associated with recurrent falls after adjusting for important confounders. Moreover, stratifying the sample by a history of falls/fracture revealed a significant association only among those with a history of falls/fracture (and not in those without a

history of falls/fracture). These findings suggest that the benefits of antidepressant use in older adults be weighed against the increased risk of falling, especially in those at high risk of these geriatric outcomes. Future comparative effectiveness research is needed to investigate relative safety and efficacy among antidepressants for older adults in other settings.

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References

1. King, MB. Falls. In: Halter, J.; Ouslander, J.; Tinetti, M.; Studenski, S.; High, K.; Asthana, S., editors. Hazzard's Geriatric Medicine and Gerontology. 6th. New York, NY: McGraw-Hill; 2009. p. 659-670.
2. Kvelde T, McVeigh C, Toson B, et al. Depressive symptomatology as a risk factor for falls in older people: systematic review and meta-analysis. J Am Geriatr Soc. 2013; 61:694–706. DOI: 10.1111/jgs.12209 [PubMed: 23617614]
3. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015; 63:2227–2246. DOI: 10.1111/jgs.13702 [PubMed: 26446832]
4. Hartikainen S, Lonnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. J Gerontol A Biol Sci Med Sci. 2007; 62:1172–1181. [PubMed: 17921433]
5. Ensrud KE, Blackwell TL, Mangione CM, et al. Central nervous system-active medications and risk for falls in older women. J Am Geriatr Soc. 2002; 50:1629–1637. [PubMed: 12366615]
6. Kerse N, Flicker L, Pfaff JJ, et al. Falls, depression and anti-depressants in later life: a large primary care appraisal. PLoS ONE. 2008; 3:e2423.doi: 10.1371/journal.pone.0002423 [PubMed: 18560599]
7. Quach L, Yang FM, Berry SD, et al. Depression, antidepressants, and falls among community-dwelling elderly people: the MOBILIZE Boston study. J Gerontol Med Sci. 2013; 68:1575–1581. DOI: 10.1093/gerona/glt084
8. Cumming RG, Kelsey JL, Nevitt MC. Methodologic issues in the study of frequent and recurrent health problems: falls in the elderly. Ann Epidemiol. 1990; 1:49–56. [PubMed: 1669489]
9. Newman AB, Haggerty CL, Kritchevsky SB, Nevitt MC, Simonsick EM. Walking performance and cardiovascular response: associations with age and morbidity—the Health, Aging and Body Composition Study. J Gerontol. 2003; 58:M715–M720.
10. Taaffe DR, Simonsick EM, Visser M, et al. Lower extremity physical performance and hip bone mineral density in elderly black and white men and women: cross-sectional associations in the Health ABC Study. J Gerontol Med Sci. 2003; 58:M934–M942.
11. Pahor M, Chrischilles EA, Guralnik JM, Brown SL, Wallace RB, Carbonin P. Drug data coding and analysis in epidemio-logic studies. Eur J Epidemiol. 1994; 10:405–411. [PubMed: 7843344]
12. Marcum ZA, Perera S, Donohue JM, et al. Analgesic use for knee and hip osteoarthritis in community-dwelling elders. Pain Med. 2011; 12:1628–1636. DOI: 10.1111/j.1526-4637.2011.01249.x [PubMed: 21992521]
13. Pit SW, Byles JE, Cockburn J. Accuracy of telephone self-report of drug use in older people and agreement with pharmaceutical claims data. Drugs Aging. 2008; 25:71–80. [PubMed: 18184031]
14. Caskie GI, Willis SL, Schaie KW, Zanjani FA. Congruence of medication information from a brown bag data collection and pharmacy records: findings from the Seattle longitudinal study. Exp Aging Res. 2006; 32:79–103. [PubMed: 16293570]

