RESEARCH

Economic Burden in Direct Costs of Concomitant Chronic Obstructive Pulmonary Disease and Asthma in a Medicare Advantage Population

Christopher M. Blanchette, PhD; Benjamin Gutierrez, PhD; Caron Ory, RN, MSN; Eunice Chang, PhD; and Manabu Akazawa, PhD, MPH

ABSTRACT

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a highly prevalent disease whose sufferers consume a large amount of resources. Among community-dwelling Medicare beneficiaries, 12% reported that they had COPD in 2002. For clinicians, differentiating COPD from asthma may be difficult, but among patients with COPD and asthma, approximately 20% have both conditions. The economic impact of concomitant asthma and COPD is potentially large but has not been studied.

OBJECTIVE: To assess the cost burden of asthma in patients with COPD in a Medicare Advantage population.

METHODS: We reviewed the database of a large health plan that contained information from more than 30 distinct plans covering approximately 25 million members. We identified Medicare beneficiaries aged 40 years or older with medical and pharmacy benefits and medical claims with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes for COPD or asthma over a 1-year identification period (calendar year 2004). We assigned patients to 2 cohorts based on diagnoses on medical claims (any diagnosis field) during 2004; the COPD cohort had at least 1 medical claim for COPD, and the COPD + asthma cohort had at least 1 claim for COPD and at least 1 claim for asthma. A patient's index date was the first date during 2004 in which there was a medical claim with a diagnosis code for COPD or asthma. To confirm diagnosis, each patient was required to have at least 1 additional claim for COPD (COPD cohort) or at least 1 claim for COPD and at least 1 claim for asthma (COPD + asthma cohort) during the 24-month period from 12 months before through 12 months after the index date. We excluded patients who (1) were not continuously enrolled during the 12 months before and after the index date and (2) did not have at least 1 pharmacy claim for a drug of any type (to verify pharmacy benefits). Outcome measures included the use of emergency room (ER) and hospital services, and cost (net provider payment after subtraction of member cost share), categorized as all-cause, non-respiratory, and respiratory-related. ER use and inpatient hospital stays were identified using place-of-service codes. A minimum of 2 consecutive dates of service (length of stay [LOS] of at least 1 day) was required to indicate an inpatient hospitalization. An LOS of at least 1 day was required to distinguish inpatient services from other services (e.g., procedures or tests) reported on claims with an inpatient place of service. Multivariate analyses adjusted for age, gender, census region, and Charlson Comorbidity Index (CCI). Ordinary least squares regression was used to predict respiratory-related total health care costs, and logistic regression was used to predict the occurrence of at least 1 acute event, defined as use of either an ER or an inpatient hospital. All 2-way interactions were considered, and only those with significant results were included in the models. All reported *P* values were 2-sided with a 0.05 significance level.

RESULTS: During 2004, 68,532 individuals within the database were enrolled in a Medicare Advantage plan. After application of the other inclusion criteria, we excluded approximately 11% of the patients who did not have 1 pharmacy claim of any type. There were 8,086 patients (11.8%) who had at least 1 medical claim with diagnosis codes for COPD and at least 1 other medical claim for either COPD or asthma and were continuously enrolled for at least 24 months. The COPD + asthma cohort numbered 1,843 patients (22.8%), and the COPD cohort numbered 6,243 patients (77.2%). Compared with COPD patients without asthma, patients with COPD + asthma were slightly younger, and a higher proportion was female. There were differences between the 2 cohorts in geographic distribution, and the COPD + asthma cohort had a higher disease severity with a mean CCI score of 2.6 (standard deviation [SD], 2.1) compared with the COPD cohort (2.3 [2.3], $P < 0.001$). Respiratory-related pharmacy costs were a relatively small part of total respiratory-related health care costs: approximately 5.7% for the COPD cohort and 8.8% for the COPD + asthma cohort. Respiratory-related costs accounted for 22.0% of total all-cause health care costs for the COPD cohort and 28.7% for the COPD + asthma cohort. Mean ([SD], median) unadjusted respiratory-related health care costs were $7,240 ([$15,057], $1,957) for the COPD + asthma cohort and $5,158 ([$11,881], $808) in the COPD cohort. After adjusting for covariates, patients in the COPD + asthma cohort were more likely to have at least 1 acute event (e.g., ER visits and hospitalizations) than patients in the COPD cohort (adjusted odds ratio, 1.6; 95% CI, 1.4-1.7) and had $1,931 (37.1%) greater adjusted respiratory-related health care costs—$7,135 versus $5,204 for the COPD cohort ($P < 0.001$).

CONCLUSION: Medicare beneficiaries with COPD and asthma incur higher health care costs and use more health care services than those with COPD without asthma.

J Manag Care Pharm. 2008;14(2):176-85

What is already known about this subject

- More than 11.4 million adults in the United States have been diagnosed with chronic obstructive pulmonary disease (COPD), which affects 5.2% of the adult population and is the fourth leading cause of death among U.S. adults.
- Among community-dwelling Medicare beneficiaries in 2002, 12% reported that they had COPD with $23,847 in average annual medical expenditures in 2002 dollars, of which $2,359 (9.9%) was for prescription drugs, and $21,488 was for hospital and other medical costs.
- The presence of other chronic lung diseases such as asthma adds to the challenge of managing COPD. Differentiating COPD from asthma may be difficult, but among patients with COPD and asthma, approximately 20% have both conditions.

What this study adds

- To our knowledge, this is the first study that examined the burden of concomitant COPD and asthma among Medicare beneficiaries. After adjustment for demographics and comorbidities, respiratory-related health care costs were 37.1% higher in patients with COPD and asthma than in patients with COPD and no evidence of asthma.
- Respiratory-related pharmacy costs were a relatively small part of total respiratory-related health care costs, approximately 5.7% for the COPD cohort and 8.8% for the COPD+asthma cohort.
- Respiratory-related costs accounted for 22.0% of total health care costs for the COPD cohort and 28.7% for the COPD+asthma cohort.

