Brief Summary of Findings on the Association Between Interstitial Lung Diseases and Severe COVID-19 Outcomes

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Overall, 7 cohort studies[1-7] and 1 modeling study[8] were retrieved that reported data on any interstitial lung disease and severe COVID-19 outcomes including mortality, intensive care unit (ICU), hospital admission, and ventilation. All studies were rated as having a moderate threat to internal validity.

- Evidence from six studies[2-4, 6-8] (N=230,262) indicates the presence of underlying interstitial lung disease (ILD) is associated with an increase in mortality. Limited evidence suggests an increase in the risk of ICU admission[2] (N=89,530) and ventilation[3] (N=483) with underlying ILD, however the evidence is insufficient to assure confidence in this assessment.
- Evidence from two cohort studies[1, 3] (N=8,256,644) conducted in Europe indicates the presence of underlying idiopathic pulmonary fibrosis is associated with an increase in mortality. Limited evidence from one study[1] (N=8,256,161) suggests increases in ICU admission and hospitalization with underlying idiopathic pulmonary fibrosis, however the evidence is insufficient to assure confidence in this assessment.
- Evidence from two cohorts[1, 2] (N=8,345,691) conducted in Europe indicates the presence of underlying sarcoidosis is associated with increases in mortality and ICU admission. Evidence from two cohort studies[1, 5] (N=8,256,982) conducted in the US and Europe suggests an increase in hospitalization with underlying sarcoidosis.
- Limited evidence from one cohort study[1] (N=8,256,161) conducted in Europe suggests underlying hypersensitivity pneumonitis, also called extrinsic allergic alveolitis, is associated with increases in mortality and hospitalization, however the evidence is insufficient to assure confidence in this assessment.
- Evidence from two cohorts[1, 3] (N=8,256,644) conducted in Europe indicates the presence of underlying interstitial lung diseases other than idiopathic pulmonary fibrosis or sarcoidosis is associated with an increase in mortality. Limited evidence from one study[1] (N=8,256,161) suggests an increase in hospitalization with underlying interstitial lung diseases other than idiopathic pulmonary fibrosis or sarcoidosis, however the evidence is insufficient to assure confidence in this assessment.
- Limited evidence from one cohort study[3] (N=483) suggests that mortality is greater among patients with moderate or severe ILD when compared to patients with mild ILD. However, the evidence is insufficient to assure confidence in this assessment.

References

1.   Aveyard P, Gao M, Lindson N, Hartmann-Boyce J, Watkinson P, Young D, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. The Lancet Respiratory Medicine 2021;9(8):909-923.
2.   Beltramo G, Cottenet J, Mariet A-S, Georges M, Piroth L, Tubert-Bitter P, et al. Chronic respiratory diseases are predictors of severe outcome in COVID-19 hospitalised patients: a nationwide study. European Respiratory Journal 2021:2004474.
3.   Drake TM, Docherty AB, Harrison EM, Quint JK, Adamali H, Agnew S, et al. Outcome of hospitalization for COVID-19 in patients with interstitial lung disease an international multicenter study. American Journal of Respiratory and Critical Care Medicine 2020;202(12):1656-1665.
4.   Estiri H, Strasser ZH, Klann JG, Naseri P, Wagholikar KB, Murphy SN. Predicting COVID-19 mortality with electronic medical records. npj Digital Medicine 2021;4(1).

5.   Halalau A, Odish F, Imam Z, Sharrak A, Brickner E, Lee PB, et al. Epidemiology, Clinical Characteristics, and Outcomes of a Large Cohort of COVID-19 Outpatients in Michigan. Int J Gen Med 2021;14:1555-1563.

6.   Kokturk N, Babayigit C, Kul S, Duru Cetinkaya P, Atis Nayci S, Argun Baris S, et al. The predictors of COVID-19 mortality in a nationwide cohort of Turkish patients. Respir Med 2021;183:106433.

7.   Oh TK, Song IA. Impact of coronavirus disease-2019 on chronic respiratory disease in South Korea: an NHIS COVID-19 database cohort study. BMC Pulmonary Medicine 2021;21(1).

8.   Mollalo A, Rivera KM, Vahabi N. Spatial statistical analysis of pre-existing mortalities of 20 diseases with COVID-19 mortalities in the continental United States. Sustainable Cities and Society 2021;67:102738.

Contents

Table of Tables

A. Methods

The aim of this review is to identify and synthesize the best available evidence on the association between interstitial lung disease (ILD) and severe COVID-19 in order to update the Centers for Disease Control and Prevention (CDC) website on underlying conditions and enable the creation of a provider-specific website with more rigorous information.

A.1. Literature Search

A list of search terms was developed to identify the literature most relevant to the population, exposure, comparator, and outcomes (PECO) question. Clinical experts and library scientists were consulted to develop a robust list of search terms. These terms were then incorporated into search strategies, and these searches were performed in OVID using the COVID-19 filter from the end of the previous literature search (December 2020). The detailed search strategies for identifying primary literature and the search results are provided in Section B.1. Subject matter experts supplemented the literature search results by recommending relevant references published before December 2020. References were included if retrieved by the chronic lung disease literature search and reported exposures and outcomes relevant to this review.
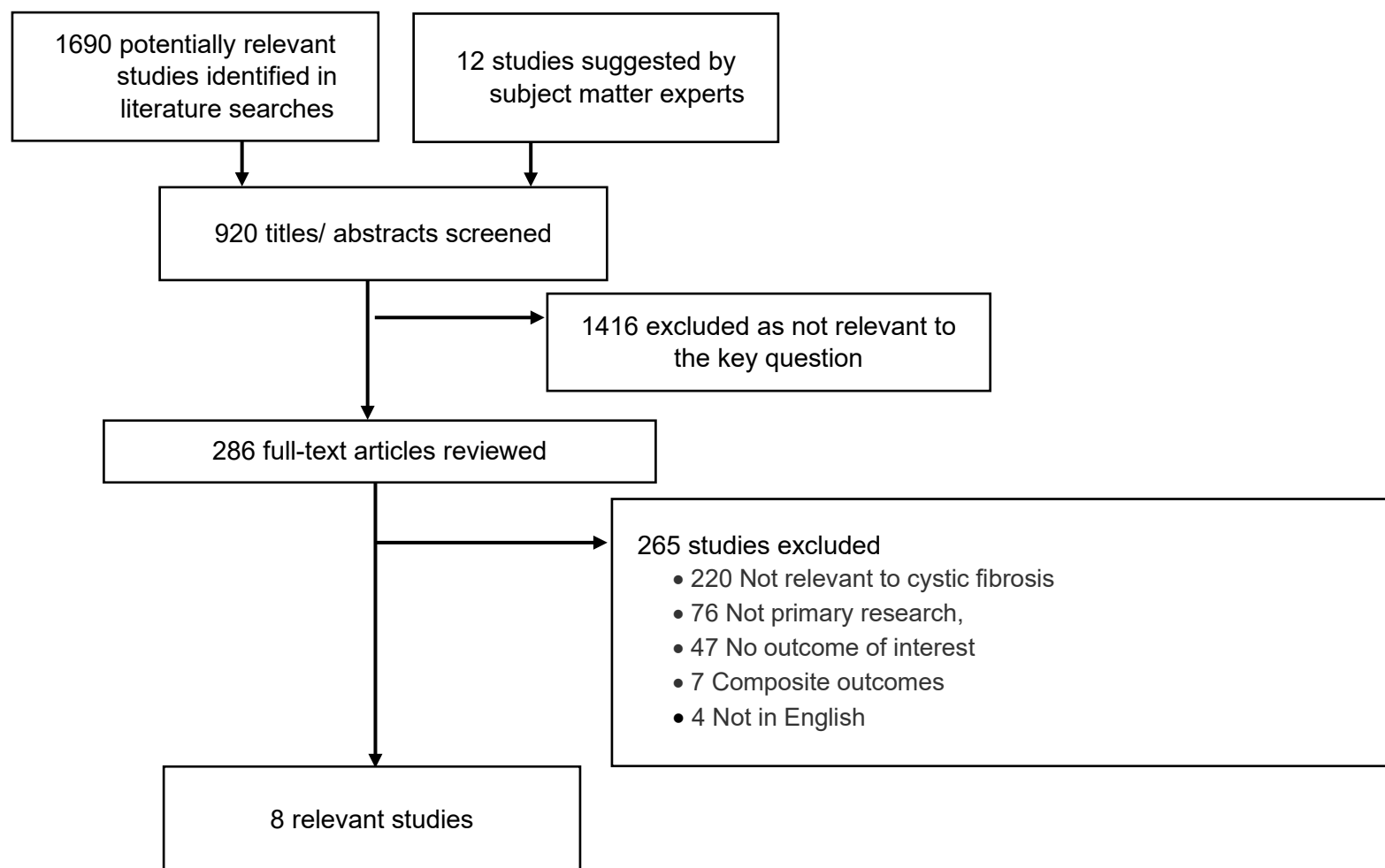
A.2. Study Selection

Titles and abstracts from references were screened by dual review (M.C., J.K.K., C.O., D.O.S., T.R., C.S., E.C.S., or M.W.). Full-text articles were retrieved if they were:
1. relevant to the PECO question;
2. primary research; and
3. written in English.

Section B.2 presents the full list of exclusion criteria. The full texts of selected articles were then screened by two independent reviewers, and disagreements were resolved by discussion (J.K.K., C.O., D.O.S., K.T.R., C.S., E.C.S., or M.W.). After the full-text screening was complete, a bibliography of the articles selected for inclusion was vetted with subject matter experts. Additional studies suggested by the subject matter experts were screened for inclusion as described above. The results of the study selection process are depicted in Figure 1.

Figure 1. Results of the Study Selection Process

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┌─────────────────────────┐        ┌─────────────────────────┐
│ 1690 potentially relevant│        │ 12 studies suggested by  │
│   studies identified in  │        │  subject matter experts  │
│    literature searches   │        │                          │
└─────────────────────────┘        └─────────────────────────┘
              │                                  │
              ▼                                  ▼
       ┌──────────────────────────────────────┐
       │    920 titles/ abstracts screened     │
       └──────────────────────────────────────┘
                        │
                        │────────►┌─────────────────────────┐
                        │         │ 1416 excluded as not     │
                        │         │ relevant to the key      │
                        │         │ question                 │
                        │         └─────────────────────────┘
                        ▼
       ┌──────────────────────────────────────┐
       │     286 full-text articles reviewed   │
       └──────────────────────────────────────┘
                        │
                        │────────►┌──────────────────────────────────┐
                        │         │ 265 studies excluded             │
                        │         │   • 220 Not relevant to cystic   │
                        │         │     fibrosis                     │
                        │         │   • 76 Not primary research,     │
                        │         │   • 47 No outcome of interest    │
                        │         │   • 7 Composite outcomes         │
                        │         │   • 4 Not in English             │
                        ▼         └──────────────────────────────────┘
       ┌──────────────────────────┐
       │     8 relevant studies    │
       └──────────────────────────┘
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A.3. Data Extraction and Synthesis

Methodologic data and results of relevant outcomes from the studies meeting inclusion criteria were extracted into standardized evidence tables. Data and analyses were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as $p \leq 0.05$.

A.4. Aggregation of the Evidence

The internal validity associated with each study was assessed using scales developed by the Division of Healthcare Quality Promotion and scores were recorded in the evidence tables. Table 4 in Section B.3.c. includes the signaling questions used to assess the quality of each study design. The strength, magnitude, precision, consistency, and applicability of results were assessed for all comparators. The overall confidence in the evidence base is reported in the aggregation tables in Section B.3.a.

A.5 Reviewing and Finalizing the Systematic Review

Draft findings, aggregation tables, and evidence tables, are presented to CDC subject matter experts for review and input. Following further revisions, the summary will be published on the CDC website.

B. Systematic Literature Review Results

B.1. Search Strategies and Results

Table 1 Chronic Lung Disease search conducted March 17, 2021

#	Search History
1	chronic lung disease
2	respiratory system disease*
3	reactive airway disease*
4	emphysema
5	chronic bronchitis
6	COPD
7	Chronic obstructive pulmonary disease
8	Asthma *
9	allergic asthma
10	irritant asthma
11	Interstitial lung disease
12	Pulmonary fibrosis
13	idiopathic pulmonary fibrosis
14	nonspecific interstitial pneumonitis
15	hypersensitivity pneumonitis
16	sarcoidosis
17	pneumoconiosis
18	asbestosis
19	coal workers pneumoconiosis
20	silicosis
21	bronchiectasis
22	cystic fibrosis
23	pulmonary vascular disease
24	pulmonary hypertension
25	bronchopulmonary dysplasia
26	bronchiolitis obliterans
27	asthma*
28	reactive airway disease*
29	CF

30	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31	Limit 30 to covid-19
32	(202012* or 2021*).dt
33	(202012* or 2021*).dc
34	32 or 33
35	31 and 34
36	Deduplicate

B.2. Study Inclusion and Exclusion Criteria

Inclusion Criteria: Studies were included at the title and abstract screen if they:
- were relevant to the key question "what is the association between interstitial lung disease and severe COVID-19?";
- were primary research;
- were written in English (can be seen as [language] in title); and
- examined humans only.

Exclusion Criteria: Studies were excluded at full text review if they:
- were not available as full-text;
- were a conference abstract, poster, letter to the editor, or reply letter;
- examined lung transplant, cancer, or immunocompromised populations;
- reported autopsy results; and
- reported only composite outcome measures for "severe COVID-19".

B.3. Evidence Review: Interstitial Lung Disease and Severe COVID-19
B.3.a. Strength & Direction of Evidence
Table 2. Evidence examined for associations with interstitial lung disease and severe COVID-19

Outcome	Results
Mortality	Overall, the evidence suggests the presence of underlying interstitial lung disease (ILD) is associated with an increase in mortality. All six studies were found to have a moderate threat to internal validity. • Strength of Association: Six studies reported adjusted measures of association ranging from 1.027 to 5.27. • Precision of Association: Three studies reported wide confidence intervals, one of which crossed the null. Three studies reported narrow confidence intervals. • Consistency of Association: All six studies reported measures of association in the same direction.

