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Regional differences in prescribing quality among elder veterans and the impact of rural residence

BC Lund^{1,2,3}, ME Charlton¹, MA Steinman⁴, and PJ Kaboli^{1,2,5}

¹Veterans Rural Health Resource Center-Central Region, VA Iowa City Health Care System, Iowa City, Iowa

²Center for Comprehensive Access & Delivery Research and Evaluation, VA Iowa City Health Care System, Iowa City, Iowa

³Department of Epidemiology, University of Iowa College of Public Health, Iowa City, Iowa

⁴Division of Geriatrics, San Francisco VA Medical Center and the University of California, San Francisco, California

⁵Division of General Internal Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, Iowa

Abstract

Purpose—Medication safety is a critical concern for older adults. Regional variation in potentially inappropriate prescribing practices may reflect important differences in health care quality. Therefore, the objectives of this study were to characterize prescribing quality variation among older adults across geographic region, and to compare prescribing quality across rural versus urban residence.

Methods—Cross-sectional study of 1,549,824 older adult veterans with regular Veterans Affairs (VA) primary care and medication use during fiscal year 2007. Prescribing quality was measured by 4 indicators of potentially inappropriate prescribing: Zhan criteria drugs to avoid, Fick criteria drugs to avoid, therapeutic duplication, and drug-drug interactions. Frequency differences across region and rural-urban residence were compared using adjusted odds-ratios.

Findings—Significant regional variation was observed for all indicators. Zhan criteria frequencies ranged from 13.2% in the Northeast to 21.2% in the South. Nationally, rural veterans had a significantly increased risk for inappropriate prescribing according to all quality indicators. However, regional analyses revealed this effect was limited to the South and Northeast, whereas rural residence was neutral in the Midwest and protective in the West.

Conclusions—Significant regional variation in prescribing quality was observed among older adult veterans, mirroring recent findings among Medicare beneficiaries. The association between rurality and prescribing quality is heterogeneous, and relying solely on national estimates may yield misleading conclusions. While we documented important variations in prescribing quality, the underlying factors driving these trends remain unknown, and they are a vital area for future research affecting older adults in both VA and non-VA health systems.

Keywords

geography; geriatrics; pharmacy; quality; rural

Older adults comprise 13% of the United States population yet consume approximately one-third of prescriptions.¹ A national (United States) survey of non-institutionalized people over 65 years found that 71% of men and 81% of women use at least one medication per week, and 19% of men and 23% of women use 5 or more.² Expanding drug regimens yield important therapeutic benefits, but they also place older adults at risk for adverse drug events, as number of medications is a powerful risk factor.³⁻⁵ In addition, advancing age is associated with increased physiological susceptibility to adverse drug events, due to both increased pharmacodynamic sensitivity and impaired drug clearance from renal and hepatic dysfunction.⁶ The combined impact of these factors makes medication safety a critical public health concern for older adults.

In addition to quantity, the quality of medication prescribing is important for older adults. Prescribing quality refers to the safe and effective use of medications and, as with other domains of health care quality, is often measured using quality indicators. Prescribing quality indicators commonly include explicitly defined lists of prescribing scenarios that represent potentially inappropriate prescribing practices and are typically ascertained from electronic administrative data. The term *potentially* is used because practices considered inappropriate in most cases may be justifiable under certain clinical circumstances. A frequently used example is the Beers criteria, a list of medications where risk generally outweighs benefit for patients over 65 years of age, as established by a consensus panel of experts.⁷⁻⁹ Prescribing quality indicators, such as the Beers criteria, have been linked to risk for adverse drug events.¹⁰⁻¹⁷

