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Dual Health Care System Use and High-Risk Prescribing in Patients With Dementia

A National Cohort Study

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Background: Recent federal policy changes attempt to expand veterans' access to providers outside the Department of Veterans Affairs (VA). Receipt of prescription medications across unconnected systems of care may increase the risk for unsafe prescribing, particularly in persons with dementia.

Objective: To investigate the association between dual health care system use and potentially unsafe medication (PUM) prescribing.

Design: Retrospective cohort study.

Setting: National VA outpatient care facilities in 2010.

Participants: 75 829 veterans with dementia who were continuously enrolled in Medicare from 2007 to 2010; 80% were VA-only users, and 20% were VA–Medicare Part D (dual) users.

Measurements: Augmented inverse propensity weighting was used to estimate the effect of dual-system versus VA-only prescribing on 4 indicators of PUM prescribing in 2010: any exposure to Healthcare Effectiveness Data and Information Set (HEDIS) high-risk medication in older adults (PUM-HEDIS), any daily exposure to prescriptions with a cumulative Anticholinergic Cognitive Burden (ACB) score of 3 or higher (PUM-ACB), any antipsychotic prescription (PUM-antipsychotic), and any PUM exposure (any-PUM). The annual number of days of each PUM exposure was also examined.

Results: Compared with VA-only users, dual users had more than double the odds of exposure to any-PUM (odds ratio [OR], 2.2 [95% CI, 2.2 to 2.3]), PUM-HEDIS (OR, 2.4 [CI, 2.2 to 2.8]), and PUM-ACB (OR, 2.1 [CI, 2.0 to 2.2]). The odds of PUM-antipsychotic exposure were also greater in dual users (OR, 1.5 [CI, 1.4 to 1.6]). Dual users had an adjusted average of 44.1 additional days of any-PUM exposure (CI, 37.2 to 45.0 days).

Limitation: Observational study design of veteran outpatients only.

Conclusion: Among veterans with dementia, rates of PUM prescribing are significantly higher among dual-system users than with VA-only users.

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Dementia is a growing public health priority that affects all health care systems in the United States (1). As a national health care organization, the U.S. Department of Veterans Affairs (VA) cares for one of the country's largest cohorts of persons with dementia (2). Because of the aging veteran population and its range of dementia risk factors (for example, traumatic brain injury, depression, and posttraumatic stress disorder), the prevalence of dementia in veterans is expected to double by 2030. Therefore, improving dementia care quality is among the VA's top strategic planning priorities and a national priority area in Healthy People 2020 (2, 3).

Dementia care is challenging for health care systems (4). The average patient with dementia has 4 comorbid conditions and receives care from 5 different providers annually (5). Medication management is particularly challenging because the average patient takes 5 different drugs, and 16% of patients take 9 or more (6). Although several medications may be indicated, using a greater number of medications (7) and prescribers (8) is a major risk factor for potentially unsafe medication (PUM) prescribing. Thus, provision of highly coordinated care is fundamental to prescribing safety in patients with dementia.

Recent federal policy changes to expand access to care may have unintended consequences that thwart the VA's efforts to enhance care coordination. In 2006, the introduction of the Medicare Part D prescription drug program expanded veterans' access to medications through non-VA health care systems, in which eligibility for Part D is independent of VA benefits. In 2014, the Patient Protection and Affordable Care Act offered expanded access to health care benefits, including medication coverage, through Medicaid and other payers. Most recently, the Veterans Access, Choice, and Accountability Act expanded access to non-VA health care to veterans who could not schedule an appointment within 30 days and those living more than 40 miles from the nearest VA facility. Although beneficial in some respects, policies that expand veterans' access to non-VA care may have the unintended consequence of negatively affecting quality of care (9–11), including safe and effective prescribing (12).

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Dual use of VA and non-VA health care on prescribing quality and safety has not previously been studied. However, prior research has shown such use to be associated with duplication and overuse of other health services (9) and worse health outcomes (11). Use of both VA and non-VA prescribing may be particularly hazardous for veterans with dementia who have complex medication needs and impaired cognitive and functional abilities, and in turn may be more vulnerable to increased care fragmentation.

This study examined the prevalence and effect of dual use of VA and Part D medications on prescribing safety among a national cohort of more than 75 000 veteran outpatients with dementia who were eligible for both VA and Part D prescription benefits. This research may assist in guiding national dementia care policies and calls for improving coordination across federal systems of care (12–14).

METHODS

Data Sources

We linked national patient-level data from 2007 to 2010 from the VA and Centers for Medicare & Medicaid Services. The VA data comprised the data sets from the VA Medical SAS files about patient demographics, diagnosis codes, and diagnosis dates for all inpatient and outpatient visits and VA Pharmacy Benefits Management Services data for dispensed outpatient medications. We included 6 Centers for Medicare & Medicaid Services data files: the Medicare Provider Analysis and Review file summarizing stays in inpatient hospitals and skilled-nursing facilities, Minimum Data Set file containing information on stays in Medicare- or Medicaid-certified long-term care facilities, outpatient facility file comprising claims submitted by institutional outpatient providers (for example, hospital outpatient departments, outpatient rehabilitation facilities, and renal dialysis facilities), carrier file containing claims from physicians and other noninstitutional providers and freestanding facilities (for example, independent clinical laboratories and freestanding ambulatory surgical centers), enrollment files, and event files containing information on prescription drugs dispensed through Part D (**Appendix Table 1**, available at Annals.org).

Sample

We identified all veterans with a diagnosis of Alzheimer disease or related dementia who were aged 68 years or older on 1 January 2010 (n = 508 998) (15). Veterans younger than 68 years were excluded because of lack of Medicare eligibility during the lookback period of 2007 to 2009. A 3-year lookback period has been shown to maximize the sensitivity of identifying persons with dementia using claims data (sensitivity, 0.80) (16). To identify active VA users, we excluded veterans with no VA outpatient encounter in 2010, including those with only VA emergency department visits (n = 324 690). We also excluded veterans not continuously enrolled in Medicare Parts A and B during 2007 to 2010 (n = 22 295) because of lack of availability of medical claims, those with Medicare-managed care or employer-sponsored creditable drug coverage (n = 47 905) during 2010 for whom non-VA prescribing could not be assessed, veterans with no prescriptions through the VA or Part D in 2010 (n = 10 593), and those receiving all prescriptions through Part D in 2010 (n = 2791). A small number of veterans living in Puerto Rico (n = 1045) were excluded because there is no comparable ZIP code or county-level data. Finally, we excluded veterans who spent 31 days or more in a hospital or nursing facility in 2010 (n = 23 850). The final sample included 75 829 veterans.

