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Geographic variation in poststroke depression among veterans with acute stroke

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Abstract—This study compared patterns of poststroke depression (PSD) detection among veterans with acute stroke in eight U.S. geographic regions. Department of Veterans Affairs (VA) medical and pharmacy data as well as Medicare data were used. International Classification of Diseases-9th Revision depression codes and antidepressant medication dispensing were applied to define patients' PSD status 12 months post-stroke. Logistic regression models were fit to compare VA PSD diagnosis and overall PSD detection between the regions. The use of VA medical data alone may underestimate the rate of PSD. Geographic variation in PSD detection depended on the data used. If VA medical data alone were used, we found no significant variation. If VA medical data were used along with Medicare and VA pharmacy data, we observed a significant variation in overall PSD detection across the regions after adjusting for potential risk factors. VA clinicians and policy makers need to consider enrollees' use of services outside the system when conducting program evaluation. Future research on PSD among veteran patients should use VA medical data in combination with Medicare and VA pharmacy data to obtain a comprehensive understanding of patients' PSD.

Key words: geographic variation, ICD-9, Medicare, poststroke depression, PSD detection, rehabilitation, stroke, "stroke belt," VA, veterans.

INTRODUCTION

Depression after stroke is common. While some estimates range from as low as 12 percent to as high as 80 percent [1–2], most estimates indicate that poststroke depression (PSD) occurs among approximately 25 to 40 percent of stroke survivors [3–6]. Studies show that PSD negatively affects patients' functional recovery and quality of life and is associated with increased morbidity, mortality, and healthcare use [7–11]. Although PSD can be effectively treated with potentially life-saving outcomes [8,12–14], it is often underdiagnosed and undertreated [2,13]. Currently, no documentation is available regarding geographic variation in PSD detection. Understanding such

Abbreviations: AOR = adjusted odds ratio, BRFSS = Behavioral Risk Factor Surveillance System, FW = Far West, FY = fiscal year, GL = Great Lakes, ICD-9 = International Classification of Diseases-9th Revision, ME = Mideast, PL = Plains, PSD = poststroke depression, SE = Southeast, SW = Southwest, VA = Department of Veterans Affairs.

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variation could provide important clues for identifying patient and system factors that may contribute to the underdiagnosis and undertreatment of PSD.

Significant geographic variation in stroke epidemiology and disparities in stroke incidence and prevalence have been demonstrated [15–19]. In a recent study of the 2005 Behavioral Risk Factor Surveillance System (BRFSS) survey, for example, overall stroke prevalence was reported as 2.6 percent among noninstitutionalized U.S. adults and the weighted, age-adjusted stroke prevalence varied across the states, with the lowest in Connecticut (1.5%) and the highest in Mississippi (4.3%) [20]. This overall estimate of stroke prevalence was comparable to previous study reports [16]. The BRFSS report showed that most states with high prevalence were clustered in the Southeast (SE) region, except for a few additional states in other regions (Illinois, Michigan, Missouri, Nevada, Texas, and West Virginia) that also had high stroke prevalence (≥3.0%). This clustering of high stroke prevalence in the SE corresponded to the high stroke mortality rates previously observed in that region, which is traditionally known as the "stroke belt" [21–22]. No obvious simple explanation exists for the observed variation in stroke prevalence. Among the many different findings, the contributing factors to the variation included differences in the prevalence of stroke risk factors (e.g., high blood pressure, high blood cholesterol levels, diabetes, smoking, physical inactivity, and obesity) [18–19] and sociocultural and socioeconomic variations (e.g, cultural norms for diet and exercise, income, social isolation, and access to healthcare and preventable services) between the areas of high and low stroke prevalence [22]. Further studies addressing potential explanations for the stroke belt are still underway, including "The Reasons for Geographic and Racial Differences in Stroke Study" [19].

The Department of Veterans Affairs (VA), through the Veterans Health Administration, maintains the largest integrated healthcare delivery system in the United States and provides care to more than 5.2 million veterans each year at more than 1,300 sites. As such, VA medical databases provide unique resources for examining PSD detection and comparing geographic variation in PSD. However, many veterans covered by the VA healthcare system are also eligible for healthcare plans outside the VA system and many of them are dual- or triple-system users. For example, we recently found that among the 1,953 VA stroke inpatients living in the state of Florida, 30 percent were VA-only users, 60 percent were VA-Medicare dual users, 3 percent were VA-Medicaid dual users, and 7 percent were triple users within the first 12 months of their acute stroke hospitalization [23]. Consequently, obtaining veterans' PSD information from non-VA sources, such as other Federal and private plans, to gain a complete picture of their PSD status is important. Furthermore, VA provides its enrollees a comprehensive pharmacy benefit that could be a rich information source for identifying patients with PSD diagnosed outside the VA.

