


ORIGINAL ARTICLE

Frequency and predictors of the potential overprescribing of antidepressants in elderly residents of a geographically defined U.S. population

William V. Bobo¹  | Brandon R. Grossardt² | Maria I. Lapid³ | Jonathan G. Leung⁴ | Cynthia Stoppel³ | Paul Y. Takahashi⁵ | Robert W. Hoel⁴ | Zheng Chang⁶ | Christian Lachner¹ | Mohit Chauhan¹ | Lee Flowers³ | Scott M. Brue⁷ | Mark A. Frye³ | Jennifer St. Sauver⁸ | Walter A. Rocca^{8,9} | Bruce Sutor³

¹Department of Psychiatry & Psychology, Mayo Clinic, Jacksonville, Florida

²Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

³Department of Psychiatry & Psychology, Mayo Clinic, Rochester, Minnesota

⁴Department of Pharmacy Services, Mayo Clinic, Rochester, Minnesota

⁵Department of Primary Care Internal Medicine, Mayo Clinic, Rochester, Minnesota

⁶Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

⁷Biomedical Informatics Support System, Mayo Clinic, Rochester, Minnesota

⁸Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

⁹Department of Neurology, Mayo Clinic, Rochester, Minnesota

Correspondence

William V. Bobo, Department of Psychiatry & Psychology, Mayo Clinic, Jacksonville, FL. Email: bobo.william@mayo.edu

Funding information

This work was supported by a Mayo Clinic CTSA award (to WVB) through grant number UL1 TR002377 from the National Center for Advancing Translational Sciences

Abstract

The purpose of this study was to estimate the extent of potential antidepressant overprescribing in a geographically defined U.S. population, and to determine the indications and factors that account for it. We conducted a cohort study of new antidepressant prescriptions for elderly residents of Olmsted County, Minnesota, 2005-2012, using the Rochester Epidemiology Project medical records-linkage system. Indications for antidepressants were abstracted from health records for all cohort members. Potential antidepressant overprescribing was defined based on regulatory approval, the level of evidence identified from a standardized drug information database, and multidisciplinary expert review. Predictors of potential antidepressant overprescribing were investigated using logistic regression models, stratified by general antidepressant indication (general medical indication, specific psychiatric diagnosis, and non-specific psychiatric symptoms). Potential antidepressant overprescribing occurred in 24% of 3199 incident antidepressant prescriptions during the study period, and involved primarily newer antidepressants that were prescribed for non-specific psychiatric symptoms and subthreshold diagnoses. Potential antidepressant overprescribing was associated with nursing home residence, having a higher number of comorbid medical conditions and outpatient prescribers, taking more concomitant medications, having greater use of urgent or acute care services in the year preceding the index antidepressant prescription, and being prescribed antidepressants via telephone, e-mail, or patient portal. In conclusion, potential antidepressant overprescribing occurred in elderly persons and involved mainly newer antidepressants used for non-specific psychiatric symptoms

Abbreviations: AD, antidepressant; MC, Mayo Clinic; NAMCS, National Ambulatory Medical Care Survey; NDF-RT, National Drug File-Reference Terminology; OMC, Olmsted Medical Center; PHQ-9, Patient Health Questionnaire-9; SNRIs, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2019 The Authors. *Pharmacology Research & Perspectives* published by John Wiley & Sons Ltd, British Pharmacological Society and American Society for Pharmacology and Experimental Therapeutics.

(NCATS), a component of the National Institutes of Health (NIH). The Rochester Epidemiology Project is funded by the National Institute on Aging of the National Institutes of Health under award number R01 AG034676. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

and subthreshold diagnoses, and was associated with indicators of higher clinical complexity or severity and with prescribing without face-to-face patient contact.

KEYWORDS

antidepressants, cohort study, elderly, overuse, prescribing

1 | INTRODUCTION

In the last 30 years, there have been large increases in the use of antidepressants, which are among the most commonly prescribed medications in the U.S.^{1,2} Although increases in antidepressant prescribing have occurred across the age spectrum,^{3,4} the largest increases have occurred in elderly persons.^{5,6} The rapid growth of antidepressant use in elderly populations has raised questions about the appropriateness of this practice.⁷

Evidence suggests that medication prescribing for many chronic health conditions in elderly persons is often inappropriate,⁸ with associated increases in morbidity and economic burden.⁹ In the case of antidepressants, available studies also suggest that potential overprescribing may be common among elderly persons,^{10,11} an important consideration given that some antidepressants, particularly those with anticholinergic side-effects, are associated with potentially serious health risks when taken by older adults.¹² Yet, questions remain about the extent of potential antidepressant overprescribing in elderly patients, and the specific indications and factors that account for it. Most of the available studies used data from surveys or electronic databases to investigate antidepressant prescribing practices among elderly persons nested within large patient cohorts.¹³⁻¹⁹ However, the antidepressant indications were inferred using diagnosis codes or self-report, which may not have accurately accounted for the specific intended antidepressant indications.¹³⁻¹⁵

In addition, several studies employed rudimentary definitions of antidepressant overprescribing, such as the absence of a psychiatric diagnosis, off-label antidepressant use, or the prescribing of antidepressants that appear on drug-to-avoid lists.^{16,20-23} These approaches are reliable, but may overlook acceptable non-psychiatric and off-label indications for antidepressants, including those with few alternative treatments, and may inaccurately consider some medications to be always inappropriate to prescribe to elderly persons without taking into consideration implicit factors such as medical context and clinical judgment. As a result, some authors have suggested that a combination of explicit and implicit methods for defining overprescribing may be more useful than the use of either approach individually.²⁴

We thus conducted a cohort study of new antidepressant prescriptions given to elderly residents of Olmsted County, Minnesota (1/1/2005 to 12/31/2012), using the Rochester Epidemiology Project (REP) medical records-linkage system. Indications for antidepressants

were abstracted directly from the narrative text of health records, which permitted the accurate identification of the specific intended indications. To increase the clinical relevance of this research, potential antidepressant overprescribing was defined based on regulatory approval, on the level of evidence identified from a standardized drug information database, and on a multidisciplinary expert review of important but less empirically supported antidepressant indications.

2 | MATERIALS AND METHODS

2.1 | Study population

We used the medical records-linkage system of the REP to identify all persons aged ≥ 65 years who received an antidepressant prescription between 1/1/2005 and 12/31/2012, and had continuous residence in Olmsted County, MN during the year preceding the date of the first qualifying antidepressant prescription ($n = 4754$). We excluded persons who had not given permission to use their medical records for research ($<3\%$ of the overall population). The REP captures nearly the entire population of Olmsted County as compared to U.S. Census estimates.²⁵ Extensive details about the REP have been reported elsewhere.^{25,26} Information on the age, sex, and self-reported race was obtained electronically from computerized REP indexes. The study was approved by the Institutional Review Boards of the Mayo Clinic (MC) and the Olmsted Medical Center (OMC).

2.2 | Drug prescription records

All inpatient (at the time of discharge) and outpatient drug prescriptions written for the study population between 12/14/2004 and 12/31/2012 were obtained from MC and OMC using linked electronic prescription records.²⁷ MC and OMC provide most of the medical care for the residents of Olmsted County. Since 2002, both institutions have used proprietary electronic prescription systems. Electronic prescriptions were obtained from the proprietary systems, converted into RxNorm codes retrospectively, and grouped using the National Drug File-Reference Terminology (NDF-RT) classification system.^{27,28}

Combination drugs with multiple ingredients were counted under the NDF-RT category for the main ingredient or under a combination drug category when applicable. Specific drug exposure data elements

included drug name, form, dosage, frequency, quantity prescribed, date prescribed, and number of refills. The days of supply for a given prescription were calculated using the following formula: Days of supply = (quantity prescribed/number of pills to be taken per day)* (1 + number of refills).

2.3 | Incident antidepressant prescriptions

Antidepressant drug prescriptions were electronically extracted for all persons aged ≥ 65 years during the study period using the aforementioned approach (Supplementary Table S1). The index date was defined as the date of the earliest qualifying antidepressant prescription—that is, the first prescription for an antidepressant during the study period. Incident antidepressant prescriptions were then identified based on having no evidence of antidepressant prescriptions within 180 days preceding the index date, and having no days of supply from older non-qualifying antidepressant prescriptions extending into the 180 day time window preceding the index date. Vortioxetine was approved in the U.S. for treating major depression in 2013, and was therefore not included as a study drug.

