

Comorbidities, Patient Knowledge, and Disease Management in a National Sample of Patients with COPD

R. Graham Barr, MD, DrPH,^{a,b,c} Bartolome R. Celli, MD,^d David M. Mannino, MD,^e Thomas Petty, MD,^f Stephen I. Rennard, MD,^g Frank C. Sciurba, MD,^h James K. Stoller, MD, MS,ⁱ Byron M. Thomashow, MD,^b Gerard M. Turino, MD^j

^aDivision of General Medicine, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY; ^bDivision of Pulmonary, Allergy and Critical Care, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY; ^cDepartment of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY; ^dPulmonary and Critical Care Division, Caritas-St Elizabeth's Medical Center, Tufts University, Boston, Mass; ^eDepartment of Preventive Medicine and Environmental Health, University of Kentucky College of Public Health, Lexington; ^fDepartments of Medicine, University of Colorado and Rush-Presbyterian St Luke's, Chicago, Ill; ^gPulmonary and Critical Care Medicine Section, Department of Internal Medicine, University of Nebraska Medical Center, Omaha; ^hDivision of Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, Pa; ⁱDepartment of Pulmonary, Allergy, and Critical Care Medicine, Cleveland Clinic, Cleveland, Ohio; ^jJames P. Mara Center, St-Luke's-Roosevelt Hospital, New York, NY.

ABSTRACT

OBJECTIVE: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States but is often undertreated. COPD often overlaps with other conditions such as hypertension and osteoporosis, which are less morbid but may be treated more aggressively. We evaluated the prevalence of these comorbid conditions and compared testing, patient knowledge, and management in a national sample of patients with COPD.

METHODS: A survey was administered by telephone in 2006 to 1003 patients with COPD to evaluate the prevalence of comorbid conditions, diagnostic testing, knowledge, and management using standardized instruments. The completion rate was 87%.

RESULTS: Among 1003 patients with COPD, 61% reported moderate or severe dyspnea and 41% reported a prior hospitalization for COPD. The most prevalent comorbid diagnoses were hypertension (55%), hypercholesterolemia (52%), depression (37%), cataracts (31%), and osteoporosis (28%). Only 10% of respondents knew their forced expiratory volume in 1 second (95% confidence interval [CI], 8-12) compared with 79% who knew their blood pressure (95% CI, 76-83). Seventy-two percent (95% CI, 69-75) reported taking any medication for COPD, usually a short-acting bronchodilator, whereas 87% (95% CI, 84-90) of patients with COPD and hypertension were taking an antihypertensive medication and 72% (95% CI, 68-75) of patients with COPD and hypercholesterolemia were taking a statin.

CONCLUSION: Although most patients with COPD in this national sample were symptomatic and many had been hospitalized for COPD, COPD self-knowledge was low and COPD was undertreated compared with generally asymptomatic, less morbid conditions such as hypertension.

© 2009 Elsevier Inc. All rights reserved. • *The American Journal of Medicine* (2009) 122, 348-355

KEYWORDS: Asthma; Chronic bronchitis; Chronic obstructive pulmonary disease; Comorbidities; Emphysema

Funding: The COPD Foundation and National Institutes of Health HL077612 and HL075476.

Conflict of Interest: See last page of article.

Authorship: All authors had access to the data and played a role in writing this manuscript.

Requests for reprints should be addressed to R. Graham Barr, MD, DrPH, Columbia University Medical Center, 630 West 168th Street, New York, NY 10032.

E-mail address: rgb9@columbia.edu

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death in the United States and is projected to be the third most common cause of death by the

year 2020.¹ In 2004, 120,000 persons in the United States died of COPD,² an increase of 67% from 1980³ and more than twice the number who died of congestive heart failure.² The

number of patients diagnosed by a physician as having COPD in the United States increased from approximately 7 million in 1980 to 12 million in 2004, higher than the prevalence of both stroke and congestive heart failure.⁴

COPD is a leading cause of hospitalizations in older adults⁵ and accounted for 15.4 million physician office visits in the United States in 2003, approximately the same as coronary heart disease, stroke, and congestive heart failure combined.² The cost of COPD care was approximately \$37.2 billion in 2004, including \$20.9 billion in direct health care expenditures, \$7.4 billion in indirect morbidity costs, and \$8.9 billion in indirect mortality costs.² Morbidity, mortality, and costs from COPD will continue to increase.⁶

Patients with COPD might have a worse prognosis than patients with other commonly treated conditions. For example, the 15-year cumulative incidence of fatal coronary heart disease in the National Health and Nutrition Examination Survey II was 5.1% and 3.0% among men and women with hypercholesterolemia, respectively, and 5.0% and 3.4% among men and women with hypertension, respectively.⁷ By comparison, the 22-year cumulative incidence of fatal COPD among National Health and Nutrition Examination Survey I participants with moderate-to-severe airflow obstruction was 7.8% based on only pre-bronchodilator measures, and all-cause mortality was 51%.⁸ Post-bronchodilator measures necessary for the diagnosis of COPD were not available in National Health and Nutrition Examination Survey I; COPD mortality is likely to have been higher still among those with actual COPD.