Ensuring high-quality prescribing among older adults is particularly relevant to the Veterans Affairs (VA) Health Care System, where 45% of enrolled veterans are over 65 years of age.¹⁸ Prescribing quality data in VA are limited, but available data suggest that older adult veterans are at similar or slightly lower risk for inappropriate prescribing compared to non-VA patient groups.^{19,20} One vital piece of missing information is whether significant regional variations in inappropriate prescribing practices exist across VA facilities. Regional variation often reflects discrepancies in the implementation of best practices, and comparisons of high versus low performing sites may identify mechanisms for improving performance.²¹ A recent analysis of national Medicare data revealed significant regional variation, with the highest concentration of potentially inappropriate prescribing found in the Southern US and the lowest rates in the Northeast and upper Midwest.²² Similar geographic distributions of prescribing quality have been previously reported among older adults in both outpatient and inpatient settings.^{23,24} The most direct interpretation of these findings are differences in provider-level characteristics, where different approaches to pharmacotherapy lead to patients in low performing regions being exposed to riskier medication regimens. However, prescribing is also influenced by system-level factors such as differences in health system organization, access to prescription drug benefits, and higher copayments for newer (and potentially safer) medications. As regional variation in many of these system-level factors is eliminated, including use of a national formulary, VA presents a unique opportunity to study prescribing quality. If the extent of regional variation is significantly lower in VA, or follows a different pattern, it is likely that system-level factors play an important role in driving regional differences in prescribing quality. However, if regional variation patterns extend to VA, then provider-level factors may play a more substantial role in driving prescribing quality.

In addition to regional differences, a focal point for VA has been ensuring equal health care access and quality for rural veterans. Approximately 3.3 million veterans, 41% of total VA enrollees, live in rural areas.²⁵ Rural residence has been associated with problems accessing health care, worse health status, and higher prevalence of chronic diseases.²⁶⁻³⁰ While there do not appear to be important disparities in access to prescription medications,³¹ some

studies suggest that rural residents may be at increased risk for inappropriate prescribing.^{23,32} Perhaps most importantly, rural residence has been linked recently to increased risk for fatal adverse drug reactions, which may be mediated by differences in prescribing quality.³³ However, the potential impact of rurality on prescribing quality has not been sufficiently studied.

The objective of this study was to fill these important knowledge gaps by characterizing geographic variation in potentially inappropriate prescribing practices among older adults in VA, as measured by 4 separate indicators of prescribing quality. To accomplish this objective, we examined prescribing quality variation across 4 major US geographic regions, and we compared rural versus urban residence.

METHODS

National VA data for fiscal year (FY) 2007 were obtained from the Austin Information Technology Center. This research was approved by the University of Iowa institutional review board and the Iowa City Veterans Affairs Research and Development Committee.

Patients

The target population was older adults receiving outpatient primary care services and medications from VA. Patients were selected if they were 65 years or older, had at least one outpatient VA primary care visit, and demonstrated regular use of outpatient VA medications during FY 2007. Primary care visits were identified using clinic stop codes from the Medical SAS Outpatient datasets.³⁴ Regular medication use was defined by a history of outpatient medication fills where the days supply periods spanned at least 240 of the 365 days of FY 2007.³⁵ Patients were excluded if they had a nursing home admission during FY 2007.

Prescribing Quality Measures

Four prescribing quality measures were examined and all were patient-level dichotomous indicators for the presence of a potentially inappropriate prescribing practice during FY 2007. The first indicator was drugs to avoid, as defined by Zhan criteria.³⁶ The Zhan criteria consist of medications to be avoided in older adults irrespective of dose, duration and concurrent disease states, as adapted from the 1997 Beers criteria.⁸ The second prescribing quality indicator was drugs to avoid, independent of diagnoses or conditions, according to Fick criteria.⁹ To eliminate the overlap between criteria sets, we limited Fick criteria to those not included in the Zhan criteria. As the Zhan criteria are essentially a subset of the Fick criteria, we could have elected to use just the Fick criteria. However, we retained the Zhan criteria as a separate quality indicator for several reasons. First, Zhan criteria drugs have been labeled as inappropriate for older adults since 1997 and have had more opportunity for dissemination into practice, whereas the new criteria introduced by Fick and associates have been available only since 2003. Second, it is possible that the newly added Fick criteria are less clinically significant than the older Zhan criteria. Third, the existing prescribing quality data for VA are based on Zhan criteria.^{19,37} Finally, the decision to use 2 mutually exclusive criteria sets allowed us to ascertain whether variation in prescribing quality was consistent across multiple independent indicators.

