Blanchette et al. Int J Respir Pulm Med 2016, 3:044
Volume 3 | Issue 2
ISSN: 2378-3516

International Journal of
Respiratory and Pulmonary Medicine

Original Research Article: Open Access

Prevalence of Depression/Anxiety among Medicare Beneficiaries with Chronic Obstructive Pulmonary Disease and Association with Acute Exacerbations

Christopher M. Blanchette[1]*, Melissa Roberts[2], Hans Petersen[3] and Anne Fuhlbrigge[4]

[1]*Department of Public Health Sciences, University of North Carolina, USA*

[2]*Lovelace Clinic Foundation, USA*

[3]*Lovelace Respiratory Research Institute, USA*

[4]*Brigham and Women's Hospital & Harvard Medical School, USA*

***Corresponding author:** *Christopher M. Blanchette, PhD, MBA, Associate Professor of Public Health Sciences, College of Health & Human Services, University of North Carolina at Charlotte, 9201 University City Blvd., CHHS 476, Charlotte, NC 28223, USA, Tel: 704-687-5610, E-mail: cblanche@uncc.edu*

Abstract

Objective: To assess the association of exacerbations with depression/anxiety among Medicare beneficiaries with chronic obstructive pulmonary disease.

Methods: A prevalent cohort of Medicare beneficiaries aged 65+ with COPD (chronic bronchitis, emphysema, bronchiectasis, chronic airway obstruction) was constructed from a 5% sample of Medicare beneficiaries. Existence of depression/anxiety was identified via healthcare services or prescription drug claims. Baseline characteristics were assessed (1/1/2006-6/31/2006) and patients followed from first depression/anxiety claim until 12/31/2007 for all-cause and respiratory-related healthcare cost and utilization. Prevalence estimates of co-occurring COPD and depression/anxiety were approximated. The occurrence and frequency of moderate (outpatient encounter with an oral corticosteroid and/or an antibiotic claim, or COPD-related emergency department visit) or severe (COPD-related hospital admission) COPD exacerbation was compared between patients with and without comorbid depression/anxiety using binary logistic and negative binomial regression models, respectively.

Results: 137,275 subjects met inclusion criteria. Depression/anxiety was present in 45% (61,900). After controlling for sex, age, region, race, Charlson comorbidity score, use of COPD-related medications, and moderate and severe exacerbations in the baseline period, enrollees with depression/anxiety were 54% more likely to have a moderate COPD exacerbation (OR 1.54, 95% CI 1.42-1.67) and 82% more likely to have a severe COPD exacerbation (OR 1.82, 95% CI 1.54-2.16).

Conclusion: Over half of Medicare beneficiaries with COPD also have depression/anxiety. Depression/anxiety is associated with a greater likelihood of COPD exacerbations. More attention to the co-existence and management of depression/anxiety among COPD patients may help reduce the occurrence and frequency of COPD exacerbations. Future research should explore the impact of managing depression/anxiety on reducing COPD exacerbations.

Keywords

Chronic obstructive pulmonary disease, Depression, Anxiety, Comorbidity

Introduction

Depression and anxiety impact 15% to 30% of the U.S. elderly at some point in their lifetimes [1,2]. If untreated or under-treated, depression and anxiety increase an individual's use of healthcare services [3], risk of comorbidity [4] and mortality [5], and also lead to reductions in functional status and productivity [4]. The economic burden associated with anxiety and related disorders is estimated at $42.3 - $46.6 billion annually [6,7]. These figures consist of direct medical costs, as well as indirect costs, associated with morbidity, reduced productivity, and mortality.

COPD is a preventable and treatable disease characterized by persistent airflow obstruction [8]. It is the third leading cause of death in the United States and there is an estimated 15 million Americans diagnosed with COPD [9]. The prevalence is highest in adults aged 65 and older, with a rate of 64.2 per 1,000 persons [10]. In 2010 COPD-related costs in the US were estimated at $49.9 billion, of which $29.5 billion were from direct medical costs, $8 billion were indirect morbidity costs and $12.4 billion were in indirect mortality costs [11]. COPD is responsible for approximately five to six clinical encounters per patient per year - a magnitude of over 15 million outpatient visits per year. In 2000 alone, COPD was responsible for 1.5 million emergency department visits and 726,000 hospitalizations in the United States [12,13]. The complexity of morbidity due to COPD is significantly increased with the addition of a mental illness such as depression and/or anxiety disorders or a chronic physical illness. Approximately 42% to 57% of individuals with COPD also suffer from depression [14,15]. Prevalence of anxiety disorders in COPD patients ranges from 10 to 24% [16,17]. In particular, a growing body of literature suggests that elderly patients with COPD who experience depression or anxiety may not be optimally treated.