Patients with COPD may be predisposed to developing muscle weakness,^{9,10} osteoporosis,^{11,12} depression,^{13,14} and possibly cardiovascular disease,¹⁵⁻¹⁹ and some studies suggest that these comorbidities contribute to mortality in COPD.²⁰ Although comorbidities seem to be common in COPD, the reported prevalence varies tremendously in different studies²¹⁻²⁴ and national data are lacking. We therefore interviewed a national sample of patients with COPD to describe comorbid conditions in COPD and to compare testing, self-knowledge and management of COPD with that of prevalent but less morbid coexisting diagnoses.

MATERIALS AND METHODS

Participants were drawn from a national sample of 4003 households in which 1 or more persons reported a diagnosis of a form of COPD. COPD was ascertained by the questionnaire item, "Have you ever been diagnosed by a physician as having: emphysema; chronic obstructive pulmonary

disease (COPD); [or] alpha-one antitrypsin deficiency?" Patients with COPD with a co-diagnosis of asthma were not excluded because of the overlap of these 2 conditions in clinical practice. The sampling frame was derived from an ongoing series of national surveys identifying households

with members with various disease conditions. The use of this commercial compiled list increased the likelihood that each contacted household included a person with COPD. The list excluded households that had previously indicated they were not willing to participate in surveys. The survey was conducted by Schulman, Ronca and Bucuvalas, Inc (New York, NY) and performed between December 29, 2005, and February 17, 2006. Participants were interviewed using an established computer-assisted telephone interview approach. The response rate (number interviewed/[valid telephone numbers – deaths

– no contacts]) was 52%, and the completion rate (number interviewed/eligible units contacted) was 87%.

Questionnaire Items

Participants were asked about the diagnosis and severity of COPD using previously validated questionnaire items, as available. Dyspnea severity was measured by the modified Medical Research Council (MRC) Dyspnea Index.²⁵ COPD-related items were used as previously described.²⁶ Participants were asked about physician diagnoses of comorbid conditions, in addition to symptoms that are considered diagnostic (eg, for heartburn and reflux²⁷) and medication use. A panel of COPD experts, including physicians, patients, and representatives from COPD organizations, helped draft the questionnaire. Validation of the responses was beyond the scope of the current study.

Statistical Analysis

Data are presented as proportions and means with standard deviations or medians with interquartile ranges, as appropriate. One-sample 95% confidence intervals (CIs) were calculated for binomial data using the normal-theory method. Associations between categorical factors were tested with the chi-square test and Mantel-Hanzel test for trend, as appropriate. All *P* values were 2-tailed, with a *P* value less than .05 considered statistically significant. Analyses were performed using SAS 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

The characteristics of the 1003 patients who responded to the survey, stratified by gender, are shown in Table 1. The mean age (\pm standard deviation) was 61 \pm 10 years, and

CLINICAL SIGNIFICANCE

- Comorbidities in COPD were common in this national survey of patients with COPD.
- Patient self-knowledge about their COPD was lower than for cardiovascular comorbidities even though diagnostic testing by physicians was similar.
- COPD was undertreated compared with generally asymptomatic, less morbid conditions such as hypertension.

Table 1 Characteristics of Participants in a National Sample of 1003 Patients with Chronic Obstructive Pulmonary Disease

	Women N = 581 (58%)	Men N = 422 (42%)	P Value
Age category (%), y			
40-49	20	10	<.001
50-59	36	29	
60-69	26	35	
≥70	18	26	
Region (%)			.86
Northeast	12	11	
Midwest	30	29	
South	36	28	
West	22	22	
Race/Ethnicity (%)			.85
White	88	89	
African American	6	5	
Hispanic	3	2	
Other	3	4	
Educational attainment			.91
No high school degree	13	17	
High school degree	38	34	
Some college	37	31	
College graduate	12	18	
Work status			<.001
Full-time	12	21	
Part-time or unemployed	16	12	
Disabled	34	20	
Retired	32	47	
Other	6	0	
Gross household income in 2004			<.001
≤\$15,000	41	23	
\$15,001-\$25,000	18	21	
\$25,001-\$35,000	16	18	
\$35,001-\$50,000	13	17	
≥\$50,001	4	6	
Ever smoker (%)	93	96	.04
Current smoking (%)	47	39	.01
Pack-years (mean ± SD)	32 ± 13	37 ± 13	.32
Concurrent diagnosis of asthma (%)	62	37	<.001
Symptoms every/most days for 3 consecutive months or more in past year (%)			
Coughed	66	60	.06
Brought up phlegm	56	56	.99
Current degree of dyspnea (%), MRC Scale			.43
None (0)	2	4	
I only get breathless after strenuous exercise (1)	9	15	
I get breathless when hurrying on level ground or walking up a slight incline (2)	23	26	
I walk slower than people my own age (3)	13	10	
I have to stop for breath when walking on level ground at my own pace (3)	13	14	

