

In-Hospital Mortality Following Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Background: Acute exacerbations of chronic obstructive pulmonary disease (COPD) are a frequent cause of hospitalization in the United States. Previous studies of selected populations of patients with COPD have estimated in-hospital mortality to range from 4% to 30%. Our objective was to obtain a generalizable estimate of in-hospital mortality from acute exacerbation of COPD in the United States and to identify predictors of in-hospital mortality using administrative data.

Methods: We performed a cross-sectional study utilizing the 1996 Nationwide Inpatient Sample, a data set of all hospitalizations from a 20% sample of nonfederal US hospitals. The study population included 71 130 patients aged 40 years or older with an acute exacerbation of COPD at hospital discharge. The primary outcome assessed was in-hospital mortality.

Results: In-hospital mortality for patients with an acute exacerbation of COPD was 2.5%. Multivariable analyses identified older age, male sex, higher income, nonroutine admission sources, and more comorbid conditions as independent risk factors for in-hospital mortality.

Conclusions: Mortality during hospitalization in this nationwide sample of patients with acute exacerbations of COPD was lower than that of previous studies of select populations. This estimate should provide optimism to both clinicians and patients regarding prognoses from COPD exacerbations requiring hospitalization. Our results indicate that the use of administrative data can help to identify subsets of patients with acute exacerbations of COPD that are at higher risk of in-hospital mortality.

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CHRONIC OBSTRUCTIVE pulmonary disease (COPD) results in substantial morbidity and mortality. Patients with COPD experience acute exacerbations or “flares” characterized by increased dyspnea, sputum production, and/or sputum purulence. These exacerbations result in approximately 500 000 hospitalizations annually in the United States¹ and are most often precipitated by respiratory tract infections, congestive heart failure, arrhythmias, or unidentified causes.² Exacerbation of COPD is the fourth leading cause of death³ and represents a significant health burden for the US population.

Previous studies of selected patient populations have estimated in-hospital mortality from acute exacerbation of COPD to range from 4% to 30%.^{2,4-15} However, because these estimates are derived from selected populations, they are likely to underestimate or overestimate the mortality risk for the “average” patient admitted with an acute exacerbation of COPD in the United States.

Studies on acute exacerbation of COPD have also identified various risk factors for in-hospital mortality, but have primarily focused on physiologic risk factors.^{2,5,10-14} Identification of these risk factors often requires additional testing that may not always be readily available for every patient. In contrast, administrative data are routinely collected and are frequently available to clinicians, hospital administrators, and insurers. Risk prediction models based on these administrative data may permit comparisons of quality of care and outcomes across regions, health plans, hospitals, and physicians.¹⁶ In addition, because administrative data are generally available at the time of hospital admission, these data may provide clinicians and health care planners the opportunity to allocate additional health care resources to patients at higher risk for poor outcomes earlier in the course of disease than physiologic data that are collected after admission.

The purpose of this study was to obtain generalizable estimates of in-hospital mortality in patients admitted for

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acute exacerbation of COPD, describe the admission characteristics of these patients, and identify risk factors for in-hospital mortality based on administrative data routinely collected in this population.

METHODS

STUDY DESIGN AND POPULATION

We conducted a cross-sectional study of patients who were part of the 1996 Nationwide Inpatient Sample (NIS).¹⁷ Patients were included for analysis if they carried a primary discharge diagnosis of chronic obstructive bronchitis with acute exacerbation (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* code of 491.21).¹⁸ Patients with a 491.21 discharge diagnosis were selected for this study, as it is the only code to record an acute exacerbation of COPD. Patients with other COPD-related ICD-9-CM discharge diagnoses, representing 22.5% of codes used for patients with COPD in this data set (491.x [chronic bronchitis], 492.x [emphysema], or 496.x [chronic airway obstruction, not elsewhere classified]), were excluded since these diagnostic codes are likely to include patients admitted for reasons other than exacerbations of their respiratory disease. Patients younger than 40 years were excluded to minimize misclassification of disease status since most patients with COPD present after the fifth decade.¹⁹

DATABASE

The 1996 NIS data set is part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality. This administrative database contains patient information on hospitalizations from a 20% sample of acute care, nongovernmental hospitals in the United States. Hospitals represented in the NIS were chosen based on a stratified probability sample of hospitals with sampling probabilities in proportion to the number of hospitals in each stratum. Strata were determined from hospital characteristics that include region, size, teaching status, urban or rural location, and ownership. The information collected in this database comes from over 900 hospitals located in 19 states and contains approximately 6.5 million records for the year 1996.