Previous work assessing the burden of anxiety and depression within COPD patients has relied primarily on small patient samples, self-reported depression survey information, and has often used non-U.S. populations [18-21]. This limits generalizability and fails to provide national estimates of the burden of comorbid conditions in

ClinMed International Library

Citation: Blanchette CM, Roberts M, Petersen H, Fuhlbrigge A (2016) Prevalence of Depression/Anxiety among Medicare Beneficiaries with Chronic Obstructive Pulmonary Disease and Association with Acute Exacerbations. Int J Respir Pulm Med 3:044

Received: October 20, 2016: **Accepted:** April 16, 2016: **Published:** April 19, 2016

COPD beneficiaries. This study sought to determine the prevalence of co-occurring COPD and depression or anxiety in a fee-for-service Medicare population, and to assess moderate and severe exacerbations among those with COPD and depression/anxiety as compared to those with COPD without co-occurring depression/anxiety.

Study Design and Sample

The study used both a cross-sectional and a cohort design. The cross-sectional design was used to estimate the prevalence of COPD and co-occurring depression or anxiety, while the cohort design was used to assess the impact of anxiety and/or depression on the occurrence and frequency of COPD exacerbations.

Data

This study used data from the Centers for Medicare and Medicaid Services (CMS) Chronic Condition Data Warehouse (CCW) from January 1, 2006 through December 31, 2007 for the 5% sample population and was restricted to enrollees who were at least 65 years of age by December 31, 2006 and who had both Part A and Part B Medicare coverage. The CCW was created specifically to assist in research related to improving the quality of care and reducing the cost of care for chronically ill Medicare enrollees. The CCW includes beneficiary demographic and enrollment information as well as information on whether beneficiaries have one of 21 chronic conditions. The 5% sample is generated from the 100% sample of eligible enrollees. Sampling is based on digits in the Health Insurance Claim number. The CCW captured data pertains to a mostly fee-for-service population as managed care administrative claims are not captured within the database. The CCW beneficiary demographic, enrollment and chronic condition status information for all enrollees in the 5% sample was used for prevalence assessments. Claims data for the beneficiaries with COPD and all associated subdiagnoses (chronic bronchitis, emphysema, bronchiectasis and airflow obstruction) within the 5% sample was used in the comparative analyses and comprised claims for institutional and non-institutional care under Medicare Parts A, B, and D. Those beneficiaries identified for the COPD cohort of the CCW were identified by CMS from a claim indicating COPD or any subdiagnoses (International Classification of Disease, 9th edition Clinical-Modification (ICD-9-CM) codes 491.xx (chronic bronchitis), 492.xx (emphysema), 494.xx (bronchiectasis), or 496 (chronic airway obstruction)). Beneficiaries were included with a COPD identification date earlier than July 1, 2007.

Cross-sectional design

The cross-sectional analysis was conducted using the 2006 CCW data. Beneficiaries were included if they had a COPD "First Occurrence" date that was prior to or equal to, December 31, 2006. The existence of a depression or anxiety comorbidity was established by an ICD-9-CM claim in 2006 that met the depression/anxiety criteria (see Patient Selection Measures below) or existence of pharmacy claims for antidepressant and anxiolytic prescriptions.

Cohort design

The cohort section of the study included patients from the CCW who had a COPD "First Occurrence" date earlier than July 1, 2007 and had at least one pharmacy claim during 2006 to demonstrate part D coverage and use. Those beneficiaries who met the selection criteria for depression/anxiety measure between July 1, 2006 and June 30, 2007 were identified as "cases" and the date of the first indication of depression/anxiety was deemed the "index date." Those who did not have evidence of a depression/anxiety diagnosis or a prescription claim for one of the antidepressant or anxiolytic medications were deemed "controls". Three time periods of observation were used including 1) July 1, 2006 through June 30, 2007: the review period for evidence of comorbid depression/anxiety and assignment of index date; 2) a 6-month pre-index period (earliest date - January 1, 2006) was used to estimate baseline characteristics, and 3) a post-index period that began for each patient after the occurrence of the anxiety/depression index event and continued through December 31, 2007.