Table 1 Continued

	Women N = 581 (58%)	Men N = 422 (42%)	P Value
I have to stop for breath after walking a few minutes on level ground (4)	30	23	
I am too breathless to leave the house (5)	10	8	
Health status (%)			.001
Excellent	1	3	
Very good	7	8	
Good	21	31	
Fair	38	31	
Poor	32	28	
COPD hospitalization ever (%)	44	38	.09
No. of COPD hospitalizations in last 5 y			
1	16	25	.47
2-4	44	54	
≥5	31	18	
Health insurance ^a			
Government			
Medicare	48	48	.95
Medicaid	22	10	<.001
Veterans Administration	4	17	<.001
Employer-based	33	37	.01
Self-financed	15	13	.43
None	11	14	.39
Insurance coverage of drug costs			.26
Most or all	62	68	
Some, little or none	34	29	

MRC = Medical Research Council.

^aMore than 1 response was permitted.

58% were women. Respondents lived mostly in the Midwest and the South of the United States and were predominantly white. Half had no education beyond high school. Ninety-five percent noted a history of daily cigarette use, and 47% of women and 39% of men smoked cigarettes regularly at the time of the survey. A co-diagnosis of asthma was common, particularly among women.

Patients with COPD in the survey were generally symptomatic and made extensive use of the health care system. Sixty-one percent reported moderate or severe dyspnea on exertion (MRC Dyspnea Index ≥ 3), 63% described chronic cough, 55% reported chronic sputum production, and 55% reported at least 1 bronchitic episode per year. Forty-one percent reported being hospitalized for a COPD exacerbation, and during the past year, 30% had visited doctors 3 to 5 times, 22% had visited doctors 6 to 10 times, and 33% had visited doctor more than 10 times.

Comorbid Conditions

Table 2 shows the frequencies of comorbid diagnoses and nonrespiratory symptoms reported by the 1003 patients with

COPD stratified by gender. Hypertension (55%) and hypercholesterolemia (52%) were the most prevalent comorbidities, followed in frequency by depression, cataracts, and osteoporosis. Sleep apnea and diabetes each occurred in approximately one quarter of patients with COPD. Twenty-two percent reported angina, 19% reported a history of myocardial infarction, and 14% reported a history of a cerebrovascular event (with overlap). Eleven percent reported chronic kidney disease, and 6% reported congestive heart failure. Of the 6% with cancer, colon (0.7%), prostate (0.6%), lung (0.5%), and breast (0.4%) cancers were most common. The prevalence of comorbid conditions was generally similar among women and men, except for depression, osteoporosis, and cardiovascular disease. Symptoms of joint pain, gastroesophageal reflux disease, and sinus problems were highly prevalent (Table 2) and more commonly reported by women than men.

The median number of comorbid conditions among these patients with COPD was 9 (interquartile range, 6-12). The frequency distribution of the total number of comorbidities is shown in Figure 1. The mean MRC Dyspnea Index increased monotonically with the number of comorbid conditions from 2.3 among those with 1 to 5 comorbid conditions to 4 among those with 20 or more comorbid conditions (Figure 2).

Table 2 Prevalence of Comorbid Diagnoses and Symptoms Among a National Sample of Patients with Chronic Obstructive Pulmonary Disease

	Percent of Patients with COPD Reporting Condition		
	Women N = 581	Men N = 422	P Value
Physician diagnosis			
Hypertension	53	57	.15
Hypercholesterolemia	54	49	.14
Depression	44	27	<.001
Cataracts	31	32	.65
Osteoporosis	39	12	<.001
Sleep apnea	25	28	.28
Diabetes	25	26	.78
Angina	20	24	.23
Heart attack	14	27	<.001
Stroke	16	11	.01
Glaucoma	7	7	.86
Congestive heart failure	7	3	.01
Cancer	6	4	.47
Symptoms			
Joint pain	77	66	<.001
Heartburn or acid reflux	68	60	.02
Sinus problems > 1-2 times/y	65	51	<.001
Erectile dysfunction	—	37	—

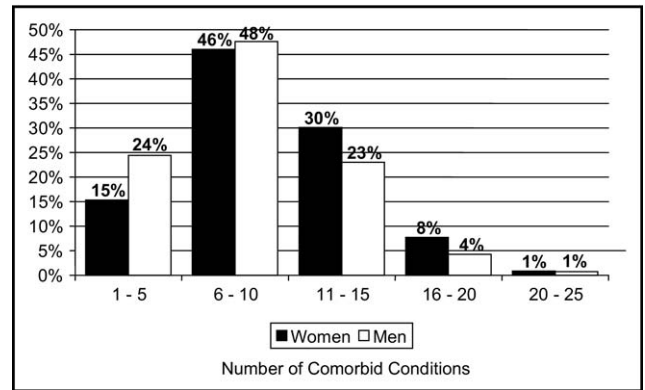


Figure 1 Frequency distribution of comorbid conditions among patients with COPD.

