

available at www.sciencedirect.comjournal homepage: www.elsevier.com/locate/rmed

Economic implications of comorbid conditions among Medicaid beneficiaries with COPD[☆]

Pei-Jung Lin^{a,*}, Fadia T. Shaya^b, Steven M. Scharf^c

^a Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA 02111, USA

^b Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD 21201, USA

^c Division of Pulmonary and Critical Care Medicine, University of Maryland Sleep Disorders Center, Baltimore, MD 21201, USA

Received 22 June 2009; accepted 15 November 2009
Available online 2 December 2009

KEYWORDS

COPD;
Cost;
Utilization;
Comorbidity;
Medicaid

Summary

Objectives: To characterize a comprehensive comorbidity profile and to explore the economic implications of comorbidity among patients with chronic obstructive pulmonary disease (COPD).

Methods: This retrospective cohort study analyzed medical claims from the Maryland Medicaid database. We employed a 1:2 case–control design to select COPD patients ($n = 1388$) and demographically matched controls ($n = 2776$) aged 40 to 64 years with 24 months of continuous enrollment. Odds ratios were employed to compare comorbidity differences, including 17 conditions defined by the Charlson Comorbidity Index (CCI) and 6 additional conditions commonly observed in COPD patients. We estimated the incremental medical utilization and medical cost by specific condition.

Results: Compared with the controls, Medicaid COPD patients had higher comorbidity burden and were more likely to have myocardial infarction, congestive heart failure, cerebrovascular disease, peptic ulcer, mild liver disease, hypertension, sleep apnea, tobacco use, and edema. COPD patients on average had 24% more medical claims (81.4 vs. 65.4, $p < 0.001$) and were 33% more expensive than controls (\$7603 vs. \$5732, $p < 0.001$). Ten conditions defined by the CCI as well as hypertension, tobacco use, and edema were associated with incremental medical utilization and cost in COPD patients; depression was associated with incremental medical utilization but not cost.

[☆] An abstract of this manuscript was presented at the International Society for Pharmacoeconomics and Outcomes Research 14th Annual International Meeting, May 16–20, 2009.

* Corresponding author. Tel.: +1 617 636 4616; fax: +1 617 636 5560.
E-mail address: plin@tuftsmedicalcenter.org (P.-J. Lin).

Conclusions: The high burden of comorbidity in COPD patients translates into additional medical utilization and cost. Effective disease management and treatment protocols are needed to reduce comorbidity burden. The development of a COPD-specific comorbidity measure may be used to identify high-risk subgroups and to predict utilization and cost.

© 2009 Elsevier Ltd. All rights reserved.

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease that affects approximately 24 million U.S. adults, including 12 million diagnosed patients and 12 million undiagnosed.¹ COPD is a major cause of disability and hospitalizations in adults and has remained the fourth leading cause of death in the U.S. for the past decade.² The annual cost of COPD was estimated at \$42.6 billion in 2007, with \$26.7 billion (63%) attributable to direct health care costs, in which hospital care accounting for the largest share (\$11.3 billion or 42%).¹

Comorbid conditions are highly prevalent among individuals with COPD. A case–control study in a Dutch primary care population reported that 73% of COPD patients had one or more comorbidity, compared to 63% in controls (odds ratio = 1.6; 95% confidence interval: 1.10–2.33).³ Data from a managed care organization showed that COPD patients on average had 3.7 comorbidities, compared to 1.8 comorbidities for controls ($p < 0.001$).⁴ In an analysis of patients with COPD undergoing pulmonary rehabilitation, 51% reported at least one chronic comorbidity, with metabolic diseases (e.g., systemic hypertension, diabetes and/or dyslipidaemia) and heart diseases (e.g., chronic heart failure and/or coronary heart disease) being the most common conditions (61% and 24%, respectively).⁵