More than 11.6 million adults in the United States have been diagnosed with chronic obstructive pulmonary disease (COPD), and it has become the 4th leading cause of death among U.S. adults.[1] The costs associated with COPD are substantial.[1-3] Among community-dwelling Medicare beneficiaries in 2002, 12% reported that they had COPD with an average annual spending on prescription drugs of $2,359 and medical spending of $21,488.[2] Emergency room (ER) visits and hospitalizations for COPD are common, particularly among the elderly. In 2004, approximately 65% of patients discharged with diagnoses of COPD were aged 65 years and older.[1] Among patients hospitalized with COPD exacerbations, approximately 50% experienced rehospitalization within 24 months.[4] As a result, health care expenditures for Medicare beneficiaries with COPD were 2.4 times those of all-aged Medicare beneficiaries in 1992.[5] While therapies that improve lung function have been shown to reduce health care spending, managing patients with COPD has become a major challenge for health care professionals, public and private health care payers, and policymakers.[6-9]

Further adding to this challenge is managing COPD in the presence of other chronic lung diseases such as asthma. In 2004, more than 3.3 million individuals aged 65 years and older reported that they had been told by health care professionals that they had asthma.[10] Between 1995 and 2004, the rates of hospitalization with asthma listed as the primary diagnosis declined within all age groups except those aged 65 years and older. While differentiating between COPD and asthma may be difficult for clinicians, there has been increased awareness that asthma and COPD coexist in approximately 20% of COPD patients.[11] According to a 20-year study, patients with active asthma were 12 times more likely to develop COPD during their lifetimes than patients without asthma.[12] While the pathogeneses of asthma and COPD differ, both are characterized by bronchial obstruction and airway inflammation, which often lead to ER visits and hospitalizations. In a 1992 study of Medicare beneficiaries, patients with COPD and comorbid conditions such as pneumonia or congestive heart failure incurred higher expenditures (1.6 and 2.1 times higher, respectively) than similarly aged Medicare patients with COPD and without these comorbidities.[5] However, to our knowledge, little has been published about the impact of concomitant COPD and asthma in the elderly population.

The Centers for Medicare & Medicaid Services (CMS) require that health plans that offer Medicare Advantage plans and prescription drug plans include quality assurance programs such as chronic care improvement and medication therapy management programs.[13] Quality assurance and disease management programs are costly to implement.[14] A common approach has been to target various intervention intensity levels based on cost patterns within a population, whereby the most costly patients receive the most intensive interventions, and the less costly patients receive the less intensive interventions.[15] To do so, identifying a costly subset with characteristics that may be effectively intervened upon is vital. Therefore, because of the high prevalence of both COPD and asthma, we conducted a study to identify the cost burden of concomitant COPD and asthma within a Medicare Advantage population.

Methods

Data Source

This analysis used data from a proprietary database owned by Integrated Health Care Information Services (IHCIS), Inc. The IHCIS *National Managed Care Benchmark Database* is Health Insurance Portability and Accountability Act (HIPAA) compliant and contains patient-level and service-level managed care claims and membership information from more than 30 distinct health plans covering approximately 25 million members. During 2004, 68,532 individuals within the IHCIS dataset were enrolled in a Medicare Advantage plan.

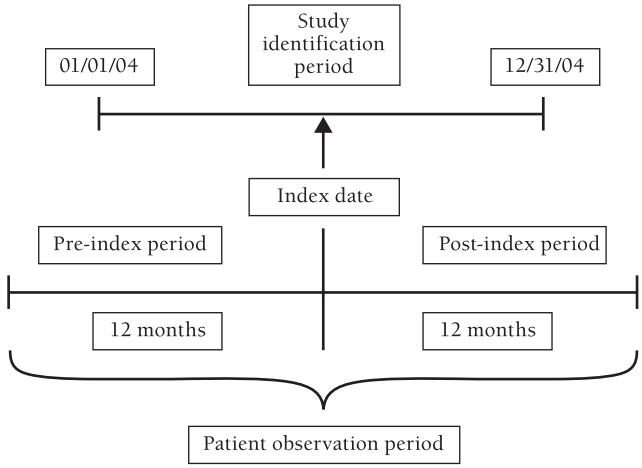
Study Design

This was a retrospective cohort analysis. Eligible patients had medical claims with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes (in any of the 5 diagnosis fields available on the claims) for asthma and/or COPD during the identification period: January 1 through December 31, 2004 (Table 1).[16] The index date was the date of the first medical or hospital claim during the identification period with an ICD-9-CM code for asthma or COPD. A 12-month period before the index date was used to identify pre-index characteristics, and a 12-month period after the index date was used to identify health care utilization and cost outcomes. Continuous enrollment was defined as enrollment in the health plan during the 12 months before the index date (pre-index period) through the 12 months after the index date (post-index period). The observation period for each patient was defined as the 24-month period from the beginning of the pre-index period to the end of the post-index period (Figure 1). To ensure that all

