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Potentially Suboptimal Prescribing for Older Veteran Nursing Home Patients with Dementia

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CONFLICT OF INTEREST:

Dr. Semla serves on the Omnicare, Inc. Pharmacy and Therapeutics Committee, and he is a member of AARP's Caregiving Advisory Panel. He is an author and editor for LexiComp, Inc; his spouse is an employee of AbbVie and owns stock in AbbVie, Abbott Labs, and Hospira. The remaining authors have no conflicts to report.

PRESENTATION OF WORK

This work was presented at the 27th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, August 15, 2011, Chicago, Illinois.

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Abstract

Background—Nursing home patients with dementia may be more likely to suffer adverse drug events from suboptimal prescribing. Previous studies have not had national samples nor have they examined multiple types of suboptimal prescribing by dementia severity.

Objective—To examine the prevalence of, and factors associated with, potentially suboptimal prescribing in older Veteran nursing home patients with dementia.

Methods—This is a retrospective descriptive study of 1303 Veterans 65 years or older admitted between 1/1/04–6/3/05 with dementia for long stays (90+ days) to 133 Veterans Affairs Community Living Centers. Dementia severity was determined by Cognitive Performance Scale and functional status dependencies.

Results—Overall, 70.2% with mild-moderate dementia (n = 1076) had underuse as they did not receive an acetylcholinesterase inhibitor (AChEI), and 27.2% had evidence of inappropriate use due to a drug-disease or drug-drug-disease interaction. Of the 227 with severe dementia, 36.1% had overuse by receiving an AChEI, lipid-lowering or other agents, and 25.1% had evidence of inappropriate use due to a drug-disease or drug-drug interaction. Multinomial logistic regression analyses among those with mild to moderate dementia identified that living in the South versus other regions was the single factor associated with all three types of suboptimal prescribing. In those with severe dementia, antipsychotic use was associated with all three suboptimal prescribing types.

Conclusions—Potentially suboptimal prescribing was common in older Veteran nursing home patients with dementia. Clinicians should develop a heightened awareness of these problems. Future studies should examine associations between potentially suboptimal prescribing and health outcomes in patients with dementia.

Keywords

dementia; nursing home; Veterans; drug utilization; quality

INTRODUCTION

Suboptimal prescribing can be defined as potential under-, over-, or inappropriate medication use.¹ Suboptimal prescribing can lead to considerable morbidity, especially in older patients with dementia who may be more vulnerable to adverse drug events.^{2–4} This is important as more than one half of nursing home patients have some form of dementia.⁵

In patients with mild to moderate dementia, potentially suboptimal prescribing can include the underuse of acetylcholinesterase inhibitors (AChEIs) because omission of these agents may prevent an improvement in cognition.⁶⁻⁸ In patients with severe dementia and limited life expectancy, medications (e.g., lipid lowering agents) that may harm or not improve quality of life can be overused.^{4,6,9,10} Drug-drug (e.g., AChEI and an anticholinergic) and drug-disease (e.g., benzodiazepine use that can worsen cognition) interactions are two important types of inappropriate prescribing for nursing home residents with both mild-moderate and severe dementia.^{6,11}

To the best of our knowledge, no published studies have stratified dementia patients in nursing homes by severity and simultaneously examined potential under-, over-, or inappropriate medication use. Most previous studies examined only one type of suboptimal drug use.¹⁰ The objective of this study is to examine the prevalence of, and factors associated with, potentially suboptimal prescribing in older Veteran nursing home patients with and mild-moderate or severe dementia.

METHODS

Study Design, Setting, Data Sources and Sample

This was a retrospective descriptive study of 3,692 long-stay (90 days or more) patients age 65 or older admitted to any one of the 133 Veteran Affairs (VA) Community Living Centers (CLCs) located in the U.S. between January 1, 2004 and June 30, 2005. Residents admitted for respite or hospice care were excluded.