The impact of comorbidities on COPD patients can be introduced in different ways, such as association with higher hospitalization and mortality rates^{6,7} and poorer quality of life.^{8,9} In a cohort of 51,353 patients who were discharged after an exacerbation of COPD in the Veterans Affairs health care system during the period of 1999 and 2003, the risk of rehospitalization increased with asthma and pulmonary hypertension.⁷ Sin and colleagues reviewed the role of comorbidities in COPD mortality and found that certain comorbidities such as cardiovascular diseases and lung cancer were associated with higher mortality rates in mild and moderate COPD, whereas respiratory failure was the main cause of death in more advanced COPD, although the exact nature of the causal pathways remains unclear.¹⁰

In this analysis, we examined the impact of individual comorbidity and overall disease profile on the medical utilization and cost of COPD patients because comorbidity is an important source of elevated economic burden in this population. In related work, we found that Medicaid COPD patients who have concomitant sleep apnea (known as the “overlap syndrome”¹¹) incurred significantly more medical utilization and higher medical cost than patients without sleep apnea.¹² Other studies indicate that COPD patients with concomitant asthma used more medical services and incurred higher cost than those without asthma based on data from a Medicaid managed care population¹³ and a Medicare Advantage population.¹⁴ In another study that

compared expenditure and utilization patterns of elderly Medicare beneficiaries with COPD ($n = 42,472$) versus all Medicare beneficiaries ($n = 1,221,615$), higher comorbidity, as measured by the Deyo-adapted Charlson Comorbidity Index (CCI), was associated with higher health care expenditures.¹⁵ As health care costs continue to escalate, understanding the economic implications associated with comorbidity can help health plans and providers to develop disease management programs that can better manage patients with COPD, improve care coordination, and potentially reduce cost. In this study, we performed a more thorough examination of comorbidities than previous studies, which typically address only limited comorbidities or explore the economic burden of comorbidity measured by a composite index such as the CCI. Our investigation included additional comorbidities that are particularly relevant to COPD patients. The results can help to inform efforts to develop a COPD-specific comorbidity measure for high-risk identification. Using data from a Medicaid population enabled us to explore the economic implications of comorbidity in a frail population.

Materials and methods

Data source

Data were obtained from the Maryland Medicaid database for 2001 through 2003, which contained all claims records for medical inpatient hospitalization, outpatient care, and physician office visits. During the study period, there were more than 445,000 Medicaid beneficiaries, representing approximately 10% of the overall state population. The Medicaid beneficiaries were disproportionately African American (>50%) and females (>60%).

Cohort selection

The eligible study population was comprised of Medicaid beneficiaries who were aged 40 to 64 years on the date of January 1, 2001, and were enrolled in one of seven contracted managed care organizations. We excluded beneficiaries younger than 40 years of age because they are not at high risk for COPD; beneficiaries aged 65 and older also were excluded because they may have been dually enrolled in Medicaid and Medicare and therefore their claims data may be incomplete. All sample beneficiaries were required to have continuous enrollment during the 12 months before the index date (defined as the date of the first medical claim with a COPD diagnosis) through the 12 months after the index date. Medical utilization data were collected from the index date through the end of the post-index period. We identified beneficiaries with a COPD diagnosis

(ICD-9-CM diagnosis codes 491.xx, 492.xx, and 496.xx) in the primary, secondary, or tertiary diagnosis field in their medical claims during the study period. A total of 7236 beneficiaries met the criteria of having 12 months pre-index period and 12 months post-index period; of these, 2411 beneficiaries (33.3%) had diagnosed COPD. Then, we employed a 1:2 case-control design to select 1388 COPD patients and 2776 demographically matched non-COPD controls with similar age (± 5 yrs), sex, and race.

Measures of economic burden

In evaluating the economic burden, resource use was measured by overall medical utilization (defined as the total number of service claims) and the total medical cost for individual categories including physician visits, outpatient services, and inpatient services. Outpatient care was defined as a practice within a hospital but not being admitted to the hospital (i.e., inpatient); physician care was defined as a practice outside of a hospital. Because the Medicaid managed care claims data do not contain actual costs for each service claim, we estimated medical cost by using the average unit cost for each type of service and imputed the cost values based on the Medicaid fee schedule.

