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Comparative analysis of COVID-19-related mortality risk in chronic lower respiratory disease and interstitial lung disease

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To the editor,

Coronavirus disease 2019 (COVID-19) has resulted in significant deaths. Individuals with pre-existing chronic lung diseases (CLD) are expected to be more susceptible to both contracting COVID-19 and experiencing adverse outcomes. However, previous studies comparing the prevalence of CLD in patients with COVID-19, compared to the general population, have yielded conflicting findings (1). In contrast to prior research, our study aims to investigate COVID-19-related mortality risk in decedents with two primary groups of CLD: interstitial lung disease (ILD) and chronic lower respiratory disease (CLRD). Through this investigation, we aim to provide valuable insights for clinical management and public health strategies. This retrospective, population-based study utilized death certificate data provided by the National Center for Health Statistics, accessible via the Centers for Disease Control and Prevention (CDC) website (2). Similar to previous investigations, individuals with COVID-19, ILD, and CLRD were identified through International Classification of Diseases (10th Revision) codes using the CDC Multiple Cause of Death database (3). Individuals under the age of 45 were excluded from the analysis due to the rarity of CLRD and ILD diagnoses in this age group. To compare the risk of COVID-19 in individuals with CLRD and ILD relative to those without CLD, logistic regression analysis was conducted to determine the adjusted odds ratio (OR), accounting for sex, age group, and race. Since our study used existing data without patient identifiers, it did not require institutional review board approval. Additional information can be found in Table 1.

In our investigation spanning the period from April 2020 to December 2021 in the U.S., we identified 5,372,894 documented deaths. Of these, 87.9% had no documented CLD, 11.1% were associated with CLRD, and 1.1% with ILD. Notably, COVID-19 infection was prevalent in 14.5% of decedents without CLD. The prevalence of COVID-19 infection among CLRD-related deaths was significantly lower at 11.5% (OR 0.77). and for ILD, it was 13.3% (OR 0.88). Similarly, COVID-19 was listed as the underlying cause of death in 13.2% of the decedents without CLD, and in only 9.9% of those with CLRD (OR 0.72) and 11.9% of those with ILD (OR 0.89). Among female decedents, compared to those without CLD, the prevalence of COVID-19 infection was 22% lower in those with CLRD and 18% lower in those with ILD. Conversely, among male decedents, COVID-19 infection rates were similarly lower by 25% in those

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Table 1. Prevalence of COVID-19 Infection among Deceased Individuals with and without Chronic Lung Disease.

	Decedents without Chronic Lung Disease		Decedents with Chronic Lower Respiratory Disease			Decedents with Interstitial Lung Disease		
Variable	**Total Deaths**	**COVID-19 Present (%)**	**Total Deaths**	**COVID-19 Present (%)**	**Adjusted Odds Ratio[a] (95% CI)**	**Total Deaths**	**COVID-19 Present (%)**	**Adjusted Odds Ratio[b] (95% CI)**
Overall	4727444	687236 (14.5)	596762	68595 (11.5)	0.77 (0.76-0.77)	60444	8026 (13.3)	0.88 (0.86-0.90)
Gender								
Female	2285726	308461 (13.5)	293406	33339(11.4)	0.78 (0.77-0.79)	26585	3255 (12.2)	0.82 (0.79-0.86)
Male	2441718	378775 (15.5)	303356	35256 (11.6)	0.75 (0.74-0.76)	33859	4771 (14.1)	0.91 (0.88-0.94)
Age (years)								
45-54	325215	50754 (15.6)	17822	2262(12.7)	0.89 (0.85-0.93)	1748	484 (27.7)	2.24 (2.01-2.49)
55-64	693243	106808 (15.4)	82790	8354(10.1)	0.65 (0.64-0.67)	6091	1410 (23.1)	1.68 (1.58-1.78)
65-74	1021233	161232(15.8)	159997	17870 (11.2)	0.70 (0.69-0.72)	14666	2329 (15.9)	1.08 (1.03-1.13)
75-84	1199791	180036 (15.0)	188230	22573 (12.0)	0.72 (0.71-0.73)	20967	2312 (11.0)	0.61 (0.59-0.64)
≥ 85	1487962	188406 (12.7)	147923	17536(11.9)	0.91 (0.89-0.92)	16972	1491 (8.8)	0.62 (0.59-0.66)
Race								
Black	634348	104106 (16.4)	54960	8116 (14.8)	0.88 (0.86-0.90)	4478	932 (20.8)	1.34 (1.24-1.44)
White	3650476	461675(12.6)	514201	54681 (10.6)	0.82 (0.81-0.83)	49280	5628 (11.4)	0.88 (0.86-0.91)
Hispanic	442620	121455(27.4)	27601	5798 (21.0)	0.69 (0.67-0.71)	6686	1466 (21.9)	0.74 (0.70-0.78)
UCD								
COVID-19	n/a	625980 (13.2)	n/a	58932 (9.9)	0.72 (0.71-0.72)	n/a	7224 (11.9)	0.89 (0.87-0.91)