The NIS data set includes primary and secondary discharge diagnoses, primary and secondary procedures, demographic characteristics, hospital characteristics, insurance status, and other administrative information (eg, hospital charges and length of stay).

OUTCOME AND INDEPENDENT VARIABLES

The primary outcome studied was in-hospital mortality. Secondary outcomes included length of stay, total charges, mechanical ventilation utilization, and discharge disposition of patients. These secondary outcomes were chosen to further characterize the morbidity of acute exacerbations of COPD. Descriptive (independent) variables included age, sex, race, and median income by ZIP code. In addition, insurance status, comorbidity, and admission source for each hospitalization were also analyzed. All independent variables were modeled as categorical variables.

Patient age was grouped by quartiles. Patient race was defined as white, black, Hispanic, Asian, American Indian, or other. Patient income was characterized in this data set by the median income within the patient's residence ZIP code area (<\$25 000, \$25 001-\$30 000, \$30 001-\$35 000, and >\$35 000). Patient discharge disposition was categorized as routine (dis-

charged home); or requiring short-term hospitalization, skilled nursing, intermediate health care facility, another type of health care facility (hospice, rehabilitation center, psychiatric facility), or home health care; discharged against medical advice; or death. Categories for patient insurance included Medicare, Medicaid, private insurance including health maintenance organizations (HMOs), self-pay, no charge, or other (Title V, worker's compensation, and other government sources). Admission source was defined as routine (referrals from physicians, clinics, and HMOs), from the emergency department, from a long-term care facility, transfer from another hospital, or secondary to a court order. Procedure codes 967, 967.1, and 967.2 were used to identify patients having received mechanical ventilation during their hospitalization.

To analyze the relationship of comorbidity to in-hospital mortality we used the Deyo-adapted Charlson Index (D-CI) as a measure of comorbid illness.^{20,21} This index is based on 17 diagnostic categories identified from ICD-9-CM discharge diagnoses. Typically, the D-CI assigns a weight from 1 to 6 for each comorbid condition based on previously defined adjusted relative risks, giving the index a range from 0 to 33. In this analysis, we found no meaningful differences in our results when using the weighted or unweighted D-CI. To facilitate interpretation of results, we modeled comorbidity using the unweighted D-CI (range, 1-17). All patients had a D-CI score of at least 1, since all patients carried a diagnosis of COPD. The D-CI was then considered as an ordinal variable with categories of 1, 2, 3, 4, and 5 or more comorbid illnesses. Patients with 5 or more comorbid illnesses were categorized as one group because of the small number of patients with comorbidities in this range.

ANALYSES

In the first stage of the analysis, we used descriptive statistics to characterize the patient sample, using proportions, means with SDs, or medians with interquartile ranges (IQRs) where appropriate. In bivariate analyses of in-hospital mortality with independent variables, we used χ^2 tests or *t* tests. The χ^2 test for trend was used to look for significant changes in risk within ordered categories. Additional bivariate analyses were performed using simple logistic regression with in-hospital mortality as the outcome of interest and all other variables considered as independent variables. Multivariable logistic regression models were then constructed to estimate risk of in-hospital mortality associated with independent variables after adjusting for other independent variables.

Because patients with COPD exacerbations may have different mortality risks depending on their source of admission (eg, routine admission vs emergency department), we developed 3 models: (1) a *full model* consisting of all eligible patients, (2) an *ED model* consisting of patients admitted from the emergency department, and (3) a *routine model* consisting of patients considered as routine hospital admissions. We did not find meaningful differences in results between these 3 models, so only multivariable analyses from the full model are reported in this article. Receiver operating characteristics for the full model were analyzed through the sequential addition of each variable to determine the model's cumulative predictive abilities.

The proportion of admissions for COPD exacerbation in the NIS data varied by hospital region (Northeast, 1.7%; Midwest, 1.7%; South, 2.2%; and West, 1.7%), hospital location (urban, 1.7% and rural, 2.9%), and hospital teaching status (teaching, 1.2% and nonteaching, 2.2%). Since outcomes may be correlated within groups of patients defined by these hospital characteristics, we used robust methods in the estimation of standard errors for primary and secondary outcomes.²²

Table 1. Population Characteristics for 71 130 Patients Admitted With an Acute Exacerbation of COPD

