Journal of Respiratory Biology and Translational Medicine

SCIEPublish

Article

Emerging Risk Factors and Temporal Patterns in Hospitalized Patients with COPD: A Retrospective Analysis of the NIS Data (2019–2023)

Xin Li [1], Jiaqian Liu [1], Soumik Purkayastha [1], Victor Brodzik Talisa [1,2], Franziska J. Rosser [3] and Ying Ding [1,*]

[1] Department of Biostatistics and Health Data Science, School of Public Health, University of Pittsburgh, 130 De Soto Street, Pittsburgh, PA 15261, USA; xil519@pitt.edu (X.L.); jil289@pitt.edu (J.L.); soumik@pitt.edu (S.P.); vit13@pitt.edu (V.B.T.)

[2] Department of Critical Care Medicine, School of Medicine, University of Pittsburgh, 3550 Terrace Street, Alan Magee Scaife Hall, Suite 600, Pittsburgh, PA 15213, USA

[3] Division of Pulmonary Medicine, Department of Pediatrics, School of Medicine, University of Pittsburgh, 4401 Penn Avenue, Pittsburgh, PA 15224, USA; franziska.rosser2@chp.edu (F.J.R.)

* Corresponding author. E-mail: yingding@pitt.edu (Y.D.)

Received: 6 September 2026; Revised: 20 October 2026; Accepted: 23 October 2026; Available online: 4 November 2026

ABSTRACT: Chronic obstructive pulmonary disease (COPD) is associated with substantial hospitalization burden. We evaluated temporal changes in associations of COVID-19 and major comorbidities with clinical and hospital utilization outcomes among COPD hospitalizations from 2019 to 2023. National Inpatient Sample data were used to identify hospitalizations with any COPD diagnosis. Outcomes included in-hospital mortality, acute kidney injury (AKI), total hospital charges, and time-to-routine discharge. Year-specific logistic, linear, and Fine–Gray models were adjusted for demographics, hospital characteristics, COVID-19, and comorbidities. Cohorts included 881,008, 737,636, 714,315, 714,230, and 748,441 hospitalizations in 2019–2023, respectively. COVID-19 had the strongest association with mortality in 2020 (adjusted odds ratio, 5.95; 95% confidence interval [CI], 5.78–6.13), declining to 1.48 (95% CI: 1.41–1.56) in 2023. Similar attenuation was observed for AKI, total charges, and time to routine discharge. Malnutrition remained consistently associated with adverse outcomes. Metastatic cancer showed higher odds of mortality (range, 2.59–3.13 across 2019–2023), chronic kidney disease with higher odds of AKI (range, 2.99–3.37), and dementia with lower routine discharge rate (adjusted subdistribution hazard ratio range, 0.52–0.55). COVID-19 associations with adverse outcomes were strongest early in the pandemic and attenuated, whereas chronic comorbidity associations remained relatively stable.

Keywords: Chronic obstructive pulmonary disease; COVID-19; Acute kidney injury; Hospital utilization; National Inpatient Sample; Time-to-routine discharge

© 2026 The authors. This is an open access article under the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory condition that affects millions of people worldwide and represents a major public health challenge. It is estimated that COPD accounts for approximately 5% of all deaths globally, making it one of the leading causes of mortality [1]. COPD develops gradually and is often underdiagnosed in its early stages because symptoms such as chronic cough and shortness of breath may not be immediately recognized [2]. The major risk factors for COPD, including cigarette smoking and exposure to indoor or outdoor air pollution, are common in daily life and difficult to avoid [3].

COPD frequently leads to substantial healthcare utilization and serious health complications [4]. Patients with COPD often experience worsening respiratory symptoms and acute exacerbations that require hospitalization. These hospitalizations are associated with severe complications such as acute kidney injury (AKI), and they contribute to increased in-hospital mortality, longer hospital stays, and higher hospitalization costs [5]. As a result, COPD places a considerable burden on both healthcare systems and affected patients.

Since the emergence of the COVID-19 pandemic in 2020, patients with COPD have been shown to face higher risks of severe illness and mortality when infected with SARS-CoV-2 [6]. In addition to COVID-19 infection, other clinical conditions, such as malnutrition and obstructive sleep apnea (OSA), are commonly observed among patients with COPD and may further worsen respiratory function and overall health status [7,8]. These factors may increase the risk of poor outcomes and highlight the need to better understand clinical risks among hospitalized patients with COPD.

Although previous studies have examined hospitalized patients with COPD, many of them focused on specific outcomes or limited time periods. Less attention has been paid to how the effects of major risk factors may vary across different years, especially before and after the COVID-19 pandemic. Furthermore, hospitalized patients may experience different discharge dispositions, including routine discharge, transfer to another care facility, or in-hospital death. These competing outcomes complicate the evaluation of hospital length of stay and require appropriate statistical approaches [9].

Therefore, this study aimed to examine associations between COVID-19 and major comorbidities and clinical and hospital utilization outcomes among hospitalized patients with COPD, and to assess how these associations evolved from 2019 to 2023.

2. Materials and Methods

2.1. Data Source

This study used data from the Healthcare Cost and Utilization Project (HCUP), a family of healthcare databases developed by the Agency for Healthcare Research and Quality (AHRQ) [10]. Specifically, we used the National Inpatient Sample (NIS), one of the largest all-payer inpatient databases in the United States, which contains encounter-level information from a 20% stratified sample of hospitalizations at U.S. community hospitals. The NIS provides a large, nationally representative source of inpatient data, including patient demographics, hospital characteristics, diagnoses and procedures (coded using ICD-10-CM and ICD-10 procedure codes), length of stay (LOS), discharge disposition, and total hospital charges. In this study, we analyzed annual NIS data from 2019 through 2023 to examine clinical and hospital utilization outcomes among patients with COPD, with analyses conducted separately for each year. Institutional review board approval and informed consent were not required.

2.2. Study Cohort

Figure 1 shows the selection of hospitalized patients with COPD from the NIS and the year-specific study cohorts from 2019 through 2023. Because the NIS is released annually as discharge-level datasets,

five datasets from 2019 through 2023 were included in the analysis. The study population included hospitalizations with COPD identified from any diagnosis position using ICD-10-CM diagnosis code J44. Table S1 lists the ICD-10-CM codes used in the present study. Because the NIS is a discharge-level database, each record represents a single hospitalization rather than a unique patient. The year 2019 was treated as the pre-COVID-19 reference year.