Diagnostic Testing for Chronic Obstructive Pulmonary Disease and Comorbid Conditions

Eighty-two percent reported undergoing spirometry in the prior year, whereas 77% had a chest x-ray and 45% had a computerized axial tomography scan. Sixty-nine percent had undergone cardiac stress testing, and 24% reported a prior cardiac catheterization. Overall, 22% underwent bone densitometry, 21% underwent a sleep study, and 7% underwent a carotid ultrasound.

Self-Knowledge of Chronic Obstructive Pulmonary Disease and Comorbid Conditions

Of the 55% of patients with COPD who reported hypertension, 79% knew their blood pressure (95% CI, 76-83). Of the 52% of patients with COPD who reported hypercholesterolemia, 37% knew their cholesterol level (95% CI, 32-42). In contrast, of the 1003 patients with COPD surveyed, only 10% reported knowing their forced expiratory volume in 1 second (FEV₁) or percent predicted FEV₁ (95% CI, 8-12). There was no difference in knowledge of FEV₁ by gender (P = .47).

Chronic Obstructive Pulmonary Disease Management

Despite the severity of symptoms and frequency of health care use reported by patients with COPD in this survey,

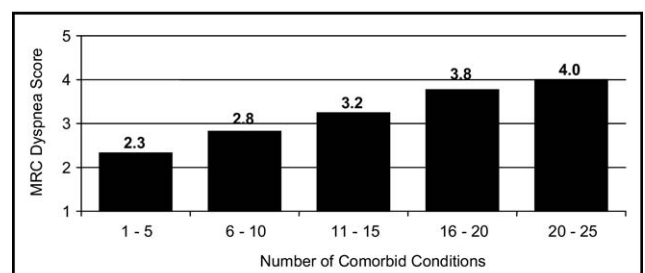


Figure 2 Severity of dyspnea by number of comorbid conditions. MRC = Medical Research Council.

Table 3 Prevalence of Medication Use for Chronic Obstructive Pulmonary Disease and Comorbid Diagnoses and Symptoms Among a National Sample of Patients with Chronic Obstructive Pulmonary Disease

	Percent of Patients with COPD with Condition Taking Medication ^a		
	Women N = 581	Men N = 422	P Value
Medication (any) for COPD (%)	74	69	.10
Among patients without diagnosis of asthma	66	63	.45
Among patients with diagnosis of asthma	79	79	.89
Comorbid diagnoses			
Medication (any) for hypertension ^a (%)	87	86	.63
Statin for hypercholesterolemia ^a (%)	68	76	.05
Medication (any) for depression ^a (%)	72	64	.13
Medication (any) for osteoporosis ^a (%)	63	45	.02
Continuous positive airway pressure for obstructive sleep apnea ^a (%)	48	45	.57
Medication for diabetes mellitus ^a (%)			
Insulin	28	44	.01
Oral hypoglycemic	67	68	.88
Medication for coronary artery disease ^a (%)			
Aspirin	52	72	<.001
Other cardiac medication	61	45	<.001
Medication for stroke ^a (%)			
Aspirin	50	67	.07
Warfarin	34	38	.64
Medication (any) for glaucoma ^a (%)	55	52	.78
Comorbid symptoms			
Medications for joint pain ^a (%)			<.001
Prescription analgesic only	45	32	
Over-the-counter analgesic only	19	17	
Both	10	8	
Regular medication (any) for heartburn or acid reflux ^a (%)	68	57	.004
Medication (any; more than 1-2 times/y) for sinus problems ^a (%)	68	64	.29

^aAmong those reporting comorbid condition (the prevalence of comorbid conditions is listed in Table 2).

72% (95% CI, 69-75) reported taking any regular medication for COPD (Table 3). Most commonly, this medication was a short-acting bronchodilator (55% of patients with COPD). Twenty-six percent of patients with COPD reported use of a combination long-acting beta agonist and an inhaled corticosteroid, and 15% reported use of a long-

acting inhaled anticholinergic. Forty percent reported daily nebulizer use, 35% used oxygen daily, and 15% had participated in pulmonary rehabilitation. Sixty-five percent reported receiving influenza vaccination during the past year.