Characteristic (n)	No. (%)
Age group, y (71 125)	
40-63	19 012 (26.7)
64-71	17 870 (25.1)
72-78	17 863 (25.1)
≥79	16 380 (23.0)
Race (57 518)	
White	49 810 (86.6)
Black	4300 (7.5)
Hispanic	2605 (4.5)
Asian	435 (0.8)
American Indian	84 (0.2)
Other	284 (0.5)
Sex (71 124)	
Female	40 085 (56.4)
Male	31 039 (43.6)
Median income by ZIP code, \$ (67 669)	
0-25 000	26 678 (39.6)
25 001-30 000	14 839 (21.9)
30 001-35 000	9816 (14.5)
≥35 001	16 236 (24.0)
Insurance status (71 009)	
Medicare	51 556 (72.6)
Private, including HMO	11 384 (16.0)
Medicaid	5481 (7.7)
Self-pay	1423 (2.0)
Other	1121 (1.6)
No charge	44 (0.1)
Admission source (68 935)	
Routine	21 330 (30.9)
Emergency department	45 158 (65.5)
Another hospital	1327 (1.9)
Long-term care facilities	1110 (1.6)
Court/law enforcement	10 (0.01)
Devo-adapted Charlson Index (71 130)	
1	39 072 (54.9)
2	21 942 (30.9)
3	8095 (11.4)
4	1729 (2.4)
≥5	292 (0.4)

Abbreviations: COPD, chronic obstructive pulmonary disease; HMO, health maintenance organization.

We assessed collinearity among independent variables using variance inflation factors. In addition, forward and backward stepwise logistic regression was used to identify the most parsimonious model. Odds ratios are reported with 99% confidence intervals. When hypothesis testing was performed, statistical significance was assumed at a level of $P < .01$. The goodness of fit for the multiple logistic regression models was assessed using the Hosmer-Lemeshow test.²³ All analyses were performed using STATA version 6 software (Stata Corp, College Station, Tex).

RESULTS

Of the approximately 6 million admissions in the 1996 NIS database, 72 891 (1.1%) carried the ICD-9-CM code of 491.21 for chronic obstructive bronchitis with acute exacerbation and were considered for analysis. After exclusion of individuals younger than 40 years, there were 71 130 admissions available for analysis. Characteristics of this patient population are listed in **Table 1**. Study

participants were predominantly older than 64 years, white, with Medicare insurance, from areas of low median incomes by ZIP code, and primarily admitted through the emergency department. During 1996, the mean age of admitted individuals was 69.9 (SD, 11.2) years and more women were admitted than men (56.4% vs 43.6%).

The median length of stay was 5 (IQR, 3-7) days and the median charge per admission was \$6975 (IQR, \$4530-\$11 171). Of the patients discharged from the hospital, 70.1% were considered to be routine discharges, 13.0% needed home health care assistance, 7.7% required skilled nursing facilities, 5.5% required "other" facilities, 1.3% were transferred to short-term hospitals, 0.7% left against medical advice, and 2.5% died in the hospital. Three percent of patients required mechanical ventilation during the course of their admission. The average number of comorbid illnesses using the D-CI was 1.6 (SD, 0.8).

Patients who died following an acute exacerbation of COPD were older (74.1 ± 9.3 years vs 69.8 ± 11.2 years; $P < .001$), had a higher level of comorbid illness (D-CI, 2.1 ± 1.0 vs 1.6 ± 0.8 ; $P < .001$), required longer hospitalizations (7 days [IQR, 3-7] vs 5 days [IQR, 3-15]; $P < .001$), and acquired higher charges (\$15 200 [IQR, \$7191-\$35 857] vs \$6905 [IQR, \$4502-\$10 935]; $P < .001$) than those who were alive at hospital discharge.

The relationships between mortality and the variables of interest are shown in **Table 2**. In the bivariate analyses, mortality from acute exacerbation of COPD increased with age quartile and median income. The highest rate of mortality was observed among whites (2.7%), men (2.8%), those with Medicare insurance (2.9%), and those admitted from nonroutine sources (2.8%). Patients requiring mechanical ventilation experienced a higher mortality rate than those who did not (27.8% vs 1.7%; $P < .001$). The odds ratios for mortality from simple logistic regression for each variable are summarized in Table 2. Statistically significant increases in mortality were seen for patients who were older, male, from areas with higher incomes, had Medicare insurance, were admitted from a nonroutine source, and had a greater number of comorbid illnesses. Primary and secondary outcomes varied significantly across hospital region, location, and teaching status (**Table 3**).