A hierarchical list of antidepressant classes was used to identify a primary antidepressant in cases of antidepressant combination pharmacotherapy (the prescribing of two or more antidepressants on or within 15 days of the index date). However, no incident use of two or more antidepressants was observed in this time window.

2.4 | Review of health records

Electronic and paper health records of all cohort members with a qualifying antidepressant prescription according to REP prescription records were reviewed to verify that the qualifying prescriptions were incident prescriptions, and to then confirm subject age and the antidepressant drug name and dose on the index date.

Additional data for study variables were also extracted from cohort members' health records on the index date and in the preceding 365 days. This information included the setting of the visit resulting in an antidepressant prescription, specialty of the antidepressant prescriber, cohort member residence (community dwelling, nursing home/assisted living), general medical and psychiatric comorbidity, and variables indicating medical service use (total number of outpatient visits, emergency room visits, hospitalizations, and number of health care providers that issued any prescription during the 365 days prior to the index date). General medical comorbidity was defined as the total number of chronic non-psychiatric health conditions (non-communicable illness; and not cured once acquired or anticipated to last ≥ 3 months²⁹) that were under active management on the index date or in the preceding 365 days based on medical record review.

2.5 | Antidepressant indications

For each cohort member, the antidepressant indication specified in health records on the index date was abstracted. In most cases, this included a specific psychiatric or general medical diagnosis. When non-

specific psychiatric complaints or symptoms were listed as the antidepressant indication, the verbatim text from all clinical notes on the index date that referred to the signs or symptoms prompting the antidepressant prescription was abstracted for further review (discussed below). When the text from clinical notes on the index date referenced other clinical notes written prior to the index date, the relevant verbatim text from those earlier clinical notes was also abstracted.

2.6 | Potential antidepressant overprescribing

A list of acceptable indications for specific antidepressants or antidepressant classes was constructed via a two-step process. First, information from the U.S. Food & Drug Administration (FDA) web site and the Micromedex 2.0/DRUGDEX database (Thomson Micromedex, Greenwood Village, CO) were used to generate a preliminary list of evidence-supported antidepressant-indication pairs, based on information from both sources available in June 2013. Evidence-supported indications were defined as: (a) having FDA approval, or (b) a DRUGDEX efficacy rating of "effective" or "favors efficacy," and an evidence rating of A or B, and a recommendation score of I (recommended) or IIa (recommended in most cases). Second, antidepressant-indication pairs with weaker support (e.g., DRUGDEX evidence rating of A or B and a recommendation score of IIb [recommended in some cases]) were subjected to literature review and further discussion by a multidisciplinary consensus work group that consisted of two general psychiatrists (WVB, BS), one geriatric psychiatrist (MIL), one geriatric internal medicine specialist (PYT), and two pharmacists specializing in neuropsychiatric disorders (JGL) and geriatric medicine (RWH). The final list of antidepressant-indication pairs representing acceptable use was approved by the multidisciplinary consensus work group (Supplementary Tables S2 and S3).

When antidepressants were prescribed for non-specific psychiatric complaints or symptoms, the verbatim text referring to the antidepressant indication that was abstracted from clinical notes was reviewed by two general psychiatrists (WVB, BS), who determined whether diagnostic criteria were met for at least one acceptable use indication. Disagreements between the two general psychiatrist reviewers were resolved by a geriatric psychiatrist (MIL).

Potential antidepressant overprescribing was defined as meeting any of the following criteria: (a) antidepressant prescribing for a specific general medical or psychiatric diagnosis not included in Supplementary Tables S2 or S3; (b) antidepressant prescribing for non-specific psychiatric complaints adjudicated as not meeting diagnostic criteria for a condition in Supplementary Tables S2 or S3; or (c) no listed antidepressant indication.

2.7 | Statistical analysis

The associations between independent variables and potential antidepressant overprescribing were investigated using univariate logistic regression, with stratification by general antidepressant indication (general medical diagnosis, specific psychiatric diagnosis, and non-specific psychiatric symptoms). The independent variables for

TABLE 1 Population characteristics stratified by indication

Characteristic	Total, N (%) ^a	General medical indication Persons, N (%) ^a	Psychiatric indication, specific Persons, N (%) ^a	Psychiatric indication, non-specific Persons, N (%) ^a	P-value comparison ^b
Sex					
Women	1973 (61.7)	448 (65.1)	1111 (61.0)	414 (60.0)	0.10
Men	1226 (38.3)	240 (34.9)	710 (39.0)	276 (40.0)	
Age when prescribed					
65-69 y	736 (23.0)	193 (28.1)	416 (22.8)	127 (18.4)	<0.0001
70-74 y	670 (20.9)	173 (25.1)	378 (20.8)	119 (17.2)	
75-79 y	599 (18.7)	133 (19.3)	332 (18.2)	134 (19.4)	
80-84 y	576 (18.0)	109 (15.8)	337 (18.5)	130 (18.8)	
85-89 y	381 (11.9)	52 (7.6)	224 (12.3)	105 (15.2)	
90+ y	237 (7.4)	28 (4.1)	134 (7.4)	75 (10.9)	
Calendar year					
2005-2006	950 (29.7)	216 (31.4)	558 (30.6)	176 (25.5)	0.01
2007-2008	801 (25.0)	174 (25.3)	428 (23.5)	199 (28.8)	
2009-2010	777 (24.3)	151 (21.9)	440 (24.2)	186 (27.0)	
2011-2012	671 (21.0)	147 (21.4)	395 (21.7)	129 (18.7)	
Race					
White race	2946 (92.1)	621 (90.3)	1668 (91.6)	657 (95.2)	0.002
Non-white race ^c	253 (7.9)	67 (9.7)	153 (8.4)	33 (4.8)	
Education level					
HS/GED or less	1602 (50.1)	349 (50.7)	901 (49.5)	352 (51.0)	0.73
Some college or more	1597 (49.9)	339 (49.3)	920 (50.5)	338 (49.0)	
Type of antidepressant prescribed					
SSRIs	1390 (43.5)	39 (5.7)	793 (43.5)	558 (80.9)	<0.0001
SNRIs	161 (5.0)	119 (17.3)	34 (1.9)	8 (1.2)	
Bupropion	103 (3.2)	1 (0.1)	93 (5.1)	9 (1.3)	
Mirtazapine	394 (12.3)	71 (10.3)	220 (12.1)	103 (14.9)	
TCA	525 (16.4)	456 (66.3)	64 (3.5)	5 (0.7)	
Trazadone/Nefazodone	626 (19.6)	2 (0.3)	617 (33.9)	7 (1.0)	
Setting of prescription					
Outpatient	2719 (85.0)	619 (90.0)	1554 (85.3)	546 (79.1)	<0.0001
Inpatient	156 (4.9)	21 (3.1)	112 (6.2)	23 (3.3)	
Other ^d	324 (10.1)	48 (7.0)	155 (8.5)	121 (17.5)	
Mode of prescription					
Office visit	2965 (92.7)	654 (95.1)	1724 (94.7)	587 (85.1)	<0.0001
Tele./email/portal ^e	234 (7.3)	34 (4.9)	97 (5.3)	103 (14.9)	
Living					
Community dwelling	2773 (86.7)	629 (91.4)	1584 (87.0)	560 (81.2)	<0.0001
Nursing home/other	426 (13.3)	59 (8.6)	237 (13.0)	130 (18.8)	
Type of prescriber					
Non-physician	178 (5.6)	34 (4.9)	97 (5.3)	47 (6.8)	<0.0001
Primary care physician	2435 (76.1)	444 (64.5)	1411 (77.5)	580 (84.1)	
Psychiatrist	140 (4.4)	1 (0.1)	136 (7.5)	3 (0.4)	
Other specialists	433 (13.5)	206 (29.9)	170 (9.3)	57 (8.3)	
Unknown	13 (0.4)	3 (0.4)	7 (0.4)	3 (0.4)	

(Continues)