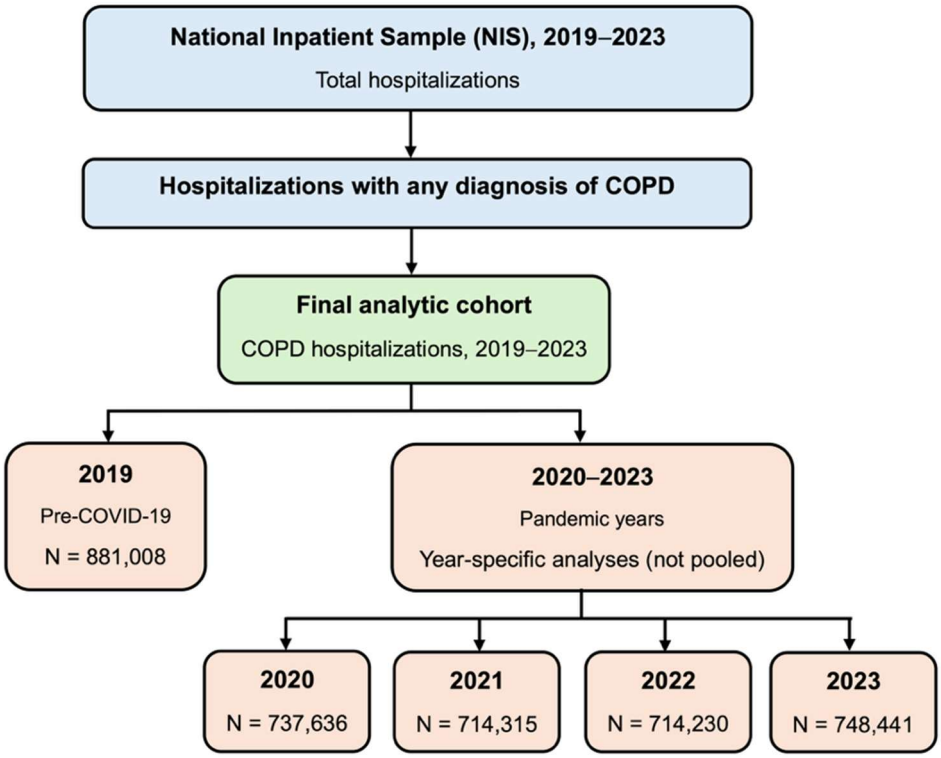


Figure 1. Selection of Hospitalizations with Any Diagnosis of COPD From the National Inpatient Sample, 2019–2023.

2.3. Outcomes and Covariates

The primary outcome was in-hospital mortality. Secondary outcomes included AKI, total hospital charges, and time-to-routine discharge from the hospital. We examined the distribution of total hospital charges to assess skewness and the need for transformation. AKI was identified using ICD-10-CM diagnosis codes. Because Present on Admission (POA) indicators were not available, AKI could not be distinguished as a pre-existing condition or an in-hospital complication. Accordingly, AKI was analyzed as an in-hospital complication, acknowledging the potential for misclassification, given its typically acute onset. Time-to-routine discharge was analyzed as a time-to-event analogue of LOS, focusing on routine discharge to home. Because patients may experience alternative outcomes that preclude routine discharge, a competing risks model was used, with routine discharge as the event of interest and in-hospital death and transfer-related dispositions treated as competing events. Patient demographics, hospital characteristics, and comorbidities were identified from the database using ICD-10-CM codes. Detailed definitions and coding specifications for all covariates are available in the database documentation [11]. Covariates included demographic and hospital characteristics, COVID-19 status, malnutrition, OSA, chronic kidney disease, chronic heart failure, and selected Elixhauser comorbidity measures representing pre-existing or independent comorbid conditions.

2.4. Statistical Analysis

Baseline characteristics and in-hospital outcomes were compared between patients with and without COVID-19. Continuous variables were summarized as mean ± standard deviation or median (IQR), as appropriate, and compared using the Wilcoxon rank-sum test. Categorical variables were summarized as frequencies and percentages and compared using Pearson's chi-square test.

Comorbidities with a prevalence below 3% were excluded from the analysis to improve the stability and reliability of model estimates. Univariable regression analyses were conducted for the remaining comorbidities, and those with a p value ≤ 0.001 were selected for inclusion in the multivariable models. Demographic (e.g., age, sex, and insurance status) and hospital-level characteristics (e.g., bed size, hospital teaching status, and ownership of hospital) were included a priori in all multivariable models.

Analyses were conducted using complete cases, and no imputation was performed.

Separate models were fitted for each year from 2019 to 2023 to evaluate how associations between risk factors and outcomes changed over time. To improve comparability across years, a consistent set of covariates was used for each outcome whenever possible.

Logistic regression models were used for in-hospital mortality and AKI, and results were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). Total hospital charges were inflation-adjusted to 2023 U.S. dollars before analysis and log-transformed before regression modeling, and additionally adjusted for discharge disposition, with the results reported as percent changes. Fine–Gray subdistribution hazards models were used to analyze time-to-routine discharge, treating routine discharge as the event of interest and in-hospital death and transfer-related dispositions as competing events [12–14]. This approach accounts for competing events that preclude routine discharge. Results were reported as subdistribution hazard ratios (sHRs) with 95% CIs. As a secondary analysis, the in-hospital mortality model was repeated in a restricted cohort of hospitalizations with COPD listed as the primary diagnosis to evaluate whether the association between COVID-19 and mortality was consistent among admissions primarily attributable to COPD. All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

Discharge-level sampling weights were not applied in the regression analyses; therefore, the results should be interpreted as associations within the analytic sample rather than nationally representative estimates. All statistical analyses were performed using R software, version 4.5.

3. Results

The analytic cohorts included 881,008 hospitalized patients with COPD in 2019, 737,636 in 2020, 714,315 in 2021, 714,230 in 2022, and 748,441 in 2023. Among hospitalized patients with COPD from 2020 through 2023, the proportion with COVID-19 was 5.52% in 2020, 7.89% in 2021, 8.72% in 2022, and 4.33% in 2023.

3.1. Patient Demographics, Comorbidities, and Hospital Characteristics

Table 1 summarizes the baseline characteristics of hospitalized patients with COPD by COVID-19 status from 2020 to 2023. The proportions of hospitalized patients with COPD who had COVID-19 were 5.52%, 7.89%, 8.72%, and 4.33% in 2020, 2021, 2022, and 2023, respectively, suggesting that the burden of COVID-19 among hospitalized patients with COPD increased from 2020 to 2022 and then declined in 2023.

Table 1. Baseline Characteristics of Hospitalized Patients with COPD from 2019 to 2023, Stratified by COVID-19 Status.

Characteristic	2019	2020			2021			2022			2023		
	Overall	Without COVID-19	With COVID-19	*p* Value	Without COVID-19	With COVID-19	*p* Value	Without COVID-19	With COVID-19	*p* Value	Without COVID-19	With COVID-19	*p* Value
	N = 881,008	*N* = 696,946 (94.5%)	*N* = 40,690 (5.5%)		*N* = 657,933 (92.1%)	*N* = 56,382 (7.9%)		*N* = 651,975 (91.3%)	*N* = 62,255 (8.7%)		*N* = 716,071 (95.7%)	*N* = 32,370 (4.3%)	
Demographic													
Age				<0.001			<0.001			<0.001			<0.001
Mean (SD)	69.5 (12.0)	69.3 (11.9)	72.6 (11.1)		69.5 (11.7)	70.5 (11.5)		69.9 (11.6)	71.8 (11.4)		70.2 (11.4)	73.4 (10.9)	
Median (IQR)	70.0 (61.0–78.0)	70.0 (61.0–78.0)	73.0 (65.0–81.0)		70.0 (62.0–78.0)	71.0 (63.0–79.0)		70.0 (62.0–78.0)	72.0 (64.0–80.0)		71.0 (62.0–79.0)	74.0 (66.0–82.0)	
Female	461,458 (52.4%)	358,020 (51.4%)	19,785 (48.6%)	<0.001	340,687 (51.8%)	28,549 (50.6%)	<0.001	341,124 (52.3%)	32,149 (51.6%)	0.001	374,720 (52.3%)	16,946 (52.4%)	>0.9
Elective admission	101,334 (11.5%)	78,814 (11.3%)	1544 (3.8%)	<0.001	71,838 (10.9%)	1804 (3.2%)	<0.001	69,049 (10.6%)	2058 (3.3%)	<0.001	74,367 (10.4%)	1071 (3.3%)	<0.001
Median Household Income				0.077			<0.001			<0.001			<0.001
0–25th percentile	316,029 (36.5%)	250,641 (36.7%)	14,863 (37.2%)		237,366 (36.8%)	21,022 (38.0%)		231,911 (36.1%)	21,741 (35.4%)		256,794 (36.6%)	10,694 (33.7%)	
26th to 50th percentile	239,502 (27.7%)	201,417 (29.5%)	11,692 (29.2%)		178,231 (27.6%)	16,006 (28.9%)		181,974 (28.3%)	17,213 (28.0%)		203,395 (29.0%)	9301 (29.3%)	
51st to 75th percentile	189,770 (21.9%)	139,915 (20.5%)	8023 (20.1%)		138,224 (21.4%)	11,625 (21.0%)		138,682 (21.6%)	13,535 (22.1%)		150,138 (21.4%)	7032 (22.2%)	
76th to 100th percentile	120,042 (13.9%)	91,684 (13.4%)	5420 (13.6%)		91,975 (14.2%)	6701 (12.1%)		90,247 (14.0%)	8886 (14.5%)		91,330 (13.0%)	4717 (14.9%)	
Injury Diagnosis Reported				<0.001			<0.001			<0.001			<0.001
No injury	803,892 (91.2%)	630,707 (90.5%)	38,865 (95.5%)		593,788 (90.3%)	53,714 (95.3%)		588,665 (90.3%)	57,742 (92.8%)		645,393 (90.1%)	30,066 (92.9%)	
Primary injury	37,467 (4.3%)	34,042 (4.9%)	433 (1.1%)		33,084 (5.0%)	666 (1.2%)		32,285 (5.0%)	1434 (2.3%)		35,355 (4.9%)	668 (2.1%)	