TABLE 1 Diagnosis, Procedure, and Drug Codes With Descriptions

Code	Description
ICD-9-CM Codes	
Asthma	
493.0x	Extrinsic asthma
493.1x	Intrinsic asthma
493.8x	Other forms of asthma
493.9x	Asthma, unspecified
Chronic obstructive pulmonary disease (COPD)	
491.xx	Chronic bronchitis
492.xx	Emphysema
496.xx	Chronic airway obstruction, not elsewhere classified
Asthma and COPD	
Any of the asthma codes listed above AND any of the COPD codes listed above OR	
493.2x	Asthma with COPD
Respiratory-Related	
460.xx-466.xx	Acute respiratory infections
470.xx-478.xx	Other diseases of the upper respiratory tract
480.xx-487.xx	Pneumonia and influenza
490.xx-496.xx	Chronic obstructive pulmonary disease and allied conditions
500.xx-508.xx	Pneumoconioses and other lung disease due to external agents
510.xx-519.xx	Other diseases of respiratory system
Respiratory-Related Drugs	
Acetylcysteine	
Albuterol	
Aminophylline	
Beclomethasone dipropionate	
Budesonide	
Cromolyn sodium	
Dyphylline	
Epinephrine	
Flunisolide	
Flunisolide/menthol	
Fluticasone propionate	
Fluticasone/salmeterol	
Formoterol fumarate	
Guaifenesin/dyphylline	
Ipratropium bromide	
Isoetharine hydrochloride	
Levalbuterol hydrochloride	
Levalbuterol tartrate	
Metaproterenol sulfate	
Methylprednisolone	
Methylprednisolone sodium succinate	
Mometasone furoate	
Montelukast sodium	
Nedocromil sodium	
Omalizumab	
Pirbuterol acetate	
Prednisolone	
Prednisone	
Salmeterol xinafoate	
Terbutaline sulfate	
Theophylline anhydrous	
Tiotropium bromide	
Triamcinolone acetonide	
Zafirlukast	
Zileuton	

FIGURE 1 Study Timeline



study patients had a pharmacy benefit so that we could accurately measure pharmacy claims cost, each patient was required to have at least 1 pharmacy claim for any medication during the observation period.

Patient Selection

COPD Cohort

Each patient (aged 40 years and older) had to have at least 1 medical claim with an ICD-9-CM code for COPD (491.xx for chronic bronchitis, 492.xx for emphysema, or 496.xx for chronic airway obstruction not classified elsewhere) during the identification period (calendar year 2004). The index date was defined as the date of the first medical claim with a COPD diagnosis during the identification period. To confirm diagnosis, each patient was required to have at least 1 additional medical claim with an ICD-9-CM code for COPD during the 24-month observation period (from 12 months before through 12 months after the index date). Any patient who had a medical claim with an ICD-9-CM code for asthma during the observation period was included in the COPD+asthma cohort if the patient met the sampling requirements for that cohort, or excluded from the study if the patient did not meet the sampling requirements for the COPD+asthma cohort.

COPD+Asthma Cohort

Each patient (aged 40 years and older) had to have at least 1 medical claim with an ICD-9-CM code for COPD and at least 1 medical claim for asthma (493.0x, 493.1x, 493.8x, 493.9x) during the identification period. The first medical claim for each diagnosis was identified, and the earlier of the 2 dates within the

identification period was selected as the index date. To confirm diagnoses, each patient was required to have at least 1 additional medical claim for COPD and at least 1 additional claim for asthma during the observation period. If a medical claim with an ICD-9-CM code for COPD and asthma (493.2x) was used during the identification period, the criterion for each disease was met, and the date of that claim was used as the index date. However, to qualify for the study, these patients still had to have either (1) at least 1 additional claim with an ICD-9-CM code for COPD and asthma (493.2x) or (2) at least 1 additional medical claim for COPD and at least 1 additional claim for asthma within the observation period.

Outcome Variables

The primary outcomes of interest were (1) respiratory-related health care costs and (2) occurrence of an acute event, defined as a respiratory-related ER visit or hospitalization. Place-of-service codes were used to identify office visits, ER visits, and inpatient hospitalizations. A minimum of 2 consecutive dates of service (length of stay [LOS] of at least 1 day) was required to indicate an inpatient hospitalization. An LOS of at least 1 day was required to distinguish inpatient services from other services (e.g., procedures or tests) reported on claims with an inpatient place of service.

Pharmacy, medical, and total health care costs were reported as respiratory-related, not respiratory-related, and all-cause. The IHCIS dataset includes standardized costs that reflect net provider payments after subtraction of member cost-share. Pharmacy claims for all respiratory medications were considered respiratory-related (Table 1). Medical claims with respiratory diagnoses listed as primary diagnoses were considered respiratory-related (ICD-9-CM diagnosis codes 460.xx-519.xx). Outcome measures derived from health care utilization claims included outpatient physician visits, all other outpatient visits, ER visits, hospitalizations with an LOS of at least 1 day, total inpatient days per patient, and ER and/or hospitalizations with an LOS of at least 1 day. If a patient had an ER visit that advanced to a hospitalization, it was considered a hospitalization. If a patient had an ER visit that did not advance to a hospitalization, it was considered an ER visit.

The number of patients who received outpatient treatment for acute exacerbations of COPD was reported. Outpatient treatment for a COPD exacerbation was defined as (1) at least 1 medical claim for an outpatient physician visit with ICD-9-CM code for COPD as the primary diagnosis and (2) at least 1 pharmacy claim with a National Drug Code (NDC) number[17] for a 14-day (or fewer) course of an oral corticosteroid or antibiotic, either of which was filled within 2 days of the outpatient physician visit.[18] If the concomitant ICD-9-CM code for COPD+asthma (493.2x) was used, it was considered a COPD diagnosis for this metric.