TABLE 1 (Continued)

Characteristic	Total, N (%) ^a	General medical indication Persons, N (%) ^a	Psychiatric indication, specific Persons, N (%) ^a	Psychiatric indication, non-specific Persons, N (%) ^a	P-value comparison ^b
Number of other medical conditions ^f					
0-3	821 (25.7)	237 (34.4)	444 (24.4)	140 (20.3)	<0.0001
4-6	1309 (40.9)	260 (37.8)	799 (43.9)	250 (36.2)	
7-10	856 (26.8)	161 (23.4)	481 (26.4)	214 (31.0)	
11 or more	213 (6.7)	30 (4.4)	97 (5.3)	86 (12.5)	
Number of other prescriptions ^g					
0-3	671 (21.0)	174 (25.3)	368 (20.2)	129 (18.7)	0.06
4-6	1119 (35.0)	223 (32.4)	635 (34.9)	261 (37.8)	
7-10	1074 (33.6)	222 (32.3)	622 (34.2)	230 (33.3)	
11 or more	335 (10.5)	69 (10.0)	196 (10.8)	70 (10.1)	
Number of outpatient visits in previous 365 d					
0-3	752 (23.5)	130 (18.9)	494 (27.1)	128 (18.6)	<0.0001
4-6	916 (28.6)	185 (26.9)	541 (29.7)	190 (27.5)	
7-10	766 (23.9)	175 (25.4)	426 (23.4)	165 (23.9)	
11 or more	765 (23.9)	198 (28.8)	360 (19.8)	207 (30.0)	
Number of outpatient prescribers ^h					
0-1	997 (31.2)	168 (24.4)	656 (36.0)	173 (25.1)	<0.0001
2	919 (28.7)	220 (32.0)	536 (29.4)	163 (23.6)	
3	580 (18.1)	129 (18.8)	317 (17.4)	134 (19.4)	
4 or more	703 (22.0)	171 (24.9)	312 (17.1)	220 (31.9)	
Number of emergency room visits in previous 365 d					
None	1841 (57.5)	435 (63.2)	1036 (56.9)	370 (53.6)	0.002
1	813 (25.4)	152 (22.1)	484 (26.6)	177 (25.7)	
2	319 (10.0)	58 (8.4)	187 (10.3)	74 (10.7)	
3	116 (3.6)	19 (2.8)	62 (3.4)	35 (5.1)	
4 or more	110 (3.4)	24 (3.5)	52 (2.9)	34 (4.9)	
Number of hospitalizations in previous 365 d					
None	2144 (67.0)	490 (71.2)	1214 (66.7)	440 (63.8)	0.002
1	712 (22.3)	141 (20.5)	420 (23.1)	151 (21.9)	
2	215 (6.7)	30 (4.4)	126 (6.9)	59 (8.6)	
3 or more	128 (4.0)	27 (3.9)	61 (3.3)	40 (5.8)	

AD, antidepressant; SNRIs, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

^aThe percent values represent the proportion of persons with the given characteristic (i.e., the rows within a characteristic sum to 100%).

^bP-values are for statistical comparisons of the distribution of characteristics across indication types. For example, there are significant differences in the age distribution of persons across the three indication groups. Only 11.7% of persons with a general medical indication for AD prescriptions were ≥ 85 y of age, whereas the frequencies of persons ≥ 85 y of age with a specific psychiatric indication or with a non-specific psychiatric indication were higher (19.7% and 26.1%, respectively).

^cNon-white race includes Blacks, Asians, mixed race, Hispanic, and Other types as self-reported by persons.

^dOther settings include nursing home, emergency room, and unknown settings.

^eIncludes telephone, email, online medical portal, and other types of non-office visits.

^fOther chronic conditions being treated at time of incident AD prescription.

^gOther prescription medications taken at time of incident AD prescription.

^hNumber of unique health care providers who prescribed at least one medication in the 365 d before incident AD prescription.

this study were selected based on prior knowledge of factors that may influence the risk of potential overprescribing of medications to elderly people across multiple treatment settings and to older adults with chronic diseases.^{17,20,30-34} Multivariable logistic regression

models were adjusted for sex, age (six strata), calendar year (four strata), non-white race (including Black, Asian, mixed race, Hispanic [non-White], and other types based on self-report), and education level (high school graduate and above vs less than high school

graduate). Additional multivariable logistic regression models included all independent variables that is the setting of the prescription, mode of the prescription (office visit, telephone/email/patient portal message), living situation, type of antidepressant prescriber, number of medical diagnoses, number of prescribed medications, number of outpatient prescribers, and the number of outpatient visits, emergency room visits, and hospitalizations in the previous year (strata shown in Tables 1-3). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using robust standard errors. Statistical testing for linear trends in ORs was conducted, where relevant, by equidistant coding of each stratum (e.g., 0, 1, 2, etc.). All statistical tests were two-sided at the 0.05 alpha level, and all analyses were performed using SAS statistical software (version 9.4 SAS Institute Inc., Cary, NC).

3 | RESULTS

As shown in Table 1, the study cohort was predominantly White and included more women than men. A total of 3199 incident antidepressant prescriptions occurred during the study period. The most commonly prescribed antidepressants were selective serotonin reuptake inhibitors (SSRIs, 44% of antidepressant prescriptions during the study period), trazodone/nefazodone (20%, nearly all for trazodone), tricyclic antidepressants (TCAs, 16%), and mirtazapine (12%). The majority (57%) of antidepressant prescriptions were for specific psychiatric indications, whereas a roughly equal proportion of prescriptions were for non-specific psychiatric symptoms (22%) and general medical diagnoses (21%).

Potential antidepressant overprescribing occurred in nearly 24% of all incident antidepressant prescriptions. SSRIs accounted for the majority (74%) of the 758 prescriptions with potential overprescribing, followed by mirtazapine (19%). The proportion of prescriptions classified as potential overprescribing within each drug class, regardless of indication, was highest for SSRIs (40.6%), followed by mirtazapine (37.5%) and serotonin-norepinephrine reuptake inhibitor (SNRIs) (8.7%). As shown in Table 2, the proportions of prescriptions classified as potential overprescribing within each drug class were highest for SSRIs, SNRIs, and mirtazapine when antidepressants were prescribed for general medical indications and specific psychiatric indications.

Rates of potential antidepressant overprescribing were highest when they were prescribed for non-specific psychiatric indications (18%), followed by specific psychiatric indications (3.5%) and general medical indications (2.5%). As shown in Supplementary Tables S4 and S5, the most common non-specific psychiatric indications for SSRIs and mirtazapine were non-specific depressive and anxiety symptoms, depressive symptoms related to loss of a spouse, unspecified behavioral changes, and having a possible depressive or anxiety disorder. The most frequently observed general medical indications for SSRIs and mirtazapine overprescribing included appetite stimulation and unspecified fatigue (Supplementary Table S4).

Potential antidepressant overprescribing was associated with inpatient prescribing (OR 5.61, 95% CI 2.04-15.40 vs outpatient), prescribing in other non-ambulatory settings (OR 2.59, 95% CI 1.20-5.59

vs outpatient), nursing home residence (OR 5.75, 95% CI 2.88-11.50 vs community dwelling), increasing number of medical conditions ($P = 0.006$ for trend), and increasing number of emergency room visits ($P = 0.0001$ for trend) and hospitalizations ($P < 0.0001$ for trend) in the year preceding the index date when antidepressants were prescribed for general medical indications (Table 3). Increasing number of comorbid medical conditions ($P = 0.004$ for trend) and outpatient prescribers ($P = 0.003$ for trend) were associated with potential overprescribing when antidepressants were prescribed for specific psychiatric diagnoses. Only receiving the prescription via telephone, e-mail, or patient portal (OR 2.48, 95% CI 1.23-4.99 vs an office visit) was significantly associated with potential antidepressant overprescribing for non-specific psychiatric indications. The risk of potential antidepressant overprescribing did not differ significantly by type of prescriber.

