Geographic Variation in Chronic Obstructive Pulmonary Disease Exacerbation Rates

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BACKGROUND: Exacerbations are important disease events for patients with chronic obstructive pulmonary disease (COPD) as they are relatively frequent, result in significant resource use and can indicate worsening disease. Little is known about variation in COPD exacerbation rates across a health system in various geographic regions.

OBJECTIVE: To compare COPD exacerbation rates by regional service networks called Veterans Integrated Service Network (VISN) in the Veterans Health Administration (VA) system.

DESIGN: Retrospective, observational study.

SUBJECTS: Patients with a COPD diagnosis from October 1999 to September 2000 with follow-up to September 2002.

MEASUREMENTS: Acute exacerbations of COPD during the baseline and follow-up periods.

RESULTS: A total of 198,981 patients were identified. Average exacerbation rate at baseline was 0.503 events per person per year. In the follow-up period, there were 187,686 exacerbations experienced by 87,494 persons (44.0% of cohort). During follow-up, the average adjusted exacerbation rate was 0.589 per person per year and varied from 0.335 (95% CI, 0.328–0.342) in VISN 1 to 0.749 (95% CI, 0.735–0.763) in VISN 9. Using the median rate of exacerbation during the baseline period as the referent, 9 VISNs had lower adjusted rate ratios and 12 VISNs had higher adjusted rate ratios in the follow-up period.

CONCLUSIONS: Geographic variation in the VA VISN system supports evidence that the medical care system including provider factors, and less so patient factors, affect COPD exacerbations. Understanding the reasons underlying this variation in COPD exacerbation rates may lead to improvements in future care and outcomes.

KEY WORDS: COPD; exacerbation; geographic variation; outcomes.

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BACKGROUND

Acute exacerbations of chronic obstructive pulmonary disease (COPD) are important events to both patients and providers. Acute exacerbations are characterized by recent onset of deterioration in patients' clinical and functional states caused by worsening of COPD. These acute events lead to increased medication utilization, outpatient physician visits, emergency department visits, and hospitalizations, which all contribute to the overall burden of COPD. Acute exacerbations with hospitalizations, in particular, account for a large proportion of the direct health care costs associated with COPD.^{1,2} There is also evidence that acute exacerbations may accelerate the decline in lung function as lung function may not recover completely after an exacerbation.^{3–5} Additionally, patients who have frequent exacerbations have a reduced quality of life.^{6–9}

In 2003, there were more than 500,000 patients with a COPD diagnosis within the Veterans Health Administration (VA) system. The majority of these patients were cared for by general medicine practitioners.¹⁰ The VA system is divided into regional service networks, called Veterans Integrated Service Networks (VISN) based on geographic location. In 2000, there were 22 VISNs in the VA system that provided integrated care to veterans within their geographic location. In 1999, Ashton et al. reported significant geographic variation in health care utilization (i.e., length of hospitalizations and number of clinic visits) for several chronic diseases including COPD.¹¹ In addition, there was significant variation in the quality of care for acute exacerbations of COPD in the inpatient setting across 360 hospitals in the United States.¹²

Little is known about regional and health system variation in the outcomes of COPD, especially COPD exacerbations. Examining variation in COPD exacerbation rates may help identify factors associated with lower rates of exacerbations and ultimately improve the quality of COPD care. Because the VA is the largest integrated health care network in the United States, it provides a distinct opportunity to investigate geographic variation in COPD exacerbation rates. The objective of this analysis was to compare COPD exacerbation rates across VISNs in the VA system.

METHODS

This was an observational study approved by the Human Studies Subcommittee of the Hines VA Hospital.

We identified a cohort of patients with a COPD diagnosis during the baseline period, which was between October 1,

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1999 and September 30, 2000 (Fiscal Year [FY] 2000), in the VA administrative data. Patients were followed for events from October 1, 2000 through September 30, 2002. To be included, patients met the following criteria: 1) had at least 1 visit with the primary ICD-9 code for COPD (ICD-9 491.x, 492.x, 496) in FY 2000; 2) received VA care at least once before FY 2000; 3) received outpatient prescriptions from the VA; and 4) were alive as of October 1, 2000.

