The Economic Burden of Comorbid Obstructive Sleep Apnea Among Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

BACKGROUND: Chronic obstructive pulmonary disease (COPD) imposes a substantial burden on patients and the health care system. The presence of comorbid obstructive sleep apnea (OSA) has been shown to increase the risk of morbidity and mortality in patients with COPD. There is limited information available on the incremental economic burden of comorbid OSA among patients with COPD.

OBJECTIVE: To estimate the incremental health care resource utilization (HCRU) and direct medical costs associated with having comorbid OSA among individuals with COPD in a nationally representative commercially insured population in the United States.

METHODS: We identified individuals with a diagnosis of COPD between January 2008 and December 2014, with and without OSA, from the IQVIA PharMetrics Plus database. The index date was defined as the first claim with a diagnosis of COPD. All baseline characteristics were measured in the 12-month pre-index period, and all outcomes were measured in the 12-month post-index period. The odds of experiencing one or more hospitalizations and emergency room (ER) visits were compared between individuals with and without comorbid OSA using logistic regression models. Twelve-month total, physician office visit, and other outpatient costs were compared between individuals with and without OSA using generalized linear models. To account for a high proportion of zero costs, 2-part models were fit to examine inpatient, ER visit, and pharmacy costs. Average marginal costs were estimated to compare the costs of individuals with and without OSA. All costs represented direct medical costs from the health plan perspective.

RESULTS: Following application of inclusion and exclusion criteria, the study sample included 85,940 individuals with COPD alone and 7,942 individuals with COPD and OSA. The odds of experiencing a hospitalization and an ER visit were significantly higher in the COPD-OSA cohort than in the COPD-only cohort (hospitalization OR=1.45, 95% CI=1.35-1.53; ER visit OR=1.24, 95% CI=1.18-1.30). The average difference in total cost between individuals with and without comorbid OSA was \$8,144 (95% CI=\$7,295-\$8,993). The average difference in costs for physician office visits and other outpatient services was \$392 (95% CI=\$351-\$433) and \$2,831 (95% CI=\$2,463-\$3,200), respectively. Among individuals with a non-zero, strictly positive inpatient cost, the average difference in inpatient costs was \$2,792 (95% CI=\$1,354-\$4,230). Similarly, among individuals with strictly positive pharmacy and ER costs, the average difference in costs between individuals with and without comorbid OSA was \$1,772 (95% CI=\$1,590-\$1,953) and \$144 (95% CI=\$101-\$188), respectively.

CONCLUSIONS: Total medical cost and costs for inpatient, ER, pharmacy, physician office visit, and other outpatient services were higher among COPD patients with comorbid OSA compared to patients without. The economic burden of comorbid OSA among patients with COPD in the commercially insured U.S. population is substantial.

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What is already known about this subject

- Studies have shown that comorbid obstructive sleep apnea (OSA) increases the risk of exacerbations and mortality in patients with chronic obstructive pulmonary disease (COPD).
- Comorbid sleep apnea syndrome was documented to be associated with higher medical utilization and costs in COPD patients in the Maryland Medicaid population.

What this study adds

- To our knowledge, this is the first study to examine the economic burden of comorbid OSA among COPD patients in the commercially insured U.S. population.
- Patients diagnosed with COPD and OSA had significantly higher all-cause 12-month health care costs (total, inpatient, emergency room, pharmacy, physician office visit, and other outpatient) than patients without OSA.

Chronic obstructive pulmonary diseases (COPD) and obstructive sleep apnea (OSA) are highly prevalent respiratory diseases that impose a substantial burden on individuals, the health care system, and society.^{1,2} COPD is a disease that can have a high burden of physical symptoms, such as shortness of breath and fatigue, compromising patients' ability to perform daily living activities.^{3,4} COPD has also been associated with a decline in mental health and health-related quality of life.⁵ In 2011, approximately 14 million adults in the United States reported having a COPD diagnosis,⁶ and COPD was the fourth leading cause of U.S. deaths in 2016.⁷ Additionally, COPD was estimated to have an economic impact of \$49.9 billion in 2010 due to direct and indirect health care costs.⁸

OSA is estimated to affect 29.4 million U.S. adults, representing 12% of the adult population.⁹ OSA has also been shown to impose a substantial economic burden, with the estimated cost of diagnosing and treating OSA in the United States being approximately \$12.4 billion in 2015.⁹