Outcome	Results
	• Applicability of Association: The populations and settings were directly applicable to the question. Five studies were conducted in high-income countries, four of which were in the US or Europe,
	Six studies suggested an increased risk of mortality in patients with ILD.
	– Five cohort studies[2-4, 6, 7] (N=230,262) reported an effect measure suggesting that underlying ILD is associated with an increase in mortality in patients with COVID-19 .
	o Of these studies, three[3, 6, 7] (N=124,023) reported wide confidence intervals, decreasing confidence in the measure of effect. One study[3] (N=483) had a small sample size. Another study[7] (N=122,040) which reported a confidence interval that spanned the null, was conducted in South Korea and reported a low rate of ILD among the study population (421/122,040 (0.3%)). The other study[6] (N=1,500) was the only study reporting on ILD that was conducted in a middle-income country and reported few events.
	o One study[4] (N=16,709) reported an increase in the odds and risk of mortality among patients with interstitial pulmonary disease after adjusting for age, sex, and history of underlying conditions.
	– One modeling study[8] (N=NR) evaluating the geospatial distributions of COVID-19 mortality in the US reported an association between county-level COVID-19 case fatality rates and county-level, age-adjusted mortality due to ILD among counties with high COVID-19 mortality that were surrounded by counties with high COVID-19 mortalities. There was a protective association among counties with low COVID-19 mortality that were surround by counties with low COVID-19 mortalities.
ICU admission	The evidence is limited but suggests the presence of underlying ILD is associated with an increase in ICU admission. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity.
	– One large retrospective cohort[2] (N=89,530) conducted in France reported an increase in odds of ICU admission among patients with ILD compared to patients with no underlying chronic lung disease. After adjusting for obesity, diabetes, hypertension, heart failure, atherosclerotic heart disease, sex, and age as a continuous variable, the increased odds of ICU admission remained.

Outcome	Results
Ventilation	The evidence is limited on the association between underlying ILD and the risk of ventilation but suggests a protective effect for underlying ILD. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. − One prospective cohort study[3] (N=483) evaluating outcomes among ILD patients hospitalized in Denmark, Germany, Italy, the Republic of Ireland, Spain, and the UK suggested a decrease in the prevalence of ventilation among patients with ILD compared to those without (3.7% vs. 9.0%, p=NR), however the study population size was small.

Table 3. Evidence examined for associations between idiopathic pulmonary fibrosis and severe COVID-19

Outcome	Results
Mortality	The evidence suggests the presence of underlying idiopathic pulmonary fibrosis is associated with an increase in mortality. Both studies were found to have a moderate threat to interval validity (Aveyard 2021 and Drake 2020) • Strength of Association: Two studies reported adjusted measures of association ranging from 1.47 to 1.74. • Precision of Association: One study reported a wide confidence interval that did not cross the null. One study reported a narrow confidence interval. • Consistency of Association: Both studies reported measures of association in same direction. • Applicability of Association: Both studies were implemented in Europe. Two cohort studies[1,3] (N=8,256,644) reported that underlying idiopathic pulmonary fibrosis is associated with an increase in mortality in patients with COVID-19. In the larger study[1] (N=8,256,161), this increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. The smaller study[3] (N=483) reported results adjusting for age and comorbidity. − One study[3] (N=483) reported a wide confidence interval and a small sample size, decreasing confidence in the measure of effect.
ICU admission	The evidence is limited but suggests the presence of underlying idiopathic pulmonary fibrosis associated with an increase in ICU admission. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. − One large retrospective cohort[1] (N=8,256,644) conducted in England suggested an increase in the hazard of ICU admission among patients with idiopathic pulmonary fibrosis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities; however, confidence intervals were

Outcome	Results
	wide and crossed the null, decreasing confidence in the measure of effect. The study reported a small number of events and the hazard of ICU admission was calculated among the entire study population, not limited to those hospitalized with COVID-19.
Hospitalization	The evidence is limited but suggests the presence of underlying idiopathic pulmonary fibrosis associated with an increase in hospitalization. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. − One large retrospective cohort[1] (N=8,256,161) conducted in England reported an increase in the hazard of hospitalization among patients with idiopathic pulmonary fibrosis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities.

Table 4. Evidence examined for associations between sarcoidosis and severe COVID-19

Outcome	Results
Mortality	The evidence suggests the presence of underlying sarcoidosis is associated with an increase in mortality. Both studies were found to have a moderate threat to internal validity. • Strength of Association: Two studies reported adjusted measures of association ranging from 1.41 to 2.11. • Precision of Association: Both studies reported wide confidence intervals, one of which crossed the null. • Consistency of Association: Both studies reported measures of association in same direction. • Applicability of Association: Both studies were implemented in Europe. − Two large cohort studies[1,2] (N=8,345,691) reported an increase in mortality among patients with sarcoidosis and both were found to have a moderate threat to internal validity. In one study[1], this increase in sarcoidosis remained after adjusting for age and sex, other demographic factors, or other comorbidities. In the other[2], the increase in pulmonary sarcoidosis remained after adjusting for age, sex, and other underlying medical conditions. o Both studies reported wide confidence intervals and one[1] crossed the null, decreasing confidence in the measure of effect. Both studies reported a small number of events.
ICU admission	The evidence suggests the presence of underlying sarcoidosis is associated with an increase in ICU admission. Both studies were found to have a moderate threat to interval validity. • Strength of Association: Two studies reported adjusted measures of association ranging from 1.51 to 2.65. • Precision of Association: Both studies reported wide confidence intervals, one of which crossed the null. • Consistency of Association: Both studies reported measures of association in same direction. • Applicability of Association: Both studies were implemented in Europe.

Outcome	Results
	– Two cohorts[1,2] (N=8,345,691) suggested an increase in ICU admission among patients with sarcoidosis . In one study[1], this increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. In the other[2], the increase remained after adjusting for age, sex, and other underlying medical conditions. o Both studies reported wide confidence intervals and one[1] crossed the null, decreasing confidence in the measure of effect. Both studies reported a small number of events, and one[1] calculated the hazard of ICU admission among the entire study population, not limited to only those hospitalized with COVID-19.
Hospitalization	The evidence is limited but suggests the presence of underlying sarcoidosis is associated with an increase in hospitalization. Both studies were found to have a moderate threat to internal validity. • Strength of Association: One study reported an adjusted measure of association of 1.36 and one study did not report a measure of association. • Precision of Association: One study reported a narrow confidence interval, and one study did not report a confidence interval. • Consistency of Association: One study reported an association, and one found no association. • Applicability of Association: Both studies were implemented in US or Europe. Two studies suggested an increased risk of hospitalization in patients with sarcoidosis. – One large retrospective cohort study[1] (N=8,256,161) conducted in England reported an increase in the hazard of hospitalization among patients with sarcoidosis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. – One retrospective cohort study[5] (N=821) in Michigan, US suggested an increase in the rate of hospitalization for people with sarcoidosis, however this difference was not statistically significant (2.3% vs. 0.5%, p=0.123). Of note, the prevalence of sarcoidosis was low in this study (6/821 (0.7%)).

Table 5. Evidence examined for associations between hypersensitivity pneumonitis (extrinsic allergic alveolitis) and severe COVID-19

Outcome	Results
Mortality	The evidence is limited but suggests the presence of underlying hypersensitivity pneumonitis, also called extrinsic allergic alveolitis, is associated with an increase in mortality. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. One retrospective cohort[1] (N=8,256,161) conducted in England suggested an increase in the hazard of mortality among patients with extrinsic allergic

Outcome	Results
	alveolitis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. o This study reported a wide confidence interval that spanned the null, decreasing confidence in the measure of effect. This study reported a small number of events.
Hospitalization	The evidence is limited but suggests the presence of underlying hypersensitivity pneumonitis or extrinsic allergic alveolitis is associated with an increase in hospitalization. Aggregation indices cannot be measured for one study, and the study was found to have a moderate threat to internal validity. One retrospective cohort[1] (N=8,256,161) conducted in England suggested an increase in the hazard of hospitalization among patients with extrinsic allergic alveolitis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. o This study reported a wide confidence interval that spanned the null, decreasing confidence in the measure of effect. This study reported a small number of events.

Table 6. Evidence examined for associations between other interstitial lung diseases and severe COVID-19

Outcome	Results
Mortality	The evidence suggests the presence of underlying other ILD excluding either idiopathic pulmonary fibrosis or sarcoidosis are associated with an increase in mortality. Both studies were found to have a moderate threat to internal validity. • Strength of Association: Two studies reported adjusted measures of association ranging from 1.50 to 2.05. • Precision of Association: Both studies reported wide confidence intervals that did not span the null. • Consistency of Association: Both studies reported measures of association in same direction. Applicability of Association: Both studies were implemented in Europe. – Two cohort studies[1, 3] (N=8,256,644) reported an increase in mortality among patients with other ILD excluding either idiopathic pulmonary fibrosis or both idiopathic pulmonary fibrosis and sarcoidosis. One study[3] (N=483) had a small study size and the other[1] (N=8,256,161) reported a small number of events.
Hospitalization	The evidence is limited but suggests the presence of underlying other ILD excluding either idiopathic pulmonary fibrosis or sarcoidosis are associated with an increase in hospitalization. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. – One large retrospective cohort[1] (N=8,256,161) conducted in England reported an increase in the hazard of hospitalization among patients with other ILD, excluding idiopathic pulmonary fibrosis or sarcoidosis. This increase remained after adjusting for age and sex, other demographic factors, or other comorbidities. This

Outcome	Results
	study reported a wide confidence interval decreasing confidence in the measure of effect; however, it does not span the null. This study reported a small number of events.

Table 7. Evidence examined for associations between severity of interstitial lung disease and severe COVID-19

Outcome	Results
Mortality	The evidence is limited regarding the association between the severity of underlying ILD and the risk of mortality. Aggregation indices cannot be measured for one study, which was found to have a moderate threat to internal validity. − One prospective cohort study[3] (N=483) conducted in Denmark, Germany, Italy, the Republic of Ireland, Spain, and the UK reported that mortality was greater among patients with moderate or severe ILD when compared to patients with mild ILD. o The analysis comparing severity levels was restricted to only those patients with ILD, limiting the confidence in the results as the sample size decreased.

B.3.b. Extracted Evidence

Table 8. Extracted Studies Reporting the Association between Interstitial Lung Disease and Severe COVID-19 Outcomes

Study	Population and Setting	Intervention	Definitions	Results
Author: Aveyard[1] **Year:** 2021 **Data Extractor:** TR **Reviewer:** DOS **Study design:** Retrospective cohort study **Study Objective:** To assess whether chronic lung disease or use of inhaled corticosteroids (ICS) affects the	**Population:** N= 8,256,161 **Setting:** 1,205 general practices **Location:** England, UK **Study dates:** January 24, 2020-April 30, 2020 **Inclusion criteria:** All patients aged 20 years and older registered with one of the 1,205 general practices in England contributing to the QResearch database (version 44, uploaded March 23, 2020) were included in this population cohort study. Data were linked to Public Health England's database of SARS-CoV-2 testing and English hospital admissions, ICU admissions, and deaths for COVID-19. **Exclusion criteria:** NR (Not reported)	**Health Condition Category:** Chronic lung disease, Risk factors, Multiple comorbid conditions, Cancer **Medical Condition, n/N (%):** COPD: 193,520/8,256,161 (2.3%) Asthma: 1,090,028/8,256,161 (13.2%) Bronchiectasis: 41271/8,256,161 (0.5%) Cystic fibrosis: 2081/8,256,161 (<1%) Sarcoidosis: 17624/8,256,161 (0.2%) Extrinsic allergic alveolitis: 2331/8,256,161 (<1%)	**Medical Condition(s):** *COPD:* ND (Not defined) *Asthma:* ND *Bronchiectasis:* ND *Cystic fibrosis:* ND *Sarcoidosis:* ND *Extrinsic allergic alveolitis:* ND *Idiopathic pulmonary fibrosis:* ND *Other interstitial lung diseases:* ND *Lung cancer:* ND **Severity Measure(s):** *Active asthma:* having at least one	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio for all other respiratory diseases, ethnicity, socioeconomic status, region of England, body-mass index, smoking status, non-smoking-related illness (hypertension, type 1 diabetes, chronic liver disease, chronic neurological disease) and smoking-related illness (coronary heart disease, stroke, atrial fibrillation, type 2 diabetes, chronic kidney disease)* *HR: Hazard Ratio* *Mortality, n/N (%):* COPD: • aHR: 1.54 (95% CI: 1.42-1.67)

Study	Population and Setting	Intervention	Definitions	Results
risk of contracting severe COVID-19. **Internal validity assessment (IVA) Score:** 24 (moderate)		Idiopathic pulmonary fibrosis: 7454/8,256,161 (0.1%) Other interstitial lung diseases: 5677/8,256,161 (0.1%) Lung cancer: 10792/8,256,161 (0.1%) **Control/Comparison group, n/N (%):** COPD: 8,062,641/8,256,161 (97.7%) Asthma: 7,166,133/8,256,161 (86.6%) Bronchiectasis: 8,214,890/8,256,161 (99.5%) Cystic fibrosis: 8,254,080/8,256,161 (99.9%) Sarcoidosis: 8,238,537/8,256,161 (99.8%) Extrinsic allergic alveolitis: 8,253,830/8,256,161 (99.9%) Idiopathic pulmonary fibrosis: 8,248,707/8,256,161 (99.9%) Other interstitial lung diseases: 8,250,484/8,256,161 (99.9%) Lung cancer: 8,245,369/8,256,161 (99.9%)	prescription for asthma medication *Severe asthma:* being prescribed at least three different classes of medication for asthma in the year before cohort entry **Clinical marker:** NR **Treatment/ Associated Therapy:** NR Inhaled corticosteroids (ICS): commonly used treatments for airways disease **Outcome Definitions:** *Mortality:* confirmed or suspected COVID-19 (ICD-10 codes U07.1 and U07.2) on the death certificate, including deaths in and out of hospital *ICU admission: a*dmission to an ICU with severe COVID-19 (ICD-10 code U07.1 or U07.2) in Intensive Care National Audit and Research Centre (ICNARC) records *Intubation:* NR *Ventilation:* NR *Hospitalization:* positive test for SARS-CoV-2 and appearing in the	• HR: 6.66 (95% CI: 6.19-7.18) • COPD: 811/193,520 (0.4%) Asthma: • aHR: 0.99 (95% CI: 0.91-1.07) • HR: 0.96 (95% CI: 0.89-1.04) • Asthma: 762/1,090,028 (0.1%) Cystic fibrosis: • Cystic fibrosis: 0/2081 (0%) Bronchiectasis: • aHR: 1.12 (95% CI: 0.94-1.33) • HR: 4.77 (95% CI: 4.03-5.65) • Bronchiectasis: 138/41,271 (0.3%) Sarcoidosis: • aHR: 1.41 (95% CI: 0.99-1.99) • HR: 2.53 (95% CI: 1.79-3.58) • Sarcoidosis: 32/17,624 (0.2%) Extrinsic allergic alveolitis: • aHR: 1.56 (95% CI: 0.78-3.13) • HR: 4.82 (95% CI: 2.41-9.65) • Extrinsic allergic alveolitis: 8/2,331 (0.3%) Idiopathic pulmonary fibrosis: • aHR: 1.47 (95% CI: 1.12-1.92) • HR: 12.09 (95% CI: 9.42-15.53) • Idiopathic pulmonary fibrosis: 62/7,454 (0.8%) Other interstitial lung diseases: • aHR: 2.05 (95% CI: 1.49-2.81) • HR: 11.37 (95% CI: 8.48-15.25) • Other interstitial lung diseases: 45/5,677 (0.8%) Lung cancer: • aHR: 1.77 (95% CI: 1.37-2.29) • HR: 8.33 (95% CI: 6.46-10.74) • Lung cancer: 60/10,792 (0.6%) *ICU admission, n/N (%):* COPD: • aHR: 0.89 (95% CI: 0.68-1.17) • HR: 1.68 (95% CI: 1.29-2.18) • COPD: 59/193,520 (<0.1%)

