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

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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.
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 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 the 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
| Characteristic                        | Total, N (%)  | General medical indication, Persons, N (%)  | Psychiatric indication, specific, Persons, N (%)  | Psychiatric indication, non-specific, Persons, N (%)  | P-value comparison |
|--------------------------------------|---------------|---------------------------------------------|-----------------------------------------------|-------------------------------------------------|------------------|
| **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 racec                      | 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<sup>d</sup>                    | 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<sup>e</sup>       | 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)
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. 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.
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 over-prescribing 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. 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...
| Characteristic                      | General medical indication (N = 688) | Psychiatric indication, specific (N = 1821) | Psychiatric indication, non-specific (N = 690) |
|------------------------------------|-------------------------------------|---------------------------------------------|------------------------------------------------|
|                                    | Persons N                           | Pot. Over-prescribing N (%)<sup>a</sup>     | Pot. Over-prescribing N (%)<sup>a</sup>       | Pot. Over-prescribing N (%)<sup>a</sup>       |
|                                    |                                     | P-value compare<sup>b</sup>                  | P-value compare<sup>b</sup>                   | P-value compare<sup>b</sup>                   |
| Sex                                |                                     |                                              |                                                |                                                |
| Women                              | 448                                 | 51 (11.4)                                   | 1111                                           | 68 (6.1)                                      |
|                                    |                                     | 0.79                                         | 0.96                                            | 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)                                      | 416                                            | 19 (4.6)                                      |
|                                    |                                     | <0.0001                                      | 0.51                                           | 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)                                     | 558                                            | 40 (7.2)                                      |
|                                    |                                     | 0.001                                        | 0.37                                           | 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)                                    | 1668                                           | 103 (6.2)                                     |
|                                    |                                     | 0.13                                         | 0.64                                           | 0.96                                           |
| Non-white race<sup>c</sup>         | 67                                  | 4 (6.0)                                      | 153                                            | 8 (5.2)                                       |
|                                    |                                     |                                              | 33                                             | 27 (81.8)                                     |
| Education level                    |                                     |                                              |                                                |                                                |
| HS/GED or less                     | 349                                 | 41 (11.7)                                    | 901                                            | 58 (6.4)                                      |
|                                    |                                     | 0.92                                         | 0.55                                           | 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)                                    | 793                                            | 82 (10.3)                                     |
|                                    |                                     | <0.0001                                      | <0.0001                                        | 558                                            |
| 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)                                     | 1554                                           | 99 (6.4)                                      |
|                                    |                                     | <0.0001                                      | 0.15                                           | 0.34                                           |
| Inpatient                          | 21                                  | 8 (38.1)                                     | 112                                            | 8 (7.1)                                       |
|                                    |                                     |                                              | 23                                             | 19 (82.6)                                     |
| Other<sup>d</sup>                  | 48                                  | 13 (27.1)                                    | 155                                            | 4 (2.6)                                       |
|                                    |                                     |                                              | 121                                            | 105 (86.8)                                    |
| Mode of prescription               |                                     |                                              |                                                |                                                |
| Office visit                       | 654                                 | 76 (11.6)                                    | 1724                                           | 109 (6.3)                                     |
|                                    |                                     | 0.98                                         | 0.09                                           | 0.02                                           |
| Tele./email/portal<sup>e</sup>     | 34                                  | 4 (11.8)                                     | 97                                             | 2 (2.1)                                       |
|                                    |                                     |                                              | 103                                            | 93 (90.3)                                     |
| Living                             |                                     |                                              |                                                |                                                |
| Community dwelling                 | 629                                 | 53 (8.4)                                     | 1584                                           | 101 (6.4)                                     |
|                                    |                                     | <0.0001                                      | 0.20                                           | 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)                                    | 97                                             | 7 (7.2)                                       |
|                                    |                                     | 0.002                                        | 0.67                                           | 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)
| Characteristic | General medical indication (N = 688) | Psychiatric indication, specific (N = 1821) | Psychiatric indication, non-specific (N = 690) |
|----------------|------------------------------------|----------------------------------------------|-----------------------------------------------|
|                | Persons N N (%)a P-value compareb  | Persons N Pot. Over-prescribing N (%)a P-value compareb | Persons N Pot. Over-prescribing N (%)a P-value compareb |
| Other specialists | 206 13 (6.3) 0.0002 | 170 12 (7.1) 0.003 | 57 47 (82.5) 0.65 |
| Unknown         | 3 0 (0.0)                | 7 0 (0.0)             | 3 2 (66.7)                              |