Second injury	39,649 (4.5%)	32,197 (4.6%)	1392 (3.4%)	31,061 (4.7%)	2002 (3.6%)	31,025 (4.8%)	3079 (4.9%)	35,323 (4.9%)	1636 (5.1%)
Insurance			<0.001		<0.001		<0.001		<0.001
Medicare	635,631 (72.2%)	493,085 (70.8%)	30,690 (75.6%)	465,044 (70.8%)	40,044 (71.2%)	463,299 (71.2%)	46,327 (74.5%)	509,632 (71.3%)	25,126 (77.8%)
Medicaid	105,703 (12.0%)	88,340 (12.7%)	3265 (8.0%)	84,015 (12.8%)	5878 (10.4%)	80,988 (12.4%)	6557 (10.5%)	81,418 (11.4%)	2545 (7.9%)
Private insurance	97,814 (11.1%)	78,481 (11.3%)	4725 (11.6%)	73,182 (11.1%)	7473 (13.3%)	72,869 (11.2%)	6388 (10.3%)	85,581 (12.0%)	3112 (9.6%)
Self-pay	17,825 (2.0%)	14,338 (2.1%)	410 (1.0%)	12,839 (2.0%)	751 (1.3%)	11,411 (1.8%)	813 (1.3%)	11,129 (1.6%)	328 (1.0%)
No charge	1622 (0.2%)	1326 (0.2%)	50 (0.1%)	1028 (0.2%)	89 (0.2%)	796 (0.1%)	79 (0.1%)	826 (0.1%)	27 (0.1%)
Other	21,538 (2.4%)	20,484 (2.9%)	1478 (3.6%)	20,853 (3.2%)	2040 (3.6%)	21,781 (3.3%)	2009 (3.2%)	25,859 (3.6%)	1167 (3.6%)
Hospital-level									
Hospital Bed Size			<0.001		<0.001		<0.001		<0.001
Small	211,960 (24.1%)	169,506 (24.3%)	10,485 (25.8%)	162,303 (24.7%)	14,904 (26.4%)	163,748 (25.1%)	16,726 (26.9%)	183,258 (25.6%)	9025 (27.9%)
Medium	264,545 (30.0%)	203,980 (29.3%)	12,086 (29.7%)	189,859 (28.9%)	17,029 (30.2%)	193,418 (29.7%)	18,876 (30.3%)	209,506 (29.3%)	9580 (29.6%)
Large	404,503 (45.9%)	323,460 (46.4%)	18,119 (44.5%)	305,771 (46.5%)	24,449 (43.4%)	294,809 (45.2%)	26,653 (42.8%)	323,307 (45.2%)	13,765 (42.5%)
Hospital Teaching Status			<0.001		<0.001		<0.001		<0.001
Rural	113,064 (12.8%)	88,548 (12.7%)	5552 (13.6%)	79,802 (12.1%)	8838 (15.7%)	82,172 (12.6%)	8956 (14.4%)	86,189 (12.0%)	4342 (13.4%)
Urban non-teaching	182,884 (20.8%)	139,551 (20.0%)	8106 (19.9%)	126,641 (19.2%)	11,997 (21.3%)	118,161 (18.1%)	11,835 (19.0%)	121,296 (16.9%)	5783 (17.9%)
Urban teaching	585,060 (66.4%)	468,847 (67.3%)	27,032 (66.4%)	451,490 (68.6%)	35,547 (63.0%)	451,642 (69.3%)	41,464 (66.6%)	508,586 (71.0%)	22,245 (68.7%)
Control/ ownership of hospital			0.007		0.300		<0.001		<0.001
Government	92,134 (10.5%)	74,265 (10.7%)	4488 (11.0%)	68,216 (10.4%)	5901 (10.5%)	67,173 (10.3%)	6414 (10.3%)	74,544 (10.4%)	3347 (10.3%)

Private nonprofit	652,410 (74.1%)	510,882 (73.3%)	29,544 (72.6%)		491,922 (74.8%)	41,991 (74.5%)		487,737 (74.8%)	47,442 (76.2%)		540,224 (75.4%)	25,083 (77.5%)	
Private investor-owned	136,464 (15.5%)	111,799 (16.0%)	6658 (16.4%)		97,795 (14.9%)	8490 (15.1%)		97,065 (14.9%)	8399 (13.5%)		101,303 (14.1%)	3940 (12.2%)	
Comorbidity													
Malnutrition	78,005 (8.9%)	63,509 (9.1%)	3824 (9.4%)	0.052	61,634 (9.4%)	5028 (8.9%)	<0.001	63,060 (9.7%)	6519 (10.5%)	<0.001	74,994 (10.5%)	3584 (11.1%)	<0.001
Obstructive sleep apnea	133,034 (15.1%)	103,356 (14.8%)	5973 (14.7%)	0.400	101,387 (15.4%)	8378 (14.9%)	<0.001	99,093 (15.2%)	8377 (13.5%)	<0.001	111,882 (15.6%)	4815 (14.9%)	<0.001
AIDS/HIV	6258 (0.7%)	5164 (0.7%)	256 (0.6%)	0.010	5089 (0.8%)	303 (0.5%)	<0.001	5015 (0.8%)	486 (0.8%)	0.800	5920 (0.8%)	237 (0.7%)	0.065
Alcohol abuse	56,116 (6.4%)	50,147 (7.2%)	1132 (2.8%)	<0.001	46,946 (7.1%)	2008 (3.6%)	<0.001	43,376 (6.7%)	2838 (4.6%)	<0.001	47,319 (6.6%)	1370 (4.2%)	<0.001
Autoimmune conditions	N/A	32,421 (4.7%)	1821 (4.5%)	0.100	30,913 (4.7%)	2847 (5.0%)	<0.001	30,463 (4.7%)	3144 (5.1%)	<0.001	35,473 (5.0%)	1766 (5.5%)	<0.001
Lymphoma	8097 (0.9%)	6275 (0.9%)	336 (0.8%)	0.120	5883 (0.9%)	565 (1.0%)	0.009	5878 (0.9%)	806 (1.3%)	<0.001	6427 (0.9%)	456 (1.4%)	<0.001
Leukemia	6383 (0.7%)	5155 (0.7%)	290 (0.7%)	0.500	4923 (0.7%)	483 (0.9%)	0.004	4703 (0.7%)	659 (1.1%)	<0.001	5087 (0.7%)	317 (1.0%)	<0.001
Metastatic cancer	31,200 (3.5%)	26,628 (3.8%)	603 (1.5%)	<0.001	25,003 (3.8%)	960 (1.7%)	<0.001	24,304 (3.7%)	1623 (2.6%)	<0.001	27,174 (3.8%)	896 (2.8%)	<0.001
Non-metastatic solid cancer	38,725 (4.4%)	31,394 (4.5%)	1193 (2.9%)	<0.001	30,342 (4.6%)	1797 (3.2%)	<0.001	29,837 (4.6%)	2490 (4.0%)	<0.001	34,306 (4.8%)	1478 (4.6%)	0.064
Dementia	73,573 (8.4%)	58,742 (8.4%)	6876 (16.9%)	<0.001	54,926 (8.3%)	5607 (9.9%)	<0.001	53,142 (8.2%)	7081 (11.4%)	<0.001	58,357 (8.1%)	3993 (12.3%)	<0.001
Depression	157,932 (17.9%)	127,044 (18.2%)	6798 (16.7%)	<0.001	120,703 (18.3%)	9001 (16.0%)	<0.001	116,616 (17.9%)	10,062 (16.2%)	<0.001	133,029 (18.6%)	5691 (17.6%)	<0.001
Diabetes, uncomplicated	105,731 (12.0%)	80,678 (11.6%)	5306 (13.0%)	<0.001	74,164 (11.3%)	6769 (12.0%)	<0.001	73,250 (11.2%)	6755 (10.9%)	0.004	76,962 (10.7%)	3321 (10.3%)	0.005
Diabetes, with complications	228,337 (25.9%)	191,391 (27.5%)	13,144 (32.3%)	<0.001	184,029 (28.0%)	17,149 (30.4%)	<0.001	183,495 (28.1%)	17,890 (28.7%)	0.002	207,495 (29.0%)	9625 (29.7%)	0.003
Drug abuse	48,241 (5.5%)	42,287 (6.1%)	1022 (2.5%)	<0.001	41,079 (6.2%)	2216 (3.9%)	<0.001	39,648 (6.1%)	2897 (4.7%)	<0.001	44,684 (6.2%)	1394 (4.3%)	<0.001