Study	Population and Setting	Intervention	Definitions	Results
			Hospital Episode Statistics dataset as an in-patient within 30 days of that test or having an International Classification of Diseases (ICD)-10 code U07.1 for confirmed COVID-19 or U07.2 for suspected COVID-19 *Non-elective readmissions*: NR **Comments:** None	Asthma: • aHR: 1.08 (95% CI: 0.93-1.25) • HR: 1.05 (95% CI: 0.91-1.22) • 213/1,090,028 (<0.1%) Bronchiectasis: • aHR: 1.47 (95% CI: 0.91-2.36) • HR: 2.37 (95% CI: 1.49-3.78) • Bronchiectasis: 18/41,271 (<0.1%) Sarcoidosis: • aHR: 1.51 (95% CI: 0.81-2.81) • HR: 3.06 (95% CI: 1.64-5.70) • Sarcoidosis: 10/17,624 (0.1%) Idiopathic pulmonary fibrosis: • aHR: 1.97 (95% CI: 0.85-4.55) • HR: 4.48 (95% CI: 2.01-9.99) • Idiopathic pulmonary fibrosis: 6/7,454 (0.1%) *Hospitalization, n/N (%):* COPD: • aHR: 1.54 (95% CI: 1.45-1.63) • HR: 5.09 (95% CI: 4.83-5.36) • COPD: 1,555/193,520 (0.8%) Asthma: • aHR: 1.18 (95% CI: 1.13-1.24) • HR: 1.22 (95% CI: 1.17-1.28) • Asthma: 2,266/1,090,028 (0.2%) Bronchiectasis: • aHR: 1.34 (95% CI: 1.20-1.50) • HR: 4.53 (95% CI: 4.06-5.07) • Bronchiectasis: 319/41,271 (0.8%) Cystic fibrosis: • aHR: 1.55 (95% CI: 0.65-3.73) • HR: 1.37 (95% CI: 0.57-3.30) • Cystic fibrosis: 5/2,081 (0.2%) Sarcoidosis: • aHR: 1.36 (95% CI: 1.10-1.68) • HR: 2.74 (95% CI: 2.21-3.39) • Sarcoidosis: 84/17,624 (0.5%) Extrinsic allergic alveolitis:

Study	Population and Setting	Intervention	Definitions	Results
				• aHR: 1.35 (95% CI: 0.82-2.21) • HR: 3.97 (95% CI: 2.43-6.48) • Extrinsic allergic alveolitis: 16/2,331 (0.7%) Idiopathic pulmonary fibrosis: • aHR: 1.59 (95% CI: 1.30-1.95) • HR: 8.80 (95% CI: 7.29-10.62) • Idiopathic pulmonary fibrosis: 110/7,454 (1.5%) Other interstitial lung diseases: • aHR: 1.66 (95% CI: 1.30-2.12) • HR: 7.57 (95% CI: 6.02-9.53) • Other interstitial lung diseases: 73/5,677 (1.3%) Lung cancer: • aHR: 2.24 (95% CI: 1.89-2.65) • HR: 7.92 (95% CI: 6.70-9.36) • Lung cancer: 139/10,792 (1.3%) **Severity of Condition:** *Mortality, n/N (%):* Active asthma: • aHR: 1.05 (95% CI: 0.96-1.15) • HR: 1.62 (95% CI: 1.49-1.77) • Active asthma: 602/535,126 (0.1%) Severe asthma: • aHR: 1.08 (95% CI: 0.98-1.19) • HR: 1.78 (95% CI: 1.62-1.95) • Severe asthma: 476/385,702 (0.1%) *ICU admission, n/N (%):* Active asthma: • aHR: 1.34 (95% CI: 1.14-1.58) • HR: 1.73 (95% CI: 1.47-2.03) • Active asthma: 165/535,126 (<0.1%) Severe asthma: • aHR: 1.30 (95% CI: 1.08-1.58) • HR: 1.79 (95% CI: 1.49-2.15)

Study	Population and Setting	Intervention	Definitions	Results
				• Severe asthma: 124/385,702 (<0.1%) *Hospitalization, n/N (%):* Active asthma: • aHR: 1.26 (95% CI: 1.20-1.33) • HR: 1.95 (95% CI: 1.85-2.05) • Active asthma: 1,720/535,126 (0.3%) Severe asthma: • aHR: 1.29 (95% CI: 1.22-1.37) • HR: 2.14 (95% CI: 2.02-2.26) • Severe asthma: 1,369/385,702 (0.4%) **Duration of Condition:** NR **Treatment/ Associated Therapy:** *Mortality:* ICS: • aHR: 1.15 (95% CI: 1.01-1.31) • HR: 2.63 (95% CI: 2.44-2.84) *ICU admission:* ICS: • aHR: 1.63 (95% CI: 1.18-2.24) • HR: 2.10 (95% CI: 1.78-2.46) *Hospitalization:* ICS: • aHR: 1.13 (95% CI: 1.03-1.23) • HR: 2.72 (95% CI: 2.60-2.85) **Comorbid Conditions:** NR **Risk Markers:** *Mortality among COPD patients, n/N (%):* Age: p<0.001 40-59: • HR: 4.61 (95% CI: 2.93-7.26) • Died: 20/31,175 (0.06%) 60-79:

Study	Population and Setting	Intervention	Definitions	Results
				• HR: 2.26 (95% CI: 1.99-2.57) • Died: 310/115,046 (0.30%) ≥ 80: • HR: 1.28 (95% CI: 1.16-1.42) • Died: 481/46,194 (1.04%) Sex: p=0.005 Women: • HR: 1.77 (95% CI: 1.56-2.00) • Died: 321/92,676 (0.35%) Men: • HR: 1.42 (95% CI: 1.28-1.57) • Died: 490/100,844 (0.49%) Ethnic group: p=0.009 White: • HR: 1.55 (95% CI: 1.41-1.69) • Died: 635/161,376 (0.39%) Asian: • HR: 1.01 (95% CI: 0.70-1.44) • Died: 33/4,463 (0.74%) Black: • HR: 1.10 (95% CI: 0.70-1.73) • Died: 20/1,900 (1.05%) Chinese: • HR: 0.68 (95% CI: 0.09-5.05) • Died: <5/178 (2.81%) Other or not recorded: • HR: 1.89 (95% CI: 1.56-2.29) • Died: 122/25,603 (0.48%) Smoking status: Non-smoker: p=0.360 • HR: 1.51 (95% CI: 1.27-1.79) • Died: 145/23,935 (0.61%) Ex-smoker: • HR: 1.52 (95% CI: 1.37-1.67) • Died: 547/104,638 (0.52%) Current smoker: • HR: 1.72 (95% CI: 1.37-2.14) • Died: 145/64,775 (0.22%) *ICU admission among COPD patients, n/N (%):* Age: p=0.466 40-59:

Study	Population and Setting	Intervention	Definitions	Results
				• HR: 1.40 (95% CI: 0.69-2.83) • ICU admission: 8/31,175 (0.03%) 60-79: • HR: 0.90 (95% CI: 0.66-1.22) • ICU admission: 45/115,046 (0.04%) ≥ 80: • HR: 1.21 (95% CI: 0.51-2.85) • ICU admission: 6/46,194 (0.01%) Sex: p=0.025 Women: • HR: 1.43 (95% CI: 0.91-2.27) • ICU admission: 20/92,676 (0.02%) Men: • HR: 0.74 (95% CI: 0.53-1.04) • ICU admission: 39/100,844 (0.04%) Ethnic group: p=0.826 White: • HR: 0.91 (95% CI: 0.66-1.26) • ICU admission: 42/161,376 (0.03%) Asian: • HR: 0.74 (95% CI: 0.30-1.79) • ICU admission: 5/4,463 (0.11%) Black: • HR: 1.18 (95% CI: 0.44-3.20) • ICU admission: <5/1,900 (0.26%) Other or not recorded: • HR: 0.79 (95% CI: 0.38-1.54) • ICU admission: 8/25,603 (0.03%) Smoking status: p=0.732 Non-smoker: • HR: 0.76 (95% CI: 0.38-1.54) • ICU admission: 8/23,935 (0.03%) Ex-smoker: • HR: 0.89 (95% CI: 0.65-1.21)

Study	Population and Setting	Intervention	Definitions	Results
				• ICU admission: 45/104,638 (0.04%) Current smoker: • HR: 1.18 (95% CI: 0.51-2.72) • ICU admission: 6/64,775 (0.01%) *Hospitalization among COPD patients, n/N (%):* Age: p<0.0001 40-59: • HR: 2.57 (95% CI: 2.08-3.17) • Hospitalized: 91/31,175 (0.29%) 60-79: • HR: 1.93 (95% CI: 1.78-2.09) • Hospitalized: 725/115,046 (0.63%) ≥ 80: • HR: 1.31 (95% CI: 1.21-1.42) • Hospitalized: 739/46,194 (1.60%) Sex: p=0.090 Women: • HR: 1.63 (95% CI: 1.50-1.78) • Hospitalized: 635/92,676 (0.69%) Men: • HR: 1.49 (95% CI: 1.38-1.60) • Hospitalized: 920/100,844 (0.91%) Ethnic group: p=0.0002 White: • HR: 1.55 (95% CI: 1.46-1.66) • Hospitalized: 1,223/161,376 (0.76%) Asian: • HR: 0.98 (95% CI: 0.76-1.27) • Hospitalized: 61/4,463 (1.4%) Black: • HR: 1.17 (95% CI: 0.85-1.61) • Hospitalized: 39/1,900 (2.10%) Chinese:

Study	Population and Setting	Intervention	Definitions	Results
				• HR: 1.33 (95% CI: 0.33-5.45)
				• Hospitalized: <5/178 (2.81%)
				Other or not recorded:
				• HR: 1.83 (95% CI: 1.59-2.10)
				• Hospitalized: 230/25,603 (0.90%)
				Smoking status: p=0.0002
				Non-smoker:
				• HR: 1.37 (95% CI: 1.21-1.56)
				• Hospitalized: 253/23,935 (1.06%)
				Ex-smoker:
				• HR: 1.51 (95% CI: 1.41-1.62)
				• Hospitalized:1,031/104,638 (0.99%)
				Current smoker:
				• HR: 1.94 (95% CI: 1.69-2.23)
				• Hospitalized: 265/64,775 (0.41%)
				Mortality among asthma patients, n/N (%):
				Age: p=0.001
				20-39:
				• HR: 2.11 (95% CI: 1.00-4.42)
				• Died: 9/459,751 (<0.01%)
				40-59:
				• HR: 1.27 (95% CI: 0.95-1.69)
				• Died: 54/352,853 (0.02%)
				60-79:
				• HR: 1.09 (95% CI: 0.96-1.24)
				• Died: 275/218,881 (0.13%)
				≥ 80:
				• HR: 0.85 (95% CI: 0.77-0.95)
				• Died: 424/58,543 (0.72%)
				Sex: p=0.628
				Women:
				• HR: 0.97 (95% CI: 0.86-1.08)
				• Died: 362/571,497 (0.06%)
				Men:
				• HR: 1.01 (95% CI: 0.90-1.12)
				• Died: 400/518,531 (0.08%)
				Ethnic group: p=0.448

Study	Population and Setting	Intervention	Definitions	Results
				White: • HR: 0.96 (95% CI: 0.87-1.05) • Died: 514/84.083 (0.61%) Asian: • HR: 1.00 (95% CI: 0.78-1.27) • Died: 80/68,014 (0.12%) Black: • HR: 0.97 (95% CI: 0.72-1.32) • Died: 48/2,835 (1.69%) Chinese: • HR: 0.95 (95% CI: 0.22-4.03) • Died: <5/3,503 (0.14%) Other or not recorded: • HR: 1.14 (95% CI: 0.94-1.38) • Died: 118/206,076 (0.06%) Smoking status: p=0.396 Non-smoker: • HR: 0.99 (95% CI: 0.89-1.10) • Died: 374/624,797 (0.06%) Ex-smoker: • HR: 0.99 (95% CI: 0.88-1.11) • Died: 341/257,566 (0.13%) Current smoker: • HR: 0.91 (95% CI: 0.65-1.26) • Died: 40/193,373 (0.02%) *ICU admission among asthma patients, n/N (%):* Age: p=0.015 20-39: • HR: 2.16 (95% CI: 1.40-3.33) • ICU admission: 28/459,751 (0.01%) 40-59: • HR: 1.03 (95% CI: 0.81-1.30) • ICU admission: 78/352,853 (0.02%) 60-79: • HR: 1.03 (95% CI: 0.83-1.27) • ICU admission: 103/218,881 (0.05%) ≥ 80: • HR: 0.61 (95% CI: 0.22-1.69)

Study	Population and Setting	Intervention	Definitions	Results
				• ICU admission: <5/58,543 (0.01%) Sex: p=0.021 Women: • HR: 1.36 (95% CI: 1.07-1.74) • ICU admission: 84/571,497 (0.01%) Men: • HR: 0.95 (95% CI: 0.79-1.15) • ICU admission: 129/518,531 (0.02%) Ethnic group: p=0.230 White: • HR: 1.18 (95% CI: 0.97-1.43) • ICU admission: 124/784,083 (0.02%) Asian: • HR: 0.94 (95% CI: 0.65-1.34) • ICU admission: 34/68,014 (0.05%) Black: • HR: 1.33 (95% CI: 0.88-2.02) • ICU admission: 26/28,352 (0.09%) Chinese: • HR: 0.99 (95% CI: 0.13-7.56) • ICU admission: <5/3,503 (0.14%) Other or not recorded: • HR: 0.77 (95% CI: 0.52-1.13) • ICU admission: 28/206,076 (0.01%) Smoking status: p=0.725 Non-smoker: • HR: 1.06 (95% CI: 0.88-1.28) • ICU admission: 124/624,797 (0.02%) Ex-smoker: • HR: 1.14 (95% CI: 0.90-1.45) • ICU admission: 81/257,566 (0.03%) Current smoker: • HR: 0.79 (95% CI: 0.36-1.73)

Study	Population and Setting	Intervention	Definitions	Results
				• ICU admission: 7/193,373 (<0.01%) *Hospitalization among asthma patients, n/N (%):* Age: p<0.0001 20-39: • HR: 1.59 (95% CI: 1.37-1.86) • Hospitalized: 206/459,751 (0.04%) 40-59: • HR: 1.43 (95% CI: 1.29-1.57) • Hospitalized: 507/352,853 (0.14%) 60-79: • HR: 1.19 (95% CI: 1.10-1.28) • Hospitalized: 847/218,881 (0.39%) ≥ 80: • HR: 0.93 (95% CI: 0.86-1.00) • Hospitalized: 706/58,543 (1.21%) Sex: p=0.0001 Women: • HR: 1.29 (95% CI: 1.21-1.37) • Hospitalized: 1,238/571,497 (0.22%) Men: • HR: 1.08 (95% CI: 1.01-1.15) • Hospitalized: 1,028/518,531 (0.20%) Ethnic group: p=0.868 White: • HR: 1.20 (95% CI: 1.14-1.27) • Hospitalized: 1,539/748,083 (0.21%) Asian: • HR: 1.16 (95% CI: 1.01-1.33) • Hospitalized: 252/68,014 (0.37%) Black: • HR: 1.10 (95% CI: 0.93-1.31) • Hospitalized: 149/28,352 (0.53%)