An analytic database was created from three data sources: 1) Minimum Data Set (MDS 2.0); 2) medication dispensing information from the VA Pharmacy Benefits Management Services (PBM); and 3) Medical SAS[®] files.¹² The MDS was completed at nursing home admission and contains information about the functional, psychological and health status needs of residents.¹³ The VA PBM data includes the following information for each drug dispensed during the first 90 days following admission: 1) start date; 2) drug name; 3) strength; 4) dosage form; 5) directions for use; 6) VA therapeutic class; and 7) amount dispensed.^{12,14} International Classification of Diseases-9 (ICD-9) Clinical Modification codes for inpatient and outpatient diagnoses in the year prior to admission were extracted from the Medical SAS[®] files.¹⁵

The study sample (n = 1303) included those with dementia identified during a VA hospitalization or outpatient visit in the year prior to CLC admission (ICD-9 codes: Alzheimer's [AD]- 331.0; 290.0; Other 046.1, 331.82, 294.8, 290.1x, 331.19; Vascular [VaD]-290.4x. These codes have been used by to identify dementia patients in previous national studies of Veterans.^{16,17} In this sample, 392 Veterans were coded as having AD, 180 had VaD, and the remaining 731 were coded as other dementias (including not otherwise specified). The relatively large other dementia category is consistent with that reported by a recent VA study and is partly due to the fact that the code of dementia, not otherwise specified (ICD-9 code 294.8), is offered in the VA electronic medical record as one of three top choices for clinicians to select.¹⁸ In a subsequent chart review by two clinicians of a sample of veteran patients coded as other dementia, over half appeared to

have a specific type of dementia (most commonly AD or VaD).¹⁸ To determine dementia severity, we used the admission MDS assessment to determine residents' cognitive function using the Cognitive Performance Scale [CPS], which has scores ranging from 0 to 6 (with higher scores representing worse cognition).¹⁹ Sensitivity and specificity for the CPS in detecting residents with cognitive impairment is similar to that of the Mini Mental State Exam.¹⁹ We also determined admission activities of daily living (ADL) dependencies; the ADL identifies the amount of assistance needed from staff for five activities (bathing, dressing, grooming, toileting and eating) and has scores ranging from 0 to 20 points (with higher scores representing more dependencies).²⁰ Following the study recommendations of van der Steen et al., severe dementia was defined as a CPS score ≤ 5 and ADL score ≤ 10 .²¹ All others were categorized as having mild-moderate dementia. The Pittsburgh VA Research and Human Subjects Committees approved the study.

Main Outcome Measures

Three types of potential suboptimal medication use anytime during the first 90 days after admission to a VA CLC was determined in patients with mild-moderate and severe dementia. First, potential underuse was operationally defined as no pharmacy dispensing of an AChEI (i.e., donepezil, tacrine, galantamine, rivastigmine) to those in the mild-moderate dementia group. The rationale is that many experts recommend AChEI treatment for those with mild-moderate dementia (i.e., AD, VaD, or Lewy body dementia) as it may improve cognitive function.⁶⁻⁸ Second, potential overuse was operationally defined in the severe dementia group as medications/classes for which patients are unlikely to derive benefit given their shortened life expectancy and risk of adverse drug events.^{6,9,10} Holmes et al. convened 12 geriatricians and reached consensus on seven medications/classes examined in this study that should never be used in these patients (i.e., AChEIs, antiplatelet agents [e.g. clopidogrel], lipid lowering agents [e.g., statins]; antineoplastics [e.g., cyclophosphamide], immune modulators [e.g., etanercept], leukotriene receptor antagonists [e.g., montelukast] and sex hormones [e.g., testosterone]).^{9,10} It is important to note that in 2006 (one year after the Holmes et al. panel was convened and the current study data were collected) the Food and Drug Administration approved the indication for donepezil use in those with severe dementia. The third outcome measure was potentially inappropriate use and was operationally defined in both the mild-moderate and severe dementia groups as evidence of either clinically important drug-disease interactions and/or clinically important drug-drug interactions.^{6,11} Clinically important drug-disease interactions included the following concomitant medications that can worsen cognitive function: 1) anticholinergics; 2) barbiturates, and 3) benzodiazepine receptor agonists.^{6,11} Highly anticholinergic drugs were those included in the Beers criteria (e.g., first generation antihistamines, tertiary tricyclic antidepressants, gastrointestinal antispasmodics).¹¹ Clinically important drug-drug interactions included: 1) highly anticholinergic drugs that can block the pharmacodynamic effects of AChEIs; 2) cimetidine, ketoconazole, paroxetine or erythromycin that can inhibit the hepatic metabolism of galantamine, and 3) ketoconazole or quinidine that can inhibit the hepatic metabolism of donepezil.⁶

For the analysis in those with mild-moderate dementia, three groups were created: 1) underuse only; 2) inappropriate use only, or 3) both under and inappropriate drug use. In

those with severe dementia, three groups were created: 1) overuse only; 2) inappropriate use only, or 3) both over and inappropriate use.