15. McEvoy, GK., editor. AHFS Drug Information 2004. Bethesda, MD: American Society of Hospital Pharmacists; 2011.
16. Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of community dwelling older people: effect of the recall interval. J Am Geriatr Soc. 2005; 53:2190–2194. [PubMed: 16398908]
17. Hanlon JT, Boudreau RM, Roumani YF, et al. Number and dosage of central nervous system medications on recurrent falls in community elders: the Health, Aging and Body Composition study. J Gerontol Med Sci. 2009; 64A:492–498. DOI: 10.1093/gerona/gln043
18. Semla, TP.; Beizer, JL.; Higbee, MD., editors. Geriatric Dosage Handbook. 19th. Hudson, OH: Lexi-Comp; 2014.
19. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. J Clin Psychiatry. 1987; 48:314–318. [PubMed: 3611032]
20. Rooks RN, Simonsick EM, Klesges LM, Newman AB, Ayonayon HN, Harris TB. Racial disparities in health care access and cardiovascular indicators in black and white older adults in the Health ABC study. J Aging Health. 2008; 20:599–614. DOI: 10.1177/0898264308321023 [PubMed: 18625758]
21. Radloff LS. The CES-D Scale: a self-report depression scale for research use in the general population. Appl Psychol Meas. 1977; 1:385–401.
22. Mehta KM, Yaffe K, Brenes GA, et al. Anxiety symptoms and decline in physical function over 5 years in the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2007; 55:265–270. [PubMed: 17302665]
23. Liang K, Zeger S. Longitudinal data analysis using generalized linear models. Biometrika. 1986; 73:13–22.
24. Diggle, PJ.; Heagerty, P.; Liang, K.; Zeger, S., editors. Analysis of Longitudinal Data. 2nd. New York, NY: Oxford University Press; 2002.
25. Darowski A, Chambers SCF, Chambers DJ. Antidepressants and falls in the elderly. Drugs Aging. 2009; 26:381–394. DOI: 10.2165/00002512-200926050-00002 [PubMed: 19552490]
26. Tinetti ME. Clinical practice: preventing falls in elderly persons. N Engl J Med. 2003; 348:42–49. [PubMed: 12510042]
27. Gribbin J, Hubbard R, Gladman J, Smith C, Lewis S. Serotonin-norepinephrine reuptake inhibitor antidepressants and the risk of falls in older people: case–control and case-series analysis of a large UK primary care database. Drugs Aging. 2011; 28:895–902. DOI: 10.2165/11592860-000000000-00000 [PubMed: 22054230]

Table 1

Characteristics of the Sample at Baseline (n = 2948).

Variables	Overall Mean ± SD or n (%)	Antidepressant Use, Mean ± SD or n (%), n = 170	No antidepressant Use, Mean ± SD or n (%), n = 2778	*P* Value
Demographics				
Female gender (missing, n = 0)	1522 (51.6)	107 (62.9)	1415 (50.9)	0.002
Black race (missing, n = 0)	1203 (40.8)	41 (24.1)	1162 (41.8)	<0.001
Pittsburgh site (missing, n = 0)	1466 (49.7)	77 (45.3)	1389 (50.0)	0.23
Age (missing, n = 0)	73.6 (2.9)	73.4 (2.7)	73.6 (2.9)	0.37
Education				0.08
Postsecondary	1260 (42.7)	87 (51.2)	1173 (42.2)	
High school graduate	954 (32.4)	49 (28.8)	905 (32.6)	
<High school (missing, n = 7)	727 (24.7)	33 (19.4)	694 (25.0)	
Married (missing, n = 186)	1531 (52.0)	96 (56.5)	1435 (51.7)	0.36
Health behaviors				
Current smoker (missing, n = 2)	302 (10.2)	20 (11.8)	282 (10.2)	0.75
Alcohol use (≥1 drink per week; missing, n = 12)	847 (28.7)	41 (24.1)	806 (29.0)	0.37
Health status				
Pulmonary disease (missing, n = 0)	298 (10.1)	18 (10.6)	280 (10.1)	0.83
Arthritis (missing, n = 37)	1650 (56.0)	106 (62.4)	1544 (55.6)	0.22
Urinary problems (missing, n = 0)	495 (16.8)	40 (23.5)	455 (16.4)	0.02
Cerebrovascular disease (missing, n = 0)	231 (7.8)	18 (10.6)	213 (7.7)	0.17
Peripheral arterial disease (missing, n = 79)	149 (5.1)	6 (3.5)	143 (5.2)	0.64
Benign prostatic hyperplasia (missing, n = 0)	692 (23.5)	36 (21.2)	656 (23.6)	0.47
Coronary heart disease (missing, n = 52)	631 (21.4)	35 (20.6)	596 (21.5)	0.20
Congestive heart disease (missing, n = 44)	85 (2.9)	6 (3.5)	79 (2.8)	0.55
Diabetes (missing, n = 3)	440 (14.9)	21 (12.4)	419 (15.1)	0.57
Vision problems (missing, n = 2)				0.97
Excellent/Good sight	2346 (79.6)	136 (80.0)	2210 (79.6)	
Fair sight	519 (17.6)	30 (17.7)	489 (17.6)	
Poor to completely blind	81 (2.8)	4 (2.4)	77 (2.8)	
Body mass index (kg/m^2) (missing, n = 0)				0.31
Underweight/Normal (<24.9)	947 (32.2)	61 (35.9)	886 (31.9)	
Overweight (25.0-29.9)	1257 (42.6)	63 (37.1)	1194 (43.0)	
Obese (30+)	744 (25.2)	46 (27.1)	698 (25.1)	
Excellent/Very good/Good self-rated health (missing, n = 4)	2479 (84.1)	134 (78.8)	2345 (84.4)	0.12
Self-reported hypertension[a] (missing, n = 0)				0.56
Controlled	775 (26.3)	48 (28.2)	727 (26.2)	
Uncontrolled	723 (24.5)	36 (21.2)	687 (24.7)	
Cognitive impairment (3MS < 80)[a] (missing, n = 12)	284 (9.6)	13 (7.7)	271 (9.8)	0.45
Drugs that increase risk of falls[a] (benzodiazepines, antipsychotics, opioids; missing, n = 0)	248 (8.4)	49 (28.8)	199 (7.2)	<0.001