Study	Population and Setting	Intervention	Definitions	Results
				Chinese: • HR: 1.07 (95% CI: 0.43-2.67) • Hospitalized: 5/3,503 (0.14%) Other or not recorded: • HR: 1.15 (95% CI: 1.02-1.29) • Hospitalized: 321/206,076 (0.16%) Smoking status: p=0.286 Non-smoker: • HR: 1.18 (95% CI: 1.11-1.25) • Hospitalized: 1,205/624,797 (0.19%) Ex-smoker: • HR: 1.16 (95% CI: 1.07-1.25) • Hospitalized: 868/257,566 (0.34%) Current smoker: • HR: 1.32 (95% CI: 1.12-1.55) • Hospitalized: 182/193,373 (0.09%) **Long-term Sequelae:** NR
Author: Beltramo[2] Year: 2021 Data Extractor: MC Reviewer: DOS Study design: Cohort Study Objective: To describe and compare chronic respiratory diseases (CRD) in hospitalized	Population: N= 89,530 COVID-19 patients Setting: Public and private hospitals Location: France Study dates: COVID-19 cohort: March 1 - April 30, 2020 Inclusion criteria: For the COVID-19 cohort, all patients hospitalized for COVID-19 during the study dates were included and identified by the primary, related, or associated diagnoses by the ICD-10 codes U0710, U0711, U0712, U0714 or U0715, regardless of their age. Data obtained from the national Programme de Medicalisation des Systemes d'Information (PMSI) database. Exclusion criteria: NR	Health Condition Category: Chronic heart disease, Chronic lung disease, Cancer Medical Condition, n/N (%): Pulmonary hypertension: 341/89,530 (0.38%) Any CRD: 14351/89530 (16.0%) Chronic respiratory failure: 1433/89,530 (1.60%) Sleep apnea: 3581/89,530 (4.00%) Chronic obstructive pulmonary disease (COPD): 4866/89,530 (5.44%)	Medical Condition(s): *Pulmonary hypertension*: ICD-10 I270 *Any CRD*: includes chronic respiratory failure, asthma, COPD, ILD, pulmonary hypertension, sarcoidosis, CF, and lung cancer *Chronic respiratory failure*: ICD-10 J961 *Sleep apnea*: ICD-10 G473 *COPD*: ICD-10 J40, J41, J42, J44 *Emphysema*: ICD-10 J43, J982	**Severe COVID-19:** *aOR: Adjusted odds ratio; adjusted for obesity, diabetes, hypertension, heart failure, atherosclerotic heart disease, sex, and age as a continuous variable* *OR: Odds ratio* *Mortality, n/N (%):* Pulmonary hypertension: • aOR: 1.24 (95% CI: 0.91-1.67) • OR: 2.01 (95% CI: 1.50-2.68) • Pulmonary hypertension: 96/341 (28.2%) • No CRD: 11222/75179 (14.93%) • p<0.05 Any CRD:

Study	Population and Setting	Intervention	Definitions	Results
patients suffering from COVID-19 or influenza (2018-2019 season), and to describe and compare respiratory complications for COVID-19 patients with CRD to COVID-19 patients without CRD and to influenza patients. IVA Score: 24 (moderate)		Emphysema: 1426/89,530 (1.59%) Asthma: 3273/89,530 (3.66%) Cystic fibrosis (CF): 20/89,530 (0.02%) Interstitial lung disease (ILD): 1611/89,530 (1.80%) Pulmonary sarcoidosis: 159/89,530 (0.18%) Lung cancer: 977/89,530 (1.09%) Control/Comparison group, n/N (%): No CRD: 75179/89530 (84.0%)	*Asthma*: ICD-10 J45, J46 *CF*: ICD-10 E840 *ILD*: ICD-10 J84 *Pulmonary sarcoidosis*: ICD-10 D86 *Lung cancer*: ICD-10 C34, C45 Severity Measure(s): NR Clinical marker: NR Treatment/ Associated Therapy, n/N (%): NR Outcome Definitions: *Mortality:* in-hospital mortality during hospitalization *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR Comments: none	- Any CRD: 3363/14351 (23.43%) - No CRD: 11222/75179 (14.93%) - p<0.0001 Chronic respiratory failure: - aOR: 1.30 (95% CI: 1.06-1.59) - OR: 2.10 (95% CI: 1.74-2.54) - Chronic respiratory failure: 413/1433 (28.8%) - No CRD: 11222/75179 (14.93%) - p<0.05 Sleep apnea: - aOR: 0.95 (95% CI: 0.85-1.06) - OR: 1.12 (95% CI: 1.02-1.25) - Sleep apnea: 672/3581 (18.8%) - No CRD: 11222/75179 (14.93%) - p<0.05 COPD: - aOR: 1.14 (95% CI: 1.06-1.22) - OR: 1.72 (95% CI: 1.61-1.84) - COPD: 1229/4886 (25.3%) - No CRD: 11222/75179 (14.93%) - p<0.05 Emphysema: - aOR: 1.01 (95% CI: 0.83-1.22) - OR: 1.18 (95% CI: 0.99-1.42)

Study	Population and Setting	Intervention	Definitions	Results
				• Emphysema: 312/1426 (21.8%) • No CRD: 11222/75179 (14.93%) Asthma: • aOR: 0.82 (95% CI: 0.71-0.94) • OR: 0.51 (95% CI: 0.45-0.58) • Asthma: 310/3273 (9.5%) • No CRD: 11222/75179 (14.93%) • p<0.05 Cystic fibrosis: • 0/20 (0.0%) ILD: • aOR: 1.20 (95% CI: 1.05-1.28) • OR: 1.41 (95% CI: 1.24-1.61) • ILD: 363/1611 (22.5%) • No CRD: 11222/75179 (14.93%) • p<0.05 Pulmonary sarcoidosis: • aOR: 2.11 (95% CI: 1.36-3.26) • OR: 1.38 (95% CI: 0.92-2.09) • Pulmonary sarcoidosis: 32/159 (20.1%) • No CRD: 11222/75179 (14.93%) Lung cancer: • aOR: 3.67 (95% CI: 3.20-4.21) • OR: 3.64 (95% CI: 3.20-4.14) • Lung cancer: 402/977 (41.2%)

Study	Population and Setting	Intervention	Definitions	Results
				• No CRD: 11222/75179 (14.93%) • $p < 0.05$ *ICU admission, n/N (%):* Pulmonary hypertension: • aOR: 1.73 (95% CI: 1.27-2.37) • OR: 1.97 (95% CI: 1.46-2.65) • Pulmonary hypertension: 97/341 (28.5%) • No CRD: 12119/75179 (16.12%) • $p < 0.05$ Any CRD: • Any CRD: 2985/14351 (20.80%) • No CRD: 12119/75179 (16.12%) • $p < 0.0001$ Chronic respiratory failure: • aOR: 1.03 (95% CI: 0.81-1.30) • OR: 1.18 (95% CI: 0.94-1.49) • Chronic respiratory failure: 320/1433 (22.3%) • No CRD: 12119/75179 (16.12%) Sleep apnea: • aOR: 1.39 (95% CI: 1.27-1.53) • OR: 2.74 (95% CI: 2.52-2.98) • Sleep apnea: 1172/3581 (32.7%) • No CRD: 12119/75179 (16.12%) • $p < 0.05$ COPD:

Study	Population and Setting	Intervention	Definitions	Results
				• aOR: 1.16 (95% CI: 1.07-1.26) • OR: 1.47 (95% CI: 1.37-1.58) • COPD: 986/4866 (20.6%) • No CRD: 12119/75179 (16.12%) • p<0.05 Emphysema: • aOR: 1.83 (95% CI: 1.56-2.16) • OR: 2.09 (95% CI: 1.78-2.45) • Emphysema: 405/1426 (28.4%) • No CRD: 12119/75179 (16.12%) • p<0.05 Asthma: • aOR: 1.23 (95% CI: 1.12-1.36) • OR: 1.35 (95% CI: 1.23-1.48) • Asthma: 640/3273 (19.6%) • No CRD: 12119/75179 (16.12%) • p<0.05 Cystic fibrosis: • aOR: 0.60 (95% CI: 0.1-2.60) • OR: 0.63 (95% CI: 0.15-2.73) • Cystic fibrosis: 2/20 (10.0%) • No CRD: 12119/75179 (16.12%) ILD: • aOR: 2.42 (95% CI: 2.14-2.72)

Study	Population and Setting	Intervention	Definitions	Results
				• OR: 2.77 (95% CI: 2.47-3.11) • ILD: 527/1611 (32.7%) • No CRD: 12119/75179 (16.12%) • p<0.05 Pulmonary sarcoidosis: • aOR: 2.65 (95% CI: 1.83-3.84) • OR: 2.94 (95% CI: 2.07-4.19) • Pulmonary sarcoidosis: 53/159 (33.3%) • No CRD: 12119/75179 (16.12%) • p<0.05 Lung cancer: • aOR: 0.77 (95% CI: 0.63-0.94) • OR: 0.78 (95% CI: 0.64-0.94) • Lung cancer: 117/977 (12.0%) • No CRD: 12119/75179 (16.12%) • p<0.05 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Drake[3]	Population: N=483 patients	**Health Condition Category:** Chronic heart	Medical Condition(s):	**Severe COVID-19:**

Study	Population and Setting	Intervention	Definitions	Results
Year: 2020 Data Extractor: JKK Reviewer: DOS Study design: Cohort Study Objective: To assess outcomes in patients with ILD hospitalized for COVID-19 versus those without ILD in a contemporaneous age-, sex-, and comorbidity-matched population. IVA Score: 24 (moderate)	Setting: tertiary ILD centers and secondary care hospitals Location: Denmark, Germany, Italy, Republic of Ireland, Spain, and the UK Study dates: March 1-May 1, 2020 Inclusion criteria: Physicians admitting patients with ILD were asked to identify all patients with a preexisting diagnosis of ILD admitted to the hospital during study period. Diagnosis of COVID-19 based on a SARS-CoV-2-positive PCR swab and/or clinicoradiological diagnosis. ILD patients were propensity-score matched to control patients identified through the ISARIC4C CCP-UK database at a 2:1 ratio. Exclusion criteria: Incomplete or minimal data or no diagnosis of COVID-19.	disease, Diabetes, Chronic Lung Disease, Risk Factors, Multiple Comorbid Conditions **Medical Condition, n/N (%):** Chronic heart disease: 138/483 (28.6%) Hypertension: 222/483 (46.0%) Diabetes: 147/483 (30.4%) Interstitial lung disease (ILD): 161/483 (33.3%) • Idiopathic pulmonary fibrosis (IPF): 68/161 (42.2%) **Control/Comparison group, n/N (%):** No chronic heart disease: 345/483 (71.4%) No hypertension: 261/483 (54.0%) No diabetes: 336/483 (69.6%) No ILD: 322/483 (66.7%)	*Chronic Heart Disease:* ND *Hypertension:* ND *Diabetes:* type 1 or type 2 *ILD:* any of the following conditions: chronic hypersensitivity pneumonitis, connective tissue disease-related ILD, IPF, rheumatoid-related ILD, sarcoidosis, Age-related ILD/presbyotic lung, ANCA vasculitis, asbestosis, autoimmune pneumonitis, chronic eosinophilic pneumonia, combined emphysema, and pulmonary fibrosis, desquamative interstitial pneumonia, non-specific interstitial pneumonia, organizing pneumonia, PPFE, smoking related ILD, or unclassifiable ILD *IPF:* ND Severity Measure(s): Moderate/Severe ILD: FVC<80% Mild ILD: FVC>80%	*aHR: Adjusted hazard ratio (95% CI); matched adjusted analysis* *Mortality, n/N (%):* Chronic Heart Disease: • aHR: 0.98 95%CI: (0.60-1.60); p=0.942 Hypertension: • aHR: 0.95 (95%CI: 0.60-1.50); p=0.817 Diabetes: • aHR: 1.24 (95%CI: 0.77-2.00); p=0.377 ILD: • aHR: 1.60 (95%CI: 1.17-2.18); p=0.003 • ILD: 79/161 (49.1%) • No ILD: 114/322 (35.4%) • p=0.013 Non-IPF ILD: • aHR: 1.50 (95%CI: 1.02–2.21); p=0.040 IPF: • aHR: 1.74 (95%CI: 1.16–2.60); p=0.007 *Mortality among non-obese patients:* ILD: • aHR: 1.09 (95%CI: 0.65-1.82); p=0.748 *Mortality among non-ILD patients:* Obesity: • aHR: 1.12 (95%CI: 0.71-1.77); p=0.628 *Ventilation, n/N (%):* • ILD: 6/161 (3.7%) • No ILD: 29/322 (9.0%)

Study	Population and Setting	Intervention	Definitions	Results

			Clinical marker: NR
			
			Treatment/ Associated Therapy: NR
			
			Outcome Definitions:
			Mortality: in-hospital mortality
			ICU admission: NR
			Intubation: NR
			Ventilation: ND
			Hospitalization: NR
			Non-elective readmissions: NR
			
			Comments: None
				Severity of Condition:
				Mortality, n/N (%):
				Moderate/Severe ILD:
				  • aHR: 1.72 (95%CI: 1.05 – 2.83); p=0.032
				  • Moderate/severe ILD: 42/69 (60.9%)
				  • Mild ILD: 27/69 (39.1%)
				  • p=0.039
				
				Duration of Condition: NR
				
				Treatment/ Associated Therapy: NR
				
				Comorbid Conditions:
				Mortality, n/N (%):
				Obesity:
				Obese &ILD:
				  • aHR: 2.27 (95%CI: 1.39–3.71); p=0.001
				
				Risk Markers:
				Mortality, n/N (%):
				Sex, male:
				  • aHR: 1.98 (1.14-3.43); p=0.015
				Female <60 years:
				  • ILD: 3/11 (27%)
				  • No ILD: 8/25 (32%)
				Female 60-75 years:
				  • ILD: 10/21 (48%)
				  • No ILD: 14/35 (40%)
				Female >75 years:
				  • ILD: 4/19 (21%)
				  • No ILD: 18/42 (43%)
				Male <60 years:
				  • ILD: 2/8 (25%)
				  • No ILD: 5/31 (16%)
				Male 60-75 years:
				  • ILD: 27/49 (55%)
				  • No ILD: 23/86 (27%)