In logistic regression models that included all independent variables, nursing home residence (for general medical indication, OR 2.98, 95% CI 1.29-6.93 vs community dwelling), having 11 or more medical conditions (for specific psychiatric diagnosis, OR 3.31, 95% CI 1.43-7.70 vs 0-3 medical conditions), and having four or more outpatient prescribers in the year preceding the index date (for specific psychiatric diagnosis, OR 2.32, 95% CI 1.15-4.67) were associated with potential antidepressant overprescribing (Table 4). Having four or more outpatient prescribers and more than one hospital admission in the year preceding the index date were associated with reduced risk of potential antidepressant overprescribing when antidepressants were prescribed for non-specific psychiatric symptoms/complaints.

4 | DISCUSSION

Potential antidepressant overprescribing occurred in nearly one-quarter of elderly residents of a geographically defined U.S. population. Potential antidepressant overprescribing was predicted by nursing home residence, having a higher number of comorbid medical conditions and outpatient prescribers, taking more concomitant medications, having greater use of acute care services in the year preceding the index antidepressant prescription, and receiving the prescription via telephone, e-mail, or patient portal. Our study provides new information about the extent and predictors of potential antidepressant overprescribing in elderly patients who received antidepressants for specific general medical conditions, specific psychiatric diagnoses, or non-specific psychiatric symptoms or complaints. Although potential antidepressant overprescribing was common in our study, the majority of incident antidepressant prescriptions were for appropriate indications, as defined in our study.

Analogous to previous studies, our definition of potential overprescribing considered regulatory approval and the level of scientific support based on ratings from the DRUGDEX compendium.^{19,35} Although this approach is strictly standardized, it runs the risk of classifying practices supported by reasonable evidence or clinical consensus as potential overprescribing. Accordingly, our definition of potential

TABLE 2 Frequencies of incident potential antidepressant overprescribing stratified by indication

Characteristic	General medical indication (N = 688)			Psychiatric indication, specific (N = 1821)			Psychiatric indication, non-specific (N = 690)		
	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b
Sex									
Women	448	51 (11.4)	0.79	1111	68 (6.1)	0.96	414	333 (80.4)	0.14
Men	240	29 (12.1)		710	43 (6.1)		276	234 (84.8)	
Age when prescribed									
65-69 y	193	8 (4.1)	<0.0001	416	19 (4.6)	0.51	127	104 (81.9)	0.61
70-74 y	173	11 (6.4)		378	21 (5.6)		119	95 (79.8)	
75-79 y	133	12 (9.0)		332	20 (6.0)		134	117 (87.3)	
80-84 y	109	24 (22.0)		337	27 (8.0)		130	107 (82.3)	
85-89 y	52	12 (23.1)		224	15 (6.7)		105	85 (81.0)	
90+ y	28	13 (46.4)		134	9 (6.7)		75	59 (78.7)	
Calendar year									
2005-2006	216	12 (5.6)	0.001	558	40 (7.2)	0.37	176	144 (81.8)	0.99
2007-2008	174	21 (12.1)		428	24 (5.6)		199	162 (81.4)	
2009-2010	151	19 (12.6)		440	29 (6.6)		186	154 (82.8)	
2011-2012	147	28 (19.0)		395	18 (4.6)		129	107 (82.9)	
Race									
White race	621	76 (12.2)	0.13	1668	103 (6.2)	0.64	657	540 (82.2)	0.96
Non-white race ^c	67	4 (6.0)		153	8 (5.2)		33	27 (81.8)	
Education level									
HS/GED or less	349	41 (11.7)	0.92	901	58 (6.4)	0.55	352	287 (81.5)	0.65
Some college or more	339	39 (11.5)		920	53 (5.8)		338	280 (82.8)	
Type of antidepressant prescribed									
SSRIs	39	13 (33.3)	<0.0001	793	82 (10.3)	<0.0001	558	469 (84.1)	0.02
SNRIs	119	2 (1.7)		34	5 (14.7)		8	7 (87.5)	
Bupropion	1	0 (0.0)		93	0 (0.0)		9	8 (88.9)	
Mirtazapine	71	55 (77.5)		220	20 (9.1)		103	72 (69.9)	
TCA	456	9 (2.0)		64	2 (3.1)		5	5 (100.0)	
Trazadone/Nefazodone	2	1 (50.0)		617	2 (0.3)		7	6 (85.7)	
Setting of prescription									
Outpatient	619	59 (9.5)	<0.0001	1554	99 (6.4)	0.15	546	443 (81.1)	0.34
Inpatient	21	8 (38.1)		112	8 (7.1)		23	19 (82.6)	
Other ^d	48	13 (27.1)		155	4 (2.6)		121	105 (86.8)	
Mode of prescription									
Office visit	654	76 (11.6)	0.98	1724	109 (6.3)	0.09	587	474 (80.7)	0.02
Tele./email/portal ^e	34	4 (11.8)		97	2 (2.1)		103	93 (90.3)	
Living									
Community dwelling	629	53 (8.4)	<0.0001	1584	101 (6.4)	0.20	560	462 (82.5)	0.64
Nursing home and other	59	27 (45.8)		237	10 (4.2)		130	105 (80.8)	
Type of prescriber									
Non-physician	34	10 (29.4)	0.002	97	7 (7.2)	0.67	47	35 (74.5)	0.53
Primary care physician	444	57 (12.8)		1411	87 (6.2)		580	480 (82.8)	
Psychiatrist	1	0 (0.0)		136	5 (3.7)		3	3 (100.0)	

(Continues)

TABLE 2 (Continued)

Characteristic	General medical indication (N = 688)			Psychiatric indication, specific (N = 1821)			Psychiatric indication, non-specific (N = 690)		
	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b	Persons N	Pot. Over-prescribing N (%) ^a	P-value compare ^b
Other specialists	206	13 (6.3)		170	12 (7.1)		57	47 (82.5)	
Unknown	3	0 (0.0)		7	0 (0.0)		3	2 (66.7)	
Number of other medical conditions ^f									
0-3	237	12 (5.1)	0.0002	444	20 (4.5)	0.003	140	112 (80.0)	0.65
4-6	260	32 (12.3)		799	45 (5.6)		250	203 (81.2)	
7-10	161	30 (18.6)		481	32 (6.7)		214	178 (83.2)	
11 or more	30	6 (20.0)		97	14 (14.4)		86	74 (86.0)	
Number of other prescriptions ^g									
0-3	174	9 (5.2)	0.01	368	16 (4.3)	0.15	129	105 (81.4)	0.66
4-6	223	26 (11.7)		635	34 (5.4)		261	211 (80.8)	
7-10	222	34 (15.3)		622	47 (7.6)		230	190 (82.6)	
11 or more	69	11 (15.9)		196	14 (7.1)		70	61 (87.1)	
Number of outpatient visits in previous 365 d									
0-3	130	14 (10.8)	0.75	494	22 (4.5)	0.32	128	101 (78.9)	0.75
4-6	185	19 (10.3)		541	34 (6.3)		190	157 (82.6)	
7-10	175	20 (11.4)		426	29 (6.8)		165	138 (83.6)	
11 or more	198	27 (13.6)		360	26 (7.2)		207	171 (82.6)	
Number of outpatient prescribers ^h									
0-1	168	21 (12.5)	0.63	656	32 (4.9)	0.006	173	142 (82.1)	0.16
2	220	21 (9.5)		536	25 (4.7)		163	142 (87.1)	
3	129	18 (14.0)		317	23 (7.3)		134	111 (82.8)	
4 or more	171	20 (11.7)		312	31 (9.9)		220	172 (78.2)	
Number of emergency room visits in previous 365 d									
None	435	34 (7.8)	<0.0001	1036	58 (5.6)	0.71	370	305 (82.4)	0.82
1	152	19 (12.5)		484	31 (6.4)		177	141 (79.7)	
2	58	15 (25.9)		187	13 (7.0)		74	63 (85.1)	
3	19	3 (15.8)		62	6 (9.7)		35	30 (85.7)	
4 or more	24	9 (37.5)		52	3 (5.8)		34	28 (82.4)	
Number of hospitalizations in previous 365 d									
None	490	38 (7.8)	<0.0001	1214	71 (5.8)	0.53	440	367 (83.4)	0.61
1	141	25 (17.7)		420	24 (5.7)		151	123 (81.5)	
2	30	8 (26.7)		126	11 (8.7)		59	46 (78.0)	
3 or more	27	9 (33.3)		61	5 (8.2)		40	31 (77.5)	

AD, antidepressant; SNRIs, serotonin-norepinephrine reuptake inhibitor; TCA, Tricyclic antidepressant.