Patient selection measures

Measures of patient selection include COPD and affective disorder diagnoses, and matching criteria including age and sex. Claim-defined depression/anxiety was defined as at least one or more inpatient claims or two or more outpatient claims for service with an ICD-9-CM code for depression and/or anxiety disorders, including generalized anxiety, social phobias, obsessive-compulsive disorders, and others (ICD-9-CM 300.0, 300.00, 300.01, 300.02, 300.09, 300.21, 300.22, 300.23, 300.3, 309.24, and 309.81).

Outcome measures

COPD exacerbations were measured during the post-index period and were defined as either moderate or severe [22]. Moderate exacerbations were measured as an outpatient encounter in conjunction with a pharmacy claim (within ten days) for an oral corticosteroid (OCS) and/or an antibiotic, or an emergency department visit with a primary diagnosis code indicating COPD. A hospital admission with a primary diagnosis code indicating COPD was considered a severe exacerbation. If a patient had a moderate exacerbation within 2 weeks of a severe exacerbation, that episode was considered one event: a severe exacerbation.

Covariate measures

A comorbidity index was utilized to characterize the populations. The index was assessed using the Deyo adaptation of the Charlson index, an index originally developed to predict risk of death in hospitalized patients that includes 17 groups of comorbidities [23]. We calculated the index in two ways: (1) using hospitalization diagnosis codes only (patients with no admissions received an index score of "0") and, (2) using outpatient encounter diagnosis codes. For the outpatient score, we required that two encounters with a given comorbidity diagnosis be present on separate dates in order for that comorbidity to be considered present. This served to exclude diagnosis codes in the claims records that may have represented a "rule-out" rather than an actual diagnosis. The existence of a comorbidity was assessed for the cross-sectional and cohort designs using ICD-9-CM diagnosis codes from claims, a common approach to measuring comorbidity in health services research [24,25].

Socio-demographic characteristics comprising age, sex, race, ethnicity, and Medicare geographic location (U.S. regions) were assessed and used as covariates in the logistic and negative binomial regression models. We also assessed moderate and severe COPD exacerbations and utilization of COPD treatment medications in the pre-index period. COPD medications included: short-acting beta agonists (SABA), bronchodilators, inhaled corticosteroids (ICS), long-acting beta agonists (LABA), ICS-LABA combinations, anticholinergics and theophylline.

Analysis

We examined annual prevalence overall and prevalence stratified by age and sex. Prevalence of COPD in a Medicare population was estimated using a denominator population of Medicare beneficiaries with 12 months enrollment during 2006 or who died during 2006, with the numerator as the beneficiaries in the denominator population with COPD. Prevalence of COPD with depression/anxiety was estimated using the beneficiaries with COPD as the denominator, and of those, the beneficiaries with COPD and depression/anxiety as the numerator.

COPD exacerbations were stratified by categories of exacerbation - moderate or severe. The number of exacerbations was assessed using a negative binomial model, which accounts for variability among patients. Occurrence of a moderate and severe exacerbation was estimated using logistic regression models.

Results

Cross-sectional prevalence estimates

We identified 1,591,413 enrollees meeting the criteria of 12 months of FFS coverage (or coverage until time of death). Of those

Table 1: Cross-sectional study: Sample characteristics by comorbid depression/anxiety.

	Total	*COPD with Depression/Anxiety*	*COPD without Depression/Anxiety*
	N (%)	N (%)	N (%)
Row percentages for prevalence rates			
Total Patients	137,275 (100%)	61,900 (45%)	75,375 (55%)
Column percentages for proportions within groups			
Male	65,276 (48%)	23,533 (38%)	41,743 (55%)
Females	71,999 (52%)	38,367 (62%)	33,632 (45%)
Age Category			
65-69 years	23,099 (17%)	10,433 (17%)	12,666 (17%)
70-74 years	30,523 (22%)	13,282 (21%)	17,241 (23%)
75-79 years	31,968 (23%)	13,859 (22%)	18,109 (24%)
80-84 years	26,766 (19%)	12,104 (20%)	14,662 (19%)
85+ years	24,919 (18%)	12,222 (20%)	12,697 (17%)
Race			
White	122,501 (89%)	55,490 (90%)	67,011 (89%)
African-Americans	9,178 (7%)	3,695 (6%)	5,483 (7%)
Hispanic	2,424 (2%)	1,460 (2%)	964 (1%)
Other	3,172 (2%)	1,255 (2%)	1,917 (3%)

