

Comorbidities, Oxygen Therapy Use and Rehospitalization in US Patients with Severe COVID-19

Jhamb, Sumit¹; Khan, Simi¹; Taneja, Havisha¹; Sachdev, Arunima¹; Mazumder Dibyajyoti¹; Buikema, Ami²

¹ Optum Global Advantage, Health Economics and Outcomes Research, Noida, India

² Health Economics and Outcomes Research, Optum, Eden Prairie, MN, United States of America

BACKGROUND & OBJECTIVES

- COVID-19 is a debilitating condition and is reported to be the 2nd leading cause of death in the U.S. in 2021.[1] In patients with COVID-19 disease, underlying comorbid conditions impose a substantial impact on rehospitalization, morbidity and mortality.[2,3] Currently, there is limited evidence using real-world data to assess factors impacting rehospitalization and death following discharge in hospitalized patients with COVID-19.[3]

Study Objectives:

- Evaluate demographic & clinical characteristics of COVID-19 hospitalized patients with respiratory and non-respiratory co-morbid conditions.
- Identify potential factors causing 60 days rehospitalization in COVID-19 patients after initial hospitalization.
- Identify and compare length of stay (LOS) at initial hospitalization in COVID-19 patients with or without rehospitalization.

METHODS

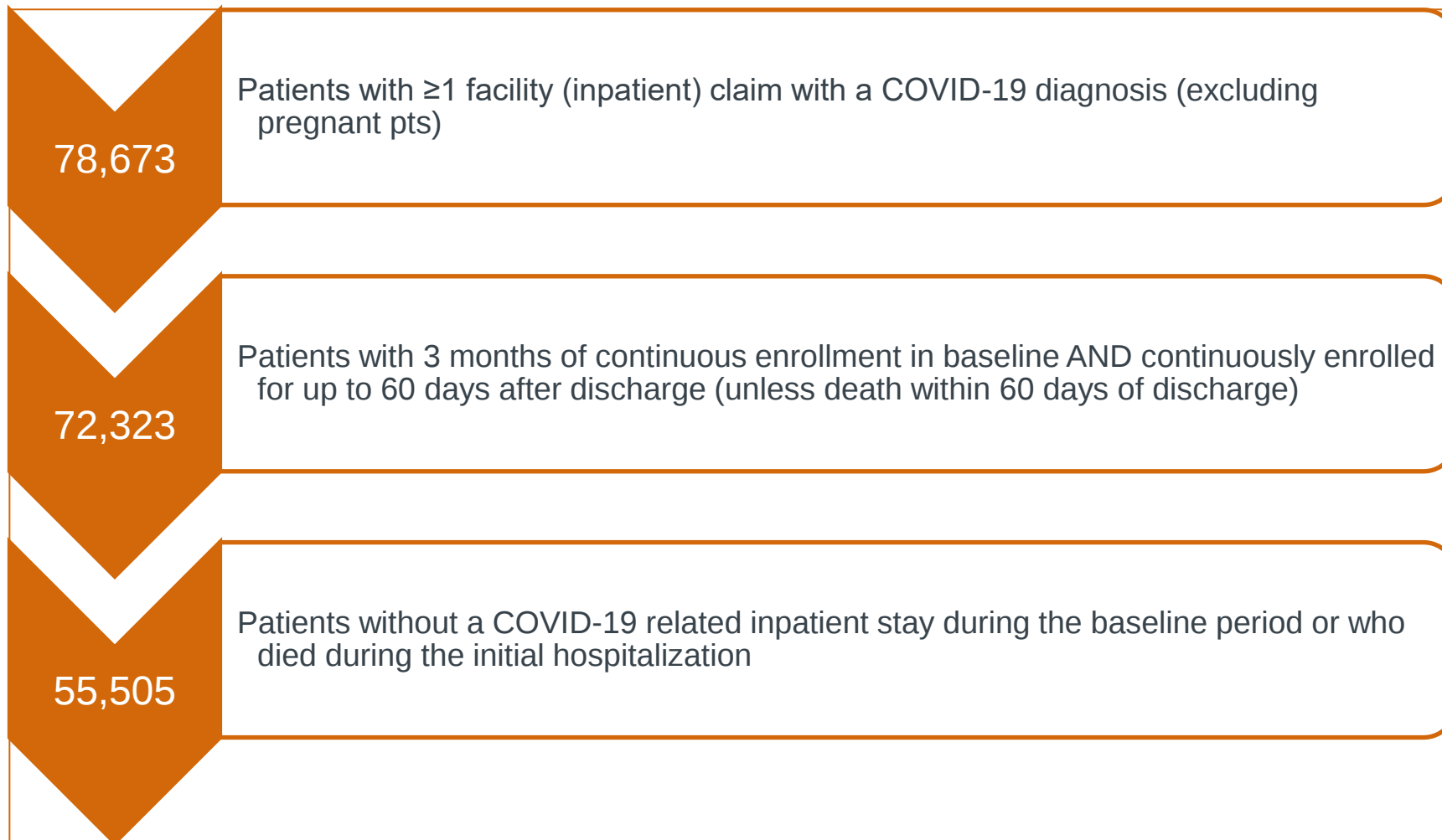
Data Source and Study Design

- This was a retrospective study of hospitalized patients diagnosed with COVID-19 (ICD-10 U07.1) in the United States between April 01, 2020 and December 31, 2020 using Optum's de-identified administrative claims database.
- The first index date (index date 1) was defined as the date of initial COVID-19 related hospitalization; the second index date (index date 2) was defined as the date of discharge from hospital.
- Patients were continuously enrolled for 3 months pre-index date 1 (and including index date 1) to capture baseline comorbidities.
- Patients were observed for up to 60 days post-discharge (post-index date 2) to the earliest of disenrollment from the health plan, end of the study period, or death.
- COVID-19 related rehospitalization was identified based on an inpatient stay with a diagnosis indicating COVID-19
- Month and year of death were available in the database and date of death was assigned as last day during the month of death. Patients who were discharged during the same month and year as their death record were considered to have died during their initial COVID-19 hospitalization and were excluded.

Inclusion/Exclusion Criteria

- Pregnant women were excluded from the study sample.
- Patients with evidence of a COVID-19 related hospital stay during the baseline period were excluded from the analysis.

Figure 1. Patient Attrition



Analysis

- All variables were analyzed descriptively, and results are presented stratified by whether or not the patient was rehospitalized following discharge.
- Means and standard deviations are presented for continuous variables; counts and percentages are presented for categorical variables.
- Kaplan-Meier (KM) analysis was conducted to examine the rehospitalization rates at different time points post-discharge.
- Four multivariable Cox proportional hazard regressions were conducted to identify factors associated with risk of rehospitalization, death, rehospitalization or death, and rehospitalization accounting for death as a competing event (Fine and Gray Model).
- Covariates included in a multivariable models were based on clinical rationale and/or statistical significance. The results are expressed as hazard ratio (HR) and the variables in the final model with a p-value <0.05 were considered statistically significant.
- Statistical analyses were completed in SAS version 9.4.

RESULTS

- A total 78,673 patients hospitalized with COVID-19 were identified; 55,505 (70.6%) were eligible for the final analysis (**Figure 1**).