Measures of comorbidity burden

Comorbidity burden was measured using the CCI with the Deyo modification^{16,17} and 6 additional conditions commonly observed in COPD patients. The CCI originally was developed as a risk measure of one-year mortality rate based on hospital chart abstraction.¹⁶ The CCI contains 17 categories of comorbidities with each assigned a weight of 1, 2, 3, or 6, reflecting the magnitude of the adjusted relative risks associated with each comorbidity. The CCI score then sums the weights for all conditions with a total maximum score of 33. We created 17 dummy variables representing each condition category: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease (COPD was removed to avoid double-counting), rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, any malignancy, moderate or severe liver disease, metastatic solid tumor, and acquired immune deficiency syndrome (AIDS).

Because some other comorbidities also are commonly found in COPD patients but are not captured in the CCI, we created 6 dummy variables to indicate these conditions,^{3,4,12,18} including hypertension (ICD-9-CM diagnosis codes: 401.xx–405.xx), depression (ICD-9-CM diagnosis codes: 296.2x, 296.3x, 311.xx), sleep apnea (ICD-9-CM diagnosis codes: 780.51, 780.53), tobacco use (ICD-9-CM diagnosis codes: 305.1x, V15.82), edema (ICD-9-CM diagnosis codes: 782.3), and pulmonary heart disease (ICD-9-CM diagnosis codes: 415.xx–416.xx).

We employed three measures to determine the comorbidity burden: (1) mean CCI score, (2) comorbidity prevalence rates and odds ratios (ORs) from logistic regressions to describe the odds for a COPD patient of having a particular comorbid condition relative to the odds for a non-COPD

control of having it; and (3) the total number of comorbidities, including 17 conditions defined by the CCI and 6 additional conditions of interest (categorized as 0, 1–2, 3–4, and ≥ 5).

Analysis

Chi-square tests were used to compare differences in binary variables; *t*-tests were used to compare differences in continuous variables as appropriate between beneficiaries with and without COPD. A generalized linear model (GLM) was performed to estimate the average medical utilization and cost by specific comorbidity. The dependent variables included age, sex, race, comorbidity dummies, and interaction terms between COPD and these comorbidities, allowing the impact of comorbidity to differ between beneficiaries with and without COPD. The incremental medical utilization associated with each comorbid condition was calculated by taking the difference of mean medical utilization between COPD patients and controls; the same procedure was repeated for calculating the incremental medical cost.

Results

Baseline characteristics

The demographic characteristics and unadjusted annual mean medical utilization and cost in the pre-index period are summarized in Table 1. As a result of matching, COPD patients and controls had similar demographic characteristics, with a mean age of 49 years, 78.2% female, and 63.3% African American. The matched sample was slightly younger than the original sample before matching and included more females and African Americans.

Beneficiaries with COPD had significantly higher medical utilization, as measured by the mean number of medical claims, than non-COPD controls (90.1 vs. 61.6, $p < 0.001$) in the pre-index period. Physician office visits accounted for the largest share of medical utilization (61.7% in COPD patients and 64.1% in non-COPD controls). The mean medical cost also was higher in COPD patients (\$8763 vs. \$5270, $p < 0.001$). The largest share of medical cost was attributed to inpatient care: 53.1% of total medical cost among COPD patients and 41.5% among non-COPD controls. Compared to the original sample, the matched cohorts had slightly higher medical utilization and higher medical cost.

Comorbidity burden

Beneficiaries with COPD had significantly higher comorbidity burden than controls (mean CCI score = 1.56 vs. 1.37, $p = 0.004$). Among comorbidities included in the CCI, the prevalence rates of diabetes (27.7%), congestive heart failure (17.9%), chronic pulmonary disease (15.7%), and cerebrovascular disease (10.7%) were high in COPD patients (Table 2). Although these comorbidities also were prevalent among controls, COPD patients were significantly more likely to have congestive heart failure (OR = 2.62; 95% confidence interval [CI]: 2.15, 3.18) and cerebrovascular disease (OR = 1.73; 95% CI: 1.38, 2.18) as well as mild liver disease (OR = 1.89; 95% CI: 1.23, 2.91) and myocardial

Table 1 Characteristics of the study sample.