The objective of this study was to use automated administrative data from multiple sources to compare geographic variation in PSD detection among a national sample of VA patients diagnosed with acute stroke across eight different geographic regions.

METHODS

Data Sources

National data were extracted from three major locations. First, we used the VA Austin Automation Center; databases used included the Patient Treatment File Main file and the Functional Status Outcomes Database for inpatient care information, the Event and Visit files for outpatient care data, and the Beneficiary Identification and Records Locator Subsystem death file for patients' mortality information. Second, we used the VA Pharmacy Benefits Management Strategic Health Group; the Pharmacy Benefit Management file was obtained for patient antidepressant dispensing and daily dosage information. Third, we used the VA Information Resource Center; veteran-Medicare merged data used for this study included the Denominator file for Medicare beneficiary's eligibility and sociodemographic information, the Medicare Provider Analysis and Review file for Medicare inpatient care, the Carrier file for noninstitutional care, and the Outpatient file for institutional outpatient care.

The calendar year Medicare data were converted into equivalent fiscal years (FYs) to ensure the compatibility of these different timeframes since the VA data are stored by Federal FY. Further, we used a dual-system matching strategy developed by Fleming et al. [24] to ensure that a patient identified in one database was the same person in the other. Full details about the matching criteria and results are reported elsewhere [9].

Sample Selection

Our study cohort consisted of 5,593 VA stroke patients. These patients had received inpatient care for acute stroke within the VA during FY 2001, survived 60 days or more after the index admission, and had an index length of stay less than 365 days. An existing high-specificity algorithm that is based on International Classification of Diseases-9th Revision (ICD-9) stroke codes [25] and has a high predictive value for identifying persons with acute stroke events was modified by including ICD-9 code 436.xx for acute, but ill-defined, cerebrovascular diseases [25–26].

Dependent Variables

Dependent variables were VA PSD diagnosis and overall PSD detection. First, VA PSD diagnosis was established if a patient had an ICD-9 depression code as a primary or secondary diagnosis recorded in the VA inpatient or outpatient databases within 12 months of the index stroke. The ICD-9 depression codes used included 296.2x (single episode or unspecified major depressive disorders), 296.3x (recurrent major depressive disorders), 311.xx (depressive disorder, not elsewhere classified), 300.4 (reactive depression), 309.0 (depressive reaction acute), and 309.1 (depressive reaction prolonged). These codes were previously reported in related studies of depression among VA enrollees [27–28].

Second, the overall PSD detection variable was an extension of a previous outcome measure, which provided an even more comprehensive measurement of PSD status of the study sample by including patients' PSD detected both inside and outside the VA healthcare system. The following databases and steps were applied in creating this outcome measure: first, we abstracted depression-related diagnosis codes from the VA databases as described previously; then, the same ICD-9 depression diagnosis codes were applied to Medicare inpatient and outpatient data; and finally, additional unique veterans were identified by abstracting their prescription dispensing records in concordance with the guideline-recommended minimum daily dosage for antidepressant medications on the VA formulary for the 12 months after the index stroke [28–29]. **Table 1** shows the antidepressants and guideline-recommended minimum daily dosages that we used. We used the minimal daily dosage to reduce the number of patients treated with low-dose antidepressants for pain control or insomnia. This latter approach helped identify the patients who were likely treated for depression but did not have a depression ICD-9 code either in the VA medical data or the Medicare data.

Table 1.
Antidepressant guideline-recommended minimum daily dosage (milligrams/day) by patient age.

Antidepressant	Patient Age	
	≥65	<65
Sertraline	25	50
Paroxetine	10	20
Citalopram*	20	20
Fluoxetine	10	20
Fluvoxamine*	100	100
Amitriptyline	NR	50
Desipramine	25	100
Doxepin	30	75
Imipramine	30	75
Nortriptyline	30	75
Protriptyline	15	15
Trimipramine	50	75
Clomipramine	75	75
Trazodone	25	150
Buproprion	50	200
Phenelzine	45	45
Tranylcypromine	20	20
Maprotiline	25	75
Nefazodone	100	200
Venlafaxine	50	75
Mirtazapine	15	15
Amoxapine	50	100

*These antidepressants were not addressed in 1997 Department of Veterans Affairs depression guidelines; minimum daily dosage for these medications derived from expert consensus.
NR = not recommended.