The coexistence of OSA and COPD in individuals has been reported to range from 2.9% to as high as 65.9%.¹⁰ When COPD and OSA coexist in the so-called overlap syndrome, increased risk for morbidity and mortality have been reported.¹¹ The presence of OSA has been shown to increase COPD exacerbations and mortality when compared with COPD-only patients.¹¹ Additionally, COPD patients with comorbid OSA have been

reported to have poorer health-related quality of life, partly due to worsened sleep disturbance and more pronounced nocturnal oxygen desaturation.¹²

While the clinical burden of COPD-OSA overlap syndrome has been studied, the economic burden has not been fully quantified in the United States. In a study conducted using Maryland Medicaid claims data (2001-2003), beneficiaries with COPD and sleep apnea syndrome incurred higher annual medical costs compared with beneficiaries without sleep apnea syndrome, highlighting the financial burden of COPD and comorbid sleep apnea in the Maryland Medicaid population.¹³ However, the incremental economic burden of OSA in commercially insured U.S. COPD patients is yet unknown.

A better understanding of the incremental economic burden of comorbid OSA among COPD patients will help create the context for important decisions such as whether reimbursement mechanisms for OSA diagnostic testing and treatment should be reevaluated to improve patient access to treatment and whether COPD patients should be actively screened and treated for OSA. Accurate and current estimates of health care resource utilization (HCRU) and costs are warranted to better understand the added economic burden of comorbid OSA in patients with COPD, and the economic benefits that may potentially be achieved by optimizing the treatment of patients with COPD and comorbid OSA and lowering the risk of adverse health outcomes.

The objective of this study was to estimate the incremental HCRU and direct medical costs associated with having comorbid OSA among individuals with COPD in a nationally representative U.S. commercially insured population. The analysis was performed from the U.S. commercial payer perspective.

Methods

Study Design and Data Source

The 10% random sample of enrollees within the IQVIA PharMetrics Plus database was used for this retrospective cohort study. The PharMetrics Plus database is composed of fully adjudicated health plan claims data and enrollment information for over 190 million commercially insured individuals since 2006 from national and subnational health plans and self-insured employer groups throughout the United States.¹⁴ This study was deemed exempt by the Institutional Review Board at the University of Maryland, Baltimore.

Study Sample

Individuals aged 18 years and older were included in the study if they had at least 1 claim with a COPD diagnosis code (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 491.xx, 492.xx, and 496.xx) between January 1, 2008, and December 31, 2014. The index date was defined as the date of the first claim with a COPD diagnosis during the study time frame. All individuals were

required to have continuous enrollment during the 12 months before the index date to capture pre-index baseline characteristics and 12 months after the index date to ensure complete outcome measurement during follow-up. Individuals with COPD and comorbid asthma (ICD-9-CM diagnosis codes 493.0x, 493.1x, 493.2x, 493.8x, and 493.9x), that is, asthma-COPD overlap syndrome, in the 12-month pre-index period were excluded from the study, since these individuals are known to be clinically different from individuals with COPD only and incur higher health care costs.¹⁵

Study Cohorts

Individuals with COPD were split into 2 mutually exclusive cohorts on the basis of their OSA status in the pre-index period, which was our main exposure of interest. Individuals with at least 1 claim including a diagnosis of OSA (ICD-9-CM diagnosis code 327.23) during the 12-month pre-index period were categorized as individuals with COPD and comorbid OSA; individuals without a diagnosis of OSA were categorized as individuals with COPD without OSA.

Baseline Measures

Baseline characteristics including age, sex, and geographic region were measured at the index date. Comorbidity burden was measured using the Charlson Comorbidity Index with Quan modification in the 12-month pre-index period.¹⁶ Because obesity has been shown to be correlated with OSA and higher health care cost, the presence of a diagnosis of obesity (ICD-9-CM diagnosis code 278.xx) was identified in the 12-month pre-index period. Pre-index oxygen use and COPD-related hospitalizations were used as proxy measures for COPD severity.¹⁷