Hypertension, complicated	336,111 (38.2%)	273,945 (39.3%)	19,003 (46.7%)	<0.001	261,643 (39.8%)	24,064 (42.7%)	<0.001	264,291 (40.5%)	28,758 (46.2%)	<0.001	298,694 (41.7%)	15,824 (48.9%)	<0.001
Hypertension, uncomplicated	290,388 (33.0%)	226,219 (32.5%)	13,733 (33.8%)	<0.001	211,591 (32.2%)	19,339 (34.3%)	<0.001	209,541 (32.1%)	19,383 (31.1%)	<0.001	228,267 (31.9%)	9733 (30.1%)	<0.001
Chronic lung disease	817,561 (92.8%)	656,245 (94.2%)	40,588 (99.7%)	<0.001	620,746 (94.3%)	56,177 (99.6%)	<0.001	615,900 (94.5%)	61,737 (99.2%)	<0.001	680,843 (95.1%)	32,072 (99.1%)	<0.001
Obesity	195,713 (22.2%)	164,673 (23.6%)	10,868 (26.7%)	<0.001	162,532 (24.7%)	16,179 (28.7%)	<0.001	161,896 (24.8%)	14,698 (23.6%)	<0.001	181,818 (25.4%)	7456 (23.0%)	<0.001
Peripheral vascular disease	100,147 (11.4%)	79,654 (11.4%)	3136 (7.7%)	<0.001	78,151 (11.9%)	4532 (8.0%)	<0.001	76,834 (11.8%)	6166 (9.9%)	<0.001	86,434 (12.1%)	3285 (10.1%)	<0.001
Hypothyroidism	151,639 (17.2%)	121,399 (17.4%)	7394 (18.2%)	<0.001	115,061 (17.5%)	9633 (17.1%)	0.016	116,415 (17.9%)	11,018 (17.7%)	0.300	132,719 (18.5%)	6436 (19.9%)	<0.001
Other thyroid disorders	11,414 (1.3%)	9444 (1.4%)	404 (1.0%)	<0.001	9640 (1.5%)	757 (1.3%)	0.020	10,280 (1.6%)	929 (1.5%)	0.110	12,054 (1.7%)	562 (1.7%)	0.500
Chronic kidney disease	246,587 (28.0%)	201,937 (29.0%)	12,740 (31.3%)	<0.001	192,443 (29.2%)	15,777 (28.0%)	<0.001	190,782 (29.3%)	18,927 (30.4%)	<0.001	215,163 (30.0%)	10,296 (31.8%)	<0.001
Chronic heart failure	125,306 (14.2%)	106,881 (15.3%)	6680 (16.4%)	<0.001	104,526 (15.9%)	8815 (15.6%)	0.120	108,479 (16.6%)	10,953 (17.6%)	<0.001	129,244 (18.0%)	6317 (19.5%)	<0.001

p values compare hospitalizations with and without COVID-19 within each calendar year and were calculated using Wilcoxon rank-sum tests for continuous variables and Pearson chi-square tests for categorical variables. Autoimmune conditions were not available in the 2019 NIS and are reported as N/A. Abbreviations: IQR = interquartile range; SD = standard deviation.

Patients with COPD were centered at approximately 70 years old, and those with COVID-19 were older than those without COVID-19 in these years (2020: 72.6 *vs.* 69.3; 2021: 70.5 *vs.* 69.5; 2022: 71.8 *vs.* 69.9; 2023: 73.4 *vs.* 70.2; $p < 0.001$). Compared with patients without COVID-19, those with COPD and COVID-19 were less likely to be female in 2020–2022 ($p \leq 0.001$), whereas the sex distribution was similar between groups in 2023. Elective admission was much less common in the COVID-19 group across all years (2020: 11.3% *vs.* 3.8%; 2021: 10.9% *vs.* 3.2%; 2022: 10.6% *vs.* 3.3%; 2023: 10.4% *vs.* 3.3%; $p < 0.001$). Compared with patients without COVID-19, those with COVID-19 were more likely to have no reported injury diagnosis and generally had a higher proportion of Medicare coverage and a lower proportion of Medicaid coverage. Among patients without COVID-19, these characteristics are similar to those observed in the 2019 cohort.

Hospital-level characteristics also differed between the two groups. Patients with COVID-19 were slightly more likely to be admitted to small hospitals (24.3% *vs.* 25.8% in 2020, 24.7% *vs.* 26.4% in 2021, 25.1% *vs.* 26.9% in 2022, and 25.6% *vs.* 27.9% in 2023; $p < 0.001$). They were also more likely to be treated in rural hospitals (2021: 12.1% *vs.* 15.7%; 2022: 12.6% *vs.* 14.4%; 2023: 12.0% *vs.* 13.4%; $p < 0.001$).

In general, among patients with COPD, those with COVID-19 had a heavier comorbidity burden than those without COVID-19. Higher prevalence ($p < 0.001$) of dementia, diabetes with complications, complicated hypertension, and obesity was observed in the COVID-19 group across all years. These findings indicate that the COVID-19 and non-COVID-19 groups were not directly comparable at baseline and further support adjustment for comorbidities in the multivariable models.