	Original sample (n = 7236)		Matched sample (n = 4164) ^a		P-value ^b
	COPD (n = 2411)	Non-COPD (n = 4825)	COPD (n = 1388)	Control (n = 2776)	
Mean age, years (s.d.)	52.4 (6.7)	49.2 (6.9)	49.3 (6.5)	48.9 (6.6)	0.109
Female, %	66.5	75.5	78.2	78.2	—
Race, %					
White	54.3	35.7	32.8	32.8	—
African American	43.0	60.8	63.3	63.3	—
Other	2.7	3.6	3.9	3.9	—
Unadjusted mean number of medical claims in the post-index period (s.d.)	89.0 (88.4)	61.2 (63.6)	90.1 (86.9)	61.6 (64.3)	<0.001
Physician office	56.5 (55.6)	39.4 (39.4)	55.6 (51.7)	39.5 (40.1)	<0.001
Inpatient	15.2 (30.3)	7.3 (19.8)	15.9 (31.2)	7.5 (21.0)	<0.001
Outpatient	17.2 (25.0)	14.5 (23.4)	18.6 (25.8)	14.6 (22.9)	<0.001
Unadjusted mean medical cost in the post-index period, \$ (s.d.)	8453 (11,367)	5212 (7891)	8763 (11,611)	5270 (8121)	<0.001
Physician office	2006 (1975)	1397 (1397)	1974 (1834)	1401 (1424)	<0.001
Inpatient	4464 (8867)	2147 (5810)	4651 (9146)	2186 (6164)	<0.001
Outpatient	1983 (2873)	1668 (2692)	2138 (2971)	1683 (2634)	<0.001

COPD: chronic obstructive pulmonary disease; s.d.: standard deviation.

^a 1:2 case–control matched on age (± 5 yrs), sex, and race.

^b P-values were derived from comparisons between COPD patients and demographically matched controls without COPD.

infarction (OR = 1.55; 95% CI: 1.07, 2.24). The prevalence rates of other comorbidities included in the CCI did not differ for COPD patients and controls.

For the six additional comorbidities we assessed, hypertension was highly prevalence in both groups (63.4% vs. 56.4%; OR = 1.34; 95% CI: 1.17, 1.53). COPD patients were more likely to have sleep apnea (OR = 3.06; 95% CI: 2.09, 4.47), tobacco use (OR = 2.18; 95% CI: 1.80, 2.62), and edema (OR = 1.49; 95% CI: 1.18, 1.89) than controls. Depression was prevalent in both cohorts (63.4% vs. 56.4%), but the prevalence rate did not differ between COPD patients and controls (OR = 1.11; 95% CI: 0.92, 1.34).

In terms of total number of comorbidities, 50.6% of COPD patients had 1–2 comorbidities, compared to 55.6% in controls. However, 28.5% and 8.4% of COPD patients had 3–4 and ≥ 5 comorbidities, respectively, compared to 21.8% and 3.7% in controls. Only 12.5% of COPD patients had none of the 23 comorbidities examined, compared to 18.9% in controls ($p < 0.001$).

Incremental medical utilization and medical cost by comorbidity

Because of the low prevalence rates (<1%) of dementia, hemiplegia or paraplegia, renal disease, any malignancy, metastatic solid tumor, and pulmonary heart disease, we excluded these comorbidities and calculated adjusted mean medical utilization and medical cost for the remaining 18 conditions. Overall, COPD patients had 24% higher medical utilization, measured by number of medical claims, than controls (81.4 vs. 65.4, $p < 0.001$), after controlling for demographic characteristics and comorbidity burden (Table 3). The greatest incremental medical

utilization was attributable to diabetes with chronic complications (148.3 vs. 81.5, $p < 0.001$), peptic ulcer disease (137.7 vs. 88.2, $p < 0.001$), and mild liver disease (131.5 vs. 96.4, $p < 0.001$). All other comorbidities, except myocardial infarction, malignancy, moderate or severe liver disease and sleep apnea, were associated with incremental medical utilization.