Measures

Dependent Variables: PUMs for Older Adults With Dementia

We constructed 3 indicators of PUM exposure in 2010: any exposure to Healthcare Effectiveness Data and Information Set (HEDIS) high-risk drugs (PUM-HEDIS) (17), any exposure to prescriptions with a cumulative score of 3 or higher on the Anticholinergic Cognitive Burden (ACB) scale (PUM-ACB), and any prescription for antipsychotic medication (PUM-antipsychotic). For each PUM type, we also calculated the number of days of exposure. We based PUM-HEDIS on the 2010 HEDIS list of potentially harmful drugs in elderly adults (17). We assessed PUM-ACB using the ACB scale, which is an expert-based, validated index that classifies each medication by severity of anticholinergic effect on cognition: 0 (none), 1 (mild), 2 (moderate), or 3 (severe) (18). Total ACB score for each day in 2010 was calculated for all patients by summing ACB scores across their medications for that day. Higher ACB scores are associated with greater anticholinergic load, with scores of 3 or higher indicating a clinically relevant burden (19). Antipsychotics are associated with increased mortality in patients with dementia and now carry a black box warning from the U.S. Food and Drug Administration (20, 21). We defined PUM-antipsychotic exposure as the receipt of at least 1 prescription for an atypical or conventional antipsychotic in 2010 (22). Finally, we created a variable—any-PUM—indicating any PUM-HEDIS, PUM-ACB, or PUM-antipsychotic exposure. Further, any-PUM exposure days are the sum of PUM-HEDIS, PUM-ACB, and PUM-antipsychotic exposure days in 2010. A day in which a patient was exposed to all 3 types of PUMs would count as 3 exposure days. Therefore, any-PUM exposure days could theoretically exceed 365 days.

Please see **Appendix Tables 2** to **4** (available at Annals.org) for details about medications classified as PUM-HEDIS, PUM-ACB, and PUM-antipsychotic.

Independent Variable: VA Users of Medicare–Part D

We defined the VA–Part D drug benefit user group as a dichotomous variable: VA-only users obtained all 2010 prescriptions through the VA, and VA–Part D users obtained at least 1 prescription from each source.

Covariates

Covariates were included if they were expected to affect the likelihood of dual use or risk for exposure to PUMs. Age, sex, race, U.S. census region, county-level rurality (23), distance to nearest VA medical center, VA enrollment priority status, and use of VA home-based primary care in 2009 were captured from VA data. Missing VA race/ethnicity values were filled in using race/ethnicity data from Medicare files. Clinical factors were derived using 2007 to 2009 health care utilization data for all inpatient, outpatient, and emergency department visits in both VA and non-VA settings, specifically using the VA Medical SAS files for all inpatient and outpatient visits and Medicare Provider Analysis and Review files, outpatient claims, and carrier claims. Clinical factors included the individual and total count of Elixhauser comorbid conditions in 2008 to 2009 (24), type of dementia (Alzheimer only, vascular dementia only, other dementing disorders only, or multiple dementia types coded in 2007 to 2009), memantine use in 2009 as a proxy for moderate or severe dementia, and counts of emergency department visits and hospitalizations in 2009. The number of days alive in 2010 was captured using the date of death in the Medicare enrollment file. Veterans Integrated Service Networks (VISNs) dummy variables were included to account for VISN-level fixed effects.

Statistical Analysis

The primary hypothesis was that dual users would be at greater risk for exposure to each of the 4 PUM categories than VA-only users. To address potential for selection bias, we used augmented inverse probability weighting (AIPW) propensity score methods to estimate the average effect of drug benefit user group and PUM exposure. We used the teffects aipw command in STATA, version 13 (StataCorp). Augmented inverse probability weighting combines 2 models: inverse probability weighting in the drug benefit user group selection propensity model with regression adjustment in the outcomes model (PUM exposure) (25). When these 2 approaches are combined, AIPW is called "doubly robust estimation" because only 1 of the 2 models needs to be correctly specified to obtain an unbiased estimator. Specifically, logistic regression was used in the propensity model to estimate the probability of belonging to either user group, and weighted logistic regression and weighted linear regression were used to model PUM exposure and the number of days of PUM exposure, respectively (25). All covariates described here were included in both the drug benefit user group selection and PUM exposure models. To account for the highly skewed nature of the days of PUM exposure variables, we estimated SEs and 95% CIs using a bias-corrected bootstrap approach (26). With less than 2% missing data across all variables, hot-deck imputation was used to derive a single complete data set (27).

Sensitivity Analysis

We conducted many sensitivity analyses. First, we examined the level of residual confounding necessary to produce the odds ratio (OR) observed for any-PUM (28). Second, we reviewed an alternative definition of dual use: proportion of total prescriptions (VA and Medicare) received from the VA. Because we hypothesized a curvilinear relationship, we included a quadratic term in these models. Third, we assessed potential confounding by stratifying all analyses by VISN. After stratification, results were pooled. We did 2 additional sensitivity analyses (results available upon request). We tested for undue influence of unusual cases in the AIPW analysis by excluding the lowest and highest 2.5% of propensity scores (29). Finally, we ran a model that included veterans who spent 31 days or more in a hospital or nursing facility in 2010.

Role of the Funding Source

The U.S. Department of Veterans Affairs had no role in the study design, data collection and analysis, manuscript preparation, or the decision to submit the manuscript for publication.

RESULTS

Study Sample

The sample included 75 829 older veteran outpatients with dementia, dually enrolled in VA care and fee-for-service Medicare, with at least 1 prescription from the VA or Part D in 2010. The mean age was 82 years; 98% were men, and 88% were non-Hispanic white persons. Nearly 20% (19.7%) were dual users, whereas 80% were VA-only users.

Balancing Covariates Via Inverse Propensity Score Weighting

Compared with VA-only users, dual users lived in the Northeast, lived farther from the nearest VA facility, had no service-connected disability, had more comorbid conditions, used memantine, and had multiple hospitalizations in 2009 (**Appendix Table 5**, available at Annals.org). After AIPW adjustment, no covariates had a standardized difference greater than 10%, which indicated sufficient balance between dual- and VA-only users. This is reflected in the comparison between the unadjusted and AIPW-adjusted differences across covariates.