enrollees, 1,343,785 enrollees were age 65 or older for the year 2006 and of these, 170,965 had evidence of COPD, providing an estimate of 12.7% for the prevalence of COPD among FFS Medicare beneficiaries age 65 and older. Among women the prevalence was 11.8% and among men, 14.0%. Individuals with COPD were more likely to be White (90% compared to 88%) and older, with 61% 75 years or older compared to 55% among individuals without COPD.

Of enrollees with COPD in 2006 (170,965), 61,900 enrollees (36.2%) were identified as meeting criteria for comorbid depression/anxiety, 75,375 (44.1%) had no evidence of depression/anxiety, and the remaining 33,690 (19.7%) had some evidence of depression/anxiety, but did not meet our inclusion criteria of at least 2 outpatient encounters. One-half of the 61,900 identified with comorbid depression/anxiety were identified based on a depression diagnosis without an accompanying prescription while 8.0% were identified based solely on a prescription claim, and 42.0% based on evidence of both a prescription and a diagnosis. Using these percentages, 604,703 (application of the 5% sample metrics to the 100% population) Medicare FFS enrollees with COPD met criteria for comorbid depression/anxiety.

The analysis population consisted of 137,275 beneficiaries, consisting of 61,900 (45%) with and 75,375 (55%) without evidence of depression/anxiety. Beneficiaries with some evidence of depression/anxiety (33,690) were excluded, as they did not meet criteria for the depression/anxiety definition. Depression/anxiety was more prevalent among beneficiaries age 85 and older (49% compared to 45% overall, $p < 0.0001$). Women had a higher prevalence of comorbid depression/anxiety compared with men (53% versus 36%, $p < 0.0001$). Interestingly, among Hispanics, 60% had evidence of depression/anxiety compared to 40% of African-Americans and other race/ethnicities.

Among those with comorbid depression/anxiety, significantly more women than men had evidence of comorbid depression/anxiety based on evidence of both a diagnosis and a prescription (49.2% versus 30.5%, $p < 0.0001$), while the percentage with comorbid depression/anxiety based only on a depression/anxiety prescription was approximately equal (7.8% versus 8.2%, $p = 0.16$). Among minority populations, there was wide variation in the percentage of individuals with evidence of both a depression/anxiety diagnosis and medication; the percentage was only 39.3% among African-Americans while it was 59.8% among Hispanics, the highest of all race/ethnicities (Table 1).

Cohort baseline characteristics

Of the 137,275 enrollees within the cross-sectional analysis, 31,279 met the criteria for the cohort analysis, which required at least 6-month pre-index and post-index periods over two years of data to assess temporal associations. Of the total sample of 31,279, 41% (12,701) of enrollees had evidence of depression/anxiety. Similar to the cross sectional analysis, individuals included in the cohort analysis with comorbid depression/anxiety were more likely to be female (42% versus 28%, $p < 0.0001$), white (87% versus 83%, $p < 0.0001$) and Hispanic (4% versus 3%, $p < 0.0001$) and had more comorbidities than those without depression/anxiety (Inpatient Charlson Index Score = 0, 71% versus 82%, $p < 0.0001$ and Outpatient Charlson Index Score = 0, 37% versus 47%, $p < 0.0001$). There were no differences between enrollees with and without comorbid depression/anxiety with respect to use of the COPD medications ICS, OCS, SABA, leukotriene modifiers, or methylxanthines. A greater number of enrollees without depression/anxiety had pre-index utilization of tiotropium (13% versus 10%, $p < 0.0001$) and ICS/LABA combination therapies (19% versus 16%, $p < 0.0001$), and a greater number of enrollees with depression/anxiety had some antibiotic (52% versus 48%, $p < 0.0001$) or ipratropium (15% versus 13%, $p < 0.0001$) utilization (Table 2).