In terms of incremental medical cost (Table 4), COPD patients on average were 33% more expensive than controls (\$7603 vs. \$5732, $p < 0.001$), after controlling for demographic characteristics and comorbidity burden. COPD patients who had diabetes with chronic complications cost \$7755 more than controls ($p < 0.001$). Peptic ulcer disease and mild liver disease were associated with \$7146 ($p < 0.001$) and \$6050 ($p < 0.001$) higher medical cost, respectively, in COPD patients. The following comorbidities also significantly increased the medical cost for COPD patients: congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, rheumatologic disease, diabetes, AIDS, hypertension, tobacco use, edema. Although depression was associated with incremental medical utilization, COPD patients with depression did not incur significantly higher medical cost compared to controls (\$9057 vs. \$7725, $p = 0.067$).

Discussion

In this study, we examined the prevalence rates of 23 comorbid conditions and their economic implications among Medicaid COPD patients compared to a control group with similar demographic characteristics. We found that COPD patients had a substantial comorbidity burden, in terms of higher CCI score, higher ORs for 9 out of the 23 conditions assessed, and higher total number of

Table 2 Comorbidity prevalence for COPD and matched control cohorts.

Comorbidity (%)	COPD (n = 1388)	Control (n = 2776)	Odds ratio (95% CI)
Mean CCI score (s.d.)	1.56 (2.07)	1.37 (2.03)	p-value = 0.004
Comorbidities included in the CCI			
Myocardial infarction	3.75	2.45	1.55 (1.07, 2.24)
Congestive heart failure	17.94	7.71	2.62 (2.15, 3.18)
Peripheral vascular disease	4.83	3.93	1.24 (0.91, 1.69)
Cerebrovascular disease	10.73	6.48	1.73 (1.38, 2.18)
Dementia	0.07	0.18	— ^a
Chronic pulmonary disease ^b	15.71	15.49	1.02 (0.85, 1.21)
Rheumatologic disease	3.60	4.25	0.84 (0.60, 1.18)
Peptic ulcer disease	3.39	1.98	1.73 (1.17, 2.57)
Mild liver disease	2.95	1.59	1.89 (1.23, 2.91)
Diabetes	27.74	27.56	1.01 (0.87, 1.17)
Diabetes with chronic complications	3.75	3.49	1.08 (0.76, 1.52)
Hemiplegia or paraplegia	0.58	0.72	— ^a
Renal disease	0	0	— ^a
Any malignancy, including leukemia and lymphoma	5.98	4.90	1.24 (0.93, 1.64)
Moderate or severe liver disease	0.79	0.36	— ^a
Metastatic solid tumor	0.65	0.68	— ^a
AIDS	5.55	6.74	0.81 (0.62, 1.07)
Comorbidities not included in the CCI			
Hypertension	63.40	56.38	1.34 (1.17, 1.53)
Depression	14.19	12.97	1.11 (0.92, 1.34)
Sleep apnea	4.90	1.66	3.06 (2.09, 4.47)
Tobacco use	18.23	9.29	2.18 (1.80, 2.62)
Edema	9.44	6.52	1.49 (1.18, 1.89)
Pulmonary heart disease	0.22	0	— ^a
Total number of comorbidities			
0	12.54	18.88	p-value < 0.001
1-2	50.58	55.55	
3-4	28.46	21.83	
≥5	8.42	3.74	

AIDS: acquired immune deficiency syndrome; CCI: Charlson Comorbidity Index; CI: confidence interval; COPD: chronic obstructive pulmonary disease.

^a Odds ratio was not reported because too few patients had this comorbidity.

^b Excluding COPD.

comorbidities than controls. The high burden of comorbidities was associated with incremental medical utilization and medical cost, suggesting that disease management interventions are needed to improve care for the comprehensive disease burden among COPD patients.

To control for confounding due to comorbidity differences between groups, researchers have numerous comorbidity measures to choose from. The CCI and its adaptations are by far the most widely used comorbidity measure in mortality analysis because it was constructed to predict mortality outcome and because the scores are easy to compute based on administrative data. However, using the CCI alone to control for confounding in health utilization and cost models may not be optimal. Previous economic evaluations in COPD have used other generic comorbidity measures, such as the Elixhauser Comorbidity Index¹⁹ and the Comorbidity Symptom Scale,⁸ but generic measures (including the CCI) may be limited in their ability to capture the comorbidity profile specific to the COPD population. We found that some conditions, such as hypertension,

depression, tobacco use and edema, that are not included in the CCI also may have substantial clinical and economic implications for COPD patients. Our findings can be used to identify additional comorbid conditions that are particularly relevant for COPD patients. These comorbid conditions subsequently can inform efforts to develop a COPD-specific comorbidity measure, which can be used as a managerial tool for targeting high-risk patients for more tailored disease management interventions.