Unadjusted Results

Among the study sample (**Table 1**), 44% were exposed to at least 1 type of PUM. Compared with VA-only users, the prevalence of any-PUM exposure among dual users was 19.8 percentage points higher (95% CI, 19.0 to 20.7 percentage points), with an additional 44.8 days of any-PUM exposure (CI, 40.2 to 48.4 percentage points). A similar pattern emerged for the specific PUM measures. Compared with VA-only users, dual users were more likely to be exposed to PUM-HEDIS (10.7 percentage points [CI, 10.0 to 11.4 percentage points]), PUM-ACB (18.4 percentage points [CI, 17.5 to 19.3 percentage points]), and PUM-antipsychotic (5.2 percentage points [CI, 4.6 to 5.8 percentage points]). Dual users had an additional 6.4 days of PUM-HEDIS exposure (CI, 5.2 to 7.6 days), 30.1 days

Table 1. Unadjusted Use of PUMs Among Older Veterans With Dementia Who Used VA Outpatient Services in 2010, by Source of Prescription Medications

PUM Exposure	VA-Part D Use (n = 14 941)	VA-Only Use (n = 60 888)	Difference (95% CI)*
Any-PUM†			
Exposure, %	59.0	39.1	19.8 (19.0–20.7)‡
Mean exposure days (SD) [range]§	159.0 (216.0) [0–1095.0]	114.3 (198.0) [0–1095.0]	44.8 (40.2–48.4)
PUM-HEDIS‖			
Any HEDIS drug exposure, %	20.5	9.8	10.7 (10.0–11.4)‡
Mean exposure days (SD) [range]	20.5 (66.0) [0–365.0]	14.1 (58.0) [0–365.0]	6.4 (5.2–7.6)
PUM-ACB**			
Exposure, %	53.8	35.4	18.4 (17.5–19.3)‡
Mean exposure days (SD) [range]	104.7 (137.0) [0–365.0]	74.6 (126.0) [0–365.0]	30.1 (27.5–32.6)
PUM-antipsychotic††			
Prescription, %	16.7	11.4	5.2 (4.6–5.8)‡
Mean exposure days (SD) [range]	33.8 (93.0) [0–365.0]	25.6 (83.0) [0–365.0]	8.2 (6.3–9.8)

ACB = Anticholinergic Cognitive Burden; HEDIS = Healthcare Effectiveness Data and Information Set; PUM = potentially unsafe medication; VA = U.S. Department of Veterans Affairs.
* All comparisons across medication user groups were statistically significant at the $P < 0.001$ level. The Pearson chi-square test was used for binary outcomes. Bias-corrected bootstrapping was used to assess the number of days.
† Includes exposure to PUM-HEDIS, PUM-ACB, and PUM-antipsychotic.
‡ Values are percentage points.
§ The sum of PUM-HEDIS, PUM-ACB, and PUM-antipsychotic-exposure days in 2010. A day in which a patient was exposed to all 3 types of PUMs would count as 3 exposure days.
‖ Exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults.
** Daily exposure to drugs that have a cumulative ACB scale score of ≥3.
†† Any prescription for antipsychotic medication.

of PUM-ACB exposure (CI, 27.5 to 32.6 days), and 8.2 days of PUM-antipsychotic exposure (CI, 6.3 to 9.8 days).

AIPW-Adjusted Results

Dual Versus VA-Only Users

In the AIPW-adjusted analyses (Table 2), compared with VA-only users being a dual user more than doubled the odds of any type of PUM exposure (OR, 2.2 [CI, 2.2 to 2.3]); the adjusted difference was 19.1 percentage points (CI, 18.1 to 20.7 percentage points). Dual users had an adjusted average of 44.1 additional days of any-PUM exposure (CI, 37.2 to 45.0 days). Dual users also had more than double the odds of PUM-HEDIS exposure (OR, 2.4 [CI, 2.2 to 2.8]); the adjusted difference was 10.9 percentage points (CI, 10.2 to 11.7 percentage points). Dual users had an adjusted average of 6.6 additional days of PUM-HEDIS exposure (CI, 5.4 to 7.9 days). Odds of PUM-ACB exposure were 2.1 times higher for dual users than VA-only users (OR, 2.1 [CI, 2.0 to 2.2]), with an adjusted difference of 17.6 percentage points (CI, 16.7 to 18.6 percentage points). Dual users had an adjusted average of 27.6 additional days of PUM-ACB exposure (CI, 25.1 to 30.1 days). Odds of PUM-antipsychotic exposure were 1.5 times higher for dual users than VA-only users (OR, 1.5 [CI, 1.4 to 1.6]), with an adjusted difference of 4.6 percentage points (CI, 3.9 to 5.3 percentage points). Dual users had an adjusted average of 6.8 additional days of PUM-antipsychotic exposure (CI, 5.1 to 8.4 days).

All results were robust across the described sensitivity analyses.

Unobserved Confounder Assessment

We focused sensitivity analyses on any-PUM (Appendix Figure 1, available at Annals.org). For the dual- versus VA-only use finding, a relative risk ratio greater than 7.0 between an unobserved confounder and any-PUM exposure would be needed to nullify the observed OR of 2.2. Even if an unobserved cofounder met this threshold, an OR of 6.0 or greater between the confounder and dual use would be needed to nullify the observed result.

Alternative Definition of Dual Use

Analyses of dual use measured as the proportion of prescriptions received from the VA showed the expected curvilinear relationship. The risk for exposure to PUMs was highest when seeking prescriptions in near-equal proportions from the VA and Part D (Appendix Figure 2, available at Annals.org).

Potential Effect Modification by VISNs

Although minor variation was observed across VISNs (Appendix Figure 3, available at Annals.org), stratified pooled results did not differ substantively from nonstratified results.

DISCUSSION

Our analysis of a national cohort of more than 75 000 veterans with dementia showed higher rates of PUM prescribing for those receiving prescriptions from both VA and Medicare providers. The prevalence of exposure to PUMs was high overall (44%), but was par-

ticularly high in dual users (59%) than VA-only users (39%). Adjusted results were similar. Compared with VA-only users, dual users had more than double the odds of exposure to any-PUM or PUM-HEDIS. Dual use also doubled the odds of PUM-ACB exposure. Dual users with dementia were at greater risk for receiving prescriptions for antipsychotics. Compared with VA-only users, dual users had an average of 1 additional week of PUM-antipsychotic and PUM-HEDIS exposure and 1 additional month of PUM-ACB exposure.