Independent Variables

Based on previous literature, our independent variables included demographic characteristics, health status factors, and site level indicators.^{10,16, 22–24} Demographics derived from the admission MDS assessment included categorical variables 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, above high school).

Health status factors were derived from the admission MDS assessment, Medical SAS[®] files, and VA PBM data. These factors included a continuous ADL dependencies measure from the admission MDS.²⁰ Using ICD-9 codes from the Medical SAS[®] files, we created a continuous variable for the Charlson Comorbidity Index based on the methods of Deyo et al., which creates a score (range 0–34) based on the presence of 17 chronic conditions (excluding dementia).^{25,26} From VA PBM data, we created dichotomous medication use variables (i.e., hypnotics, antidepressants, antipsychotics, mood stabilizers, and memantine) and a categorical variable for polypharmacy involving the remaining medications (i.e., 0–1, 2–4, 5+ prescribed drugs at admission). Dichotomous variables for psychiatric/neurological problems (i.e., aggressive behavior, post-traumatic stress disorder [PTSD], other anxiety disorder, depression [Depression Rating Scale-DRS scores>3], seizure disorder, Parkinson's disease, neuropathic pain, bipolar disease, schizophrenia, hypertension) were created using either ICD-9 codes from Medical SAS[®] files or MDS admission assessments.^{24,27} Categorical variables for site level indicators were created for urban/rural status, census region (i.e., Northeast, Midwest, South, West), facility size (i.e., small [<60 beds], medium [60–120 beds], and large [>120 beds]), and whether the patient resided in an Alzheimer's/ Dementia Special Care Unit.^{16,24}

Statistical Analyses

Descriptive statistics summarized independent variables and main outcome measures. To include the approximately 1% of patients with missing data on education, we created a dummy variable for a “missing” category. By dementia severity group status, we summarized the number of patients with evidence of potential overuse, underuse, and inappropriate use. Multinomial logistic regression analysis using a backward selection approach ($\alpha = 0.10$) identified those health status factors and site level indicators to be included with the demographic characteristics in the final models. Among those with mild-moderate dementia, we used multinomial logistic regression to identify demographic, health status and site level factors associated with underuse only, inappropriate use only, or both.²⁸ We also conducted logistic multinomial regression analysis in those with severe dementia to identify demographic, health status and site level factors associated with potential overuse only, potential inappropriate use only, or both.²⁸ We report 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 CLC patients who had mild-moderate dementia (n = 1,076) to those with severe dementia (n = 227). Those with mild-moderate dementia were less likely to have greater ADL dependencies, aggressive behavior, seizure disorder, or Parkinson's disease. Patients with mild-moderate dementia were more likely to have a greater number of comorbidities (on average), other anxieties, depression, neuropathic pain, and to use antidepressants.

In those with mild-moderate dementia, 70.2% were not receiving an ACHEI, indicating potential underuse (Table 2). Among those with severe dementia, 36.1% had potential overuse; the most common medication classes involved were ACHEIs (23.4%), lipid lowering agents (12.8%), and antiplatelet agents (5.3%).

Table 2 also shows potentially inappropriate drug use among both groups of patients with dementia. The overall prevalence of potentially inappropriate medication use did not differ significantly by dementia severity (27.2% for those with mild-moderate dementia versus 25.1% for those with severe dementia; $p = 0.51$). The most common drug-disease interactions were the use of anticholinergics (24.4% and 19.8% vs. respectively) and benzodiazepines (4.5% and 6.6%, respectively), both of which could exacerbate dementia. The most common drug-drug interaction for both dementia groups involved concomitant use of an anticholinergic with an ACHEI (7.9% and 5.3%, respectively). There were few other drug-drug interactions with ACHEIs.

