Published in final edited form as:
J Am Geriatr Soc. 2011 August ; 59(8): 1412–1420. doi:10.1111/j.1532-5415.2011.03522.x.

Potential Underuse, Overuse and Inappropriate Use of Antidepressants in Older Veteran Nursing Home Patients

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Abstract

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Author Contributions: Dr. Hanlon conceived of and designed the study, acquired the data, supervised the analyses and interpreted of the data, and drafted the initial manuscript. Mr. Wang preformed the analyses and assisted in the interpretation of data and preparation of the manuscript. Dr. Castle served as an expert on the creation and use of MDS scales as important covariate and contributed to the design, analyses, and interpretation of data for this study and assisted in preparing the manuscript. Drs. Handler, Semla, Pugh, Berlowitz and Dysken served on the expert panel that created the explicit criteria for evaluating potentially inappropriate antidepressant use and all contributed to the design, analyses, and interpretation of data for this study and assisted in preparing the manuscript. Dr. Stone assisted in the development of the study design, and analytic plan, oversaw the statistical analyses preformed by Mr. Wang and contributed to the interpretation of data for this study and assisted in preparing the manuscript.

Presentations: International Conference on Pharmacoepidemiology & Therapeutic Risk Management, August 17, 2009, Providence, RI and Gerontological Society of America Annual Meeting, November 19, 2009, Atlanta, GA

Conflict of Interest Disclosures: None reported

Objective—To examine prevalence and patient/site level factors associated with potential underuse, overuse and inappropriate use of antidepressants in older Veterans Affairs (VA) Community Living Center (CLC) patients.

Design—Longitudinal study.

Settings—133 VA CLCs.

Patients—3,692 veterans 65 years or older admitted between 1/1/04-6/3/05 with long stays (90+days).

Measurements—Prevalence of potential underuse, inappropriate use and overuse of antidepressants in patients with and without depression (as documented by International Classification of Diseases-9 Clinical Modification codes or Depression Rating Scale).

Results—Selective serotonin reuptake inhibitors were the most commonly prescribed antidepressant. Of the 877 patients with depression, 25.4% did not receive an antidepressant suggesting potential underuse. Among depressed patients who received antidepressants, 43.1% had potential inappropriate use due primarily to problems seen with drug-drug and drug-disease interactions. Of the 2,815 patients who did not have depression, 1190 (42.3%) were prescribed one or more antidepressants; of these only 48 of 1190 (4.0%) had a FDA-approved labeled indication-suggesting potential overuse. Overall only 17.6% of antidepressant use was appropriate (324/1844). The only consistent patient factor associated with potential underuse and overuse use was taking an antipsychotic without evidence of schizophrenia (underuse-adjusted relative risk ratio [ARRR] 0.56, 95% confidence interval [CI] 0.33-0.94; overuse-Adjusted Odds Ratio 1.52, 95% CI 1.21-1.91). Both having moderate/severe pain (ARRR 1.54, 95% CI 1.08-2.20) and the prescribing of an anxiolytic/hypnotic (ARR 1.33, 95% CI 1.02-1.74) increased the risk of potential inappropriate antidepressant use.

Conclusion—Potential problems with the use of antidepressants were frequently observed in older US veteran CLC patients. Future studies are needed to examine the true risks and benefits of antidepressant use in CLC and non-VA nursing homes.

Keywords

aged; nursing homes; depression; pharmacoepidemiology

INTRODUCTION

Depression is common among older nursing home patients.[1] One seminal study reported a 12% prevalence rate for major depression using the American Psychiatric Association's Diagnostic and Statistical Manual of Psychiatric Disorders (DSM-III-R) criteria in older patients in a 1,100 bed nursing home.[2,3] In addition, minor, subsyndromal, or subthreshold depression was seen in an additional 30% of these older nursing home patients.[3] In contrast, a more recent national study of nursing homes found that only 20% of older patients had a diagnosis of depression indicated via their quarterly Minimum Data Set (MDS) assessment.[4] Depression is important to treat in older nursing home patients and is commonly associated with morbidity (e.g., hospitalization, functional status decline) and mortality.[1]

Depression in nursing homes can be treated with one or a combination of the following modes of treatment: electroconvulsive therapy, psychological/psychiatric intervention, and antidepressant therapy. [1] Antidepressant therapy is the most common treatment in nursing home patients. [1] Moreover, the prevalence of antidepressant use in US nursing home patients has increased over 100% from 21.9% in 1996 to 47.5% in 2006.[5] This prevalence rate of 47.5% is consistent with the national rate of antidepressant use in Veterans Affairs

(VA) Community Living Centers (CLC). [6] Despite these high rates, data are conflicting regarding possible undertreatment of depression in nursing home residents. Recent national information shows that less than 5% of nursing home patients with symptoms of depression determined via the quarterly MDS assessments were untreated with an antidepressant. [7] In contrast, a 2000 study of Ohio nursing home patients found that 23% of those with a depression diagnosis did not receive an antidepressant. [8] Concomitantly, there is limited information that suggests potential overuse and inappropriate use of antidepressants may be problematic in older nursing home patients. [9,10] Given this background, the objectives of this study are to estimate the prevalence and patient/site level factors associated with potential underuse, inappropriate use and overuse of antidepressants in older VA CLC patients.