The proportion taking any regular medication was higher among patients with COPD with a co-diagnosis of asthma than among those with COPD only (79% vs 64%, respectively; $P < .001$). There were no significant differences in treatment for COPD by gender.

Management of Comorbid Conditions

Table 3 also shows medication use for comorbid conditions stratified by gender. Figure 3 presents the distribution of the total number of noninhaler prescription medications taken by patients with COPD per day.

Eighty-seven percent (95% CI, 84-90) of patients with COPD and hypertension were taking an antihypertensive medication. The proportion of patients with COPD with hypertension who took antihypertensive medications was significantly greater than the proportion of patients with COPD who took COPD medications. Seventy-two percent (95% CI, 68-75) of patients with COPD and hypercholesterolemia were taking a statin, which was similar to the proportion of patients with COPD who took any COPD medication and greater than the proportion who took a long-acting bronchodilator (41%; 95% CI, 38-44).

Twelve percent of surveyed patients reported having no health care insurance; 30% of those with health insurance reported having no, little, or only some medication coverage; and approximately one third described co-pay amounts as moderate or large. Lack of or inadequate health insurance coverage seemed to have a substantial negative impact on the use of health services by patients with COPD (Figure 4).

DISCUSSION

This national survey of patients with diagnosed COPD suggested that comorbid diagnoses of hypertension, hypercho-

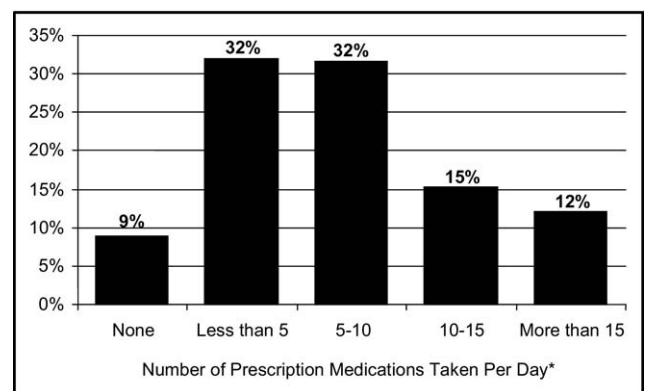


Figure 3 Frequency distribution of prescription medications taken per day among patients with COPD. *Inhaled and nebulized treatments were not included in these totals.

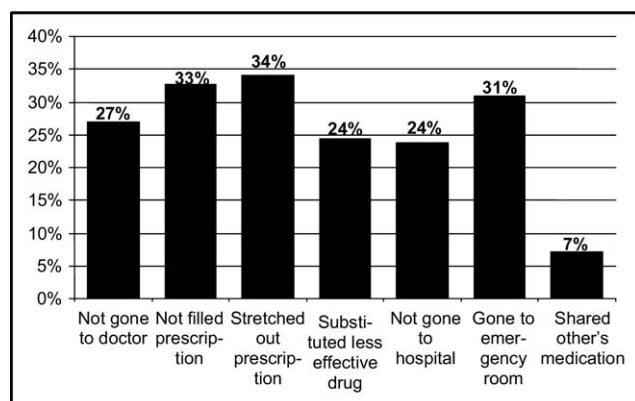


Figure 4 Percent of participants who answered in the affirmative to the question: "During the past 12 months, as a result of costs or lack of coverage have you . . .?"

lesterolemia, depression, and osteoporosis occur frequently in patients with COPD. Although this was a COPD survey and despite similar amounts of clinical testing, patients' knowledge of their cholesterol levels and blood pressure far exceeded their knowledge of their FEV₁. COPD was undertreated compared with other conditions, such as hypertension, which is generally asymptomatic and causes fewer hospitalizations and deaths than COPD.²

Several regional studies have examined the prevalence of comorbidities in COPD,^{23,24,28,29} with the prevalence of cardiac disease ranging from 13% to 71%, the prevalence of arthritis ranging from 10% to 36%, the prevalence of diabetes ranging from 2% to 22%, and the prevalence of cancer ranging from 4% to 15%. The present study showed, in general, higher prevalences of most comorbid conditions than many of the prior studies. Possible sources of variation in estimates across studies include differing severity of COPD, differing methods of ascertaining comorbidities (eg, direct inquiry vs interrogating administrative databases), and differing definitions. Notably, most of the prior studies performed chart or administrative data reviews rather than the direct patient survey performed here, and none were national or representative samples.