Multivariable analyses (Table 2), after accounting for correlation of outcomes within groups defined by hospital characteristics, confirmed the results of the bivariate analyses with the exception of insurance status. Insurance status was no longer significantly related to in-hospital mortality after adjusting for other independent variables. The Hosmer-Lemeshow test suggests that the full model demonstrated a good fit ($P > .32$). There was no evidence for significant collinearity among the independent variables. Receiver operating characteristic analyses of the full model showed an area under the curve of 0.70. The **Figure** demonstrates that the increase in predictive power of the full model is principally owing to the addition of age and the D-CI. Stepwise multiple logistic regression indicated that age, sex, admission source, D-CI, and median income by ZIP code provided the most parsimonious model.

Table 2. Bivariate and Multivariable Analysis of In-Hospital Deaths

Characteristic (n)	In-Hospital Deaths, No. (%)	Unadjusted OR (99% CI)	Adjusted OR* (99% CI)
Age groups, y †‡ (71 093)			
40-63	232 (1.2)	1.00	1.00
64-71	410 (2.3)	1.90 (1.54-2.35)	1.60 (1.31-1.97)
72-78	535 (3.0)	2.50 (2.04-3.07)	1.94 (1.74-2.15)
≥79	601 (3.7)	3.08 (2.52-3.77)	2.27 (1.86-2.76)
Race (57 493)			
White	1338 (2.7)	1.00	1.00
Black	87 (2.0)	0.75 (0.56-1.00)	0.83 (0.64-1.06)
Hispanic	56 (2.2)	0.80 (0.56-1.14)	0.81 (0.50-1.31)
Asian	6 (1.4)	0.51 (0.18-1.46)	0.42 (0.18-0.99)
American Indian	2 (2.4)	0.88 (0.14-5.59)	1.10 (0.18-6.77)
Other	7 (2.5)	0.92 (0.34-2.46)	1.02 (0.52-2.00)
Sex (71 092)			
Female	903 (2.3)	1.00	1.00
Male	874 (2.8)	1.25 (1.11-1.43)	1.22 (1.06-1.42)
Median income by ZIP code, \$ †‡ (67 638)			
0-25 000	578 (2.2)	1.00	1.00
25 001-30 000	381 (2.6)	1.19 (1.01-1.42)	1.20 (0.97-1.48)
30 001-35 000	264 (2.7)	1.25 (1.03-1.52)	1.17 (0.98-1.40)
≥35 001	481 (3.0)	1.38 (1.18-1.63)	1.31 (1.06-1.60)
Insurance status† (70 977)			
Medicare	1472 (2.9)	1.00	1.00
Private, including HMO	189 (1.7)	0.57 (0.47-0.70)	0.87 (0.69-1.08)
Medicaid	72 (1.3)	0.45 (0.33-0.62)	0.91 (0.73-1.12)
Self-pay	21 (1.5)	0.51 (0.29-0.90)	0.70 (0.36-1.34)
Other	20 (1.8)	0.62 (0.34-1.11)	1.27 (0.67-2.41)
No charge	1 (2.3)	0.79 (0.06-10.72)	2.07 (0.28-15.02)
Admission source†‡ (68 903)			
Routine	396 (1.9)	1.00	1.00
Emergency department	1189 (2.6)	1.43 (1.23-1.66)	1.39 (1.15-1.67)
Another hospital	83 (6.3)	3.52 (2.56-4.86)	2.93 (1.99-4.34)
Long-term care facilities	56 (5.1)	2.81 (1.93-4.10)	1.99 (1.13-3.53)
Court/law enforcement	0
Deyo-adapted Charlson Index†‡ (71 130)			
1	576 (1.5)	1.00	1.00
2	676 (3.1)	2.12 (1.83-2.46)	1.98 (1.67-2.35)
3	366 (4.5)	3.16 (2.66-3.77)	2.70 (2.19-3.27)
4	130 (7.5)	5.43 (4.20-7.04)	4.82 (3.59-6.44)
≥5	30 (10.3)	7.65 (4.60-12.71)	5.70 (4.08-7.89)

Abbreviations: CI, confidence interval; HMO, health maintenance organization; OR, odds ratio.

*Adjusted OR based on a multivariable logistic regression that includes age quartiles, race, sex, median income by ZIP code, insurance status, admission source, and Deyo-adapted Charlson Index. The model accounts for possible correlation of outcomes among patients in strata defined by hospital region, location, and teaching status.

† χ^2 Test of trends for bivariate analyses, $P < .01$.

‡ χ^2 Test of trends for multivariable analyses, $P < .01$.

COMMENT

Using a large, nationally representative administrative database of hospitalizations in the United States, we found that the overall mortality for adults 40 years or older with an acute exacerbation of COPD was 2.5% (99% confidence interval, 2.4%-2.7%). In addition, we identified specific patient subgroups at higher risk for in-hospital mortality.

