Brief Summary of Findings on the Association Between Underlying Liver Diseases and Severe COVID-19 Outcomes

Prepared and reviewed by

Megan Hofmeister, MD, MS, MPH; Physician; Epidemiology Research Team, Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention (CDC)

Erin C. Stone, MPH, MA; Public Health Analyst; Division of Healthcare Quality Promotion, National Center for Zoonotic and Emerging Infectious Diseases, CDC

Devon L. Okasako-Schmucker, MPH; Program Analyst; Eagle Global Scientific

Mylaica Conner Henry, MPH; Communications Specialist/Technical Writer; Eagle Global Scientific

Jill Kumasaka; ORISE Fellow; Division of Healthcare Quality Promotion, National Center for Zoonotic and Emerging Infectious Diseases, CDC

Tashika M. Robinson, MPH; Program Analyst III; Eagle Global Scientific, LLC

Christine Nam So, MPH; Program Analyst III; Eagle Global Scientific

Marwan Wassef, MPH; Data Analyst; Chenega Corporation

Kanta Devi Sircar, PhD, MPH, Epidemiologist, Underlying Conditions, Core Clinical Unit, Clinical Disease and Health Services Team, Health Systems and Worker Safety Task Force, CDC COVID-19 Response, CDC

Contact: CDC Info contact us form

Overall, 64 cohort and case-control studies were retrieved that reported data on any underlying liver disease and severe COVID-19 outcomes including mortality, intensive care unit (ICU) admission, intubation, ventilation, and hospitalization. All studies were rated as having moderate to low threat to internal validity.

- Any underlying chronic liver disease was associated with increased risk of mortality[1-39], ICU admission[2, 4, 8, 9, 16, 17, 22, 35, 37, 40], intubation[12, 20, 27, 41,], ventilation[2, 9, 15, 18, 20, 37, 42], and hospitalization[4, 8, 12, 17, 18, 22, 23, 36, 37, 43-46]. [Part B Table 2]
    - Hepatitis B was not associated with an increased risk of severe COVID-19 outcomes[38, 45, 47-51]. [Part B Table 4]
    - Hepatitis C was not associated with an increased risk of mortality[54] or ICU admission[54]. Inconsistent results limit the conclusions that can be made regarding the risk of hospitalization[45, 52] in people with underlying hepatitis C. [Part B Table 5]
    - Autoimmune hepatitis (AIH) may be associated with an increased risk of severe COVID-19 outcomes. Limited evidence from one study[37] suggested an increase in the odds of mortality, ICU admission, and ventilation was associated with AIH in COVID-19 patients; however, one study is insufficient evidence to draw conclusions. [Part B Table 6]
    - Non-alcoholic fatty liver disease (NAFLD) was not associated with an increased risk of mortality[2, 37, 53-55]. Inconsistent findings limit the conclusions that can be drawn regarding the risk of ICU admission in COVID-19 patients with underlying NAFLD (four studies). The data suggested that an increase in the rate of mechanical ventilation was associated with underlying NAFLD, however, the confidence in this result is limited because it is based on one cohort study. [Part B Table 7]
    - Alcohol-related liver disease (ALD) may be associated with an increased risk of severe COVID-19 outcomes Limited data from one study[37] suggested an increase in the odds of mortality was associated with ALD in COVID-19 patients; however, one study is insufficient evidence to draw conclusions. [Part B Table 8]
- A comparison between different underlying liver diseases suggested no difference in the risk of mortality between hepatitis B, hepatitis C, NAFLD, and fatty liver disease. [35, 37, 56] One[56] of the three studies reported an increase in the hazard of mortality was associated with underlying alcohol-related liver disease; however, conclusions associated with these findings are limited because they are based on only one study. [Part B Table 9]
- Increasing severity of liver disease was associated with a strong increase in the risk of mortality in patients with COVID-19. [10, 27, 52, 54, 57-60] Underlying liver diseases, measures of severity, and severity score thresholds varied across studies. [Part B Table 10]
    - Cirrhosis was associated with an increase in the risk of mortality and hospitalization in COVID-19 patients compared to COVID-19 patients with no underlying cirrhosis. [2, 23, 27, 35, 37, 54, 56, 61-63] [Part B Table 10]
- Comorbidities: Limited data from one study[52] suggested an increase in the risk of mortality, ICU admission, and hospitalization when comparing patients with hepatitis C, COVID-19, and ≥3 comorbidities with patients with COVID-19 alone. However, when examining the effect of specific comorbid conditions in addition to liver disease, the only condition associated with a consistent increase in risk of severe COVID-19 outcomes was diabetes.[18, 37, 56] [Part B Table 11]

Table A. Association Between Underlying Liver Diseases and Severe COVID-19 Outcomes

Underlying liver disease	Mortality	ICU admission	Intubation	Ventilation	Hospitalization
Hepatitis B	X	X	NR	X	X
Hepatitis C	X	X	NR	NR	I
Autoimmune hepatitis	✓(+)	✓(+)	NR	✓(+)	X
NAFLD	X	I	NR	✓(+)	NR
Alcoholic liver disease	✓(+)	NR	NR	NR	NR
Cirrhosis	✓(+)	NR	NR	NR	✓(+)

X = no association between the indicated severe COVID-19 outcome for patients with the indicated underlying liver condition compared to those without; ✓(+) = positive association (increased odds, risk, or rate); ✓(-) = negative association (decreased odds, risk, or rate); NR = not reported, data not available for assessment; I = inconsistent results between available studies preclude the ability to draw a conclusion about the association between the underlying liver disease and the indicated severe COVID-19 outcome

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A. Methods

The aim of this review is to identify and synthesize the best available evidence on the association between chronic liver conditions 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 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 Part B. Subject matter experts supplemented the literature search results by recommending relevant references published before December 2020. References were included if retrieved by the chronic liver disease literature search and reported exposures and outcomes relevant to this review.

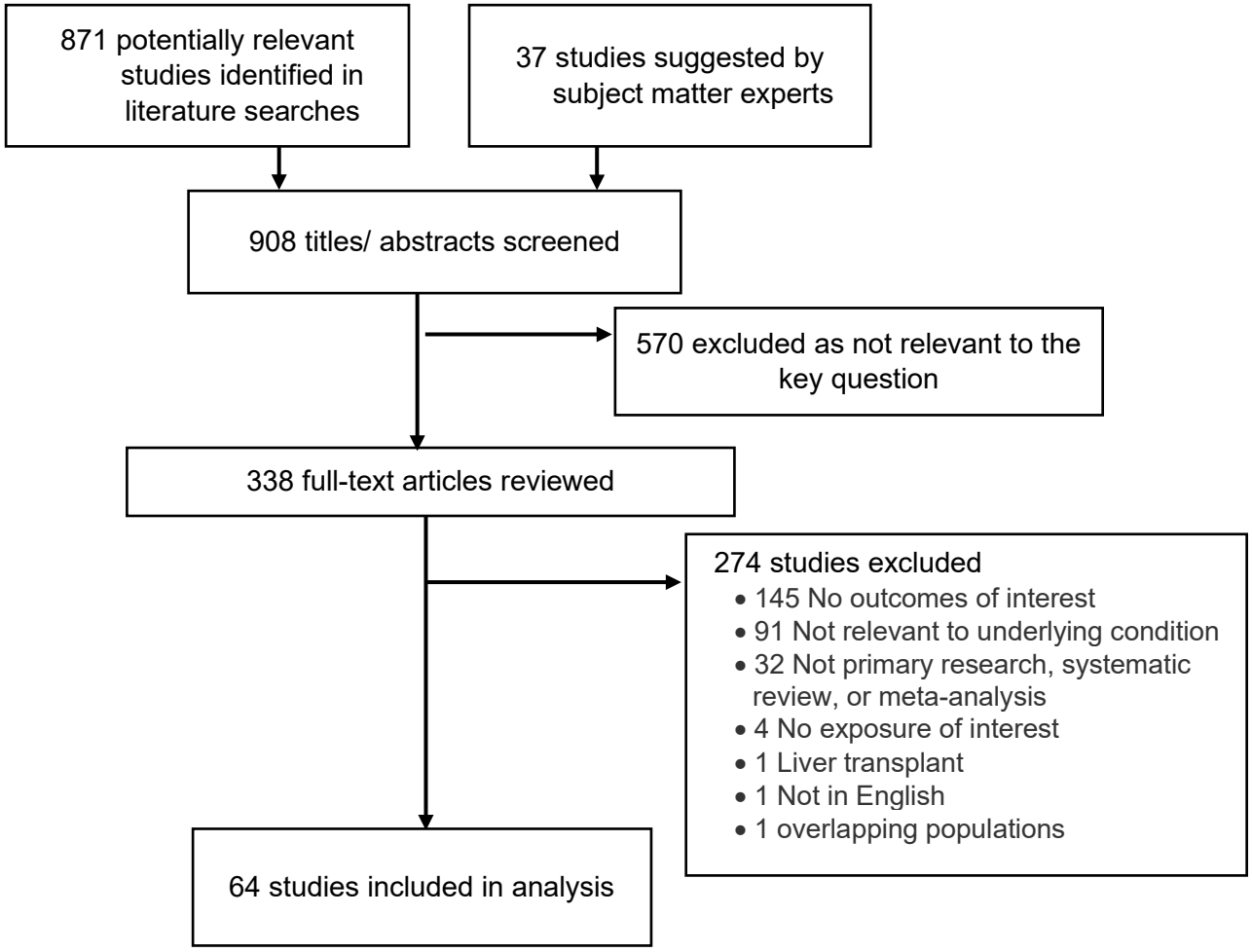
A.2. Study Selection

Titles and abstracts from references were screened by dual review (J.K.K., C.O., D.O.S., K.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.

The Part B 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



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. Part B includes the 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 the *Part B*.

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 Liver Disease Search Conducted February 18, 2021

#	Search History
1	liver disease*
2	cirrhosis
3	NAFLD
4	MAFLD
5	liver injur*
6	Hepatitis
7	Hemochromatosis
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Limit 8 to covid-19
10	(202012* or 2021*).dt
11	(202012* or 2021*).dc
12	10 or 11
13	9 and 12
14	Remove duplicates from 13

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 chronic liver disease and severe COVID-19?";
    - Exposures: Chronic liver disease, underlying liver disease, CLD, MAFLD, NAFLD, NASH, hepatitis B, hepatitis C, cirrhosis (severity).
    - Outcomes: mortality, ICU admission, intubation, ventilation, and hospitalization
- 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 liver transplant, liver cancer, or immunocompromised populations;
- reported autopsy results; and
- reported only composite outcome measures for "severe COVID-19".

B.3. Evidence Review: Chronic Liver Disease and Severe COVID-19 Outcomes

B.3.a. Strength & Direction of Evidence

Table 2 The Association Between Chronic Liver Disease and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence[1-38] suggests the presence of underlying chronic liver disease is associated with an increased risk, hazard, or odds of mortality. All studies were found to have a moderate to low threat to internal validity except for one cohort[3]. • Strength of Association: Thirty-eight studies[1-38] reported univariable and multivariable measures of association ranging from a high of 6.08 to a low of 0.68. Eleven these studies[1-10, 15]reporting multivariable analyses with measures of association between 1.19 and 2. • Precision of Association: Of the 21 studies reporting confidence intervals, 16 studies reported wide confidence intervals. • Consistency of Association: Overall, the evidence is consistent in the direction of increased risk of mortality. • Applicability of Association: The populations and settings were directly applicable to the question Summary of Evidence: • Twenty-four studies (N = 18,258,486), 22 cohort[1-7, 9, 11-24] and two case-control studies[8, 25] reported an effect measure suggesting that underlying chronic liver disease is associated with an increase in mortality in patients with COVID-19. o Of these studies, ten[2, 11, 15, 17-19, 21, 24] (N = 208,000) reported confidence intervals that span the null or non-significant results, decreasing confidence in the measure of effect most of these studies had small sample sizes and low numbers of events. • Eleven studies (N = 26,168), ten cohort[26-35] and one case-control study[36] reported an effect measure suggesting no association between underlying chronic liver disease and mortality in patients with COVID-19. • Three cohort studies[10, 37, 38] (N = 3,640) reported effect measures suggesting a protective association between underlying chronic liver disease and mortality in patients with COVID-19; however, the confidence intervals for these effect measures span the null, decreasing the confidence in this measure of effect.
ICU Admission	Evidence suggests the presence of underlying chronic liver disease is associated with an increased rate or odds of ICU admission. All studies were found to have a moderate to low threat to internal validity. • Strength of Association: Five studies [2, 4, 8, 17, 37] reported univariable and multivariable measures of effect. ranging from 1.2 – 3.48. Statistically significant, adjusted measures of effect ranged from 1.37 – 2.71. • Precision of Association: Confidence intervals were wide for all five odds ratios reported in the studies and crossed the null in one[4]. • Consistency of Association: The evidence is consistent in the direction of increased risk of ICU admission. • Applicability of Association: The populations and settings were directly applicable to the question. Summary of Evidence:

	• Seven studies (N = 847,421), one case control[8] and six cohort studies[2, 4, 17, 22, 37] reported an increase in the odds or rate of ICU admission in patients with underlying liver disease compared with patients with no liver disease. ○ Three of these studies[2, 4, 37] (N = 4,579)reported statistically significant results when adjusted for risk factors. • Four cohort studies[9, 16, 35, 40] (N = 17,109) reported no difference in the rate of ICU admission among COVID-19 patients with and without underlying liver disease.
Intubation	Overall, the evidence[12, 20, 27, 41] suggests the presence of underlying chronic liver disease is associated with an increased rate or odds of intubation. All studies were found to have a moderate to low threat to internal validity. • Strength of Association: No measures of association were reported. • Precision of Association: Confidence intervals were not calculated in these studies; however, a statistically significant difference was only reported in one study.[27] • Consistency of Association: Overall, the evidence is consistent in the direction of increased risk of intubation, however this generally did not reach statistical significance. • Applicability of Association: The populations and settings were directly applicable to the question. Summary of Evidence: • Four studies (N = 178,190), one nested case-control study[41] and three cohort studies[12, 20, 27] reported higher rates of intubation in patients with liver disease compared with patients with no liver disease, however this difference reached statistical significance in only one study.[27]
Ventilation	Evidence from seven studies[2, 9, 15, 18, 20, 37, 42] suggests the presence of underlying chronic liver disease is associated with an increased rate or odds of ventilation or mechanical ventilation. All studies were found to have a moderate to low threat to internal validity. • Strength of Association: Two US cohort studies[2, 15] reported higher adjusted odds of ventilation in patients with underlying liver disease between 1.42 and 2.08. One Spanish cohort study[9] reported a reduction in the adjusted odds of ventilation in patients with underlying liver disease. • Precision of Association: Confidence intervals were narrow in two studies[9, 15] and wider in the third study[2] however none of these confidence intervals crossed the null. • Consistency of Association: Tour studies[2, 15, 20, 37] (N = 13,553) suggest an increase in ventilation and an increased risk of ventilation, and two studies[9, 18] reported a decrease in the rate or risk of ventilation however when considering the country in which these studies were conducted, studies conducted in the US, China, and multiple countries reported increased risk of ventilation, and two Spanish studies reported a reduction in the odds of ventilation. • Applicability of Association: The populations and settings were directly applicable to the question. Summary of Evidence: • Four cohort studies[2, 15, 20, 37] (N = 13,553) reported an increase in the adjusted odds or rate of ventilation in COVID-19 patients with underlying liver disease compared to patients with no underlying liver disease.

	• Three cohort studies[9, 18, 42] (N = 12,769) reported an increase in mechanical ventilation for COVID-19 patients with and without underlying liver disease.
Hospitalization	The evidence from thirteen studies[4, 8, 12, 17, 18, 22, 23, 36, 37, 43-46] suggests the presence of underlying chronic liver disease is associated with an increased rate or odds of hospitalization. All studies were found to have a high to low threat to internal validity. • Strength of Association: In studies that measured the odds or risk of hospitalization, the association ranged from 1.3 to 3.26. • Precision of Association: Confidence intervals were relatively narrow for all associations and crossed one. • Consistency of Association: There were inconsistencies in the evidence, however overall, the largest sample sizes were in the direction of an increase in risk. • Applicability of Association: The populations and settings were directly applicable to the question. Summary of Evidence: • Eight studies (N = 329,045), one case-control[12] and seven cohort studies[17, 18, 23, 36, 37, 43, 44] reported an increase in the odds, risk or rate of hospitalization in patients with underlying liver disease compared to patients with no underlying liver disease. ○ One of these studies[44] (N = 257) reported wide confidence intervals that cross the null, reducing the confidence in these results. • Three studies (N = 504,008), one cohort[8] and two case-control studies[45, 46] reported no difference in rates or odds of hospitalization in COVID-19 patients with and without underlying liver disease. • Two cohort studies[4, 22] (N = 209,930) reported a reduction in the rate or odds of hospitalization in COVID-19 patients with and without underlying liver disease.

Table 3 The Association Between Hepatitis Mortality and COVID-19 Case Fatality Ratio

Outcome	Results
Case fatality ratio	One study is insufficient to determine the overall odds of case fatality due to underlying hepatitis in patients with COVID-19. • One geospatial analysis[39] (N = NR) reported a strong, statistically significant increase in the odds of a high COVID-19 case fatality in clustered counties with a high hepatitis mortality rate.

Table 4 The Association Between Hepatitis B Virus (HBV) Infection and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence suggested no difference in the risk, odds, or rate of mortality when comparing patients with HBV to those without. • Strength of Association: The association was not strong, ranging from 0.26 – 1.14

	• Precision of Association: Confidence intervals were wide for all findings • Consistency of Association: overall, the evidence is inconsistent in direction. • Applicability of Association: the populations and settings were all in China, reducing applicability of these findings. Six studies[38, 47-51] (N = 6,440) reported on data on mortality and HBV in COVID-19 patients, and all were found to have a moderate to low threat to internal validity. • Two Chinese cohort studies[47, 48] (N = 1,810) reported increased rates of mortality among patients with underlying HBV compared to those with no HBV, however these differences did not reach statistical significance. • Three Chinese cohort studies[38, 49, 50] (N = 4,010) reported no difference in the hazard or rate of mortality in patients with and without underlying HBV. One of these studies (Liu J [50]) reported no events. • One Chinese cohort study[51] (N = 620) reported a reduction in the risk of mortality among patients with and without underlying HBV, however the confidence interval was wide and crossed the null, reducing the confidence in these findings.
ICU admission	Evidence from two studies [38, 47] suggested no difference in the rate of ICU admission when comparing patients with HBV to those without. Both studies were found to have a moderate to low threat to internal validity. • Strength of Association: No measures of association were reported, but the rates diverse across studies. • Precision of Association: No confidence intervals were reported. • Consistency of Association: Overall, the evidence is inconsistent in direction. • Applicability of Association: The populations and settings were all in China, reducing applicability of these findings. Summary of Evidence: • One cohort study[38] (N = 536) reported higher rates of ICU admission in COVID-19 patients with HBV compared to those without, however this difference was not reported as being significant. • One cohort study[47] (N = 1,590) reported lower rates of ICU admission in COVID-19 patients with HBV compared to those without, however this difference was not reported as being significant.
Ventilation	Evidence from two studies[38, 47] suggested no difference in the rate of ventilation for patients with HBV compared to those without. All studies were found to have a moderate to low threat to internal validity. • Strength of Association: No measures of association were reported. • Precision of Association: No confidence intervals or p-values were reported. • Consistency of Association: The direction of results is consistent. • Applicability of Association: The populations and settings were all in China, reducing applicability of these findings. Summary of Evidence:

	• Two cohort studies[38, 47] (N = 3,663) of Chinese patients reported an increase in the rate of ventilation in patients with HBV and COVID-19 compared with patients with COVID-19 only, however there were few events in the HBV groups, and this was not reported as statistically significantly different.
Hospitalization	Limited evidence from one study[45] suggested no difference in hospitalization for patients with HBV compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One study[45] (N = 821) reported no difference in hospitalization rates between COVID-19 patients with and without underlying HBV. There was a small number of events in this study.