The high prevalence of comorbidity in COPD is likely multifactorial and associated with age, multisystem impact of tobacco exposure, and pathogenic features associated with or as a result of primary lung pathophysiology. The frequency of comorbid conditions in patients with COPD in part probably reflects the age of the COPD population. According to the National Health Interview Survey in 2003-2004, 28% of men and 16% of women aged more than 65 years reported having cardiac disease, 48% of men and 54% of women reported having hypertension, 20% of men and 18% of women reported having diabetes, and 44% of men and 55% of women reported having arthritis.³⁰ However, 95% of patients with COPD have a smoking history, and smoking is a major risk factor for a large number of other diseases, including coronary artery disease, cerebrovascular and peripheral vascular disease, lung cancer and other

malignancies, erectile dysfunction, cataracts, osteoporosis, peptic ulcer disease, and the metabolic syndrome.³¹ Recent investigations have documented associations of comorbid conditions with COPD independent of common risk factors, such as tobacco exposure.^{9,32-34} Speculation on the mechanisms behind such associations include common genetic mechanisms resulting in synchronous pathology in multiple organ systems, systemic effects related to the pulmonary and systemic vasculature, or a systemic inflammatory response linked to the lung parenchymal and airway inflammatory processes in COPD.

Medications also might contribute to the development of comorbidities in COPD. Bronchodilators might contribute to tachyarrhythmias and tremors, although randomized clinical trials of long-acting β -agonists suggest that these effects probably do not translate into increased cardiovascular mortality.³⁵ Inhaled anticholinergics affect intraocular pressure and bladder function and may have cardiovascular effects.^{36,37} Inhaled corticosteroids predispose patients to cataracts and skin bruising and might increase osteoporosis and risk of pneumonia.³⁵ Systemic corticosteroids, often overused in COPD care,²⁶ could contribute to diabetes, hypertension, osteoporosis, muscle dysfunction, and adrenal insufficiency.

Numerous studies have suggested that comorbidities are a common cause of or contributor to COPD hospitalizations.³⁸ In the Lung Health Study, a study of mild COPD, 12.8% of the 5887 smokers were hospitalized, with 42% for cardiovascular events versus 14% for pulmonary complications.³⁹ In a Kaiser Permanente study of more than 45,000 patients with COPD, heart failure was the leading cause of hospitalization, followed by myocardial infarction and stroke.²⁰ Kinnunen et al⁴⁰ found that comorbidities were associated with an increased duration of COPD hospitalizations; the mean length-of-stay in patients without comorbidity was 7.7 days compared with 10.5 days if a concurrent disease was present. Most studies evaluating cause of death in COPD suggest that patients with COPD are more likely to die of comorbid conditions rather than of COPD,⁴¹⁻⁴⁴ with most deaths from cardiovascular disease or malignancy, although this varies with the severity of COPD.

A striking finding in our study was that patients with COPD demonstrated better recall of their blood pressure and cholesterol than of their FEV₁. Although this is not surprising in the context of the greater public education regarding hypertension and hypercholesterolemia than about COPD, the fact that lung function is a stronger independent predictor of survival than blood pressure or cholesterol level, not only among patients with COPD but also in the general elderly population,⁴⁵ suggests the irony of this observation and the need for more public education about COPD. The National Institutes of Health recently initiated a major initiative, called the "Learn More, Breathe Better Campaign," to increase awareness of and understanding about COPD.⁴⁶

COPD was less commonly treated than less symptomatic and less morbid conditions, such as hypertension and hy-

percholesterolemia, despite the increasing number of proven medications for the treatment of COPD. Recent randomized clinical trials show the effectiveness of long-acting β -agonists, long-acting anticholinergics, and long-acting β -agonist-inhaled corticosteroid combinations for long-term bronchodilation, improvement in quality of life, and prevention of exacerbations,^{35,37} although definitive evidence for their effects on change in lung function and mortality requires further testing in randomized clinical trials.

The diagnosis of COPD in this study was not validated in the patient surveys but was based on patient report. On the other hand, almost all patients had a substantial smoking history and most had prominent symptoms of chronic dyspnea. The prevalence of overlap with asthma, particularly among women, reflected real-world clinical practice and diagnostic challenges. Previous studies have documented a gender discrepancy in the diagnosis of asthma compared with COPD in which women are preferentially diagnosed with asthma given the same clinical history.⁴⁷ Notably, the underuse of COPD medications was more marked in patients with COPD without a co-diagnosis of asthma compared with those with a co-diagnosis of asthma. Comorbid diagnoses also were not validated, although the high prevalence of appropriate medication use for these diagnoses suggested that they were accurate. The survey was performed in a national sample, but the sample was not representative, potentially limiting the generalizability of the results. The sampling frame may have increased the estimated prevalence of comorbidities and reported use of all medications compared with a representative sample.