Outcome Measures

We examined the number of hospitalizations and ER visits per patient in the 12-month post-index period, and the odds of experiencing 1 or more hospitalizations and ER visits were compared between the 2 cohorts. We calculated all-cause total medical cost per patient in the 12-month post-index period by summing all costs from the claims files over that period. We also stratified the cost by HCRU category (inpatient, ER, pharmacy, physician office visit, and other outpatient, which included lab/pathology, radiology, and outpatient surgical or rehabilitation services). Costs were compared between individuals with and without OSA as a ratio and as the average marginal cost. All costs evaluated were direct medical costs obtained from the dollar amount paid by the health plan to a provider/facility for services rendered. Costs were adjusted to 2018 U.S. dollars using the annual medical care component of the Consumer Price Index to account for inflation.¹⁸

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TABLE 1 Baseline Characteristics of the Study Sample

	Individuals with COPD (n = 85,940)		Individuals with COPD and OSA (n = 7,942)		P Value ^a
Age in years, mean (SD)	60.7	(11.9)	59.3	(10.5)	<0.01
Age in years, n (%)					<0.01
<40	3,517	(4.09)	264	(3.32)	
40-54	21,442	(24.95)	2,153	(27.11)	
55-64	31,295	(36.41)	3,296	(41.50)	
≥65	29,686	(34.54)	2,229	(28.07)	
Sex, n (%)					<0.01
Female	43,358	(50.45)	3,105	(39.10)	
Male	42,567	(49.53)	4,836	(60.89)	
Geographic region, n (%)					<0.01
East	22,395	(26.06)	1,836	(23.12)	
South	28,774	(33.48)	2,779	(34.99)	
Midwest	25,489	(29.66)	2,505	(31.54)	
West	9,282	(10.80)	822	(10.35)	
Pre-index oxygen use, n (%)					<0.01
No	80,646	(93.84)	6,496	(81.79)	
Yes	5,294	(6.16)	1,446	(18.21)	
Pre-index COPD-related hospitalization, n (%)					<0.01
No	81,916	(95.32)	7,459	(93.92)	
Yes	4,024	(4.68)	483	(6.08)	
CCI, n (%)					<0.01
1	65,919	(76.70)	5,377	(67.70)	
≥2	20,021	(23.30)	2,565	(32.30)	

^aChi-square test was used for categorical variables, and Student's t-test was used for continuous variables.

CCI = Quan-modified Charlson Comorbidity Index; COPD = chronic obstructive pulmonary disease; OSA = obstructive sleep apnea; SD = standard deviation.

Statistical Analysis

Chi-square tests and Student's t-tests were performed to compare baseline characteristics, unadjusted rates of hospitalizations and ER visits experienced, and costs of the COPD-only and COPD-OSA cohorts. Chi-square tests were used to compare categorical data, and Student's t-tests were used to compare continuous data.

A logistic regression was performed to compare the odds of experiencing 1 or more hospitalizations and ER visits in the COPD-OSA cohort versus the COPD-only cohort. A generalized linear model (GLM) with a gamma distribution and a log link was fit to compare total costs, physician office visit costs, and other outpatient costs for individuals with comorbid OSA versus individuals without OSA. To account for a high proportion of zero costs, a two-part model was fit to examine inpatient, ER visit, and pharmacy costs. The first part of the model consisted of a logit model estimating the odds of having any costs, and the second part was a GLM with a gamma distribution and a log link modeling the expected cost conditional on having non-zero, strictly positive costs.

The average marginal total cost and the average marginal cost for each HCRU category were estimated by computing the marginal effect at each observation level and then calculating

the sample average of individual marginal effects to obtain the overall average marginal effect.¹⁹ The 95% confidence intervals (CIs) for the average marginal costs were estimated using the delta method. Baseline characteristics were adjusted for in all analyses. We were unable to report or include obesity as a covariate in the analyses because few individuals had evidence of this diagnosis. A modified Parks test was used to determine data support for the assumption that the cost and HCRU data follow the distribution chosen for the GLM,²⁰ and Ramsey's Regression Equation Specification Error Test (RESET) was performed to verify the link.²¹ All analyses were performed using SAS Studio (SAS Institute, Cary, NC), and a *P* value less than 0.05 was considered statistically significant.

Sensitivity Analysis

To test the robustness of the estimated outcomes, a sensitivity analysis was conducted for all outcomes with additional covariates for index year (2008, 2009, 2010, 2011, 2012, 2013, and 2014) added to the model. This was done to ensure that changes in clinical practice patterns and new COPD treatments approved within the study time period had no effect on the estimated outcomes. We also conducted a sensitivity analysis excluding individuals with a diagnosis code for obesity to examine if this led to changes in the overall results.