Table 1. Demographic and Clinical Characteristics by Reprehospitalization Status

	Rehospitalization (N=4,334)	No Reprehospitalization (51,171)	P-value
Age (mean±SD)	72.54 ± 12.07	68.14 ± 14.30	
0-29 years (n, %)	26 (0.60%)	830 (1.6%)	<.0001
30-49 years (n, %)	178 (4.1%)	4,688 (9.1%)	<.0001
50-64 years (n, %)	671 (15.5%)	11,118 (21.7%)	<.0001
65-74 years (n, %)	1,364 (31.5%)	16,098 (31.5%)	0.9860
75-84 years (n, %)	1,417 (32.7%)	12,806 (25.0%)	<.0001
>85 years (n, %)	678 (15.6%)	5,631 (11.0%)	<.0001
Gender (n, %)			
Male	2,302 (53.1%)	25,291 (49.4%)	<.0001
Race/Ethnicity (n, %)			
African American	377 (8.7%)	4,224 (8.2%)	0.3087
Caucasian	857 (19.8%)	9,414 (18.4%)	0.0250
Asian	40 (0.9%)	473 (0.9%)	0.9925
Hispanic	266 (6.1%)	3,218 (6.3%)	0.6935
Unknown/Unidentified	2,794 (64.5%)	33,842 (66.1%)	0.0260
Region (n, %)			
Midwest	1,031 (23.8%)	14,244 (27.8%)	<.0001
Northeast	592 (13.7%)	6,603 (12.9%)	0.1550
South	2,368 (54.64%)	25,872 (50.6%)	<.0001
West	343 (7.9%)	4,452 (8.7%)	0.0770
Smoking History (n, %)			
Obesity/Overweight (n, %)	91 (2.1%)	728 (1.4%)	0.0004
Insurance Type (n, %)			