Study	Population and Setting	Intervention	Definitions	Results
				Male >75 years: • ILD: 33/53 (62%) • No ILD: 46/103 (45%) **Long-term Sequelae:** NR
Author: Estiri[4] Year: 2021 Data Extractor: DOS Reviewer: MW Study design: Cohort Study Objective: To predict risk of mortality and study risk factors for death across different age groups. IVA Score: 25 (moderate)	Population: N=16709 Setting: Medical system consisting of 10 hospital Location: MA, US Study dates: March 3 - November 10, 2020 Inclusion criteria: Electronic health record (EHR) data from patients with a confirmed case for COVID-19 (confirmed PCR test) who had at least 1 year of medical history (i.e., a 1-year time difference between the first and last medical record before the COVID-19 positive PCR test) with medical system. Included data from beginning of electronic record (as far back as January 1, 2020) up to 14 days prior to the positive COVID-19 PCR test date. Exclusion criteria: NR	Health Condition Category: Cerebrovascular Disease, Chronic Heart Disease, Neurocognitive Disorders, Diabetes, Chronic Kidney Disease, Chronic Lung Disease, Risk Factors, Immunocompromised Status, Blood Disorders, Cancer Medical Condition, n/N (%): Cerebrovascular accident: 1337/16709 (8.0%) Thoracic aortic aneurysm: 212/16709 (0.1%) Abdominal aortic aneurysm: 151/16709 (0.9%) Atrial fibrillation and flutter: 1262/16709 (7.6%) Aortic valve disorder: 727/16709 (4.4%) Cardiomegaly: 893/16709 (5.3%) Coronary artery disease: 1924/16709 (11.5%) Heart failure: 1382/16709 (8.3%) Hyperlipidemia: 5733/16709 (34.3%) Hypertension: 6539/16709 (39.1%)	Medical Condition(s): *Cerebrovascular accident:* ICD9 434.x, 436, 437.x, 438.x; ICD10 I63.x, I69.x, G46.x *Thoracic aortic aneurysm:* ICD9 441.1, 441.2; ICD10 I71.1, I71.2 *Abdominal aortic aneurysm:* ICD9 441.3, 441.4; ICD10 I71.3, I71.4 *Atrial fibrillation and flutter:* ICD9 427.3x; ICD10 I48.x *Aortic valve disorder:* IDC9 424.1; ICD10 I35.x *Cardiomegaly:* ICD9 429.3; ICD10 I51.7 *Coronary artery disease:* ICD9 414.x; ICD10 I25.x, R93.1; ERX 705113; OMA NSPA3 *Heart failure:* ICD9 428.3x, 428.4x; ICD10 I50.3x, I50.4x, ICD9 398.91, 402.11, 402.91, 404.01, 404.11, 404.13, 404.91,	**Severe COVID-19:** *aOR: Adjusted odds ratio from Generalized Linear Model (GLM) boosting model; median over 10 model iterations; model included age, history of pneumonia, type 2 diabetes mellitus with complications, heart failure, chronic kidney disease, interstitial pulmonary disease, chronic obstructive pulmonary disease, pulmonary embolism, benign prostate hypertrophy, atrial fibrillation and flutter, hypertensive urgency or emergency, coronary artery disease, gout, lung neoplasm, history of a cerebrovascular accident, abdominal aortic aneurysm, cardiomegaly, and female* *RR: Univariate relative risk* *OR: Univariate odds ratio* *Mortality, n/N (%):* Cerebrovascular accident: • aOR: 1.009 (IQR: 0.003) • RR: 5.10 (95%CI: 4.45-5.84) • OR: 6.07 (95%CI: 5.16-7.11) • Non-survivors: 255/830 (30.7%) • Survivors: 1082/15,879 (6.9%) • p<0.001

Study	Population and Setting	Intervention	Definitions	Results
		Hypertensive emergency: 353/16709 (2.1%) Mitral valve disorder: 1131/16709 (6.8%) Occlusion of the carotid artery: 573/16709 (3.4%) Pulmonary hypertension: 322/16709 (1.9%) Tricuspid valve disorder: 695/16709 (4.2%) Ventricular tachycardia: 331/16709 (2.0%) Parkinson's disease: 165/16709 (1.0%) Epilepsy: 623/16709 (3.7%) Diabetes mellitus, type 1: 590/16709 (3.5%) Diabetes mellitus, type 2 with complications: 2082/16709 (12.5%) Diabetes mellitus, type 2 without complications: 3018/16709 (18.1%) End-stage renal disease: 383/16709 (2.3%) Chronic kidney disease: 1554/16709 (9.3%) Chronic obstructive pulmonary disease (COPD): 910/16709 (5.4%) Interstitial pulmonary disease: 260/16709 (1.6%) Obstructive sleep apnea: 1657/16709 (9.9%) Pulmonary embolism: 940/16709 (5.6%) Rheumatoid arthritis: 396/16709 (2.4%) Anemia: 4974/16709 (29.8%)	404.93, 428.0, 428.1, 428.2x, 428.4x; ODA MLFT5; ICD10 I09.81, I13.0, I11.0, I50.2x, I50.82, I50.84, I50.89, I50.4x, I50.9 *Hyperlipidemia:* ICD9 272.x; ICD10 E78.x *Hypertension:* ICD9 401.x, 405.x, 642.13, 997.91; ICD10 I10.x, O10.x, O11.x; ERX 100141; LMA 953; OMA MTDH2 *Hypertensive emergency:* ICD9 401.0, 405.01, 405.09; ICD10 I16.x *Mitral valve disorder:* ICD9 424.0; ICD10 I34.x *Occlusion of the carotid artery:* ICD9 433.1; ICD10 I65.2x *Pulmonary hypertension:* ICD9 416.0; ICD10 I27.x *Tricuspid valve disorder:* IDC9 387.0; ICD10 I36.x *Ventricular tachycardia:* IDC9 427.1; ICD10 I47.2 *Parkinson's disease:* ICD9 332.x; ICD10 G21.x *Epilepsy:* ICD9 345.x, 649.4x; ICD10 G40.x, Z82.0	Thoracic aortic aneurysm: • RR: 3.43 (95%CI: 2.51-4.67) • OR: 3.92 (95%CI: 2.67-5.60) • Non-survivors: 35/830 (4.2%) • Survivors: 177/15,879 (1.1%) • $p<0.001$ Abdominal aortic aneurysm: • aOR: 1.006 (IQR: 0.000) • RR: 5.70 (95%CI: 4.35-7.46) • OR: 7.47 (95%CI: 5.12-10.68) • Non-survivors: 41/830 (4.9%) • Survivors: 110/15,879 (0.7%) • $p<0.001$ Atrial fibrillation and flutter: • aOR: 1.016 (IQR: 0.003) • RR: 5.77 (95%CI: 5.05-6.60) • OR: 7.05 (95%CI: 6.00-8.26) • Non-survivors: 266/830 (32.0%) • Survivors: 996/15,879 (6.3%) • $p<0.001$ Aortic valve disorder: • RR: 5.66 (95%CI: 4.87-6.59) • OR: 7.09 (95%CI: 5.86-8.54) • Non-survivors: 170/830 (20.5%)

Study	Population and Setting	Intervention	Definitions	Results
		Peripheral vascular disease: 674/16709 (4.0%) Breast neoplasm: 407/16709 (2.4%) Lung neoplasm: 190/16709 (1.1%) Prostate neoplasm: 314/16709 (1.9%) Control/Comparison group, n/N (%): No cerebrovascular accident: 15372/16709 (92.0%) No thoracic aortic aneurysm: 16497/16709 (98.7%) No abdominal aortic aneurysm: 16558/16709 (99.1%) No atrial fibrillation and flutter: 15447/16709 (92.4%) No aortic valve disorder: 15982/16709 (95.6%) No cardiomegaly: 15816/16709 (94.7%) No coronary artery disease: 14785/16709 (88.5%) No heart failure: 15327/16709 (91.7%) No hyperlipidemia: 1097616709 (65.7%) No hypertension: 10170/16709 (60.9%)	*Diabetes mellitus, type 1:* ICD9 25.x1, 250.x3; ICD10 E10.x *Diabetes mellitus, type 2 with complications:* ICD9 249.x, 250.x0, 250.x2; ICD10 E08.x, E09.x, E11.x, E13.x *Diabetes mellitus, type 2 without complications:* ICD9 240.0x, 250.0x; ICD10 E08.9, E11.9, E13.9 *End-stage renal disease:* ICD9 458.21, 585.5, 585.6, 996.68, 996.68, 996.73, V45.1, V45.11, V45.12, V56.x; ICD10 N18.5, N18.6, I13.11, I13.2, I12.0, I95.3, T85.611x, T85.621A, T85.691A, T85.71XD, T82.41Xx, T82.43Xx, T82.49Xx, Y62.2, Y84.1, Z49.01, Z49.02, Z49.3, Z91.15, Z99.2; ERX122830, LMA 3772, OMA BASX6 *Chronic kidney disease:* ICD9 585.x; ICD10 D63.1, E08.22, E09.22, E10.22, E11.22, E13.22, I12.x, I13.x, N18.x *COPD:* ICD9 434.x, 436, 437.x, 438.x; ICD10 I63.x, I69.x, G46.x	• Survivors: 557/15,879 (3.5%) • $p<0.001$ Cardiomegaly: • aOR: 1.006 (IQR: 0.000) • RR: 4.03 (95%CI: 3.43-4.74) • OR: 4.67 (95%CI: 3.85-5.63) • Non-survivors: 154/830 (18.6%) • Survivors: 739/15,879 (4.7%) • $p<0.001$ Coronary artery disease: • aOR: 1.014 (IQR: 0.003) • RR: 5.52 (95%CI: 4.85-6.28) • OR: 6.28 (95%CI: 5.62-7.55) • Non-survivors: 347/830 (41.8%) • Survivors: 1577/15,879 (10.0%) • $p<0.001$ Heart failure: • aOR: 1.047 (IQR: 0.011) • RR: 6.31 (95%CI: 5.54-7.19) • OR: 7.79 (95%CI: 6.67-9.08) • Non-survivors: 301/830 (36.3%) • Survivors: 1081/15,879 (6.8%) • $p<0.001$ Hyperlipidemia:

Study	Population and Setting	Intervention	Definitions	Results
		No hypertensive emergency: 16356/16709 (97.9%) No mitral valve disorder: 15578/16709 (93.2%) No occlusion of the carotid artery: 16136/16709 (96.6%) No pulmonary hypertension: 16387/16709 (98.1%) No tricuspid valve disorder: 16014/16709 (95.8%) No ventricular tachycardia: 16378/16709 (98.0%) No Parkinson's disease: 16544/16709 (99.0%) No epilepsy: 16086/16709 (96.3%) No diabetes mellitus, type 1: 16119/16709 (96.5%) No diabetes mellitus, type 2 with complications: 14627/16709 (87.5%) No diabetes mellitus, type 2 without complications: 13691/16709 (81.9%) No end-stage renal disease: 16326/16709 (97.7%) No chronic kidney disease: 15155/16709 (90.7%) No COPD: 15799/16709 (94.6%) No interstitial pulmonary disease: 16449/16709 (98.4%)	*Interstitial pulmonary disease:* ICD9 516.x; ICD10 J84.x *Obstructive sleep apnea:* ICD9 780.57, 780.53, 327.23; ICD10 G47.33 *Pulmonary embolism:* ICD9 415.x, 453.x, 445.x, 673.x; ICD10 I26.x, I74.x, I75.x, I82.x, O88.x, Z86.711, Z86.718 *Rheumatoid arthritis:* ICD9 714.x; ICD10 M05.x, M06.x, M08.x *Anemia:* ICD9 280.x, 281.x, 282.x, 283.x, 285.x; ICD10 D50.x, D50.x-53.x, D55.x-D59.x, D60x-D64.x, O90.81, O99.01x *Peripheral vascular disease:* ICD9 443.9; ICD10 I73.9 *Breast neoplasm:* ICD9 174.x; ICD10 C50.x *Lung neoplasm:* ICD9 162.x (excluding x=0); ICD10 C34.x *Prostate neoplasm:* ICD9 185.x; ICD10 C61.x Severity Measure(s): NR Clinical marker: NR	• RR: 4.04 (95%CI: 3.50-4.65) • OR: 4.37 (95%CI: 3.76-5.08) • Non-survivors: 563/830 (67.8%) • Survivors: 5170/15,879 (32.7%) • p<0.001 Hypertension: • RR: 6.61 (95%CI: 5.58-7.84) • OR: 7.25 (95%CI: 6.10-8.68) • Non-survivors: 672/830 (81.0%) • Survivors: 5867/15,879 (37.2%) • p<0.001 Hypertensive emergency: • aOR: 1.015 (IQR: 0.021) • RR: 3.87 (95%CI: 3.07-4.88) • OR: 4.51 (95%CI: 3.38-5.94) • Non-survivors: 64/830 (7.7%) • Survivors: 289/15,879 (1.8%) • p<0.001 Mitral valve disorder: • RR: 3.98 (95%CI: 3.42-4.63) • OR: 4.57 (95%CI: 3.82-5.43) • Non-survivors: 186/830 (22.4%) • Survivors: 945/15,879 (6.0%) • p<0.001

Study	Population and Setting	Intervention	Definitions	Results
		No obstructive sleep apnea: 15052/16709 (90.1%) No pulmonary embolism: 15769/16709 (94.4%) No rheumatoid arthritis: 16313/16709 (97.6%) No anemia: 11735/16709 (70.2%) No peripheral vascular disease: 16035/16709 (96.0%) No breast neoplasm: 16302/16709 (97.6%) No lung neoplasm: 16519/16709 (98.9%) No prostate neoplasm: 16395/16709 (98.1%)	Treatment/ Associated Therapy: NR Outcome Definitions: *Mortality:* from various data sources and included mortality unrelated to visit *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR Comments: None	Occlusion of the carotid artery: • RR: 5.23 (95%CI: 4.42-6.18) • OR: 6.47 (95%CI: 5.23-7.96) • Non-survivors: 130/830 (15.7%) • Survivors: 443/15,879 (2.8%) • p<0.001 Pulmonary hypertension: • RR: 4.91 (95%CI: 3.96-6.07) • OR: 6.06 (95% CI: 4.59-7.91) • Non-survivors: 73/830 (8.8%) • Survivors: 249/15,879 (1.6%) • p<0.001 Tricuspid valve disorder: • RR: 4.12 (95%CI: 3.47-4.91) • OR: 4.82 (95% CI: 3.90-5.91) • Non-survivors: 126/830 (15.2%) • Survivors: 569/15,879 (3.6%) • p<0.001 Ventricular tachycardia: • RR: 5.42 (95%CI: 4.44-6.63) • OR: 6.89 (95% CI: 5.28-8.90) • Non-survivors: 82/830 (9.9%) • Survivors: 249/15,879 (1.6%) • p<0.001 Parkinson's disease:

Study	Population and Setting	Intervention	Definitions	Results
				• RR: 4.02 (95%CI: 2.92-5.53) • OR: 4.76 (95% CI: 3.16-6.96) • Non-survivors: 32/830 (3.9%) • Survivors: 133/15,879 (0.8%) • p<0.001 Epilepsy: • RR: 2.45 (95%CI: 1.95-3.08) • OR: 2.65 (95% CI: 2.03-3.40) • Non-survivors: 72/830 (8.7%) • Survivors: 551/15,879 (3.5%) • p<0.001 Diabetes mellitus, type 1: • RR: 3.20 (95%CI: 2.60-3.93) • OR: 3.58 (95% CI: 2.80-4.53) • Non-survivors: 87/830 (10.5%) • Survivors: 503/15,879 (3.2%) • p<0.001 Diabetes mellitus, type 2 with complications: • aOR: 1.047 (Interquartile Range (IQR): 0.015) • RR: 3.82 (95%CI: 3.35-4.39) • OR: 4.30 (95% CI: 3.69-4.99) • Non-survivors: 293/830 (35.3%) • Survivors: 1789/15,879 (11.3%)

Study	Population and Setting	Intervention	Definitions	Results
				• p<0.001 Diabetes mellitus, type 2 without complications: • RR: 3.47 (95%CI: 3.05-3.96) • OR: 3.81 (95% CI: 3.30-4.40) • Non-survivors: 360/830 (43.4%) • Survivors: 2658/15,879 (16.8%) • p<0.001 End-stage renal disease: • RR: 4.74 (95%CI: 3.87-5.80) • OR: 5.78 (95% CI: 4.46-7.41) • Non-survivors: 83/830 (10.0%) • Survivors: 300/15,879 (1.9%) • p<0.001 Chronic kidney disease: • aOR: 1.042 (IQR: 0.014) • RR: 6.83 (95%CI: 6.01-7.77) • OR: 8.48 (95% CI: 7.29-9.85) • Non-survivors: 342/830 (41.2%) • Survivors: 1212/15,879 (7.7%) • p<0.001 COPD: • aOR: 1.024 (IQR: 0.021) • RR: 4.77 (95%CI: 4.10-5.55) • OR: 5.70 (95% CI: 4.74-6.82)

Study	Population and Setting	Intervention	Definitions	Results
				• Non-survivors: 179/830 (21.6%) • Survivors: 731/15,879 (4.6%) • p<0.001 Interstitial pulmonary disease: • aOR: 1.027 (IQR: 0.025) • RR: 4.32 (95%CI: 3.36-5.54) • OR: 5.17 (95% CI: 3.76-7.00) • Non-survivors: 53/830 (6.4%) • Survivors: 207/15,879 (1.3%) • p<0.001 Obstructive sleep apnea: • RR: 2.84 (95%CI: 2.49-3.24) • OR: 3.04 (95% CI: 2.64-3.51) • Non-survivors: 128/830 (15.4%) • Survivors: 1529/15,879 (9.7%) • p<0.001 Pulmonary embolism: • aOR: 1.018 (IQR: 0.019) • RR: 3.55 (95%CI: 3.01-4.19) • OR: 4.02 (95% CI: 3.30-4.86) • Non-survivors: 145/830 (17.5%) • Survivors: 795/15,879 (5.0%) • p<0.001 Rheumatoid arthritis:

Study	Population and Setting	Intervention	Definitions	Results
				• RR: 2.36 (95%CI: 1.78-3.14) • OR: 2.54 (95% CI: 1.83-3.46) • Non-survivors: 45/830 (5.4%) • Survivors: 351/15,879 (2.2%) • $p<0.001$ Anemia: • RR: 3.38 (95%CI: 2.96-3.87) • OR: 3.64 (95% CI: 3.16-4.20) • Non-survivors: 489/830 (58.9%) • Survivors: 4485/15,879 (28.4%) • $p<0.001$ Peripheral vascular disease: • RR: 5.04 (95%CI: 4.28-5.92) • OR: 6.15 (95% CI: 5.02-7.48) • Non-survivors: 145/830 (17.5%) • Survivors: 529/15,879 (3.4%) • $p<0.001$ Breast neoplasm: • RR: 2.62 (95%CI: 2.01-3.42) • OR: 2.86 (95% CI: 2.09-3.84) • Non-survivors: 51/830 (6.1%) • Survivors: 356/15,879 (2.3%) • $p<0.001$ Lung neoplasm:

Study	Population and Setting	Intervention	Definitions	Results
				• aOR: 1.012 (IQR: 0.000) • RR: 4.75 (95%CI: 3.62-6.23) • OR: 5.86 (95%CI: 4.09-8.22) • Non-survivors: 43/830 (5.2%) • Survivors: 147/15,879 (0.9%) • p<0.001 Prostate neoplasm: • RR: 3.63 (95%CI: 2.82-4.68) • OR: 4.19 (95%CI: 3.07-5.62) • Non-survivors: 54/830 (6.5%) • Survivors: 260/15,879 (1.6%) • p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%):* Female: • aOR: 0.972 (IQR: 0.017) • RR: 0.67 (95%CI: 0.58-0.76) • OR: 0.65 (95%CI: 0.57-0.75) • Non-survivors: 391/830 (47.1%)

Study	Population and Setting	Intervention	Definitions	Results
				• Survivors: 9,168/15,879 (58.1%) • p<0.001 Ethnicity, Hispanic: • RR: 0.32 (95%CI: 0.22-0.47) • OR: 0.31 (95%CI: 0.20-0.45) • Non-survivors: 27/830 (3.3%) • Survivors: 1,567/15,879 (9.9%) • p<0.001 Race, White: • RR: 2.36 (95%CI: 2.03-2.74) • OR: 2.45 (95%CI: 2.10-2.88) • Non-survivors: 608/830 (73.3%) • Survivors: 8,374/15,879 (53%) • p<0.001 Race, Black or African American: • RR: 0.84 (95%CI: 0.69-1.03) • OR: 0.84 (95%CI: 0.67-1.03) • Non-survivors: 104/830 (12.5%) • Survivors: 2,326/15,879 (14.7%) • p=0.102 Age: • aOR: 2.816 (IQR: 0.052) Age, under 45 years: • RR: 0.04 (95%CI: 0.02-0.06)

Study	Population and Setting	Intervention	Definitions	Results
				• OR: 0.03 (95%CI: 0.02-0.05) • Non-survivors: 21/830 (2.5%) • Survivors: 6,903/15,879 (43.7%) • p<0.001 Age, 45-65 years: • RR: 0.39 (95%CI: 0.33-0.47) • OR: 0.38 (95%CI: 0.31-0.45) • Non-survivors: 142/830 (17.1%) • Survivors: 5,629/15,879 (35.7%) • p<0.001 Age, 65-85 years: • RR: 3.88 (95%CI: 3.41-4.43) • OR: 4.30 (3.73-4.96) • Non-survivors: 385/830 (46.4%) • Survivors: 2,659/15,879 (16.8%) • p<0.001 Age, over 85 years: • RR: 8.35 (95%CI: 7.35-9.49) • OR: 11.36 (95%CI: 9.65-13.36) • Non-survivors: 282/830 (34.0%) • Survivors: 688/15,879 (4.4%) • p<0.001 Smoking history: • RR: 2.09 (95%CI: 1.76-2.50)

Study	Population and Setting	Intervention	Definitions	Results
				• OR: 2.21 (95%CI: 1.82-2.67) • Non-survivors: 137/830 (16.5%) • Survivors: 1304/15,879 (8.3%) • p<0.001 **Long-term Sequelae:** NR
Author: Halalau[5] Year: 2021 Data Extractor: MW Reviewer: DOS Study Design: Cohort Study Objective: To describe the demographics, initial clinical presentation, and outcomes of a large cohort of outpatients with COVID-19. IVA Score: 23 (moderate)	Population: N=821 Setting: Large healthcare system including 8 hospitals Location: Michigan, USA Study dates: Up to April 12, 2020 Inclusion criteria: Patients who tested positive for SARS-CoV-2 at any date up to April 1, 2020, after evaluation at any of the emergency departments across the 8 study hospitals, and subsequently discharged home. Laboratory confirmation for COVID-19 was defined as a positive result of real-time RT-PCR assay of nasopharyngeal swabs. Testing was offered if patients experienced moderate cough or fever over 100.4°F, and if they had chronic kidney disease, heart disease, diabetes, chronic lung disease, were receiving immunosuppression medication, or were immunocompromised due to cancer treatment, recent surgeries, or other conditions. Exclusion criteria: All patients with a negative test for SARS-CoV-2.	Health Condition Category: Chronic Heart Disease, Chronic Liver Disease, Neurocognitive Disorders, Diabetes, Chronic Kidney Disease, Chronic Lung Disease, Risk Factors, Immunocompromised Status, Blood Disorders, Cancer Medical Condition, n/N (%): Cerebrovascular Disease: 71/821 (8.6%) Transient Ischemic Attack: 48/821 (5.8%) Hypertension: 261/821 (31.8%) Hyperlipidemia: 168/821 (20.5%) Coronary Artery Disease: 125/821 (15.2%) Heart failure: 18/821 (2.2%) Cardiac arrhythmia: 116/821 (14.1%) Chronic liver disease: 11/821 (1.3%) Chronic Hepatitis B: 1/821 (0.1%)	Medical Condition(s): *Cerebrovascular Disease:* ND *Hypertension:* ND *Hyperlipidemia:* ND *Coronary Artery Disease:* ND *Heart failure:* ND *Cardiac arrhythmia:* ND *Chronic liver disease:* ND *Chronic Hepatitis B:* ND *Chronic Hepatitis C:* ND *Cognitive impairment or dementia:* ND *Seizure disorder:* ND *Transient Ischemic Attack:* ND *Psychiatric Disorder:* ND *Diabetes Mellitus:* ND *Prediabetes:* ND *Chronic kidney disease:* ND *COPD:* ND	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariate regression model included age, BMI, diabetes mellitus, obstructive sleep apnea, hypertension, COPD, dementia, and chronic kidney disease* *Hospitalization, n/N (%):* Cerebrovascular disease: • Admitted patients: 10/86 (11.6%) • Outpatients: 61/735 (8.3%) • p=0.299 Transient Ischemic Attack: • Admitted patients: 8/86 (9.3%) • Outpatients: 40/735 (5.4%) • p=0.149 Hypertension: • Admitted patients: 45/86 (52.3%) • Outpatients: 216/735 (29.4%) • p<0.001 Hyperlipidemia: • Admitted patients: 29/86 (33.7%) • Outpatients: 139/735 (18.9%)

Study	Population and Setting	Intervention	Definitions	Results
		Chronic Hepatitis C: 1/821 (0.1%) Cognitive impairment or dementia: 153/821 (18.6%) Seizure disorder: 150/821 (18.3%) Psychiatric Disorder: 103/821 (12.5%) Diabetes Mellitus: 279/821 (34%) Prediabetes: 82/821 (10.2%) Chronic kidney disease: 86/821 (10.5%) Chronic obstructive pulmonary disease (COPD): 74/821 (9%) Bronchial Asthma: 92/821 (11.2%) Obstructive Sleep Apnea: 171/821 (20.8%) Interstitial Lung Disease: 0/821 (0%) Pulmonary hypertension: 8/821 (1%) Sarcoidosis: 6/821 (0.7%) Venous thromboembolic disease: 103/821 (12.5%) Rheumatologic disorders: 146/821 (17.8%) Immunosuppression: 11/821 (1.3%) Cancer: 75/821 (9.1%) Control/Comparison group, n/N (%): None of the above: 295/821 (35.9%)	*Bronchial Asthma:* ND *Obstructive Sleep Apnea:* ND *Interstitial Lung Disease:* ND *Pulmonary hypertension:* ND *Sarcoidosis:* ND *Venous thromboembolic disease:* ND *Rheumatologic disorders:* ND *Immunosuppression:* ND *Venous thromboembolic disease:* ND *Cancer:* ND Severity Measure(s): NR Clinical marker: NR Treatment/ Associated Therapy: NR Outcome Definitions: *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* Emergency department visits for the patients that resulted in admission to hospital	• p=0.001 Coronary artery disease: • Admitted patients: 24/86 (27.9%) • Outpatients: 101/735 (13.7%) • p=0.001 Heart failure: • Admitted patients: 2/86 (2.3%) • Outpatients: 16/735 (2.2%) • p=1.0 Cardiac arrhythmia: • Admitted patients: 15/86 (17.4%) • Outpatients: 101/735 (13.7%) • p=0.351 Chronic liver disease: • Admitted patients: 0/86 (0%) • Outpatients: 11/735 (1.5%) • p=0.617 Chronic hepatitis B: • Admitted patients: 0/86 (0%) • Outpatients: 1/735 (0.1%) • p=1.0 Chronic hepatitis C: • Admitted patients: 0/86 (0%) • Outpatients: 1/735 (0.1%) • p=1.0 Cognitive impairment or dementia: • Admitted patients: 30/86 (34.9%)

Study	Population and Setting	Intervention	Definitions	Results
			Non-elective readmissions: NR Comments: None	• Outpatients: 123/735 (16.7%) • p <0.001 Seizure disorder: • Admitted patients: 27/86 (31.4%) • Outpatients: 123/735 (16.7%) • p=0.001 Psychiatric Disorder: • Admitted patients: 9/86 (10.5%) • Outpatients: 94/735 (12.8%) • p=0.538 Diabetes Mellitus: • aOR: 3.27 (95%CI: 1.49-7.15), p=0.003 • Admitted patients: 64/86 (74.4%) • Outpatients: 215/735 (29.3%) • p<0.001 Prediabetes: • Admitted patients: 22/86 (25.6%) • Outpatients: 62/735 (8.4%) • p<0.001 Chronic kidney disease: • Admitted patients: 15/86 (17.4%) • Outpatients: 71/735 (9.7%) • p=0.026 COPD: • Admitted patients: 34/86 (39.5%) • Outpatients: 40/735 (5.4%) • p<0.001

Study	Population and Setting	Intervention	Definitions	Results
				Bronchial Asthma: • Admitted patients: 12/86 (14.0%) • Outpatients: 80/735 (10.9%) • p=0.393 Obstructive Sleep Apnea: • aOR: 3.44 (95%CI: 1.11-10.65), p=0.032 • Admitted patients: 31/86 (36.0%) • Outpatients: 140/735 (19.0%) • p<0.001 Interstitial Lung Disease: • Admitted patients: 0/86 (0%) • Outpatients: 0/735 (0%) • p=N/A Pulmonary hypertension: • Admitted patients: 0/86 (0%) • Outpatients: 8/735 (1.1%) • p=1.0 Sarcoidosis: • Admitted patients: 2/86 (2.3%) • Outpatients: 4/735 (0.5%) • p=0.123 Venous thromboembolic disease: • Admitted patients: 11/86 (12.8%) • Outpatients: 92/735 (12.5%) • p=0.942 Rheumatologic disorders: • Admitted patients: 24/86 (28.9%)