Exacerbations

Acute exacerbations were identified using a combination of inpatient, outpatient, and pharmacy data. Exacerbations were defined based on the presence of an ICD-9 code related to COPD and/or specific to an exacerbation (ICD-9 490, 491, 491.0, 491.1, 491.2, 491.21, 491.22, 491.8, 491.9, 492.x, 486) with one of the following: 1) an inpatient hospitalization; 2) an emergency department visit; or 3) an outpatient visit with either an oral steroid or antibiotic prescription dispensed within 5 days of the visit. To avoid identifying chronic users of steroids and antibiotics as having an acute exacerbation, a new prescription had to be filled within 5 days of the outpatient event and the days supply for that prescription must have been less than 30 days. Outpatient visits that included a diagnosis for infections other than respiratory infections (e.g., cellulitis) were not included as an exacerbation. Exacerbations were assumed to last 30 days and after 30 days a new acute exacerbation could be identified.^{13,14}

Covariates

Covariates measured during the baseline period included: patient characteristics (e.g., sex, age, race), comorbidities (e.g., hypertension [ICD-9, 401–405], diabetes [ICD-9, 250], heart disease [ICD-9, 410–414], gastrointestinal [GI] disease [ICD-9, 530–537], musculoskeletal problems [ICD-9, 710–739], cancer [ICD-9, 140–208]), and baseline health care utilization (i.e., primary care contacts, pulmonary specialist contacts, hospitalizations).

Climate data were obtained through the U.S. Department of Commerce National Climatic Data Center (National Oceanic and Atmospheric Administration Satellite and Information Service website).¹⁵ Climate categories were created from annual average temperatures and the annual average range in temperatures. Quartiles were created for each of the measures; categories were also created that divided the measures in 5-degree gradients. Geographic region of the country (e.g., Northeast, South, Midwest, and West) and latitudes and longitudes were considered as covariates because of the difference in climate.

We included influenza-like illness rates as a covariate in the analysis to control for regional variation in acute respiratory illnesses that were not classified as COPD exacerbations. Our intent was to control for differences in flu and flu-like illness that could potentially impact the rate of COPD exacerbations that were identified. The influenza-like illness rates were obtained from weekly surveillance reports from the Center for Disease Control and Prevention (CDC) (<http://www.cdc.gov/flu/weekly/fluactivity.htm>). The rates reported by the CDC were summarized by VISN based on geographic location. The average annual rate for each region was determined based on

the proportion of physician visits associated with the influenza-like illness.

Analysis

Patient characteristics were summarized from baseline year data. Counts and percentages were used to describe categorical variables. In evaluating exacerbations, we compared the bivariate relationship between baseline covariates and exacerbation rates in the follow-up period. Because the focus was on exploring regional variation in exacerbation rates, VISN was our primary covariate of interest. The outcome of interest, COPD exacerbations, represents a nonnegative count with overdispersion and a frequency of zero counts significantly higher than that expected for a Poisson distribution. Therefore, we used negative binomial regression models to compare the rate of exacerbations in the follow-up period while controlling for other covariates.^{16–18} Covariates that had a significant bivariate relationship with follow-up exacerbation rates and/or changed the point estimates for 25% of the VISNs by more than 10% were included in the final model. Covariates included in the final model were baseline exacerbation rate, comorbidities, race, age, health care utilization, and climate (i.e., average annual temperature quartiles and latitude). In the negative binomial regression analysis, the standard errors were corrected using the Huber/White/sandwich estimate of variance in STATA to account for within VISN correlation. A *p* value less than 0.05 was considered statistically significant.

RESULTS

There were 198,981 patients identified for inclusion in the analysis. Of this cohort, 97.9% were male, 67.6% were White, and 77.9% were over 60 years of age (Table 1). The plurality of patients identified resided in the South (*N*=84,338 (42.4%)). Baseline health care utilization is shown in Table 2. During the baseline period, 97.8% of the patients had at least 1 primary care visit and 35.9% of patients had at least 1 pulmonary specialist visit.

Figure 1 provides a map of the United States indicating the VISNs.¹⁹ The sample size within VISNs ranged from 3,654 (VISN 5) to 19,597 (VISN 16). During the baseline year, 108,174 exacerbations were experienced by 68,190 persons. The baseline exacerbation rate was 0.503 events (95% CI, 0.499–0.507) per person/year. There was nearly a twofold difference in baseline exacerbation rates across VISNs, ranging from 0.320 (95% CI, 0.304–0.335) to 0.606 (95% CI, 0.588–0.624) exacerbations per person/year. At baseline there was no significant relationship between exacerbation rates and influenza-like illness when stratified by low (blue), medium (yellow), and high (red) rates of influenza-like illness (Fig. 2).

The adjusted model for exacerbation rates during follow-up included baseline exacerbation rate, comorbidities, age, race, health care utilization and climate. Table 3 shows unadjusted and adjusted rate ratios for the covariates in the final model. During follow-up, the rate of exacerbations was higher among older age groups and increased as the number of exacerbations during the baseline period increased.