Cohort bivariate statistics

In the post-index period, a far greater proportion of enrollees with evidence of depression/anxiety had claims for acute exacerbation treatments such as antibiotics (59% versus 45%, $p < 0.0001$) as well as OCS use (23% versus 18%, $p < 0.0001$) and chronic medications such as ICS (7 % versus 6%, $p < 0.0001$), ipratropium (17% versus 13%, $p < 0.0001$), and SABA (23% versus 20%, $p < 0.0001$). The use of ICS/LABA combinations (19% versus 20%, $p < 0.0001$) and tiotropium (13% versus 15%, $p < 0.0001$) remained more prevalent among enrollees without depression/anxiety. More enrollees with depression/anxiety experienced moderate (11% versus 8%, $p < 0.0001$) and severe exacerbations (3% versus 1%, $p < 0.0001$) than enrollees without depression/anxiety (Table 3).

Cohort adjusted risk of exacerbation

After adjusting for sex, age category, region, race, Charlson score, and use of COPD-related medications in the baseline period, patients with depression/anxiety were 54% were more likely to have a moderate exacerbation (OR 1.54; 95% CI, 1.42 to 1.67) and a 82% more likely to have a severe exacerbation (OR 1.82; 95% CI, 1.54 to

Table 2: Cohort study: Baseline characteristics.

	Total *		COPD with Depression/Anxiety		COPD without Depression/ Anxiety	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**
Number of Patients	31,279	100.00%	12,701	100.00%	18,578	100.00%
Age [Mean (SD)]	77.2	(7.45)	77.6	(7.72)	77.0	(7.24)
Male	11,357	36.31%	3,515	27.67%	7,842	42.21%
Region of U.S.*						
Boston	2,119	6.77%	903	7.11%	1,216	6.55%
New York	2,572	8.22%	934	7.35%	1,638	8.82%
Philadelphia	2,887	9.23%	1,069	8.42%	1,818	9.79%
Atlanta	8,587	27.45%	3,873	30.49%	4,714	25.37%
Chicago	4,634	14.82%	1,776	13.98%	2,858	15.38%
Dallas	3,772	12.06%	1,545	12.16%	2,227	11.99%
Kansas City	1,915	6.12%	787	6.20%	1,128	6.07%
Denver	826	2.64%	315	2.48%	511	2.75%
San Francisco	3,107	9.93%	1,112	8.76%	1,995	10.74%
Seattle	860	2.75%	387	3.05%	473	2.55%
Race/Ethnicity						
White	26,510	84.75%	11,103	87.42%	15,407	82.93%
African-Americans	2,487	7.95%	753	5.93%	1,734	9.33%
Hispanic	1,051	3.36%	538	4.24%	513	2.76%
Other Races:	1,231	3.94%	307	2.42%	924	4.97%
Inpatient Charlson Index						
Score = 0	24,127	77.13%	8,960	70.55%	15,167	81.64%
Score = 1	3,234	10.34%	1,707	13.44%	1,527	8.22%
Score ≥ 2	3,918	12.53%	2,034	16.01%	1,884	10.14%
Outpatient Charlson Index						
Score = 0	13,480	43.10%	4,733	37.26%	8,747	47.08%
Score = 1	7,643	24.43%	3,316	26.11%	4,327	23.29%
Score = 2	4,832	15.45%	2,158	16.99%	2,674	14.39%
Score ≥ 3	5,324	17.02%	2,494	19.64%	2,830	15.23%
Drugs Pre-Index (% with any fills)						
Antibiotics	15,510	49.59%	6,564	51.68%	8,946	48.15%
ICS/LABA combination	5,572	17.81%	2,055	16.18%	3,517	18.93%
Inhaled cortico-steroid (ICS)	2,048	6.55%	821	6.46%	1,227	6.60%
Injected Steroids	62	0.20%	43	0.34%	19	0.10%
Ipratropium	4,266	13.64%	1,870	14.72%	2,396	12.90%
Long-acting beta-agonist (LABA)	694	2.22%	252	1.98%	442	2.38%
Leukotriene modifiers	2,730	8.73%	1,143	9.00%	1,587	8.54%
Methylxanthines	1,187	3.79%	484	3.81%	703	3.78%
Oral corticosteroids (OCS)	6,164	19.71%	2,549	20.07%	3,615	19.46%
Short-acting beta-agonist (SABA)	6,212	19.86%	2,496	19.65%	3,716	20.00%
Tiotropium	3,767	12.04%	1,280	10.08%	2,487	13.39%
any of above drugs †	22,367	71.51%	9,045	71.21%	13,322	71.71%

*enrollees in non-U.S. region were not included

†use of omalizumab and mast cell stabilizers are also included but not reported because of cell size report restrictions

2.16). Depression/Anxiety was also shown to increase the frequency of moderate exacerbations by 44% (IRR 1.44, 95% CI, 1.334 to 1.55) and severe exacerbations by 82% (IRR 1.82; 95% CI, 1.53 to 2.15) (Table 4).