Independent Variables or Geographic Regions

In this study, we applied the classification of the U.S. Department of Commerce Bureau of Economic Analysis to group patients' residential states into eight geographic regions as shown in **Table 2**. These regional groupings were based primarily on homogeneity of the states in economic and sociodemographic characteristics, and they are the most frequently used groupings of states in the United States for economic analysis [30].

Sociodemographic Variables

Sociodemographic variables included age, sex, race, marital status, priority for VA care, and mortality. Patient priority for VA medical care was created based upon the Means Test Indicator in the VA medical database. Full details about the Means Test Indicator and the patient priority for VA care are reported elsewhere [9].

Table 2.
Geographic regions defined by U.S. Department of Commerce Bureau of Economic Analysis.

Region	States
New England	Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
Mideast	Delaware, District of Columbia, Maryland, New Jersey, New York, Pennsylvania
Great Lakes	Illinois, Indiana, Michigan, Ohio, Wisconsin
Plains	Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota
Southeast	Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, West Virginia
Southwest	Arizona, New Mexico, Oklahoma, Texas
Rocky Mountain	Colorado, Idaho, Montana, Utah, Wyoming
Far West	Alaska, California, Hawaii, Nevada, Oregon, Washington

Clinical and Disease Severity Variables

Clinical and disease severity variables used for this study were stroke type (ischemic vs all others), comorbidity, and hospitalization admission source (hospital referral vs all other sources) during index hospitalization. These clinical measurements have been used previously as severity proxies in stroke-related outcome studies [31–34]. A modified Charlson comorbidity index was used to assess the patients' medical comorbid conditions at the index hospitalization, with higher weighted summary scores being associated with a more severe burden of comorbidity [35].

Statistical Analysis

All data were analyzed using SAS, version 9.1 (SAS Institute; Cary, North Carolina). Descriptive statistics were obtained on the sociodemographic, clinical and disease severity, as well as PSD variables. Chi-square tests on discrete variables and *F*-tests on continuous variables were performed to compare these variables between the regions. We used multivariate logistic procedures to estimate the geographic variation in PSD detection, while controlling for the sociodemographic and clinical and disease severity factors discussed previously.

RESULTS

Table 3 shows the demographics, clinical characteristics, and PSD detection of the study sample by region. The distribution of the overall study sample (N = 5,593) ranged from 2.5 percent in New England to 33.2 percent in the SE across the eight regions. Among the demographic and clinical variables presented, significant differences ($p < 0.01$) in patient age, race, marital status, and admission source (hospital referral vs all others) between the regions were apparent. Specifically, compared with the others, patients in the Rocky Mountain region were older, more likely to be white and married, and less likely to be referred from a hospital for the index hospitalization. In contrast, patients in the Great Lakes (GL), SE, and Far West (FW) regions were the youngest; patients in the Mideast (ME) were less likely to be white; patients in the FW were less likely to be married; and patients in the FW and GL were more likely to have hospital referrals for the index hospitalization. In addition, significant variation ($p < 0.05$) was shown across the regions in unadjusted VA PSD diagnosis and overall PSD detection 12-months poststroke.

The results from logistic regression analyses showed no significant geographic variation in PSD diagnosis within the VA system (**Table 4**). Nevertheless, significant geographic variation was present in overall PSD detection, after adjusting for patient demographics and clinical factors. Specifically, patients in the ME were less likely (adjusted odds ratio [AOR] 0.77, $p < 0.01$) and patients in the Plains (PL) and Southwest (SW) were more likely (AOR 1.23 and 1.21, respectively, $p < 0.05$) to be diagnosed with PSD than patients in the SE. Other statistically significantly factors ($p < 0.01$) associated with both VA and overall PSD detection included younger age and being nonwhite. Additional factors associated with overall PSD detection included high priority for VA care, more comorbid conditions, and admission source for index hospitalization.