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TABLE 2 Unadjusted 12-Month Prevalence and Rates of Hospitalizations and ER Visits in the COPD-Only Cohort and the COPD-OSA Cohort

	Individuals with COPD (n = 85,915)		Individuals with COPD and OSA (n = 7,942)		P Value ^a
	n	%	n	%	
No hospitalizations	59,429	69.2	4,705	59.2	<0.01
≥ 1 hospitalization	26,486	30.8	3,237	40.8	
No ER visits	57,691	67.2	4,882	61.5	<0.01
≥ 1 ER visit	28,224	32.9	3,060	38.5	
	Mean	SD	Mean	SD	P Value ^a
Number of hospitalizations (including nonutilizers)	0.55	1.20	0.77	1.43	<0.01
Number of hospitalizations if ≥ 1 hospitalization	1.80	1.55	1.90	1.69	<0.01
Number of ER visits (including nonutilizers)	1.76	6.19	2.12	8.62	<0.01
Number of ER visits if ≥ 1 ER visit	5.36	9.87	5.49	13.20	0.49

^aChi-square test was used for categorical variables, and Student's *t*-test was used for continuous variables.

COPD = chronic obstructive pulmonary disease; ER = emergency room; OSA = obstructive sleep apnea; SD = standard deviation.

Additionally, we changed the inclusion criteria to require at least 2 claims with a COPD diagnosis code, at least 30 days apart, to examine if this led to changes in the estimated outcomes.

Results

Baseline Characteristics

A total of 93,882 patients with COPD met the study inclusion and exclusion criteria. A flowchart showing the selection of the study sample is available in Appendix A (available in online article), and patients' baseline characteristics are shown in Table 1. Twenty-five individuals only had claims that were denied, so those individuals were excluded from the analysis. We included 85,915 patients with COPD without OSA and 7,942 patients with COPD and OSA in the analysis.

HCRU: Hospitalizations/ER Visits—Descriptive Analysis

Unadjusted rates of hospitalizations and ER visits are presented in Table 2. A higher proportion of individuals with comorbid OSA experienced hospitalizations and ER visits compared with individuals without OSA (40.8% vs. 30.8%; $P < 0.01$ for hospitalizations; 38.5% vs. 32.9%; $P < 0.01$ for ER visits). The mean number of hospitalizations and ER visits were both higher in the COPD-OSA cohort (0.77 vs. 0.55; $P < 0.01$ for hospitalizations; 2.12 vs. 1.76; $P < 0.01$ for ER visits).

HCRU: Hospitalizations/ER Visits - Adjusted Regression Analysis

Adjusted for baseline characteristics, the odds of experiencing a hospitalization were significantly higher in the COPD-OSA cohort than in the COPD-only cohort (odds ratio [OR] = 1.45; 95% CI = 1.38-1.53; $P < 0.01$). The odds of experiencing an ER visit were also significantly higher in the COPD-OSA cohort (OR = 1.24; 95% CI = 1.18-1.30; $P < 0.01$).

Health Care Costs—Descriptive Analysis

The unadjusted mean 12-month costs of individuals in the COPD-OSA cohort and the COPD-only cohort are presented in Table 3. The mean (SD) 12-month total cost for individuals with COPD and comorbid OSA was \$32,566 (\$61,981) compared with \$20,342 (\$47,472) for individuals with COPD without OSA. Individuals with comorbid OSA also had higher inpatient, ER, pharmacy, physician office visit, and other outpatient costs than individuals with COPD only ($P < 0.01$). Inpatient and other outpatient costs represented the majority of costs in both cohorts.

Health Care Costs—Adjusted Regression Analysis

Total costs of individuals with COPD and comorbid OSA were estimated to be 40% higher than individuals with COPD only ($P < 0.01$; Table 4). Physician office visit and other outpatient costs were also estimated to be 45% and 37% higher for individuals with COPD and comorbid OSA, respectively ($P < 0.01$). The odds of having any inpatient, ER, and pharmacy costs among those with COPD and comorbid OSA were 45%, 27%, and 22% higher, respectively, than individuals with COPD only ($P < 0.01$). Among individuals with non-zero, strictly positive inpatient, ER, and pharmacy costs, inpatient costs were estimated to be 10% higher for individuals with comorbid OSA compared with individuals without ($P < 0.01$); ER costs were estimated to be 17% higher for individuals with comorbid OSA compared with individuals without ($P < 0.01$); and pharmacy costs were estimated to be 46% higher for individuals with OSA ($P < 0.01$; Table 4).