Number of other medical conditionsf

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| 0-3        | 237 12 (5.1)                  |
| 4-6        | 260 32 (12.3)                 |
| 7-10       | 161 30 (18.6)                 |
| 11 or more | 30 6 (20.0)                   |

Number of other prescriptionsg

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| 0-3        | 174 9 (5.2) 0.01 |
| 4-6        | 223 26 (11.7) 0.016 |
| 7-10       | 222 34 (15.3) 0.015 |
| 11 or more | 69 11 (15.9) 0.01 |

Number of outpatient visits in previous 365 d

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| 0-3        | 130 14 (10.8) 0.75 |
| 4-6        | 185 19 (10.3) 0.015 |
| 7-10       | 175 20 (11.4) 0.016 |
| 11 or more | 198 27 (13.6) 0.01 |

Number of outpatient prescribersh

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| 0-1        | 168 21 (12.5) 0.63 |
| 2          | 220 21 (9.5) 0.006 |
| 3          | 129 18 (14.0) 0.13 |
| 4 or more  | 171 20 (11.7) 0.016 |

Number of emergency room visits in previous 365 d

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| None       | 435 34 (7.8) <0.0001 |
| 1          | 152 19 (12.5) 0.006 |
| 2          | 58 15 (25.9) 0.74 |
| 3          | 19 3 (15.8) 0.35 |
| 4 or more  | 24 9 (37.5) 0.016 |

Number of hospitalizations in previous 365 d

|            | Persons N N (%)a P-value compareb |
|------------|----------------------------------|
| None       | 490 38 (7.8) <0.0001 |
| 1          | 141 25 (17.7) 0.53 |
| 2          | 30 8 (26.7) 0.53 |
| 3 or more  | 27 9 (33.3) 0.03 |

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                                  |                           |                                |                                 |                                 |                                     |                                 |
| 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)                | 0.004                           | 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                            |