Variables	Overall Mean ± SD or n (%)	Antidepressant Use, Mean ± SD or n (%), n = 170	No antidepressant Use, Mean ± SD or n (%), n = 2778	*P* Value
No. of prescription medications[a,b] (missing, n = 0)	1.8 (2.0)	2.33 (2.13)	1.76 (1.99)	<0.001
Health status (conditions for which antidepressants are prescribed)				
Self-reported depression (missing, n = 1)	277 (9.4)	88 (51.8)	189 (6.8)	<0.001
Depressive symptoms (Short CES-D ≥ 10[a]; missing, n = 27)	168 (5.7)	27 (15.9)	141 (5.1)	<0.001
Bodily pain (any in past 30 days; missing, n = 3)	1942 (65.9)	120 (70.6)	1822 (65.6)	0.38
Sleep problems (missing, n = 0)	691 (23.4)	111 (65.3)	1579 (56.8)	0.03
Anxiety symptoms (missing, n = 0)	414 (14.0)	47 (27.7)	367 (13.2)	<0.001
Access to care				
Hospitalization in previous 12 months (missing, n = 0)	435 (14.8)	35 (20.6)	400 (14.4)	0.03
Private physician (missing, n = 0)	2319 (78.7)	139 (81.8)	2180 (78.5)	0.31
Prescription insurance (missing, n = 0)	1861 (63.1)	116 (68.2)	1745 (62.8)	0.16
Flu shot in previous 12 months (missing, n = 0)	2039 (69.2)	124 (72.9)	1915 (68.9)	0.27

Abbreviations: 3MS, Modified Mini-Mental Status Exam; CES-D, Center for Epidemiologic Studies Depression Scale.

[a] Time varying.

[b] Excluding drugs that increase the risk of falls and antidepressants.

Table 2

Antidepressant Use Over Time.[a]

Antidepressant Medication Use	Year 1 (n = 2948), n (%)	Year 2 (n = 2811), n (%)	Year 3 (n = 2679), n (%)	Year 5 (n = 2489), n (%)	Year 6 (n = 2388), n (%)
Any use	170 (5.8)	189 (6.7)	219 (8.2)	220 (8.8)	235 (9.8)
SDD ≥2	67 (2.3)	78 (2.8)	75 (2.8)	74 (3.0)	88 (3.7)
SDD 1-2	97 (3.3)	120 (4.3)	156 (5.8)	176 (7.1)	189 (7.9)
SDD <1	11 (0.4)	19 (0.7)	26 (1.0)	22 (0.9)	27 (1.1)
Long-term use (≥2 years)	74 (2.5)	100 (3.6)	104 (3.9)	119 (4.8)	122 (5.1)
Short-term use	94 (3.2)	98 (3.5)	129 (4.8)	117 (4.7)	144 (6.0)
Specific class use					
SSRI	73 (2.5)	90 (3.2)	123 (4.6)	139 (5.6)	158 (6.6)
TCA	70 (2.4)	71 (2.5)	59 (2.2)	44 (1.8)	44 (1.8)
Others[b]	31 (1.1)	41 (1.5)	51 (1.9)	49 (2.0)	44 (1.8)

Abbreviations: SDD, standardized daily dose; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

[a]Medication data not available at year 4.

[b]Others: trazodone, bupropion, venlafaxine, mirtazapine, phenelzine.

Table 3

Prevalence of Falls Over Time, Overall and by Antidepressant Use.