Discussion

Our findings indicate that comorbid depression or anxiety is highly prevalent among older adult Medicare enrollees with COPD. Our findings in the cross-sectional study demonstrate 36% of patients with COPD have evidence of depression/anxiety, suggesting over half a million enrollees suffer from the comorbidity. Our findings compare to those of Moussas *et al.* who found 49% of 132 patients with pulmonary disease in Greece had symptoms of depression and 27% had symptoms of anxiety [19]. While another study by Jennings *et al.* who found 32% of 194 COPD patients discharged from a pulmonary rehabilitation to experience depression within one year [21]. Qian *et al.* found 21.6% of Medicare beneficiaries with COPD to have a diagnosis of depression and over 80% of those to receive antidepressant treatment. These estimates may be lower because the measure did not include anxiety as well, nor did it assess medication only as a potential sensitivity measure [26].

Patients with depression/anxiety were more likely to experience a moderate or severe COPD exacerbation and experience these more frequently. These findings suggest that depression/anxiety has a significant impact on respiratory function and COPD stability and that management of symptoms in this population may differ from those without depression.

Our findings on the occurrence and frequency of exacerbations were similar to those of other recent studies, which have assessed COPD and depression comorbidity. In a managed care population of COPD patients aged 40 and older, Dalal *et al.* found patients with depression/anxiety 77% more likely to experience a COPD-related hospitalization and 48% more likely to experience a COPD-related ER visit, where we found a likelihood of 82% for severe exacerbation defined as a COPD-related hospitalization and 54% for a moderate exacerbation defined as an outpatient encounter in conjunction with a pharmacy claim (within ten days) for an OCS and/or an antibiotic, or an emergency department visit with a primary diagnosis code indicating COPD [27]. Among a cohort of 491 patients with COPD in China, Xu *et al.* found depression/anxiety associated with a 77% increased incidence of exacerbations requiring hospitalizations, 51% with symptoms, and 56% with healthcare intervention [18].

Table 3: Cohort study: Post-index differences by depression/anxiety.

	Total		COPD with Depression/ Anxiety		COPD without Depression/Anxiety		
	N	%	N	%	N	%	Difference, P value †
Number of Patients	31,279	100.00%	12,701	100.00%	18,578	100.00%	
Drugs Post-Index (N, % with any fills)							
Antibiotics	15,913	50.87%	7,493	59.00%	8,420	45.32%	< 0.0001
ICS/LABA combination	6,110	19.53%	2,419	19.05%	3,691	19.87%	0.0718
Inhaled cortico-steroid (ICS)	2,118	6.77%	934	7.35%	1,184	6.37%	0.0007
Injected Steroids	96	0.31%	68	0.54%	28	0.15%	< 0.0001
Ipratropium	4,578	14.64%	2,165	17.05%	2,413	12.99%	< 0.0001
Long-acting beta-agonist (LABA)	719	2.30%	290	2.28%	429	2.31%	0.8807
Leukotriene Modifiers	2,817	9.01%	1,237	9.74%	1,580	8.50%	0.0002
Methylxanthines	1,216	3.89%	510	4.02%	706	3.80%	0.3335
Oral cortico-steroids (OCS)	6,294	20.12%	2,871	22.60%	3,423	18.43%	< 0.0001
Short-acting beta-agonist (SABA)	6,578	21.03%	2,907	22.89%	3,671	19.76%	< 0.0001
Tiotropium	4,470	14.29%	1,657	13.05%	2,813	15.14%	< 0.0001
any of above drugs*	23,103	73.86%	9,978	78.56%	13,125	70.65%	< 0.0001
Utilization (N, % with any event)							
Moderate Exacerbation	2,821	9.02%	1,396	10.99%	1,425	7.67%	< 0.0001
Severe Exacerbation	587	1.88%	318	2.50%	269	1.45%	< 0.0001
Utilization (Mean events, SD)							
Moderate Exacerbation	0.10	(0.31)	0.12	(0.34)	0.08	(0.29)	< 0.0001
Severe Exacerbation	0.02	(0.15)	0.03	(0.17)	0.02	(0.13)	< 0.0001

SD: standard deviation

*use of omalizumab and mast cell stabilizers are also included but not reported because of cell size report restrictions

†p-values are calculated using chi-square test for frequency differences and t-test for mean differences

Table 4: Cohort study: Adjusted association of depression/anxiety and COPD exacerbation.