The third prescribing quality indicator was therapeutic duplication, defined as concurrent use of more than one medication from a modified VA drug class.^{17,38} The fourth prescribing quality indicator was the concurrent use of 2 medications with the potential to produce clinically significant drug-drug interactions, according to a leading reference.³⁹ This resource for drug-drug interactions has been used as a prescribing quality indicator in prior

work.¹⁷ It is essential for the therapeutic duplication and drug-drug interaction indicators that the implicated medications were administered concurrently, and not given sequentially. A validated algorithm was applied to establish a cross-sectional active drug list for each patient at the midpoint of FY 2007, and thereby yielded medications that were taken concurrently at a point in time.⁴⁰ The therapeutic duplication and drug-drug interaction indicators were determined from these cross-sectional drug regimens.

Geographic Variables

Rural or urban residence was determined according to the VA U/R/H designation. This method uses the latitude and longitude of the veteran's residential address to assign him or her to 1 of 3 groups: urban, rural, or highly rural.⁴¹ VA considers veterans living in census tracts designated as Urbanized Areas (identified populations of at least 50,000 by the US Census Bureau) as urban. Veterans living in counties with average population density of < 7 residents per square mile are considered highly rural. The remaining veterans failing to meet either of these designations are considered rural. For this analysis, rural and highly rural veterans were grouped together. Based on where they received care, each veteran was assigned to a Veteran Integrated Service Network (VISN) and aggregated to larger geographic regions based on the best overlapping boundaries with US census regions. VISNs 1, 2, 3, and 4 were assigned to the Northeast region; VISNs 10, 11, 12, 15, and 23 to the Midwest; VISNs 5, 6, 7, 8, 9, 16, and 17 to the South; and VISNs 18, 19, 20, 21, and 22 to the West.

Statistical Analysis

Odds ratios and 95% confidence intervals were estimated by multiple logistic regression using SAS procedure LOGISTIC (SAS version 9.2, SAS Institute Inc., Cary, North Carolina). All odds ratios were adjusted for age and sex to account for differences in prescribing quality measures across regions that could be attributable to interregional variation in these demographic characteristics.

RESULTS

Patients

A total of 1,959,212 older adult veterans had at least one outpatient VA primary care visit in FY 2007. Of these, 1,565,492 (79.9%) were also regular VA medication users. After excluding 9,434 (0.6%) patients with missing geocoding data and 6,234 (0.4%) patients with nursing home admissions, a total of 1,549,824 veterans were selected. The mean age was 75.8 (S.D. = 6.4) years, with an interquartile range of 71-81, and 27,419 (1.8%) were women. The mean number of active medications at the midpoint of the fiscal year (April 1, 2007) was 5.5 (S.D. = 3.3).

Prescribing Quality Violations

The most common violations for each prescribing quality indicator are found in Table 1. The most common Zhan criteria violation was oxybutynin, which was taken by 3.4% of older adult veterans during FY2007. Common Fick criteria violations included doxazosin (3.8%), high-dose ferrous sulfate (2.9%), and high-dose short-acting benzodiazepines (2.7%). Concurrent use of 2 or more antidepressants (2.0%) was the most frequent therapeutic duplication, followed by antiulcer medications (1.1%) and short-acting beta-agonists (0.8%). The most frequent drug-drug interaction pair was concurrent use of simvastatin and verapamil (0.9%).

Prescribing Quality Variation by Region

Prescribing quality indicator violations were common nationally, including 17.9% of veterans who received a Zhan criteria medication during FY 2007 (Table 2). However, significant regional differences were observed, with the lowest prevalence in the Northeast (13.2%), and increasing across the Midwest (15.9%) and West (18.9%), and the highest prevalence in the South (21.2%). Fick criteria violations were also common nationally (16.5%), and they displayed the same regional pattern with the lowest prevalence rates in the Northeast (13.3%) and highest rates in the South (18.9%). Therapeutic duplication was less common, with a national prevalence of 6.4% and a pattern of regional variation similar to Zhan and Fick criteria. The final prescribing quality indicator, drug-drug interactions, was the least common nationally (3.75%), displayed the least amount of regional variation, and had a different pattern of variation. Drug interaction prevalence was significantly higher in the South than other regions, but it did not differ between Northeast and Midwest regions, and it was significantly lower in the West than any other region.