	Year 2 (n = 2948), n (%)	Year 3 (n = 2811), n (%)	Year 4 (n = 2679), n (%)	Year 6 (n = 2489), n (%)	Year 7 (n = 2388), n (%)
≥2 Falls	240 (8.1)	210 (7.5)	229 (8.6)	259 (10.4)	206 (8.6)
Any antidepressant use at prior assessment	28/170 (16.5)	31/189 (16.4)	37/219 (16.9)	52/220 (23.6)	38/235 (16.2)
No antidepressant use at prior assessment	212/2778 (7.6)	179/2622 (6.8)	192/2460 (7.8)	207/2269 (9.1)	168/2153 (7.8)

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Table 4

Association Between Antidepressant Use and Recurrent Falls, With and Without Controlling for Covariates (Including Depressive Symptoms).

Antidepressant Medication Use[a]	Bivariate OR (95% CI)	Adjusted OR (95% CI)[b]
Any use	1.99 (1.60-2.48)	1.48 (1.12-1.96)
Long duration (≥2 years)	1.77 (1.31-2.40)	1.31 (0.88-1.95)
Short duration	1.79 (1.36-2.36)	1.47 (1.04-2.00)
SDD ≥2	1.35 (0.90-2.02)	1.03 (0.64-1.65)
SDD 1-2	1.91 (1.47-2.49)	1.59 (1.15-2.18)
SDD <1	1.57 (0.81-3.04)	1.18 (0.49-2.87)
Specific class use[c]		
SSRI	2.23 (1.68-2.97)	1.62 (1.15-2.28)
TCA	1.61 (1.08-2.40)	1.27 (0.76-2.13)
Others[d]	1.79 (1.07-3.00)	1.34 (0.72-2.50)

Abbreviations: OR, odds ratio; SDD, standardized daily dose; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

[a] Reference group is “No Use.”

[b] Controlling for variables forced into the model (ie, site, drugs that increase the risk of falls, self-reported depression, depressive symptoms per Center for Epidemiologic Studies Depression Scale–10, bodily pain, sleep problems, and anxiety symptoms) and those from forward selection procedures (ie, age, pulmonary disease, arthritis, urinary problems, cerebrovascular disease, diabetes, vision problems, hospitalization in previous 12 months, and private physician).

[c] Each antidepressant subclass was run as a separate model and controlled for antidepressant subclass use other than the subclass being evaluated.

[d] Others: trazodone, bupropion, venlafaxine, mirtazapine, phenelzine.

Table 5

Bivariate and Multivariable Association Between Antidepressant Use and Recurrent Falls Stratified by History of Falls and/or Fracture (After Age 45 Years) at Baseline.

	History of Falls/Fracture (n = 1092)		No History of Falls/Fracture (n = 1856)	
Antidepressant Medication Use[a]	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**[b]	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**[b]
Any use	2.02 (1.51-2.69)	1.83 (1.28-2.63)	1.83 (1.30-2.59)	0.97 (0.60-1.56)
Long duration (≥2 years)	1.61 (1.09-2.39)	1.38 (0.82-2.30)	1.84 (1.15-2.95)	1.30 (0.69-2.42)
Short duration	1.85 (1.30-2.64)	1.77 (1.17-2.68)	1.61 (1.03-2.51)	0.79 (0.42-1.48)
SDD ≥2	1.39 (0.81-2.40)	1.06 (0.57-1.97)	1.13 (0.63-2.06)	0.98 (0.48-2.01)
SDD 1-2	1.80 (1.26-2.57)	1.99 (1.31-3.01)	1.97 (1.34-2.88)	1.17 (0.71-1.93)
SDD <1	1.16 (0.41-3.31)	0.75 (0.18-3.05)	2.22 (0.99-4.93)	1.89 (0.67-5.36)
Specific class use[c]				
SSRI	2.12 (1.49-3.02)	1.92 (1.24-2.97)	2.21 (1.40-3.48)	1.11 (0.62-2.01)
TCA	1.86 (1.11-3.09)	1.47 (0.77-2.82)	1.25 (0.64-2.41)	0.86 (0.35-2.13)
Others[d]	1.90 (0.90-4.01)	2.22 (0.99-4.94)	1.65 (0.80-3.40)	0.76 (0.27-2.12)

Abbreviations: OR, odds ratio; SDD, standardized daily dose; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

[a] Reference group is “No Use.”

[b] Controlling for variables forced into the model (ie, site, drugs that increase the risk of falls, self-reported depression, depressive symptoms per Center for Epidemiologic Studies Depression Scale–10, bodily pain, sleep problems, and anxiety symptoms) and those from forward selection procedures (ie, age, pulmonary disease, arthritis, urinary problems, cerebrovascular disease, diabetes, vision problems, hospitalization in previous 12 months, and private physician).

[c] Each antidepressant subclass was run as a separate model and controlled for antidepressant subclass use other than the subclass being evaluated.

[d] Others: trazodone, bupropion, venlafaxine, mirtazapine, phenelzine.