METHODS

Study Design, Setting, Data Sources and Sample

This was a longitudinal study of 3,692 long-stay (90 days or more) patients age 65 or older admitted to any one of the 133 VA CLCs located in the US between January 1, 2004 and June 30, 2005. The mission of these CLCs (previously called Nursing Home Care Units), with varying bed sizes, is to provide compassionate care to eligible veterans with sufficient functional impairment to require this level of service. Veterans with chronic stable conditions including dementia, those requiring rehabilitation or short term specialized services such as respite or intravenous therapy, or those who need inpatient hospice can receive this type of care in the VA CLCs. These CLCs are located in 21 regions across the US called Veterans Integrated Services Networks (VISNs). The development of a merged database that included Minimum Data Set (MDS), and medication dispensing information from the Pharmacy Benefits Management Services (PBM) used for this study was recently described. [6] Briefly, all veterans receiving care in a VA CLC were evaluated by CLC staff using the MDS 2.0. MDS version 2.0 is a reliable standardized tool to identify the functional, psychological and health status needs of residents, and to evaluate the quality of care for these residents. [11] All MDS data were collected via resident interviews, staff interviews and reviews of medical records. For all CLC patients, the MDS was completed at admission (within 14 days of admission), and quarterly thereafter (within 90 days of previous evaluation) and at the time of any significant change in status (e.g., major change in cognitive function or functional status decline). The VA PBM provided all prescription data for the defined study cohort. These data included the following information for each drug dispensed: 1) start date; 2) drug name; 3) strength; 4) dosage form; 5) directions for use; 6) VA therapeutic class; and 7) amount dispensed. To the merged database mentioned previously, we also linked International Classification of Diseases-9 (ICD-9) Clinical Modification codes for inpatient and outpatient diagnoses in the previous year from the VA National Patient Care Database (NPCD) records. This final merged database, which was prepared by using encrypted identifiers that were consistent across the three individual databases, was used to conduct the present analyses.

The sample was first stratified by depression status determined by ICD-9 codes. Specifically, we identified any hospitalization or outpatient visit to a VA in the previous year where depression was addressed and noted using ICD-9 codes (296.2, 296.3, 298.0x, 300.4x, 309.1x, 311.xx, 301.12, 309.0x). [12,13] This approach was chosen because it was utilized in two previous VA studies examining the quality of depression care in outpatients and a previous study using ICD-9 codes to identify depression found acceptable specificity (88%) but lower sensitivity (52%). [12-14] Thus while this approach may underestimate the "true rate" of depression it is likely to be more accurate than just using the listing of depression on a patients problem list or in Section I of the MDS entitled "Disease Diagnoses".[11] To assure that we did not misclassify those who did not have VA health

service utilization in the previous year and to improve sensitivity, we also included those with a high likelihood of depression on admission (MDS Depression Rating Scale [DRS] scores>3).[15] The DRS is a summary of seven symptoms detected by nursing home staff that capture verbal and non-verbal indicators of depressed mood and has been shown to be a reliable (sensitivity 91% and specificity 69% with a psychiatrist diagnosis) and valid measure of depression among nursing home residents when compared to other depression scales and a psychiatrist diagnosis. [15] A total of 877 patients were included in the depression sample (i.e., 796 by ICD-9 codes and 181 by DRS >3 only) and the remaining 2,815 had no documented depression. This study was approved by the Pittsburgh VA Institutional Review Board and Research and Development Committees.

Main Outcome Measures

Antidepressants on the VA national formulary in 2004/2005 (VA Classes CN 601, CN609, CN802) included those in the following 4 discrete groups: 1) tricyclic antidepressants (TCA-amitriptyline, desipramine, doxepin, nortriptyline), 2) selective serotonin reuptake inhibitors (SSRI-paroxetine, sertraline, fluoxetine, citalopram), 3) serotonin-norepinephrine reuptake inhibitors (SNRI-venlafaxine), and 4) other antidepressants (i.e., trazodone, mirtazapine, methylphenidate, bupropion). Methylphenidate was included as it is frequently used to treat depression in the elderly.