Prescribing Quality by Rural Residence

A total of 676,870 (43.7%) older adult veterans were rural residents. When compared to their urban counterparts, rural veterans were significantly more likely to have a prescribing quality indicator violation across all 4 measures (Table 3). The greatest difference was observed for Zhan criteria, where violation prevalence was 18.7% among rural residents, compared to 17.2% among urban residents (adjusted OR = 1.10). Smaller but statistically significant odds-ratios were observed for the remaining prescribing quality indicators.

Recognizing that the impact of rurality may differ across geographic regions, separate rural-urban comparisons were conducted for individual US regions (Table 4). Consistent with national findings, rural veterans were at increased risk for prescribing quality violations in the South and Northeast. For example, the Zhan criteria odds-ratios were 1.22 and 1.11 for the South and Northeast, respectively. However, prescribing quality was equivalent between rural and urban veterans in the Midwest, and rural veterans were at lower risk in the West. Importantly, the pattern and magnitude of regional variation in urban-rural differences were generally consistent across all 4 prescribing quality measures.

DISCUSSION

Significant regional variation in prescribing quality was observed among older adults receiving primary care in VA. The frequency of inappropriate prescribing was highest in the South and lowest in the Northeast. This pattern mirrors a recent study among Medicare beneficiaries, using data from the same time period.²² Furthermore, this pattern has remained consistent over time. A study using 1999 data for community dwelling elders found older adults in the New England and Middle Atlantic census regions had significantly lower odds of inappropriate prescribing compared to the East South Central region.²³ Similar regional patterns have been observed in the inpatient setting.²⁴ The consistency of regional variation over time, across setting, between VA and non-VA systems, and among different quality measures, likely reflects differences in the general climate of clinical practice that extend beyond specific institutions or health care systems.

In addition to geographic region, prescribing quality varied significantly by rural residence. Potentially inappropriate prescribing was significantly more common among rural veterans across 4 independent quality indicators. However, the magnitude of the differences was likely to be of modest clinical significance. The largest difference was seen with Zhan criteria, where 18.7% of rural veterans received a potentially inappropriate medication, compared to 17.2% of urban veterans. Prior studies of rural-urban differences in prescribing

quality have had mixed results, which could be explained by an apparently small effect size.^{23,32,36,42,43} It is unlikely that rural veterans experience significant barriers to obtaining medication refills in VA due to the mail delivery system where refills can be requested in-person, by phone, or online. However, disparities in medication access could still arise from barriers to accessing the physicians and other providers who write prescriptions. This concern is the basis for most studies of rural-urban differences, where quality measures typically reflect the absence of some health care service. In contrast, all 4 measures of prescribing quality examined in this study reflect access to treatment that should *not* have been received. Therefore, our findings cannot be attributed to impaired health care access, but perhaps they could be described as diminished access to high-quality care. For example, our findings could be explained by restricted access to specialty geriatrics care, given that 90% of geriatricians are located in urban areas.⁴⁴

Looking beyond the national average, we further examined the impact of rural residence within specific geographic regions and documented a clinically significant interaction. Consistent with the national average, rurality was associated with greater rates of potentially inappropriate prescribing in the Northeast and the South. However, rural veterans were at significantly lower risk for inappropriate prescribing in the West, and they faced equivalent risk in the Midwest. This observation has important implications for future research. Most studies examine rurality as a single variable and assume a constant effect across geographic regions. Based on this assumption we would have concluded that rural veterans were at an increased risk for inappropriate prescribing. However, we discovered that rural residence could be associated with increased, decreased or equivalent risk, depending on the region. Therefore, national implementation of policy or interventions could be misguided and inefficient, when potential rural disparities are limited to specific geographic regions. Only one prior study has similarly examined regional differences in the impact of rural residence on health care quality.⁴⁵ In parallel to our findings, this study found that rural individuals received lower quality diabetes care in the South but equivalent or higher quality care in other geographic regions. The authors attributed this finding to the higher proportion of non-whites in the South, but they could not provide direct analytic support for this hypothesis. The extent to which racial disparities could explain our findings is unknown, and it is an important avenue for future research.