To our knowledge, this study is the first to examine the effect of dual-system use on prescribing safety among veterans. Our results are consistent with previous research on dual use of other health services, which found poorer quality of care and health outcomes among veteran dual users (9–11, 30–34). Although future research should investigate the mechanisms by which use of both VA and non-VA drug benefits increases the risk for PUM prescribing, our findings have several possible explanations. First, dual-system use may disrupt key aspects of care continuity necessary for safe prescribing to patients with dementia (35). For example, research by Byrne and colleagues (36) suggests that VA and private systems are not sufficiently integrated to facilitate exchange of crucial patient diagnostic, laboratory, and prescribing information (12). The absence of electronic information exchanges places much of the burden on cognitively impaired veterans or their family caregivers to communicate complex information across systems in which veterans are presumably seeing different prescribers. Second, VA-only users may have been protected by the evidence-based, national VA formulary and other VA medication restrictions (for example, criteria for use and prior authorization). Unlike Part D, which places few restrictions on drugs, the VA uses an integrated, nationalized formulary that includes ongoing review of medication safety and effectiveness and administrative infrastructure capable of restricting PUMs when necessary (37). Finally, although PUM exposure was more common among dual users (59%), the high rate of exposure in VA-only users (39%) is consistent with prior research (38). The persistent challenge of PUM prescribing in older adults, even within an integrated health care system, further underscores the need for increased screening and interventions to reduce such prescribing.

The finding that dual users were exposed to an additional month of high-ACB medications and an additional week of antipsychotics is concerning. The U.S. Food and Drug Administration acknowledged the elevated mortality risk associated with antipsychotic prescribing to patients with dementia through black box warnings as early as 2005. Exposure to drugs with strong anticholinergic properties increases cognitive impairment (39), risk for falls (40), and all-cause mortality (39). Anticholinergics also may work antagonistically in dementia therapies designed to boost acetylcholine (41) and increase the risk for an anticholinergic–acetylcholinesterase inhibitor prescribing cascade (42).

These findings have important policy and clinical implications for patients with dementia. First, for the benefits of dual use (such as increased access) to outweigh the risks, careful comanagement of care between VA and non-VA providers is critical. Successful comanagement requires that health information exchange between systems—currently the responsibility of veterans and caregivers—needs to improve. Pilot programs, such as the VA Virtual Lifetime Electronic Record, have shown great potential for facilitating health information sharing between VA and non-VA providers (43). Efforts to rapidly implement such programs, particularly to vulnerable veterans, are urgently needed to keep pace with recent policies designed to expand access to non-VA providers.

Second, pharmacist-led medication management is known to decrease the use of unsafe medications (44). The VA pharmacists could serve as "medication coordination managers" for high-risk, dual-system–using veterans. In addition to improving safety, pharmacists could help reduce patient, caregiver, and physician burden by assisting with communication of medication information across systems.

Our analysis has several limitations. First, the sample is representative of veterans with dementia who are enrolled in Medicare fee-for-service and use VA outpatient facilities. Although our sample represents one of

Table 2. Adjusted Use of PUMs Among Older Veterans With Dementia Who Used VA Outpatient Services in 2010, by Source of Prescription Medications

PUM Exposure	VA–Part D Use vs. VA-Only Use	
	Unadjusted	Adjusted by AIPW Propensity Score Methods
Any-PUM*		
Difference (95% CI)†	19.8 (19.0–20.7)	19.1 (18.1–20.7)
OR (95% CI)	2.2 (2.2–2.3)	2.2 (2.1–2.3)
Days (95% CI)¶	44.8 (40.9–48.6)	44.1 (37.2–45.0)
PUM-HEDIS‡		
Difference (95% CI)†	10.7 (10.0–11.4)	10.9 (10.2–11.7)
OR (95% CI)	2.4 (2.3–2.5)	2.4 (2.2–2.8)
Days (95% CI)¶	6.5 (5.4–7.6)	6.6 (5.4–7.9)
PUM-ACB§		
Difference (95% CI)†	18.5 (17.5–19.3)	17.6 (16.7–18.6)
OR (95% CI)	2.1 (2.1–2.2)	2.1 (2.0–2.2)
Days (95% CI)¶	30.4 (28.1–32.7)	27.6 (25.1–30.1)
PUM-antipsychotic‖		
Difference (95% CI)†	5.2 (4.6–5.8)	4.6 (3.9–5.3)
OR (95% CI)	1.5 (1.5–1.6)	1.5 (1.4–1.6)
Days (95% CI), *n*¶	8.2 (6.5–9.7)	6.8 (5.1–8.4)

ACB = Anticholinergic Cognitive Burden; AIPW = augmented inverse probability weighting; HEDIS = Healthcare Effectiveness Data and Information Set; OR = odds ratio; PUM = potentially unsafe medication; VA = U.S. Department of Veterans Affairs.

* Includes exposure to PUM-HEDIS, PUM-ACB, and PUM-antipsychotic.

† Percentage points.

‡ Exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults.

§ Daily exposure to drugs that have a cumulative ACB scale score of ≥3.

‖ Any prescription for antipsychotic medication.

¶ Bias-corrected bootstrapped 95% CIs.

the country's largest cohorts of persons with dementia, it may not be representative of all Medicare-eligible veterans with dementia. Future research should assess whether use of both VA- and non-VA prescribing presents risks for all older veterans, including those without dementia who have access to Medicare drug benefits; those enrolled in Medicare-managed care; or those using other non-VA drug benefits. Second, although our propensity score approach addresses potential confounding from observed variables, unobserved factors may bias results. Rule-out sensitivity analyses, however, suggest any unobserved confounder would need to be extremely strong to negate observed results. Third, given the lack of information on characteristics of VA and Medicare prescribers in our prescription data, we cannot determine whether prescriber characteristics influenced the results. Finally, our measures do not capture the full range of PUM prescribing scenarios, nor is every instance of exposure to our chosen measures necessarily unsafe. We did not assess duplication of therapies, drug–drug interactions, drug–disease interactions, or unsafe over-the-counter medications (6), which are important areas for future investigation.