To operationally define potential underuse and inappropriate use of antidepressants in the depression group, we consulted two specific authoritative sources: 1) a guideline from the American Medical Directors Association (AMDA) and 2) quality of care indicators from the Centers for Medicare and Medicaid Services (CMS) for appropriate use of antidepressants for treating depression in nursing homes.[16,17] We also turned to the Veterans Health Administration and Department of Defense (VHA/DOD) guideline for treating adults with depression and to another from England that focused on treating older adults with depression in the primary care setting. [18,19] Using a previously published and validated approach, we created explicit criteria for potentially inappropriate use that was reviewed, edited and agreed upon by our expert panel consisting of a nurse pharmacoepidemiology researcher (MJP), a geriatric clinical pharmacist (TPS), two geriatricians (SMH, DRB) and a geriatric psychiatrist/psychopharmacologist (MWD).[20] Potential inappropriate use in those in the depression group was ascertained by applying these explicit criteria to determine if there were one or more problems in five specific quality areas: 1) selection (e.g., choosing an antidepressant such as amitriptyline which has anticholinergic/orthostasis effects); 2) maintenance dosage exceeding or below minimum effective dosage (i.e., highest daily dose during the 90 day period to account for the time needed to “start low and go slow” or titrate new antidepressants); 3) clinically important drug-drug interactions; 4) clinically important drug-disease interactions; and 5) therapeutic duplication (i.e. use of two or more TCAs, SSRIs, or SNRIs concomitantly) (**see Appendix I).** Potential underuse in the depressed group was noted by the lack of an order for an antidepressant during the 90 day follow-up period. The rational for this operational definition is that many experts recommend antidepressant treatment for a period of time ranging from one to three years to reduce the likelihood of major depression reoccurrence and relapse in older depressed patients. [17,18] All persons in the depressed group taking an antidepressant that were not considered potentially inappropriate were included in the appropriate use category.

To operationally define potential overuse in those without depression, we consulted two specific authoritative sources: 1) a joint statement of the members of the Long Term Care Professional Leadership Council (LTCPLC) and 2) the Food and Drug Administration (FDA) web site. [21,22] Potential overuse of antidepressant use in euthymic patients was operationally defined as lack of a FDA-approved labeled indication (**see footnote of Table 2**

for further details). [21,22] We used ICD-9 codes to determine these indications using previously established methods. [23] Appropriate use of antidepressants in those without depression was defined as any use not deemed to be overuse.

Independent Variables

Based on previous literature, our independent variables included demographic characteristics, health status factors and psychiatric/neurological problems.[10, 23,24] Using data from the admission MDS, categorical variables were created for age (65-74, 75-84, 85+), race (black, white, or other), gender (male or female) and educational level (less than high school, high school, greater than high school).

Regarding health status factors, we created a continuous variable for activities of daily living (ADL) dependencies from the admission MDS, which had a range from 0 to 20 points and identifies the amount of assistance needed from staff for five activities (bathing, dressing, grooming, toileting and eating). [25] We created a continuous variable for the Charlson comorbidity index based on the methods of Deyo which creates a score (range 0-34) that is calculated based on the presence of 18 chronic conditions documented in the electronic medical record via ICD-9-codes. [26,27] We also quantified the number of prescribed drugs at admission (excluding those specified below). We also created a dichotomous variable for physical restraint use as noted on the MDS. In addition, we examined dichotomous variables for individual conditions noted on the admission MDS (i.e., cancer, chronic obstructive pulmonary disease [COPD], diabetes, arteriosclerotic heart disease, arthritis, hip fracture history, hypertension, and osteoporosis).

Psychiatric/neurological problem variables were created using ICD-9 codes from VA hospitalizations or outpatient visits in the previous year. Specifically, we created dichotomous variables for cerebrovascular accident (CVA), seizure disorder, Parkinson's disease, any neuropathic pain, bipolar disease, posttraumatic stress disorder (PTSD), other anxiety disorder, Alzheimer's, vascular or other dementia.[27] To supplement these psychiatric/neurological problems, data from the admission MDS evaluation were also used to create a dichotomous variables for behavioral problems and moderate/severe pain, and a categorical variable for cognitive function (i.e., Cognitive Performance Score [CPS] –intact, mild/moderate, severe). [28, 29] Finally, from PBM data we created a dichotomous variable denoting use of individual medication classes (i.e., antipsychotics [CN701 and 709] in those patients without schizophrenia, anxiolytic/hypnotics [in CN302 and 309], acetylcholinesterase inhibitors [ACHEI] and memantine [in CN900]). We also included two dichotomous variables (i.e., bed size and geographic region) to control for potentially confounding site factors. [5]

Statistical Analyses

Descriptive statistics summarized independent variables and study outcomes. To include the approximately 3% of patients with missing data on education or cognitive performance status in the analyses, we created dummy variables for a “missing” category. By depression group status, we summarized the number of patients who were prescribed individual classes of antidepressants (i.e., TCAs, SSRIs, SNRIs, others) and types of potentially inappropriate antidepressant use by problem type. We conducted a multinomial regression analysis to identify patient factors associated with (i) underuse or inappropriate use versus appropriate use (reference group) of antidepressants among patients with depression. We conducted a multivariable logistic regression analysis in those without depression by first removing from the sample those with labeled (“ appropriate use”), and compared overuse with the reference group no use of antidepressants.[30] We used a backward selection approach (alpha=0.10) to identify those health status factors and psychiatric/neurological conditions to be added to the

patient demographic characteristics and site factors in the final models. We report estimated adjusted relative risk ratios (RRRs) and 95% confidence intervals (CIs); robust standard errors adjusted for clustering by CLC. Multi-parameter Wald tests quantified the association of each outcome with categorical variables with more than two levels. Statistical analyses were performed using SAS® (version 9; Cary, NC) and Stata® (College Station, TX) software.