Commercial	479 (11.0%)	13,229 (25.8%)	<.0001
Medicare	3,855 (88.9%)	37,942 (74.1%)	<.0001
Comorbidities (n, %)			
Hypertension	3,023 (69.7%)	29,015 (56.7%)	<.0001
Heart failure	1,056 (24.4%)	6,801 (13.3%)	<.0001
Other CVDs	2,775 (64.0%)	23,838 (46.6%)	<.0001
Stroke	355 (8.2%)	2,594 (5.07%)	<.0001
Sickle Cell Disease	12 (0.3%)	80 (0.2%)	0.0611
Type 1 Diabetes Mellitus	149 (3.4%)	867 (1.7%)	<.0001
Type 2 Diabetes Mellitus	2,033 (46.9%)	18,722 (36.6%)	<.0001
Asthma	310 (7.1%)	3,397 (6.6%)	0.1929
COPD	998 (23.0%)	7,166 (14.0%)	<.0001
Other Pulmonary Diseases	775 (17.9%)	5,759 (11.2%)	<.0001
Liver Disease	205 (4.7%)	1,253 (2.4%)	<.0001
Kidney Disease	1,646 (37.9%)	12,241 (23.9%)	<.0001
HIV	19 (0.4%)	192 (0.4%)	0.5164
Immunodeficiency	271 (6.2%)	1,681 (3.3%)	<.0001
Cancer	838 (19.3%)	6,903 (13.5%)	<.0001
Dementia	628 (14.5%)	5,303 (10.3%)	<.0001
Transplantation	3 (0.07%)	8 (0.02%)	0.0161
Oxygen therapy use (n, %)	2 (0.05%)	67 (0.13%)	0.1283

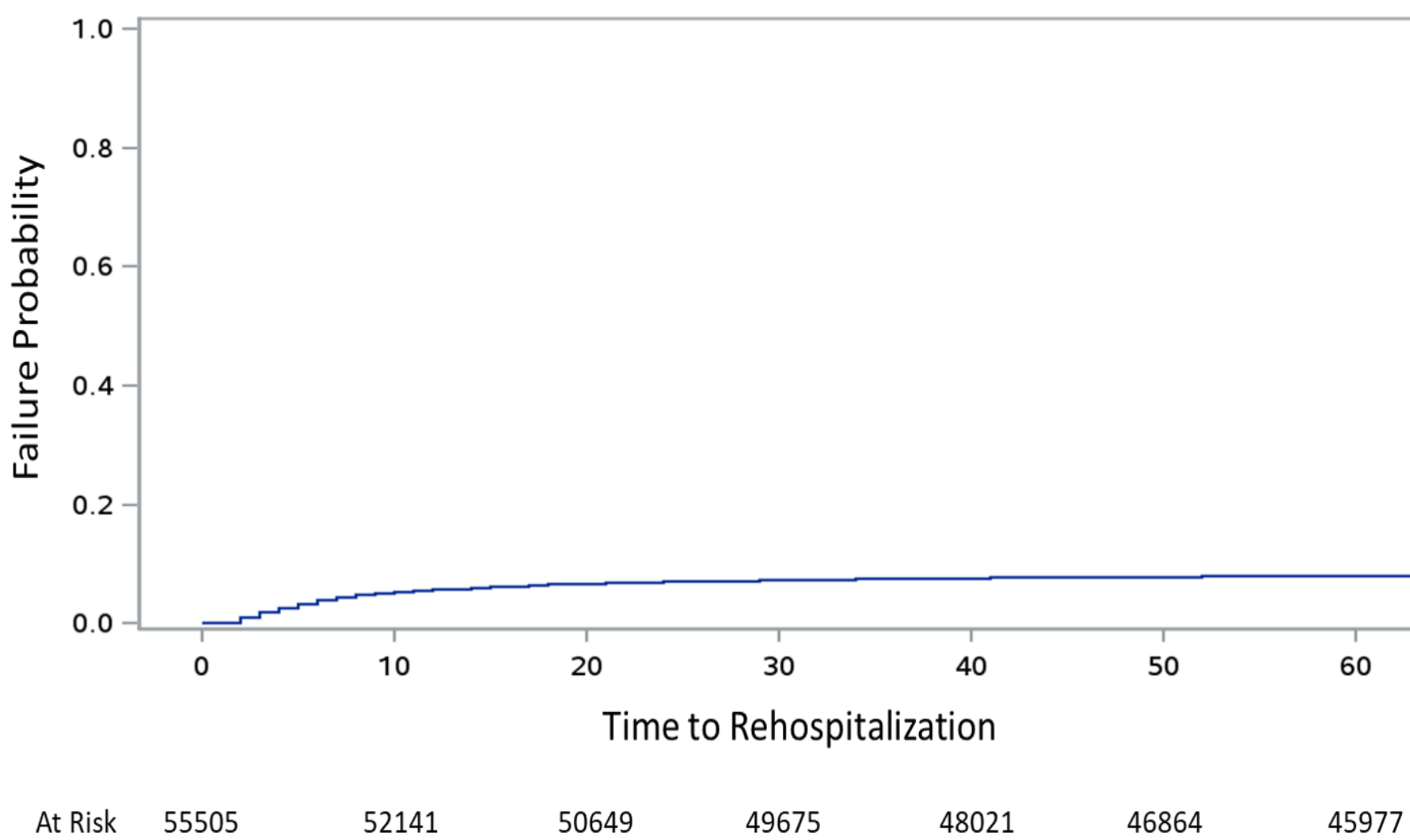
Abbreviations: COPD: chronic obstructive pulmonary disease; CVD: cardiovascular; HIV: human immunodeficiency virus