Event	Odds Ratio	95% CI	IRR	95% CI
Moderate Exacerbation	1.54	(1.42 - 1.67)	1.44	(1.34 - 1.55)
Severe Exacerbation	1.82	(1.54 - 2.16)	1.82	(1.53 - 2.15)

IRR: Incidence Rate Ratio; 95% CI, 95% Confidence Intervals;

Both the logistic regression (OR) and the negative binomial model (IRR) adjusted for sex, age, region, race; Charlson score, use of COPD-related medications, and moderate and severe exacerbations in the baseline period.

This study provides a significant amount of information on the burden, treatment, and outcomes of COPD when associated with comorbid affective disorder. This is the first study to estimate the presence of depression and anxiety in Medicare patients with COPD and the potential risk that comorbidity places on the occurrence of exacerbations. However, this study is not without limitations. Most of these limitations include those consistent with any observational study using administrative claims data and include potential selection bias, missing data, misclassification, and confounding. Administrative data also lacks clinically rich information that does not appear on a claim, such as the result of a test. In this study, lung function was not available due to the nature of the data. Care was taken to adjust for known threats to the internal validity of retrospective analysis including confounding, selection, incidental truncation, and omitted variables. Model diagnostic tests and informal analysis was used to assess the evidence for residual unmodeled systematic variation. Because the data are reliant on claims submitted by providers and administered by CMS, there is the chance that claims are mislabeled such that the patients do not have COPD or that some COPD patients either are mislabeled as having an affective disorder or not having an affective disorder; this potential for mislabeling is why we used several measures to identify depression and anxiety and did not rely solely on ICD-9-CM claims for the disease, as recent articles have discovered ICD-9 diagnosis from claims alone has poor positive predictive value [26]. There has also been debate over the use of OR and RR when outcomes are common (> 10%) in cohort studies. The argument against the use of the odds ratio states that the odds ratio may overestimate the relative risk [28]. However, there is also a body of evidence that suggests that using the odds ratio is preferred [29]. We have used ORs here as reported in previous studies [27,18]. We addressed the major flaws of the study to ensure reliable and important results that will benefit both COPD patients with and without affective disorders and potentially reduce exacerbation events.

Conclusions

Comorbid depression or anxiety appears to be highly prevalent in a Medicare population of older adults, with 36% of patients with documentation of the comorbidity. COPD patients with evidence of depression or anxiety are more likely to experience a COPD exacerbation and more frequently. More attention to the co-existence and management of the symptoms associated with these comorbidities may lead to a reduction in the occurrence and frequency of COPD exacerbations.

Acknowledgements

The authors would like to thank Alan Kamada, PharmD and Anand Dalal, PhD, MBA of GlaxoSmithKline for comments. This study was supported by a grant from GlaxoSmithKline (CAD113281).

Disclosures

The authors received unrestricted grant funding for this study from GlaxoSmithKline (CAD113281)

References

1. Judd LL (1997) Surveys show that 20-30% of elderly patients exhibit SSD symptomatology. International Medicine World Report 12: 33-34.
2. Unützer J, Patrick DL, Simon G, Grembowski D, Walker E, et al. (1997) Depressive symptoms and the cost of health services in HMO patients aged 65 years and older. A 4-year prospective study. JAMA 277: 1618-1623.
3. Frasure-Smith N, Lespérance F, Gravel G, Masson A, Juneau M, et al. (2000) Depression and health-care costs during the first year following myocardial infarction. J Psychosom Res 48: 471-478.
4. McIntyre RS, O'Donovan C (2004) The human cost of not achieving full remission in depression. Can J Psychiatry 49: 10S-16S.
5. Frasure-Smith N, Lespérance F, Talajic M (1993) Depression following myocardial infarction. Impact on 6-month survival. JAMA 270: 1819-1825.
6. Greenberg PE, Sisitsky T, Kessler RC, Finkelstein SN, Berndt ER, et al. (1999) The economic burden of anxiety disorders in the 1990s. J Clin Psychiatry 60: 427-435.
7. DuPont RL, Rice DP, Miller LS, Shiraki SS, Rowland CR, et al. (1996) Economic costs of anxiety disorders. Anxiety 2: 167-172.

8. Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2013.

9. Kosacz NM, Punturieri A, Croxton TL, Ndenecho MN, Kiley JP, et al. (2012) Chronic obstructive pulmonary disease - among adults - United States, 2011. MMWR 61: 938-943.

10. Centers for Disease Control and Prevention (2011) National Center for Health Statistics. National Health Interview Survey Raw Data. Analysis performed by the American Lung Association Research and Health Education Division using SPSS and SUDAAN software.

11. Confronting COPD in America (2000) Schulman, Ronca and Bucuvalas, Inc. (SRBI) Funded by Glaxo Smith Kline.

12. Mannino DM (2002) COPD: epidemiology, prevalence, morbidity and mortality, and disease heterogeneity. Chest 121: 121S-126S.

13. Radin A, Cote C (2008) Primary care of the patient with chronic obstructive pulmonary disease-part 1: frontline prevention and early diagnosis. Am J Med 121: S3-12.

14. Yohannes AM, Baldwin RC, Connolly MJ (2000) Depression and anxiety in elderly outpatients with chronic obstructive pulmonary disease: prevalence, and validation of the BASDEC screening questionnaire. Int J Geriatr Psychiatry 15: 1090-1096.

15. Lacasse Y, Rousseau L, Maltais F (2001) Prevalence of depressive symptoms and depression in patients with severe oxygen-dependent chronic obstructive pulmonary disease. J Cardiopulm Rehabil 21: 80-86.

16. Karajgi B, Rifkin A, Doddi S, Kolli R (1990) The prevalence of anxiety disorders in patients with chronic obstructive pulmonary disease. Am J Psychiatry 147: 200-201.

17. Yellowlees PM, Alpers JH, Bowden JJ, Bryant GD, Ruffin RE (1987) Psychiatric morbidity in patients with chronic airflow obstruction. Med J Aust 146: 305-307.

18. Xu W, Collet JP, Shapiro S, Lin Y, Yang T, et al. (2008) Independent effect of depression and anxiety on chronic obstructive pulmonary disease exacerbations and hospitalizations. Am J Respir Crit Care Med 178: 913-920.

19. Moussas G, Tselebis A, Karkanias A, Stamouli D, Ilias I, et al. (2008) A comparative study of anxiety and depression in patients with bronchial asthma, chronic obstructive pulmonary disease and tuberculosis in a general hospital of chest diseases. Ann Gen Psychiatry 7: 7.

20. Jennings JH, Digiovine B, Obeid D, Frank C (2009) The association between depressive symptoms and acute exacerbations of COPD. Lung 187: 128-135.

21. van den Bemt L, Schermer T, Bor H, Smink R, van Weel-Baumgarten E, et al. (2009) The risk for depression comorbidity in patients with COPD. Chest 135: 108-114.

22. Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, et al. (2007) Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med 356: 775-789.

23. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 45: 613-619.

24. Klabunde CN, Potosky AL, Legler JM, Warren JL (2000) Development of a comorbidity index using physician claims data. J Clin Epidemiol 53: 1258-1267.

25. Elixhauser A, Steiner C, Harris DR, Coffey RM (1998) Comorbidity measures for use with administrative data. Med Care 36: 8-27.

26. Qian J, Simoni-Wastila L, Langenberg P, Rattinger GB, Zuckerman IH, et al. (2013) Effects of depression diagnosis and antidepressant treatment on mortality in Medicare beneficiaries with chronic obstructive pulmonary disease. J Am Geriatr Soc 61: 754-761.

27. Dalal AA, Shah M, Lunacsek O, Hanania NA (2011) Clinical and economic burden of depression/anxiety in chronic obstructive pulmonary disease patients within a managed care population. COPD 8: 293-299.

28. McNutt LA, Wu C, Xue X, Hafner JP (2003) Estimating the relative risk in cohort studies and clinical trials of common outcomes. Am J Epidemiol 157: 940-943.

29. Cook TD (2002) Advanced statistics: up with odds ratios! A case for odds ratios when outcomes are common. Acad Emerg Med 9: 1430-1434.