Other study variables included age, gender, geographic region, and pre-index characteristics, including Charlson Comorbidity Index (CCI, defined in the text that follows) scores, the individual CCI components, and select other comorbid conditions.[19] The CCI contains 19 categories of comorbidities, defined using ICD-9-CM diagnosis codes. Each category has an associated weight based on adjusted risk of 1-year mortality. The overall score reflects the cumulative increased likelihood of 1-year mortality. A higher score reflects a more severe comorbidity burden. For this analysis, we used an adapted version of the clinical index developed by Charlson and her colleagues, which is based on medical record review and contains 17 categories of comorbidities.[20] These categories include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, moderate or severe liver disease, diabetes with complications, hemiplegia or paraplegia, renal disease, malignant neoplasms, metastatic solid tumors, and acquired immune deficiency syndrome. COPD and asthma are assigned to the chronic pulmonary disease category and are considered a single comorbidity. Because it is possible that some of the study patients were newly diagnosed with a pulmonary condition on the index date, and these pulmonary conditions were not reported as pre-index comorbidities, not all study patients met the CCI criterion for chronic pulmonary disease.

Statistical Analysis

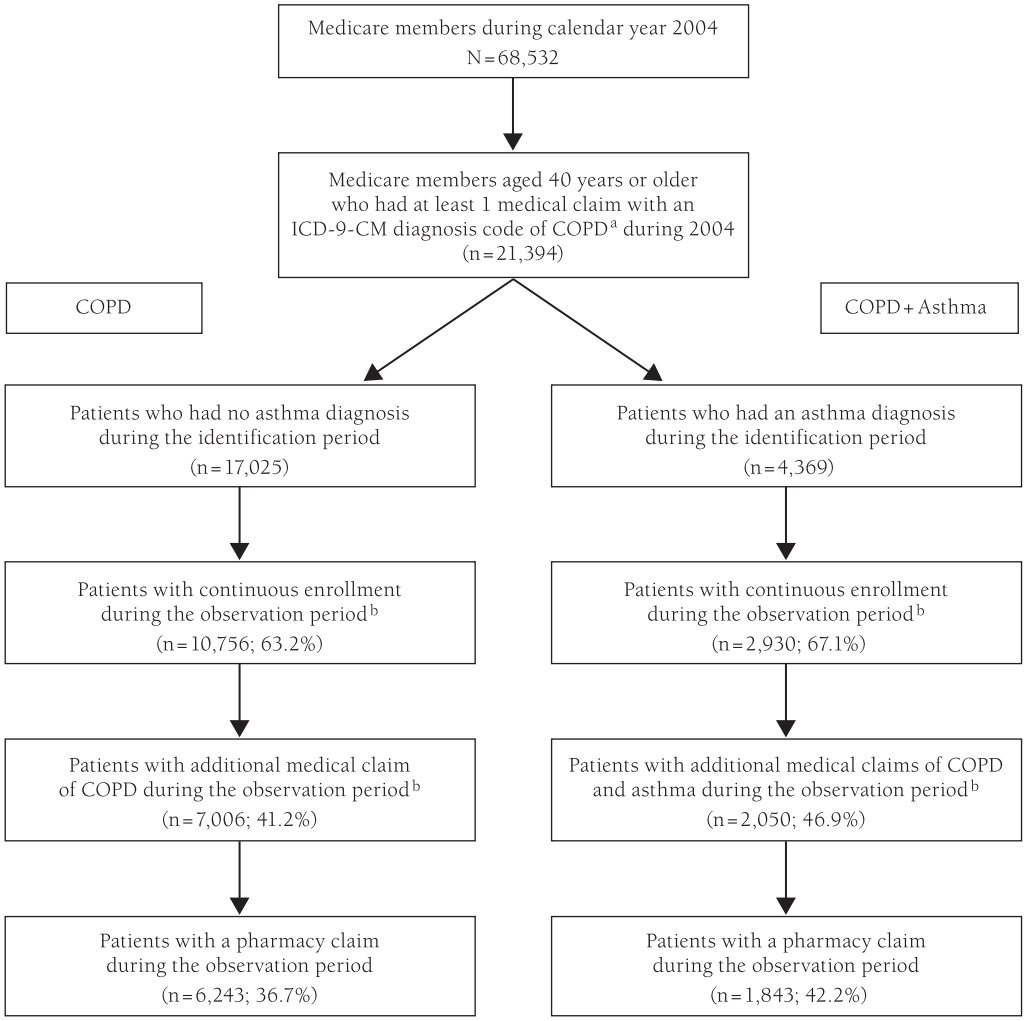
All data transformations and statistical analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, NC). To compare pre-index characteristics between the 2 cohorts, the Pearson chi-square test was used for categorical variables, and the *t*-test was used for continuous variables. To compare medians, the non-parametric median test was used.

Multivariate regression models were used to adjust for baseline characteristics. The independent variables included age, gender, census region, and CCI score. For the models, we created 3 census regions: Northeast, West, and Midwest/South/unknown. All 2-way interactions were considered, and only those with significant results were included in the models. Age by region was the only significant interaction included in all models. For the dependent variable of respiratory-related total health cost, analysis of covariance (an extension of ordinary least squares regression) was used, and adjusted means (also known as least squares means) were estimated and compared. We estimated adjusted means by applying into the model the grand means of age and CCI score and the grand proportion of each category of gender and census region. For the dichotomous dependent variable indicating an acute event (i.e., ER use or inpatient hospital use with LOS $\geq$1 day), logistic regression was used and adjusted odds ratios were reported. All statistical tests were 2-sided with a level of significance of 0.05.

Results

Application of the final inclusion criterion of at least 1 pharmacy claim of any type resulted in the exclusion of 10.9% (n=763)

FIGURE 2 Patient Selection



[a] *The ICD-9-CM codes with descriptions are listed in Table 1. The identification period was the 12-month period from January 1 through December 31, 2004.*
[b] *The index date was the date of the first diagnosis in the identification period. The 24-month observation period included 12 months pre-index and 12 months post-index.*
COPD=chronic obstructive pulmonary disease; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification.

of patients in the COPD cohort and 10.1% (n=207) patients in the COPD+asthma cohort (Figure 2). Among the remaining 8,086 patients who met the study criteria, 6,243 (77.2%) were stratified to the COPD cohort and 1,843 (22.8%) to the COPD+asthma cohort. Compared with the COPD cohort, COPD+asthma cohort patients were slightly younger, and a higher percentage was female. Geographic representation also differed between cohorts ($P<0.001$), but in both cohorts, approximately 75% of patients were in the northeastern United States, and the geographic location for 12%-13% of the patients was unknown (Table 2).