RESULTS

Table 1. compares the characteristics of those CLC patients who were depressed (n=877) with those who were not (n=2815). The groups were similar in regards to most characteristics. Whites and those with more comorbidities were more likely to be in the depressed than the non depressed group. Those in the non depressed group had more ADL dependencies and more severe cognitive impairment than those in the depressed group. The most common medication class taken by those without schizophrenia in both groups was antipsychotics.

Table 2. summarizes antidepressant use overall and by specific classes for patients with and without depression. The most common antidepressant class used by both groups was SSRIs. No use of monoamine oxidase inhibitors [MAOI] was documented. Of the 877 patients with depression, only 74.6% (n=654) took an antidepressant which suggests potential underuse was evident in 25.4% (n=223) of these patients. Among patients without depression, 42.3% took an antidepressant which suggests potential overuse as only 48 of these 1190 taking an antidepressant had evidence of a FDA approved labeled indication. Thus only 4.0% of antidepressant use among those without depression was appropriate.

Table 3. summarizes potential inappropriate drug use among patients with depression. Nearly six in ten patients' with depression (n=378) who received an antidepressant had one or more prescribing problems. Thus appropriate antidepressant use was seen in 276/654 (42.5%). Drug-drug and drug-disease interactions were the most common problems whereas therapeutic duplication and selection were the least frequent prescribing problems. By combining appropriate use regardless of depression group (48 + 276/1190 +654=17.6%), less than 2 in 10 antidepressant prescriptions were not problematic.

Table 4. summarizes the results of the multivariable multinomial logistic regression models for potential underuse, and inappropriate use of antidepressant versus appropriate use among those who were depressed. Factors significantly associated with a reduced risk of potential underuse in patients with depression included polypharmacy (i.e., taking > 5 medications), having a history of cancer, or taking an antipsychotic without evidence of schizophrenia; the only factor associated with an increased risk of potential underuse were having ADL dependencies. Regarding potential inappropriate use, blacks and those with cancer were significantly less likely to have this problem. Those who had with moderate to severe pain and those taking an anxiolytic/hypnotic were at significantly increase risk of inappropriate use (rather than appropriate use).

Table 5. summarizes the results of the multivariable logistic regression models for potential overuse versus no antidepressant use among those who were not depressed. Patients aged 85 and older had a significantly reduced risk of overuse, and the risk of overuse decreased with increasing comorbidity index score. Overuse was significantly more likely in those with mild/moderate cognitive impairment, polypharmacy (i.e., taking > 5 medications), CVA, other anxiety, taking an antipsychotic without evidence of schizophrenia.

DISCUSSION

In this study, nearly 50% of all older long stay veteran nursing home patients received an antidepressant which is consistent with the rate of nearly 48% of non-VA nursing home residents taking an antidepressant.[6] That depression was found in nearly 25% of patients is also consistent with previously published studies. [3,10] However, we found that nearly 25% of those with depression did not receive an antidepressant suggesting potential underuse. This rate is considerably less than the 45% of nursing home residents with MDS-reported depression who were found to be untreated with an antidepressant in a multi-state US sample.[10] However, it is consistent with the rates from more recent studies that still show that between 21-34% of nursing home patients with depression do not receive an antidepressant.[8,31] Our multivariable analyses of factors associated with underuse of antidepressants suggest that prescribers may be more cautious in those with greater ADL dependencies. This may reflect appropriate concern about the likelihood of antidepressant adverse effects is greater than the potential benefits in these vulnerable patients. Hopefully the rate of antidepressant underuse will be further reduced by better detection and monitoring of depression by the valid, reliable, and frequently used PHQ-9, which is replacing DRS in MDS version 3.0, and is scheduled to be implemented in non VA CLCs in the fall of 2010 and VA CLCs in early 2011.[32]

Among persons who were depressed and receiving an antidepressant, over 40% had evidence of potentially inappropriate use with one or more prescribing problems. The least frequent problems were therapeutic duplication and selection. Medication selection was potentially problematic primarily because TCAs are notorious for their orthostatic hypotension and anticholinergic effects which can increase the risk of falls and cognitive impairment in older adults. [16-18] Under- and over-dosing problems were seen in nearly 9% of depressed patients. We found that underdosing was most common with sertraline and trazodone, and venlafaxine. Trazodone may have been misclassified as underdosed because they may have been prescribed to manage sleep and weight loss, despite little evidence-based data to support these indications.[33] Drug –drug interactions were seen in one in four antidepressant users who were depressed. Two of the three most common drug–drug interaction was the use of multiple drugs that increase serotonin (and thus increase the risk of serotonin syndrome); this would include the use of multiple antidepressants regardless of therapeutic intent.[34] Additionally, the use of paroxetine or fluoxetine or bupropion which are potent inhibitors of CY2D6 hepatic enzymes, can decrease the clearance of important substrate drugs such as metoprolol, and other antidepressants (i.e., TCA, venlafaxine) that could result in preventable adverse drug events. [35] Drug-disease interactions were just as common in this patient group and frequently involved the prescribing of antidepressants in patients with a history of a fall. It is important to note that the risk of falls with SSRIs is the same as that of tricyclic antidepressants.[36] The only potentially modifiable risk factors associated with potential inappropriate prescribing of antidepressants in this study were patients having moderate/severe pain and the prescribing of an anxiolytic/hypnotic.