Table 3 shows the results of the multinomial logistic regression analyses among those with mild-moderate dementia. Blacks were less likely than whites to have inappropriate use only or both under and inappropriate use (i.e., significance of the predictor across the 3 responses). Those prescribed 5+ medications, were diagnosed with bipolar disorder, schizophrenia and/or took memantine were significantly more likely than those without these characteristics to have potential underuse only or both under and inappropriate use. Those taking an antidepressant were significantly more likely than those who did not to have inappropriate use only or both inappropriate and underuse. Those living in the South were less likely than those living elsewhere to have evidence of suboptimal prescribing.

Table 4 shows the results of the multinomial logistic regression analyses among those with severe dementia. The probability of overuse only or both overuse and inappropriate use increased significantly with the number of comorbidities. Only antipsychotic use was associated with a higher risk of all three types of potential suboptimal drug use (i.e., overuse, inappropriate use or both).

DISCUSSION

Our study shows that seven in ten older Veterans with mild-moderate dementia residing in these CLCs did not receive an ACHEI (i.e., potential underuse). However, the overall the proportion of those with mild-moderate dementia receiving an ACEI (28.7%) is comparable to the 30.0% reported based on the 2004 National Nursing Home Study.²³ That study reported that the oldest old, those with worse functional status, user of antidepressants or

antipsychotics, and residents of larger nursing homes were more likely to use an AChEI. In our study, only the South region was significantly associated with less underuse of AChEIs in those with mild-moderate dementia. Therefore, clinicians practicing in regions besides the southern US should have heightened awareness and consider the use of AChEIs in those with mild-moderate dementia.

Regarding potential overuse, nearly one quarter of older Veterans with severe dementia received AChEI agents (i.e., potential over-use). This compares with a national study by Tjia et al. of 5,406 non-VA nursing home residents with advanced dementia where 36.4% took an AChEI.¹⁰ Clinicians should assess patients with severe dementia and consider whether discontinuation of AChEIs is indicated. Besides AChEIs in those with severe dementia, up to nearly 13% of these patients took a lipid lowering agent. In contrast, the same Tjia et al. study reported 22.4% received a lipid lowering agent.¹⁰ In the current study among those with severe dementia, only antipsychotic use was associated with a higher risk of overuse, inappropriate use or both. Therefore, clinicians evaluating the appropriateness of antipsychotic use should be aware that overuse and inappropriate use are more likely in those with severe dementia.

Potentially inappropriate prescribing due to drug-disease or drug-drug interactions regardless of dementia severity was common. Anticholinergic use was the most common medication class involved in drug-disease interactions. The most common drug-drug interaction in nearly a quarter of AChEI users (100/386) was the concomitant use of a highly anticholinergic agent, which can reduce the pharmacological effectiveness. The proportion with this specific drug-drug interaction is similar to the 27.1% rate reported in a study of 3,251 non-VA nursing home patients from Indiana.²² These findings have some clinical implications. One issue is for health care professionals working with older nursing home patients with dementia who receive an AChEI is to be more vigilant in avoiding the use of anticholinergic medications given their potential for worsening cognition, as well as increasing the risk of constipation, urinary retention, and syncope.¹¹ In most cases a suitable alternative is available. For example in patients with seasonal allergies, nasal steroids are preferable to highly anticholinergic and sedative first generation antihistamines.²⁹ Another emerging and important issue is for clinicians to reexamine the need for continuing certain medications in patients with shortened life expectancy, such as those with severe dementia.^{9,10} Several reviews have addressed the ethics of not prescribing certain medications, as well as techniques for medication discontinuation and avoidance of adverse drug withdrawal events.^{3,4,30}