Previous studies of subpopulations of patients with acute exacerbations of COPD have demonstrated a 6-fold range in in-hospital mortality.^{2,4-14} These estimates were derived from analyses of specific subpopulations, including the elderly (5%-11%),^{2,6,11} patients admitted for acute respiratory failure (11%-26%),^{2,4,9,10,12,14} patients admitted to pulmonary specialty wards or urban hospitals (4%-14%),^{5,8} or intensive care units (8%-26%).^{4,7,11,13}

Comparisons of subgroups of patients in the present study suggest that our findings are consistent with previous reports that focused on subpopulations of COPD, supporting the validity of the mortality estimate in the present study. For example, we found that patients older than 65 years had an in-hospital mortality risk of 3.0%, similar to the 5.0% reported in a study limited to elderly COPD patients from a Medicare claims database (age ≥65 years).⁶ Likewise, the high in-hospital mortality rate among patients requiring mechanical ventilation in the present study is consistent with findings reported by Senoff and colleagues⁴ (27.8% vs 31.8%, respectively).

In the present study, we identified several risk factors for in-hospital mortality using information that is obtainable from administrative databases. Most predictors of in-hospital mortality reported in previous studies have focused on physiologic variables related to se-

Table 3. Outcomes for Patients Admitted With an Acute Exacerbation of COPD Stratified by Hospital Region, Teaching Status, and Hospital Location

Outcome	Hospital Region				Teaching Status		Hospital Location	
	Northeast	Midwest	South	West	Nonteaching	Teaching	Urban	Rural
In-hospital mortality, %*	3.1	2.2	2.2	2.8‡	2.4	2.9‡	2.7	1.8‡
Requiring mechanical ventilation, %†	3.2	2.3	2.9	4.0‡	2.6	4.7‡	3.4	1.7‡
Mortality in those requiring mechanical ventilation, %	30.0	22.7	31.7	22.7‡	32.0	38.3‡	28.2	26.0‡
Median LOS (interquartile range), d	5 (4-8)	4 (3-7)	5 (3-7)	4§ (3-6)	5 (3-7)	4 (3-7)	5 (3-7)	4§ (3-6)

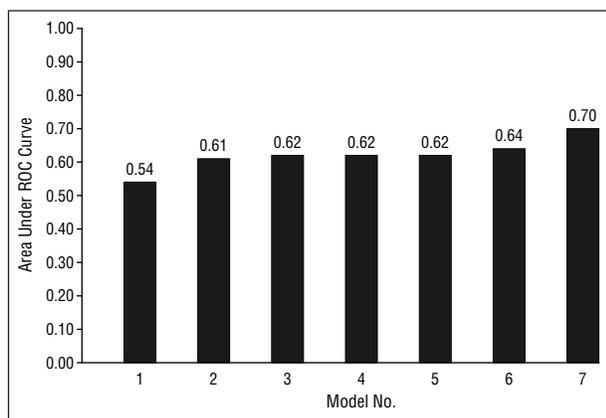
Abbreviations: COPD, chronic obstructive pulmonary disease; LOS, length of stay.

*Percentage of patients with COPD exacerbation who died in the hospital.

†Percentage of patients with COPD exacerbation requiring mechanical ventilation.

‡ $P < .001$ by χ^2 test for differences in outcome across hospital region, teaching status, or location.

§ $P < .001$ by Kruskal-Wallis test for differences across hospital region and hospital location.



Each model number represents the stepwise addition of the following variables: 1, median income by ZIP code; 2, age; 3, sex; 4, race; 5, insurance status; 6, admission source; and 7, Deyo-adapted Charlson Index. Note that age and Deyo-adapted Charlson Index have the greatest contribution to the predictive ability of the full model. ROC indicates receiver operating curve.

verity of illness such as impaired oxygenation (lower PaO₂-fraction of inspired oxygen ratio and higher alveolar to arterial oxygen gradient),^{2,5} lower arterial pH,^{12,14} and higher acute physiology scores.^{2,11,13} The addition of physiologic data to administrative data is likely to improve the predictive abilities of models based on administrative data alone. Nevertheless, in the present study, several risk factors for in-hospital mortality were identified using information readily available from an administrative database.