To the best of our knowledge this is one of the first studies to examine potential overuse of antidepressants in nursing home patients. In patients without depression, only a small number of cases (n= 48 of 1190) had a FDA approved labeled indication for the antidepressants. One explanation is that a recent study showed that US physicians have limited knowledge of which indications are FDA approved versus being off-label. [37] Of potential concern is the recent report that five antidepressants are among the top 25 drugs used off label with inadequate efficacy evidence.[38] One factor associated with potential overuse was anxiety for which there is evidence that specific antidepressants classes (and not just individual agents) may be effective and this use is supported by various nursing

home organizations.[21] Finally, it is notable that co-prescribing of antipsychotics (in those without schizophrenia) was associated with an increased the risk of antidepressant overuse.

So what are the implications of these results? One is that that there are prescribing quality issues involving antidepressants that clinicians should be aware of in VA CLCs. It is likely that similar prescribing issues are also occurring at similar levels in non-VA nursing homes given their equally high rates of antidepressant use. [5] What is not clear is the effect that this antidepressant prescribing quality has on nursing home patient outcomes. Nonetheless, it is clinically sensible to consider ways to address this quality prescribing problem. Three recently published articles describe successful approaches used in randomized controlled trials (i.e., academic detailing, pharmacist interventions, multidisciplinary teamwork, computerized decision support systems) to improve psychotropic prescribing for nursing home patients.[39-41] It is interesting to note though that none of these studies examined changing the quality of antidepressant prescribing. In part to address this issue, the VA is currently launching a variety of initiatives including increasing the availability and integration of psychologists and psychiatrists services in CLCs as well as increasing staff education. Similar initiatives in non-VA nursing homes will be also be necessary to address the stigma associated with diagnosing and treating psychiatric problems in nursing homes and historically low reimbursement rates for non-psychiatrist providers.

This study has a number of potential limitations. There is potential misclassification because depression was not diagnosed by an independent research psychiatrist, but according to ICD-9 codes along with severity of depressive symptoms based on MDS data. However, examining alternative classifications of depression including shortening the lookback period for ICD-9 codes to 6 months or using the listing of depression in the MDS did not substantially change the depression sample. The application of explicit criteria to evaluate the quality of prescribing is limited because they can not take into account individual patient characteristics. It is also important to note that the rate of potential underuse may be somewhat inflated because patients may have been receiving effective non-pharmacological treatment that is not captured by this or other studies. We also applied some explicit guideline criteria published in 2006 or later to data from 2004-2005 which does not allow for prior dissemination of this information to providers. Finally it is unclear what the generalizability of the current findings are to non-VA nursing home settings given that the majority of their patients are older females and the use of some antidepressant medications may be different in VA due to their use of a national formulary.

Despite these potential limitations, we conclude that potential problems with the use of antidepressants were observed frequently in older US veteran nursing home patients. Future studies are needed to examine the true risks and benefits of antidepressant use in nursing homes.

Acknowledgments

Sponsors' Roles: The organizations that funded this study had no role in the design, methods, analysis, or preparation of this paper.

Funding: This study was supported by National Institute of Aging grants (P30AG024827, T32 AG021885, K07AG033174, R01AG034056, R56AG027017, 3U01 AG012553), a National Institute of Mental Health grant (R34 MH082682), a National Institute of Nursing Research grant (R01 NR010135), Agency for Healthcare Research and Quality grants (R01 HS017695, R01 HS018721, K12 HS019461) and a VA Health Services Research grant (IIR-06-062).

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	Yes*	No	Yes*	No	Yes*	No	Yes*	No	Yes	No	Yes	No	Yes	Nos*	Yes	Non	Y N	
Employment or Affiliation		X		X		X		X		X		X		X		X		X
Grants/Funds		X		X		X		X		X		X		X		X		X
Honoraria		X		X		X		X		X		X		X		X		X
Speaker Forum		X		X		X		X		X		X		X		X		X
Consultant		X		X		X		X		X		X		X		X		X
Stocks		X		X		X		X		X		X		X		X		X
Royalties		X		X		X		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X		X		X		X
Board Member		X		X		X		X		X		X		X		X		X
Patents		X		X		X		X		X		X		X		X		X
Personal Relationship		X		X		X		X		X		X		X		X		X

* For “yes”, provide a brief explanation:

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Table 1

Patient and Facility Characteristics for Older Depressed and Non-Depressed Veterans in Community Living Centers