There are several important limitations to consider. First, our study was limited to older adults, and variation patterns may be different for younger populations. While further examination of younger patient groups is warranted, older adults represent a key population of interest for prescribing quality. Second, our study was limited to veterans, and thus predominantly comprised men. However, a prior study of Medicare beneficiaries found similar regional patterns in prescribing quality during the same time period.²² Therefore, our findings do not seem to apply only to men, or to individuals receiving care in VA. A third limitation is the use of prescribing quality indicators, derived from electronic administrative data, as a measure of inappropriate prescribing. These indicators do not account for individual differences and thus reflect prescribing practices that can only be considered to be potentially inappropriate. While it has been argued that these indicators may have insufficient specificity for patient-level analyses,⁴⁶ they can still serve as valid proxy measures of inappropriate prescribing at larger aggregate levels.⁴⁷ As long as the positive predictive value does not vary systematically by geographic region, then variations in *potentially* inappropriate prescribing will mirror underlying variations in *actual* inappropriate prescribing. Furthermore, the observation of similar geographic variation patterns across 3 independent indicators supports the validity of our findings. The one indicator that did not follow the same pattern of regional variation was drug-drug interactions. It is noteworthy that VA employs drug-drug interaction screening software that is common across all VA medical centers, which could explain why less regional variation

was observed with this indicator. However, there is still the opportunity for variation arising from differences in how clinicians respond to the warnings presented by the software. Finally, we were limited to prescription medications supplied through the VA and thus did not have access to information concerning medications acquired through other sources such as Medicare part D, private insurance, or purchased out-of-pocket.

In summary, we observed clinically meaningful regional variation in prescribing quality across VA, consistent with a prior report involving Medicare beneficiaries.²² This suggests that regional variation in prescribing quality is not a function of specific system-level characteristics of VA, and interventions designed to reduce variation may struggle against endemic regional differences in prescribing practices. On the other hand, the closed nature of the VA system and the standardized electronic medical record may make interventions to improve prescribing quality more feasible than in non-VA systems. Our second key finding was that rural veterans were at increased risk for inappropriate prescribing overall, but that this effect varied by region. This finding suggests that the impact of rurality on health care access and quality is complex, and that being a rural veteran in the West is different from being a rural veteran in the South. Further, the one-size-fits-all approaches to ensuring access to high-quality health care for rural veterans may not be effective, and in many regions such approaches may be unwarranted. While this study documented important variations in prescribing quality, the underlying factors driving these trends remain unknown, and they are a vital area for future research affecting older adults in both VA and non-VA health systems.

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Table 1

Most Common Violations for Each Prescribing Quality Indicator

Zhan Criteria, Drugs to Avoid	%	Therapeutic Duplication	%
1. Oxybutynin	3.4%	1. Antidepressants	2.0%
2. Cyclobenzaprine	2.2%	2. Antiulcer medications	1.1%
3. Dipyridamole	2.2%	3. Short-acting beta-agonists	0.8%
4. Amitriptyline	2.0%	4. Opioid analgesics	0.6%
5. Propoxyphene	1.9%	5. Sedative-hypnotics	0.4%
Fick Criteria, Drugs to Avoid^a	%	Drug Interaction	%
1. Doxazosin	3.8%	1. Simvastatin-verapamil	0.9%
2. Ferrous sulfate > 325 mg/d	2.9%	2. Simvastatin-amiodarone	0.7%
3. Short-acting benzodiazepines ^b	2.7%	3. Aspirin-warfarin	0.4%
4. Clonidine	2.1%	4. Atenolol-valsartan	0.4%
5. Daily fluoxetine	2.0%	5. Aspirin-ibuprofen	0.4%