The COPD+asthma cohort had more comorbidities, with a mean CCI score of 2.6 (standard deviation [SD] ±2.1) compared with 2.3 [±2.3] for the COPD cohort ($P<0.001$, Table 3). Congestive heart failure, chronic pulmonary diseases, rheumatologic disease, peptic ulcer disease, mild-to-moderate diabetes, pneumonia, and acute upper respiratory infections were more prevalent in the COPD+asthma cohort and peripheral vascular disease, and metastatic solid tumors were more prevalent in the COPD cohort. Except for rates of pulmonary disease, these comorbidity differences were slight.

Unadjusted Health Care Utilization and Costs

Unadjusted health care utilization metrics are presented in Table 4. Respiratory-related resource utilization rates in the COPD+asthma cohort were higher than in the COPD cohort for every utilization metric except total inpatient days. The proportions of patients who received outpatient treatment for COPD exacerbations did not significantly differ by cohort (7.1% for COPD+asthma vs. 7.8% for COPD; $P=0.279$).

Unadjusted health care costs, including pharmacy, medical, and total (pharmacy+medical), stratified as respiratory-related, not respiratory-related, and all-cause, are presented in Table 5. Unadjusted mean respiratory-related costs for the post-index period were higher for the COPD+asthma cohort than for the COPD cohort ($7,240 vs. $5,158; $P=0.001$). The median all-cause health care costs for the post-index period were higher for the COPD+asthma cohort than the COPD cohort ($12,513 vs. $10,146; $P<0.001$, Table 5). Respiratory-related pharmacy costs were a relatively small part of total respiratory-related health care costs, approximately 5.7% for the COPD cohort and 8.8% for the COPD+asthma cohort. Respiratory-related costs accounted for 22.0% of total health care costs for the COPD cohort and 28.7% for the COPD+asthma cohort.

TABLE 2 Pre-index Characteristics

	COPD	COPD + Asthma	*P* Value
	N = 6,243	N = 1,843	
Age, mean [SD]	73.9 [5.0]	73.0 [6.0]	<0.001 [a]
Age group (years)	**% patients (n)**	**% patients (n)**	<0.001 [b]
40-54	0.8% (50)	2.1% (38)	
55-64	3.3% (203)	5.6% (104)	
65-74	40.2% (2,508)	41.5% (764)	
75+	55.8% (3,482)	50.8% (937)	
Gender			<0.001 [b]
Female	51.6% (3,220)	59.6% (1,099)	
Region			<0.001 [c]
Midwest	0% (0)	0.1% (1)	
Northeast	74.5% (4,649)	78.5% (1,447)	
South	0.1% (8)	0.1% (2)	
West	13.4% (834)	8.4% (154)	
Unknown	12.0% (752)	13.0% (239)	

[a] *Student's t-test.*
[b] *Pearson chi-square test.*
[c] *Fisher's exact test.*
COPD = chronic obstructive pulmonary disease.

TABLE 3 Pre-index Comorbid Conditions

Condition	COPD	COPD + asthma	*P* Value
	N = 6,243	N = 1,843	
	Mean [Standard Deviation]		***P* Value [a]**
Charlson Comorbidity Index	2.3 [2.3]	2.6 [2.1]	<0.001
	% Patients (n)		***P* Value [b]**
Myocardial infarction	7.2 (449)	6.8 (126)	0.602
Congestive heart failure	18.3 (1,141)	21.3 (392)	0.004
Peripheral vascular disease	10.5 (654)	8.2 (151)	0.004
Cerebrovascular disease	15.2 (951)	13.7 (252)	0.098
Dementia	1.8 (110)	1.2 (22)	0.091
Chronic pulmonary disease	60.2 (3,756)	92.5 (1,705)	<0.001
Rheumatologic disease	2.9 (183)	3.9 (72)	0.035
Peptic ulcer disease	2.3 (142)	3.1 (58)	0.034
Mild liver disease	0.5 (32)	0.5 (10)	0.875
Mild-to-moderate diabetes	20.7 (1,293)	24.8 (457)	<0.001
Diabetes with chronic complications	4.2 (261)	5.0 (93)	0.111
Paraplegia or hemiplegia	0.6 (35)	0.8 (14)	0.333
Renal disease	4.2 (265)	3.7 (69)	0.342
Any malignancy/lymphoma/leukemia	15.8 (985)	14.3 (263)	0.116
Moderate or severe liver disease	9.7 (607)	10.0 (185)	0.689
Metastatic solid tumor	2.2 (139)	1.2 (23)	0.008
AIDS	0.0 (1)	0.0 (0)	0.587
Acute upper respiratory infection*	15.3 (953)	23.1 (425)	<0.001
Pneumonia*	12.8 (796)	18.8 (347)	<0.001

[a] *Student's t-test.*
[b] *Pearson chi-square test.*
* *Not a component of CCI.*
AIDS = acquired immune deficiency syndrome; CCI = Charlson Comorbidity Index; COPD = chronic obstructive pulmonary disease.