Our data show that hypertension was the most common condition in both groups: 63% in COPD patients and 56% in controls, higher than any comorbid conditions included in the CCI. The hypertension prevalence rates are higher than previously reported^{3,4} possibly because our sample was drawn from a Medicaid population in which African Americans account for a greater proportion relative to the general population, and African Americans have been shown to be at high risk of hypertension.²⁰ In our sample, hypertension was associated with higher medical services claims and higher medical cost in COPD patients. The

Table 3 Incremental medical utilization for COPD and matched control cohorts by comorbidity.

Comorbidity ^a	Adjusted mean medical utilization		Incremental utilization	P-value
	COPD (n = 1388)	Control (n = 2776)		
Overall	81.4	65.4	16.0	<0.001
Comorbidities included in the CCI				
Myocardial infarction	106.2	102.8	3.4	0.767
Congestive heart failure	127.8	103.6	24.2	<0.001
Peripheral vascular disease	107.8	84.7	23.1	0.018
Cerebrovascular disease	119.7	102.0	17.7	0.011
Chronic pulmonary disease ^b	91.9	73.6	18.3	<0.001
Rheumatologic disease	114.8	87.1	27.7	0.007
Peptic ulcer disease	137.7	88.2	49.5	<0.001
Mild liver disease	131.5	96.4	35.1	0.014
Diabetes	96.6	77.9	18.7	<0.001
Diabetes with chronic complications	148.3	81.5	66.8	<0.001
Any malignancy, including leukemia and lymphoma	122.6	124.2	-1.6	0.849
Moderate or severe liver disease	143.4	147.8	-4.4	0.879
AIDS	121.5	96.8	24.7	0.003
Comorbidities not included in the CCI				
Hypertension	86.5	69.9	16.6	<0.001
Depression	98.3	80.6	17.7	0.001
Sleep apnea	95.1	84.3	10.8	0.357
Tobacco use	93.9	77.6	16.3	0.003
Edema	116.3	89.3	27.0	<0.001

Note: Medical utilization was measured by the number of service claims.

AIDS: acquired immune deficiency syndrome; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease.

^a Six comorbidities with <1% of prevalence were excluded. These conditions were dementia, hemiplegia or paraplegia, renal disease, moderate or severe liver disease, metastatic solid tumor, and pulmonary heart disease.

^b Excluding COPD.

incremental economic burden may be due to the fact that hypertension frequently is reported in hospitalized patients with COPD²¹ and that inpatient care account for the majority of medical cost (as observed in our sample). Managing COPD patients may be especially challenging with the presence of comorbidities because of their complex health care needs and taking multiple medications. For instance, COPD patients may over use systemic corticosteroids, which could contribute to increased blood pressure, osteoporosis, diabetes, muscle dysfunction, and adrenal insufficiency.²²

Among the 17 conditions included in the CCI, the prevalence rates of congestive heart failure, myocardial infarction, and cerebrovascular disease were significantly higher in COPD patients than controls. Congestive heart failure and cerebrovascular disease also were associated with high incremental medical utilization and cost in COPD patients. In a cohort of more than 45,000 COPD patients enrolled in an integrated health care system, congestive heart failure was the leading cause of hospitalization, followed by myocardial infarction and cerebrovascular disease among all cardiovascular diseases.²³ The age-adjusted hospitalization risk ratios (RR) for COPD patients compared to the demographically matched controls were significantly higher for these comorbidities: congestive heart failure RR = 5.55 (95% CI: 4.71, 5.73), myocardial infarction

RR = 2.14 (95% CI: 1.95, 2.36), and cerebrovascular disease RR = 1.51 (95% CI: 1.37, 1.66).²³ The associated high economic implications (as observed in our sample) and high hospitalization risk suggest that COPD patients with cardiovascular diseases may be a suitable subgroup for more tailored interventions and disease management.