This study has a number of potential limitations. First, there is potential disease misclassification because dementia and its severity were not determined by an independent research neurologist using standardized diagnostic criteria. Second, the criteria for suboptimal drug use were developed by consensus of an expert panel. Currently, to the best of our knowledge, evidence-based predictive validity data is not available for these criteria. Third, potential overuse of AChEIs in those with severe may have been overestimated in part because interpretation of the VA criteria for use at the time of the study may have varied at each CLC.¹⁰ Fourth, overuse would be overestimated if a discontinuation was attempted, but because of patient deterioration, the AChEI was restarted. Despite this, it is

important to keep in mind that the benefit in dementia patients is modest at best (only one third of those with mild to moderate Alzheimer's improved 4 points or more on a 70 point ADAS-Cog scale).^{6,7} Fifth, potential underuse of ACHEIs may also be overestimated in patients in whom it was started and stopped due to adverse drug events/perceived lack of efficacy. Sixth, our power was limited, particularly in the multinomial modeling, due to the relatively small sample of those with severe dementia, those who were female, and those with specific psychiatric conditions. Finally, our findings in a primarily male VA nursing home population may not generalize to non-VA nursing home settings where a majority of dementia patients is older and female.

CONCLUSIONS

We conclude that potentially suboptimal prescribing was common in older Veteran nursing home patients with dementia. Clinicians should develop a heightened awareness for these problems. Future studies should examine the impact that potentially inappropriate prescribing has on dementia patient health outcomes. Further study is also needed to better understand dementia patient, family, and prescriber preferences for intensifying, discontinuing or not initiating certain medications and the impact that these prescribing actions have on health outcomes in dementia patients.

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Table 1

Characteristics of Older Veteran Nursing Home Patients by Dementia Severity

Factors	Mild to Moderate Dementia (n = 1076)	Severe Dementia (n = 227)	p-value
	n (%)	n (%)	
<i>Demographics</i>			
Age			
65–74	261 (24.3)	48 (21.1)	
75–84	621 (57.7)	130 (57.3)	
85+	194 (18.0)	49 (21.6)	
Race			
White	889 (82.6)	166 (73.1)	
Black	133 (12.4)	33 (14.5)	
Other	54 (5.0)	28 (12.3)	
Female gender	30 (2.8)	7 (3.1)	0.81
Education			
Below High School	341 (31.7)	74 (32.6)	0.29
High School	475 (44.1)	111 (48.9)	
Above High School	250 (23.2)	41 (18.1)	
Missing	10 (0.9)	1 (0.4)	
ADL Dependence (mean ± SD)	8.69 (6.13)	16.8 (3.49)	<0.01
Comorbidity Index excluding dementia (mean ± SD)	2.10 (1.93)	1.48 (1.47)	<0.01
Polypharmacy			
0–1	416 (38.7)	74 (32.6)	0.05
2–4	392 (36.4)	79 (34.8)	
5+	268 (24.9)	74 (32.6)	
Aggressive behavior	149 (13.8)	46 (20.3)	0.01
PTSD	106 (9.9)	14 (6.2)	0.08
Other anxiety	118 (11.0)	12 (5.3)	0.01
Depression	354 (32.9)	41 (18.1)	<0.01
Seizure disorder	59 (5.5)	23 (10.1)	0.01
Parkinson's disease	82 (7.6)	31 (13.7)	<0.01
Neuropathic pain	242 (22.5)	24 (10.6)	<0.01
Bipolar disease	54 (5.0)	6 (2.6)	0.12
Schizophrenia	121 (11.2)	24 (10.6)	0.77
Hypertension	705 (65.5)	135 (59.5)	0.08
Use of hypnotic	5 (0.5)	0 (0.0)	0.30
Use of antidepressant	571 (53.1)	86 (37.9)	<0.01
Use of antipsychotic	445 (41.4)	95 (41.9)	0.89
Use of mood stabilizer	183 (17.0)	33 (14.5)	0.36
Use of memantine	73 (6.8)	16 (7.0)	0.89
<i>Site Level Indicators</i>			
Rural	301 (28.0)	54 (23.8)	0.20

Factors	Mild to Moderate Dementia (n = 1076)	Severe Dementia (n = 227)	p-value
	n (%)	n (%)	
Region			0.23
North East	264 (24.5)	60 (26.4)	
Midwest	179 (16.6)	39 (17.2)	
South	472 (43.9)	106 (46.7)	
West	161 (15.0)	22 (9.7)	
Bed Size			0.73
Small (<60)	92 (8.6)	23 (10.1)	
Medium (60–120)	519 (48.2)	109 (48.0)	
Large (>120)	465 (43.2)	95 (41.9)	
Alzheimer's/Dementia			0.36
Special Care Unit	231 (21.5)	55 (24.2)	