The average marginal total cost (i.e., the average difference in total cost between individuals with and without comorbid OSA) was \$8,144 (95% CI = \$7,295-\$8,993; $P < 0.01$; Table 5). The average marginal cost for other outpatient services was \$2,831 (95% CI = \$2,463-\$3,200; $P < 0.01$), and the

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TABLE 3 Unadjusted Mean 12-Month Costs in the COPD-Only Cohort and the COPD-OSA Cohort

	Individuals with COPD (n = 85,915)		Individuals with COPD and OSA (n = 7,942)		P Value ^a
	Mean (SD)	%	Mean (SD)	%	
Total cost	\$20,342 (\$47,472)	100.0	\$32,566 (\$61,981)	100.0	<0.01
Cost per HCRU category					
Inpatient	\$8,512 (\$34,535)	41.8	\$14,041 (\$46,029)	43.1	<0.01
ER visit	\$265 (\$1,163)	1.3	\$397 (\$1,510)	1.2	<0.01
Pharmacy	\$3,007 (\$7,638)	14.8	\$5,011 (\$13,233)	15.4	<0.01
Physician office visit	\$871 (\$1,104)	4.3	\$1,282 (\$1,476)	3.9	<0.01
Other outpatient	\$7,689 (\$21,575)	37.8	\$11,837 (\$25,308)	36.3	<0.01

^aStudent's *t*-test was used to test for differences in mean costs.

COPD = chronic obstructive pulmonary disease; ER = emergency room; HCRU = health care resource utilization; OSA = obstructive sleep apnea; SD = standard deviation.

average marginal cost for physician office visits was \$392 (95% CI = \$351-\$433; $P < 0.01$). The average marginal probability of having a non-zero, strictly positive inpatient, ER visit, and pharmacy cost from the logit part of the 2-part models are presented in Appendix B (available in online article). Among individuals with a non-zero, strictly positive inpatient cost, the average marginal cost for inpatient stays was \$2,792 (95% CI = \$1,354-\$4,230; $P < 0.01$). Similarly, among individuals with a non-zero, strictly positive pharmacy cost, the average marginal cost for pharmacy services was \$1,772 (95% CI = \$1,590-\$1,953; $P < 0.01$). The average marginal cost for ER visits, given that individuals have a non-zero, strictly positive ER cost, was \$144 (95% CI = \$101-\$188; $P < 0.01$).

Sensitivity Analysis

The results from the sensitivity analysis remained consistent with the original analysis. Adjusting for index year did not have a significant effect on the outcome estimates. The odds of experiencing a hospitalization in the COPD-OSA cohort was 1.43 times the odds of experiencing a hospitalization in the COPD-only cohort (OR = 1.43; 95% CI = 1.36-1.51). The odds of experiencing an ER visit was also higher in the COPD-OSA cohort (OR = 1.22; 95% CI = 1.16-1.28). Total cost was estimated to be 1.38 times higher in the COPD-OSA cohort ($P < 0.01$). Office visit costs were found to be 1.45 times higher in the COPD-OSA cohort ($P < 0.01$), and other outpatient costs were found to be 1.35 times higher ($P < 0.01$). The relative cost ratios for inpatient, ER visit, and pharmacy costs remained consistent with the results of the original analysis.

The average marginal total cost of \$7,731 (95% CI = \$6,891-\$8,571), and the average marginal cost for each HCRU category were similar to the estimates from the original analysis. Additionally, excluding individuals with a diagnosis of obesity did not change the results of the adjusted regression analyses. Requiring at least 2 claims with a COPD diagnosis to be included in the study sample also yielded outcome estimates that were similar to the estimates from the original analysis.