3.2. In-Hospital Mortality and Complications

Patients with COPD and a concurrent diagnosis of COVID-19 had higher in-hospital mortality than those without COVID-19 from 2020 to 2023 (Table 2). The mortality rate among patients without COVID-19 was relatively stable over time, ranging from 3.8% to 4.1%, whereas mortality in the COVID-19 group was substantially higher in 2020 and 2021 (19.6% and 16.6%, respectively), and subsequently declined to 9.2% in 2022 and 6.0% in 2023. As shown in Table S2 and Figure 2A, COVID-19 was associated with a substantially increased mortality risk in patients with COPD early in the pandemic, with the magnitude of the association declining over time. The aORs were 5.954 (95% CI, 5.783–6.130) in 2020 and 4.908 (95% CI, 4.778–5.041) in 2021, decreasing to 2.262 (95% CI, 2.193–2.333) in 2022 and 1.484 (95% CI, 1.413–1.558) in 2023. By contrast, metastatic cancer remained consistently strongly associated with in-hospital mortality across the years, with aORs ranging between 2.594 and 3.134 during 2019–2023. Malnutrition and non-metastatic solid cancer also showed stable associations with increased in-hospital mortality.

For AKI, chronic kidney disease was the most consistently associated factor, with aORs ranging from 2.991 to 3.372 during 2019–2023. The association between COVID-19 and AKI was strongest in 2020 and declined progressively through 2023, whereas malnutrition and obesity showed relatively stable associations over time (Figure 2B; Table S3).

Table 2. Clinical and Hospital Utilization Outcomes Among Hospitalized Patients with COPD From 2019 to 2023, Stratified by COVID-19 Status.

Outcomes	2019	2020				2021				2022				2023			
	Overall	Overall	Without COVID-19	With COVID-19	*p* Value	Overall	Without COVID-19	With COVID-19	*p* Value	Overall	Without COVID-19	With COVID-19	*p* Value	Overall	Without COVID-19	With COVID-19	*p* Value
	N = 881,008	*N* = 737,636	*N* = 696,946	*N* = 40,690		*N* = 714,315	*N* = 657,933	*N* = 56,382		*N* = 714,230	*N* = 651,975	*N* = 62,255		*N* = 748,441	*N* = 716,071	*N* = 32,370	
In-Hospital Mortality					<0.001				<0.001				<0.001				<0.001
Alive	850,918 (96.6%)	702,742 (95.3%)	670,033 (96.2%)	32,709 (80.4%)		678,260 (95.0%)	631,271 (96.0%)	46,989 (83.4%)		681,814 (95.5%)	625,307 (95.9%)	56,507 (90.8%)		719,225 (96.1%)	688,812 (96.2%)	30,412 (94.0%)	
Died	29,858 (3.4%)	34,634 (4.7%)	26,685 (3.8%)	7949 (19.6%)		35,877 (5.0%)	26,498 (4.0%)	9379 (16.6%)		32,227 (4.5%)	26,490 (4.1%)	5737 (9.2%)		29,016 (3.9%)	27,068 (3.8%)	1948 (6.0%)	
AKI					<0.001				<0.001				<0.001				<0.001
No AKI	680,763 (77.3%)	551,057 (74.7%)	524,888 (75.3%)	26,169 (64.3%)		528,401 (74.0%)	491,043 (74.6%)	37,358 (66.3%)		529,344 (74.1%)	486,336 (74.6%)	43,008 (69.1%)		554,544 (74.1%)	531,625 (74.2%)	22,919 (70.8%)	
AKI	200,245 (22.7%)	186,579 (25.3%)	172,058 (24.7%)	14,521 (35.7%)		185,914 (26.0%)	166,890 (25.4%)	19,024 (33.7%)		184,886 (25.9%)	165,639 (25.4%)	19,247 (30.9%)		193,897 (25.9%)	184,446 (25.8%)	9451 (29.2%)	
Total Charges ($)					<0.001				<0.001				<0.001				<0.001
Mean (SD)	77,625 (114,015)	84,575 (126,963)	82,999 (123,412)	111,588 (174,888)		85,985 (128,268)	83,695 (123,077)	112,668 (175,740)		83,008 (125,688)	81,938 (123,032)	94,200 (150,242)		87,944 (127,042)	87,566 (126,235)	96,306 (143,491)	
Median (IQR)	46,278 (25,594, 87,675)	49,646 (27,358, 94,892)	49,093 (27,110, 93,649)	60,570 (32,515, 120,304)		50,739 (27,927, 96,815)	49,870 (27,515, 94,874)	62,440 (34,120, 122,681)		49,133 (27,211, 93,487)	48,698 (26,941, 92,621)	54,095 (30,283, 102,522)		52,643 (29,577, 99,024)	52,384 (29,405, 98,792)	58,025 (33,703, 104,148)	
LOS by disposition, mean (SD), days																	
Routine Discharge	4.6 (4.7)	4.8 (5.0)	4.7 (4.9)	6.6 (6.2)	<0.001	4.9 (5.3)	4.8 (5.2)	6.4 (6.6)	<0.001	5.0 (5.4)	4.9 (5.3)	5.9 (7.3)	<0.001	4.8 (5.3)	4.8 (5.1)	5.5 (7.4)	<0.001
Died	7.4 (10.5)	8.0 (10.5)	7.3 (10.8)	10.6 (9.3)	<0.001	8.7 (10.8)	7.5 (10.5)	12.0 (10.9)	<0.001	8.4 (11.1)	7.8 (10.9)	10.9 (11.6)	<0.001	7.9 (11.1)	7.7 (10.8)	10.9 (13.6)	<0.001

Transfer to acute hospital	5.2 (9.2)	5.5 (10.9)	5.3 (10.5)	7.3 (15.0)	<0.001	5.7 (10.3)	5.4 (9.3)	9.0 (17.4)	<0.001	5.9 (11.3)	5.7 (10.4)	8.8 (19.1)	<0.001	5.4 (8.2)	5.3 (8.0)	7.9 (11.2)	<0.001
Transfer to another facility	8.1 (8.3)	8.7 (9.0)	8.4 (8.8)	11.3 (10.8)	<0.001	9.1 (9.8)	8.7 (9.3)	13.3 (13.2)	<0.001	9.3 (10.3)	9.0 (9.7)	12.4 (14.3)	<0.001	9.0 (10.0)	8.8 (9.6)	11.1 (14.9)	<0.001

Total charges were inflation-adjusted to 2023 U.S. dollars using the Consumer Price Index. *p* values compare hospitalizations with and without COVID-19 within each calendar year and were calculated using Pearson chi-square tests for categorical outcomes and Wilcoxon rank-sum tests for continuous outcomes. Abbreviations: AKI = acute kidney injury; IQR = interquartile range; LOS = length of stay; SD = standard deviation.

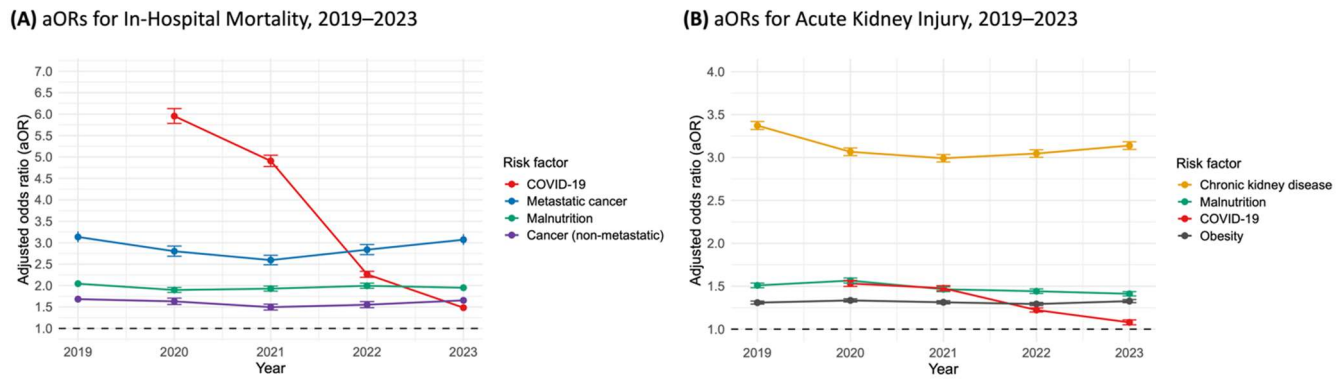


Figure 2. Temporal Trends in Adjusted Effect Estimates and 95% CIs for Top Risk Factors of Two Clinical Outcomes Among Hospitalized Patients With COPD, 2019–2023. (**A**) aORs for in-hospital mortality; (**B**) aORs for acute kidney injury. aOR, adjusted odds ratio; CI, confidence interval.