Factor	Depressed (n=877) n (%)	Not Depressed (n=2,815) N (%)	p-value
Demographics			
Age			
65-74	265 (30.22)	869 (30.87)	
75-84	468 (53.36)	1,458 (51.79)	0.69
85+	144 (16.42)	488 (17.34)	
Race			
White	760 (86.66)	2,221 (78.90)	
Black	87 (9.92)	412 (14.64)	<0.01
Other	30 (3.42)	182 (6.47)	
Female gender	37 (4.22)	66 (2.34)	<0.01
Education			
Below high school	253 (28.85)	859 (30.52)	
High school	404 (46.07)	1,312 (47.68)	0.51
Above high school	208 (23.72)	614 (21.81)	
Not Assessed	12 (1.37)	30 (1.07)	
Health Status			
ADL dependence (Mean ±SD)	8.58 (6.31)	9.27 (6.55)	<0.01
Comorbidity index (Mean ±SD)	2.95 (2.29)	2.62 (2.21)	<0.01
Other Medications			
0-5	243 (27.71)	744 (26.43)	0.31
6-10	258 (29.42)	786 (27.92)	
11-15	158 (18.02)	587 (20.85)	
16+	218 (24.86)	698 (24.80)	
COPD	259 (29.53)	747 (26.54)	0.08
Diabetes	309 (35.23)	1,077(38.26)	0.11
Cancer	162(18.47)	472(16.77)	0.24
Arthritis	255(29.08)	756(26.86)	0.20
ASHD	233 (26.57)	656 (23.30)	0.05
Hip fracture	43 (4.90)	144 (5.12)	0.80
Hypertension	588 (67.05)	1,879 (66.75)	0.87
Osteoporosis	58 (6.61)	160 (5.68)	0.31
Neurological/Psychiatric Problems			
Cerebrovascular accident	152 (17.33)	507 (18.01)	0.65
Seizure disorder	52 (5.93)	146 (5.19)	0.39
Parkinson's	80 (9.12)	146 (5.19)	<0.01
Any neuropathic pain	266 (30.33)	609 (21.63)	<0.01
Bipolar disease	22 (2.51)	64 (2.27)	0.69
Schizophrenia	86 (9.81)	283 (10.05)	0.83

Factor	Depressed (n=877) n (%)	Not Depressed (n=2,815) N (%)	p-value
PTSD	124 (14.14)	121 (4.30)	<0.01
Other Anxiety	148 (16.88)	133 (4.72)	<0.01
Alzheimer's	106 (12.09)	286 (10.16)	0.11
Vascular dementia	89 (10.15)	150 (5.33)	<0.01
Other dementia	336 (38.31)	753 (26.75)	<0.01
Behavior problem	171 (19.50)	347 (12.33)	<0.01
Moderate/severe pain	223 (25.43)	645 (22.91)	0.13
Cognitive function			
Intact	442 (50.40)	1,497 (53.18)	
Mild/Moderate	325 (37.06)	880 (31.26)	<0.01
Severe	90 (10.26)	384 (13.64)	
Not assessed	20 (2.28)	54 (1.92)	
Use of antipsychotic in those without schizophrenia	214 (24.40)	512 (18.19)	<0.01
Use of anxiolytic/hypnotic	68 (7.75)	163 (5.79)	0.04
Use of ACHEI	156 (17.79)	363 (12.90)	<0.01
Use of Memantine	35 (3.99)	78 (2.77)	0.07
Site Level Indicators			
Bed Size			
Small (<60)	126 (14.37)	384 (13.64)	0.81
Medium (60-120)	416 (47.43)	1,328 (47.18)	
Large (>120)	335 (38.20)	488 (39.18)	
Region			
North East	221 (25.20)	695 (24.69)	0.30
Midwest	191 (21.78)	556 (19.75)	
South	331 (37.74)	1,158 (41.14)	
West	134 (15.28)	406 (14.42)	

Abbreviations: ACHEI= acetylcholinesterase inhibitors; ADL= activities of daily living; ASHD=arteriosclerotic heart disease; COPD=chronic obstructive pulmonary disease; PTSD=post traumatic stress disorder

Table 2

Antidepressant Medication Use Among Older Depressed and Non-Depressed Veteran Community Living Center Patients

Variables	Depressed (n=877) N (%)	Not Depressed (n=2815) N (%)	p-value
Any Antidepressant Use	654 (74.6)*	1190 (42.3)†	<0.01
Antidepressant Class Use*			
SSRI	494 (56.4)	754 (26.8)	<0.01
SNRI	44 (5.0)	42 (1.5)	<0.01
TCA	32 (3.7)	87 (3.1)	0.30
Other	290 (33.1)	546 (19.4)	<0.01

Abbreviations: SNRI=serotonin-norepinephrine reuptake inhibitor; SSRI=selective serotonin reuptake inhibitor; TCA=tricyclic antidepressants

*Use of specific classes adds to greater than 74.6% since some patients took more than one agent concomitantly.

†Only 48 of 1190 (4.0%) receiving an antidepressants had a FDA approved labeled indication (venlafaxine for panic disorder, generalized anxiety disorder, and social phobia; doxepin for moderate pruritus due to atopic dermatitis or lichen simplex chronicus; bupropion for smoking cessation; methylphenidate for narcolepsy or attention deficit disorder; escitalopram for generalized anxiety disorder; fluvoxamine-social phobia or obsessive compulsive disorder; fluoxetine for obsessive compulsive disorder, or panic disorder; duloxetine for diabetic peripheral neuropathy; paroxetine for generalized anxiety disorder or obsessive-compulsive disorder or panic disorder or posttraumatic stress disorder or social phobia; sertraline for obsessive compulsive disorder or panic disorder or posttraumatic

Table 3

Potentially Inappropriate Antidepressant Use Among Those with Depression By Type of Problem and Overall (n=877)