We report evidence that prescribing safety may be inadvertently compromised when national policies expand patient access to several poorly coordinated health care systems. Policymakers should consider implementing electronic health information exchanges and additional medication therapy management services across systems to keep pace with recent policies designed to expand veterans' access to non-VA providers and protect vulnerable patients from risks associated with dual-system use.

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Appendix Table 1. List of ICD-9-CM Diagnosis Codes Indicating Alzheimer Disease and Related Disorders or Senile Dementia, per Medicare's Chronic Conditions Warehouse

ICD-9-CM Diagnosis Code	Description
331.0	Alzheimer's disease
331.11	Pick's disease
331.19	Other frontotemporal dementia
331.2	Senile degeneration of brain
331.7	Cerebral degeneration in diseases classified elsewhere
290.0	Senile dementia, uncomplicated
290.1	Presenile dementia (brain syndrome with presenile dementia)
290.10	Presenile dementia, uncomplicated
290.11	Presenile dementia, with delirium
290.12	Presenile dementia, with delusional features
290.13	Presenile dementia, with depressive features
290.20	Senile dementia, with delusional features
290.21	Senile dementia, with depressive features
290.3	Senile dementia, with delirium
290.40	Arteriosclerotic dementia, uncomplicated
290.41	Arteriosclerotic dementia, with delirium
290.42	Arteriosclerotic dementia, with delusional features
290.43	Arteriosclerotic dementia, with depressive features
294.0	Amnestic syndrome (Korsakoff's psychosis or syndrome, nonalcoholic)
294.1	Dementia in conditions classified elsewhere
294.10	Dementia in conditions classified elsewhere without behavioral disturbance
294.11	Dementia in condition classified elsewhere with behavioral disturbance
294.8	Other specific organ brain syndrome (chronic)
797	Senile without mention of psychosis

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Appendix Table 2. Medications Classified as PUM-HEDIS*

Antianxiety (includes combination drugs)
- Aspirin-meprobamate
- Meprobamate

Antiemetics
- Scopolamine
- Trimethobenzamide

Analgesics (includes combination drugs)
- Ketorolac (oral only)

Antihistamines (includes combination drugs)
- APAP/dextromethorphan/diphenhydramine
- APAP/diphenhydramine/phenylephrine
- APAP/diphenhydramine/pseudoephedrine
- Acetaminophen-diphenhydramine
- Carbetapentane/diphenhydramine/phenylephrine
- Codeine/phenylephrine/promethazine
- Codeine-promethazine
- Cyproheptadine
- Dexchlorpheniramine
- Dexchlorpheniramine/dextromethorphan/pseudoephedrine
- Dexchlorpheniramine/guaifenesin/pseudoephedrine
- Dexchlorpheniramine/hydrocodone/phenylephrine
- Dexchlorpheniramine/methscopolamine/pseudoephedrine
- Dexchlorpheniramine-pseudoephedrine
- Dextromethorphan-promethazine
- Diphenhydramine
- Diphenhydramine/hydrocodone/phenylephrine
- Diphenhydramine-magnesium salicylate
- Diphenhydramine-phenylephrine
- Diphenhydramine-pseudoephedrine
- Hydroxyzine hydrochloride
- Hydroxyzine pamoate
- Phenylephrine-promethazine
- Promethazine

Antipsychotic, typical
- Thioridazine

Amphetamines
- Amphetamine-dextroamphetamine
- Benzphetamine
- Dexmethylphenidate
- Dextroamphetamine
- Diethylpropion
- Methamphetamine
- Methylphenidate
- Phendimetrazine
- Phentermine

Barbiturates
- Butabarbital
- Mephobarbital
- Pentobarbital
- Phenobarbital
- Secobarbital

Long-acting benzodiazepines (includes combination drugs)
- Amitriptyline-chlordiazepoxide
- Chlordiazepoxide
- Chlordiazepoxide-clidinium
- Diazepam
- Flurazepam

Calcium-channel blockers
- Nifedipine–short-acting only

Gastrointestinal antispasmodics
- Dicyclomine
- Propantheline

Appendix Table 2–Continued

Belladonna alkaloids (includes combination drugs)
- Atropine (oral only)
- Atropine/CPM/hyoscyamine/PE/scopolamine
- Atropine/hyoscyamine/PB/scopolamine
- Atropine-difenoxin
- Atropine-diphenoxylate
- Atropine-edrophonium
- Belladonna
- Belladonna/ergotamine/phenobarbital
- Butabarbital/hyoscyamine/phenazopyridine
- Hyoscyamine
- Hyoscyamine/methenam/m-blue/phenyl salicyl

Skeletal muscle relaxants (includes combination drugs)
- ASA/caffeine/orphenadrine
- ASA/carisoprodol/codeine
- Aspirin-carisoprodol
- Aspirin-methocarbamol
- Carisoprodol
- Chlorzoxazone
- Cyclobenzaprine
- Metaxalone
- Methocarbamol
- Orphenadrine

Oral estrogens (includes combination drugs)
- Conjugated estrogen
- Conjugated estrogen-medroxyprogesterone
- Esterified estrogen
- Esterified estrogen-methyltestosterone
- Estropipate

Oral hypoglycemics
- Chlorpropamide

Narcotics (includes combination drugs)
- ASA/caffeine/propoxyphene†
- Acetaminophen-pentazocine
- Acetaminophen-propoxyphene†
- Belladonna-opium
- Meperidine
- Meperidine-promethazine
- Naloxone-pentazocine
- Pentazocine
- Propoxyphene hydrochloride†
- Propoxyphene napsylate†

Vasodilators
- Dipyridamole–short-acting only
- Ergot mesyloid
- Isoxsuprine

Others (including androgens and anabolic steroids, thyroid drugs, urinary anti-infectives)
- Methyltestosterone
- Nitrofurantoin
- Nitrofurantoin macrocrystals
- Nitrofurantoin macrocrystals-monohydrate
- Thyroid desiccated

APAP = acetaminophen; ASA = aspirin; CPM = chlorpheniramine; HEDIS = Healthcare Effectiveness Data and Information Set; PB = phenobarbital; PE = phenylephrine; PUM = potentially unsafe medication.
* Exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults.
† Propoxyphene is no longer available in the United States.