^aThe percent values represent the potential AD overprescribing in the respective characteristic strata. Potential AD overprescribing was determined by the review of the complete medical record information available.

^bP-values are for statistical comparisons of the frequencies of potential AD overprescribing within an indication type. For example, the frequencies of potential AD overprescribing differed significantly across age strata in the general medical indication group (ranging from 4.1% in the 65-69 y age stratum and increasing to 46.4% in the 90+ y age stratum; P-value for comparison <0.0001). By contrast, there were no significant differences in the potential AD overprescribing frequencies across the age strata in the specific psychiatric indication group (P = 0.51) and in the non-specific psychiatric indication group (P = 0.61).

^cNon-white race includes Blacks, Asians, mixed race, Hispanic, and Other types as self-reported by persons.

^dOther settings include nursing home, emergency room, and unknown settings.

^eIncludes telephone, email, online medical portal, and other types of non-office visits.

^fOther chronic conditions being treated at time of incident AD prescription.

^gOther prescription medications taken at time of incident AD prescription.

^hNumber of unique health care providers who prescribed at least one medication in the 365 d before incident AD prescription.

TABLE 3 Predictors of potential antidepressant overprescribing^a in elderly persons (one characteristic at a time)

Characteristic	General medical indication		Psychiatric indication, specific		Psychiatric indication, non-specific	
	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value
Setting of prescription						
Outpatient	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Inpatient	5.61 (2.04-15.4)	0.001	1.09 (0.52-2.31)	0.82	0.99 (0.32-3.06)	0.99
Other ^d	2.59 (1.20-5.59)	0.02	0.37 (0.13-1.02)	0.06	1.69 (0.94-3.05)	0.08
Mode of prescription						
Office visit	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Tele/email/portal ^e	0.88 (0.29-2.73)	0.83	0.30 (0.07-1.22)	0.09	2.48 (1.23-4.99)	0.01
Living	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Community dwelling	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Nursing home and other	5.75 (2.88-11.5)	<0.0001	0.54 (0.27-1.08)	0.08	0.97 (0.56-1.67)	0.90
Type of prescriber						
Non-physician	1.96 (0.81-4.76)	0.14	1.23 (0.55-2.79)	0.61	0.61 (0.30-1.25)	0.18
Primary care physician	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Psychiatrist	Non-estimable ^f	—	0.58 (0.23-1.46)	0.24	Non-estimable ^f	—
Other specialists	0.53 (0.27-1.02)	0.06	1.15 (0.61-2.17)	0.66	0.91 (0.44-1.89)	0.81
Unknown	Non-estimable ^f	—	Non-estimable ^f	—	0.41 (0.03-4.76)	0.47
Number of other medical conditions ^g						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	2.20 (1.06-4.57)	0.03	1.26 (0.73-2.17)	0.41	1.03 (0.60-1.75)	0.92
7-10	3.15 (1.47-6.75)	0.003	1.48 (0.82-2.67)	0.19	1.16 (0.66-2.05)	0.60
11 or more	2.69 (0.82-8.86)	0.10	3.60 (1.71-7.59)	0.001	1.50 (0.70-3.20)	0.30
Number of other prescriptions ^h						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	2.07 (0.90-4.76)	0.09	1.21 (0.65-2.23)	0.55	0.90 (0.52-1.56)	0.71
7-10	2.16 (0.96-4.85)	0.06	1.73 (0.95-3.14)	0.07	1.03 (0.58-1.82)	0.92
11 or more	1.73 (0.64-4.70)	0.28	1.67 (0.79-3.55)	0.18	1.47 (0.64-3.41)	0.37
Number of outpatient visits in previous 365 d						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	0.77 (0.35-1.72)	0.53	1.43 (0.82-2.49)	0.20	1.19 (0.67-2.12)	0.55
7-10	0.78 (0.35-1.74)	0.54	1.50 (0.85-2.67)	0.16	1.29 (0.71-2.36)	0.40
11 or more	0.87 (0.41-1.86)	0.72	1.61 (0.89-2.91)	0.11	1.21 (0.69-2.14)	0.51

(Continues)

TABLE 3 (Continued)

Characteristic	General medical indication			Psychiatric indication, specific			Psychiatric indication, non-specific		
	OR (95% CI) ^b	P-value	P-trend ^c	OR (95% CI) ^b	P-value	P-trend ^c	OR (95% CI) ^b	P-value	P-trend ^c
0-1	1.00 (ref)	—	0.81	1.00 (ref)	—	0.003	1.00 (ref)	—	0.14
2	0.79 (0.39-1.59)	0.51		0.94 (0.55-1.62)	0.83		1.43 (0.78-2.62)	0.25	
3	1.19 (0.57-2.50)	0.65		1.49 (0.85-2.60)	0.16		1.03 (0.57-1.88)	0.91	
4 or more	0.80 (0.39-1.65)	0.55		2.07 (1.23-3.49)	0.01		0.75 (0.44-1.26)	0.27	
Number of emergency room visits in previous 365 d									
None	1.00 (ref)	—	0.0001	1.00 (ref)	—	0.44	1.00 (ref)	—	0.65
1	1.55 (0.82-2.93)	0.18		1.12 (0.71-1.76)	0.64		0.84 (0.53-1.34)	0.46	
2	3.74 (1.78-7.85)	0.001		1.22 (0.65-2.29)	0.54		1.23 (0.60-2.49)	0.57	
3	1.16 (0.28-4.75)	0.83		1.62 (0.66-3.97)	0.29		1.36 (0.50-3.70)	0.55	
4 or more	6.24 (2.19-17.8)	0.001		0.96 (0.29-3.18)	0.94		1.02 (0.40-2.59)	0.96	
Number of hospitalizations in previous 365 d									
None	1.00 (ref)	—	<0.0001	1.00 (ref)	—	0.39	1.00 (ref)	—	0.17
1	2.24 (1.25-4.04)	0.007		0.93 (0.57-1.51)	0.77		0.84 (0.51-1.38)	0.49	
2	3.31 (1.21-9.03)	0.02		1.47 (0.74-2.89)	0.27		0.68 (0.35-1.33)	0.26	
3 or more	4.80 (1.84-12.5)	0.001		1.34 (0.51-3.48)	0.55		0.69 (0.31-1.53)	0.36	

AD, antidepressant; CI, 95% confidence interval; OR, odds ratio.

^aThe AD prescription was found to represent potential overprescribing by the review of the complete medical record information available.

^bAll odds ratios and P-values represent the comparative risk of potential antidepressant overprescribing between strata for a given risk factor, by general antidepressant indication. Statistical testing for linear trends in ORs was conducted, where relevant, by equidistant coding of each stratum (P-trend). For example, when antidepressants were prescribed for specific psychiatric indications, there were non-significant associations between having 2 (P = 0.83) or 3 (P = 0.16) outpatient prescribers in the year preceding the incident antidepressant prescription and the risk of potential antidepressant overprescribing as compared with the reference group (having 0-1 outpatient prescribers). Having four or more outpatient prescribers significantly increased the risk of potential antidepressant overprescribing, compared with the reference group (P = 0.01). Formal testing of linear trend in odds ratios was statistically significant (P-trend = 0.003). All analyses were adjusted for sex, age (six strata), calendar year (four strata), non-white race (Blacks, Asians, mixed race, Hispanic, and Other types as self-reported by persons), and education level (>HS vs ≤HS).

^cP-value testing for a linear trend in the ORs by equidistant coding of each stratum (e.g., 0, 1, 2, etc.).

^dOther settings include nursing home, emergency room, and unknown settings.

^eIncludes telephone, email, online medical portal, and other types of non-office visits.

^fOR was non-estimable because of small sample size and corresponding complete separation of persons into AD prescriptions that were either all "justified" or all "unjustified".

^gOther chronic conditions being treated at time of incident AD prescription.

^hOther prescription medications taken at time of incident AD prescription.

ⁱNumber of unique health care providers who prescribed at least one medication in the 365 d before incident AD prescription.