Abbreviations: UCD – Underlying cause of Death. Data were obtained from the Centers for Disease Control and Prevention Multiple Cause of Death Database (https://wonder.cdc.gov/mcd-icd10.html). International Classification of Diseases-10 codes used are as follows: COVID-19: U07.1, Chronic lower respiratory disease: J40-J47, Interstitial lung disease (excluded pneumoconiosis): J84, J67, D86.0 and D86.2. Decedents without Chronic Lung Disease group comprises all decedents who do not have chronic lower respiratory disease or interstitial lung disease. Those <45 years old were excluded as the diagnoses of chronic lower respiratory disease or interstitial lung disease were rare in this age group. Race was categorized according to US Census standards as non-Hispanic White (White), Hispanic, non-Hispanic Black (Black). Other races were excluded due to small numbers in individual categories. The time period examined was April 2020 – Dec 2021. [a]The overall odds (adjusted for age, gender and race) of COVID-19 in decedents with Chronic Lower Respiratory Disease compared to those without Chronic Lung Disease (excluding Chronic Lower Respiratory Disease and Interstitial Lung Disease). The overall odds (adjusted for age, gender and race) of COVID-19 in decedents with Interstitial Lung Disease compared to those without Chronic Lung Disease. All data are covered by the provisions of the Public Health Service Act [42 U.S.C. 242 m (d)] and the data can be used for publication without additional permission.

with CLRD, but only 9% lower in those with ILD. Stratifying by age groups revealed diverse patterns. Compared to those without CLD, COVID-19 infection rates were 11-30% lower in CLRD decedents aged 45-74 years. In contrast, individuals with ILD in the same age range experienced notably higher rates; 124% higher in the 45–54 year age group and 68% higher in the 55-64 year age group. However, both CLRD and ILD decedents ≥ 75 years exhibited lower infection rates. Analyzing by race also revealed significant disparities. Compared to those without CLD, COVID-19 infection rates were 12% lower in Black decedents with CLRD but 34% higher with ILD. Among Whites, rates were 18% lower in CLRD and 12% lower in ILD decedents, while in Hispanics, they were 31% lower in CLRD decedents and 26% lower in ILD decedents. Unlike prior research that compared CLD patients to healthy populations (4-6), our study's comparison group of non-CLD decedents likely represents a sicker population, making it a more appropriate comparison. Our analysis revealed a 23% lower COVID-19 prevalence in CLRD decedents and a 12% lower prevalence in ILD decedents compared to non-CLD decedents. This aligns with previous research indicating lower CLD prevalence in hospitalized COVID-19 patients compared to the general population (6). While several studies suggest individuals with CLD face increased risk of severe disease (5, 7), a large community cohort found a low absolute risk of death from COVID-19 across all CLD groups (4), consistent with our findings. The lower prevalence of COVID-19 in decedents with CLD may be due to several factors. Individuals with CLD might adhere more strictly to preventive measures and vaccinations due to their perceived