TABLE 4 Unadjusted Health Care Utilization for 12 Months of Post-index Follow-Up

	Respiratory Related			Not Respiratory Related			All Cause		
	COPD n = 6,243	COPD + Asthma n = 1,843	*P* Value	COPD n = 6,243	COPD + Asthma n = 1,843	*P* Value	COPD n = 6,243	COPD + Asthma n = 1,843	*P* Value
Outpatient physician visits[a]	2.7 [3.0] 2.0	4.8 [4.7] 4.0	<0.001[b] <0.001[c]	14.3 [12.3] 11.0	15.5 [11.9] 13.0	<0.001[b] <0.001[c]	17.0 [12.7] 14.0	20.3 [13.0] 17.0	<0.001[b] <0.001[c]
All other outpatient visits[a]	0.8 [2.3] 0.0	1.1 [3.4] 0.0	<0.001[b] <0.001[c]	5.1 [11.2] 2.0	5.5 [10.0] 2.0	0.182[b] <0.001[c]	5.9 [11.8] 2.0	6.6 [11.2] 3.0	0.020[b] <0.001[c]
% (n) patients with ER visit[d]	13.5% (841)	21.7% (400)	<0.001[e]	38.7% (2,415)	43.3% (798)	<0.001[e]	43.7% (2,727)	51.4% (947)	<0.001[e]
% (n) patients with LOS ≥ 1[f]	20.6% (1,288)	26.3% (484)	<0.001[e]	30.6% (1,909)	36.3% (669)	<0.001[e]	41.1% (2,564)	47.4% (873)	<0.001[e]
Total inpatient days[a]	8.7 [9.9] 5.0	9.6 [13.3] 6.0	0.167[b] <0.283[c]	17.5 [25.2] 8.0	15.3 [21.9] 7.0	0.032[b] <0.126[c]	17.4 [25.4] 8.0	17.0 [24.4] 8.0	0.731[b] <0.591[c]
% (n) patients with ER visit[d] or LOS ≥ 1 day[f]	28.3% (1,768)	37.8% (696)	<0.001[e]	47.1% (2,940)	53.1% (978)	<0.001[e]	52.7% (3,291)	60.6% (1,117)	<0.001[e]
% (n) patients with outpatient visit for COPD exacerbation	7.8% (488)	7.1% (130)	0.279[e]	n/a	n/a	n/a	n/a	n/a	n/a

[a] *Mean [SD] median.*
[b] *Student's t-test.*
[c] *Median test.*
[d] *Denotes a claim with a place of service of emergency room.*
[e] *Pearson chi-square test.*
[f] *Denotes claims with an inpatient place of service and a date span of 2 or more consecutive days, (i.e. LOS of at least 1 day).*
COPD = chronic obstructive pulmonary disease; ER = emergency room; LOS = length of stay.

TABLE 5 Unadjusted Health Care Costs for 12 Months of Post-index Follow-Up

	Respiratory Related			Not Respiratory Related			All Cause		
Mean [SD] Median	COPD N = 6,243	COPD + Asthma n = 1,843	*P* Value	COPD n = 6,243	COPD + Asthma n = 1,843	*P* Value	COPD n = 6,243	COPD + Asthma n = 1,843	*P* Value[a]
Pharmacy costs	$294 [$638] $2	$634 [$961] $244	<0.001[a] <0.001[b]	$1,316 [$1,889] $844	$1,375 [$1,861] $812	0.236[a] <0.233[b]	$1,610 [$2,044] $1,095	$2,009 [$2,269] $1,405	<0.001[a] <0.001[b]
Medical costs	$4,864 [$11,805] $514	$6,606 [$14,960] $1,111	<0.001[a] <0.001[b]	$17,018 [$31,596] $5,927	$16,645 [$26,397] $6,973	0.612[a] <0.001[b]	$21,882 [$36,620] $8,503	$23,252 [$33,957] $10,150	0.135[a] <0.001[b]
Total health care costs	$5,158 [$11,881] $808	$7,240 [$15,057] $1,957	<0.001[a] <0.001[b]	$18,334 [$31,992] $7,249	$18,021 [$26,735] $8,271	0.673[a] 0.001[b]	$23,492 [$37,002] $10,146	$25,261 [$34,307] $12,513	0.056[a] <0.001[b]

[a] *Student's t-test.*
[b] *Median test.*
COPD = chronic obstructive pulmonary disease.

Adjusted Health Care Utilization and Costs

After adjusting for age, gender, region, and CCI score, the COPD+asthma cohort was 1.6 times as likely to have ER and/or hospital use as compared with the COPD cohort (95% [CI], 1.4-1.7; Table 6). The COPD+asthma cohort ($7,135; 95% CI, $6,556-$7,714) had higher adjusted respiratory-related total health care costs than did the COPD cohort ($5,204; 95% CI, $4,888-$5,519, $P<0.001$; Table 7).

TABLE 6 Logistic Regression (N=8,086) Predicting Occurrence of Acute Event (Respiratory-Related Emergency Room Use or Inpatient Hospital Use With Length of Stay at Least 1 Day)

	Coefficient Estimate	Standard Error	Pr > Chi-Square
Parameter			
Intercept	-0.80	0.71	0.260
Age	0.00	0.01	0.923
Gender (female vs. male)	0.00	0.05	0.924
Region (Northeast vs. Midwest/South/unknown)	-3.11	0.84	0.002
Region (West vs. Midwest/South/unknown)	2.23	1.28	0.082
Age*Region Northeast	0.04	0.01	0.002
Age*Region West	-0.03	0.02	0.066
CCI	0.06	0.01	<0.001
Cohort (asthma+COPD vs. COPD)	0.44	0.06	<0.001
	Lower 95% CI for Odds Ratio	**Adjusted Odds Ratio Estimate**	**Upper 95% CI for Odds Ratio**
Cohort (asthma+COPD vs. COPD)	1.4	1.6	1.7

Max-rescaled R-square=0.03; c-statistic=0.596.
CCI=Charlson Comorbidity Index; CI=confidence interval; COPD=chronic obstructive pulmonary disease.