A greater number of comorbid illnesses were associated with increased risk of in-hospital mortality in the present study. In contrast, Connors and colleagues² found that the number of preexisting comorbid illnesses was not a significant predictor of in-hospital mortality among patients admitted with severe COPD. This finding may have been due to the higher overall severity of illness in their population compared with the present investigation (eg, 11% vs 2.5% in-hospital mortality in the overall cohort). In their study, the number of comorbid conditions may not have provided additional information for mortality risk since they examined a stratum of patients already at an elevated risk of death. In contrast, in our population, which was designed to select patients across a broad range of illness severity and was not restricted to specific patient subpopulations (ie, patients admitted

to an intensive care unit, patients with acute respiratory failure, or patients with a prognosis of less than 6 months), the number of comorbid conditions influenced mortality. There has been some criticism of the adaptation of the Charlson index to administrative databases. The ICD-9-CM discharge diagnosis codes used in this study may have underestimated the presence of comorbid conditions when compared with detailed chart abstraction.²⁴ Nevertheless, the derived D-CI has still been shown to have similar predictive abilities for mortality when compared with a score derived from chart abstraction.^{24,25} We demonstrated that the addition of the D-CI to the prediction model resulted in a definitive improvement in the model's predictive ability. This finding suggests, not surprisingly, that while demographic and admission characteristics may be useful in the prediction of in-hospital mortality, an individual patient's clinical health status provides additional information in determining mortality risk.

Few studies have reported sex as a risk factor for in-hospital mortality in acute exacerbations of COPD.^{11,13} Heuser and colleagues,¹¹ in a study of 3050 patients with lower respiratory tract disease admitted to the intensive care unit initially found that men were more likely to die. Their estimate of the higher risk of in-hospital mortality (odds ratio, 1.25; $P = .07$) is consistent with the findings in the present study. The increased mortality risk for male sex found by Heuser and colleagues and in the present study may reflect the observation that men are more likely than women to seek care later in the course of the disease and thus carry a worse prognosis.²⁶

The finding of an income over \$35 000 compared with an income of less than \$25 000 as an independent risk factor for in-hospital mortality was unexpected. Most studies that have looked at variables of socioeconomic status have generally found increased morbidity and mortality from COPD in patients with lower socioeconomic status.²⁷⁻³² A potential explanation for this finding is that thresholds for hospital admission may be influenced by income so that patients with higher incomes were admitted for more severe exacerbations of COPD, while patients with lower incomes and fewer resources were admitted for milder exacerbations of COPD. Although we adjusted for comorbid illnesses, confounding from factors related to severity of illness could have occurred. As a result, it would appear as if patients with higher incomes are at greater risk of dying in the hospital. In ad-

dition, data concerning patient income is represented by the median income within the patient's residence ZIP code. Because ecological data³³ have been used to generalize the income of all patients living within a given area, we believe this finding should be interpreted with caution.

While many studies have shown race-related differences in health care delivery and outcomes for across a number of diseases,³⁴⁻³⁷ our results do not demonstrate significant differences by race in hospital mortality from COPD exacerbations. The absence of a significant difference between blacks and whites is especially interesting given that black patients may present to the emergency department later in their disease course with greater severity of illness compared with white patients.³⁷⁻⁴⁰ These results should therefore provide some optimism concerning potential racial disparities in outcomes of acute exacerbations of COPD.

Nonroutine admissions were found to be associated with a higher risk of in-hospital mortality compared with patients referred by "routine" sources (physicians, clinics, or HMOs). Patients transferred from another hospital were at highest risk compared with those admitted from the emergency department or long-term care facilities. Previous studies have indicated that frequent trips to the emergency department or to a physician's office are associated with an increased risk of hospitalization,⁴¹ but the importance of source of admission has not previously been reported for in-hospital mortality from acute exacerbations of COPD. Presumably patients transferred from another hospital require additional resources that were not available at the initial hospital, which suggests that they have greater illness severity and carry a higher mortality risk. Similarly, patients admitted from the emergency department or transferred from a long-term care facility may have a higher acuity of disease, placing them at a higher risk of mortality.

The present study has 2 principal strengths. First, this is the largest study to date of in-hospital mortality in patients presenting with an acute exacerbation of COPD. In addition, the generalizability of these results is enhanced as the data from the NIS are derived from a stratified sample of all nonfederal US hospitals and the observations in this study are not limited to specific subpopulations of patients.

The major limitation in this study is that accuracy of the diagnosis of COPD exacerbation is dependent on proper ICD-9-CM coding. Though the lack of unique patient identifiers in the NIS data set prevented a validation study, a previous study² found that ICD-9-CM codes correctly classified 87% of patients with an acute COPD exacerbation. To minimize potential misclassification we limited our analyses to individuals 40 years and older since most patients with COPD present after the fifth decade.¹⁹ The lack of unique patient identifiers also prevented us from identifying whether multiple admissions existed for an individual represented in the NIS data set. As a result, variables associated with multiple hospital admissions could lead to an underestimation of the mortality risk attributable to that variable. For example, if older individuals were more likely to have multiple admissions, our mortality risk estimate would underestimate the true risk of death due to older age.