Table 5 The Association Between Hepatitis C Virus (HCV) Infection and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence from one study[54] suggested no difference in the risk of mortality for patients with HCV compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[54] (N = 1,950) of propensity score matched patients reported no difference in the risk of mortality in patients with HCV and COVID compared with patients with COVID-19 alone.
ICU Admission	Limited evidence from one study[54] suggested no difference in the risk of ICU admission for patients with HCV compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[54] (N = 1,950) of propensity score matched patients reported no difference in the risk of ICU admission in patients with HCV and COVID compared with patients with COVID-19 alone.
Hospitalization	Evidence from two studies studies[45, 52] suggested inconsistent results for the rate of hospitalization of patients with HCV compared to those without. Both studies were found to have a moderate to low threat to internal validity. • Strength of Association: No measures of association were reported. • Precision of Association: No confidence intervals were reported however results were significant for one study and not for the other. • Consistency of Association: The direction of results is inconsistent. • Applicability of Association: The populations and settings were all in the USA. Summary of Evidence:

	• One cohort study[52] (N = 1,950) of propensity score matched patients reported an increase in the risk of hospitalization in patients with HCV and COVID compared with patients with COVID-19 alone. • One cohort study[45] (N = 821) reported no difference in hospitalization rates between COVID-19 patients with and without underlying HCV. There was a small number of events in this study.

Table 6 The Association Between Autoimmune Hepatitis (AIH) and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Limited evidence consisted of one study[37] suggested an increase in the risk of mortality for patients with autoimmune hepatitis (AIH) compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[37] (N = 1,701) reported an increased risk of mortality in patients with AIH when compared with propensity score matched patients with non-AIH liver disease or with no underlying liver disease, however confidence intervals were wide and crossed the null.
ICU Admission	Overall, the evidence consisted of one study suggesting an increase in the risk of ICU admission for patients with AIH compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[37] (N = 1,701) reported increased risk of ICU admission in patients with AIH when compared with no underlying liver disease. This trend was seen when patients with AIH were compared with patients with non-AIH liver disease, however confidence intervals were wide and crossed the null.
Ventilation	Overall, the evidence consisted of one study reporting an increase in the risk of ventilation for patients with AIH compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[37] (N = 1,701) reported an increase in the rate of intubation for patients with AIH compared with no liver disease, however when patients with AIH were compared with propensity score matched patients with non-AIH liver disease, there was no association between AIH and ventilation.
Hospitalization	Overall, the evidence consisted of one study suggesting no association between hospitalization and underlying AIH compared to patients with no liver disease or other underlying liver diseases. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence:

	• One cohort study[37] (N = 1,701) reported no association between hospitalization and AIH when compared with patients with no underlying liver disease or patients with other underlying liver diseases.

Table 7 The Association Between Non-alcoholic Fatty Liver Disease and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence suggested no difference in the adjusted odds or rate of mortality of patients with non-alcoholic fatty liver disease (NAFLD) compared to those without. • Strength of Association: For studies reporting measures of effect, the magnitude ranged from 0.98 to 4.25, and the majority of evidence suggested no difference • Precision of Association: confidence intervals were wide for both studies reporting measures of association • Consistency of Association: Overall, the results are inconsistent • Applicability of Association: the populations and settings were international for studies suggestion no association, with increases in mortality in Turkey Summary of Evidence: • Five studies[2, 37, 53-55] reported on data on mortality and NAFLD in COVID-19 patients, and all were found to have a moderate to low threat to internal validity. ○ One cohort study[53] in Turkey (N = 343) reported higher adjusted odds of mortality for COVID-19 patients with NAFLD than those without. ○ Four cohort studies[2, 37, 54, 55] (N = 2,537) reported no difference in mortality for COVID-19 patients with and without NAFLD
ICU admission	Overall, the evidence was inconclusive on the risk of ICU admission for patients with non-alcoholic fatty liver disease (NAFLD) compared to those without. • Strength of Association: One study reported an adjusted measure of association of 2.3, and one study reported a significant increase in rate. • Precision of Association: The confidence interval was wide for the study reporting a measure of association • Consistency of Association: Overall, the results are inconsistent • Applicability of Association: the populations and settings were international for studies suggestion no association, with increases in ICU admission in USA and Turkey Four studies[2, 53-55]reported on data on ICU and NAFLD in COVID-19 patients, and all were found to have a moderate to low threat to internal validity. Summary of Evidence: • Two cohort studies[2, 53] in Turkey & USA (N = 706) reported higher adjusted odds of or rate of mortality for COVID-19 patients with NAFLD than those without liver disease.

	• Two cohort studies[54, 55] in the UK and China (N = 473) reported no difference in mortality for COVID-19 patients with NAFLD and without liver disease
Ventilation	Overall, the evidence consisted of one study suggesting an increase in the risk of ventilation for patients with NAFLD compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[2] (N = 363) reported a higher rate of mechanical ventilation for patients with NAFLD compared to patients without CLD.

Table 8 The Association Between Alcoholic Liver Disease and Severe COVID-19 Outcomes

Outcome	Results
Mortality	Overall, the evidence consisted of one study reported an increase in the risk of mortality for patients with alcoholic liver disease compared to those without. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[37] (N = 1,701) reported a significant increase in the adjusted odds of mortality in patents with alcoholic liver disease compared with patients with no liver disease.

Table 9 Comparison Between Different Underlying Chronic Liver Diseases Examined for Association with Mortality Due to COVID-19

Health Condition	Results
All types compared	Overall, the evidence suggested no difference in the hazard or odds of mortality for patients with differing underlying liver disease, with the exception of one study reporting an increase in mortality for patients with alcohol-related liver disease (ALD). • Strength of Association: For studies reporting measures of effect, the range was 0.81-1.25, except for ALD compared with other liver diseases where the hazard ratio was 2.69. • Precision of Association: Confidence intervals were wide for all studies reporting measures of association. • Consistency of Association: The results are consistent across studies. • Applicability of Association: The populations and settings were diverse and applicable. Summary of Evidence: • Two studies[35, 56] reported on data on mortality and different liver diseases in COVID-19 patients, and all were found to have a moderate to low threat to internal validity.

	○ One cohort study[56] (N = 867) reported only alcohol-related liver disease (ALD) was associated with increased hazard of mortality when compared with HCV. NAFLD, HBV and other types of liver disease were not significantly associated with and increased hazard of mortality. ○ One cohort study[35] (N = 127) reported no difference in mortality among patients with underlying HBV, HCV, and fatty liver disease.
Autoimmune hepatitis (AIH) compared with non-autoimmune hepatitis liver diseases	Overall, the evidence consisted of one study suggesting no association between hospitalization and underlying AIH compared to patients with other underlying liver diseases. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[37] (N = 1,701) reported no differences in the rates of severe COVID-19 outcomes including mortality, ICU admission, intubation, and hospitalization between patients with AIH and non-AIH liver diseases.

Table 10 Increasing Severity of Underlying Chronic Liver Diseases Examined for Association with Mortality Due to COVID-19

Health Condition	Results
Chronic Liver Disease	Evidence from eight studies[10, 27, 52, 54, 57-60] indicates there is an increasing risk of severe COVID-19 outcomes associated with increasing severity of chronic liver disease in COVID-19 patients. Underlying liver diseases, measures of severity and severity scores thresholds varied across studies. All studies were found to have a moderate to low threat to internal validity. • Strength of Association: The adjusted measure of association for more severe liver conditions ranged from 2.18 – 12.41. • Precision of Association: The confidence intervals were wide for all studies. • Consistency of Association: The results are consistent. • Applicability of Association: Populations and settings are applicable to this question. Summary of Evidence: • Six studies[10, 52, 57-60] (N = 174,853) reported an increase in the risk of mortality was associated with increasing severity of underlying liver condition of any kind. Underlying conditions, measures of severity and severity scores thresholds varied across studies. • Two studies[27, 54] (N = 3,545) reported no difference in mortality was associated with differing severity of liver disease among COVID-10 patients. ○ One cohort study[54] (N = 193) reported no difference in the rate of NAFLD + FIB4 >1.45 or NAFLD + FIB 4 >3.25 in patients who died with those who were discharged.

	○ One cohort study[27] (N = 3,352) reported no difference in the rate of mortality between patients with decompensated liver disease and patients with compensated liver disease.
Cirrhosis	Evidence from ten studies[2, 23, 27, 35, 37, 54, 56, 61-63] indicates there is an increasing risk of severe COVID-19 outcomes associated with cirrhosis in COVID-19 patients, regardless of the underlying liver condition. All studies were found to have a high to low threat to internal validity. Underlying conditions, measures of severity and severity scores thresholds varied across studies. • Strength of Association: The adjusted measure of association for cirrhosis ranged from 2.03 – 12.5. • Precision of Association: The confidence intervals were wide for all studies. • Consistency of Association: The results are consistent. • Applicability of Association: Populations and settings are applicable to this question. Summary of Evidence: • Eight studies[2, 23, 27, 37, 56, 61-63] (N = 12,945) reported an increase in the risk of mortality was associated with increasing severity of underlying liver condition of any kind. • Two smaller studies[35, 54] (N = 320) reported no difference in mortality or ICU admission for COVID-19 patients with underlying liver disease, regardless of the presence of cirrhosis.

Table 11 Increasing Severity of Underlying Chronic Liver Diseases Examined for Association with Mortality Due to COVID-19

Health Condition	Results
Chronic liver disease and increasing number of comorbidities	Limited evidence from one cohort study[52] suggested an increasing risk of severe COVID-19 outcomes is associated with an increasing number of comorbidities in addition to underlying liver disease, however this is insufficient to determine an association. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[52] (N = 1,950) reported an increase in risk of mortality, ICU admission, and hospitalization when comparing patients with HCV, COVID-19 and ≥3 comorbidities with patients with COVID-19 alone.
Chronic Liver Disease and Diabetes	Evidence from 2 studies[37, 56] indicates there is an increasing risk of mortality associated with liver disease and diabetes in COVID-19 patients. Both studies were found to have a moderate threat to internal validity. • Strength of Association: The adjusted measure of association for cirrhosis ranged from 2.03 – 12.5. • Precision of Association: The confidence intervals were wide for all studies. • Consistency of Association: The results are consistent. • Applicability of Association: Populations and settings are applicable to this question. Summary of Evidence:

	• 2 studies[37, 56] (N = 2,568) suggested an increase in mortality associated with chronic liver disease (CLD) and diabetes in patients compared to patients with CLD alone.
	  • One cohort study[56] (N = 867) found an increase in the hazard of mortality when comparing patients with CLD and diabetes to patients with CLD only.
	  • One cohort study[37] (N = 1,701) suggested an increase in the odds of mortality in patients with autoimmune hepatitis and diabetes compared with patients with CLD when adjusting for multiple variables, however the confidence interval crossed the null.

Chronic Liver Disease and Hypertension, Cardiovascular Disease, Chronic Obstructive Pulmonary Disease, or Obesity	Evidence from two cohort studies[37, 56] suggested inconsistent results in the odds of mortality in patients with CLD and multiple comorbidities when compared to patients with CLD only. Both studies were found to have moderate threat to internal validity. • Strength of Association: The adjusted measure of association for cirrhosis ranged from 1.07 – 1.13. • Precision of Association: The confidence intervals were wide for both studies. • Consistency of Association: The results are consistent. • Applicability of Association: Populations and settings are applicable to this question. Summary of Evidence: • Two cohort studies[37, 56](N = 2,568) reported inconsistent results for mortality in patients with CLD and hypertension, cardiovascular disease, COPD, or obesity compared with patients with CLD alone. Inconsistent results limit the conclusions that can be drawn for the interaction of underlying liver disease and these specific comorbidities and the resulting mortality.
Chronic Liver Disease and Obesity	Evidence from two cohort studies[18, 37]suggested inconsistent results in the odds of mortality in patients with CLD and obesity when compared to patients with CLD only. Both studies were found to have moderate threat to internal validity. • Strength of Association: The univariable measure of association for cirrhosis ranged from 1.07 to 1.13. • Precision of Association: The confidence intervals were wide for both studies. • Consistency of Association: The results are inconsistent. • Applicability of Association: Populations and settings are applicable to this question. Summary of Evidence: • One single center cohort study[18] (N = 447) reported a significant increase in the odds of mortality among patients with CLD who were obese compared to patients with CLD only [OR 7.2 (95% CI: 1.13-45.96), p=0.037].

	• One cohort study[37] (N = 1,701) examining three registries of patients from 35 countries suggested no difference in the adjusted odds of mortality in patients with CLD and COPD when compared to patients with CLD only [aOR 1.07 (95% CI: 0.69-1.65), p=0.767].
HCV + comorbidities	Limited evidence from one study[52]suggested no association between mortality, ICU admission, or hospitalization and different comorbidities in COVID-19 patients with HCV. Aggregation indices cannot be measured with only one study which was found to have a moderate threat to internal validity. Summary of Evidence: • One cohort study[52] (N = 1,950) reported no difference in mortality, ICU admission, or hospitalization for patients with and without HCV by comorbidities.

B.3.b. Extracted Evidence

Table 12 Extracted Studies Reporting the Association between Chronic Liver Diseases and Severe COVID-19 Outcomes

Study	Population and Setting	Intervention	Definitions	Results
Author: Alizadehsani[28] **Year:** 2021 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To analyze risk factor predictions, clinical outcomes, and mortality in COVID-19 patients. **IVA Score:** 20 (Moderate)	**Population:** N = 1,002 **Setting:** 2 hospitals **Location:** Iran **Study dates:** March 5 - May 4, 2020 **Inclusion criteria:** Patients with laboratory-confirmed COVID-19 pneumonia **Exclusion criteria:** Significant missing data **Population:** N = 319 n = 123 COVID-19 n = 196 Healthy	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 3/123 (2.4%) **Control/Comparison group, n/N (%):** No liver disease: 120/123 (97.6%)	**Medical Condition(s):** *Liver disease:* ND **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	**Severe COVID-19:** *Mortality, n/N (%)* Liver disease: • Dead: 0/15 (0%) • Alive: 3/108 (2.7%) • p=1 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	Setting: Imaging department of tertiary hospital **Location:** Iran **Study dates:** March 3 - April 8, 2020 **Inclusion criteria:** Patients with flu-like symptoms during the COVID-19 pandemic referred to the imaging department. COVID-19 was diagnosed in suspicious cases via lung CT reviewed by radiologist with >14 years of experience in chest imaging. **Exclusion criteria:** NR			
Author: Bahardoust[11] **Year:** 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To describe the clinical characteristics and outcomes of COVID-19 infection among patients with underlying liver diseases and determine the risk factors for severe COVID-19 among them.	**Population:** N =1002 **Setting:** 2 hospitals **Location:** Iran **Study dates:** March 5 - May 4, 2020 **Inclusion criteria:** Patients with laboratory-confirmed COVID-19 pneumonia **Exclusion criteria:** Significant missing data	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** CLD: 81/1002 (8%) **Control/Comparison group, n/N (%):** CLD: 921/1002 (92%)	Data retrieved from medical records **Medical Condition(s):** *Liver Disease*: including cirrhosis, grade II or higher fatty liver, and viral hepatitis **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: diagnosis confirmed via real-time PCR and CT scan *Mortality*: ND *Readmission*: readmission to hospital **Comments:** None	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N (%):* • *OR: 1.85 (95% CI: 0.91-3.77) • Liver Disease: 10/81 (12.4%) • No Liver Disease: 65/921 (7%) • p=0.018 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Readmission, n/N (%):

Study	Population and Setting	Intervention	Definitions	Results
IVA Score: 21 (moderate)				• *OR: 0.92 (95% CI: 0.43-1.97) • CLD: 8/81 (9.8%) • No CLD: 98/921 (10.6%) • p=0.42
Author: Bajaj [61] **Year:** 2021 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To describe the 90-day post discharge outcomes in patients admitted with cirrhosis+COVID-19, cirrhosis alone, and COVID-19 alone. **IVA Score:** 19 (moderate)	**Population:** N = 214 **Setting:** 7 medical centers **Location:** North America **Study dates:** March - May 2020 **Inclusion criteria:** Non-elective hospitalizations of patients admitted with PCR-confirmed COVID-19 alone, cirrhosis alone, and PCR-confirmed COVID-19 plus cirrhosis. **Exclusion criteria:** Subjects with organ transplant, HIV, and unclear cirrhosis/COVID-19 diagnoses.	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Cirrhosis (& COVID-19): 29/214 (13.5%) **Control/Comparison group, n/N (%):** No cirrhosis (& COVID-19): 93/214 (43.4%) Cirrhosis only: 92/214 (43.0%)	**Medical Condition(s):** *Cirrhosis*: diagnosed by liver biopsy or clinical/imaging features **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: death and hospice *Non-elective readmissions*: non-elective readmissions within 90-days of discharge **Comments:** Authors report 4 deaths among cirrhosis (& COVID-19) group in text but reported 3 in Table 1.	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N (%):* • 15/214 (7.0%) • *OR: 10.61 (95% CI: 1.06-106.37) • Cirrhosis (& COVID-19): 3/29 (10.3%) • No cirrhosis (& COVID-19): 1/93 (1.1%) • p<0.05 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: • *OR: 5 (95% CI: 1.95-12.76) • Cirrhosis (& COVID-19): 13/29 (44.8%) • No cirrhosis (& COVID-19): 13/93 (14.0%) • P=0.002
Author: Bennett[12] **Year:** 2021 **Data Extractor:** CO **Reviewer:** ECS/DOS **Study design:** Cohort	**Population:** N = 1,926,526 patients **Setting:** 34 medical centers **Location:** USA **Study dates:** January 1 – December 7, 2020	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 5237/174568 (3.0%) **Control/Comparison group, n/N (%):** No liver disease: 169331/174568 (97.0%)	Data retrieved from medical records **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:**	**Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* **Severe COVID-19, n/N (%):** COVID-19: 174,568/1,926,526 (9.1%) Mortality: 3,775/1,926,526 (0.2%) Ventilation: 2,790/1,926,526 (0.1%) Hospitalization: 32,472/1,926,526 (1.7%) *Mortality among all hospitalized with disease, n/N (%):* Liver disease: • *OR: 1.47 (95% CI: 1.30-1.66) • 344/3,775 (9.1%)