CONCLUSIONS

Comorbidities are common in COPD and likely add to the complexity and cost of care. Although patients with COPD take a large number of medications, relatively few of these medications are for COPD. This discrepancy may relate to poor physician and patient knowledge about COPD²⁶ or reflect the more limited evidence base for COPD compared with other leading causes of death. Although advances in COPD pathophysiology and clinical research are needed to have a full impact, better education and optimal use of existing therapeutic strategies are warranted to improve symptoms and reduce hospitalizations in patients with COPD.

ACKNOWLEDGMENTS

We thank the COPD Foundation, which commissioned the survey, and the firm of Schulman, Ronca and Bucuvalas, Inc, which administered the survey, performed initial data analyses, and assisted with some aspects of the initial manuscript preparation.

References

1. Petty TL. Definition, epidemiology, course, and prognosis of COPD. *Clin Cornerstone*. 2003;5:1-10.
2. *National Heart Lung Blood Institute Factbook FY-2006*. Bethesda, MD: National Institutes of Health/National Heart, Lung, and Blood Institute; 2007.
3. Hoyert DL, Arias E, Smith BL, et al. *Death: Final Data for 1999. National Vital Statistics Reports 2001*. Hyattsville, MD: National Center for Health Statistics; 2001. US Dept of Health and Human Services publication (PHS) 2001-1120;2001.
4. Schiller JS, Adams PF, Nelson ZC. Summary health statistics for the U.S. population: National Health Interview Survey, 2003. *Vital Health Stat 10*. 2005;1:1-104.
5. Mannino DM. COPD: epidemiology, prevalence, morbidity and mortality, and disease heterogeneity. *Chest*. 2002;121(5 Suppl):121S-126S.
6. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet*. 1997;349:1498-1504.
7. Mensah GA, Brown DW, Croft JB, Greenlund KJ. Major coronary risk factors and death from coronary heart disease: baseline and follow-up mortality data from the Second National Health and Nutrition Examination Survey (NHANES II). *Am J Prev Med*. 2005;29(5 Suppl 1):68-74.
8. Mannino DM, Buist AS, Petty TL, et al. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow-up study. *Thorax*. 2003;58:388-393.
9. Wouters EF, Creutzberg EC, Schols AM. Systemic effects in COPD. *Chest*. 2002;121(5 Suppl):127S-130S.
10. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. A statement of the American Thoracic Society and European Respiratory Society. *Am J Respir Crit Care Med*. 1999;159(4 Pt 2):S1-40.
11. de Vries F, van Staa TP, Bracke MS, et al. Severity of obstructive airway disease and risk of osteoporotic fracture. *Eur Respir J*. 2005; 25:879-884.
12. Jorgensen NR, Schwarz P, Holme I, et al. The prevalence of osteoporosis in patients with chronic obstructive pulmonary disease: a cross sectional study. *Respir Med*. 2007;101:177-185.
13. Himelhoch S, Lehman A, Kreyenbuhl J, et al. Prevalence of chronic obstructive pulmonary disease among those with serious mental illness. *Am J Psychiatry*. 2004;161:2317-2319.
14. Norwood R, Norwood R. Prevalence and impact of depression in chronic obstructive pulmonary disease patients. *Curr Opin Pulm Med*. 2006;12:113-117.
15. Sin DD, Man SF. Why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular diseases? The potential role of systemic inflammation in chronic obstructive pulmonary disease. *Circulation*. 2003;107:1514-1519.
16. Schunemann HJ, Dorn J, Grant BJ, et al. Pulmonary function is a long-term predictor of mortality in the general population: 29-year follow-up of the Buffalo Health Study. *Chest*. 2000;118:656-664.
17. Friedman GD, Klatsky AL, Siegelab AB. Lung function and outcome of myocardial infarction. *N Engl J Med*. 1976;295:1323.
18. Curkendall SM, Lanes S, de Luise C, et al. Chronic obstructive pulmonary disease severity and cardiovascular outcomes. *Eur J Epidemiol*. 2006;21:803-813.
19. Curkendall SM, DeLuise C, Jones JK, et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada. *Ann Epidemiol*. 2006;16:63-70.
20. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest*. 2005;128:2005-2011.
21. van Manen JG, Bindels PJ, IJzermans CJ, et al. Prevalence of comorbidity in patients with a chronic airway obstruction and controls over the age of 40. *J Clin Epidemiol*. 2001;54:287-293.
22. Mapel DW, Dedrick D, Davis K. Trends and cardiovascular comorbidities of COPD patients in the Veterans Administration Medical System, 1991-1999. *COPD*. 2005;2:35-41.
23. Soriano JB, Visick GT, Muellerova H, et al. Patterns of comorbidities in newly diagnosed COPD and asthma in primary care. *Chest*. 2005; 128:2099-2107.