Several study limitations are attributable to the nature of the Medicaid data employed in our study. First, female, low-income populations and minorities, especially African Americans, were over-represented in our sample. Some comorbidities, such as hypertension, may be more prevalent in this population. Generalizing our results to other populations should be made with caution. Second, COPD commonly is undiagnosed¹ and COPD patients could consume substantial health care services and costs prior to diagnosis.^{19,24} The potential non-differential misclassification bias due to undiagnosed COPD could weaken the association between comorbidity and economic burden. Third, there are inherent limitations, such as coding bias, in using large administrative claims data. The diagnosis coded in patients' claims may be the most important condition or the condition that is most likely to result in payment. In our study, sample selection and comorbidity identification was based on the ICD-9-CM diagnosis codes recorded in claims files. Due to lacking clinical details (e.g. pathophysiologic data) in Medicaid claims data, we

Table 4 Incremental medical cost for COPD and matched control cohorts by comorbidity.

Comorbidity ^a	Adjusted mean annual cost, \$		Incremental cost, \$	P-value
	COPD (n = 1388)	Control (n = 2776)		
Overall	7603	5732	1871	<0.001
Comorbidities included in the CCI				
Myocardial infarction	11,791	11,976	-185	0.903
Congestive heart failure	14,610	10,862	3748	<0.001
Peripheral vascular disease	11,122	7209	3913	0.003
Cerebrovascular disease	13,184	11,004	2180	0.018
Chronic pulmonary disease ^b	8915	6753	2162	0.002
Rheumatologic disease	10,452	7234	3218	0.019
Peptic ulcer disease	14,350	7204	7146	<0.001
Mild liver disease	14,331	8281	6050	0.001
Diabetes	9127	6696	2431	<0.001
Diabetes with chronic complications	14,313	6558	7755	<0.001
Any malignancy, including leukemia and lymphoma	12,075	11,241	834	0.460
Moderate or severe liver disease	18,970	23,587	-4617	0.226
AIDS	13,160	9586	3574	0.001
Comorbidities not included in the CCI				
Hypertension	8021	6200	1821	<0.001
Depression	9057	7725	1332	0.067
Sleep apnea	7155	7203	-48	0.975
Tobacco use	9643	6876	2767	<0.001
Edema	11,353	8187	3166	<0.001

AIDS: acquired immune deficiency syndrome; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease.

^a 6 Comorbidities with <1% of prevalence were excluded. These conditions were dementia, hemiplegia or paraplegia, renal disease, moderate or severe liver disease, metastatic solid tumor, and pulmonary heart disease.

^b Excluding COPD.

were unable to determine the extent to which the diagnoses were accurate. We also did not have information on COPD severity, which may lead to underestimate or overestimate of the economic burden due to comorbidity differences. Future research using alternative data sources, such as COPD registries or retrospective chart reviews, may be needed to validate our findings. Finally, our cost estimates were based on the Medicaid fee schedule for the medical service rendered rather than the actual costs for each type of service, which were not available in the Medicaid managed care claims data. Therefore, our cost estimation can only serve as proxies. This method is deemed reliable and valid since it draws cost information from the same Medicaid population.

Our findings highlight the high prevalence rates of comorbidities in Medicaid COPD patients and the substantial economic implications of comorbidity. Additional conditions not included in the commonly used CCI, such as hypertension, depression, tobacco use and edema, may have substantial economic impact on COPD patients. Future research is needed to articulate and characterize specific pathways to high utilization and cost associated with particular comorbid conditions. The development of a COPD-specific comorbidity measure may be used to identify high-risk subgroups and to predict utilization and cost.

Conflict of interest statement

This manuscript was prepared without any contract or funding from a sponsor. The authors declared no conflicts of interest.

Acknowledgment

All authors contributed to the conception and study design, data analysis, interpretation of data, drafting and revising the manuscript, and the final approval of the version to be submitted. The authors were grateful for Dr. Christopher Blanchette and attendees of the International Society for Pharmacoeconomics and Outcomes Research 14th Annual International Meeting for providing helpful comments on this study.