Study	Population and Setting	Intervention	Definitions	Results
Study Objective: To develop predictive and diagnostic computational tools and to inform critical decisions. **IVA Score:** 22 (moderate)	**Inclusion criteria:** Adults ≥18 years with any encounter after 1/1/2020 with one of a set of *a priori*-defined SARS-CoV-2 laboratory tests, or a "strong positive" diagnostic code, or two "weak positive" diagnostic codes during the same encounter or on the same date prior to 5/1/2020. **Exclusion criteria:** NR		*Mortality*: Hospital mortality or discharge to hospice; WHO Severity 10 *Severe (invasive ventilation):* hospitalized with invasive ventilation; WHO Severity 7-9 *Hospitalized*: ND *COVID-19:* via PCR or antigen testing **Comments:** Because data are aggregated from many health systems and 4 common data models that vary in granularity, some sites have systematic missingness of some variables.	*Severe (invasive ventilation):* Liver disease: • *OR: 1.00 (95% CI: 0.86-1.17) • 187/2,790 (6.7%) *Hospitalized:* Liver disease: • *OR: 3.26 (95% CI: 3.08-3.45) • 2176/32472 (6.7%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers, n/N (%):** NR **Long-term Sequelae:** NR
Author: Berenguer [62] **Year:** 2020 **Data Extractor:** JKK **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To analyze the characteristics and predictors of death in hospitalized patients with COVID-19 in Spain. **IVA Score:** 25 (moderate)	**Population:** N = 4,035 patients **Setting:** 127 hospitals **Location:** Spain **Study dates:** Start of COVID-19 in Spain-March 17, 2020 **Inclusion criteria:** Those admitted to Spanish hospitals with lab-confirmed COVID-19 by RT-PCR. **Exclusion criteria:** No lab-confirmed COVID-19, no data on outcome, or no admission date.	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N 9%):** Liver Cirrhosis: 54/3998 (1.3%) **Control/Comparison group, n/N (%):** No Liver Cirrhosis: 3944/3998 (98.6%) Total of 141 patients (3.6%) were discharged and readmitted during the study period, a median time of 5 days (IQR, 2-9 days) after discharge; only one hospital admission episode was considered for purposes of analysis	Comorbidities were defined as diagnoses included in the medical record **Medical Condition(s):** *Liver Cirrhosis*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/Associated Therapy:** NR **Outcome Definitions:** *Mortality*: all-cause mortality *ICU/High Dependency Unit Admission*: ND *Mechanical Ventilation*: ND **Comments:** None	**Severe COVID-19:** *aHR = Multivariable cox proportional hazards model using covariates clustered according to clinical or sociodemographic strata; hazard ratio [HR] (95% CI)* *HR = Univariable cox proportional hazards model; hazard ratio [HR] (95% CI)* **Odds ratio [OR] (95% CI) calculated by ERT* *Mortality, n/N(%):* Liver Cirrhosis: • *HR: 2.03 (95% CI: 1.31-3.13) • *OR: 2.43 (95% CI: 1.42-4.17) • Deceased: 26/1116 (2.3%) • Alive: 28/2882 (1.0%) • p=0.001 *ICU/High Dependency Unit Admission, n/N (%):* 736/3,988 (18.5%) • Deceased: 312/1,122 (27.8%) • Alive: 424/2,866 (14.8%) • p<0.001

Study	Population and Setting	Intervention	Definitions	Results
				Mechanical ventilation, n/N (%): 619/3,992 (15.5%) • Deceased: 283/1,119 (25.3%) • Alive: 336/2,873 (11.7%) • p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Bergman[8] **Year:** 2021 **Data Extractor:** DOS **Reviewer**: CS **Study design:** Case-control **Study Objective:** To investigate the importance of potential medical and demographic risk factors for COVID-19 diagnosis, hospitalization (with or without ICU admission), and subsequent all-cause mortality during the first wave of COVID-19. **IVA Score:** 26 (low)	**Population:** N =502,656 **Setting:** Nationwide registries **Location:** Sweden **Study dates:** Up to mid-September 2020 **Inclusion criteria:** All cases of COVID-19 confirmed in Sweden until mid-September 2020. Reporting confirmed cases to is required by law. Control population comprised of random sample of 5 non-diagnosed individuals for each COVID-19 case. Each control was residing in Sweden on January 1,	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 511/68,575 (0.7%) **Control/Comparison group, n/N (%):** Liver disease: 2,628/434,081 (0.6%)	**Medical Condition(s):** *Liver disease:* ICD10 K70-K77 **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* All-cause mortality until October 1, 2020 *ICU admission:* ICU hospitalization for confirmed COVID-19 (ICD-10 U071) *Intubation:* NR *Ventilation:* NR *Hospitalization:* non-ICU hospitalization with confirmed COVID-19 (ICD-10 U071) *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted hazard ratio; cox regression; model included demographic variables, comorbidities, and prescription medications: Adjusted hazard ratio; cox regression; model included demographic variables, comorbidities, and prescription medications* *HR: Unadjusted hazard ratio* *aOR: Adjusted odds ratio; multinomial logistic regression; model included demographic variables, comorbidities, and prescription medications: Adjusted odds ratio; multinomial logistic regression; model included demographic variables, comorbidities, and prescription medications* *OR: Unadjusted odds ratio; univariable logistic regression* *Mortality:* Liver disease: • aHR: 1.27 (95% CI: 1.09-1.46) • HR: 4.10 (95% CI: 3.57-4.72) *ICU admission, n/N (%):* Liver disease: • aOR: 1.37 (95% CI: 1.05-1.79) • OR: 4.46 (95% CI: 3.48-5.72) • ICU admission: 66/2494 (2.6%)

Study	Population and Setting	Intervention	Definitions	Results
	2020 and was alive on January 31, 2020. **Exclusion criteria:** Persons were excluded if they had missing data on at least one of the included variables.			*Hospitalization, n/N (%):* Liver disease: • aOR: 1.07 (95% CI: 0.93-1.23) • OR: 3.52 (95% CI: 3.11-3.98) • Hospitalized: 285/13,589 (2.1%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Butt[52] **Year:** 2021 **Data Extractor:** JKK **Reviewer:** DOS **Study design:** Matched case-control **Study Objective:** to determine the impact of HCV infection upon the rates of acute care hospitalization, ICU admission and all-cause mortality **IVA Score:** 22 (moderate)	**Population:** N =1,950 patients **Setting:** VA medical centers **Location:** US **Study dates:** NR **Inclusion criteria:** Veterans with positive HCV antibody and at least one positive HCV RNA based on Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES) and had a propensity score matched HCV uninfected controls; controls identified based on negative	**Health Condition Category:** Chronic liver disease, Comorbid conditions, Risk factors **Medical Condition, n/N (%):** Hepatitis C Virus Positive (HCV+): 975/1950 (50%) **Control/Comparison group, n/N (%):** Hepatitis C Virus Negative (HCV-): 975/1950 (50%) HCV antibody test or undetectable HCV RNA who remained negative during the duration of recorded follow-up; propensity score matching was based on age, race, sex, body mass index, and presence of hypertension, diabetes, coronary artery disease, stroke or cancer, smoking status, and alcohol use; the nearest-neighbor matching (1:1) technique with a caliper of 0.25 standard deviation was used	Presence of comorbidities was defined using ICD-9/10 diagnostic codes, laboratory values and/or pharmacy prescription for specific conditions **Medical Condition(s):** *HCV+:* positive HCV antibody test **Severity Measure(s):** *Fibrosis 4 (FIB-4):* used to calculate liver fibrosis stage; calculated using an average of two values closet to, but before baseline **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19:* positive RT-PCR *Mortality*: all-cause mortality *ICU Admission*: admitted or transferred to an ICU setting for any duration of time	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N(%)* • *OR (95% CI): 1.02 (0.71-1.46) • HCV+: 64/975 (6.6%) • HCV-: 63/975 (6.5%) • p=0.93 Mortality, rate per 1000 person-yrs. (95% CI): • HCV+: 4.9 (3.8-6.2) • HCV-: 4.6(3.6-5.9) • p=0.78 *ICU Admission, n/N(%)* • *OR: 1.05 (95% CI: 0.80-1.37) • HCV+: 127/975 (13.0%) • HCV-: 122/975 (12.5%) • p=0.73 *Hospitalization, n/N(%)* • *OR: 1.41 (95% CI: 1.14-1.76) • HCV+: 234/975 (24%) • HCV-: 178/975 (18.3%) • p=0.002 **Severity of Condition: n/N (%), rate**

Study	Population and Setting	Intervention	Definitions	Results
	HCV antibody test in same year **Exclusion criteria:** Veterans with HIV or HBV coinfection at any time point		*Hospitalization*: any admission to an acute care facility that occurred within 14 days after a positive SARS-CoV-2 test **Comments:** None	*Mortality, rate per 1000 person-years (95% CI); n/N (%):* FIB-4 > 3.25, p=0.88 • HCV+: 7.4 (3.3-16.6); 6/64 (9.4%) • HCV-: 6.3 (0.8-45.1); 1/63 (1.6%) FIB-4=1.45-3.25, p=0.81 • HCV+: 5.1 (3.4-7.6);24/64 (37.5%) • HCV-: 5.5 (3.2-9.6); 13/63 (20.6%) FIB-4 < 1.45, p=0.98 • HCV+: 4.5 (3.2-6.4); 31/64 (48.4%) • HCV-: 4.5 (3.4-6.1); 44/63 (69.8%) FIB-4 missing, p=0.85 • HCV+: 4.2 (1.3-13.0); 3/64 (4.7%) • HCV-: 3.6 (1.5-8.8); 5/63 (7.9%) *ICU Admission, rate per 1000 person-years (95% CI); n/N (%):* FIB-4 > 3.25 • HCV+: 11.2 (5.8-21.5); 9/127 (7.1%) • HCV-: 12.7 (3.1-50.8); 2/122 (1.6%) FIB-4=1.45-3.25 • HCV+: 10.4 (7.9-13.8); 49/127 (38.6%) • HCV-: 12.4 (8.6-17.9); 29/122 (23.8%) FIB-4 < 1.45 • HCV+: 9.4 (7.3,12); 64/127 (50.4%) • HCV-: 8.9 (7.2-11); 86/122 (70.5%) FIB-4 missing • HCV+: 7 (2.9-16.8); 5/127 (3.9%) • HCV-: 3.6 (1.5-8.8); 5/122 (4.1%) *Hospitalization, rate per 1000 person-years (95% CI); n/N (%):* FIB-4 > 3.25 • HCV+: 27.4 (18-41.6); 22/234 (9.4%) • HCV-: 6.3 (0.8-45.1); 1/178 (0.6%) FIB-4=1.45-3.25 • HCV+: 20.7 (16.9,25.3); 97/234 (41.5%) • HCV-: 15.4 (11.1-21.4); 36/178 (20.2%)

Study	Population and Setting	Intervention	Definitions	Results
				FIB-4 < 1.45 • HCV+: 14.7 (12.1-17.9); 100/234 (42.7%) • HCV-: 13.5 (11.4-16); 130/178 (73.0%) FIB-4 missing • HCV+: 21 (12.6-34.8); 15/234 (6.4%) • HCV-: 8 (4.4-14.5); 11/178 (6.2%) **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** *n/N (%) calculated by ERT* *Mortality, rate per 1000 person-years (95% CI); n/N (%):* ≥3 comorbidities, p=0.82 • HCV+: 10.4 (5.9-18.4); 12/64 (18.8%) • HCV-: 9.4 (5.1-17.6); 10/63 (15.9%) 1-2 comorbidities, p=0.66 • HCV+: 4.5 (3.2-6.4); 32/64 (50.0%) • HCV-: 4.0 (2.9-5.7); 33/63 (52.4%) No comorbidities: p=0.73 • HCV+: 4.1 (2.6-6.4); 20/64 (31.3%) • HCV-: 4.6 (2.9-7.1); 20/63 (31.7%) *ICU Admission, rate per 1000 person-years (95% CI); n/N (%):* ≥3 comorbidities: • HCV+: 16.5 (10.5-25.9); 19/127 (15.0%) • HCV-: 16.1 (10-25.9); 17/122 (13.9%) 1-2 comorbidities: • HCV+: 9.4 (7.3-11.9); 66/127 (52%) • HCV-: 8.9 (7-11.2); 72/122 (59.0%) No comorbidities: • HCV+: 8.7 (6.4-11.7); 42/127 (33.1%) • HCV-: 7.6 (5.4-10.7); 33/122 (27.0%) *Hospitalization, rate per 1000 person-years (95% CI); n/N (%):* ≥3 comorbidities: • HCV+: 34.8 (25.5-47.5); 40/234 (17.1%) • HCV-: 19.9 (13-30.5); 21/178 (11.8%) 1-2 comorbidities: • HCV+: 17.5 (14.6-20.9); 123/234 (52.6%)

Study	Population and Setting	Intervention	Definitions	Results
				• HCV-: 12 (9.8-14.6); 97/178 (54.5%) No comorbidities: • HCV+: 14.7 (11.6-18.5); 71/234 (30.3%) • HCV-: 13.8 (10.7-17.8); 60/178 (33.7%) **Risk Markers:** *n/N (%) calculated by ERT* *Mortality, rate per 1000 person-years (95% CI); n/N (%):* Age, ≤60 years: p=0.55 • HCV+: 1.3 (0.3-5.5); 2/64 (3.1%) • HCV-: 2.3 (0.8-6.1); 4/63 (6.3%) Age, >60-70 years: p=0.97 • HCV+: 3.4 (2.3-5.1); 26/64 (40.6%) • HCV-: 3.4 (2.2-5.1); 23/63 (36.5%) Age, >70 years: p=0.36 • HCV+: 8.8 (6.3-12.2); 36/64 (56.3%) • HCV-: 7.1 (5.1-9.8); 36/63 (57.1%) Sex, Male: p=0.70 • HCV+: 5 (3.9-6.5); 64/64 (100%) • HCV-: 4.7 (3.7-6.1); 62/63 (98.4%) Sex, Female: • HCV+: 0/64 (0%) • HCV-: 2.4 (0.3-17.3); 1/63 (%) *ICU Admission, rate per 1000 person-years (95% CI); n/N (%):* Age, ≤60 years: • HCV+: 8.2 (4.6-14.5); 12/127 (9.4%) • HCV-: 5.2 (2.7-10); 9/122 (7.4%) Age, >60-70 years: • HCV+: 9.5 (7.5-12); 71/127 (55.9%) • HCV-: 8.4 (6.4-10.9); 56/122 (45.9%) Age, >70 years: • HCV+: 10.8 (8,14.5); 44/127 (34.6%) • HCV-: 11.2 (8.7,14.6); 57/122 (46.7%) Race, White: • HCV+: 8.5 (6-12.2); 31/127 (24.4%) • HCV-: 7.8 (5.5-11.2); 30/122 (24.6%) Race, Black: • HCV+: 10.6 (8.5-13.3); 78/127 (61.4%) • HCV-: 10 (7.9-12.6); 74/122 (60.7%) Race, Hispanic: • HCV+: 6.7 (3-14.9); 6/127 (4.7%) • HCV-: 11.3 (6-21); 10/122 (8.2%) Race, Other/Unknown:

Study	Population and Setting	Intervention	Definitions	Results
				• HCV+: 10.1 (5.7-17.8); 12/127 (9.4%) • HCV-: 5.8 (2.9-11.6); 8/122 (6.6%) Sex, Male: • HCV+: 9.8 (8.2-11.6); 123/127 (96.9%) • HCV-: 9.2 (7.7-11); 121/122 (99.2%) Sex, Female: • HCV+: 9.2 (3.4-24.5); 4/127 (3.1%) • HCV-: 2.4 (0.3-17.3); 1/122 (0.8%) *Hospitalization, rate per 1000 person-years (95% CI); n/N (%):* Age, ≤60 years: • HCV+: 18.5 (12.7-27); 27/234 (11.5%) • HCV-: 11.5 (7.4-17.9); 20/178 (11.2%) Age, >60-70 years: • HCV+: 18 (15.2-21.4); 135/234 (57.7%) • HCV-: 13.1 (10.7-16.2); 88/178 (49.4%) Age, >70 years: • HCV+: 17.6 (14-22.2) 72/234 (30.8%) • HCV-: 13.8 (10.9-17.5) 70/178 (39.3%) Race, White: • HCV+: 16.6 (12.8-21.3); 60/234 (25.6%) • HCV-: 11 (8.1-14.9); 42/178 (23.6%) Race, Black: • HCV+: 18.6 (15.7-22); 136/234 (58.1%) • HCV-: 14.5 (12-17.5); 107/178 (60.1%) Race, Hispanic: • HCV+: 12.3 (6.8-22.2); 11/234 (4.7%) • HCV-: 11.3 (6-21); 10/178 (5.6%) Race, Other/Unknown: • HCV+: 22.7 (15.6-33.1); 27/234 (11.5%) • HCV-: 13.8 (8.8-21.7); 19/178 (10.7%) Sex, Male: • HCV+: 18.2 (16-20.7); 229/234 (97.9%) • HCV-: 13.5 (11.7-15.7); 177/178 (99.4%) Sex, Female: • HCV+: 11.5 (4.7-27.7); 5/234 (2.1%) • HCV-: 2.4 (0.3-17.3); 1/178 (0.6%) **Long-term Sequelae:** NR
Author: Campos-Murguia [60]	**Population:** N = 432 Patients	**Health Condition Category:** Chronic liver disease (CLD), Risk factors	**Medical Condition(s):** *Metabolic dysfunction-associated fatty liver disease (MAFLD)*: ND	**Severe COVID-19:** NR **Severity of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
Year: 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To evaluate the presence of MAFLD and liver fibrosis in patients with COVID-19 and its association with prognosis. **IVA Score:** 24 (moderate)	**Setting:** tertiary care center **Location:** Mexico **Study dates:** March 1-May 19, 2020 **Inclusion criteria:** >18 years old, any sex, with a confirmed diagnosis of SARS-CoV-2 infection by RT-PCR; only patients with severe disease requiring treatment with oxygen were included; only CT scans with images from the liver at the level of the right portal vein branch and from the upper pole of the spleen to the splenic hilum were included. **Exclusion criteria:** Patients with in-hospital stays >28 days, transferred from or to another hospital, those who solicited voluntary discharge or those lacking follow-up data; patients with known or recent diagnosis of liver disease different from MAFLD (e.g., autoimmune liver diseases, alcohol, hepatitis C or B infections, history of liver transplantation)	**Medical Condition, n/N (%):** Metabolic dysfunction-associated fatty liver disease (MAFLD)/liver steatosis: 176/432 (40.7%) Liver fibrosis: 37/176 (21.0&) Obesity: 184/432 (42.6%) **Control/Comparison group, n/N (%):** No metabolic dysfunction-associated fatty liver disease (MAFLD)/liver steatosis: 256/432 (59.3%) No liver fibrosis: 139/176 (79.0%) No obesity: 248/432 (57.4%)	*Liver steatosis:* determined by computed tomography scan (CT); criteria for diagnosis included having attenuation coefficient ≤ 40 Hounsfield units (HU), in an area of 20cm^2 between the segments VII and VIII in the liver and b) attenuation coefficient ≥10 HU in an area of 5 cm^2 in the splenic parenchyma; liver/spleen ratio (L/S ratio) <0.70 was used as a cutoff value to discriminate between patients with or without severe liver steatosis *Obesity:* BMI > 30 kg/m2 **Severity Measure(s):** *MALFD:* • *Liver fibrosis:* assessed using the NAFLD fibrosis score (NFS score), and when altered, the AST to platelet ratio index (APRI) score; bi-step approach was done in patients with diagnosis of liver steatosis by CT scan, using as a first evaluation the NAFLD fibrosis score (NFS); participants with NFS values > -1.455 – 0.675 (indeterminate) or >0.675 (severe fibrosis F3,F4) were analyzed by the AST to Platelet Ratio Index (APRI), and when the result in this index was >1.0, the individuals were finally classified as high-risk of severe liver fibrosis • No fibrosis **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU Admission:* ND *Intubation:* ND **Comments:** None	**Cox regression analysis [HR] (95% CI), n/N (%) among MAFLD population* *Multivariable logistic regression [aOR] (95% CI) among MAFLD population* **Calculated by ERT* *Mortality, n/N(%)*: Fibrosis: • *HR: 2.543 (95% CI: 1.147-5.637), p=0.022 • *OR: 2.08 (95% CI: 0.88-4.92) • Severe fibrosis: 10/37 (32.3%) • No fibrosis: 21/139 (15%) • p=0.024 *ICU Admission, n/N(%):* • *OR: 1.81 (95% CI: 0.83-3.96) • Severe fibrosis: 13/37 (39.4%) • No fibrosis: 32/139 (22.9%) • p=0.051 *Intubation:* Fibrosis: • aHR: 3.243 (95% CI: 1.355-7.760), p=0.008 **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality:* Sex, female: • *HR: 0.424 (95% CI: 0.154-1.171), p=0.098 Age: • *HR: 1.035 (95% CI: 1.002 – 1.070), p=0.040 BMI: • *HR: 1.087 (95% CI: 1.029 – 1.147), p=0.003 *Intubation:* Sex, female: • aHR: 0.478 (95% CI: 0.202 – 1.131), p=0.09 Age: • aHR: 0.980 (0.969 – 0.991), p=0.001 BMI:

Study	Population and Setting	Intervention	Definitions	Results
	and those with cancer, HIV or use of drugs that could cause fatty liver.			• aHR: 1.086 (1.025-1.150), p=0.005 **Long-term Sequelae:** NR
Author: Cao[26] **Year:** 2020 **Data Extractor:** MW **Reviewer:** ECS **Study design:** Cohort **Study Objective:** To investigate clinical and laboratory features and short-term outcomes of patients with Corona Virus Disease 2019 (COVID-19). **IVA Score:** 22 (moderate)	**Population:** N =102 **Setting:** Hospital **Location:** Wuhan, China **Study dates:** January 3 - February 1, 2020 **Inclusion criteria:** All patients with COVID-19 admitted to Hospital in Wuhan, China, between January 3 and February 1, 2020 were included. **Exclusion criteria:** COVID-19 with minimally symptomatic or asymptomatic SARS-CoV-2 infection	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 2/102 (2%) **Control/Comparison group, n/N (%):** No Chronic liver disease: 100/102 (98%)	**Medical Condition(s):** ND **Severity Measure(s):** NR **Clinical marker:** ND **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* non-survivors followed up to discharge **Comments:** Number of patients with chronic liver disease is reported at 4; however, authors report 1 non-survivor and 2 survivors with chronic liver disease	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N (%):* 17/102 (16.7%) Chronic liver disease: • *OR: 2.59 (95% CI: 0.22-30.34) • Non-survivors: 1/17 (5.9%) • Survivors: 2/85 (2.4%) • p= 0.462 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Chen [49] **Year:** 2020 **Data Extractor:** ECS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To investigate the potential risk factors associated with fatal outcomes from COVID-19 through a	**Population:** N =1,590 patients **Setting:** 575 hospitals **Location:** China **Study dates:** December- January 31, 2020 **Inclusion criteria:** hospitalized, lab-	**Health Condition Categories:** Chronic liver disease **Medical Condition, n/N (%):** Hepatitis B infection: 28/1590 (1.8%) **Control/Comparison group, n/N (%):** No Hepatitis B infection: 1562/1590 (98.2%)	All data extracted from medical records **Medical Condition(s):** *Hep B*: ND **Severity Measure(s):** NR **Clinical marker:** Blood leukocyte count: >10×10^9/L or <4×10^9/L Lymphocyte count: <1.5×10^9/L Platelet count: <150×10^9/L C-reactive protein level: <10/L Procalcitonin level: >0.5 ng/mL Lactose dehydrogenase: ≥250U/L	**Severe COVID-19:** Medical conditions according to fatality: *Multivariable cox regression/ proportional hazard ratio [aHR] 95%CI; n/N (%)* *Univariable cox regression/ proportional hazard ratio [HR] 95%CI; n/N (%)* **Odds ratio [OR] 95% CI calculated by ERT* Hepatitis B infection: • HR: 1.06 (95%CI: 0.15-7.69), p= 0.95 • *OR: 1.14 (95% CI: 0.15-8.59) • Fatal: 1/50 (2.0%) • Non-Fatal: 27/1540 (1.8%) • p=0.594

Study	Population and Setting	Intervention	Definitions	Results
Multivariable Cox regression analysis and a nomogram model. **IVA Score:** 23 (moderate)	confirmed COVID-19 cases. **Exclusion criteria:** Patients with incomplete records.		Aspartate aminotransferase: >40U/L **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: diagnosis confirmed by a positive real-time reverse transcriptase-polymerase chain reaction assay or high-throughput sequencing findings from nasal or pharyngeal swab specimens *Hospitalization*: admitted to participating hospital *Ventilation*: NIV, IMV, ECMO **Comments:** Data was analyzed for risk of having the disease among those who died vs. those who did not die. For the purposes of this review, analysis of mortality among those with and without the disease would be correct.	**Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Factors/ Risk Marker:** NR **Long-term Sequelae:** NR
Author: Chishinga[4] **Year:** 2020 **Data Extractor:** DOS **Reviewer:** CS **Study design:** Cohort **Study Objective:** To understand the clinical disease spectrum and risk factors for severe disease among COVID-19 patients from Fulton County, GA in order to inform public health programs and clinical providers in this highly affected geographic region. **IVA Score:** 24 (moderate)	**Population:** N = 2,851 **Setting:** State database developed by public health department **Location:** GA, US **Study dates:** March 2 - May 31, 2020 **Inclusion criteria:** Individuals diagnosed with laboratory-confirmed SARS-CoV-2 infection who resided in Fulton County, Georgia. A laboratory confirmation for SARS-CoV-2 was	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** *Mortality-related data:* Chronic liver disease: 14/1969 (0.7%) *ICU-related data:* Chronic liver disease: 11/1650 (0.7%) *Hospitalization-related data:* Chronic liver disease: 17/2820 (0.6%) **Control/Comparison group, n/N (%):** *Mortality-related data:* No chronic liver disease: 1339/1969 (68.0%) *ICU-related data:* No chronic liver disease: 1289/1650 (78.1%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* all-cause mortality *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression model includes age categories, sex, chronic renal disease, neurologic disease, diabetes mellitus, cardiovascular disease, immunocompromised, chronic lung disease, chronic liver disease, and "other chronic diseases", with long-term care facilities as random effects: Adjusted odds ratio; multivariable logistic regression model includes age categories, sex, chronic renal disease, neurologic disease, diabetes mellitus, cardiovascular disease, immunocompromised, chronic lung disease, chronic liver disease, and "other chronic diseases", with long-term care facilities as random effects* *OR: Odds ratio* *Mortality, n/N (%):* Chronic liver disease: • aOR: 1.9 (0.4-8.2) : 1.9 (0.4-8.2) • OR: 3.2 (95%CI: 0.9-11.7) • Chronic liver disease: 4/14 (28.6%) • No chronic liver disease: 111/1339 (8.3%)

Study	Population and Setting	Intervention	Definitions	Results
	defined as a positive result of real-time RT-PCR or antigen test. **Exclusion criteria:** Cases that had missing outcome information were excluded from analyses and assumed that they were missing at random.	*Hospitalization-related data:* No chronic liver disease: 1854/2820 (65.7%)		*ICU admission, n/N (%):* Chronic liver disease: • aOR: 1.2 (0.3-5.4): 1.2 (0.3-5.4) • OR: 2.2 (95%CI: 0.5-8.7) • Chronic liver disease: 3/11 (27.3%) • No chronic liver disease:163/1289 (12.6%) *Hospitalization, n/N (%):* Chronic liver disease: • aOR: 0.6 (0.2-1.9): 0.6 (0.2-1.9) • OR: 2.0 (95%CI: 0.8-5.4) • Chronic liver disease: 7/17 (41.2%) • No chronic liver disease: 508/1854 (27.4%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Chow[43] **Year:** 2020 **Data Extractor:** CS **Reviewer:** MW **Study design:** Cohort **Study Objective:** NR **IVA Score:** 20 (moderate)	**Population:** N = 122,653 **Setting:** Hospitals **Location:** 50 states, 4 territories and affiliated islands, the District of Columbia, and New York City of the U.S. **Study dates:** February 12-March 28, 2020 **Inclusion criteria:** Laboratory-confirmed COVID-19 cases	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 41/7162 (0.6%) **Control/Comparison group, n/N (%):** None of the above conditions: 4470/7162 (62.4%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* estimated for persons aged ≥19 years because of the small sample size of cases in children with underlying health conditions *Intubation:* NR *Ventilation:* NR *Hospitalization:* estimated for persons aged ≥19 years because of the small	**Severe COVID-19:** *ICU Admission (among all), n/N (%), or Median (IQR):* Chronic liver disease: • Chronic liver disease: 7/41 (17.1%) • No conditions: 99/4470 (2.2%) *Hospitalized, n/N (%), or Median (IQR):* Chronic liver disease: • Chronic liver disease: 16/41 (39.0%) • No conditions: 404/4470 (9.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR

Study	Population and Setting	Intervention	Definitions	Results
	Exclusion criteria: Cases among persons repatriated to the U.S. from Wuhan, China, and the Diamond Princess cruise ship.		sample size of cases in children with underlying health conditions *Non-elective readmissions*: NR **Comments:** None	**Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Cui[29] **Year:** 2020 **Data Extractor:** CS **Reviewer:** MW **Study design:** Cohort **Study Objective:** To evaluate the factors associated with death in patients with coronavirus disease 2019 by clarifying the clinical characteristics and immune responses. **IVA Score:** 24 (moderate)	**Population**: N = 836 **Setting:** Hospital **Location:** Wuhan, China **Study dates:** January 14- March 26, 2020 **Inclusion criteria:** Patients with confirmed COVID-19 by nucleic acid test or IgG and/or IgM serology test who were transferred or admitted to the isolation ward of a Wuhan hospital between January 14 and March 9, 2020 were included. **Exclusion criteria:** Patients who were not discharged before March 26th were excluded.	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease (CLD): 22/836 (2.6%) **Control/Comparison group, n/N (%):** No CLD: 814/836 (97.4%)	**Medical Condition(s):** *CLD:* ND **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	**Severe COVID-19:** *aOR: Multivariable Logistic Regression, adjustments NR, adjustments NR* *OR: Univariable Logistic Regression* *Mortality, n/N (%), or Median (IQR):* CLD • Deceased: 3/137 (2.2%) • Survivor: 19/699 (2.7%) • p=0.724 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Ding[38] **Year:** 2020 **Data Extractor:** JKK **Reviewer:** DOS	**Population:** N = 2,073 patients **Setting:** 3 inpatient medical centers **Location:** China	**Health Condition Category:** Chronic liver disease **Medical Condition:** n/N (%) Liver Disease: 204/2,073 (9.8%) • Hepatitis B Virus Positive (HBV+): 134/536 (25.0%)	**Medical Condition(s):** *Liver Disease*: MAFLD, HCV, HBV, compensated cirrhosis, or decompensated cirrhosis *HBV+*: diagnosed based on viral serology and ICD-10 diagnosis codes	**Severe COVID-19:** *Univariable Cox proportional hazards model hazard ratios [HR] (95% CI); n/N (%)* **Odds ratio [OR] (95%C) calculated by ERT* *Mortality, n/N (%):* Liver disease: • HR: 0.688 (95% CI: 0.413-1.148), p=0.148

Study	Population and Setting	Intervention	Definitions	Results
Study design: Cohort **Study Objective:** To explore the evolution and clinical significance of abnormal liver chemistries and the impact of hepatitis B infection on outcome in patients with COVID-19 **IVA Score:** 23 (moderate)	**Study dates:** January 18-April 25, 2020 **Inclusion criteria:** Laboratory-confirmed COVID-19 patients via RT-PCR with symptoms of fever, or respiratory symptoms such as cough or dyspnea, showing the radiologic features of viral pneumonia. **Exclusion criteria:** Patients <18 years old, pregnant, with malignancies, acute fatal organ injury (acute coronary syndrome, acute stroke, and acute pulmonary embolism), or decompensated or end-stage of chronic organ dysfunction (end-stage renal diseases, decompensated cirrhosis, or severe congestive heart failure) at admission, HIV-positive, with organ transplantation or on long-term use of immunosuppressants before admission, with surgical diseases and received emergency operation immediately after admission, without	• Hepatitis C Virus Positive (HCV+): 39/2,073 (1.9%) • MAFLD: 20/2,073 (1.0%) • Compensated Cirrhosis: 11/2,073 (0.5%) • Decompensated Cirrhosis: 3/2,073 (0.1%) **Control/Comparison group:** n/N (%) No liver Disease: 1,869/2,073 (90.2%) • Hepatitis B Virus Negative (HBV-): 402/536 (75.0%) • Hepatitis C Virus Negative (HCV-): 2034/2079 (97.8%) • No MAFLD: 2,053/2,073 (99.0%) • No Compensated Cirrhosis: 2,062/2,073 (99.5%) • No Decompensated Cirrhosis: 2,070/2,073 (99.9%)	*HCV+*: diagnosed based on viral serology and ICD-10 diagnosis codes *MAFLD*: diagnosed by ultrasonic scan, or CT measurements of steatosis with the exclusion of secondary causes including hepatitis B *Compensated Cirrhosis*: measured by ultrasound scan or computed tomography (CT); in 11 patients with compensated cirrhosis, 5 for hepatitis B virus infection, 1 for hepatitis C virus infection, 1 for with hepatitis B and hepatitis C virus co-infection, 1 for with history of alcohol abuse, 2 for with schistosomiasis, and 1 was cirrhosis of unknown cause *Decompensated Cirrhosis*: assessed according to the Clinical Practice Guidelines of European Association for the Study of the Liver; all 3 patients were with HBV infection **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** COVID-19: positive RT-PCR assay *Hospitalization*: ND *ICU Admission*: ND *Mechanical Ventilation*: ND *Mortality*: in-hospital mortality **Comments:** None	• *OR: 0.67 (95% CI: 0.38-1.17) • Deceased: 14/200 (7.0%) • Alive: 190/1873 (10/1%) • p=0.196 *Mechanical Ventilation, n/N (%):* • *OR: 1.55 (95% CI: 0.88-2.72) • HBV+: 21/134 (15.7%) • HBV-: 43/402 (10.7%) • p=0.166 HCV+: 7/39 (17.9%) MAFLD: 1/20 (5.0%) Compensated Cirrhosis: 0/11 (0.0%) Decompensated Cirrhosis: 1/3 (33.3%) *ICU Admission, n/N (%):* • *OR: 1.81 (95% CI: 0.95-3.46) • HBV+: 16/134 (11.9%) • HBV-: 28/402 (7.0%) • p=0.102 • HCV+: 5/39 (12.8%) • MAFLD: 1/20 (5.0%) Compensated Cirrhosis: 0/11 (0.0%) Decompensated Cirrhosis: 1/3 (33.3%) *Hospitalization, n/N (%):* Chronic Liver Disease: • HCV+: 5/39: (12.8%) • MAFLD: 1/20 (5.0%) **Severity of Condition:** *Hospitalization, n/N (%):* Cirrhosis: • Compensated cirrhosis: 0/11 (0.0%) • Decompensated cirrhosis: 1/3 (33.3%) **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR

Study	Population and Setting	Intervention	Definitions	Results
	core data sets such as results of liver chemistries, routine blood counts, coagulation profile, blood tests of hepatitis B antigen, antibodies against HCV or chest CT imaging, who died within 12 hours after admission, or were transferred to another hospital.			**Risk Markers:** NR **Long-term Sequelae:** NR
Author: Dong [13] **Year:** 2021 **Data Extractor:** MC **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To retrospectively analyze and compare the clinical characteristics and prognosis between the comorbidity group and the non-comorbidity group, in order to assess risk factors affecting survival from the phrase of infection peak in Wuhan. **IVA Score:** 23 (moderate)	**Population:** N = 278 **Setting:** Academic tertiary care hospital **Location:** China **Study dates:** February 8-March 9, 2020 **Inclusion criteria:** All patients aged 18 years or older diagnosed with COVID-19 using RT-PCR who visibly manifested symptoms of pneumonia on computed tomography (CT) images were eligible for the study; patient's CT imaging had to reveal multiple small patches of shadows and interstitial changes, especially in the lung periphery,	**Health Condition Category:** Chronic liver disease, Multiple comorbid conditions **Medical Condition, n/N (%):** Chronic liver disease: 7/175 (2.52%) **Control/Comparison group, n/N (%):** No comorbidity: 103/278 (37.05%)	**Medical Condition(s):** *Cardiovascular disease*: ICD-10 coding *Hypertension*: ICD-10 code *Chronic liver disease*: ICD-10 code *Diabetes mellitus*: ICD-10 code *COPD*: ICD-10 code *Malignant tumor*: ICD-10 code **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* mortality within 28 days *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N (%)* Chronic liver disease • *OR: 5.19 (95% CI: 1.04-25.87) • Chronic liver disease: 3/7 (42.86%) • No comorbidity: 13/103 (12.62%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** *Mortality, n/N (%):* • *OR: 2.77 (95% CI: 1.42-5.40) • Comorbidity: 50/175 (28.57%) • No comorbidity: 13/103 (12.62%) • p=0.002 *Ventilation* • *OR: 3.17 (95% CI: 1.63-6.16) • Comorbidity: 55/175 (31.43%) • No comorbidity: 13/103 (12.62%) • p<0.001 **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	or multiple ground-glass shadows, infiltration shadows, and lung consolidation. **Exclusion criteria:** Patients who were hospitalized for less than 24 hours, were in a state of arrest at arrival, or had incomplete clinical data.			
Author: Eshrati[7] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To determine the factors affecting the survival rate and risk of death in Iranian patients with COVID-19. **IVA Score:** 24 (moderate)	**Population:** N = 3188 patients **Setting:** Hospitals and medical centers under the supervision of the health department of Iran University of Medical Sciences **Location:** Iran **Study dates:** February 22-April 19, 2020 **Inclusion criteria:** Consecutive hospitalized patients with RT-PCR positive or lung CT scan confirmed COVID-19 from February 22-March 25, 2020. **Exclusion criteria:** Incomplete personal data, such as failure to disclose the date	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 14/3188 (0.4%) **Control/Comparison group, n/N (%):** No liver disease: 3174/3188 (99.6%)	Data retrieved from medical records **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** *Supportive therapy*: ND *Antibiotic*: ND *Antiviral treatment*: ND **Outcome Definitions:** *Mortality*: ND **Comments:** None	**Severe COVID-19:** *Univariable cox regression [HR] (95% CI), n/N (%)* *Multivariable cox regression [aHR] (95% CI), n/N (%)*Calculated by ERT* *Mortality n/N (%):* *329/3188 (10.3%)* Liver disease: • aHR: 1.33 (95% CI: 0.41-4.25), p=0.625 • *OR: 2.36 (95% CI: 0.66-8.50) • Liver disease: 3/14 (21.4%) • No liver disease: 326/3174(10.3%) • p=0.169 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	of discharge or hospitalization or other information.			
Author: Espana [57] **Year:** 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To identify factors associated with risk of death among patients with COVID-19. **IVA Score:** 26 (low)	**Population:** N = 18,768 patients; n = 3,567 nursing home residents; n = 15,201 general population **Setting:** Health system divided into 13 integrated healthcare organizations **Location:** Spain **Study dates:** February- June 29, 2020 **Inclusion criteria:** Residents of Basque Country with RT-PCR confirmed SARS-CoV-2 or positive IgM, or IgG antibody test performed due to symptoms suggestive of disease or having had contact with a positive case, from February – May 22, 2020. **Exclusion criteria:** No patients were excluded.	**Health Condition Category:** Chronic liver disease **Medical Condition:** N = NR Liver disease **Control/Comparison group:** N = NR No liver disease	Data retrieved from electronic medical records database **Medical Condition(s):** *Liver disease*: mild liver, moderate or severe liver disease **Severity Measure(s):** *Liver disease*: • Mild: NR • Moderate/Severe: NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19 mortality*: ND **Comments:** None	**Univariable logistic regression [OR] (95%CI); n/N (%)* *Multivariable logistic regression [aOR] (95% CI) adjusted for dementia, age, sex, and age; n/N (%)* COVID-19 Mortality: Liver disease: • General population: aOR 1.49 (95% CI: 1.17–1.91), p=0.0013 **Severity of Condition:** Liver disease: Mild vs no liver disease: • Nursing home residents: OR: 1.30 (95% CI: 0.90–1.89), p=0.1652 • General population: aOR 1.43 (95% CI: 1.01–2.03), p=0.0448 Moderate/severe vs. no liver disease: • Nursing home residents: OR: 0.31 (95% CI: 0.07–1.33), p=0.1145 • General population: aOR 2.47 (95% CI: 1.16–5.26), p=0.0192 **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Fisman[14] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS	**Population:** N = 21,922 patients **Setting:** 34 public health units using provincial public health case	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** CLD: 94/21,922 (0.4%) **Control/Comparison group, n/N (%):**	All data retrieved from electronic medical records **Medical Condition(s):** *CLD*: ND **Severity Measure(s):** NR	**Severe COVID-19:** **Univariable logistic regression [OR] (95% CI), p-value, n/N (%)* *Multivariable logistic regression [aOR] (95% CI), logit, n/N (%)* *Mortality:*

Study	Population and Setting	Intervention	Definitions	Results
Study design: Prediction modeling **Study Objective:** To develop and validate parsimonious, sensitive, and specific prediction rules for infection-related death in individuals with COVID-19 in Ontario. **IVA Score:** 25 (moderate)	management data system **Location:** Canada **Study dates:** January 23-May 15, 2020 **Inclusion criteria:** Patients within the public health case management system with laboratory-confirmed SARS-CoV-2 infection via validated nucleic acid amplification test, including RT-PCR and nucleic acid sequencing. **Exclusion criteria:** NR	*Calculated by ERT:* No CLD: 21,828/21,922 (99.6%)	**Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19 mortality*: ND **Comments:** None	CLD: • OR: 6.06 (95% CI: 3.50–10.46), p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Forlano [54] **Year:** 2020 **Data Extractor:** CO **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To describe the clinical characteristics and outcomes of patients with NAFLD admitted and diagnosed with COVID-19 compared with non NAFLD COVID19 positive admissions; explored association between risk factors and clinical outcomes.	**Population:** N = 193 patients **Setting:** NHS Trust **Location:** London, UK **Study dates:** February 25-June 10, 2020 **Inclusion criteria:** All consecutive adult patients admitted and diagnosed with real-time RT-PCR confirmed COVID-19 detected in nasopharyngeal swabs between February 25, 2020 - 5 April 5, 2020 and had imaging of the liver (either ultrasound or computerized tomography) dated	**Health Condition Category:** Chronic liver disease **Medical Condition:** NAFLD: 132/193 (68.4%) **Control/Comparison group:** No NAFLD: 61/193 (31.6%)	Data retrieved from medical records **Medical Condition(s):** *NAFLD*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: in-hospital mortality *ICU Admission*: ND **Comments:** None	**Severe COVID-19:** **calculated by ERT* *Mortality* • *OR: 0.93 (95% CI: 0.48-1.80) • NAFLD: 18/61 (29%) • No NAFLD: 41/132 (31%) *ICU Admission* • *OR: 0.86 (95% CI: 0.39-1.86) • NAFLD: 11/61 (18%) • No NAFLD: 27/132 (20%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
IVA Score: 22 (moderate)	within 1 year from the admission for COVID-19 or a known diagnosis of NAFLD. **Exclusion criteria:** Patients with excessive alcohol consumption or causes of liver disease other than NAFLD.			
Author: Frager[27] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To assess prognostic ability of initial admission aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels and to determine impact of preexisting liver disease on mortality and hospital course. **IVA Score:** 22 (moderate)	**Population:** N = 3352 **Setting:** Medical center **Location:** New York, USA **Study dates:** February 28, 2020 - May 22, 2020 **Inclusion criteria:** patients who had a rt-PCR positive SARS-CoV2 nasal swab, were over 18 years of age, and had an associated inpatient admission and discharge (or death) to study center **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver diseases, Risk factors **Medical Condition:** Liver disease: 457/3352 (13.6%) • Alcohol-related liver disease (ALD): 19/3352 (0.6%) • Mixed/other: 279/3352 (8.3%) • NASH/NAFLD: 74/3352 (2.2%) • Viral: 85/3352 (2.5%) Cirrhosis: 83/3352 (2.5%) • Prior history of compensated liver disease: 67/83 (80.7%) • Prior history of decompensated liver disease: 16/83 (19.3%) **Control/Comparison group:** No liver disease: 2895/3352 (86.4%) No cirrhosis: 3269/3352 (97.5%)	**Medical Condition(s):** *ALD*: ND *Mixed/other*: cholestatic liver disease, autoimmune hepatitis, hepatocellular carcinoma, and acute on chronic liver failure *NASH/NAFLD*: ND *Viral*: viral hepatitis *Cirrhosis*: ND **Severity Measure(s):** NR Cirrhosis: • Prior history of compensated liver disease • Prior history of decompensated liver disease **Clinical marker:** ND **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Intubation*: ND **Comments:** None	**Severe COVID-19, n/N (%):** **Calculated by ERT* *Mortality n/N (%):* Liver disease: • *OR: 1.16 (95% CI: 0.93-1.44) • Liver disease: 135/457 (29.5%) • No liver disease: 769/2895 (26.6%) • p=0.202 Cirrhosis: • HR: 1.67 (95% CI: 1.09-2.55), p = 0.019 • 30/83 (36.1%) *No difference in risk of death in patients with all etiologies of liver disease* *Intubation*: 630/3352 (18.8%) Liver disease: • *OR: 1.41 (95% CI: 1.11-1.78) • Liver disease: 108/457 (23.6%) • No liver disease: 522/2895 (18.0%) • p=0.005 Cirrhosis: 22/83 (26.5%) • Died: 19/22 (86.4%) • Survived: 3/22 (13.65%) Intubation was required for 21.1% of patients with ALD, 22.6% with mixed etiology, 29.7% with NASH/ NAFLD, and 22.4% with viral hepatitis **Severity of Condition:** NR *Mortality, n/N (%):*

Study	Population and Setting	Intervention	Definitions	Results
				• Prior history of decompensated liver disease: 8/16 (50%) • Prior history of compensated liver disease: 22/67 (32.8%) • *OR: 2.05 (95% CI: 0.67-6.17) • p=0.250 **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Among patients with cirrhosis:* *Mortality n/N (%):* Sex, female: • *OR: 1.12 (95% CI: 0.45-2.74) • Died: 15/30 (50%) • Survived: 25/53 (47.2%) Sex, male: • *OR: 0.89 (95% CI: 0.36-2.18) • Died: 15/30 (50%) • Survived: 28/53 (52.8%) • p=0.985 **Clinical markers:** Among patients with cirrhosis: *Mortality:* Albumin g/dL, mean (SD) • Died: 3.08 (0.78) • Survived: 3.52 (0.62) • p= 0.007 ALT U/L, median (IQR) • Died: 32.00 [16.00, 38.00] • Survived: 27.50 [19.00, 41.00] • p= 0.708 AST U/L, median (IQR) • Died: 78.00 [50.25, 103.75] • Survived: 53.00 [36.00, 84.00] • p= 0.075 Total bilirubin mg/dL, mean (SD) • Died: 2.48 (4.58) • Survived: 1.21 (1.11) • P= 0.059

Study	Population and Setting	Intervention	Definitions	Results
				INR, median (IQR) • Died: 1.30 [1.20, 1.50] • Survived: 1.20 [1.10, 1.30] • p= 0.064 Platelets k/µL, mean (SD) • Died: 145.80 (78.90) • Survived: 108.15 (66.61) • p= 0.023 **Long-term Sequelae:** NR
Author: Fried [15] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To examine patient characteristics associated with morbidity and mortality among patients hospitalized in the US. **IVA Score:** 26 (low)	**Population:** N = 11,721 patients **Setting:** 245 hospitals **Location:** 38 states in the US **Study dates:** February 15-April 20, 2020 **Inclusion criteria:** Patients ≥18 years admitted between February 15-April 20, 2020 across study hospitals with an ICD-10 code indicating COVID-19 infection or had confirmatory ICD-10 codes released after April 1, 2020. **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 147/11721 (1.3%) **Control/Comparison group, n/N (%):** No liver disease: 11574/11721 (98.7%)	Hospital claims data retrieved from hospital chargemaster **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Ventilation*: mechanical **Comments:** None	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI) adjusted for all other variables in the model, n/N (%):* **Calculated by ERT* *Mortality:* Liver disease: • aOR 1.19 (95% CI; 0.81-1.74) *Mechanical Ventilation (MV):* 1967/11721 Liver disease: • aOR: 1.42 (95% CI: 0.95-2.11) • OR: 1.50 (95% CI: 1.02-2.21) • MV: 34/1967 (1.7%) • No MV: 113/9754 (1.2%) • p=0.0382 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Galiero[1] **Year:** 2020 **Data Extractor:** MW	**Population:** N = 618 **Setting:** 18 COVID centers (11 sub-intensive COVID-19 units, 6 low-intensive adapted with	**Health Condition Category:** Chronic liver disease, Comorbid conditions **Medical Condition:** CLD: 35/618 (5.7%)	**Medical Condition(s):** *CLD*: chronic hepatopathy from HCV and HBV, NAFLD and Cirrhosis **Severity Measure(s):** NR **Clinical marker:** NR	**Severe COVID-19:** *COVID-19 mortality:* *Univariable logistic regression odds ratio [OR] (95%CI)* *Multivariable logistic regression odds ratio [aOR] (95%CI); model included age, sex, Glasgow Coma Score category, respiratory severity, chronic cardiac disease, CKD, CLD, chronic respiratory disease, and malignancies*

Study	Population and Setting	Intervention	Definitions	Results
Reviewer: DOS **Study design:** Cohort **Study Objective:** To identify comorbidities associated with in-hospital mortality, with particular focus on chronic liver disease. **IVA Score:** 23 (moderate)	respiratory devices,1 ICU) **Location:** Italy **Study dates:** March 13-June 6, 2020 **Inclusion criteria:** All adult patients (≥ 18 years) with laboratory confirmed SARS-CoV-2 infection via real-time PCR of nasal-pharyngeal swab specimen, who completed their hospitalization (discharged or dead) during study period, of whom clinical records were available. **Exclusion criteria:** All patients with either incomplete or missing clinical and laboratory data at baseline.	**Control/Comparison group:** No pre-existing condition: 166/618 (26.9%)	**Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: assessed either from data at discharge or death certificate **Comments:** None	CLD • aOR: 5.88 (95% CI: 2.39-14.46), p<0.001 • OR: 5.67 (95% CI: 2.8-11.47), p <0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** Mortality: • 0 pre-existing comorbidities: reference • 1 pre-existing comorbidity: OR: 1.61 (95% CI: 0.88-2.94), p=0.126 • 2 pre-existing comorbidities: OR: 2.48 (95% CI: 1.35-4.57), p=0.004 • ≥3 pre-existing comorbidities: OR: 3.70 (95% CI: 2.12 - 6.44), p<0.001 **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Gorgulu[16] **Year:** 2020 **Data Extractor:** DOS **Reviewer:** MW **Study design:** Cohort **Study Objective:** To determine the important effects of age, comorbidity factors, symptoms, laboratory findings, and	**Population:** N = 483 **Setting:** Level 3 hospital **Location:** Turkey **Study dates:** March - June 2020 **Inclusion criteria:** Geriatric patients aged 65 and over with COVID-19 symptoms who were	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 17/483 (3.5%) **Control/Comparison group, n/N (%):** No chronic liver disease: 466/483 (96.5%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* transfer from service to intensive care unit *Intubation:* invasive mechanical ventilation *Ventilation:* ND	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression* model includes age, COPD-bronchial asthma, malignancy, cerebrovascular disease, chronic renal failure, weakness, dry cough, throat ache, shortness of breath, ground glass opacity, and C-reactive protein model includes age, COPD-bronchial asthma, malignancy, cerebrovascular disease, chronic renal failure, weakness, dry cough, throat ache, shortness of breath, ground glass opacity, and C-reactive protein *Mortality, n/N (%):* Chronic liver disease: • Died: 4/81 (4.9%)

Study	Population and Setting	Intervention	Definitions	Results
radiological results on prognosis of patients with COVID-19 symptoms in 3 different geriatric age groups. **IVA Score:** 24 (moderate)	admitted to study hospital. **Exclusion criteria:** Patients under 65 years old or did not have COVID-19 symptoms**.**		*Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• Alive: 13/402 (3.2%) • p=0.504 *ICU admission, n/N (%):* Chronic liver disease: • ICU: 4/112 (3.6%) • Not ICU: 13/371 (3.5%) • p=0.999 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Gottlieb[63] **Year:** 2020 **Data Extractor:** CO **Reviewer:** ES/DOS **Study design:** Case-control **Study Objective:** To present clinical and demographic features of patients with laboratory-confirmed COVID-19 as of June 21, 2020; secondary outcome was to identify risk factors associated with hospitalization and critical illness. **IVA Score:** 17 (high)	**Population:** N = 8,673 patients **Setting:** One university hospital **Location:** Chicago, IL, USA **Study dates:** March 4, 2020-June 21, 2020 **Inclusion criteria:** all patients presenting to university hospital with COVID-19 **Exclusion criteria:** patients who were transferred from other inpatient hospitals	**Health Condition Category:** Chronic liver disease **Medical Condition:** Cirrhosis: 207/8673 (2.4%) **Control/Comparison group:** No Cirrhosis: 8,466/8,673 (97.6%)	Conditions extracted from electronic health records **Medical Condition(s):** *Cirrhosis*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** ND **Outcome Definitions:** *COVID-19*: Lab confirmed using molecular amplification assay and nasopharyngeal, midturbinate, or nasal swab samples. *Inpatient hospitalization*: any patient requiring admission to the hospital. For patients with more than one hospitalization (n = 376), only the most recent hospitalization was utilized *Critical illness (ICU Admission)*: a patient requiring ICU admission	**Severe COVID-19, n/N (%):** *Multivariable logistic regression odds ratio [aOR] (95%CI); n/N data for ICU Admission: NR* **Odds ratio [OR] 95% CI calculated by ERT* *Hospitalization, n/N (%)*: 1,483/8,673 (17.1%) Cirrhosis: • aOR: 2.03 (95% CI: 1.42-2.91) • *OR: 5.51 (95% CI: 4.17-7.29) • Hospitalized: 107/1483 (7.2%) • No hospitalization: 100/7190 (1.4%) *Intubation, n/N(%)*: 282/1,483 (19.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Grasselli[30]	**Population:** N = 3988	**Health Condition Category:**	**Medical Condition(s):**	**Severe COVID-19:**

Study	Population and Setting	Intervention	Definitions	Results
Year: 2020 **Data Extractor:** DOS **Reviewer:** MW **Study Design:** Cohort **Study Objective:** To describe the baseline characteristics of the patients, comorbidities, concomitant treatments at the time of hospital admission, mode and setting of ventilatory support, and the association of these characteristics with time to death. **IVA Score:** 24 (moderate)	**Setting:** ICUs **Location**: Italy **Study dates:** February 20 - May 30, 2020 **Inclusion criteria:** All consecutive patients with confirmed SARS-CoV-2 infection admitted to one of the network ICUs from February 20 to April 22, 2020. Laboratory confirmation of SARS-CoV-2 was defined as a positive result of real-time RT-PCR assay of nasal and pharyngeal swabs and, in selected cases, confirmation with RT-PCR assay from lower respiratory tract aspirates. **Exclusion criteria:** Patients with negative findings or missing results for RT-PCR for SARS-CoV-2.	Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 86/3988 (2.2%) **Control/Comparison group, n/N (%):** No comorbidities: 1302/3988 (32.6%)	*Liver disease:* chronic hepatitis, hepatic cirrhosis; medical exemptions in last 10 years (code 008, 016); hospitalization in last 5 years with ICD9 code 571.2, 571.5, 571.6, 571.8, 572.3, 456.0, 456.1, 456.2, 070 diagnosis; medications prescribed during last year with ATC code L03AB04, L03AB05, L03AB06, L03AB09, L03AB10, L03AB11, L03AB12, L03AB60, L03AB61 (DDD>50%), J05AE14, J05AX16, J05AX68, J05AX67, J05AX14, J05AX65, J05AX15 **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	*aHR: Adjusted hazard ratio; multivariable cox proportional hazards regression analysis; model includes age in years, sex, respiratory support, hypertension, hypercholesterolemia, heart disease, type 2 diabetes, malignancy, COPD, ACE inhibitor therapy, ARB therapy, statin, diuretic, PEEP at admission, FiO_2 at admission, PaO_2/FiO_2* at admission *HR: Univariate hazard ratio* *Mortality, n/N (%):* Liver disease: • HR: 1.03 (95%CI: 0.76-1.39), p=0.87 • Liver disease: 42/86 (48.8%) • No comorbidities: 490/1302 (37.6%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Guan[47] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS	**Population:** N = 1,590 patients **Setting:** 575 hospitals in 31 provinces/ autonomous regions/ provincial	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Hepatitis B: 28/1590 (1.8%) **Control/Comparison group, n/N (%):** *Percentages calculated by ERT*	Data extracted from medical records; medical conditions were determined based on patient's self-report on admission **Medical Condition(s):** *Hepatitis B*: ND	**Severe COVID-19:** **Calculated by ERT* *Mortality, n/N (%):* Hepatitis B: • *OR: 1.14 (95% CI: 0.15-8.59) • Hepatitis B: 1/28 (3.6%) • No Hepatitis B: 49/1562 (3.1%)