Abbreviations: ADL = Activities of Daily Living; PTSD = Post Traumatic Stress Disorder

Table 2

Underuse, Potential Inappropriate Prescribing, and Overuse in Older Veteran Nursing Home Patients with Dementia

	Mild to Moderate Dementia (n = 1076) n (%)	Severe Dementia (n = 227) n (%)
<i>Underuse of ACHEI</i>	755 (70.2)	
<i>Potentially Inappropriate Prescribing (Overall)</i>	293 (27.2)	57 (25.1)
<i>Drug/Disease Interaction</i>		
Anticholinergics	262 (24.4)	45 (19.8)
Barbiturates	2 (0.2)	0 (0.0)
Benzodiazepine	48 (4.5)	15 (6.6)
<i>Drug-Drug Interaction *</i>		
Anticholinergics /ACHEI	85 (7.9)	12 (5.3)
<i>Overuse (Overall)</i>		82 (36.1)
ACHEI		65 (23.4)
Lipid lowering agent		29 (12.8)
Antiplatelet agent		12 (5.3)
Other classes		8 (3.5)

Abbreviations: ACHEI = Acetylcholinesterase Inhibitor;

* One person with severe dementia had evidence of paroxetine/galantamine drug-drug interaction; 6 persons with mild-moderate dementia had a drug interaction with galantamine, and another 6 had one with donepezil.

Table 3

Factors Associated with Potential Underuse Only, Inappropriate Use Only and Both in those with Mild to Moderate Dementia (n = 1076)

Factors	Underuse Only (n = 556)	Inappropriate Only (n = 94)	Both (n = 199)
	Adj. RRR (95% CI)	Adj. RRR (95% CI)	Adj. RRR (95% CI)
<i>Demographics</i>			
Age			
65–74	reference	reference	reference
75–84	0.56 (0.34–0.93)	0.56 (0.26–1.21)	0.37 (0.19–0.73)
85+	0.70 (0.36–1.35)	1.12 (0.41–3.01)	0.53 (0.24–1.16)
Race *			
White	reference	reference	reference
Black	0.85 (0.52–1.38)	0.41 (0.19–0.88)	0.30 (0.15–0.61)
Other	1.47 (0.69–3.11)	0.22 (0.04–1.12)	1.31 (0.55–3.14)
Female gender	2.98 (0.69–12.9)	4.08 (0.76–21.99)	6.70 (1.41–31.71)
Education			
Below high school	reference	reference	reference
High school	0.86 (0.61–1.20)	0.94 (0.54–1.64)	0.96 (0.60–1.53)
Above high school	0.96 (0.58–1.58)	0.75 (0.40–1.40)	0.69 (0.38–1.26)
<i>Health Status</i>			
Comorbidity Index (excluding dementia)	1.08 (0.99–1.18)	0.98 (0.86–1.11)	1.12 (1.01–1.24)
Other Medications *			
0–1	reference	reference	reference
2–4	1.01 (0.72–1.42)	1.01 (0.61–1.68)	0.74 (0.45–1.20)
5+	2.72 (1.76–4.21)	1.12 (0.53–2.38)	2.02 (1.09–3.71)
Bipolar *	4.43 (1.31–15.08)	3.42 (0.70–16.64)	5.91 (1.65–21.13)
Schizophrenia *	2.45 (1.26–4.79)	0.89 (0.32–2.45)	3.64 (1.62–8.15)
Hypnotic use	0.28 (0.28–2.86)	too few to calculate	1.52 (0.27–8.66)
Antidepressant use *	0.83 (0.61–1.13)	2.12 (1.27–3.52)	1.59 (1.02–2.47)
Antipsychotic use	0.96 (0.91–1.01)	1.08 (1.03–1.12)	1.04 (0.99–1.08)
Memantine use *	0.32 (0.17–0.60)	0.58 (0.22–1.48)	0.09 (0.18–0.41)
<i>Site Level Indicators</i>			
Small Bed Size (<60)	reference	reference	reference
Medium Bed Size (60–120)	1.04 (0.58–1.87)	1.79 (0.67–4.77)	1.17 (0.57–2.41)
Large Bed Size (>120)	0.70 (0.36–1.35)	1.53 (0.57–4.12)	0.89 (0.42–1.89)
Rural	1.26 (0.73–2.13)	1.22 (0.72–2.07)	1.39 (0.74–2.62)
North East Region *			
Midwest Region	0.76 (0.42–1.38)	0.47 (0.25–0.87)	0.76 (0.41–1.40)
South Region	0.60 (0.37–0.97)	0.38 (0.21–0.70)	0.48 (0.27–0.86)
West Region	1.25 (0.69–2.23)	0.57 (0.18–1.74)	0.86 (0.42–1.77)