\(^a\) Dependent variable: potential antidepressant overprescribing is defined as the ratio of antidepressant prescriptions to all primary care medications prescriptions. \(^b\) OR (95% CI) = Odds ratio (95% confidence interval). \(^c\) P-value and P-trend are calculated using the generalized linear model. \(^d\) Other includes hospital, inpatient, nursing home, and long-term care facility. \(^e\) Tele/email/portal denotes telemedicine, email, and portal. \(^f\) Non-estimable indicates that the estimate is not estimable due to zero events. \(^g\) Number of other medical conditions includes all other medical conditions except the general medical indication. \(^h\) Number of other prescriptions includes all other medications except the psychiatric indication. (Continues)
| Characteristic | General medical indication | Psychiatric indication, specific | Psychiatric indication, non-specific |
|---------------|----------------------------|---------------------------------|-----------------------------------|
|               | OR (95% CI)b | P-value | P-trendc | OR (95% CI)b | P-value | P-trendc | OR (95% CI)b | P-value | P-trendc |
| 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                          |
| Setting of prescription                |                           |                                  |                                     |                                  |
| Outpatient                             | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| Inpatient                              | 3.70 (1.00-13.7)          | 0.049                            | 1.25 (0.51-3.11)                   | 0.63                             |
| Other \(^c\)                           | 3.79 (0.91-15.9)          | 0.07                             | 0.64 (0.15-2.67)                   | 0.54                             |
| Mode of prescription                   |                           |                                  |                                     |                                  |
| Office visit                           | 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                             |
| Living                                 |                           |                                  |                                     |                                  |
| Community dwelling                     | 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                             |
| Type of prescriber                     |                           |                                  |                                     |                                  |
| Non-physician                          | 1.33 (0.44-4.08)          | 0.61                             | 1.36 (0.58-3.18)                   | 0.48                             |
| Primary care physician                 | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| Psychiatrist                           | Non-estimable\(^e\)       | —                                | 0.59 (0.23-1.55)                   | 0.29                             |
| Other specialists                      | 0.52 (0.24-1.12)          | 0.09                             | 0.92 (0.45-1.89)                   | 0.83                             |
| Unknown                                | Non-estimable\(^e\)       | —                                | Non-estimable\(^e\)               | —                                |
| Number of other medical conditions\(^f\) |                           |                                  |                                     |                                  |
| 0-3                                    | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| 4-6                                    | 1.87 (0.82-4.26)          | 0.13                             | 1.13 (0.64-2.01)                   | 0.68                             |
| 7-10                                   | 1.92 (0.75-4.90)          | 0.17                             | 1.36 (0.71-2.62)                   | 0.36                             |
| 11 or more                             | 3.17 (0.80-12.6)          | 0.10                             | 3.31 (1.43-7.70)                   | 0.005                            |
| Number of other prescriptions \(^h\)   |                           |                                  |                                     |                                  |
| 0-3                                    | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| 4-6                                    | 1.09 (0.42-2.82)          | 0.87                             | 1.09 (0.57-2.07)                   | 0.79                             |
| 7-10                                   | 1.15 (0.44-3.00)          | 0.78                             | 1.45 (0.75-2.79)                   | 0.26                             |
| 11 or more                             | 0.80 (0.24-2.70)          | 0.72                             | 1.19 (0.50-2.82)                   | 0.69                             |
| Number of outpatient visits in previous 365 d |             |                                  |                                     |                                  |
| 0-3                                    | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| 4-6                                    | 0.76 (0.31-1.86)          | 0.54                             | 1.24 (0.67-2.28)                   | 0.50                             |
| 7-10                                   | 0.61 (0.23-1.63)          | 0.33                             | 1.01 (0.50-2.03)                   | 0.98                             |
| 11 or more                             | 0.45 (0.14-1.41)          | 0.17                             | 0.66 (0.28-1.51)                   | 0.32                             |
| Number of outpatient prescribers\(^h\) |                           |                                  |                                     |                                  |
| 0-1                                    | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| 2                                      | 0.85 (0.37-1.93)          | 0.69                             | 0.89 (0.49-1.60)                   | 0.69                             |
| 3                                      | 1.34 (0.52-3.47)          | 0.54                             | 1.48 (0.76-2.88)                   | 0.24                             |
| 4 or more                              | 0.88 (0.29-2.64)          | 0.82                             | 2.32 (1.15-4.67)                   | 0.02                             |
| Number of emergency room visits in previous 365 d |             |                                  |                                     |                                  |
| None                                   | 1.00 (ref)                | —                                | 1.00 (ref)                          | —                                |
| 1                                      | 0.95 (0.41-2.19)          | 0.91                             | 1.11 (0.65-1.89)                   | 0.71                             |
| 2                                      | 1.97 (0.72-5.38)          | 0.18                             | 1.08 (0.50-2.30)                   | 0.85                             |
| 3                                      | 0.74 (0.14-3.95)          | 0.73                             | 1.50 (0.50-4.51)                   | 0.47                             |
| 4 or more                              | 2.87 (0.60-13.7)          | 0.19                             | 0.69 (0.15-3.12)                   | 0.63                             |
| Number of hospitalizations in previous 365 d |             |                                  |                                     |                                  |
| None                                   | 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.

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

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).

Other settings include nursing home, emergency room, and unknown settings.

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

OR was not estimable because of small sample size and corresponding complete separation of persons into AD prescriptions that were either all "justified" or all "unjustified".

Other chronic conditions being treated at time of incident AD prescription.

Other prescription medications taken at time of incident AD prescription.

Number 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. 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.

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. 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.

Bereavement and adjustment disorder diagnoses can be quite severe and at times difficult to distinguish from major depressive disorder. 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. 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.

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. The antidepressant treatment of subthreshold depression (depressive disorder, not otherwise specified), which is distinct from adjustment disorders, is relatively under-studied. In the elderly, subthreshold depression is more common than major depression, and antidepressants may be helpful for patients with subthreshold depression and severe mood symptoms. However, we were not able to distinguish between patients with severe vs milder subthreshold depression that may not respond well to antidepressant treatment.

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. The challenges associated with managing a large number of co-occurring chronic health conditions during brief office visits may also be an important factor—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 undertreatment 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.

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

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