higher risk. Additionally, CLD decedents likely have other underlying health conditions, increasing their likelihood of death from causes other than COVID-19. Medications for CLD, such as steroids and immunomodulators, might also blunt the systemic inflammatory response to COVID-19. Our study highlights significant demographic differences in COVID-19 infection prevalence among ILD decedents. Notably, younger age groups (especially 45-64 years) and Black individuals with ILD had higher COVID-19 prevalence compared to those without CLD, contradicting the overall trend of lower COVID-19 prevalence among ILD decedents. The absence of a similar trend in CLRD decedents underscores the influence of distinct risk factors and pathophysiological mechanisms specific to various types of CLD. The age-specific disparity in ILD may be influenced by several factors. Younger individuals are more likely to have high-exposure occupations/social activities. Disparities in healthcare access, vaccination rates, and testing availability among younger individuals and marginalized communities may also exacerbate their vulnerability to COVID-19, especially with underlying ILD. Black individuals, in particular, are disproportionately affected by structural/socioeconomic inequities, potentially contributing to the higher COVID-19 prevalence rates among ILD patients in this racial group (8). Interestingly, we did not observe a similar trend of higher COVID-19 prevalence among Hispanic ILD decedents, suggesting a complex interplay of biological, cultural and socioeconomic factors influencing COVID-19 prevalence and outcomes across different races. Addressing these disparities requires targeted interventions to improve healthcare access, promote vaccination equity, and address social determinants of health to mitigate the disproportionate burden of COVID-19 on vulnerable populations. Notably, the ILD group in our study was predominantly composed of individuals with IPF-CS, identified similarly to prior studies (9), accounting for 86% of Black patients and 84% of those aged 45-64, which may limit the generalizability of our findings to non-IPF-CS ILDs. In a single exploratory sub-group analysis, we investigated whether the observed higher COVID-19 prevalence among younger and Black ILD decedents extended to those with sarcoidosis. Compared to non-CLD decedents, the COVID-19 prevalence in sarcoidosis decedents showed an OR of 1.10 (95% CI: 0.86-1.40) among Black individuals and an OR of 1.19 (95% CI: 0.90-1.56) for those aged 45-64. These findings indicate a trend similar to the overall ILD population but with less pronounced associations, suggesting that while there may be some overlap, sarcoidosis-specific factors could influence COVID-19 susceptibility differently (10, 11). This study's strength lies in its comprehensive analysis of the entire U.S. population. However, a limitation is the inability to independently verify the accuracy of diagnoses on death certificates. Nonetheless, the robustness of our findings is supported by the substantial sample size, making them unlikely due to random chance. In summary, our findings suggest that COVID-19 prevalence is generally lower in decedents with CLD compared to those without, except for ILD decedents younger than 75 years and in Black individuals. These discrepancies merit further exploration to understand the underlying factors driving the observed trends.

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References

1. Calver JF, Fabbri L, May J, Jenkins RG. COVID-19 in Patients with Chronic Lung Disease. Clin Chest Med 2023; 44: 385-393.
2. Centers for Disease Control and Prevention. Wide-Ranging Online Data for Epidemiologic Research. Multiple cause of death, 2018–2021. https://wonder.cdc.gov/mcd.html.
3. Jeganathan N, Cleland D, Sathananthan M. The association of lung cancer with pulmonary fibrosis. ERJ Open Res 2022; 8.
4. Aveyard P, Gao M, Lindson N, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. Lancet Respir Med 2021; 9: 909-923.
5. Drake TM, Docherty AB, Harrison EM, et al. Outcome of Hospitalization for COVID-19 in Patients with Interstitial Lung Disease. An International Multicenter Study. Am J Respir Crit Care Med 2020; 202: 1656-1665.
6. Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? Lancet Respir Med 2020; 8: 436-438.

7. Sanchez-Ramirez DC, Mackey D. Underlying respiratory diseases, specifically COPD, and smoking are associated with severe COVID-19 outcomes: A systematic review and meta-analysis. Respir Med 2020; 171: 106096.
8. Vasquez Reyes M. The Disproportional Impact of COVID-19 on African Americans. Health Hum Rights 2020; 22: 299-307.
9. Jeganathan N, Sathananthan M. Urban-Rural Differences in Idiopathic Pulmonary Fibrosis-Related Mortality Rates in the United States. Chest 2024; 165: 924-928.
10. Baughman RP, Lower EE. COVID-19 infections in sarcoidosis: a prospective single center study of 886 sarcoidosis patients. Sarcoidosis Vasc Diffuse Lung Dis 2021; 38: e2021029.
11. Baughman RP, Lower EE, Buchanan M, et al. Risk and outcome of COVID-19 infection in sarcoidosis patients: results of a self-reporting questionnaire. Sarcoidosis Vasc Diffuse Lung Dis 2020; 37: e2020009.