TABLE 4 Predictors of potential antidepressant overprescribing^a in elderly persons (all characteristics in multivariable model)

Characteristic	General medical indication		Psychiatric indication, specific		Psychiatric indication, non-specific	
	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value
Setting of prescription						
Outpatient	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Inpatient	3.70 (1.00-13.7)	0.049	1.25 (0.51-3.11)	0.63	1.09 (0.29-4.13)	0.90
Other ^c	3.79 (0.91-15.9)	0.07	0.64 (0.15-2.67)	0.54	0.65 (0.20-2.13)	0.48
Mode of prescription						
Office visit	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Tele./email/portal ^d	0.20 (0.03-1.31)	0.09	0.47 (0.07-3.35)	0.45	3.90 (1.07-14.21)	0.04
Living						
Community dwelling	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Nursing home and other	2.98 (1.29-6.93)	0.01	0.51 (0.25-1.06)	0.07	0.99 (0.53-1.87)	0.98
Type of prescriber						
Non-physician	1.33 (0.44-4.08)	0.61	1.36 (0.58-3.18)	0.48	0.72 (0.33-1.59)	0.42
Primary care physician	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
Psychiatrist	Non-estimable ^e	—	0.59 (0.23-1.55)	0.29	Non-estimable ^e	—
Other specialists	0.52 (0.24-1.12)	0.09	0.92 (0.45-1.89)	0.83	1.00 (0.43-2.30)	0.99
Unknown	Non-estimable ^e	—	Non-estimable ^e	—	0.62 (0.04-9.22)	0.73
Number of other medical conditions ^f						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	1.87 (0.82-4.26)	0.13	1.13 (0.64-2.01)	0.68	1.10 (0.62-1.95)	0.75
7-10	1.92 (0.75-4.90)	0.17	1.36 (0.71-2.62)	0.36	1.39 (0.72-2.69)	0.33
11 or more	3.17 (0.80-12.6)	0.10	3.31 (1.43-7.70)	0.005	1.76 (0.72-4.35)	0.22
Number of other prescriptions ^g						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	1.09 (0.42-2.82)	0.87	1.09 (0.57-2.07)	0.79	0.92 (0.51-1.66)	0.79
7-10	1.15 (0.44-3.00)	0.78	1.45 (0.75-2.79)	0.26	0.98 (0.51-1.88)	0.95
11 or more	0.80 (0.24-2.70)	0.72	1.19 (0.50-2.82)	0.69	1.58 (0.60-4.13)	0.35
Number of outpatient visits in previous 365 d						
0-3	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
4-6	0.76 (0.31-1.86)	0.54	1.24 (0.67-2.28)	0.50	1.34 (0.68-2.64)	0.39
7-10	0.61 (0.23-1.63)	0.33	1.01 (0.50-2.03)	0.98	1.86 (0.85-4.09)	0.12
11 or more	0.45 (0.14-1.41)	0.17	0.66 (0.28-1.51)	0.32	2.07 (0.89-4.82)	0.09
Number of outpatient prescribers ^h						
0-1	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
2	0.85 (0.37-1.93)	0.69	0.89 (0.49-1.60)	0.69	1.12 (0.57-2.19)	0.75
3	1.34 (0.52-3.47)	0.54	1.48 (0.76-2.88)	0.24	0.73 (0.35-1.52)	0.40
4 or more	0.88 (0.29-2.64)	0.82	2.32 (1.15-4.67)	0.02	0.43 (0.20-0.92)	0.03
Number of emergency room visits in previous 365 d						
None	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—
1	0.95 (0.41-2.19)	0.91	1.11 (0.65-1.89)	0.71	1.04 (0.59-1.82)	0.89
2	1.97 (0.72-5.38)	0.18	1.08 (0.50-2.30)	0.85	1.94 (0.79-4.78)	0.15
3	0.74 (0.14-3.95)	0.73	1.50 (0.50-4.51)	0.47	3.09 (0.89-10.7)	0.08
4 or more	2.87 (0.60-13.7)	0.19	0.69 (0.15-3.12)	0.63	2.20 (0.63-7.75)	0.22
Number of hospitalizations in previous 365 d						
None	1.00 (ref)	—	1.00 (ref)	—	1.00 (ref)	—

(Continues)

TABLE 4 (Continued)

Characteristic	General medical indication		Psychiatric indication, specific		Psychiatric indication, non-specific	
	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value	OR (95% CI) ^b	P-value
1	1.65 (0.71-3.84)	0.25	0.77 (0.42-1.39)	0.38	0.65 (0.35-1.22)	0.18
2	1.41 (0.37-5.40)	0.61	1.10 (0.46-2.63)	0.83	0.35 (0.14-0.88)	0.03
3 or more	2.20 (0.45-10.6)	0.33	0.97 (0.25-3.72)	0.96	0.30 (0.09-0.97)	0.045

AD, antidepressant; CI, 95% confidence interval; OR, odds ratio.

^aThe AD prescription was found to be unjustified by the review of the complete medical record information available.

^bAll analyses were adjusted for sex, age (six strata), calendar year (four strata), non-white race (Blacks, Asians, mixed race, Hispanic, and Other types as self-reported by persons), and education level (>HS vs ≤HS).

^cOther settings include nursing home, emergency room, and unknown settings.

^dIncludes telephone, email, online medical portal, and other types of non-office visits.

^eOR was non-estimable because of small sample size and corresponding complete separation of persons into AD prescriptions that were either all "justified" or all "unjustified".

^fOther chronic conditions being treated at time of incident AD prescription.

^gOther prescription medications taken at time of incident AD prescription.

^hNumber of unique health care providers who prescribed at least one medication in the 365 d before incident AD prescription.

overprescribing considered indications with weaker support that were subjected to literature review and multidisciplinary panel approval. Despite differences in the definitions of antidepressant overprescribing, the rates of potential overprescribing in our study were consistent with those reported in prior research. For example, Conti and colleagues reported that overuse (defined as off-label antidepressant prescribing for indications with limited/no scientific support) occurred in approximately 20% of 2005 Medical Expenditure Panel Survey respondents with self-reported antidepressant treatment.¹⁹ In another study, an estimated 26% of persons aged ≥65 years were classified as having potential antidepressant overprescribing, defined as the prescribing of antidepressants for minimal or mild depression, based on a review of ICD-9 codes and Patient Health Questionnaire-9 (PHQ-9) scores abstracted from electronic health records.³⁶

A large study that used National Ambulatory Medical Care Survey (NAMCS) data to report medication prescribing trends to a nationally representative sample of elderly adults (totaling 96 996 office based physician visits) showed high rates of anticholinergic medication prescribing.¹² The list of high-risk anticholinergic medications included tricyclic antidepressants and the SSRI, paroxetine. In our study, tricyclic antidepressants accounted for 16% of antidepressant prescriptions, but relatively few cases of antidepressant overprescribing. Instead, potential overprescribing of antidepressants in our study mainly occurred with newer antidepressants, such as SSRIs, SNRIs, and mirtazapine, which were often prescribed for non-specific psychiatric symptoms and subthreshold psychiatric diagnoses (e.g., adjustment disorders, bereavement, etc.). Our findings are thus consistent with previous studies documenting the use of antidepressants for mild or poorly defined mental health conditions or unspecified psychiatric or somatic symptoms.^{4,20,37,38}

Bereavement and adjustment disorder diagnoses can be quite severe and at times difficult to distinguish from major depressive disorder.^{39,40} Without data on the severity and duration of depressive symptoms, it is not possible to determine the number of patients in our study who were prescribed antidepressants after receiving

bereavement of adjustment disorder diagnoses, but may have been better characterized as having major depression or subthreshold depression. However, this is less of a concern for the present study, which focuses on prescribing behavior, and accounts specifically for the diagnoses prompting an antidepressant prescription, as they appeared in the medical records. Antidepressants are generally not recommended for the treatment of adjustment disorders, which are expected to resolve with time and are best treated with psychotherapy.⁴¹ Although bereavement is no longer exclusionary for a diagnosis of major depression, antidepressant treatment is generally reserved for cases of bereavement where a moderate or severe depressive syndrome is diagnosed.⁴²