It is important to note that our study cohort included 268 patients (4.8%) who were users of certain antidepressants with guideline-recommended minimum daily dosages that may have been prescribed for the management of pain (amitriptyline and imipramine) or sleep disorders (trazodone, nefazodone, and mirtazapine). However, in separate confirmation analyses, we found that the final results remained the same, with or without these 268 patients.

Table 3.
Patient characteristics by percentage or mean ± standard deviation for entire sample (N = 5,593) and by region.

Characteristic	Study Sample	Regional Sample							
		New England	Mideast	Great Lakes	Southeast	Southwest	Rocky Mountain	Far West	Plains
Frequency	100	2.5	12.5	13.1	33.2	15.3	3.1	11.3	9.0
Demographic									
Age*	67.6 ± 11.1	68.7 ± 10.5	69.1 ± 11.4	67.0 ± 10.6	67.0 ± 11.2	67.5 ± 11.2	69.3 ± 11.0	67.2 ± 11.0	68.7 ± 10.7
Male	98.2	95.7	98.3	98.4	98.3	98.4	96.6	98.6	98.4
White*	72.3	91.9	61.8	67.4	69.2	75.0	92.4	75.8	84.8
Married*	48.0	51.8	42.5	43.5	52.1	51.9	55.4	39.3	47.1
High Priority for VA Care	92.9	89.4	90.7	92.3	93.7	92.9	92.0	94.9	92.6
12-Month Mortality	11.5	9.2	10.7	10.7	12.2	13.2	11.4	9.2	12.0
Clinical Characteristics									
Ischemic Stroke	93.5	94.3	92.7	93.7	93.0	93.7	92.6	94.3	94.4
Comorbidity	0.8 ± 1.2	0.8 ± 1.0	0.9 ± 1.1	0.9 ± 1.2	0.9 ± 1.2	0.8 ± 1.1	0.9 ± 1.2	0.9 ± 1.2	0.9 ± 1.1
Hospital Referral*	4.3	3.6	1.1	5.6	4.7	2.9	0.1	7.0	3.2
Unadjusted PSD									
VA PSD Diagnosis*	20.0	19.2	16.1	21.5	18.9	21.3	25.7	20.8	22.0
Overall PSD Detection*	39.1	43.3	31.0	38.0	38.7	43.1	45.1	38.3	44.5

Note: p-values were from chi-square tests for categorical variables and F-tests for continuous variables between regions.
*$p < 0.05$.
PSD = poststroke depression, VA = Department of Veterans Affairs.

Table 4.
Adjusted odds ratio and 95 percent confidence interval for Department of Veterans Affairs (VA) poststroke depression (PSD) diagnosis and overall PSD detection.

Potential Factor	VA PSD Diagnosis	Overall PSD Detection
Region (reference = Southeast)		
New England	0.97 (0.62–1.52)	1.17 (0.82–1.66)
Mideast	0.90 (0.71–1.14)	0.77 (0.64–0.94)*
Great Lakes	1.17 (0.95–1.45)	0.98 (0.82–1.17)
Plains	1.16 (0.91–1.49)	1.23 (1.00–1.51)†
Southwest	1.17 (0.96–1.44)	1.21 (1.03–1.43)†
Rocky Mountain	1.39 (0.96–2.01)	1.19 (0.86–1.64)
Far West	1.10 (0.87–1.38)	0.95 (0.78–1.15)
Age (continuous)	0.98 (0.97–0.98)*	0.99 (0.98–0.99)*
White (reference = all others)	1.55 (1.32–1.82)*	1.60 (1.41–1.82)*
Married (reference = all others)	0.92 (0.81–1.06)	1.03 (0.92–1.15)
VA Care Priority: High (reference = low)	1.03 (0.79–1.34)	1.36 (1.09–1.70)*
Ischemic Stroke (reference = all others)	1.13 (0.86–1.49)	1.19 (0.95–1.49)
12-Month Mortality: Yes (reference = no)	0.87 (0.70–1.10)	0.95 (0.80–1.14)
Comorbidity (continuous)	1.02 (0.96–1.08)	1.08 (1.03–1.13)*
Hospital Referral: Acute (reference = all others)	1.30 (0.96–1.77)	1.58 (1.21–2.06)*

*$p < 0.01$.
†$p < 0.05$.

DISCUSSION

This study contributes to the current literature by providing a comprehensive comparison of variation in VA PSD diagnosis and overall PSD detection across eight geographic regions of the United States. PSD is a high-volume condition that negatively affects patients' recovery and quality of life. Although effective treatments for PSD are available, PSD is often underdiagnosed and undertreated, and the pattern of PSD diagnosis among VA healthcare enrollees with stroke is largely unknown.