During the follow-up period, there were 187,686 exacerbations experienced by 87,494 persons (44.0% of total cohort). After controlling for baseline exacerbation rates, race, age,

Table 1. Baseline Characteristics

	N (%)
N	198,981 (100)
Male	194,695 (97.9)
Age (years)	
<50	10,762 (5.4)
50–59	33,249 (16.7)
60–69	59,804 (30.1)
70–79	77,029 (38.7)
80–89	17,661 (8.9)
90+	476 (0.2)
Race	
Black	15,042 (7.6)
Hispanic	3,734 (1.9)
White	134,433 (67.6)
Other	781 (0.4)
Unknown	44,991 (22.6)
Comorbidities	
Hypertension	114,207 (57.4)
Heart Disease	66,293 (33.3)
Diabetes	49,810 (25.0)
Gastrointestinal Disease	49,461 (24.9)
Musculoskeletal Problems	92,734 (46.6)
Cancer	30,384 (15.3)
Baseline Exacerbation (episodes)	
0	134,865 (67.8)
1	41,625 (20.9)
2	14,143 (7.1)
3	5,195 (2.6)
4+	3,153 (1.6)
Latitude	
≥45°	11,228 (5.6)
40°–<45°	61,071 (30.7)
35°–<40°	62,173 (31.3)
<35°	64,509 (32.4)
Region	
Northeast	30,435 (15.3)
South	84,338 (42.4)
Midwest	50,013 (25.1)
West	32,666 (16.4)
Other	1,529 (0.8)

comorbidities, health care utilization, and climate, the average exacerbation rate was 0.589 per person/year and varied from 0.335 (95% CI, 0.328–0.342) in VISN 1 to 0.749 (95% CI, 0.735–0.763) in VISN 9 (Fig. 3). Compared to the VISN with

Table 2. Baseline Healthcare Utilization

	N (%)
N	198,981 (100)
Primary Care Contacts (visits)	5.3 (5.9)*
0	4,349 (2.2)
1–3	84,438 (42.4)
4–7	73,375 (36.9)
8–11	21,902 (11.0)
12+	14,917 (7.5)
Pulmonary Contacts (visits)	0.8 (1.9)*
0	127,451 (64.1)
1	36,428 (18.3)
2–3	24,553 (12.3)
4+	10,549 (5.3)
Hospitalization (admissions)	0.3 (0.8)*
0	162,249 (81.5)
1	23,076 (11.6)
2	7,700 (3.9)
3	3,145 (1.6)
4+	2,811 (1.4)

*Mean (SD)

Figure 1. Map of Veterans Integrated Service Networks. On January 2002, VISN 13 and VISN 14 merged to create VISN 23. VISN 13 included facilities in Minnesota, North Dakota, and South Dakota and VISN 14 included facilities in Iowa and Nebraska.

the median exacerbation rate at baseline, the rate ratio of exacerbations during follow-up ranged from 0.63 in VISN 1 to 1.28 in VISN 13 (Table 4). There were 9 VISNs that had lower rates of exacerbations during follow-up than the VISN with the baseline median exacerbation rate and there were 12 VISNs that had higher exacerbation rates.

DISCUSSION

Examining regional variation in health outcomes can help highlight care practices that may be associated with better outcomes, and can potentially lead to improvement in the overall care of patients. Our objective in this analysis was to examine rates of COPD exacerbations across the VA system. We found more than a twofold difference in exacerbation rates between the VISN with the lowest and highest annual exacerbation rates, and this difference remained even after controlling for factors associated with COPD exacerbations.

It may not be surprising that differences in rates of exacerbations exist across a wide geographic area like the United States where there are population and climate differences. Previous studies have found substantial geographic variation in outcomes for different disease states and procedures such as acute coronary syndrome,^{20–22} asthma,²³ and

Figure 2. Baseline exacerbation rate by VISN and influenza-like illness rate. Baseline exacerbation rate per year by VISN. Influenza-like illness rates by increasing rate as follows: Blue=low, Yellow=medium, Red=high.