Type Of Problem*	n (%)	Most Common Drugs Involved (n)
Selection	32 (3.7)	Amitriptyline (12)
		Nortriptyline (11)
		Doxepin (7)
Dosage	77 (8.8)	Trazodone (28)
		Sertraline (16)
		Venlafaxine (10)
Drug-Drug Interaction	227 (25.9)	SSRI and Trazodone (73)
		Fluoxetine or Paroxetine and Metoprolol (41)
		Mirtazapine and SSRI (15)
Drug-Disease Interaction	223 (25.4)	SSRI and Falls (73)
		Venlafaxine and Hypertension (22)
		TCA and Constipation (8)
Therapeutic Duplication	10 (1.1)	SSRI and SSRI (10)
Any Problem	378 (43.1)	

Abbreviations: TCA=tricyclic antidepressants, SSRI=selective serotonin reuptake inhibitor

*Adds to more than 43.1% because some patients had more than one type of problem

Table 4

Factors Associated with Underuse (n=223), and Inappropriate Use (n=378) Compared to Appropriate Use (reference group; n=276) of Antidepressants in Those With Depression

Factors	Underuse (n=223)		Inappropriate Use (n=378)	
Demographics	**Adj. RRR**	**95% CI**	**Adj. RRR**	**95% CI**
Age				
65-74	1.00	reference	1.00	reference
75-84	0.90	0.59-1.39	1.27	0.87-1.84
85+	0.92	0.52-1.62	1.29	0.79-2.11
Race				
White	1.00	reference	1.00	reference
Black	0.85	0.49-1.49	0.48	0.30-0.76*
Other	1.21	0.48-3.01	0.86	0.33-2.25
Female gender	1.55	0.68-3.53	0.67	0.28-1.61
Education				
Below high School	1.00	reference	1.00	reference
High school	0.84	0.55-1.28	0.89	0.59-1.33
Above high School	1.02	0.58-1.79	0.90	0.57-1.44
Not Assessed	1.15	0.27-4.81	1.23	0.26-5.83
Health Status	**Adj. RRR**	**95% CI**	**Adj. RRR**	**95% CI**
Activities of daily living score (per unit increase)	1.05	1.02-1.09*	1.02	0.99-1.04
Other Medications				
0-5	1.00	reference	1.00	Reference
6-10	0.57	0.36-0.91*	1.39	0.88-2.19
11-15	0.40	0.23-0.73*	1.58	0.94-2.66
16+	0.46	0.28-0.76*	1.79	1.09-2.94
Cancer	0.52	0.33-0.81*	0.62	0.41-0.94*
Neurological/Psychiatric Problems	**Adj. RRR**	**95% CI**	**Adj. RRR**	**95% CI**
Cerebrovascular accident	0.63	0.37-1.08	1.33	0.83-2.15
Behavior problem	1.51	0.91-2.49	0.69	0.44-1.08
Moderate/severe pain	0.79	0.51-1.21	1.54	1.08-2.20*
Use of anxiolytic/hypnotic	1.08	0.81-1.44	1.33	1.02-1.74*
Use of antipsychotic in those without schizophrenia	0.56	0.33-0.94*	0.90	0.62-1.30

Factors	**Underuse (n=223)**		**Inappropriate Use (n=378)**	
Site Level Indicators	**Adj. RRR**	**95% CI**	**Adj. RRR**	**95% CI**
Bed Size				
Small (<60)	1.00	Reference	1.00	reference
Medium (60-120)	0.90	0.49-1.66	0.97	0.56-1.66
Large (>120)	0.59	0.32-1.11	1.01	0.60-1.71
Region				
North East	1.00	Reference	1.00	reference
Midwest	0.76	0.44-1.29	0.78	0.47-1.31
South	0.61	0.38-0.99	1.03	0.66-1.60
West	0.77	0.43-1.37	1.28	0.74-2.19

Wald chi2(46)=147.57; Prob > chi2=0.0000; Log pseudolikelihood = -871.022; Pseudo R2=0.076

Abbreviations: CI=confidence interval; RRR=relative risk ratio

* p<0.05; for categorical variables, contrasts are noted as being statistically significant only when the overall effect in the equation is significant.

Table 5

Factors Associated with Overuse (n=1142) Compared to No Use (reference group; n=1625) in Those Without Depression*

Factors		Over Use (n=1142)
Demographics	**Adj. OR**	**95% CI**
Age		
65-74	1.00	Reference
75-84	0.89	0.73- 1.09
85+	0.70	0.57-0.87†
Race		
White	1.00	Reference
Black	0.82	0.65-1.03
Other	0.69	0.40-1.19
Female gender	1.28	0.81-2.01
Education		
Below high school	1.00	Reference
High school	1.08	0.88-1.33
Above high school	1.32	1.05-1.68
Not Assessed	0.63	0.27-1.43

Factors	Over Use (n=1142)	
Health Status	**Adj. OR**	**95% CI**
Comorbidity index	0.92	0.88-0.96†
Other Medications		
0-5	1.00	Reference
6-10	1.88	1.48-2.38†
11-15	2.50	1.93-3.24†
16+	3.50	2.79-4.38†
Cancer	1.27	0.99-1.63
COPD	1.21	1.00- 1.47
ASHD	1.20	0.96-1.50