Study	Population and Setting	Intervention	Definitions	Results
				• Outpatients: 122/735 (16.6%) • p=0.010 **Immunosuppression:** • Admitted patients: 1/86 (1.2%) • Outpatients: 10/735 (1.4%) • p=1.0 **Cancer:** • Admitted patients: 14/86 (16.3%) • Outpatients: 61/735 (8.3%) • p=0.015 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Hospitalization, n/N (%) or mean ±SD:* Age, years: • Admitted patients: 54.4±15.6 • Outpatients: 48.7±15.7 • p=0.002 Sex, male: • Admitted patients: 50/86 (58.1%) • Outpatients: 334/735 (45.4%) • p=0.026 Ethnicity; p=0.679 Caucasian:

Study	Population and Setting	Intervention	Definitions	Results
				• Admitted patients: 34/86 (39.5%) • Outpatients: 269/735 (36.6%) African American: • Admitted patients: 47/86 (54.6%) • Outpatients: 405/735 (55.1%) Other: • Admitted patients: 5/86 (5.8%) • Outpatients: 61/735 (8.3%) **Long-term Sequelae:** NR
Author: Kokturk[6] **Year:** 2021 **Data Extractor:** MW **Reviewer:** DOS **Study Design:** Cohort **Study Objective:** To evaluate the clinical outcomes of hospitalized patients and to predict COVID-19 mortality among highly suspected patients. **IVA Score:** 24 (moderate)	**Population:** N=1500 **Setting:** 26 Centers (17 university hospitals, 2 large tertiary hospitals, 2 secondary care hospitals and 5 private hospitals) **Location:** Turkey **Study dates:** March 11 – July 18, 2020 **Inclusion criteria:** Patients admitted to the hospital during study dates with a proven presence of a positive nucleic acid amplification test or a positive rapid antigen detection test together with clinical and radiographic findings that were strongly suggestive of COVID-19, and Highly probable cases presented with similar clinical and radiographic findings but could not be confirmed with an RT-PCR test. **Exclusion criteria:** NR	**Health Condition Category:** Cerebrovascular disease, Chronic heart disease, Chronic liver disease, Diabetes, Chronic kidney disease, Obesity, Chronic lung disease, Risk factors, Multiple comorbid conditions, Immunocompromised status, Blood disorders, Cancer **Medical Condition, n/N (%):** Cerebrovascular disease: 49/1500 (3.4%) Atherosclerosis: 145/1500 (10%) Hypertension: 402/1500 (27.4%) Heart failure: 64/1500 (4.4%) Chronic hepatic disease: 11/1500 (0.8%) Diabetes: 236/1500 (16.3%)	**Medical Condition(s):** *Cerebrovascular disease:* ND *Atherosclerosis:* ND *Hypertension:* ND *Heart failure:* ND *Chronic hepatic disease:* ND *Diabetes:* ND *Chronic kidney disease:* ND *Obesity:* BMI ≥30 *Asthma:* ND *COPD:* ND *Bronchiectasis:* ND *Interstitial lung disease:* ND *Immunosuppressive conditions:* ND *Connective tissue disorder:* ND *Malignancy:* ND *Others:* ND	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression with 1228 cases including clinical parameters, disease spectrum and comorbidities* *OR: Odds ratio; univariable logistic regression* *Mortality, n/N (%):* Cerebrovascular disease: • OR: 1.97 (95%CI: 0.69–5.65); p=0.209 • Non-survivors: 4/67 (6.3%) • Survivors: 45/1433 (3.3%) Atherosclerosis: • OR: 4.12 (95%CI: 2.34–7.26); p=0.001 • Non-survivors: 19/67 (29.2%) • Survivors: 126/1433 (9.1%) Hypertension: • OR: 3.08 (95%CI: 1.88–5.05); p=0.001 • Non-survivors: 35/67 (52.2%) • Survivors: 367/1433 (26.2%)

Study	Population and Setting	Intervention	Definitions	Results
		Chronic kidney disease: 51/1500 (3.5%) Obesity: 175/1500 (21.4%) Asthma: 111/1500 (7.7%) Chronic obstructive pulmonary disease (COPD): 90/1500 (6.2%) Bronchiectasis: 12/1500 (0.8%) Interstitial lung disease: 22/1500 (1.5%) Immunosuppressive conditions: 25/1500 (1.7%) Connective tissue disorders: 25/1500 (1.7%) Malignancy: 76/1500 (5.3%) **Control/Comparison group, n/N (%):** No cerebrovascular disease: 1451/1500 (96.7%) No atherosclerosis: 1355/1500 (90.3%) No hypertension: 1098/1500 (73.2%) No heart failure: 1436/1500 (95.7%) No chronic hepatic disease: 1489/1500 (99.3%) No diabetes: 1264/1500 (84.3%) No chronic kidney disease: 1449/1500 (96.6%) Not obese (BMI<30): 643/1500 (78.6%) No asthma: 1389/1500 (92.6%) No COPD: 1410/1500 (94%) No bronchiectasis: 1488/1500 (99.2%) No interstitial lung disease: 1478/1500 (98.5%)	**Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	Heart failure: • OR: 5.08 (95%CI: 2.51–10.27); p=0.001 • Non-survivors: 11/67 (16.9%) • Survivors: 53/1433 (3.9%) Chronic hepatic disease: • OR: 2.16 (95%CI: 0.27–17.15); p=0.466 • Non-survivors: 1/67 (1.6%) • Survivors: 10/1433 (0.7%) Diabetes: • OR: 1.28 (95%CI: 0.69–2.39); p=0.439 • Non-survivors: 13/67 (19.7%) • Survivors: 223/1433 (16.1%) Chronic kidney disease: • OR: 4.35 (95%CI: 1.96–9.68); p=0.001 • Non-survivors: 8/67 (12.3%) • Survivors: 43/1433 (3.1%) Obesity: • OR: 5.01 (95%CI: 0.66–37.80); p=0.118 • Not obesity: 18/643 (2.8%) • Obesity: 1/175 (0.5%) Asthma: • OR: 0.57 (95%CI: 0.17–1.84); p=0.345 • Non-survivors: 3/67 (4.6%) • Survivors: 108/1433 (7.9%) COPD: • OR: 5.24 (95%CI: 2.81–9.76); p=0.001 • Non-survivors: 15/67 (23.1%) • Survivors: 75/1433 (5.4%) Bronchiectasis: • OR: 1.93 (95%CI: 0.25–15.21); p=0.531 • Non-survivors: 1/67 (1.5%) • Survivors: 11/1433 (0.8%) Interstitial lung disease:

Study	Population and Setting	Intervention	Definitions	Results
		No immunosuppressive conditions: 1475/1500 (98.3%) No connective tissue disorders: 1475/1500 (98.3%) No malignancy: 1424/1500 (94.9%)		• aOR: 5.27 (95%CI: 1.17–23.8); p=0.031 • OR: 4.99 (95%CI: 1.64–15.21); p=0.005 • Non-survivors: 4/67 (6.3%) • Survivors: 18/1433 (1.3%) Immunosuppressive conditions: • OR: 5.73 (95%CI: 2.08–15.78); p=0.001 • Non-survivors: 5/67 (7.8%) • Survivors: 20/1433 (1.5%) Connective tissue disorder: • OR: 4.21 (95%CI: 1.4–12.66); p=0.001 • Non-survivors: 4/67 (6.0%) • Survivors: 21/1433 (1.4%) Malignancy: • aOR: 19.99 (95%CI: 8.14–49.1); p=0.001 • OR: 10.49 (95%CI: 5.81–18.94); p=0.001 • Non-survivors: 20/67 (30.8%) • Survivors: 56/1433 (4.1%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, n/N (%) or mean ± SD:* Age (years): • aOR: 1.09 (95%CI: 1.06–1.12); p=0.001 • OR: 1.08 (95%CI: 1.06–1.10); p=0.001 • Non-survivors: 71.3 ± 15.06

Study	Population and Setting	Intervention	Definitions	Results
				• Survivors: 50.98 ± 17.24 Age group: • OR: 6.71 (95%CI: 3.97–11.33); p=0.001 • Non-survivors ≥65: 45/379 (11.9%) • Non-survivors <65: 22/1117 (2.0%) Sex: • aOR: 2.47 (95%CI: 1.05–5.82); p=0.038 • OR: 1.96 (95%CI: 1.14–3.36); p=0.015 • Male non-survivors: 48/850 (5.6%) • Female non-survivors: 19/640 (3.0%) Smoking: Active smokers: • OR: 0.76 (95%CI: 0.26–2.23); p=0.622 • Active smoker non-survivors: 4/204 (2.0%) • Never smoker non-survivors: 23/901 (2.5%) Ex-smokers: • OR: 3.77 (95%CI: 2.08–6.84); p=0.001 • Ex-smoker non-survivors: 23/256 (9.0%) • Never smoker non-survivors: 23/901 (2.5%) Ever smokers: • OR: 2.38 (95%CI: 1.35–4.20); p=0.003 • Ever smoker non-survivors: 27/460 (5.9%) • Never smoker non-survivors: 23/901 (2.5%) **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
Author: Mollalo[8] **Year**: 2021 **Data Extractor:** DOS **Reviewer:** CS **Study design:** Predictive modeling **Study Objective:** To apply spatial and statistical analysis to better understand the geospatial distributions of the COVID-19 mortality rate (MR) and case fatality rate (CFR) in US **IVA Score:** 22 (moderate)	**Population:** N=NR **Setting:** nationwide **Location:** US **Study dates:** January 22 – November 22, 2020 **Inclusion criteria:** cumulative COVID-19 cases and deaths collected from *USAFacts*; age-adjusted mortality rates of 20 covariates collected from *University of Washington Global Health Data Exchange* **Exclusion criteria:** counties with less than 16 reported deaths were excluded from subsequent analyses	**Health Condition Category:** Cerebrovascular disease, Chronic heart disease, Chronic liver disease, Respiratory disease, Risk factors, Cancer, Blood diseases **Medical Condition:** Cerebrovascular disease: NR Cardiovascular disease: NR Cardiomyopathy & myocarditis: NR Peripheral vascular disease: NR Hypertensive heart: NR Atrial fibrillation: NR Hepatitis: NR Asthma: NR Pulmonary sarcoidosis & interstitial lung disease: NR COPD: NR Tracheal, bronchus, and lung cancer: NR Pancreatic cancer: NR Leukemia: NR Hodgkin lymphoma: NR Mesothelioma: NR HIV/AIDS: NR High-high (HH): counties with high COVID-19 mortality surrounded by counties with high COVID-19 mortalities Low-low (LL): counties with low COVID-19 mortality surrounded by counties with low COVID-19 mortalities	**Medical Condition(s):** *Cerebrovascular disease*: ND *Cardiovascular disease*: ND *Cardiomyopathy & myocarditis*: ND *Peripheral vascular disease*: ND *Hypertensive heart*: ND *Atrial fibrillation*: ND *Hepatitis*: ND *Asthma*: ND *Pulmonary sarcoidosis & interstitial lung disease*: ND *COPD*: ND *Tracheal, bronchus, and lung cancer*: ND *Pancreatic cancer*: ND *Leukemia*: ND *Hodgkin lymphoma*: ND *Mesothelioma*: ND *HIV/AIDS*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19 case fatality ratio (CFR)*:	**Severe COVID-19:** *Mixed-effects multinomial logistic regression model odds ratio [OR] (95% CI) for association between COVID-19 CFR classification (HH or LL) and mortalities of other diseases:* Cerebrovascular disease: • HH: 1.267 (95% CI: 1.169-1.374), p<0.001 • LL: 1.053 (95% CI: 0.977-1.135), p=0.180 Cardiovascular disease: • HH: 0.817 (95% CI: 0.759-0.880), p<0.001 • LL: 0.949 (95% CI: 0.884-1.018), p=0.142 Cardiomyopathy & myocarditis: • HH: 1.233 (95% CI: 1.113-1.366), p<0.001 • LL: 1.130 (95% CI: 1.024-1.246), p=0.014 Peripheral vascular disease: • HH: 1.034 (95% CI: 0.729-1.468), p=0.851 • LL: 0.953 (95% CI: 0.711-1.276), p=0.745 Hypertensive heart: • HH: 1.214 (95% CI: 1.126-1.309), p<0.001 • LL: 1.034 (95% CI: 0.963-1.109), p=0.361 Atrial fibrillation: • HH: 1.324 (95% CI: 1.130-1.551), p=0.001 • LL: 0.992 (95% CI: 0.872-1.128), p=0.902 Hepatitis: • HH: 5.602 (95% CI: 1.265-24.814), p=0.023

Study	Population and Setting	Intervention	Definitions	Results
		Control/Comparison group: Non-significant (NS): non-significant counties	proportion of recorded death over the confirmed cases	• LL: 0.808 (95% CI: 0.187-3.483), p=0.774
				Asthma:
		COVID-19 Mortality rate (MR): mean COVID-19 mortality rate per 100,000 individuals		• HH: 4.584 (95% CI: 2.583-8.137), p<0.001
				• LL: 0.818 (95% CI: 0.461-1.452), p=0.492
				Interstitial lung disease:
		Comments: none		• HH: 1.218 (95% CI: 1.012-1.466), p=0.037
				• LL: 0.826 (95% CI: 0.702-0.972), p=0.021
				COPD:
				• HH: 0.996 (95% CI: 0.976-1.016), p=0.705
				• LL: 1.028 (95% CI: 1.010-1.046), p=0.002
				Tracheal, bronchus, and lung cancer:
				• HH: 1.043 (95% CI: 1.016-1.070), p=0.002
				• LL: 0.967 (95% CI: 0.947-0.986), p=0.001
				Pancreatic cancer:
				• HH: 0.474 (95% CI: 0.377-0.596), p<0.001
				• LL: 1.343 (95% CI: 1.082-1.666), p=0.007
				Leukemia:
				• HH: 2.172 (95% CI: 1.518-3.106), p<0.001
				• LL: 0.432 (95% CI: 0.325-0.573), p<0.001
				Hodgkin lymphoma:
				• HH: 0.008 (95% CI: 0.000-1.196), p=0.059
				• LL: 48.361 (95% CI: 0.644-3633.023), p=0.078
				Mesothelioma:

Study	Population and Setting	Intervention	Definitions	Results
				• HH: 0.847 (95% CI: 0.522-1.375), p=0.502 • LL: 1.954 (95% CI: 1.130-3.380), p=0.017 HIV/AIDS: • HH: 0.850 (95% CI: 0.753-0.960), p=0.009 • LL: 2.061 (95% CI: 1.641-2.588), p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** Alcohol use disorder: • HH: 1.088 (95% CI: 0.965-1.227), p=0.168 • LL: 1.149 (95% CI: 1.044-1.266), p=0.005 Drug use disorder: • HH: 1.016 (95% CI: 0.972-1.061), p=0.491 • LL: 0.960 (95% CI: 0.928-0.992), p=0.016 **Long-term Sequelae:** NR
Author: Oh[7] **Year:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study design:** Cohort	**Population:** N=122,040 n=7,780 COVID-19 + **Setting:** National Health Insurance Service database **Location:** South Korea **Study dates:** January 1-June 26, 2020 **Inclusion criteria:** Individuals ≥20 years old, had a respiratory disease diagnosis by the International Classification of Diseases codes, and prescription	**Health Condition Category:** Cerebrovascular disease, Chronic heart disease, Chronic liver disease, Neurocognitive disorders, Diabetes, Chronic kidney disease, Chronic lung disease, Risk factors, Immunocompromised status, Blood disorders, Cancer	**Medical Condition(s):** ICD-10 codes were used to evaluate CRDs and other comorbid conditions in the study population:	**Severe COVID-19:** *aOR: Multivariable Logistic Regression: Multivariable Logistic Regression* *Mortality:* Cerebrovascular disease: • aOR: 0.57 (95% CI: 0.38-0.87); p=0.009 Hemiplegia/paraplegia:

Study	Population and Setting	Intervention	Definitions	Results
Study Objective: To investigate various chronic respiratory diseases (CRDs) that affect the risk of COVID-19 among the general population in South Korea, and to examine the effect of different CRDs on hospital mortality among patients with COVID-19 in South Korea. **IVA Score:** 25 (Moderate)	information concerning drugs and/or procedures from 2015-2020 were included. COVID-19 negative individuals were extracted from the national database using stratification methods with regard to age, sex, and residence in February 2020. **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Cerebrovascular disease: 5763/122,040 (4.6%) Hemiplegia/paraplegia: 568/122,040 (0.5%) Hypertension: 32,727/122,040 (26.3%) Congestive heart failure: 3683/122,040 (3.0%) Myocardial infarction: 1187/122,040 (1.0%) Mild liver disease: 13,612/122,040 (10.9%) Moderate or severe liver disease: 146/122,040 (0.1%) Dementia: 3926/122,040 (3.2%) Diabetes without chronic complication: 13,781/122,040 (11.1%) Diabetes: with chronic complication: 4255/122,040 (3.4%) Renal disease: 1392/122,040 (1.1%) Any chronic respiratory disease: 36,365/122,040 (29.2%) Chronic obstructive pulmonary disease (COPD): 4488/122,040 (3.6%) Asthma: 33,858/122,040 (27.2%) Interstitial lung disease: 421/122,040 (0.3%) Lung disease d/t external agent: 437/122,040 (0.4%) Obstructive sleep apnea: 550/122,040 (0.4%) Tuberculosis of lung: 608/122,040 (0.5%)	*Cerebrovascular disease:* G45.x, G46.x, H34.0, I60.x - I69.x *Hemiplegia/paraplegia:* G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0 - G83.4, G83.9 *Hypertension:* ND *Congestive heart failure:* I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5 - I42.9, I43.x, I50.x, P29.0 *Myocardial infarction:* I21.x, I22.x, I25.2 *Dementia:* F00.x - F03.x, F05.1, G30.x, G31.1 *Diabetes without chronic complication:* E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9 *Diabetes with chronic complication:* E10.2 - E10.5, E10.7, E11.2 - E11.5, E11.7, E12.2 - E12.5, E12.7, E13.2 - E13.5, E13.7, E14.2 - E14.5, E14.7 *Renal disease:* I12.0, I13.1, N03.2 - N03.7, N05.2 - N05.7, N18.x, N19.x, N25.0, Z49.0 - Z49.2, Z94.0, Z99.2	• aOR: 1.92 (95% CI: 1.03-3.59); p=0.040 Hypertension: • aOR: 1.36 (95% CI: 0.89-2.06); p=0.153 Congestive heart failure: • aOR: 1.91 (95% CI: 1.38-2.66); p<0.001 Myocardial infarction: • aOR: 0.79 (95% CI: 0.47-1.33); p=0.374 Dementia: • aOR: 1.61 (95% CI: 1.11-2.32); p=0.011 Diabetes without chronic complication: • aOR: 1.87 (95% CI: 1.35-2.59); p<0.001 Diabetes with chronic complication: • aOR: 1.61 (95% CI: 1.06-2.45); p=0.027 Renal disease: • aOR: 1.47 (95% CI: 0.87-2.47); p=0.148 Any chronic respiratory disease: • aOR: 1.19 (95% CI: 0.86-1.64); p=0.299 COPD: • aOR: 1.56 (95% CI: 1.06-2.2); p=0.024 Asthma: • aOR: 1.03 (95% CI: 0.76-1.41); p=0.834 Interstitial lung disease: • aOR: 1.83 (95% CI: 0.74-4.55); p=0.193 Lung disease d/t external agent: • aOR: 3.54 (95% CI: 1.70-7.38); p<0.001 Obstructive sleep apnea:

Study	Population and Setting	Intervention	Definitions	Results
		AIDS/HIV: 32/122,040 (0.0%) Peripheral vascular disease: 7198/122,040 (5.8%) Malignancy: 22,013/122,040 (17.7%) Metastatic solid tumor: 4072/122,040 (3.3%) Lung cancer: 769/122,040 (0.6%) **Control/Comparison group, n/N (%):** No cerebrovascular disease: 116,277/122,040 (95.3%) No hemiplegia/paraplegia: 121,472/122,040 (99.5%) No hypertension: 89,313/122,040 (73.2%) No congestive heart failure: 118,357/122,040 (97.0%) No myocardial infarction: 120,853/122,040 (99.0%) No mild liver disease: 108,428/122,040 (88.8%) No moderate or severe liver disease: 121,894/122,040 (99.9%) No dementia: 118,114/122,040 (96.8%) No diabetes without chronic complication: 108,259/122,040 (88.7%) No diabetes with chronic complication: 117,785/122,040 (96.5%) No renal disease: 120,648/122,040 (98.9%) No chronic respiratory disease: 85,675/122,040 (70.2%) No COPD: 117,552/122,040 (96.3%)	*Any chronic respiratory disease:* ND *COPD:* I27.8, I27.9, J40.x - J47.x, J60.x - J67.x, J68.4, J70.1, J70.3 *Asthma:* J45 *Interstitial lung disease:* J84.9 *Lung disease d/t external agent:* J60-J70 *Obstructive sleep apnea:* G47.33 *Tuberculosis of lung:* A15 *AIDS/HIV:* B20.x - B22.x, B24.x *Peripheral vascular disease:* I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9 *Malignancy:* except malignant neoplasm of skin; C00.x - C26.x, C30.x - C34.x, C37.x - C41.x, C43.x, C45.x - C58.x, C60.x - C76.x, C81.x - C85.x, C88.x, C90.x - C97.x *Metastatic solid tumor:* C77.x - C80.x *Lung cancer:* C34 **Severity Measure(s):** *Mild liver disease:* B18.x, K70.0 - K70.3, K70.9, K71.3 - K71.5, K71.7, K73.x, K74.x,	• aOR: 0.47 (95% CI: 0.06-3.94); p=0.486 Tuberculosis of lung: aOR: 1.65 (95% CI: 0.48-5.64); p=0.423AIDS/HIV: • aOR: 1.43 (95% CI: 0.11-19.37); p=0.788 Peripheral vascular disease: • aOR: 1.19 (95% CI: 0.81-1.76); p=0.76 Malignancy: • aOR: 1.07 (95% CI: 0.78-1.46); p=0.694 Metastatic solid tumor: • aOR: 1.37 (95% CI: 0.85-2.19); p=0.192 Lung cancer: • aOR: 1.82 (95% CI: 0.80-4.14); p=0.154 **Severity of Condition:** *Mortality:* Charlson comorbidity index: comorbidity index: • aOR: 1.80 (95% CI: 1.32-2.44); p<0.001 **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality:* Age, 10-year increase: • aOR: 2.85 (95% CI: 2.40-3.38); p<0.001 Sex, male: • aOR: 2.12 (95% CI: 1.55-2.88); p<0.001

Study	Population and Setting	Intervention	Definitions	Results
		No asthma: 88,182/122,040 (72.3%) No interstitial lung disease: 121,619/122,040 (99.7%) No lung disease d/t external agent: 121,603/122,040 (99.6%) No obstructive sleep apnea: 121,490/122,040 (99.5%) No tuberculosis of lung: 121,432/122,040 (99.5%) No AIDS/HIV: 122,008/122,040 (99.9%) No peripheral vascular disease: 114,842/122,040 (94.1%) No malignancy: 100,027/122,040 (82.0%) No metastatic solid tumor: 117,968/122,040 (96.7%) No lung cancer: 121,271/122,040 (99.4%)	K76.0, K76.2 - K76.4, K76.8, K76.9, Z94.4 *Moderate or severe liver disease:* I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7 *Charlson comorbidity index:* NDND **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** The paper reports different study sizes in the text (N=122,040; n=7,669 COVID-19+) and Figure 1 (N=124,330; n=7,780 COVID-19+).	Income level by quartile grouping: Q1 (lowest): 1 Q2: • aOR: 0.96 (95% CI: 0.59-1.57); p=0.882 Q3: • aOR: 1.08 (95% CI: 0.70-1.65); p=0.739 Q4 (highest): • aOR: 0.89 (95% CI: 0.652-1.30); p=0.554 Unknown: • aOR: 0.67 (95% CI: 0.18-2.54); p=0.560 **Long-term Sequelae:** NR

B.3.c. Internal Validity Assessments of Extracted Studies

Table 9. Internal Validity Assessments of Extracted Studies reporting the Association between Interstitial Lung Diseases and Severe COVID-19 Outcomes

Domain	Signaling question	Aveyard 2021[1]	Beltramo 2021[2]	Drake 2020[3]	Estiri 2021[4]	Halalau 2021[5]	Kokturk 2021[6]	Mollalo 2021[8]	Oh 2021[7]
	Outcome	Mortality, ICU, Hospitalization	Mortality, ICU admission	Mortality, ventilation	Hospitalization	Hospitalization	Mortality	Mortality for COVID-19 and other diseases	Mortality
		data extracted from medical records	Data extracted from hospital records	data extracted from medical records	medical records	Data extracted from electronic medical records	Data extracted from medical records	Data from USAFacts and UW Global Health Data Exchange	Data extracted from database
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1
	Well described population	1	1	1	1	1	1	1	1
	Well described setting	1	1	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	0	1	1	1	1	0	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1
Information Bias: Measurement	Measure of intervention/ exposure is valid	1	1	1	1	1	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	0	1

	Author Year	Aveyard 2021[1]	Beltramo 2021[2]	Drake 2020[3]	Estiri 2021[4]	Halalau 2021[5]	Kokturk 2021[6]	Mollalo 2021[8]	Oh 2021[7]
	Outcome	Mortality, ICU, Hospitalization	Mortality, ICU admission	Mortality, ventilation	Hospitalization	Hospitalization	Mortality	Mortality for COVID-19 and other diseases	Mortality
Domain	**Signaling question**	data extracted from medical records	Data extracted from hospital records	data extracted from medical records	medical records	Data extracted from electronic medical records	Data extracted from medical records	Data from USAFacts and UW Global Health Data Exchange	Data extracted from database
and Misclassification	Fidelity to intervention is measured	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1	0	1
	Adequately powered to detect result	0	0	0	1	0	0	0	1
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1	1	1
	Confidence interval is narrow	0	1	0	0	0	0	1	0
Confounding	Potential confounders identified	1	1	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0

	Author Year	Aveyard 2021[1]	Beltramo 2021[2]	Drake 2020[3]	Estiri 2021[4]	Halalau 2021[5]	Kokturk 2021[6]	Mollalo 2021[8]	Oh 2021[7]
	Outcome	Mortality, ICU, Hospitalization	Mortality, ICU admission	Mortality, ventilation	Hospitalization	Hospitalization	Mortality	Mortality for COVID-19 and other diseases	Mortality
Domain	**Signaling question**	data extracted from medical records	Data extracted from hospital records	data extracted from medical records	medical records	Data extracted from electronic medical records	Data extracted from medical records	Data from USAFacts and UW Global Health Data Exchange	Data extracted from database
	Adjustment for confounders in data analysis phase	1	1	1	1	0	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1	1
SCORE	Threat to internal validity	24	24	24	25	23	24	22	25
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

C. References

1. Aveyard P, Gao M, Lindson N, Hartmann-Boyce J, Watkinson P, Young D, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. The Lancet Respiratory Medicine 2021;9(8):909-923.

2. Beltramo G, Cottenet J, Mariet A-S, Georges M, Piroth L, Tubert-Bitter P, et al. Chronic respiratory diseases are predictors of severe outcome in COVID-19 hospitalised patients: a nationwide study. European Respiratory Journal 2021:2004474.

3. Drake TM, Docherty AB, Harrison EM, Quint JK, Adamali H, Agnew S, et al. Outcome of hospitalization for COVID-19 in patients with interstitial lung disease an international multicenter study. American Journal of Respiratory and Critical Care Medicine 2020;202(12):1656-1665.

4. Estiri H, Strasser ZH, Klann JG, Naseri P, Wagholikar KB, Murphy SN. Predicting COVID-19 mortality with electronic medical records. npj Digital Medicine 2021;4(1).

5. Halalau A, Odish F, Imam Z, Sharrak A, Brickner E, Lee PB, et al. Epidemiology, Clinical Characteristics, and Outcomes of a Large Cohort of COVID-19 Outpatients in Michigan. Int J Gen Med 2021;14:1555-1563.

6. Kokturk N, Babayigit C, Kul S, Duru Cetinkaya P, Atis Nayci S, Argun Baris S, et al. The predictors of COVID-19 mortality in a nationwide cohort of Turkish patients. Respir Med 2021;183:106433.

7.   Oh TK, Song IA. Impact of coronavirus disease-2019 on chronic respiratory disease in South Korea: an NHIS COVID-19 database cohort study. BMC Pulmonary Medicine 2021;21(1).
8.   Mollalo A, Rivera KM, Vahabi N. Spatial statistical analysis of pre-existing mortalities of 20 diseases with COVID-19 mortalities in the continental United States. Sustainable Cities and Society 2021;67:102738.

D. Abbreviations

Acronym	Full
95% CI	95% confidence interval
aHR	adjusted hazard ratio
aOR	adjusted odds ratio
BMI	body mass index
BPD	bronchopulmonary dysplasia
CF	cystic fibrosis
CFR	case fatality ratio
COI	conflict of interest
COPD	chronic obstructive pulmonary disease
CRD	chronic respiratory disease
ECMO	extracorporeal membrane oxygenation
EHR	electronic health record
EMR	electronic medical record
IQR	Interquartile range
GLM	generalized linear model
HH	high-high counties
HR	hazard ratio
ICD10	International Classification of Diseases 10
ICNARC	Intensive Care National Audit and Research Centre
ICS	inhaled corticosteroids
ICU	intensive care unit
ILD	interstitial lung disease
IPF	idiopathic pulmonary fibrosis
IVA	Internal validity assessments
LL	low-low counties
MR	mortality rate
ND	not defined

NR	not reviewed
OR	odds ratio
PCR	polymerase chain reaction
PECO	population, exposure, comparator, and outcomes
PMSI	Programme de Medicalisation des Systemes d'Information
RR	Rate ratio
RT-PCR	real time polymerase chain reaction