Discussion

Despite the high prevalence and mortality of asthma and COPD, little is known about their combined impact on health care utilization and costs. Our analysis had several interesting findings. Clinical characteristics of the cohorts differed significantly. Compared with the COPD-only cohort, the COPD+asthma cohort was younger, comprised a higher proportion of females, and had a greater burden of comorbidity, evidenced by higher CCI scores and prevalence of select chronic conditions. Our finding that the COPD+asthma cohort comprised a higher proportion of younger and female patients is consistent with the findings of a Centers for Disease Control and Prevention study, which reported that asthma was more often diagnosed in younger and female patients.[21] In our study, patients in the COPD+asthma cohort had a higher prevalence of respiratory-related comorbidities, including congestive heart failure, pneumonia, and upper respiratory infections. After adjusting for differences in demographics and comorbidities, the COPD+asthma cohort was 1.6 times as likely as the COPD cohort to have a respiratory-related ER visit or hospitalization. As a result, respiratory-related health care cost was significantly higher in the COPD+asthma cohort than in the COPD cohort. Among enrollees with COPD, an additional diagnosis of asthma was associated with a 37.1% increase in adjusted mean respiratory-related total health care cost. These findings demonstrate the significant economic burden posed by asthma in the presence of COPD.

Many health care organizations have turned to clinical initiatives and disease management programs to better manage patients with prevalent diseases who require frequent and costly health care services. Among patients with COPD, pharmacologic and non-pharmacologic interventions that reduce exacerbations through respiratory-related ER visits and hospitalizations have the potential to generate savings. Although our study did not address this possibility specifically, our findings suggest that it should be explored in future research. Studies have shown that select respiratory treatments such as inhaled corticosteroid and long-acting beta agonist combination products reduce bronchial obstruction and airway inflammation in patients with COPD or asthma treated in outpatient settings, thus reducing ER visits and hospitalizations.[6-8] When implementing a program, it is important to identify patients with characteristics that place them at risk of incurring more utilization and higher health care costs. Our findings suggest that patients with concomitant COPD and asthma may be an appropriate group for a focused intervention.

Limitations

There are limitations to this study. First, we may have excluded patients with very mild COPD or those who have not been diagnosed, thereby overstating per-patient health care utilization and costs. To ensure that patients had COPD, we required at least 2 medical claims for COPD, and to ensure that the patients had a pharmacy benefit, we required that they had at least 1 pharmacy claim for any medication during a 2-year period of continuous enrollment. About 10% of the patients who otherwise met the inclusion/exclusion criteria were excluded by the absence of at least 1 pharmacy claim for any drug. However, we did not require a pharmacy claim for a respiratory medication; the low median costs for respiratory-related medications suggest that we may have also captured mild COPD patients. In addition, our use of a broad range of respiratory-related diagnoses may have overestimated respiratory-related health care utilization.

Second, users of the IHCIS database are blinded from knowledge of the characteristics of individual health plans in the database, so potentially important characteristics are unknown,

TABLE 7 Ordinary Least Squares Regression of Respiratory-Related Costs on Study Cohort and Covariates (N = 8,086)

	Coefficient Estimate	Standard Error	Pr > |t|
Parameter			
Intercept	7900.01	4323.25	0.068
Age	-16.18	59.86	0.787
Gender (female vs. male)	-332.87	282.60	0.239
Region (Northeast vs. Midwest/South/unknown)	-11606.72	4935.65	0.019
Region (West vs. Midwest/South/unknown)	7181.38	7808.77	0.358
Age*Region Northeast	123.81	68.03	0.069
Age*Region West	-146.22	105.36	0.165
CCI	412.88	63.73	<0.001
Cohort (asthma + COPD vs. COPD)	1931.23	336.50	<0.001
	Lower 95% CI for Adjusted Mean[a]	**Adjusted Mean**	**Upper 95% CI for Adjusted Mean**
Asthma + COPD cohort	$6,556	$7,135	$7,714
COPD cohort	$4,888	$5,204	$5,519

[a] *Adjusted means were calculated by applying into the model the grand means of age and CCI and the grand proportion of each category of gender and census region.*

R-square = 0.02.

CCI = Charlson Comorbidity Index; CI = confidence intervals; COPD = chronic obstructive pulmonary disease.

such as the presence of annual pharmacy benefit maximum caps and plan coverage of only generic drugs, characteristics that were common among Medicare Advantage plans in 2004. Third, the relationship between COPD and/or asthma severity and study outcomes could not be explored because diagnosis codes do not provide information regarding severity levels.

Third, there are also challenges in differentiating COPD from asthma, particularly among the elderly, and it is possible that some patients may have been misdiagnosed, and therefore stratified incorrectly.[11] Fourth, administrative data are subject to coding errors and omissions, and observational designs are vulnerable to unmeasured factors that may have influenced outcomes. Our low c-statistic and *R*-squared values suggest that results could be attributable to unmeasured confounding factors. Fifth, our population was primarily from the northeastern United States so our results may not be representative of the entire U.S. population.

Seventh, results of this study reflect health care utilization and cost within our dataset for patients identified by plans as being in the Medicare Advantage program and may not reflect patterns from another population, setting, or plans that submit data on patients not coded as Medicare Advantage participants.

Conclusion

Patients with COPD and asthma use more health care services and incur higher costs than those with COPD without the presence of asthma. These patients may be an appropriate group for a focused intervention to improve disease management and outcomes.

Authors

CHRISTOPHER M. BLANCHETTE, PhD, is associate scientist and director, Center for Pharmacoeconomic & Outcomes Research, Lovelace Respiratory Research Institute, Albuquerque, New Mexico. BENJAMIN GUTIERREZ, PhD, is health economics practice leader, CARON ORY, RN, MSN, is a senior researcher, and EUNICE CHANG, PhD, is the chief statistician, Partnership for Health Analytic Research, Beverly Hills, California. MANABU AKAZAWA, PhD, MPH, is a former health outcomes fellow at the University of North Carolina, and GlaxoSmithKline, Chapel Hill, North Carolina.