Discussion

Knowledge about the economic burden of illnesses is useful when examining unmet need, evaluating the appropriateness of current policies, and planning and implementing new health policy interventions. It is well known that COPD is associated with high health care costs.²²⁻²⁴ Similar to what was observed in this study, high annual health care costs have been reported in the literature. In an analysis of commercially insured individuals with COPD in the United States,²² annual direct costs were estimated to range between \$11,395 and \$17,651 (2010 U.S. dollars) based on exacerbation frequency. The estimated costs are lower than the costs observed in our study, which is most likely because the study only included working-age individuals aged 65 years and younger.²² In another study of commercially insured patients with COPD, the mean annual health care cost was estimated to range from \$2,003 to as high as \$43,461 (2008 U.S. dollars), depending on the level of care received.²⁵

It is important to recognize that patients with COPD often have comorbidities, which may independently contribute to the economic burden of illness in the COPD population. While the clinical outcomes of COPD patients with comorbid OSA have been studied,^{11,12,26} the economic burden associated with OSA among COPD patients in the commercially insured U.S. population has not been assessed. This study offers an assessment of the health care cost burden associated with comorbid OSA among commercially insured COPD patients in the United States. We used a large sample of individuals represented in an administrative claims database. The database includes fully adjudicated medical and pharmacy claims and thus presents an ideal data source for studying the cost of covered health services among individuals diagnosed with COPD only and with comorbid OSA. The results from this study may prompt and guide payers and policymakers to design targeted disease management programs for COPD patients with comorbid OSA.

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TABLE 4 12-Month Cost Regression Results: COPD-OSA Cohort vs. COPD-Only Cohort (Reference)

	Cost Ratio (95% CI)		P Value
Total cost ^a	1.40	(1.36-1.44)	< 0.01
Cost per HCRU category			
One-part models^a			
Physician office visit	1.45	(1.40-1.50)	< 0.01
Other outpatient	1.37	(1.32-1.42)	< 0.01
Two-part models^b			
	Logit Model Odds Ratio	GLM Cost Ratio	
Inpatient	1.45 (1.38-1.53)	1.10 (1.05-1.15)	< 0.01 ^c ; < 0.01 ^d
ER visit	1.27 (1.21-1.33)	1.17 (1.12-1.22)	< 0.01 ^c ; < 0.01 ^d
Pharmacy	1.22 (1.15-1.30)	1.46 (1.41-1.51)	< 0.01 ^c ; < 0.01 ^d

^aGLM with a gamma distribution and a log link was fit.

^bA 2-part model was fit: (1) GLM (logit link and binomial distribution) and (2) GLM (gamma distribution with a log link).

^cP value from logit model.

^dP value from GLM.

CI=confidence interval; COPD=chronic obstructive pulmonary disease; ER=emergency room; GLM=generalized linear model; HCRU=health care resource utilization; OSA=obstructive sleep apnea.

Studies have found that patients with COPD and comorbid OSA have worse clinical outcomes and higher HCRU than individuals with COPD alone, including more COPD exacerbations leading to hospitalization,^{11,27} as well as increased risk of cardiovascular events and mortality.^{11,26} In a study examining the effect of comorbidities in COPD patients on HCRU and costs in a predominantly Medicare population, sleep apnea was associated with an 18% higher all-cause health care costs.²⁷ A study of Maryland Medicaid beneficiaries found that individuals with sleep apnea syndrome had higher medical service use and medical cost than beneficiaries without sleep apnea syndrome, with \$4,155 in excess annual costs.¹³

Similarly, our study comparing HCRU and costs of individuals with COPD living with and without comorbid OSA in a commercially insured population identified significantly increased economic burden attributable to comorbid OSA. The probability of experiencing hospitalizations and ER visits was higher for individuals with comorbid OSA, and these individuals incurred higher health care costs. On average, among those with a non-zero, strictly positive hospitalization cost, having comorbid OSA was associated with approximately \$2,800 higher costs due to hospitalizations. Additionally, individuals with comorbid OSA incurred higher costs for physician office visits and other outpatient services, which may be due to individuals with OSA presenting with more symptoms or complications, requiring additional work-up and/or treatment.

The results of this study and previous studies suggest that patients with COPD and comorbid OSA are at risk of increased morbidity and are likely to incur higher HCRU and health care costs. It is important to understand the totality of disease burden for patients, not just the single disease state on its own, to align health care services more closely with patients'

needs and thus reduce the overall burden of disease. Evidence of the management of comorbid conditions is often limited as patients with comorbid chronic conditions are frequently excluded from randomized clinical trials.²⁸ Despite this challenge, clinical practice guidelines should include consideration of comorbidities and how patients should be managed in the presence of these comorbidities.