3.3. Hospital Utilization Outcomes

For total hospital charges, COVID-19 infection was associated with higher total hospital charges, with adjusted increases of 17.8% (2020), 27.7% (2021), 15.4% (2022), and 14.9% (2023) compared to patients without COVID-19 (Figure 3A; Table S4). Malnutrition showed the largest adjusted association with total hospital charges each year, with total charges increasing by approximately 40%.

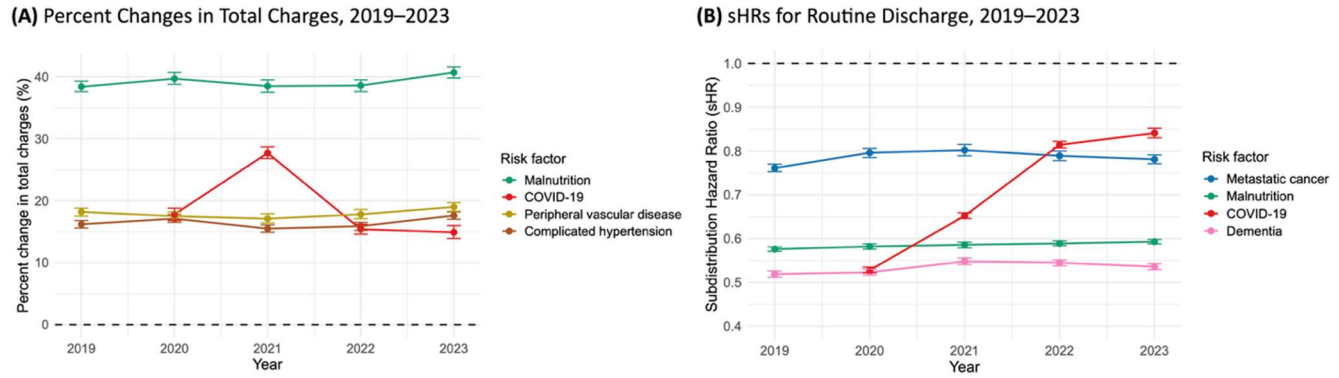


Figure 3. Temporal Trends in Adjusted Effect Estimates and 95% CIs for Top Risk Factors of Two Hospital Utilization Outcomes Among Hospitalized Patients With COPD, 2019–2023. (**A**) Percent changes in total hospital charges; (**B**) sHRs for routine discharge. sHR, subdistribution hazard ratio; CI, confidence interval.

For time-to-routine discharge, Figure 4 shows the cumulative incidence functions (CIFs) of discharge dispositions by COVID-19 status across study years. Compared with the non-COVID-19 group, patients with COVID-19 consistently showed a lower cumulative incidence of routine discharge and a higher cumulative incidence of in-hospital death. Although discharge outcomes in patients with COVID-19 improved over time, they remained worse than those observed in patients without COVID-19.

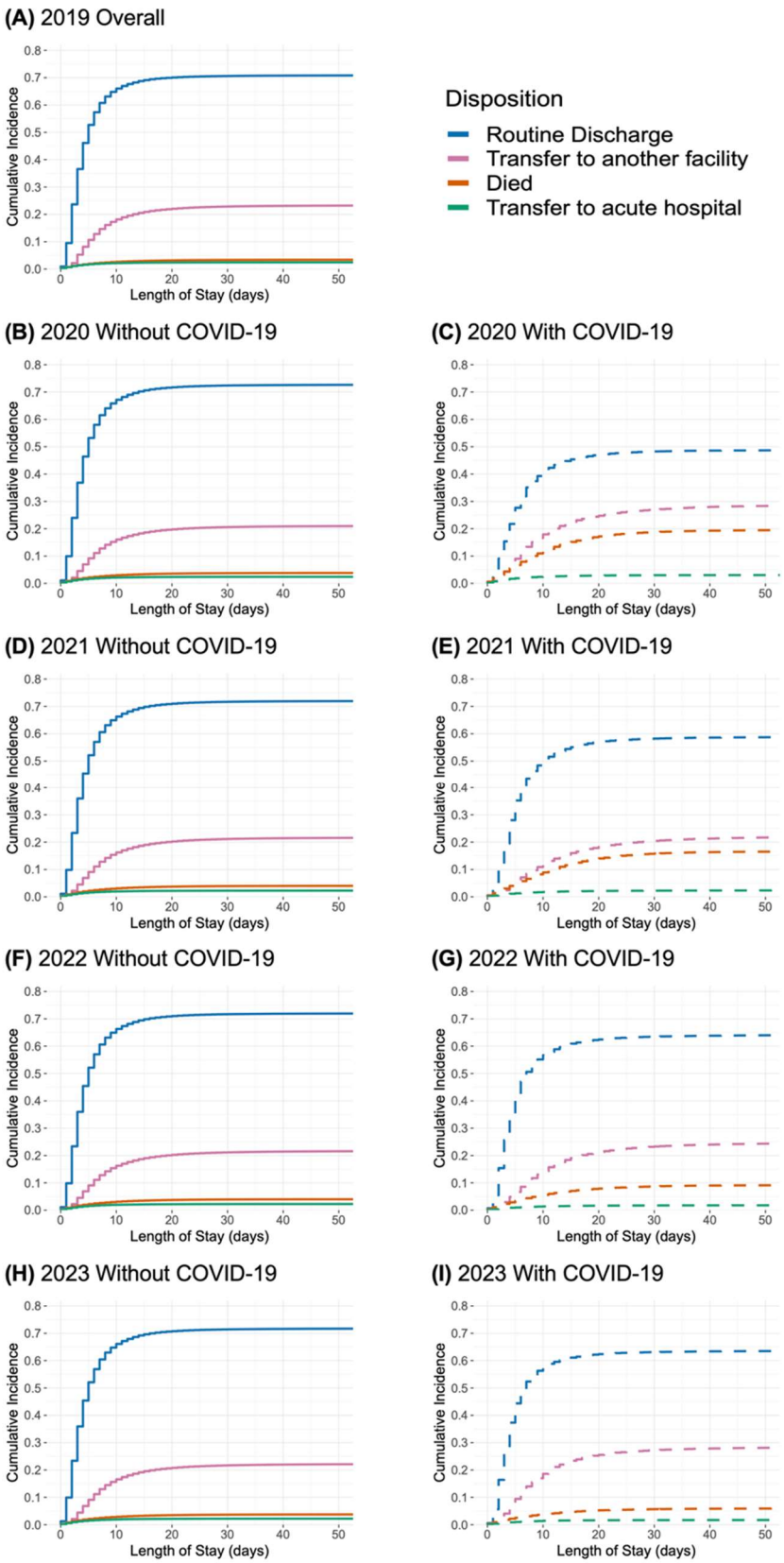


Figure 4. Cumulative Incidence Functions by Discharge Disposition Among Patients with COPD From 2019 to 2023, Stratified by COVID-19 Status. (**A**) 2019 overall; (**B**) 2020 without COVID-19; (**C**) 2020 with COVID-19; (**D**) 2021 without COVID-19; (**E**) 2021 with COVID-19; (**F**) 2022 without COVID-19; (**G**) 2022 with COVID-19; (**H**) 2023 without COVID-19; (**I**) 2023 with COVID-19.