In our study, we did not classify antidepressant prescribing for subthreshold depression and dysthymic disorder as potential overprescribing. Dysthymic disorder (persistent depressive disorder) is an accepted indication for antidepressants, based on reasonably strong evidence.⁴³ The antidepressant treatment of subthreshold depression (depressive disorder, not otherwise specified), which is distinct from adjustment disorders,⁴⁴ is relatively under-studied. In the elderly, subthreshold depression is more common than major depression,⁴⁵ and antidepressants may be helpful for patients with subthreshold depression and severe mood symptoms.⁴⁴ However, we were not able to distinguish between patients with severe vs milder subthreshold depression that may not respond well to antidepressant treatment.⁴⁶

The reasons for potential antidepressant overprescribing in our study remain unclear, but may include the availability of agents that are safer for use in the elderly, the improved detection of emotional distress in geriatric patients, and the increasing use of antidepressants in general practice.⁴⁷ The challenges associated with managing a large number of co-occurring chronic health conditions during brief office visits may also be an important factor⁴⁸—one that we were unable to assess directly in this research. However, potential antidepressant overprescribing in our study was associated with factors representing higher clinical complexity or severity. These factors included nursing

home residence, higher number of comorbid medical conditions and outpatient prescribers, taking more concomitant medications, and greater use of urgent or acute care services in the year preceding the index antidepressant prescription. These factors could predict being overprescribed nearly any class of medication, and our study did not focus on factors predicting overprescribing of medications other than antidepressants. However, our study findings are consistent with prior work showing that antidepressant overprescribing may be related to higher medical or psychosocial complexity.^{17,20}

To our knowledge, our study is the first to link new antidepressant prescriptions in response to telephone, e-mail, or electronic portal messages with potential antidepressant overprescribing in elderly patients. These platforms are increasingly important for disease management support;^{49,50} however, they may be limited by the inability to obtain and document clinical histories with sufficient detail to justify the initiation of antidepressant treatment. In our study, the level of detail in the clinical documentation describing the rationale for antidepressant prescribing during these encounters was often vague or lacking, and resulted in the adjudication of such cases as representing potential antidepressant overprescribing.

Our study had several strengths, including a well-characterized population-based cohort of elderly adults who received a new prescription for antidepressants. Our definition of potential overprescribing combined FDA approval and Micromedex DRUGDEX classifications with expert clinical review, which may have reduced the risk of misclassifying accepted but less well supported indications for antidepressants. Medical record abstraction allowed us to define the exact intended indication for antidepressants—an important feature given the focus of our study on prescribing behavior, and an important methodological advantage over the use of diagnosis codes or surveys to infer the intended antidepressant indications.

There are also limitations of this work to consider. First, some elements of antidepressant overprescribing were not assessed, such as excessive or inadequate dosing, excessive treatment duration, and drug-drug or drug-disease interactions, which may have resulted in an underestimation of potential antidepressant overprescribing. Conversely, our estimates of potential antidepressant overprescribing may have been inflated, especially for psychiatric indications, because our approach relied on how thoroughly clinicians queried about symptoms necessary for specifically defined mental health conditions and on the quality of documentation of those symptoms. This is a particularly important limitation for psychiatric diagnoses, the symptoms of which are often under-recorded in non-mental health specialty settings, where most antidepressant prescribing occurs.⁵¹ Third, reviewing the records of cases for which antidepressants were prescribed for non-specific symptoms may have reduced the overestimation of potential antidepressant overprescribing, but there were insufficient resources for applying the same level of scrutiny over all cases of appropriate antidepressant prescribing, as we defined it. This limitation may be especially important in view of growing evidence that several psychiatric diagnoses, especially in primary care settings, do not conform to diagnostic criteria.⁵¹ As such, it is unknown to what degree antidepressant prescribing for specific indications, such as depressive disorder, not

otherwise specified, may have been better classified as potential overprescribing. Fourth, our study focused on potential antidepressant overprescribing—not on outcomes of treatment or antidepressant under-use. The initiation of an antidepressant for potential overprescribing indications may have benefitted some patients, and the under-treatment of mental disorders in the elderly may be a more significant problem than antidepressant overprescribing.⁵² Fifth, the 95% confidence intervals for the odds ratios for nearly all predictors of potential antidepressant overprescribing were wide, even when results were significant, indicating relatively low precision. Finally, our cohort was representative of elderly persons residing in the Upper Midwest region of the U.S.;⁵³ however, our results may not be generalizable to cohorts with different sociodemographic or clinical characteristics, where rates of potential antidepressant overprescribing may be higher.^{17,54-56}

We conclude that potential antidepressant overprescribing in a large cohort of elderly patients mainly involved the use of newer antidepressants for non-specific psychiatric symptoms and indications. However, the majority of incident antidepressant starts did not represent potential overprescribing. When overprescribing occurred, it was associated with factors representing higher multimorbidity, clinical complexity, and severity—and with antidepressant prescribing that did not involve face to face interaction of patients with prescribers.

ORCID

William V. Bobo  <https://orcid.org/0000-0002-5674-3079>

REFERENCES

1. Chen Y, Kelton CM, Jing Y, Guo JJ, Li X, Patel NC. Utilization, price, and spending trends for antidepressants in the US Medicaid Program. *Res Social Adm Pharm*. 2008;4:244-257.
2. Mojtabai R, Olfson M. National trends in long-term use of antidepressant medications: results from the U.S. National Health and Nutrition Examination Survey. *J Clin Psychiatry*. 2014;75:169-177.
3. Moore M, Yuen HM, Dunn N, Mullee MA, Maskell J, Kendrick T. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *BMJ*. 2009;339:b3999.
4. Olfson M, Marcus SC. National patterns in antidepressant medication treatment. *Arch Gen Psychiatry*. 2009;66:848-856.
5. Maust DT, Blow FC, Wiechers IR, Kales HC, Marcus SC. National trends in antidepressant, benzodiazepine, and other sedative-hypnotic treatment of older adults in psychiatric and primary care. *J Clin Psychiatry*. 2017;78:e363-e371.
6. Hanlon JT, Handler SM, Castle NG. Antidepressant prescribing in US nursing homes between 1996 and 2006 and its relationship to staffing patterns and use of other psychotropic medications. *J Am Med Dir Assoc*. 2010;11:320-324.
7. Dowrick C, Frances A. Medicalising unhappiness: new classification of depression risks more patients being put on drug treatment from which they will not benefit. *BMJ*. 2013;347:f7140.
8. Spinewine A, Schmader KE, Barber N, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet*. 2007;370:173-184.
9. Simonson W, Feinberg JL. Medication-related problems in the elderly: defining the issues and identifying solutions. *Drugs Aging*. 2005;22:559-569.