- 5.51% of patients were rehospitalized (rehosp) after initial COVID-19 hospitalization.
- Patients who were rehospitalized were older (mean age: 72.5 years) compared to non-rehosp patients (mean age: 68.1 years) group (**Table 1**).
- The most frequent comorbidities were hypertension (69.7% vs 56.7%), other cardiovascular disease (64.0% vs 46.6%), type 2 diabetes mellitus (46.9% vs 36.6%), kidney disease (37.9% vs 23.9%), and heart failure (24.4% vs 13.3%) in rehosp and non-rehosp groups, respectively.
- There were 2.1% vs 1.4% of patients with smoking history, and 25.6% vs 22.1% were overweight/obese in rehosp vs non-rehosp group.
- Respiratory-related comorbidities such as COPD, other pulmonary disease, and asthma were 23.0% vs 14.0%, 17.9% vs 11.2%, and 7.1% vs 6.6% in rehosp vs non-rehosp patients.
- Hospital length of stay was <7 days, 7-13 days and 14+ days was 68.8% vs 63.6%, 19.0% vs 21.3%, and 12.2% vs 15.1% in rehosp vs non-rehosp group at initial hospitalization.

Kaplan Meier (KM) Analysis

- COVID-19 related rehospitalization rates at 30 and 60 days were assessed using Kaplan-Meier (KM) analysis. The KM curve shows that ~8% of patients had COVID-19 related rehospitalization (at both 30 and 60 days) after initial hospitalization (**Figure 2**).

Figure 2. Kaplan-Meier Analysis to Assess the Risk of COVID-19 Related Reprehospitalization at 30 and 60 Days After Discharge



Cox Proportional-Hazards Analysis

- Results were similar across models and showed a significantly higher risk of rehospitalization and death in patients with older age (≥65 years) and with underlying comorbid conditions (**Table 2**).
- Longer duration of the initial hospital stay was associated with death but not rehospitalization.
- In model 2, patients with overweight/obesity and asthma had significantly lower risk of death (p<.0001; p=0.0005). However, longer length of stay (LOS) for the initial hospitalization (i.e. ≥7 days) resulted in a significantly higher risk of death (p<.0001).
- The findings were similar in model 4 (competing risk model) and model 1 (**Table 2**).