The results of this study have several implications. First, this study provides an estimate of the in-hospital mortality for the "average patient" in the United States admitted with an acute exacerbation of COPD. Compared with previous estimates in selected subpopulations that suggested a higher mortality (4%-30%), we believe our findings are reason for clinicians and patients to be more optimistic about the outcomes of hospitalization. Second, while many studies have shown care or outcome disadvantages for nonwhites in the United States, our data suggest that no significant differences in in-hospital mortality from COPD exacerbations exist between nonwhites and whites. Third, while it may not be surprising that older patients and those with a greater number of comorbid illnesses were at higher risk of mortality, the higher mortality risk in men cannot be readily explained and deserves further inquiry. Fourth, secondary analyses by hospital region, location, and teaching status suggest that variation in in-hospital mortality and other outcomes are present. Whether this finding is due to differences in severity of illness on hospital admission or other factors (eg, differences in inpatient care) merits further investigation since COPD exacerbations are common and represent a substantial burden in terms of morbidity, mortality, and health care expenditures.

These findings demonstrate that administrative data collected in large patient populations can provide useful information regarding patient outcomes in acute exacerbations of COPD. Future studies may want to consider patient sex, source of hospitalization, and the number of comorbid illnesses as potential predictors of mortality when creating risk prediction models in this population.

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REFERENCES

1. Bach PB, Brown C, Gelfand SE, McCrory DC. Management of acute exacerbations of chronic obstructive pulmonary disease: a summary and appraisal of published evidence. *Ann Intern Med.* 2001;134:600-620.
2. Connors AF Jr, 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;154:959-967.