Abbreviations: Adj. = adjusted; CI = confidence interval; RRR = relative rate ratio

* $P < 0.05$ for overall multiparameter Wald test for the factor

Table 4

Factors Associated with Potential Overuse Only, Inappropriate Use Only and Both in those with Severe Dementia (n = 227)

Factors	Overuse Only (n = 55)	Inappropriate Only (N = 30)	Both (n = 27)
	Adj. RRR (95% CI)	Adj. RRR (95% CI)	Adj. RRR (95% CI)
<i>Demographics</i>			
Age			
65–74	reference	reference	reference
75–84	0.89 (0.32–2.46)	0.42 (0.14–1.28)	2.54 (0.58–11.13)
85+	1.21 (0.37–3.98)	0.44 (0.11–1.67)	1.87 (0.30–11.55)
Race			
White	reference	reference	reference
Black	0.50 (0.14–1.73)	0.17 (0.02–1.21)	0.03 (0.01–0.35)
Other	2.84 (0.71–11.35)	1.77 (0.55–5.67)	1.18 (0.17–7.93)
Female gender	4.01 (0.55–35.21)	too few to calculate	too few to calculate
Education			
Below high school	reference	reference	reference
High school	1.13 (0.41–3.09)	1.42 (0.41–4.82)	1.26 (0.33–4.79)
Above high school	0.88 (0.31–2.45)	0.80 (0.18–3.53)	0.34 (0.02–6.68)
<i>Health Status</i>			
Comorbidity index* (excluding dementia)	1.35 (1.05–1.72)	1.39 (0.97–2.00)	2.08 (1.47–2.94)
0–1 medications			
0–1 medications	reference	reference	reference
2–4 medications	1.54 (0.64–3.70)	0.24 (0.08–0.72)	0.72 (0.20–2.54)
5+ medications	0.67 (0.26–1.70)	0.29 (0.08–0.72)	1.15 (0.29–4.54)
Neuropathic pain	2.35 (0.66–8.45)	4.05 (0.91–17.93)	24.71 (6.79–89.89)
Bipolar	too few to calculate	0.12 (0.00–275.63)	0.64 (0.03–12.50)
Mood stabilizers	2.01 (0.40–9.96)	2.72 (0.37–19.84)	27.71 (4.17–184.02)
Antipsychotic use*	1.19 (1.04–1.36)	1.32 (1.13–1.54)	1.36 (1.20–1.55)
Memantine use	5.89 (0.92–37.59)	too few to calculate	4.78 (0.34–66.62)
<i>Site Level Indicators</i>			
Small Bed Size (<60)			
Small Bed Size (<60)	reference	reference	reference
Medium Bed Size (60–120)	0.34 (0.08–1.38)	2.75 (0.36–20.82)	0.15 (0.02–1.16)
Large Bed Size (>120)	1.08 (0.28–4.05)	4.48 (0.45–44.85)	0.21 (0.03–1.24)
Rural			
Rural	1.71 (0.66–4.41)	4.56 (1.37–15.14)	0.60 (0.12–2.99)
North East Region			
North East Region	reference	reference	reference
Midwest Region	0.53 (0.14–1.99)	0.79 (0.15–4.16)	0.20 (0.03–1.13)
South Region	0.84 (0.30–2.28)	1.37 (0.26–7.12)	0.28 (0.05–1.610)
West Region	0.65 (0.11–3.74)	2.84 (0.56–14.42)	0.05 (0.01–0.41)

Abbreviations: Adj. = adjusted; CI = confidence interval; RRR = relative rate ratio

* P<0.05 for overall multiparameter Wald test for the factor