^aIncludes only drugs to avoid, independent of diagnoses or conditions, that are not included in the Zhan criteria

^bShort-acting benzodiazepines in excess of the following daily doses: lorazepam, 3mg; oxazepam, 60mg; alprazolam, 2 mg; temazepam, 15mg; triazolam, 0.25mg

Table 2
Variation in Prescribing Quality Among Older Adult Veterans By Geographic Region

Indicator	National N=1,549,824 N (%)	Regional Differences			
		Northeast N=297,651 N (%)	Midwest N=406,152 N (%)	West N=261,539 N (%)	South N=584,482 N (%)
Zhan Criteria	277,148 (17.9%)	39,383 (13.2%) Reference	64,478 (15.9%) 1.23 (1.22, 1.25)	49,438 (18.9%) 1.51 (1.49, 1.53)	123,849 (21.2%) 1.75 (1.73, 1.77)
Fick Criteria ^b	256,180 (16.5%)	39,479 (13.3%) Reference	58,541 (14.4%) 1.11 (1.09, 1.12)	47,582 (18.2%) 1.47 (1.44, 1.49)	110,578 (18.9%) 1.54 (1.52, 1.56)
Therapeutic Duplication	99,672 (6.4%)	14,741 (5.0%) Reference	22,498 (5.5%) 1.11 (1.09, 1.13)	19,531 (7.5%) 1.49 (1.46, 1.53)	42,902 (7.3%) 1.47 (1.44, 1.50)
Drug-drug Interaction	58,144 (3.75%)	11,049 (3.71%) Reference	15,151 (3.73%) 1.00 (0.98, 1.03)	8,806 (3.37%) 0.90 (0.87, 0.92)	23,138 (3.96%) 1.06 (1.04, 1.08)

^aOR = odds ratio in relation to Northeast region, adjusted for age and sex

^bIncludes only drugs to avoid, independent of diagnoses or conditions, that are not included in the Zhan criteria

Table 3

Prescribing Quality Among Older Adult Veterans By Rural and Urban Residence

Indicator	Urban (N=872,954) N (%)	Rural (N=676,870) N (%)	OR (95% CI)^a
Zhan Criteria	150,298 (17.2%)	126,850 (18.7%)	
	Reference		1.10 (1.09, 1.11)
Fick Criteria ^b	142,597 (16.3%)	113,583 (16.8%)	
	Reference		1.04 (1.03, 1.05)
Therapeutic Duplication	54,408 (6.2%)	45,264 (6.7%)	
	Reference		1.05 (1.04, 1.06)
Drug –drug Interaction	32,357 (3.71%)	25,787 (3.81%)	
	Reference		1.020 (1.003, 1.037)

^aOR = odds ratio in relation to urban residence, adjusted for age and sex

^bIncludes only drugs to avoid, independent of diagnoses or conditions, that are not included in the Zhan criteria

Table 4

Regional Variation in Associations of Rural Residence and Prescribing Quality

<i>a</i> Odds-ratios (95% CI) for Rural versus Urban Residence				
Indicator	Northeast	Midwest	West	South
Zhan Criteria	1.11 (1.09, 1.14)	0.97 (0.95, 0.99)	0.89 (0.87, 0.91)	1.22 (1.20, 1.23)
Fick Criteria ^{<i>b</i>}	1.02 (1.00, 1.04)	0.99 (0.97, 1.01)	0.96 (0.94, 0.98)	1.09 (1.07, 1.10)
Therapeutic Duplication	1.07 (1.03, 1.11)	0.99 (0.96, 1.01)	0.88 (0.86, 0.91)	1.15 (1.12, 1.17)
Drug –drug Interaction	0.97 (0.93, 1.01)	0.97 (0.94, 1.00)	0.90 (0.86, 0.94)	1.11 (1.08, 1.14)

^{*a*}Odds ratio for rural versus urban residence, adjusted for age and sex

^{*b*}Includes only drugs to avoid, independent of diagnoses or conditions, that are not included in the Zhan criteria