LOS differed between patients with and without COVID-19 across all disposition categories, with patients with COVID-19 generally having longer mean LOS (Table 2).

Fine–Gray subdistribution hazards models were applied to analyze time-to-routine discharge for each year. The sHRs for COVID-19 were 0.528 (95% CI, 0.522–0.535) in 2020 and increased progressively in 2021 (sHR, 0.652; 95% CI, 0.646–0.659), 2022 (sHR, 0.814; 95% CI, 0.807–0.822), and 2023 (sHR, 0.841; 95% CI, 0.830–0.852), indicating attenuation of the association over time (Figure 3B; Table S5).

Among other comorbidities, dementia consistently showed the smallest sHR across all years, ranging from 0.52 to 0.55, indicating a lower cumulative incidence of routine discharge among patients with dementia. Malnutrition and metastatic cancer were also associated with a lower cumulative incidence of routine discharge (sHR ranging from 0.576 to 0.593 for malnutrition and sHR ranging from 0.761 to 0.802 for metastatic cancer during 2019–2023).

3.4. Secondary Analysis in Hospitalizations with COPD as the Primary Diagnosis

We conducted a secondary analysis restricted to hospitalizations in which COPD was listed as the primary diagnosis. The restricted cohort included 96,454 hospitalizations in 2019 and 58,149 in 2020. The number remained at approximately 50,000 to 51,000 per year from 2021 to 2023 (Table S6). The lower number of COPD hospitalizations during the pandemic may be partly attributable to COVID-19 being coded as the primary diagnosis, with COPD recorded as a secondary diagnosis. Mortality among patients with COVID-19 was highest in 2020 and 2021, at 8.2% and 6.8%, respectively, and declined to 3.1% in 2022 and 2.3% in 2023, whereas mortality among patients without COVID-19 remained relatively stable at approximately 1.1% to 1.2%. In multivariable logistic regression models, COVID-19 was associated with increased odds of in-hospital mortality, with the strongest association in 2020 (aOR, 8.017; 95% CI, 4.330–14.844), followed by 2021 (aOR, 5.372; 95% CI, 3.369–8.566), 2022 (aOR, 2.313; 95% CI, 1.490–3.591), and 2023 (aOR, 2.126; 95% CI, 1.120–4.034). Metastatic cancer, malnutrition, and non-metastatic solid cancer also remained consistently associated with higher in-hospital mortality across the years. Overall, these findings were consistent with the full COPD cohort analysis, although the absolute mortality rates and adjusted odds ratios differed for the primary-diagnosis cohorts. Detailed results are provided in Table S7. The lower mortality observed in the primary-diagnosis cohort is expected because these hospitalizations were primarily driven by COPD-related illness, whereas the full COPD cohort also included patients hospitalized for other serious conditions with COPD recorded as a secondary diagnosis. Consequently, the broader cohort likely had a higher burden of illness, resulting in greater overall mortality.

4. Discussion

This study examined major factors associated with clinical and hospital utilization outcomes and temporal patterns among hospitalized patients with COPD from 2019 to 2023 using the NIS database. Several important findings emerged. First, the association of COVID-19 with clinical and hospital utilization outcomes varied across years and outcomes. Across all the outcomes examined, the magnitude of association for COVID-19 was strongest in 2020 and 2021 and then declined in 2022 and 2023. Second, some chronic comorbidities, such as malnutrition, remained relatively stable over time and continued to show important associations with poor hospital outcomes. Overall, these findings suggest that both pandemic-related factors and persistent chronic conditions were associated with worse clinical and hospital utilization outcomes among hospitalized patients with COPD, but their relative importance differed by outcome and changed over time.

The strong association of COVID-19 with adverse outcomes in the early pandemic years was one of the most important findings in this study. In both descriptive analyses and multivariable models, patients with COPD who had COVID-19 experienced worse clinical and hospital utilization outcomes than those

without COVID-19, particularly in 2020 and 2021. This pattern is clinically plausible because patients with COPD have limited respiratory reserve and are more vulnerable to severe outcomes from acute respiratory infections, including COVID-19 [15]. In later years, the association of COVID-19 attenuated. A possible explanation is that vaccination, improved treatment strategies, changes in circulating variants, and increased clinical experience reduced the severity and hospital burden of COVID-19 over time [16]. Although the association of COVID-19 decreased over time, it remained an important factor, suggesting that COVID-19 remained associated with worse hospital outcomes even after the early pandemic period.

Another important finding was the stable role of chronic comorbidities across the years. Malnutrition was one of the most notable examples. It appeared as an important factor in multiple outcomes and was especially strong in the models for routine discharge and total charges. This finding is clinically plausible because malnutrition in COPD can contribute to skeletal muscle depletion, respiratory muscle weakness, reduced ventilatory capacity, impaired cough and airway clearance, and lower physiologic reserve [17]. These mechanisms may make recovery from acute respiratory illness more difficult and increase the need for supportive care during hospitalization. Similarly, metastatic cancer remained strongly and consistently associated with mortality, likely reflecting advanced systemic disease, greater tumor burden, impaired organ function, and reduced ability to tolerate acute illness [18]. Chronic kidney disease (CKD) remained the dominant factor associated with AKI, which is clinically plausible because patients with CKD have impaired baseline kidney function and reduced renal reserve, making them more vulnerable to acute kidney insults [19]. These patterns suggest that chronic underlying disease burden continued to play a major role in hospitalized patients with COPD, even when the acute association of COVID-19 became smaller.

The results for time-to-routine discharge provide additional insight into the hospital burden. In the competing risks framework, dementia, malnutrition, and metastatic cancer were all associated with lower sHR for routine discharge, indicating a lower cumulative incidence of routine discharge over time. COVID-19 was also associated with a lower cumulative incidence of routine discharge in the early pandemic years, but this association weakened in later years. These findings suggest that both acute infectious burden and chronic patient complexity can delay routine discharge, although their temporal patterns may differ. Because routine discharge was analyzed in the presence of competing events, the Fine–Gray model provided a more appropriate way to characterize discharge patterns than a standard survival model that ignores competing outcomes.

Several limitations should also be considered. First, this retrospective observational study used an administrative database, so the findings should be interpreted as associations rather than causal effects. Second, the NIS does not contain POA indicators for all relevant diagnoses in this analysis, so some conditions identified during hospitalization, such as AKI, could not always be clearly distinguished as pre-existing comorbidities versus in-hospital complications. Third, changes in data availability in the NIS across years may affect comparability. Some hospital-level and demographic variables were limited or modified in 2023, and incomplete reporting of total charges from certain states in 2023 may have influenced the charge analyses. Fourth, comorbidities were identified using year-specific HCUP Elixhauser definitions, and the included conditions were not completely identical across all years. Fifth, potential correlations among hospitalizations within the same hospital and repeated admissions of the same patient were also not accounted for (due to limitations of the NIS data), which may have overstated the precision of the estimates. Finally, discharge-level weights were not applied in the regression analyses, so the model results should be interpreted as associations within the analytic sample rather than nationally representative estimates.