First, in this cross-sectional national study, we found that one-third of the study cohort (patients with acute stroke in FY 2001) were in the SE region. While this pattern may appear to be consistent with the previous reports that most states with high stroke prevalence are clustered in the SE region [20], our intention is not to make a comparison for the following reasons. A lack of universal consensus exists about the classification of stroke patients mostly because of the heterogeneity of the disease. For example, the American Heart Association and Centers for Disease Control and Prevention consistently define stroke under the more generic heading "cerebrovascular disease" by using ICD-9 codes 430–438, excluding 435 for transient ischemic stroke [36–37]. In the BRFSS survey reports [20], respondents' stroke status was based upon their response to the question "Has a doctor or other health professional ever told you that you had a stroke?" In our current study, however, we applied a stroke ICD-9 code algorithm developed by Reker and colleagues for its high specificity and strong positive predictive value in identifying acute stroke cases among veterans [25]. We also modified the algorithm by including ICD-9 code 436.xx for acute, but ill-defined, cerebrovascular disease. As a result, counting stroke patients is highly dependent upon which ICD-9 codes are used and the fact that different ICD-9 codes yield differing results.

Second, our logistic regression results showed no significant geographic differences in VA PSD diagnosis, regardless of the geographic variation in acute stroke cases across the eight regions, even after adjusting for patients' demographic characteristics and clinical factors. This finding may reflect the results of various initiatives (e.g., Quality Enhancement Research Initiative or QUERI) that VA has in place to enhance its quality of care and implementation of evidence-based clinical guidelines, including a performance measure for annual depression screening for all veterans enrolled in VA primary care clinics [38–42].

Third, in this study, we were able to link and combine multiple sources of data (i.e., VA inpatient and outpatient data, Medicare inpatient and outpatient data, and VA pharmacy data) to obtain a more complete picture of patients' PSD status from within and outside the VA system. With these different data sources, we found that the patients' VA-PSD diagnosis nearly doubled (20.0% vs 39.1%) and that patients in the SE region were more likely to be diagnosed with PSD than patients in the ME and less likely to be diagnosed with PSD than patients in the PL and SW regions. This variation in overall PSD detection among VA patients with acute stroke may not represent PSD detection within the VA system; rather, it reflects the difference in PSD detection beyond the VA system across the eight regions.

Our findings, however, suggest that to gain a comprehensive oversight of PSD detection in VA patients, one must evaluate non-VA data sources, since 70 percent of the VA stroke patients were multiple healthcare system users [23]. This study underscores the need to use other data sources, such as Medicare data and VA pharmacy data, to investigate stroke characteristics or outcomes within the VA. Our findings also suggest that VA clinicians and policy makers need to consider enrollees' use of services outside the VA system when conducting program evaluation and developing interventional programs to improve care quality and functional recovery of their patients poststroke.

It is important to note that in this study, we were unable to obtain access to patients' prestroke depression status, and thus we were unable to adjust for patients' preexisting depression in our final analyses. Although a history of depression has been linked to an increased risk for development of PSD, the proportion of patients with PSD who have active depression at the time of their stroke is not well known. Further, the impact of preexisting depression on PSD detection, severity, treatment, and outcomes is likewise not well understood. We have chosen to use the term PSD in this study because we ascertained depression diagnosis after an acute stroke, but we realize the inherent ambiguity of this term. Future studies should attempt to address this important clinical situation.

CONCLUSIONS

Our findings indicate that clinicians in the ME region of the country should be screening more consistently for PSD among their stroke patients. Our study revealed that

factors related to the diagnosis of PSD include younger age, white race, higher VA care priority, heavier burden of comorbidity, and inpatient hospital referral.

Our findings also suggest that using VA medical data alone will likely result in an underestimate of PSD among veterans after an acute stroke, with a twofold increase in case ascertainment by using Medicare and VA pharmacy information. Although PSD detection prevalence appears to be similar across geographic regions when only VA data are examined, significant regional differences are observed when both VA pharmacy and Medicare data are included. Whether these differences are largely explained by differences in patient sociodemographic characteristics of dual-users versus VA-only users, underlying differences in the system of care, or difficulties in care coordination remains to be explored.

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