3. National Heart, Lung, and Blood Institute. Morbidity and mortality: chartbook on cardiovascular, lung, and blood diseases. 1998. US Department of Health and Human Services, Public Health Service, National Institutes of Health. Available at: <http://www.nhlbi.nih.gov/resources/docs/cht-book.htm>. Accessed June 5, 2002.
4. Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. *JAMA*. 1995;274:1852-1857.
5. Fuso L, Incalzi RA, Pistelli R, et al. Predicting mortality of patients hospitalized for acutely exacerbated chronic obstructive pulmonary disease. *Am J Med*. 1995;98:272-277.
6. Cydulka RK, McFadden ER Jr, Emerman CL, Sivinski LD, Pisanelli W, Rimm AA. Patterns of hospitalization in elderly patients with asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1997;156:1807-1812.
7. Moran JL, Green JV, Homan SD, Leeson RJ, Leppard PI. Acute exacerbations of chronic obstructive pulmonary disease and mechanical ventilation: a reevaluation. *Crit Care Med*. 1998;26:71-78.
8. Mushlin AI, Black ER, Connolly CA, Buonaccorso KM, Eberly SW. The necessary length of hospital stay for chronic pulmonary disease. *JAMA*. 1991;266:80-83.
9. Dardes N, Campo S, Chiappini MG, Re MA, Ciccirello P, Vulterini S. Prognosis of COPD patients after an episode of acute respiratory failure. *Eur J Respir Dis Suppl*. 1986;146:377-381.
10. Burk RH, George RB. Acute respiratory failure in chronic obstructive pulmonary disease: immediate and long-term prognosis. *Arch Intern Med*. 1973;132:865-868.
11. Heuser MD, Case LD, Ettinger WH. Mortality in intensive care patients with respiratory disease: is age important? *Arch Intern Med*. 1992;152:1683-1688.
12. Warren PM, Flenley DC, Millar JS, Avery A. Respiratory failure revisited: acute exacerbations of chronic bronchitis between 1961-68 and 1970-76. *Lancet*. 1980;1:467-470.
13. Portier F, Defouilloy C, Muir JF. Determinants of immediate survival among chronic respiratory insufficiency patients admitted to an intensive care unit for acute respiratory failure: a prospective multicenter study. *Chest*. 1992;101:204-210.
14. Jeffrey AA, Warren PM, Flenley DC. Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. *Thorax*. 1992;47:34-40.
15. Martin TR, Lewis SW, Albert RK. The prognosis of patients with chronic obstructive pulmonary disease after hospitalization for acute respiratory failure. *Chest*. 1982;82:310-314.
16. Iezzoni LI, ed. *Risk Adjustment for Measuring Health Outcomes*. 2nd ed. Chicago, Ill: Health Administration Press; 1997.
17. 1996 Nationwide Inpatient Sample (NIS): Healthcare Cost and Utilization Project [database]. Rockville, Md: Agency for Healthcare Research and Quality; 1999.
18. Department of Health and Human Services. *International Classification of Diseases, Ninth Revision, Clinical Modification*. 4th ed. Washington, DC: US Government Printing Office; 1991. DHHS publication (PHS)91-1260.
19. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1995;152:S77-S121.
20. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47:1245-1251.
21. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45:613-619.
22. Huber PJ. The behavior of maximum likelihood estimates under non-standard conditions. In: *Proceedings of the Fifth Symposium on Mathematical Statistics and Probability*. Berkeley: University of California Press; 1967;1:221-233.
23. Lemeshow S, Hosmer DW Jr. A review of goodness of fit statistics for use in the development of logistic regression models. *Am J Epidemiol*. 1982;115:92-106.
24. van Doorn C, Bogardus ST, Williams CS, Concato J, Towle VR, Inouye SK. Risk adjustment for older hospitalized persons: a comparison of two methods of data collection for the Charlson Index. *J Clin Epidemiol*. 2001;54:694-701.
25. Powell H, Lim LL, Heller RF. Accuracy of administrative data to assess comorbidity in patients with heart disease: an Australian perspective. *J Clin Epidemiol*. 2001;54:687-693.
26. Council on Ethical and Judicial Affairs, American Medical Association. Gender disparities in clinical decision making. *JAMA*. 1991;266:559-562.
27. Viegi G, Scognamiglio A, Baldacci S, Pistelli F, Carrozzi L. Epidemiology of chronic obstructive pulmonary disease (COPD). *Respiration*. 2001;68:4-19.
28. Prescott E, Vestbo J. Socioeconomic status and chronic obstructive pulmonary disease. *Thorax*. 1999;54:737-741.
29. Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: results from the Copenhagen City Heart Study. *Eur Respir J*. 1999;13:1109-1114.
30. Stebbings JH Jr. Chronic respiratory disease among nonsmokers in Hagerstown, Maryland, 3: social class and chronic respiratory disease. *Environ Res*. 1971;4:213-232.
31. Cohen BH, Ball WC Jr, Brashears S, et al. Risk factors in chronic obstructive pulmonary disease (COPD). *Am J Epidemiol*. 1977;105:223-232.
32. Higgins MW, Keller JB, Metzner HL. Smoking, socioeconomic status, and chronic respiratory disease. *Am Rev Respir Dis*. 1977;116:403-410.
33. Szklo M, Nieto FJ. Basic study designs in analytical epidemiology. In: *Epidemiology: Beyond the Basics*. Gaithersburg, Md: Aspen Publishers Inc; 2000:3-51.
34. Jha AK, Shlipak MG, Hosmer W, Frances CD, Browner WS. Racial differences in mortality among men hospitalized in the Veterans Affairs health care system. *JAMA*. 2001;285:297-303.
35. Krishnan JA, Diette GB, Skinner EA, Clark BD, Steinwachs D, Wu AW. Race and sex differences in consistency of care with national asthma guidelines in managed care organizations. *Arch Intern Med*. 2001;161:1660-1668.
36. Yergan J, Flood AB, LoGerfo JP, Diehr P. Relationship between patient race and the intensity of hospital services. *Med Care*. 1987;25:592-603.
37. Buckle JM, Horn SD, Oates VM, Abbey H. Severity of illness and resource use differences among white and black hospitalized elderly. *Arch Intern Med*. 1992;152:1596-1603.
38. Horner RD, Lawler FH, Hainer BL. Relationship between patient race and survival following admission to intensive care among patients of primary care physicians. *Health Serv Res*. 1991;26:531-542.
39. Johnson PA, Lee TH, Cook EF, Rouan GW, Goldman L. Effect of race on the presentation and management of patients with acute chest pain. *Ann Intern Med*. 1993;118:593-601.
40. Weissman JS, Stern R, Fielding SL, Epstein AM. Delayed access to health care: risk factors, reasons, and consequences. *Ann Intern Med*. 1991;114:325-331.
41. Murata GH, Gorby MS, Kapsner CO, Chick TW, Halperin AK. A multivariate model for the prediction of relapse after outpatient treatment of decompensated chronic obstructive pulmonary disease. *Arch Intern Med*. 1992;152:73-77.