Table 3. Association Between Patient Characteristics and Follow-up Exacerbations

	Unadjusted RR (95%CI)	Adjusted RR (95% CI)
Age (years)		
<50	1	1
50–59	1.23 (1.18–1.28)	1.19 (1.14–1.24)
60–69	1.41 (1.36–1.47)	1.32 (1.27–1.37)
70–79	1.44 (1.38–1.49)	1.33 (1.28–1.39)
80–89	1.64 (1.57–1.72)	1.41 (1.35–1.48)
90+	1.56 (1.33–1.83)	1.63 (1.39–1.92)
Race		
White	1	1
Hispanic	0.92 (0.87–0.97)	0.94 (0.87–1.01)
Black	1.08 (1.05–1.11)	1.03 (1.00–1.06)
Other	0.98 (0.86–1.10)	0.94 (0.82–1.08)
Unknown	0.57 (0.56–0.58)	0.71 (0.70–0.73)
Baseline Exacerbation		
0	1	1
1	2.49 (2.44–2.53)	1.93 (1.89–1.97)
2	4.21 (4.11–4.30)	2.79 (2.72–2.87)
3	6.12 (5.91–6.33)	3.47 (3.34–3.61)
4+	8.54 (8.12–8.98)	4.70 (4.50–4.95)
Comorbidities		
Hypertension	1.13 (1.11–1.15)	0.96 (0.95–0.98)
Heart Disease	1.41 (1.38–1.43)	1.07 (1.05–1.09)
Diabetes	1.20 (1.18–1.23)	1.02 (1.00–1.03)
Gastrointestinal Disease	1.35 (1.32–1.37)	1.04 (1.02–1.06)
Musculoskeletal Problems	1.23 (1.22–1.25)	1.04 (1.02–1.05)
Cancer	1.56 (1.53–1.59)	1.23 (1.20–1.25)
Latitude		
≥45°	1	1
40°–<45°	0.87 (0.84–0.90)	0.89 (0.85–0.93)
35°–<40°	1.09 (1.05–1.13)	1.10 (1.05–1.16)
<35°	0.95 (0.91–0.98)	1.05 (0.99–1.12)
Average Annual Temperature		
<46°	1	1
46°–51°	1.07 (1.04–1.11)	1.08 (1.05–1.11)
>51°–59°	1.25 (1.21–1.29)	1.03 (0.99–1.07)
>59°	1.11 (1.08–1.15)	0.96 (0.92–1.11)
Primary Care Contacts		
0	1	1
1–3	0.79 (0.74–0.83)	0.98 (0.92–1.14)
4–7	1.41 (1.34–1.50)	1.37 (1.29–1.45)
8–11	2.36 (2.23–2.50)	1.66 (1.56–1.77)
12+	3.24 (3.05–3.44)	1.86 (1.75–1.99)
Pulmonary Specialist Contacts		
0	1	1
1	1.48 (1.45–1.51)	1.22 (1.19–1.24)
2–3	2.23 (2.18–2.28)	1.50 (1.47–1.54)
4+	3.14 (3.05–3.23)	1.73 (1.68–1.79)
Hospitalization		
0	1	1
1	2.19 (2.14–2.23)	1.10 (1.07–1.13)
2	3.40 (3.30–3.51)	1.20 (1.16–1.24)
3	3.61 (3.45–3.79)	1.10 (1.05–1.16)
4+	5.33 (5.09–5.59)	1.29 (1.22–1.36)

major surgery for degenerative diseases of the hip, knee, and spine.²⁴ This is also consistent with studies that have evaluated variation in treatment and outcomes for COPD.^{25–28} Oftentimes these differences persist even when controlling for case-mix and risk factors across the different regions. This was true in our analysis of patients with COPD, where even after controlling for factors related to COPD exacerbation rates such as climate, age, comorbidities, and baseline exacerbation rates (a proxy for severity), substantial differences in exacerbation rates persisted. Therefore, variation in exacerbation rates

Figure 3. Adjusted exacerbation rates in follow-up period by VISN. Dashed line represents overall mean exacerbation rate per year.

appears to be related to factors other than differences in patient factors and climate.

An additional explanation for the regional variation observed in this population could be regional variation in provider care. For example, in patients with myocardial infarctions (MI), providers in New England have been shown to have higher rates of aspirin and beta-blocker use.²¹ This has been presented as a potential explanation for better outcomes for patients with an MI in New England than in other parts of the United States. We also found that exacerbation rates were lowest in New England (VISN 1) relative to other VISNs, and it is possible that treatment patterns for COPD could be different in this region. For instance, regional variation in influenza vaccination or treatment for COPD (e.g., long-acting anticholinergics, long-acting beta agonists, inhaled corticosteroids) could impact COPD exacerbation rates and account for the observed differences. An important next step is to look more closely at treatment patterns and other health system factors

Table 4. Adjusted Rate Ratios of COPD Exacerbations for Each VISN During Follow-up Compared to VISN 8