Appendix Table 3. Medications Classified as PUM-ACB, by ACB Scale Score*

ACB scale score 1
- Alimemazine
- Alverine
- Alprazolam
- Aripiprazole
- Asenapine
- Atenolol
- Bupropion
- Captopril
- Cetirizine
- Chlorthalidone
- Cimetidine
- Clidinium
- Clorazepate
- Codeine
- Colchicine
- Desloratadine
- Diazepam
- Digoxin
- Dipyridamole
- Disopyramide
- Fentanyl
- Furosemide
- Fluvoxamine
- Haloperidol
- Hydralazine
- Hydrocortisone
- Iloperidone
- Isosorbide
- Levocetirizine
- Loperamide
- Loratadine
- Metoprolol
- Morphine
- Nifedipine
- Paliperidone
- Prednisone
- Quinidine
- Ranitidine
- Risperidone
- Theophylline
- Trazodone
- Triamterene
- Venlafaxine
- Warfarin

ACB scale score 2
- Amantadine
- Belladonna
- Carbamazepine
- Cyclobenzaprine
- Cyproheptadine
- Loxapine
- Meperidine
- Methotrimeprazine
- Molindone
- Nefopam
- Oxcarbazepine
- Pimozide

ACB scale score 3
- Amitriptyline
- Amoxapine
- Atropine
- Benztropine
- Brompheniramine
- Carbinoxamine
- Chlorpheniramine
- Chlorpromazine
- Clemastine

***Appendix Table 3*–Continued**
- Clomipramine
- Clozapine
- Darifenacin
- Desipramine
- Dicyclomine
- Dimenhydrinate
- Diphenhydramine
- Doxepin
- Doxylamine
- Fesoterodine
- Flavoxate
- Hydroxyzine
- Hyoscyamine
- Imipramine
- Meclizine
- Methocarbamol
- Nortriptyline
- Olanzapine
- Orphenadrine
- Oxybutynin
- Paroxetine
- Perphenazine
- Promethazine
- Propantheline
- Propiverine
- Quetiapine
- Scopolamine
- Solifenacin
- Thioridazine
- Tolterodine
- Trifluoperazine
- Trihexyphenidyl
- Trimipramine
- Trospium

ACB = Anticholinergic Cognitive Burden; PUM = potentially unsafe medication.
* Daily exposure to drugs that have a cumulative ACB scale score of ≥3.

Appendix Table 4. Medications Classified as PUM-Antipsychotic*

- Amitriptyline
- Aripiprazole
- Asenapine
- Brexpiprazole
- Chlorpromazine
- Clozapine
- Fluoxetine
- Fluphenazine
- Haloperidol
- Iloperidone
- Loxapine
- Lurasidone
- Molindone
- Olanzapine
- Paliperidone
- Perphenazine
- Pimozide
- Prochlorperazine
- Quetiapine
- Risperidone
- Thioridazine
- Trifluoperazine
- Thiothixene
- Ziprasidone

* Any prescription for antipsychotic medication.

Appendix Table 5. Characteristics of Older Veterans With Dementia Who Used VA Outpatient Services in 2010, by Source of Prescription Medications*

Characteristic	Unadjusted		Adjusted by AIPW		
	VA-Part D Use (*n* = 14 941)	VA-Only Use (*n* = 60 888)	VA-Part D Use	VA-Only Use	Standardized Difference
Age, %					
68–74 y	12	13	13	13	−0.9
75–79 y	23	22	22	22	−1.0
80–84 y	32	29	30	30	0.2
≥85 y	33	35	35	35	1.4
Sex, %					
Female	2	2	2	2	–
Male	98	98	98	98	−0.3
Race/ethnicity, %					
Hispanic	2	3	3	3	0.6
Non-Hispanic					
White	91	88	88	89	−0.4
Black	5	8	7	7	0.2
Other	2	1	1	1	−0.2
U.S. region, %					
Northeast	20	15	16	16	0.3
Midwest	22	26	26	25	1.0
South	45	45	44	45	−0.4
West	13	14	14	14	−0.9
County rurality, %					
Large metropolitan	39	38	38	38	−1.2
Small metropolitan	35	37	36	36	0.5
Micropolitan	14	14	14	14	0.7
Noncore rural	12	11	12	12	0.2
Distance to nearest VA, *mi*	18	17	17	17	0.5
VA enrollment priority status, %					
Highly disabled	18	28	26	25	0.5
Low/moderately disabled	13	15	14	15	−0.5
Low income	27	23	24	24	0.3
No service-connected disability	42	35	36	36	−0.3
Number of comorbidities, %					
0	1	2	2	2	−0.1
1–2	17	22	21	21	−0.5
3–4	30	32	32	32	0.2
≥5	52	44	45	45	0.3
Comorbid conditions, %					
Congestive heart failure	26	21	22	22	0.2
Valvular disease	19	16	16	16	0.2
Pulmonary circulation disorder	5	4	4	4	0.4
Peripheral vascular disorder	31	25	26	26	0.3
Hypertension	79	78	78	78	0.2
Paralysis	5	5	5	5	0.4
Neurologic disorder	50	43	44	44	0.4
Chronic pulmonary disease	33	28	29	29	0.0
Diabetes					
Uncomplicated	28	26	27	27	−0.3
Complicated	18	15	15	15	0
Hypothyroidism	20	17	17	17	0.2
Renal failure	20	18	19	19	0.6
Tumor without metastasis	22	20	20	20	−0.3
Rheumatoid arthritis	4	4	4	4	−0.4
Coagulopathy	8	6	6	6	0.2
Obesity	7	6	6	6	0.1
Weight loss	8	8	8	8	0.9
Fluid and electrolyte disorder	24	21	21	21	0.5
Blood loss anemia	2	2	2	2	0.6