It was beyond the scope of this study to evaluate whether patients with COPD and comorbid OSA are adequately treated for their OSA. Among COPD patients, an important adverse health event is a COPD exacerbation that may lead to an ER visit and/or hospitalization. Future studies are needed to examine whether treatment for OSA (e.g., positive airway pressure therapy and adherence to such therapy) in this patient population lowers the risk of adverse health events, such as exacerbations leading to hospitalizations, and associated health care costs. Also, it would be interesting to examine whether health care costs differ by OSA severity in this population. It is clear that OSA imposes an added burden on patients with COPD, including an increased risk of experiencing hospitalizations. Optimizing coverage policies and enabling timely patient access to diagnostic testing and treatment and, thus, optimizing the management of this patient population may help reduce this burden. Payers and policymakers may use information from this study to develop and financially plan for tailored therapeutic interventions for improved management of patients with COPD and comorbid OSA.

Limitations

This study has some limitations to consider. This study was conducted using commercial claims data; therefore, the results cannot be generalized to the U.S. population. Obesity may have been an unmeasured confounder in this study. Except for

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TABLE 5 12-Month Average Marginal Costs: COPD-OSA Cohort vs. COPD-Only Cohort (Reference)

	Average Marginal Cost (95% CI) ^c	P Value
Total cost ^a	\$8,144 (\$7,295-\$8,993)	<0.01
Cost per HCRU category		
Inpatient ^b	\$2,792 (\$1,354-\$4,230)	<0.01
ER visit ^b	\$144 (\$101-\$188)	<0.01
Pharmacy ^b	\$1,772 (\$1,590-\$1,953)	<0.01
Physician office visit ^a	\$392 (\$351-\$433)	<0.01
Other outpatient ^a	\$2,831 (\$2,463-\$3,200)	<0.01

^aGLM with a gamma distribution and a log link was fit.

^bSecond part of a 2-part model: GLM (gamma distribution with a log link). Cost represents the cost given a non-zero cost.

^cConfidence interval estimated using the delta method.

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; GLM = generalized linear model; HCRU = health care resource utilization; OSA = obstructive sleep apnea.

in the sensitivity analysis, we did not examine the effects of obesity due to a low prevalence, based on the billing code for obesity. Obesity is rarely coded and captured in administrative claims data, and it has been shown that a claims-based diagnosis of obesity lacks sensitivity, leading to an underestimation of the true prevalence.²⁹ Additionally, it is possible that the COPD-only cohort included individuals who had OSA but had not been diagnosed, leading to misclassification bias and an underestimation of the true difference.

Despite these limitations, this study provides useful information regarding patterns of health care resource utilization and associated costs. The findings are timely, given the growing evidence regarding multimorbidity and the associated implications for HCRU and costs.³⁰⁻³³ To our knowledge, this study is the first to quantify the economic impact of comorbid OSA among commercially insured individuals with COPD from the commercial payer perspective. This study showed that the economic burden of comorbid OSA among individuals with COPD is substantial.

Conclusions

Individuals with comorbid OSA demonstrated greater HCRU and costs than individuals with COPD alone, with a higher probability of experiencing hospitalizations and ER visits. Rather than treat COPD as a sole condition on its own, the overall disease profile of patients with COPD needs to be considered, since management of the overall comorbid burden of patients may lead to a reduction in adverse health events that lead to ER visits/hospitalizations and potentially a reduction in health care costs.

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DISCLOSURES

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DATA STATEMENT

The statements, findings, conclusions, views, and opinions contained and expressed in this article are based in part on data obtained under license from IQVIA (Source: IQVIA PharMetrics Plus, January 2006-December 2015. All Rights Reserved). The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IQVIA or any of its affiliated or subsidiary entities.

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APPENDIX A Cohort Selection

COPD=chronic obstructive pulmonary disease; OSA=obstructive sleep apnea.

APPENDIX B 12-Month Average Marginal Probability of Having Any Hospitalization, ER Visit, and Pharmacy Costs (Part 1 of a 2-Part Model)

HCRU Category	Average Marginal Probability (95% CI) ^b	P Value
Inpatient ^a	0.07 (0.06-0.08)	<0.01
ER visit ^a	0.05 (0.04-0.06)	<0.01
Pharmacy ^a	0.03 (0.02-0.04)	<0.01

^aFirst part of a 2-part model: GLM (logit link and binomial distribution); COPD-OSA cohort vs. COPD-only cohort (reference).

^bCI estimated using the delta method.

CI=confidence interval; COPD=chronic obstructive pulmonary disease; ER=emergency room; GLM=generalized linear model; HCRU=health care resource utilization; OSA=obstructive sleep apnea.