24. Sidney S, Sorel M, Quesenberry CP, Jr, et al. COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. *Chest*. 2005;128:2068-2075.
25. Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54:581-586.
26. 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;118:1415.
27. Kahrilas PJ. Gastroesophageal reflux disease. *JAMA*. 1996;276:983-988.
28. Wijnhoven HA, Kriegsman DM, Hesselink AE, et al. The influence of co-morbidity on health-related quality of life in asthma and COPD patients. *Respir Med*. 2003;97:468-475.
29. 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. *Ageing*. 2006;35:33-37.
30. Adams PF, Barnes PM. Summary health statistics for the U.S. population: National Health Interview Survey, 2004. *Vital Health Stat 10*. 2006;1-104.
31. The 2004 United States Surgeon General's Report: The Health Consequences of Smoking. *N S W Public Health Bull*. 2004;15:107.
32. Agusti AG, Noguera A, Sauleda J, et al. Systemic effects of chronic obstructive pulmonary disease. *Eur Respir J*. 2003;21:347-360.
33. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: role of comorbidities. *Eur Respir J*. 2006;28:1245-1257.
34. Walter RE, Wilk JB, Larson MG, et al. Systemic inflammation and COPD: The Framingham Heart Study. *Chest*. 2008;133:19-25. Epub 2007 Oct 1.
35. Calverley PM, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med*. 2007;356:775-789.
36. Anthonisen NR, Connett JE, Kiley JP, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. *JAMA*. 1994;272:1497-1505.
37. Barr RG, Bourbeau J, Camargo CA, Jr, Ram FSF. Inhaled tiotropium for stable chronic obstructive pulmonary disease: a meta-analysis. *Thorax*. 2006;61:854-862.
38. Fabbri LM, Luppi F, Beghe B, Rabe KF. Complex chronic comorbidities of COPD. *Eur Respir J*. 2008;31:204-212.
39. Anthonisen NR, Connett JE, Enright PL, Manfreda J. Hospitalizations and mortality in the Lung Health Study. *Am J Respir Crit Care Med*. 2002;166:333-339.
40. Kinnunen T, Saynajakangas O, Tuuponen T, Keistinen T. Impact of comorbidities on the duration of COPD patients' hospital episodes. *Respir Med*. 2003;97:143-146.
41. Huiart L, Ernst P, Suissa S. Cardiovascular morbidity and mortality in COPD. *Chest*. 2005;128:2640-2646.
42. Hansell AL, Walk JA, Soriano JB. What do chronic obstructive pulmonary disease patients die from? A multiple cause coding analysis. *Eur Respir J*. 2003;22:809-814.
43. Mannino DM, Brown C, Giovino GA. Obstructive lung disease deaths in the United States from 1979 through 1993. An analysis using multiple-cause mortality data. *Am J Respir Crit Care Med*. 1997;156(3 Pt 1):814-818.
44. Camilli AE, Robbins DR, Lebowitz MD. Death certificate reporting of confirmed airways obstructive disease. *Am J Epidemiol*. 1991;133:795-800.
45. Fried LP, Kronmal RA, Newman AB, et al. Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. *JAMA*. 1998;279:585-592.
46. Learn More, Breathe Better Campaign. Available at: <http://www.nhlbi.nih.gov/health/public/lung/copd/index.htm>. Accessed February 3, 2008.
47. Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. *Chest*. 2001;119:1691-1695.

Conflict of Interest: R. Graham Barr, MD, DrPH: none. Bartolome R. Celli, MD: research grants from Glaxo Smith Kline (GSK), Boehringer Ingelheim (BI), Forrest Medical, Astra Zeneca; advisory board payments from GSK, BI, Almirall, Astra Zeneca; speakers' fees from GSK, BI, Astra Zeneca, Almirall. David Mannino, MD: research funding from GSK, Pfizer, and Novartis; consultant or speakers' fees from GSK, Pfizer, BI, Astra-Zeneca, Dey, and Sepracor. Thomas Petty, MD: none. Stephen I. Rennard, MD: research grants from Almirall, Lorillard, Centocor, Novartis, GSK, Philip Morris, Institute for Science and Health, Roche; consultancy and advisory board payments from Abbott, Johnson & Johnson, Almirall, Novartis, Altana, Roche, Anthera, Quintiles, GSK, Targegen; speakers' fees from Adams, Novartis, AstraZeneca, Pfizer. Frank C. Sciurba, MD: consultancy for Astra Zeneca, BI, Dey, GSK, Novartis, Pfizer, PneumRX, Respironics, Schering and Sepracor. James K. Stoller, MD, MS: consultancy for Talecris Biotherapeutics, BI; speaker for Grifols, Baxter, CSL-Behring, Pfizer, Talecris. Byron M. Thomashow, MD: speakers' fees and consultancy for BI, Pfizer and GSK. Gerard M. Turino, MD: research grant from BI; consultancy for Talecris Corporation.