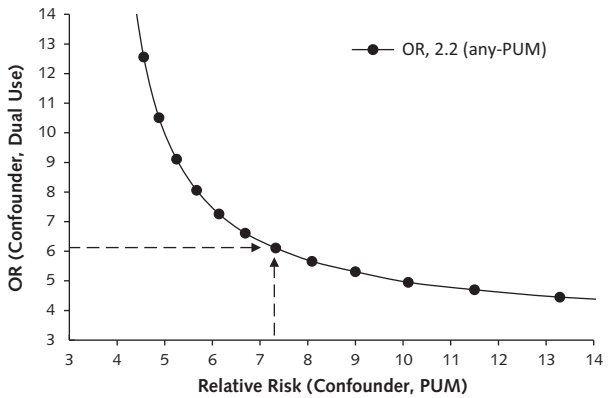
Continued on following page

Appendix Table 5–Continued

Characteristic	Unadjusted		Adjusted by Augmented Inverse Probability Weighting		
	VA-Part D Use (n = 14 941)	VA-Only Use (n = 60 888)	VA-Part D Use	VA-Only Use	Standardized Difference
Deficiency anemia	38	32	33	33	0.4
Alcohol abuse	3	3	3	3	0.5
Psychoses	16	15	15	15	−0.2
Depression	26	24	24	24	0.1
Epilepsy	4	3	3	3	−0.2
Syncope	10	8	9	9	0.1
Memantine user in 2009, %					
No	76	87	85	85	–
Yes	24	13	15	15	−0.1
In-home-based primary care, %					
No	97	93	94	94	–
Yes	4	7	6	6	1.2
Dementia type, %					
Alzheimer disease only	8	9	8	8	−0.3
Vascular dementia only	11	14	13	13	−0.4
Other dementing disorder only	33	40	39	39	−0.9
Multiple dementia diagnoses	48	38	40	39	1.3
Hospitalizations in 2009, %					
0	62	66	65	66	−0.9
1	21	20	20	20	0.6
≥2	17	14	15	14	0.5
Emergency department visits in 2009, %					
0	60	61	60	61	−0.3
1	23	23	23	23	−0.1
≥2	17	17	17	17	0.5
Days alive in 2010, *n*	352	349	350	350	0.4
VISN, %					
1	5	6	6	5	0.6
2	2	1	2	2	−0.2
3	3	6	4	4	−0.2
4	5	7	6	6	0.0
5	3	2	3	3	−0.2
6	5	5	5	5	−0.3
7	7	7	7	7	−0.3
8	10	11	9	9	−0.4
9	5	5	5	5	−0.1
10	4	3	4	3	0.4
11	5	5	5	5	0.4
12	5	5	5	5	0.8
15	5	5	5	5	−0.3
16	9	9	10	9	0.7
17	4	4	4	4	−0.3
18	4	3	4	4	−0.6
19	3	2	2	2	−0.2
20	3	3	3	3	−0.5
21	3	3	3	3	−0.7
22	3	3	3	3	−0.4
23	6	5	6	6	0.9

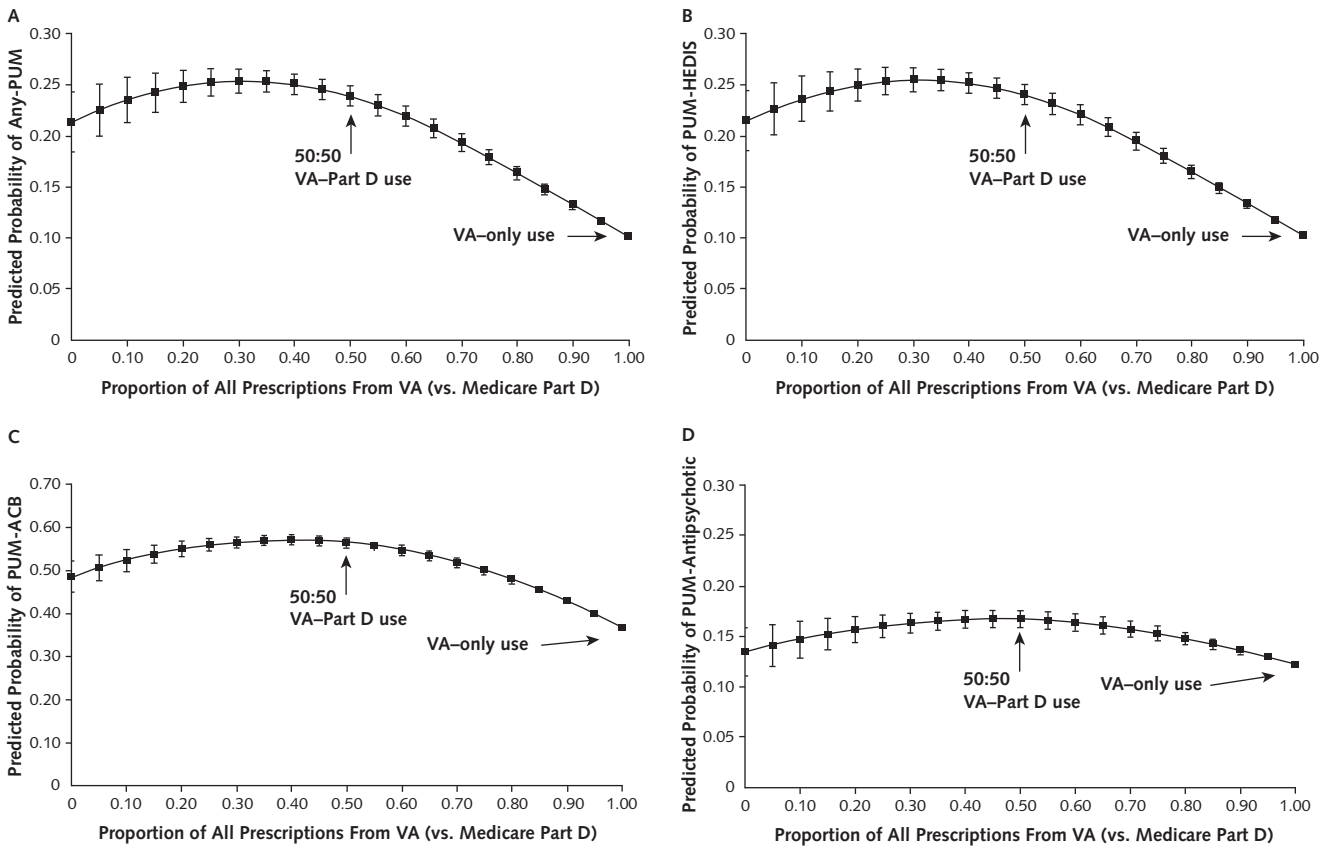
AIPW = augmented inverse probability weighting; VA = U.S. Department of Veterans Affairs; VISN = Veteran Integrated Service Network.
* Percentages may not sum to 100 due to rounding.