Factors	Over Use (n=1142)	
Neurological/Psychiatric Problems	**Adj. OR**	**95% CI**
Cerebrovascular accident	1.50	1.20-1.87†
Any neuropathic pain	1.17	0.98-1.40
PTSD	1.09	0.67-1.77
Other Anxiety	1.48	1.02-2.14†
Cognitive function		

Factors	Over Use (n=1142)	
Neurological/Psychiatric Problems	**Adj. OR**	**95% CI**
Intact	1.00	Reference
Mild/Moderate	1.24	1.02-1.50†
Severe	0.96	0.72-1.27
Not assessed	1.75	0.97-3.16
Use of antipsychotic in those without schizophrenia	1.52	1.21-1.91†

Factors	Over Use (n=1142)	
Site Level Indicators	**Adj. OR**	**95% CI**
Bed Size		
Small (<60)	1.00	Reference
Medium (60-120)	0.84	0.60-1.18
Large (>120)	1.02	0.72-1.45
Region		
North East	1.00	Reference
Midwest	1.13	0.77-1.65
South	1.16	0.80-1.69
West	1.03	0.69-1.53

Wald chi2(28)=251.75; Prob > chi2=0.000; Log pseudolikelihood = -1761.431; Pseudo R2 =0.0612

Abbreviations: ACHEI= acetylcholinesterase inhibitors; ADL= activities of daily living; ASHD=arteriosclerotic heart disease; CI=confidence interval; COPD=chronic obstructive pulmonary disease; CPS=cognitive performance scale; HS=high school; PTSD=post traumatic stress disorder, OR=odds ratio

*those with appropriate on-label antidepressant use (n=48) excluded from the model

†p<0.05

Appendix I

Explicit Criteria for Antidepressant Use in the Elderly Nursing Home Patient

Class/Agent	Selection	Minimum/ Maximum Daily Dosage (mg/ day)	Drug-Drug Interaction to Avoid	Drug-Disease Interactions*	Therapeutic Duplication
Other Antidepressants					
Bupropion	Recommended	150-300	CYP2D6 substrates†	Seizure disorder	N/A
Mirtazapine	Recommended	15-45 (30 if estimated creatinine clearance <30 ml/min)	Clonidine; Other drugs that ↑ serotonin‡	None	N/A
Trazodone	Recommended	25-150	Other drugs that ↑ serotonin‡	None	N/A
Methylphenidate	Recommended	5-20	MAOI	Hypertension, Seizure disorder, arrhythmias, long QT interval”	Other amphetamines and modafinil
Serotonin-Norepinephrine Reuptake Inhibitor [SNRI]					
Venlafaxine	Recommended	50-225	Other drugs that ↑ serotonin‡	Hypertension	N/A
Selective Serotonin Reuptake Inhibitors [SSRI]					
Citalopram,	Recommended	10-40	Other drugs that ↑ serotonin‡	Falls	Concurrent SSRI
Fluoxetine	Recommended	10-40	CYP2D6 substrates†, Other drugs that ↑ serotonin‡, phenytoin	Falls	Same as above
Paroxetine	Recommended	10-40	Anticholinergics‡,CYP2D6 substrates†; Other drugs that ↑ serotonin‡	Falls	Same as above
Sertraline	Recommended	50-200	Other drugs that ↑ serotonin‡	Falls	Same as above
Tricyclic Antidepressants [TCA]					
Amitriptyline	Not recommended[1]	10-75	Anticholinergic§ bupropion, clonidine, Other drugs that ↑ serotonin‡	Benign prostatic hypertrophy” constipation, dementia, falls, heart block, orthostatic hypotension,	Concurrent TCA
Desipramine	Recommended	10-75	Same as above	Same as above	Same as above
Doxepin	Not recommended	10-75	Same as above	Same as above	Same as above
Nortriptyline	Recommended	10-75	Same as above	Same as above	Same as above

[*] Diseases were determined from admission Minimum Data Set (v2.0) assessments and through the use of specific ICD-9 codes. While this approach may not be highly sensitive it is likely to be highly specific.

[†] CYP2D6 substrates (i.e., metoprolol, tricyclic antidepressants, venlafaxine)

[‡] Other non antidepressant drugs that increase serotonin that in combination with specific antidepressants increase the risk of serotonin syndrome (i.e., buspirone, dextromethorphan, meperidine, sumatriptan, tramadol).

[§] Non antidepressant drugs with anticholinergic activities included antiarrthymic (i.e., disopyramide), anti-emetics/anti-vertigo (i.e., meclizine, prochlorperazine), antiparkinsonians (i.e., trihexyphenidyl), antipsychotic (i.e., all conventionals and olanzapine, quetiapine), antispasmodics (e.g., belladonna, oxybutynin), cold and allergy drugs (e.g., hydroxyzine and other 1st generation antihistamines), sleep aids (i.e., diphenhydramine), and skeletal muscle relaxants (i.e., cyclobenzaprine and methocarbamol)