References

1. NHLBI. *Morbidity and Mortality chart book: chart book on cardiovascular, lung, and blood diseases*; 2007.
2. Centers for Disease Control and Prevention. Leading causes of death, <http://www.cdc.gov/nchs/FASTATS/lcod.htm>; 2008 [accessed 1.03.09].

3. van Manen JG, Bindels PJ, Cj Ij van der Zee JS, Bottema BJ, Schade E. Prevalence of comorbidity in patients with a chronic airway obstruction and controls over the age of 40. *J Clin Epidemiol* 2001;**54**(3):287–93.
4. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease. A case–control study in a health maintenance organization. *Arch Intern Med* 2000;**160**(17):2653–8.
5. Crisafulli E, Costi S, Luppi F, et al. Role of comorbidities in a cohort of patients with COPD undergoing pulmonary rehabilitation. *Thorax* 2008;**63**(6):487–92.
6. Vilkmán S, Keistinen T, Tuuponen T, Kivela SL. Survival and cause of death among elderly chronic obstructive pulmonary disease patients after first admission to hospital. *Respiration* 1997;**64**(4):281–4.
7. McGhan R, Radcliff T, Fish R, Sutherland ER, Welsh C, Make B. Predictors of rehospitalization and death after a severe exacerbation of COPD. *Chest* 2007;**132**(6):1748–55.
8. Yeo J, Karimova G, Bansal S. Co-morbidity in older patients with COPD – its impact on health service utilisation and quality of life, a community study. *Age Ageing* 2006;**35**(1):33–7.
9. Wijnhoven HA, Kriegsman DM, Hesselink AE, de Haan M, Schellevis FG. The influence of co-morbidity on health-related quality of life in asthma and COPD patients. *Respir Med* 2003;**97**(5):468–75.
10. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: role of comorbidities. *Eur Respir J* 2006;**28**(6):1245–57.
11. Krachman S, Minai OA, Scharf SM. Sleep abnormalities and treatment in emphysema. *Proc Am Thorac Soc* 2008;**5**(4):536–42.
12. Shaya FT, Lin PJ, Aljawadi MH, Scharf SM. Elevated economic burden in obstructive lung disease patients with concomitant sleep apnea syndrome. *Sleep Breath* 2009;**13**(4):315–6.
13. Shaya FT, Dongyi D, Akazawa MO, et al. Burden of concomitant asthma and COPD in a Medicaid population. *Chest* 2008;**134**(1):14–9.
14. Blanchette CM, Gutierrez B, Ory C, Chang E, Akazawa M. Economic burden in direct costs of concomitant chronic obstructive pulmonary disease and asthma in a medicare advantage population. *J Manag Care Pharm* 2008;**14**(2):176–85.
15. 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):133–8.
16. 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.
17. 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):613–9.
18. Mapel DW, Frost FJ, Hurley JS, et al. An algorithm for the identification of undiagnosed COPD cases using administrative claims data. *J Manag Care Pharm* 2006;**12**(6):457–65.
19. Akazawa M, Halpern R, Riedel AA, Stanford RH, Dalal A, Blanchette CM. Economic burden prior to COPD diagnosis: a matched case–control study in the United States. *Respir Med* 2008;**102**(12):1744–52.
20. NHLBI. Who is at risk for high blood pressure? http://www.nhlbi.nih.gov/health/dci/Diseases/Hbp/HBP_WholsAtRisk.html; 2008 [accessed 1.03.09].
21. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest* 2005;**128**(4):2005–11.
22. Barr RG, Celli BR, Martinez FJ, et al. Physician and patient perceptions in COPD: the COPD resource network needs assessment survey. *Am J Med* 2005;**118**(12):1415.
23. Sidney S, Sorel M, Quesenberry Jr CP, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. *Chest* 2005;**128**(4):2068–75.
24. Mapel DW, Robinson SB, Dastani HB, Shah H, Phillips AL, Lydick E. The direct medical costs of undiagnosed chronic obstructive pulmonary disease. *Value Health* 2008;**11**(4):628–36.