Appendix Figure 1. Rule-out sensitivity analysis for any-PUM exposure.



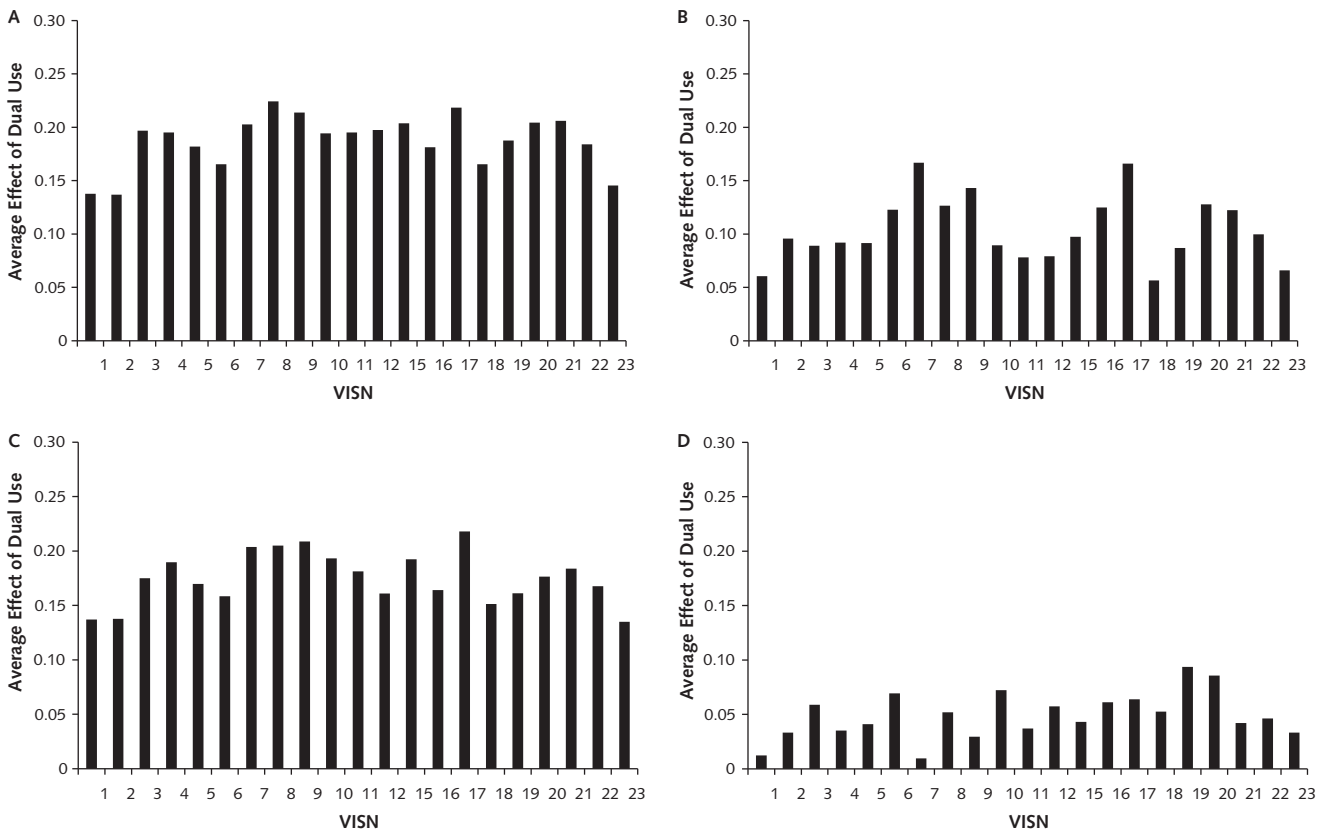
Area above the curve represents values of the levels of confounding necessary to produce the observed OR (2.2). Area below the curve represents levels of confounding that would not be sufficient on their own, after adjustment for observed confounders, to produce the observed ORs. For example, the dashed lines indicate that an unobserved confounder would need to have a relative risk of greater than 7.0 with PUM exposure and an OR of 6.0 or greater with dual use of the VA and Medicare Part D to nullify the observed adjusted OR of 2.2. ACB = Anticholinergic Cognitive Burden; any-PUM = includes exposure to PUM-HEDIS, PUM-ACB, and PUM-antipsychotic; HEDIS = Healthcare Effectiveness Data and Information Set; OR = odds ratio; PUM = potentially unsafe medication; PUM-ACB = daily exposure to drugs that have a cumulative ACB scale score of ≥3; PUM-antipsychotic = any prescription for antipsychotic medication; PUM-HEDIS = exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults; VA = U.S. Department of Veterans Affairs.

Appendix Figure 2. Predicted probability of PUM exposure, by the proportion of all VA prescriptions.



Error bars represent 95% CIs. ACB = Anticholinergic Cognitive Burden; Any-PUM = includes exposure to PUM-HEDIS, PUM-ACB, and PUM-antipsychotic; HEDIS = Healthcare Effectiveness Data and Information Set; PUM = potentially unsafe medication; PUM-ACB = daily exposure to drugs that have a cumulative ACB scale score of ≥3; PUM-antipsychotic = any prescription for antipsychotic medication; PUM-HEDIS = exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults; VA = U.S. Department of Veterans Affairs; **A**. Any-PUM exposure. **B**. PUM-HEDIS exposure. **C**. PUM-ACB exposure. **D**. PUM-antipsychotic exposure.

Appendix Figure 3. Average effect of dual use on measures of unsafe prescribing.



Each bar represents the average effect of dual use on the measure of unsafe prescribing, stratified by VISN. ACB = Anticholinergic Cognitive Burden; Any-PUM = includes exposure to PUM-HEDIS, PUM-ACB, and PUM-antipsychotic; HEDIS = Healthcare Effectiveness Data and Information Set; PUM = potentially unsafe medication; PUM-ACB = daily exposure to drugs that have a cumulative ACB scale score of ≥3; PUM-antipsychotic = any prescription for antipsychotic medication; PUM-HEDIS = exposure to any high-risk drug based on the 2010 HEDIS list of potentially harmful drugs in older adults; VISN = Veterans Integrated Service Network; **A**. Any-PUM exposure. **B**. PUM-HEDIS exposure. **C**. PUM-ACB exposure. **D**. PUM-antipsychotic exposure.