AUTHOR CORRESPONDENCE: Christopher M. Blanchette, PhD, Associate Scientist and Director, Center for Pharmacoeconomic & Outcomes Research, Lovelace Respiratory Research Institute, 2425 Ridgecrest Dr. SE, Albuquerque, NM 87108-5127. Tel.: 505.216.7695; Fax: 505.348.4802; E-mail: cblanchette@lrri.org

DISCLOSURES

GlaxoSmithKline provided funding for this project, and author Christopher M. Blanchette was an employee of GlaxoSmithKline at the time this research was conducted.

Blanchette was responsible for the study concept and design, with assistance from Gutierrez and Akazawa. Chang performed the majority of data analysis with assistance from Gutierrez. All authors contributed to data interpretation. Ory did the majority of the writing of the manuscript and contributed equally to the revision with Blanchette.

REFERENCES

1. American Lung Association. Epidemiology & Statistics Unit, Research and Program Services. *Trends in Chronic Obstructive Bronchitis and Emphysema: Morbidity and Mortality, September 2007.* American Lung Association; 2007, Available at: www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/TREND_COPD_SEPT07.PDF.

2. Stewart BS-WL, Zuckerman I, Doshi J, Shea D, Shaffer T, Zhao L. *Medication use by age and disabled Medicare beneficiaries across the spectrum of morbidity—A Chartbook:* The Peter Lamy Center on Drug Therapy and Aging, University of Maryland School of Pharmacy; Baltimore, MD, 2007, Available at: www.pharmacy.umaryland.edu/lamy/Complete%20Chartbook%20w.%20cover.pdf. Accessed January 24, 2008.

3. Tinkelman D, Nordyke RJ, Isonaka S, George D, DesFosses K, Nonikov D. The impact of chronic obstructive pulmonary disease on long-term disability costs. *J Manag Care Pharm.* 2005;11(1):25-32. Available at: www.amcp.org/data/jmcp/Research_25-32.pdf.

4. Connors Jr. AF, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Am J Respir Crit Care Med.* 1996;154(4):959-67.

5. Grasso ME, Weller WE, Shaffer TJ, Diette GB, Anderson GF. Capitation, managed care, and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1998;158(1):133-38.

6. Kardos P, Wencker M, Glaab T, Vogelmeier C. Impact of salmeterol/fluticasone propionate versus salmeterol on exacerbations in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2007; 175(2):144-94.

7. Niewoehner DE, Rice K, Cote C, et al. Prevention of exacerbations of chronic obstructive pulmonary disease with tiotropium, a once-daily inhaled anticholinergic bronchodilator: a randomized trial. *Ann Intern Med.* 2005;143(5):317-26.

8. Stempel DA, Kim J, Chernicoff HO, Legoretta A. Asthma related ER/hospitalization risk and asthma costs of fluticasone propionate/salmeterol in a single inhaler compared to fluticasone propionate and salmeterol in separate inhalers. [meeting abstract] *J Allergy Clin Immunol.* 2004; 113(2):S272.

9. U.S. Department of Health and Human Services. Respiratory Disease [Goal 24]. Healthy People 2010 (conference ed., vol II). In: U.S. Department of Health and Human Services Washington, DC, 2000. Available at: www.healthypeople.gov/document/pdf/Volume2/24Respiratory.pdf.

10. *American Lung Association, Epidemiology & Statistics Unit RaPS, Trends in Asthma Morbidity and Mortality August 2007:* American Lung Association, 2007. Available at: www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/TREND_ASTHMA2007.PDF.

11. Beeh KM, Kornmann O, Beier J, Ksoll M, Buhl R. Clinical application of a simple questionnaire for the differentiation of asthma and chronic obstructive pulmonary disease. *Respir Med.* 2004;98(7):591-97.

12. Silva GE, Sherrill DL, Guerra S, Barbee RA. Asthma as a risk factor for COPD in a longitudinal study. *Chest.* 2004;126(1):59-65.

13. Medicare Prescription Drug, Improvement, and Modernization Act: Section 722 Amending Section 1852e of Social Security Act, H.R. 1.ENR. 2003. Available at: www.cms.hhs.gov/EmplUnionPlanSponsorInfo/downloads/hr1.pdf.

14. Linden A, Roberts N, Keck K. The complete "how to" guide for selecting a disease management vendor. *Dis Manag.* 2003, 6(1):21-26. Available at: www.lindenconsulting.org/documents/DMHowTo.pdf.

15. Krumholz HM, Currie PM, Riegel B, et al. A taxonomy for disease management: a scientific statement from the American Heart Association Disease Management Taxonomy Writing Group. *Circulation.* 2006; 114(13):1432-45.

16. U.S. Department of Health and Human Services. *International Classification of Diseases, Ninth Revision, Clinical Modification,* 4th ed.: U.S. Government Printing Office, Washington, DC; 1991.

17. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. National Drug Code Directory. Available at: www.fda.gov/cder/ndc/database/default.htm.

18. Fan VS, Bryson CL, Curtis JR, et al. Inhaled corticosteroids in chronic obstructive pulmonary disease and risk of death and hospitalization: time-dependent analysis. *Am J Respir Crit Care Med.* 2003;168(12):1488-94.

19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-83.

20. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol.* 1992; 45(6):613-19.

21. Centers for Disease Control and Prevention. Self-reported asthma prevalence among adults—United States, 2000. *MMWR Morb Mortal Wkly Rep.* 2001;50(32):682-86. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5032a3.htm.