Study	Population and Setting	Intervention	Definitions	Results
Study design: Cohort **Study Objective:** To evaluate the risk of serious adverse outcomes in patients with COVID-19 by stratifying by comorbidity status. **IVA Score:** 23 (moderate)	municipalities across mainland China **Location:** China **Study dates:** December 11, 2019-January 31, 2020 **Inclusion criteria:** laboratory confirmed via real-time RT-PCR assay for nasal and pharyngeal swab specimen cases who were hospitalized at one of 575 (31.7% of total) certified hospitals admitting patients with COVID-19 **Exclusion criteria:** NR	No hepatitis B: 1562/1590 (98.2%)	**Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Severe COVID-19*: based on WHO interim guidance; high throughput sequencing or real-time RT-PCR assay findings for nasal/pharyngeal swab specimens were positive; severe cases denoted at least one major criterion (septic shock requiring vasoactive medications, or respiratory failure requiring mechanical ventilation), or at least three minor criteria (respiratory rate ≥30 breaths/min, oxygen index ≤250, multiple lobe infiltration, delirium or loss of consciousness, blood urea nitrogen ≥20 mg/dL, blood leukocyte count ≤4000 cells/dL, blood platelet count ≤100000 cells/dL, body temperature <36°C, and hypotension necessitating vasoactive drugs for maintaining blood pressure); based on 2007 American Thoracic Society Infectious Disease Society of America guidelines *Non-severe COVID-19*: based on WHO interim guidance; high throughput sequencing or real-time RT-PCR assay findings for nasal/pharyngeal swab specimens were positive; based on 2007 American Thoracic Society Infectious Disease Society of America guidelines; not defined further *ICU Admission*: NR *Ventilation*: mechanical *Composite end-point*: admission to intensive care unit, invasive ventilation, or death	*Invasive Mechanical Ventilation, n/N (%):* 50/1590 (3.1) Hepatitis B: • *OR: 2.43 (95% CI: 0.56-10.52) • Hepatitis B: 2/28 (7.1%) • No Hepatitis B: 48/1562 (3.1%) *ICU Admission, n/N (%):* Hepatitis B: • *OR: 0.55 (95% CI: 0.07-4.11) • Hepatitis B: 1/28 (3.6%) • No Hepatitis B: 98/1562 (6.3%) *Severe COVID-19, n/N (%):* Hepatitis B: • Hepatitis B: 9/28 (32.1%) • No Hepatitis B: 245/1562 (15.7%) **Severity of Condition, n/N (%):** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
			Comments: None	
Author: Gude-Sampedro [17] **Year:** 2020 **Data Extractor:** CO **Reviewer:** ECS/MW/DOS **Study design:** Cohort **Study Objective:** To develop and validate a prognostic model to identify patients with Covid-19 infection at a higher risk of hospitalization, ICU admission and death, based on their age, sex, comorbidities and geographic place of residence **IVA Score:** 24 (moderate)	**Population:** N = 10,454 patients **Setting:** NR **Location:** Spain **Study dates:** March 6, 2020-May 7, 2020 **Inclusion criteria:** Patients with COVID-19 infection confirmed by RT-PCR on nasal or throat swab samples; data were collected from the Galician Health Service database (SERGAS), a longitudinal Galicia data of the population **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition:** Liver disease: 149/10,454 (1.4%) **Control/Comparison group:** No Liver disease: 10,305/10,454 (98.6%)	Data extracted from electronic health records **Medical Condition(s):** *(ICPC-2 codes)* *Liver disease*: D97 **Severity Measure(s):** NR **Clinical marker**: NR **Treatment/ Associated Therapy**: NR **Outcome Definitions:** *COVID-19*: a positive reverse transcription polymerase chain reaction (RT-PCR) test on samples obtained from nasal or throat swabs performed in accordance with WHO protocol *Hospitalization*: NR *ICU Admission*: the patient was a candidate for ICU admission if they required mechanical ventilation or had a fraction of inspired oxygen of≥60% *Ventilation*: ND *Intubation*: ND *Mortality*: death of any cause after RT-PCR diagnosis **Comments:** None	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI)* *Odds Ratio (95%CI)* Mortality, n/N (%): 544/10,454 (5.2%) *Mortality (medical conditions), n/N (%):* Liver disease: • aOR: 1.82 (95% CI: 0.98-3.37) • 14/56 (25%) *ICU Admission*: 284/10,454 (2.7%) *ICU Admission (medical conditions), n/N (%):* Liver disease: • aOR: 2.71 (95% CI: 1.57-4.68); 18/56 (32.1%) • OR: 3.86 (95% CI: 2.17-6.86) *Hospitalization:* 2,492/10,454 (23.8%) Liver disease: 56/149 (37.5%) • OR: 1.94 (95% CI: 1.39-2.71) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Guerra Veloz[18] **Year:** 2021 **Data Extractor:** CO **Reviewer:** MW/ECS **Study design:** Cohort	**Population:** N = 447 patients **Setting:** single university hospital **Location:** Spain	**Health Condition Category:** Chronic liver disease (CLD), Comorbid conditions, Risk factors **Medical Condition:** CLD: 28/447 (6.3%) **Control/Comparison group:** No CLD: 419/447 (93.7%)	Data retrieved from electronic medical records **Medical Condition(s):** *Chronic liver disease*: chronic hepatitis B or C, alcohol-related liver disease, autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis	**Severe COVID-19, n/N (%):** *Univariable logistic regression [OR] (95% CI) for mortality in all patients with COVID-19* *Mortality (Medical conditions)* CLD: • OR: 1.82 (95% CI: 0.74-4.50), p=0.192 • CLD: 8/26 (30.8%) • No CLD: 39/200 (19.6%)

Study	Population and Setting	Intervention	Definitions	Results
Study Objective: To determine the prevalence of CLD in COVID-19 patients and analyze the course of the infection, compared with patients with non-liver disease. **IVA Score:** 22 (moderate)	**Study dates:** March 23-April 30, 2020 **Inclusion criteria:** all positive SARS-CoV-2 PCR patients admitted to university hospital from March 23rd to April 30th, 2020 **Exclusion criteria:** NR		and non-alcoholic fatty liver disease (NAFLD) **Severity Measure(s):** Advanced liver fibrosis/cirrhosis or non-advanced liver fibrosis: evaluated according to international criteria **Clinical marker:** Ferritin: ND **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: a positive result of the real-time reverse transcription PCR assay of a specimen collected via a nasopharyngeal swab Mortality: ND *Hospitalization*: ND *ICU Admission*: ND *Ventilation*: ND *Intubation*: ND **Comments:** None	• p=0.289 *Hospitalization (admitted):* • OR: 14.2 (95% CI: 3.3-60.7) • CLD: 26/28 (92.9%) • No CLD: 200/419 (47.4%) • p < 0.001 *ICU Admission:* • OR: 0.8 (95% CI: 0.22-2.84) • CLD: 3/26 (11.5%) • No CLD: 28/200 (14.0%) • p=0.507 *Ventilation:* • OR: 0.79 (95% CI: 0.17-3.62) • CLD: 2/26 (7.7%) • No CLD: 19/200 (9.5%) • p=0.555 *Intubation*: NR **Severity of Condition:** *Mortality, n/N (%)* • Advanced fibrosis: 3/7 (42.8%) • Non-advanced fibrosis: 5/21 (23.8%) • OR: 2.4 (95% CI: 0.39-14.5) **Duration of Underlying Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions, n/N (%):** *Univariable logistic regression [OR] (95% CI), p-value for mortality in patients with Chronic Liver disease and COVID-19* COPD: OR: 5.25 (95% CI: 0.90-30.70), p=0.066 Cancer: OR: 5.25 (95% CI: 0.90-30.70), p=0.066 Obesity: OR: 7.20 (95% CI: 1.13-45.96), p=0.037 **Clinical Markers:**

Study	Population and Setting	Intervention	Definitions	Results
				Univariable logistic regression [OR] (95% CI), p-value for mortality in patients with Chronic Liver disease and COVID-19 Ferritin (ng/ml): OR: 1.000 (95% CI: 0.999-1.000), p= 0.655 **Risk Markers, n/N (%):** *Univariable logistic regression [OR] (95% CI), p-value for mortality in patients with Chronic Liver disease and COVID-19* Age: • OR: 0.989 (95% CI: 0.954-1.026), p=0.562 Sex (male): • OR: 11.20 (95% CI: 1.25-100.31), p=0.031 Smoker: • OR: 12.67 (95% CI: 0.99-162.26), p= 0.051 **Long-term Sequelae:** NR
Author: Halalau[45] **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	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 11/821 (1.3%) Chronic Hepatitis B: 1/821 (0.1%) Chronic Hepatitis C: 1/821 (0.1%) **Control/Comparison group, n/N (%):** None of the above: 295/821 (35.9%)	**Medical Condition(s):** *Chronic liver disease:* ND *Chronic Hepatitis B:* ND *Chronic Hepatitis C:* 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 *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Hospitalization, n/N (%):* 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 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

Study	Population and Setting	Intervention	Definitions	Results
	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.			**Long-term Sequelae:** NR
Author: Harrison[58] **Year:** 2020 **Data Extractor:** JKK **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To determine associations between comorbidities listed and mortality among patients in the United States with COVID-19	**Population:** N = 31,461 patients **Setting:** Inpatient and outpatient care settings in 24 academic medical centers, specialty physician practices, and community hospitals **Location:** US **Study dates:** January 20th-May 26th, 2020	**Health Condition Category:** Chronic liver disease **Medical Condition: n/N (%)** Mild Liver Disease: 1,497/31,461 (4.8%) Moderate/Severe Liver Disease: 138/31,461 (0.4%) **Control/Comparison group: n/N (%)** No mild Liver Disease: 29,964/31,461 (95.2%) No moderate/Severe Liver Disease: 31,323/31,461 (99.6%)	Comorbidities identified if patient had corresponding ICD code for condition since January 1, 2015 **Medical Condition(s):** *Mild Liver Disease*: ND *Moderate/Severe Liver Disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: deaths during inpatient or outpatient visit; deaths occurring outside hospital setting were not well captured	**Severe COVID-19:** *Multivariable logistic regression, odds ratio [aOR] 95% CI; n/N (%)* *Univariable logistic regression, odds ratio [OR] 95% CI; n/N (%)* *Mortality*: Mild Liver Disease: • aOR: 1.26 (95% CI: 1.00-1.59), p=0.046 • OR: 2.15 (95% CI: 1.77-2.62), p<0.001 • Deceased: 121/1,296 (9.3%) • Alive: 1,376/30,165 (4.6%) Moderate/Severe Liver Disease: • aOR: 2.62 (95% CI: 1.53-4.47), p<0.001 • OR: 4.47 (95% CI: 2.83-7.08), p<0.001 • Deceased: 22/1,296 (1.7%) • Alive: 116/30,165 (0.4%)

Study	Population and Setting	Intervention	Definitions	Results
IVA Score: 25 (moderate)	**Inclusion criteria:** Adults 18-90 years with COVID-19 recorded in electronic medical records during study dates **Exclusion criteria:** No age or sex recorded in medical records; patients with ICD-9 code 079.89 as this code may still be used occasionally as a "catch-all" code for >50 viral infections		*COVID-19*: 1 or more in their EMR's: U07.1 COVID-19, B97.29, B34.2, or a positive test result with COVID-19 - specific laboratory *Ventilation*: invasive mechanical ventilation **Comments:** The median (IQR) estimated time in the study was 54 days (36–68)	**Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Hashemi [2] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To describe the characteristics of CLD and study the effect of existing liver-related comorbidities on the manifestations and outcomes of hospitalized adult patients with COVID-19. **IVA Score:** 23 (moderate)	**Population:** 363 patients **Setting:** Single healthcare system consisting of two tertiary centers and seven community hospitals **Location:** Massachusetts, US **Study dates:** March 11-April 2, 2020 **Inclusion criteria:** all consecutive hospitalized adults with laboratory-confirmed COVID-19 via PCR nasopharyngeal swab or tracheal as pirate **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** CLD: 69/363 (19%) • NAFLD: 55/69 (15.2%) • NAFLD + Alcohol liver disease: 1/69 (1.4%) • HCV: 6/69 (8.7%) • HBV: 2/69 (2.9%) • PBC: 1/69 (1.4%) • Compensated Cirrhosis (1 NAFLD, 4 viral, 1 alcohol, 1 HBV, 1 HCV): 6/69 (8.7%) • Decompensated cirrhosis (2 alcohol, 1 HCV): 3/69 (4.3%) **Control/Comparison group, n/N (%):** No CLD: 294/363 (81%)	All data retrieved from electronic medical records **Medical Condition(s):** *CLD*: ND • *NAFLD*: presence of diffuse hepatic steatosis on any prior imaging studies or liver histology in the absence of secondary causes of hepatic fat accumulation including significant alcohol use, long-term use of steatogenic medications or hereditary disorders • *HCV*: history of HCV viremia, including those with cured infection who have evidence of liver fibrosis on histology or non-invasive testing • *HBV*: presence of hepatitis B surface antigen for greater than 6 months, with or without detectable viremia • *Cirrhosis*: presence of morphological features of cirrhosis with or without portal hypertension on abdominal imaging and/or liver histology • *Decompensated cirrhosis*: presence of ascites or hepatic encephalopathy	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI), n/N (%); n/N calculated by ERT* **Calculated by ERT* *Mortality:* CLD: • aOR: 2.00 (95% CI: 0.94-4.28), p=0.07 • 17/69 (23.9%) No CLD: • *OR: 2.14 (95% CI: 1.12-4.07) • 39/294 (13.2%) • p=0.029 NAFLD: 9/55 (16.4%), p=0.54 Non-NAFLD CLD: 8/14 (53.9%), p<0.0001 No CLD: 39/294 (13.2%) Cirrhosis vs no CLD: • aOR: 12.5 (95% CI: 2.16-72.5), p=0.009 Non-cirrhosis CLD: • aOR: 1.47 (95% CI: 0.64-3.38), p=0.13 Cirrhosis: 55.6% • No Cirrhosis: 13.2% • p=0.0004 *ICU Admission:* CLD vs no CLD:

Study	Population and Setting	Intervention	Definitions	Results
			on active treatment or history of variceal bleeding **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *ICU Admission*: ND *Mechanical Ventilation*: ND **Comments:** None	• aOR: 1.77 (95% CI: 1.03-3.04), p=0.04 • *OR: 1.80 (95% CI: 1.06-3.06) CLD: 34/69 (49.3%) • No CLD: 103/294 (35%) • p=0.028 NAFLD: • aOR: 2.30 (95% CI: 1.27-4.17), p=0.03 • NAFLD: 28/55 (50.9%) • No CLD: 103/294 (35.2%) • p=0.0095 Non-NAFLD CLD: • 5/14 (38.5%) • No CLD: 99/294 (33.7%) • p=0.81 *Mechanical Ventilation:* CLD vs no CLD: • aOR: 2.08 (95% CI: 1.20-3.60), p=0.0092 • *OR: 2.11 (95% CI: 1.24-3.60) CLD: 33/69 (47.8%) • No CLD: 89/294 (30.3%) • p=0.0055 NAFLD: • aOR: 2.15 (95% CI: 1.18-3.91), p=0.02 • NAFLD: 27/55 (49.1%) • No CLD: 89/294 (30.4%) • p=0.006 Non-NAFLD CLD: 5/14 (38.5%) • No CLD: 89/294 (30.4%a) • p=0.54 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: He[31]	**Population:** N = 336 **Setting:** Hospital	**Health Condition Category:** Chronic liver disease, Multiple comorbid conditions	**Medical Condition(s):** *Chronic liver disease:* ND	**Severe COVID-19:** *HR: Hazard ratio; Kaplan-Meir survival curve*

Study	Population and Setting	Intervention	Definitions	Results
Year: 2020 **Data Extractor:** TR **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To investigate the clinical characteristics and outcomes of patients with severe COVID-19 and chronic obstructive pulmonary disease (COPD). **IVA Score:** 23 (moderate)	**Location:** China **Study dates:** January 20, 2020 - April 10, 2020 **Inclusion criteria:** All patients hospitalized with severe COVID-19, defined as positive for SARS-CoV-2 nucleic acid by real-time PCR or positive for SARS-CoV-2-specific IgM and IgG antibodies and at least one of the following manifestations: respiratory rate ≥30/min, oxygen saturation ≤93% in a resting state, PaO_2 /FiO_2 ≤300 mmHg, pulmonary imaging (CT/DR) showing significant progression >50% within 24 to 48 hours, respiratory failure requiring mechanical ventilation, shock, or admission to the Intensive Care Unit (ICU) for failure of other organs. **Exclusion criteria:** NR	**Medical Condition, n/N (%):** Chronic liver disease: 3/336 (0.9%) **Control/Comparison group, n/N (%):** Chronic liver disease: 333/336 (99.1%)	**Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* ND *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	*Mortality, n/N (%):* Chronic liver disease: • Non-survivors: 1/103 (0.8%) • Survivors: 2/203 (1.0%) • p=0.824 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** *Mortality among COPD patients, n/N (%):* Chronic liver disease: • Non-survivors: 0/22 (0%) • Survivors: 0/6 (0%) • Diabetes: • Non-survivors: 3/22 (13.6%) • Survivors: 2/6 (3.33%) • p=0.264 **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Higuera-de la Tijera[41] **Year:** 2021	**Population:** N = 166 patients	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):**	Data retrieved from medical records **Medical Condition(s):** *CLD*: ND	**Severe COVID-19:** Medical conditions according to intubation: *Univariable logistic regression [OR] (95%CI); n/N (%)* **Calculated by ERT*