Table 2. Four Different Models to Assess the Relative Risk of COVID-19 Related Reprehospitalization and Death among Patients with an Initial COVID-19 Hospitalization

Parameters	Category	Model 1 Outcome: Rehosp		Model 2 Outcome: Death		Model 3 Outcome: Rehosp + Death		Model 4 Outcome: Rehosp w/ Death as a Competing Event	
		Hazard Ratio	P-value	Hazard Ratio	P-value	Hazard Ratio	P-value	Hazard Ratio	P-value
Gender (Ref. Male)	Female	0.787	<.0001	0.862	<.0001	0.852	<.0001	0.787	<.0001
Age Category (Ref. 50-64)	0-29	0.832	0.3635	0.391	0.0140	0.703	0.0557	0.832	0.3631
	30-49	0.848	0.0576	0.519	<.0001	0.741	<.0001	0.848	0.0595
	65-74	1.018	0.7353	1.174	0.0024	1.099	0.0173	1.017	0.7406
	75-84	1.249	<.0001	1.795	<.0001	1.471	<.0001	1.248	<.0001
	85+	1.415	<.0001	3.027	<.0001	2.213	<.0001	1.409	<.0001
Line of Business (Ref. Medicare)	Commercial	0.533	<.0001	0.389	<.0001	0.487	<.0001	0.533	<.0001
Region (Ref. South)	Northeast	0.881	0.0064	0.698	<.0001	0.757	<.0001	0.881	0.0063
	Midwest	0.771	<.0001	1.048	0.1233	0.950	0.0421	0.771	<.0001
	West	0.926	0.1850	1.174	0.0011	1.083	0.0463	0.925	0.1775
Length of Stay (LOS) Ref. <7 days)	14+	0.618	<.0001	1.510	<.0001	1.120	<.0001	0.617	<.0001
	7-13	0.720	<.0001	1.138	<.0001	0.952	0.0584	0.720	<.0001
Heart Failure	-	1.240	<.0001	1.411	<.0001	1.351	<.0001	1.239	<.0001
Other CVDs	-	1.222	<.0001	1.299	<.0001	1.261	<.0001	1.222	<.0001
T2 Diabetes Mellitus	-	1.118	0.0008					1.119	0.0007
T1 Diabetes Mellitus	-	1.542	<.0001	1.256	0.0025	1.390	<.0001	1.542	<.0001
COPD	-	1.258	<.0001	1.249	<.0001	1.252	<.0001	1.257	<.0001
Overweight/Obesity	-			0.870	<.0001	0.923	0.0025		
Stroke	-	1.134	0.0275	1.168	0.0001	1.168	<.0001	1.132	0.0282
Asthma	-			0.829	0.0007				
Other Resp. Diseases	-	1.126	0.0065	1.287	<.0001	1.204	<.0001	1.126	0.0059
Liver Disease	-	1.351	<.0001	1.845	<.0001	1.599	<.0001	1.350	<.0001
Dementia	-			1.913	<.0001	1.595	<.0001		
Kidney Disease	-	1.230	<.0001	1.247	<.0001	1.260	<.0001	1.229	<.0001
Immunodeficiency	-	1.513	<.0001	1.303	<.0001	1.344	<.0001	1.512	<.0001
Cancer	-	1.209	<.0001	1.325	<.0001	1.247	<.0001	1.209	<.0001

LIMITATIONS

- The study used administrative claims data, thus any misclassification, miscoding, or misrepresentation of the ICD/CPT/HCPCS codes in the database may result in the under or over representation of patients in the population and other measures.
- Patients who died during the hospital discharge month were assumed to have died during their initial hospitalization in the study, which could lead to underestimation of rehospitalization risk.

CONCLUSIONS

- Patients with underlying comorbid conditions and older age have a higher risk of a COVID-19 related rehospitalization or death following an initial COVID-19 hospitalization.
- Further analysis is needed to understand the risk factors associated with all-cause rehospitalization, as well as the impact of other factors such as oxygen therapy, treatments, and optimal management strategies on rehospitalization risk for patients with COVID-19 and comorbid conditions.

References

1) <https://www.healthsystemtracker.org/brief/covid19-and-other-leading-causes-of-death-in-the-us/> 2) Donnelly JP, Wang XQ, Iwashyna TJ, Prescott HC. Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System. *JAMA*. 2021;325(3):304–306 3) Ejaz H, Alsharhi A, Zafar A et al. COVID-19 and comorbidities: Deleterious impact on infected patients. *J Infect Public Health*. 2020 Dec;13(12):1833-1839.