10. Rhee TG, Schommer JC, Capistrant BD, Hadsall R, Uden DL. Potentially inappropriate antidepressant prescriptions among older adults in office-based outpatient settings: National trends from 2002 to 2012. *Adm Policy Ment Health*. 2018;45:224-235.
11. Rhee TG. Continuing versus new antidepressant use in older adults: U.S. prescribing trends from 2006 to 2015. *Eur Geriatr Med*. 2018;9:551-555.
12. Rhee TG, Choi YC, Ouellet GM, Ross JS. National prescribing trends for high-risk anticholinergic medications in older adults. *J Am Geriatr Soc*. 2018;66:1382-1387.
13. Lockhart P, Guthrie B. Trends in primary care antidepressant prescribing 1995-2007: a longitudinal population database analysis. *Br J Gen Pract*. 2011;61:e565-e572.
14. Newman SC, Schopflocher D. Trends in antidepressant prescriptions among the elderly in Alberta during 1997 to 2004. *Can J Psychiatry*. 2008;53:704-707.
15. Mamdani MM, Parikh SV, Austin PC, Upshur RE. Use of antidepressants among elderly subjects: trends and contributing factors. *Am J Psychiatry*. 2000;157:360-367.
16. Parabiaghi A, Franchi C, Tettamanti M, et al. Antidepressants utilization among elderly in Lombardy from 2000 to 2007: dispensing trends and appropriateness. *Eur J Clin Pharmacol*. 2011;67:1077-1083.
17. Hanlon JT, Wang X, Castle NG, et al. Potential underuse, overuse, and inappropriate use of antidepressants in older veteran nursing home residents. *J Am Geriatr Soc*. 2011;59:1412-1420.
18. Nishtala PS, McLachlan AJ, Bell JS, Chen TF. Determinants of antidepressant medication prescribing in elderly residents of aged care homes in Australia: a retrospective study. *Am J Geriatr Pharmacother*. 2009;7:210-219.
19. Conti R, Busch AB, Cutler DM. Overuse of antidepressants in a nationally representative adult patient population in 2005. *Psychiatr Serv*. 2011;62:720-726.
20. Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. *Health Aff (Millwood)*. 2011;30:1434-1442.
21. Pagura J, Katz LY, Mojtabai R, Druss BG, Cox B, Sareen J. Antidepressant use in the absence of common mental disorders in the general population. *J Clin Psychiatry*. 2011;72:494-501.
22. Maust DT, Mavandadi S, Eakin A, et al. Telephone-based behavioral health assessment for older adults starting a new psychiatric medication. *Am J Geriatr Psychiatry*. 2011;19:851-858.
23. Wiechers IR, Kirwin PD, Rosenheck RA. Increased risk among older veterans of prescribing psychotropic medication in the absence of psychiatric diagnoses. *Am J Geriatr Psychiatry*. 2014;22:531-539.
24. Buetow SA, Sibbald B, Cantrill JA, Halliwell S. Appropriateness in health care: application to prescribing. *Soc Sci Med*. 1997;45:261-271.
25. St Sauver JL, Grossardt BR, Yawn BP, Melton LJ 3rd, Rocca WA. Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester epidemiology project. *Am J Epidemiol*. 2011;173:1059-1068.
26. St Sauver JL, Grossardt BR, Yawn BP, et al. Data resource profile: the Rochester Epidemiology Project (REP) medical records-linkage system. *Int J Epidemiol*. 2012;41:1614-1624.
27. Pathak J, Murphy SP, Willaert BN, et al. Using RxNorm and NDF-RT to classify medication data extracted from electronic health records: experiences from the Rochester Epidemiology Project. *AMIA Annu Symp Proc*. 2011;2011:1089-1098.
28. Savova GK, Masanz JJ, Ogren PV, et al. Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. *J Am Med Inform Assoc*. 2010;17:507-513.
29. Services USDoHaH. *Health, United States, 2010: With Special Feature on Death and Dying*. Hyattsville, MD: Centers for Disease Control and Prevention, National Center for Health Statistics. Appendix, definition of "condition." 2011:486-487.
30. Projovic I, Vukadinovic D, Milovanovic O, et al. Risk factors for potentially inappropriate prescribing to older patients in primary care. *Eur J Clin Pharmacol*. 2016;72:93-107.
31. Hiance-Delahaye A, de Schongor FM, Lechowski L, et al. Potentially inappropriate prescription of antidepressants in old people: characteristics, associated factors, and impact on mortality. *Int Psychogeriatr*. 2018;30:715-726.
32. San-Jose A, Agusti A, Vidal X, et al. Inappropriate prescribing to the oldest old patients admitted to hospital: prevalence, most frequently used medicines, and associated factors. *BMC Geriatr*. 2015;15:42.
33. Weng MC, Tsai CF, Sheu KL, et al. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. *QJM*. 2013;106:1009-1015.
34. Vezmar Kovacevic S, Simsic M, Stojkov Rudinski S, et al. Potentially inappropriate prescribing in older primary care patients. *PLoS ONE*. 2014;9(4):e95536.
35. Radley DC, Finkelstein SN, Stafford RS. Off-label prescribing among office-based physicians. *Arch Intern Med*. 2006;166:1021-1026.
36. Simon GE, Rossom RC, Beck A, et al. Antidepressants are not overprescribed for mild depression. *J Clin Psychiatry*. 2015;76:1627-1632.
37. Petty DR, House A, Knapp P, Raynor T, Zermansky A. Prevalence, duration and indications for prescribing of antidepressants in primary care. *Age Ageing*. 2006;35:523-526.
38. Cruickshank G, Macgillivray S, Bruce D, Mather A, Matthews K, Williams B. Cross-sectional survey of patients in receipt of long-term repeat prescriptions for antidepressant drugs in primary care. *Ment Health Fam Med*. 2008;5:105-109.
39. Casey P, Maracy M, Kelly BD. Can adjustment disorder and depressive episode be distinguished? Results From ODIN. *J Affect Disord*. 2006;92:291-297.
40. Friedman RA. Grief, depression, and the DSM-5. *N Engl J Med*. 2012;366:1855-1857.
41. Carta MG, Balestrieri M, Murru A, Hardoy MC. Adjustment Disorder: epidemiology, diagnosis and treatment. *Clin Pract Epidemiol Ment Health*. 2009;5:15.
42. Osborn J, Raetz J, Kost A. Seasonal affective disorder, grief reaction, and adjustment disorder. *Med Clin North Am*. 2014;98:1065-1077.
43. von Wolff A, Holzel LP, Westphal A, Harter M, Kriston L. Selective serotonin reuptake inhibitors and tricyclic antidepressants in the acute treatment of chronic depression and dysthymia: a systematic review and meta-analysis. *J Affect Disord*. 2013;144:7-15.
44. Zimmerman M, Martinez JH, Dalrymple K, Chelminski I, Young D. "Subthreshold" depression: is the distinction between depressive disorder not otherwise specified and adjustment disorder valid? *J Clin Psychiatry*. 2013;74:470-476.
45. Alexopoulos GS. Depression in the elderly. *Lancet*. 2005;365:1961-1970.
46. Williams JW, Barrett J, Oxman T, et al. Treatment of dysthymia and minor depression in primary care: a randomized controlled trial in older adults. *JAMA*. 2000;284:1519-1526.
47. Barbui C, Cipriani A, Patel V, Ayuso-Mateos JL, van Ommeren M. Efficacy of antidepressants and benzodiazepines in minor depression: systematic review and meta-analysis. *Br J Psychiatry*. 2011;198:11-16, sup 11.
48. Johnson CF, Williams B, MacGillivray SA, Dougall NJ, Maxwell M. 'Doing the right thing': factors influencing GP prescribing of antidepressants and prescribed doses. *BMC Fam Pract*. 2017;18:72.
49. Zhou YY, Kanter MH, Wang JJ, Garrido T. Improved quality at Kaiser Permanente through e-mail between physicians and patients. *Health Aff (Millwood)*. 2010;29:1370-1375.

50. Schnipper JL, Gandhi TK, Wald JS, et al. Design and implementation of a web-based patient portal linked to an electronic health record designed to improve medication safety: the Patient Gateway medications module. *Inform Prim Care*. 2008;16:147-155.
51. Mitchell AJ, Vaze A, Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. *Lancet*. 2009;374:609-619.
52. Unutzer J, Katon W, Callahan CM, et al. Depression treatment in a sample of 1,801 depressed older adults in primary care. *J Am Geriatr Soc*. 2003;51:505-514.
53. St Sauver JL, Grossardt BR, Leibson CL, Yawn BP, Melton LJ, Rocca WA. Generalizability of epidemiological findings and public health decisions: an illustration from the Rochester Epidemiology Project. *Mayo Clin Proc*. 2012;87:151-160.
54. Aspinall SL, Zhao X, Semla TP, et al. Epidemiology of drug-disease interactions in older veteran nursing home residents. *J Am Geriatr Soc*. 2015;63:77-84.
55. Dosa D, Cai S, Gidmark S, Thomas K, Intrator O. Potentially inappropriate medication use in veterans residing in community living centers: have we gotten better? *J Am Geriatr Soc*. 2013;61:1994-1999.
56. Jureidini J, Tonkin A. Overuse of antidepressant drugs for the treatment of depression. *CNS Drugs*. 2006;20:623-632.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Bobo WV, Grossardt BR, Lapid MI, et al. Frequency and predictors of the potential overprescribing of antidepressants in elderly residents of a geographically defined U.S. population. *Pharmacol Res Perspect*. 2019;e00461. <https://doi.org/10.1002/prp2.461>