Future studies could extend this work by using patient-level longitudinal datasets that allow repeated admissions to be linked over time and provide more detailed clinical information, such as POA indicators, laboratory values, or severity measures. Future research could also examine post-discharge outcomes, such as readmission or longer-term mortality, to provide a more complete picture of the hospitalization burden among patients with COPD over time.

5. Conclusions

Among hospitalized patients with COPD, associations between major risk factors and clinical and hospital utilization outcomes varied over time. The associations of COVID-19 with adverse outcomes were strongest early in the pandemic, whereas chronic comorbidities remained consistently associated with adverse outcomes. These findings highlight the importance of considering both temporal context and underlying comorbidity burden when evaluating hospitalized patients with COPD.

Supplementary Materials

The following supporting information can be found at: https://www.sciepublish.com/article/pii/1307, Table S1: Diagnosis and ICD-10-CM Codes; Table S2: Multivariable Logistic Regression Model Results for In-Hospital Mortality, 2019–2023; Table S3: Multivariable Logistic Regression Model Results for Acute Kidney Injury, 2019–2023; Table S4: Multivariable Log-Transformation Linear Regression Model Results for Total Charges, 2019–2023; Table S5: Multivariable Fine–Gray Subdistribution Model Results for Time-to-Routine Discharge, 2019–2023; Table S6: In-Hospital Mortality by Year and COVID-19 Status Among Patients With COPD as the Primary Diagnosis, 2019–2023; Table S7: Multivariable Logistic Regression Model for In-Hospital Mortality Among Patients With COPD as the Primary Diagnosis, 2019–2023.

Statement of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used ChatGPT (GPT-5.6 Sol, OpenAI) to assist with language editing, wording refinement, and manuscript formatting. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the published article.

Acknowledgments

The authors thank the Healthcare Cost and Utilization Project (HCUP) and the Agency for Healthcare Research and Quality for providing the National Inpatient Sample (NIS) database used in this study.

Author Contributions

Conceptualization, Y.D. and X.L.; Methodology, X.L., J.L., S.P. and V.B.T.; Formal Analysis, X.L.; Data Curation, X.L.; Writing—Original Draft Preparation, X.L.; Writing—Review & Editing, Y.D., J.L., S.P., V.B.T. and F.J.R.; Supervision, Y.D. All authors have read and agreed to the final version of the manuscript.

Ethics Statement

Not applicable. This study used deidentified discharge-level data from the Healthcare Cost and Utilization Project National Inpatient Sample and did not involve direct interaction with human participants.

Informed Consent Statement

Not applicable. This study used de-identified discharge-level data and involved no direct interaction with study participants.

Data Availability Statement

The de-identified discharge-level data used in this study were obtained from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS). The NIS is available to authorized users under the HCUP Data Use Agreement.

Funding

This research received no external funding.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. World Health Organization. Chronic Obstructive Pulmonary Disease (COPD). Available online: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-%28copd%29 (accessed on 18 May 2026).
2. Diab N, Gershon AS, Sin DD, Tan WC, Bourbeau J, Boulet LP, et al. Underdiagnosis and Overdiagnosis of Chronic Obstructive Pulmonary Disease. *Am. J. Respir. Crit. Care Med.* **2018**, *198*, 1130–1139. DOI:10.1164/rccm.201804-0621CI
3. Global Initiative for Chronic Obstructive Lung Disease. Pocket Guide to COPD Diagnosis, Management, and Prevention: 2024 Report. Available online: https://goldcopd.org/wp-content/uploads/2024/02/POCKET-GUIDE-GOLD-2024-ver-1.2-11Jan2024_WMV.pdf (accessed on 18 May 2026).
4. May SM, Li JTC. Burden of chronic obstructive pulmonary disease: Healthcare costs and beyond. *Allergy Asthma Proc.* **2015**, *36*, 4–10. DOI:10.2500/aap.2015.36.3812
5. Barakat M, McDonald H, Collier T, Smeeth L, Nitsch D, Quint J. Acute kidney injury in stable COPD and at exacerbation. *Int. J. Chronic Obstr. Pulm. Dis.* **2015**, *10*, 2067. DOI:10.2147/COPD.S88759
6. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. *PLoS ONE* **2020**, *15*, e0233147. DOI:10.1371/journal.pone.0233147
7. Deng M, Lu Y, Zhang Q, Bian Y, Zhou X, Hou G. Global prevalence of malnutrition in patients with chronic obstructive pulmonary disease: Systemic review and meta-analysis. *Clin. Nutr.* **2023**, *42*, 848–858. DOI:10.1016/j.clnu.2023.04.005
8. De la Fuente JRO, Greenberg P, Sunderram J. The overlap of chronic obstructive pulmonary disease and obstructive sleep apnea in hospitalizations for acute exacerbation of chronic obstructive pulmonary disease. *J. Clin. Sleep Med.* **2024**, *20*, 863–870. DOI:10.5664/jcsm.11000
9. Brock GN, Barnes C, Ramirez JA, Myers J. How to handle mortality when investigating length of hospital stay and time to clinical stability. *BMC Med. Res. Methodol.* **2011**, *11*, 144. DOI:10.1186/1471-2288-11-144
10. Healthcare Cost and Utilization Project. National Inpatient Sample (NIS). Available online: https://hcup-us.ahrq.gov/nisoverview.jsp (accessed on 18 May 2026).
11. Healthcare Cost and Utilization Project. NIS Description of Data Elements. Available online: https://hcup-us.ahrq.gov/db/nation/nis/nisdde.jsp (accessed on 18 May 2026).
12. Putter H, Fiocco M, Geskus RB. Tutorial in biostatistics: Competing risks and multi-state models. *Stat. Med.* **2007**, *26*, 2389–2430. DOI:10.1002/sim.2712
13. Austin PC, Fine JP. Practical recommendations for reporting Fine-Gray model analyses for competing risk data. *Stat. Med.* **2017**, *36*, 4391–4400. DOI:10.1002/sim.7501
14. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *J. Am. Stat. Assoc.* **1999**, *94*, 496–509. DOI:10.1080/01621459.1999.10474144
15. Singh D, Mathioudakis AG, Higham A. Chronic obstructive pulmonary disease and COVID-19: Interrelationships. *Curr. Opin. Pulm. Med.* **2022**, *28*, 76–83. DOI:10.1097/MCP.0000000000000834
16. Bhimraj A, Falck-Ytter Y, Baden LR, Bedimo R, Cawcutt K, Cheng VCC, et al. 2025 Clinical Practice Guideline Update by the Infectious Diseases Society of America on the Treatment and Management of COVID-19: Pemivibart for Pre-exposure Prophylaxis, Vilobelimab for Critical Illness, and Abatacept or Infliximab for Severe or Critical Illness. *Clin. Infect. Dis.* **2025**, *81*, i1–i5. DOI:10.1093/cid/ciaf424
17. Mete B, Pehlivan E, Gülbaş G, Günen H. Prevalence of malnutrition in COPD and its relationship with the parameters related to disease severity. *Int. J. Chronic Obstr. Pulm. Dis.* **2018**, *13*, 3307–3312. DOI:10.2147/COPD.S179609
18. Alečković M, McAllister SS, Polyak K. Metastasis as a systemic disease: Molecular insights and clinical implications. *Biochim. Biophys. Acta Rev. Cancer* **2019**, *1872*, 89–102. DOI:10.1016/j.bbcan.2019.06.002
19. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute Kidney Injury and Chronic Kidney Disease as Interconnected Syndromes. *N. Engl. J. Med.* **2014**, *371*, 58–66. DOI:10.1056/NEJMra1214243