VISN	RR (95% CI)
1	0.63 (0.56–0.70)
2	0.97 (0.86–1.08)
3	0.82 (0.73–0.94)
4	0.87 (0.79–0.95)
5	0.88 (0.79–0.99)
6	1.05 (0.96–1.15)
7	1.00 (0.93–1.09)
8 (referent)	1
9	1.11 (1.03–1.21)
10	1.13 (0.98–1.30)
11	0.94 (0.86–1.03)
12	1.01 (0.91–1.11)
13	1.28 (1.13–1.44)
14	0.97 (0.88–1.08)
15	1.03 (0.96–1.12)
16	1.01 (0.94–1.08)
17	0.90 (0.84–0.97)
18	0.96 (0.88–1.05)
19	1.04 (0.93–1.18)
20	1.16 (1.05–1.29)
21	1.05 (0.92–1.19)
22	1.00 (0.85–1.18)

that differ for COPD care in the VA to better understand reasons for the regional variation.

An advantage of conducting this analysis in a single health care system, like the Veteran's Health Administration, is that it may help remove some of the variation caused by various administrative and incentive structures across different health care systems. For example, VA physicians were salaried with financial incentives that were unaffected by patterns of practice during the time of this study. In addition, the VA patient population may be more homogeneous than other national samples, partly owing to eligibility for care, which gives highest priority to veterans with conditions related to military service and low income status. Given these factors, we may expect similar outcomes in COPD patients.

However, there are additional considerations about the VA health care system and assessment of regional variation. The primary covariate of interest was VISN, which represents both a geographically and administratively linked area. Thus, providers within a VISN may be more likely to provide similar care because they are working under the same set of rules. These regional networks, however, may not translate to similar patterns of care nationally as each network has its own administrative structure in place, including things like formularies and number and type of providers. Given this administrative structure, regional variation, as we and others have found, in studies of the VA health care system may not be particularly surprising.^{11, 22, 29-32}

There are limitations in our study that need to be acknowledged. First, the inclusion criteria included veterans with COPD, but does not account for severity of disease. More severe disease has been associated with more COPD exacerbations, which is likely to be associated with increased health care utilization.³³ We attempted to control for disease severity in the analysis by using markers of disease severity during the baseline period, including the baseline exacerbation rate and health care utilization. Second, the diagnosis of COPD was based on ICD-9 codes and not validated with spirometry. Previous studies have shown limited spirometry use in the diagnosis of COPD.¹⁰ In practice, the majority of physicians seem to be diagnosing and managing COPD based on symptoms alone. Thus, our population may include patients that are misclassified as having COPD; however, these results are reflective of real world practice patterns and applicable to patients with a clinical diagnosis of COPD. Third, there were differences in the age groups by VISN as older veterans lived in southern VISNs. Older patients may have more comorbidities and possibly more severe disease, which could result in increased COPD exacerbations. However, in our study, the southern VISNs were not necessarily associated with higher exacerbation rates and our analysis controlled for climate and age. Fourth, in January 2002, during our follow-up period, VISN 13 and VISN 14 merged to become VISN 23. The merger did not have an effect on the facilities or programs in the previous VISNs, but did merge the administrative structures. Primary care at the individual level was not expected to change; hence, we would not expect a change in effect at the provider level as a result of this merger. Fifth, another factor that is closely related to COPD exacerbations is smoking status. We did not have this information at the individual level to include in our analysis. Sixth, we used annual average temperatures, annual average range in temperatures, latitudes, and longitudes to account for the variability of the

climate. We did not include regional differences in ambient air quality, which may also contribute to COPD exacerbations. Finally, we did not account for health care system use outside the VA health care system. Tseng and colleagues³¹ have shown that for diabetic patients that are Medicare eligible, it is important to account for non-VA health care system use when assessing patterns of care and outcomes. They found that including data from Centers for Medicare and Medicaid Services (CMS) had a major impact on the observed amputation rates of patients with diabetes. In evaluating spirometry use in the diagnosis of COPD, we found that COPD patients receiving dual health care benefits with CMS misclassified only 5% as not having had spirometry within the VA system.¹⁰ It would not be particularly surprising if events for emergent situations such as myocardial infarctions were not identified if relying solely on VA data; however, if COPD exacerbations are typically non-emergent events and these patients are being seen by VA providers for their COPD, we would expect to identify the majority of events that occurred in this population.

Geographic variation in the VA health care system provides evidence that the medical care system including provider factors, and less so patient factors, affect COPD exacerbation rates. Closer examination of the VISNs in which there were lower exacerbation rates could provide useful guidance on practice patterns or interventions that could be used across the health care system. Understanding the reasons underlying this variation may lead to improvements in future care and outcomes of patients with COPD.

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