Study	Population and Setting	Intervention	Definitions	Results
Data Extractor: CS **Reviewer:** DOS **Study design:** Case-control nested in a cohort **Study Objective:** To compare characteristics of patients with severe COVID-19 due to SARS-CoV-2 who required invasive mechanical intubation versus stable hospitalized patients. **IVA Score:** 20 (moderate)	**Setting:** tertiary level hospital converted to a COVID-19 center during SARS-CoV-2 pandemic **Location:** Mexico **Study dates:** March – May 2020 **Inclusion criteria:** Laboratory-confirmed via real-time RT-PCR assay for nasal and pharyngeal swab specimens patients admitted to a COVID-19 center converted hospital **Exclusion criteria:** Patients who requested voluntary discharge	CLD: 17/166 (10.2%) **Control/Comparison group, n/N (%):** No CLD: 149/166 (89.8%)	**Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Invasive mechanical ventilation (IMV*]: patients who required IMV at any point in their clinical disease course during hospitalization **Comments:** None	Chronic liver disease: • *OR: 1.69 (95% CI: 0.50-5.63) • IMV: 4/27 (14.8%) • No IMV: 13/139 (9.3%) • p=0.3000 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Huang[55] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To investigate the clinical features and liver injury in patients with COVID-19 with NAFLD in a multicenter cohort of patients with COVID-19. **IVA Score:** 23 (moderate)	**Population:** N = 280 **Setting:** 10 designated hospitals **Location:** China **Study dates:** January 18, 2020 -February 26, 2020 **Inclusion criteria:** consecutive patients with laboratory-confirmed COVID-19 via real-time PCR of throat swab samples who were enrolled in designated hospitals	**Health Condition Category:** Chronic liver disease **Medical Condition:** NAFLD: 86/280 (30.7%) **Control/Comparison group:** No NAFLD: 194/280 (69.3%)	**Medical Condition(s):** *NAFLD*: defined using the published hepatic steatosis index (HSI) in the absence of other causes of CLD; HSI = 8 * (ALT/AST ratio) + BMI (+2 if female, +2 if diabetic); serum ALT and AST results of first test after admission used for calculation; cutoff of 366 used to define presence of NAFLD **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *ICU Admission*: ND *Mortality*: ND	**Calculated by ERT* **Severe COVID-19:** *Mortality, n/N (%):* 0/280 (0%) • *OR: 2.24 (95% CI: 0.04-114.25) • NAFLD: 0/86 (0%) • No NAFLD: 0/194 (0%) *ICU admission, n/N (%):*18/280 (6.4%) • *OR: 0.86 (95% CI: 0.29-2.49) • NAFLD: 5/86 (5.8%) • No NAFLD: 13/194 (6.7%) • p=0.78 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR

Study	Population and Setting	Intervention	Definitions	Results
	between January 18-February 26, 2020 **Exclusion criteria:** Patients with the following comorbidities: viral hepatitis (defined by positive serum hepatitis B surface antigen and/or hepatitis C antibody and/or a known history of chronic hepatitis B or chronic hepatitis C), significant alcohol consumption (defined by >30 g/day in men and >20 g/day in women), autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, or any other CLD; patients without BMI data; patients with insufficient biochemistry data		**Comments:** None	**Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Jiang Y[32] **Year:** 2020 **Data Extractor:** DOS **Reviewer:** MW **Study design:** Cohort **Study Objective:** To identify independent factors predicting all-cause mortality among older	**Population:** N = 281 **Setting:** ICUs of Infectious Disease Departments in one hospital **Location:** China **Study dates:** January 30 - April 10, 2020 **Inclusion criteria:**	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 9/281 (3.2%) **Control/Comparison group, n/N (%):** No chronic liver disease: 272/281 (96.8%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* all cause-mortality *ICU admission:* NR *Intubation:* NR	***Severe COVID-19:*** *OR: Odds ratio; binary logistic regression* *Mortality among 60-79 years age group n/N (%):* Chronic liver disease: • Died: 3/72 (4.2%) • Survived: 6/143 (4.2%) • p=1.00 Mortality among ≥80 years age group, n/N (%): Chronic liver disease: • Died: 0/42 (0%) • Survived: 0/24 (0%)

Study	Population and Setting	Intervention	Definitions	Results
adults with severe COVID-19 in Wuhan, China. **IVA Score:** 24 (moderate)	All older patients with severe COVID-19 admitted between January 30 - March 8, 2020 were enrolled if they met at least one of the following three criteria: 1) respiratory distress with a respiratory rate of ≥30 breaths per minute; 2) oxygen saturation (fingertip pulse oximetry) of ≤93% in the resting state; or 3) PO_2/FiO_2 ≤300 mmH G, based on recommendations of the National Institute for Viral Disease Control and Prevention, China. To confirm SARS-CoV-2 infection, throat swab samples were obtained from all patients upon admission and tested using real-time RT-PCR assays. **Exclusion criteria:** NR		*Ventilation:* mechanical ventilation, high flow oxygen therapy *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• p=N/A Mortality comparing 60-79 years and ≥80 years age groups, p-values: Chronic liver disease: =0.122 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Killerby[46] **Year:** 2020 **Data Extractor:** CO **Reviewer:** ES **Study design:** Case-control	**Population:** N = 531 patients **Setting:** 6 Acute care hospitals and associated outpatient clinics affiliated with a single academic health care system	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 9/531 (1.7%) **Control/Comparison group:** No liver disease: 522/531 (98.3%)	Conditions extracted from medical records **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR	**Calculated by ERT* **Severe COVID-19, n/N (%):** *Hospitalization, n/N (%):* 220/531 (41.4%) Liver disease: • *OR: 1.78 (95% CI: 0.47-6.72) • Hospitalized: 5/220 (2.3%) • Not hospitalized: 4/311 (1.3%) **Severity of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
Study Objective: To determine characteristics associated with hospitalization for covid-19. **IVA Score:** 17 (high)	**Location:** Georgia, US **Study Dates:** March 1-April 7, 2020 **Inclusion Criteria:** Patients aged ≥18 years with laboratory-confirmed COVID-19. Hospitalized patients selected sequentially from hospital-provided lists, and all non-hospitalized patients evaluated at outpatient clinics or an ED and not admitted) **Exclusion Criteria:** Persons lacking a health care visit during which a medical history could be recorded. Non-hospitalized excluded if they stayed for observation or died in ED		**Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: a positive real-time reverse transcription–polymerase chain reaction [RT-PCR] test result for SARS-CoV-2 *Hospitalization*: included stays for observation and deaths that occurred in an emergency department (ED) *ICU admission*: ND *Ventilation*: ND *Intubation*: ND **Comments:** None	**Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Factors/Risk Markers:** NR **Long-term sequelae:** NR
Author: Kim D [56] **Year:** 2020 **Data Extractor:** CO **Reviewer:** ES **Study design:** Cohort **Study Objective:** to identify predictors of mortality in patients with Chronic Liver Disease (CLD) who acquire COVID-19	**Population:** N = 867 patients **Setting:** 21 institutions **Location:** USA **Study dates:** March 1-May 30, 2020 **Inclusion criteria:** Age > 18 years, laboratory-confirmed COVID19, and presence of	**Health Condition Category:** Chronic liver disease, Comorbid conditions, Risk factors **Medical Condition:** Chronic Liver Disease • Hepatitis C virus (HCV): 190/867 (21.9%) • Hepatitis B virus (HBV): 62/867 (7.2%) • Nonalcoholic fatty liver disease (NAFLD): 456/867 (52.6%) • Alcohol-related liver disease (ALD): 94/867 (10.8%) • Cirrhosis: 247/867 (28.5%)	Data extracted from medical records and confirmed via manual chart review **Medical Condition(s):** *Chronic Liver Disease* • *Hepatitis C virus (HCV)*: ND • *Hepatitis B virus (HBV)*: ND • *Nonalcoholic fatty liver disease (NAFLD)*: ND • *Alcohol-related liver disease (ALD)*: Alcoholic liver disease; alcoholic hepatitis; without ascites; with ascites; Alcoholic fibrosis and sclerosis of liver; Alcoholic cirrhosis of liver; without ascites; with	**Severe COVID-19:** Mortality (COVID-related): 105/867 (86.7%) *Multivariable cox proportional [aHR] (95%CI) for COVID-19-related mortality among patients with chronic liver disease* Etiology of liver disease • HCV: 1 • HBV: aHR: 0.81 (95% CI: 0.23–2.83), p=0.746 • ALD: aHR: 2.69 (95% CI: 1.44–5.02), p=0.002 • NAFLD: aHR: 1.08 (95% CI: 0.59–1.97), p=0.804 • Other: aHR: 1.15 (95% CI: 0.42–3.13), p=0.782 Presence of cirrhosis • No Cirrhosis: 1 • Compensated cirrhosis: aHR: 0.90 (95% CI: 0.49–1.65), p=0.743

Study	Population and Setting	Intervention	Definitions	Results
IVA Score: 21 (moderate)	preexisting Chronic Liver Disease (CLD) **Exclusion criteria:** Patients who had undergone liver transplantation and patients with COVID-19 diagnosis based on clinical suspicion	• Compensated Cirrhosis: 134/867 (15.5%) • Decompensated Cirrhosis: 93/867 (10.7%) • Hepatocellular carcinoma: 22/867 (2.5%) **Control/Comparison group:** No chronic Liver Disease • No hepatitis C virus (HCV): 677/867 (78.1%) • No hepatitis B virus (HBV): 805/867 (92.8%) • No nonalcoholic fatty liver disease (NAFLD): 411/867 (47.4%) • No alcohol-related liver disease (ALD): • No cirrhosis: 773/867 (89.2%) • No compensated Cirrhosis: 733/867 (84.5%) • No decompensated Cirrhosis: 774/867 (89.3%) • No hepatocellular carcinoma: 845/867 (97.5%)	ascites; Alcoholic hepatic; failure; without coma; with coma; Alcoholic liver disease, unspecified • *Cirrhosis*: ND • *Compensated Cirrhosis*: ND • *Decompensated Cirrhosis*: ND • *Hepatocellular carcinoma*: ND **Severity Measure(s):** Age: • <65 • ≥65 Smoking: • Current Smoker • Past Smoker • Never Smoker **Clinical marker:** NA? **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Severe COVID-19*: death, hospitalization, oxygen requirement, intensive care unit [ICU] admission, requirement of vasopressors, or mechanical ventilation *Hospitalization*: ND *ICU Admission*: ND *Ventilation*: ND *Intubation*: ND *COVID-19 Attributable Death*: if death was clinically related to COVID-19 and there were no other unrelated causes of death. **Comments:** Lack of adequate COVID-19 testing during the early phase of the pandemic could have led to decreased representation of patients with CLD and mild COVID-19 in cohort.	• Decompensated cirrhosis: aHR: 2.41 (95% CI: 1.34–4.32), p=0.003 • Presence of HCC: aHR: 3.96 (95% CI: 1.74–8.98), p=0.001 *Multivariable model [aOR] (95%CI) for COVID-19-related mortality among patients with cirrhosis specifically* Presence of cirrhosis • Decompensated cirrhosis: aOR: 3.12 (95% CI: 1.68–5.79), p<0.001 • Presence of HCC: aOR: 3.61(95% CI: 1.58–8.25); p=0.002 • Comorbidity: COPD: aOR: 3.12 (95% CI: 1.68–5.79), p<0.001 Severe COVID-19 among patients with chronic liver disease: 535/867 (61.7%) *Multivariable Model Odds Ratio [aOR] (95%CI); n/N (%)* *Etiology of liver disease* HCV: 1 • Severe COVID-19: 130/535 (24.3%) • No Severe COVID-19: 56/322 (17.4%) HBV: aOR: 0.99 (95% CI: 0.46–2.13), p=0.973 • Severe COVID-19: 37/535 (6.9%) • No Severe COVID-19: 25/322 (7.8%) NAFLD: aOR: 0.68 (95% CI: 0.41–1.13), p=0.137 • Severe COVID-19: 256/535 (47.9%) • No Severe COVID-19: 199/322 (61.8%) ALD: aOR: 2.08 (95% CI: 0.97–4.45), p=0.059 • Severe COVID-19: 72/535 (13.5%) • No Severe COVID-19: 18/322 (5.6%) Other: aOR: 1.27 (95% CI: 0.60–2.70), p=0.536 • Severe COVID-19: 40/535 (7.5%) • No Severe COVID-19: 24/322 (7.5%) Missing: • Severe COVID-19: 0/535 (0%) • No Severe COVID-19: 0/322 (0%) *Presence of cirrhosis* No cirrhosis: 1 • Severe COVID-19: 363/535 (67.9%) • No Severe COVID-19: 254/322 (78.9%) Compensated cirrhosis: aOR: 0.70 (95% CI: 0.43–1.14), p=0.152 • Severe COVID-19: 83/535 (15.5%)

Study	Population and Setting	Intervention	Definitions	Results
				• No Severe COVID-19: 48/322 (14.9%) Decompensated cirrhosis: aOR: 2.50 (95% CI: 1.20–5.21), p=0.015 • Severe COVID-19: 77/535 (14.4%) • No Severe COVID-19: 14/322 (4.3%) Hepatocellular carcinoma OR: 2.99 (95% CI: 0.62–14.36), p=0.171 • Severe COVID-19: 18/535 (3.4%) • No Severe COVID-19: 3/322 (0.9%) Missing • Severe COVID-19: 12/535 (2.2%) • No Severe COVID-19: 6/322 (1.9%) Hospitalization: 524/867 (60.4%) ICU Admission: 199/867 (23.0%) Ventilation: 154/867 (17.8%) Intubation: NR **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions, n/N (%):** *Multivariable cox proportional [aHR] (95%CI) for mortality* *Conditions Comorbid to the Presence of Liver disease* • Diabetes: aHR: 1.82 (95% CI: 1.15–2.89), p=0.011 • Hypertension: aHR: 1.69 (95% CI: 1.04–2.76), p=0.034 • Cardiovascular disease: aHR: 0.86 (95% CI: 0.53–1.42), p=0.564 • COPD: aHR: 2.29 (95% CI: 1.32–3.96), p=0.003 *Multivariable Model Odds Ratio [OR] 95%CI for severe COVID-19* *Conditions Comorbid to the Presence of Liver disease* Diabetes: • aOR: 1.51 (95% CI: 1.04–2.19), p=0.029 • Severe COVID-19: 259/535 (48.4%) • No Severe COVID-19: 110/322 (34.2%) • p<.001 Hypertension: • aOR: 1.16 (95% CI: 0.80–1.68), p=0.434 • Severe COVID-19: 321/535 (60.0%)

Study	Population and Setting	Intervention	Definitions	Results
				• No Severe COVID-19: 165/322 (51.2%) • p=0.012 Obesity: • aOR: 1.21 (95% CI: 0.84–1.76), p=0.302 • Severe COVID-19: 213/535 (39.8%) • No Severe COVID-19: 150/322 (46.6%) • p=0.052 Hyperlipidemia: • Severe COVID-19: 218/535 (40.8%) • No Severe COVID-19: 113/322 (35.1%) • p=0.100 Cardiovascular disease: • aOR: 1.85 (95% CI: 1.09–3.13); p=0.022 • Severe COVID-19: 116/535 (21.7%) • No Severe COVID-19: 32/322 (9.9%) • p<.001 HIV: • Severe COVID-19: 16/535 (3.0%) • No Severe COVID-19: 8/322 (2.5%) • p=0.664 COPD: • aOR: 2.26 (95% CI: 1.15–4.45), p=0.019 • Severe COVID-19: 62/535 (11.6%) • No Severe COVID-19: 15/322 (4.7%) • p=0.001 Asthma: • Severe COVID-19: 61/535 (11.4%) • No Severe COVID-19: 29/322 (9.0%) • p=0.268 Other cancer: • Severe COVID-19: 45/535 (8.4%) • No Severe COVID-19: 21/322 (6.5%) • p=0.315 **Risk Markers, n/N (%):** *Multivariable cox proportional [aHR] (95%CI) for COVID-19-related mortality for patients with chronic liver disease* Age (per 10 year): 1.52 (1.27–1.82), p<0.001 Sex (male): 1.23 (0.79–1.91), p=0.359 Race/ethnicity • Non-Hispanic white: 1 • Non-Hispanic: 0.84 (0.50–1.43), p=0.524

Study	Population and Setting	Intervention	Definitions	Results
				• Hispanic: 1.20 (0.69–2.09), p=0.522 • Non-Hispanic Asian: 1.93 (0.64–5.77); p=0.244 • Other: 0.80 (0.24–2.66), p=0.711 Smoking status: • No: 1 • Past smoker: 1.39 (0.86–2.26), p=0.179 • Current smoker: 2.99 (1.56–5.72), p=0.001 *Multivariable model [OR] (95%CI) for severe COVID-19- for patients with chronic liver disease* Age (per 10 year): 1.43(1.25–1.65); p<0.001 Age category: <65 • Severe COVID-19: 330/535 (61.7%) • No Severe COVID-19: 260/322 (80.8%) • p<.001 ≥65 • Severe COVID-19: 205/535 (38.3%) • No Severe COVID-19: 62/322 (19.3%) Sex (male): 1.28 (0.90–1.81), p=0.172 • Severe COVID-19: 308/535 (57.6%) • No Severe COVID-19: 159/322 (49.5%) • p=0.022 Race/ethnicity: Non-Hispanic white: 1 • Severe COVID-19: 156/535 (29.2%) • No Severe COVID-19: 107/322 (33.2%) Non-Hispanic black: 0.83 (0.54–1.28), p=0.406 • Severe COVID-19: 152/535 (28.4%) • No Severe COVID-19: 112/322 (34.8%) Hispanic: 2.33 (1.47–3.70); p<.001 • Severe COVID-19: 148/535 (27.7%) • No Severe COVID-19: 69/322 (21.4%) Non-Hispanic Asian: 1.90 (0.85–4.27), p=0.124 • No Severe COVID-19: 14/322 (4.3%) • Severe COVID-19: 29/535 (5.7%) Other: 3.40 (1.31–8.81); p=0.012 • Severe COVID-19: 30/535 (5.4%) • No Severe COVID-19: 8/322 (2.5%) Missing • Severe COVID-19: 20/535 (3.7%) • No Severe COVID-19: 12/322 (3.7%) Alcohol use:

Study	Population and Setting	Intervention	Definitions	Results
				Do not drink currently: 1 • Severe COVID-19: 85/535 (15.9%) • No Severe COVID-19: 85/322 (26.4%) Current daily drinking: 0.98 (0.53–1.83), p=0.953 • Severe COVID-19: 70/535 (13.1%) • No Severe COVID-19: 34/322 (10.6%) Social drinking: 0.84 (0.55–1.26), p=0.390 • Severe COVID-19: 345/535 (64.5%) • No Severe COVID-19: 183/322 (56.8%) Missing • Severe COVID-19: 35/535 (6.5%) • No Severe COVID-19: 20/322 (6.2%) Smoking: Never smoker: 1 • Severe COVID-19: 278/535 (52.0%) • No Severe COVID-19: 199/322 (61.8%) Current smoker: 1.00 (0.54–1.83), p=0.990 • Severe COVID-19: 59/535 (11.0%) • No Severe COVID-19: 35/322 (10.9%) • p=0.032 Past smoker: 0.96 (0.65–1.43), p=0.855 • Severe COVID-19: 175/535 (32.7%) • No Severe COVID-19: 82/322 (25.5%) Missing • Severe COVID-19: 23/535 (4.3%) • No Severe COVID-19: 6/322 (1.9%) **Long-term Sequelae:** NR
Author: Kim SR[40] **Year:** 2020 **Data Extractor:** CS **Reviewer:** MW **Study design:** Cohort **Study Objective:** To answer important questions on COVID-19 progression and outcomes, as well as potential risk factors to intensive care unit admission. To analyze risk factors on the	**Population:** N = 2,959 **Setting:** National database; Clinical Epidemiological Information provided by the Korea Disease Control and Prevention Agency **Location:** South Korea **Study dates:** Up to April 30, 2020 **Inclusion criteria:** All patients with	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 46/2959 (1.6%) **Control/Comparison group, n/N (%):** No chronic liver disease: 2913/2959 (98.4%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR	**Severe COVID-19:** *ICU admission, n/N (%)* Chronic liver disease: • ICU: 2/133 (1.5%) • General ward: 44/2826 (1.6%) • p=1 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR

Study	Population and Setting	Intervention	Definitions	Results
progression to severity stages of COVID-19 while using national data. **IVA Score:** 20 (moderate)	confirmed COVID-19 who were released from isolation or dead until April 30, 2020 were included. **Exclusion criteria:** Patients with pregnancy-related variables or missing values for other variables were excluded.		**Comments:** None	**Long-term Sequelae:** NR
Author: Kokturk[19] **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 = 1,500 **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-	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic hepatic disease: 11/1500 (0.8%) **Control/Comparison group, n/N (%):** No chronic hepatic disease: 1489/1500 (99.3%)	**Medical Condition(s):** *Chronic hepatic disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND I*CU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**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 (%):* 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%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	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			
Author: Li C[20] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** to investigate clinical characteristics and outcomes of CLD confirmed in COVID-19 patients **IVA Score:** 23 (moderate)	**Population:** N = 104 **Setting:** Hospital **Location:** China **Study dates:** February 2, 2020-April 2, 2020 **Inclusion criteria:** All CLD and computer-generated random sample of non-CLD patients with COVID-19 at study hospital known to have treated the largest number of COVID-19 patients **Exclusion criteria:** Patients diagnosed with acute liver injury or who showed incomplete medical records	**Health Condition Category:** Chronic liver disease **Medical Condition:** CLD: 52/104 (50%) **Control/Comparison group:** No CLD: 52/104 (50%)	**Medical Condition(s):** *CLD*: included all CLD patients diagnosed with chronic viral hepatitis B and C, autoimmune liver disease, cryptogenic liver cirrhosis, NAFLD, methotrexate related liver fibrosis and alcoholic liver disease; progressive deterioration of liver functions, leading to fibrosis and cirrhosis of liver parenchyma; refers to liver disease at least 6 months; consists of diverse liver pathologies including hepatocellular carcinoma, liver cirrhosis, and inflammation (chronic hepatitis); diagnosed based on clinical features **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Invasive ventilation*: invasive mechanical ventilation **Comments:** None	**Severe COVID-19:** **Calculated by ERT* *Mortality, n/N (%):* • *OR: 22.9 (95% CI: 1.29-405.29) • p<0.01 • CLD: 9/52 (17.3%) • No CLD: 0/52 (0%) 6 patients died of respiratory and circulatory failure; 3 patients died of multiple organ dysfunction syndrome (MODS) *Invasive ventilation, n/N (%)*: • *OR: 5.42 (95% CI: 0.61-48.15) • CLD: 5/52 (9.6%) • No CLD: 1/52 (1.9%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Li G [21] **Year:** 2020	**Population:** N = 1,075 patients **Setting:** Hospitals	**Health Condition Category:** Chronic liver disease **Medical Condition:**	Data retrieved from medical records **Medical Condition(s):** *Chronic liver disease*: ND	**Severe COVID-19:** *Univariable cox regression/ proportional hazard ratio [HR] 95%CI; n/N (%)*

Study	Population and Setting	Intervention	Definitions	Results
Data Extractor: CO **Reviewer:** ECS/MW/DOS **Study design:** Cohort **Study Objective:** To explore risk factors that drive mortality in patients (who received neither dexamethasone nor remdesivir). **IVA Score:** 21 (moderate)	**Location:** China, European regions, and North America **Study dates:** January-April 2020 **Inclusion criteria:** COVID-19 patients recorded during study dates. **Exclusion criteria:** Patients who received either remdesivir or dexamethasone, were hospitalized after May 1 and had missing data of therapy or were from countries with limited online data.	Chronic liver disease: 9/399 (2%) **Control/Comparison group:** No Chronic liver disease: 390/399 (98%)	**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	*Multivariable cox regression/ proportional hazard ratio [aHR] 95%CI; n/N (%)* **Calculated by ERT* *Mortality, n/N (%)* Chronic liver disease: • HR: 1.90 (95% CI: 1.29-2.80); p=0.09 • *OR: 5.6 (95% CI: 1.14-27.3) • Non-survivor: 7/157 (5%) • Survivor: 2/242 (1%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Li Y[10] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** to compare the Fibrosis-4 (FIB-4) score for a cohort of hospitalized patients with COVID-19 and assess its association with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA, inflammatory cytokine	**Population:** 202 **Setting:** two academic centers **Location:** US **Study dates:** March 15-July 15, 2020 **Inclusion criteria:** participants enrolled in 2 cohort studies with SARS-CoV-2 real-time PCR test positive from nasopharyngeal swab and hospitalized at study hospitals	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** History of liver diseases: 65/202 (32.3%) • Chronic viral hepatitis without steatosis or cirrhosis: 1/65 (1.6%) • Steatosis: 58/65 (89.2%) • Cirrhosis: 6/65 (9.2%) **Control/Comparison group, n/N (%):** No history of liver diseases: 137/202 (67.8%)	Data retrieved from medical records **Medical Condition(s):** *History of liver diseases*: ND • *Chronic viral hepatitis without steatosis or cirrhosis*: ND • *Steatosis*: ND • *Cirrhosis*: ND **Severity Measure(s):** NR **Clinical marker:** *Fibrosis-4 score (FIB-4)*: scoring system derived from routine tests including AST, ALT, age, and platelet count (PLT) to predict advanced fibrosis in hepatitis C infection; FIB-4 <1.45 considered within the normal range with a negative predictive value of advanced fibrosis of approximately 90%.	**Severe COVID-19:** *Univariable logistic regression odds ratio [OR] (95% CI), n/N (%)* *Multivariable regression model includes sex, BMI, ethnicity, hypertension, diabetes, remdesivir trial enrollment, and history of liver disease; odds ratio [aOR] (95% CI)* *#Multivariable backward stepwise regression model includes sex, BMI, ethnicity, hypertension, diabetes, remdesivir trial enrollment, history of liver disease, CRP, lymphocyte count, LDH, and D-dimer; odds ratio [aOR] (95% CI)* **Calculated by ERT* *Mortality:* History of liver diseases: • aOR: 0.75 (95% CI: 0.25-2.29), p=0.61 • OR: 1.23 (95% CI: 0.49-3.11), p=0.66 • Death: 8/22 (36.4%) • Survival: 57/180 (31.7%)

Study	Population and Setting	Intervention	Definitions	Results
levels, and clinical outcome **IVA Score:** 23 (moderate)	**Exclusion criteria:** history of decompensated cirrhosis or cirrhosis with Model for End-Stage Liver Disease–Sodium score >10 and participants who received chemotherapy within 1 month of hospitalization		FIB-4 = (Age (year) × AST (U/L)) / (PLT (100/µL) × √ALT (U/L)) *Troponin T*: ND *C reactive protein (CRP)*: ND *Lymphocyte count*: ND *Lactate Dehydrogenase (LDH)*: ND *D-dimer*: ND **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: NR **Comments:** None	Chronic viral hepatitis without steatosis or cirrhosis among those with history of liver diseases: • Death: 0/8 (0.0%) • Survival: 1/57 (1.7%) Steatosis among those with history of liver diseases: • *OR: 0.82 (95% CI: 009.-7.89) • Death: 7/8 (87.5%) • Survival: 51/57 (89.5%) Cirrhosis among those with history of liver diseases: • *OR: 1.49 (95% CI: 0.15-14.63) • Death: 1/8 (12.5%) • Survival: 5/57 (8.8%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Clinical Markers:** *Mortality:* FIB-4 (every 1-unit increment): • aOR: 1.79 (95% CI: 1.36, 2.35), p<0.001 • #aOR: 1.63 (95% CI: 1.22, 2.17), p= 0.001 • OR: 1.75 (95% CI: 1.37-2.23), p<0.001 • Death: 16/22 (72.7%) • Survival: 47/180 (26.1%) Troponin T ≥ 15 ng/L: • #aOR: 3.78 (95% CI: 1.21, 11.79), p=0.022 • OR: 6.64 (95% CI: 2.46-17.92), p<0.001 CRP (every 10-mg/L increment) • OR: 1.02 (95% CI: 0.98-1.07), p=0.36 Lymphocyte count (every 1,000/uL increment): • OR: 0.17 (95% CI: 0.05-0.58), p=0.005 LDH (every 10-U/L increment): • OR: 1.03 (95% CI: 1.01-1.05), p=0.004 D-dimer (every 100-ng/mL increment): • #aOR: 1.05 (95% CI: 1.00, 1.09), p=0.032

Study	Population and Setting	Intervention	Definitions	Results
				• OR: 1.05 (95% CI: 1.02-1.08), p=0.004 **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Liu J [50] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** to assess the independent effect of HBV infection on the outcomes of COVID-19 as well as the progression of HBV infection **IVA Score:** 24 (moderate)	**Population:** 347 patients **Setting:** Hospital **Location:** China **Study dates:** January 1, 2020- April 12, 2020 **Inclusion criteria:** patients diagnosed with COVID-19 by nucleic acid testing with well-documented records and longitudinal follow-up (liver function testing, chest CT scan, or blood gas assay across two or more days) from January 1-March 1, 2020 **Exclusion criteria:** patients without data available at baseline (blood routine exams, liver biochemistries, CT score, blood gas assay) and subjects coinfected with HIV or has any liver disease other than hepatitis B	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Hepatitis B (HBV): 21/347(6.1%) **Control/Comparison group, n/N (%):** No HBV: 326/347 (93.9%)	Data retrieved from medical records **Medical Condition(s):** *HBV*: HBeAg-negative chronic HBV infection or HBeAG-negative CHB or pre-existing cirrhosis **Severity Measure(s):** none **Clinical marker:** None **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):* CHB: • CHB: 0/21 (0%) • No CHB: 0/326 (0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Liu R[48]	**Population:** N = 220 patients	**Health Condition Category:** Chronic liver disease	Data retrieved from medical records	**Severe COVID-19:** **calculated by ERT*

Study	Population and Setting	Intervention	Definitions	Results
Year: 2020 **Data Extractor:** CO **Reviewer:** CS/DOS **Study design:** Cohort **Study Objective:** to reveal whether COVID-19 patients with pre-existing hepatitis B (HBV) infection are predisposed to more severe illness **IVA Score:** 24 (moderate)	**Setting:** university hospital **Location:** China **Study dates:** May 1, 2019-March 30, 2020 **Inclusion criteria:** patients with confirmed SARS-CoV-2 through nasopharyngeal swab specimen high-throughput sequencing or RT-PCR and pre-existing HBV and SARS-CoV-2 mono-infected patients randomly selected to match age, sex, and comorbidities of coinfected group admitted to the hospital from January 22 to March 30, 2020; chronic hepatitis B patients measured during their follow-up visit from May 1 to November 30, 2019; healthy controls that had a physical examination in October-November 2019 **Exclusion criteria:** patients with differing pre-existing co-morbidities and of different age and sex	**Medical Condition, n/N (%):** HBV+ (& SARS-Cov-2+): 50/220 (22.7%) **Control/Comparison group, n/N (%):** HBV- (& SARS-CoV-2+): 56/220 (25.5%)	**Medical Condition(s):** *Hepatitis B*: positive for hepatitis B virus surface antigen (HBsAg) and hepatitis B virus e antigen (HBeAg) by enzyme-linked immune sorbent assays (ELISA) **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND **Comments:** None	Mortality, n/N (%): • *OR: 1.13 (95% CI: 0.27-4.78) • HBV+ (& SARS-CoV-2+): 4/50 (8%) • HBV- (& SARS-CoV-2+): 4/56 (7.14%) • p=0.868 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
Author: Maestre-Muñiz[33] **Year:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study design:** Cohort **Study Objective:** To identify risk factors for death from the COVID-19 infection among subjects admitted to a hospital in central Spain, and to analyze factors that may contribute to mortality. **IVA Score:** 24 (moderate)	**Population:** N = 444 **Setting:** Community medical center **Location:** Spain **Study dates:** February 26 – May 31, 2020 **Inclusion criteria:** Adult inpatients who were confirmed COVID-19 positive either by a nasopharyngeal swab test using real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay, or by IgG/IgM lateral flow immunoassay chromatography rapid testing and who were admitted to hospital due to respiratory failure during the study dates were included. **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 31/444 (7.0%) **Control/Comparison group, n/N (%):** No chronic liver disease: 413/444 (93.0%)	**Medical Condition(s):** *Chronic liver disease:* ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* In-hospital mortality *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Multivariable Logistic Regression: Multivariable Logistic Regression* *Mortality, n/N (%)* Chronic liver disease: • With CLD: 12/31 (38.7%) • Without CLD: 130/413 (31.5%) • p=0.405 **Severity of Condition:** **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Magro[5] **Year:** 2021 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort	**Population:** N = 2,191; N = 1,810 derivation cohort; N = 381 validation cohort **Setting:** three referral tertiary centers	**Health Condition Category:** Chronic liver disease **Medical Condition:** Chronic liver disease: 42/1810 (2.3%) **Control/Comparison group:** No chronic liver disease: 1768/1810 (97.6%)	**Medical Condition(s):** ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: in hospital death	**Severe COVID-19:** *Multivariable model in the derivation cohort of risk factors associated with in hospital mortality: aHR (95%CI), p value* *Mortality: n/N (%)* 495/1810 (27.3%) Chronic liver disease: • aHR: 1.78 (95% CI: 1.16-2.72), p=0.008

Study	Population and Setting	Intervention	Definitions	Results
Study Objective: To develop and to validate a simple clinical prediction rule for early identification of in hospital mortality of patients with COVID-19. **IVA Score:** 23 (moderate)	**Location:** Italy **Study dates:** February 22-April 30, 2020 **Inclusion criteria:** hospitalized patients with real-time RT-PCR confirmed COVID-19 from nasal and pharyngeal swab samples who were admitted between February 22-April 7, 2020 **Exclusion criteria:** NR		*ICU Admission*: ND *Ventilation*: non-invasive ventilation **Comments:** None	*ICU Admission: n/N (%)* • 242/1810 (13.4%) *Ventilation: n/N (%)* • 108/1384 (7.8%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Mallow [3] **Year:** 2020 **Data Extractor:** CO **Reviewer:** CS/DOS **Study design:** Cohort **Study Objective:** To quantify the role of the number of CDC risk factors on in-hospital mortality in a large and geographically diverse group of hospitalized COVID-19 patients. **IVA Score:** 26 (high)	**Population:** N = 21,676 patients **Setting:** 276 acute care hospitals **Location:** USA **Study dates:** March 15-April 30, 2020 **Inclusion criteria:** All hospitalizations with a confirmed COVID-19 diagnosis identified using ICD-10 code U07 and discharged between March 15-April 30, 2020 **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 936/21,676 (4.3%) **Control/Comparison group:** No Liver disease: 20,740/21,676 (95.7%)	Data retrieved from electronic medical records **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *ICU Admission*: ND **Comments:** None	**Severe COVID-19, n/N (%):** *Multivariable logistic regression [aOR] (95%CI); n/N (%) associated with mortality* **Calculated by ERT* *Mortality:* Liver disease: • aOR: 1.91 (95% CI: 1.61-2.26), p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Marjot & Buescher[64]	**Population:** N =1,701 patients	**Health Condition Category:**	Data retrieved from 3 COVID-19 registries	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI), n/N (%)*

Study	Population and Setting	Intervention	Definitions	Results
Year: 2021 **Data Extractor:** CO **Reviewer:** CS/DOS **Study design:** Cohort **Study Objective:** To evaluate the disease course and outcomes for patients with autoimmune hepatitis (AIH). **IVA Score:** 24 (moderate)	**Setting:** 3 multinational registries (COVID-Hep registry, SECURE-cirrhosis registry, and R-LIVER COVID-19) **Location:** 35 countries **Study dates:** March 25-October 24, 2020 **Inclusion criteria:** All cases of laboratory-confirmed SARS-CoV-2 infection by nasopharyngeal swabs in patients with chronic liver disease without prior liver transplantation, aged >16yrs, from any location, and with any symptom profile or disease severity; comparison group included patients without chronic liver disease **Exclusion criteria:** Cases were excluded if: SARS-CoV-2 infection was not laboratory-confirmed, the submission was a duplicate, if hospitalization status, cirrhosis status, or mortality outcome was not known or not reported, or if the	Chronic liver disease (CLD), Risk factors, Comorbid conditions **Medical Condition, n/N (%):** CLD: 932/1701 (54.8%) • Autoimmune hepatitis (AIH): 70/932 (7.5%) • Non-AIH CLD: 862/932 (92.5%) • NAFLD: 362/932 (38.8%) • ALD: 233/932 (25.0%) • HCV: 128/932 (13.7%) • HBV: 121/932 (13.0%) **Control/Comparison group, n/N (%):** No CLD: 769/1701 (45.2%)	**Medical Condition(s):** *CLD*: ND *AIH*: excludes variant syndromes and IgG4-related disease **Severity Measure(s):** CLD without cirrhosis: ND CTP-A: ND *CTP-B*: ND *CTP-C*: ND **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: detection of SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR) on nasopharyngeal swabs *Mortality*: ND *Hospitalization*: ND *ICU Admission*: ND Intubation: invasive ventilation *Ventilation*: ND **Comments:** None	*Univariable logistic regression [OR] (95% CI), n/N (%)* **calculated by ERT* *Mortality, n/N (%):* CLD: • *OR: 0.93 (95% CI: 0.74-1.18) • CLD: 190/932 (20%) • No CLD: 166/769 (22%) AIH: • *OR: 1.08 (95% CI: 0.60-1.93) • AIH: 16/70 (23%) • No CLD: 166/769 (22%) • p=0.764 AIH vs non-AIH CLD: • *OR: 1.17 (95% CI: 0.65-2.10) • AIH: 16/70 (23%) • Non-AIH CLD: 174/862 (20%) • p=0.643 Among CLD cohort: • AIH: aOR: 1.87 (95% CI: 0.81–4.34), p=0.145 • NAFLD: aOR: 0.98 (95% CI: 0.56–1.71), p=0.946 • ALD: aOR: 1.79 (95% CI: 1.06–3.01), p=0.029 • HCV: aOR: 1.05 (95% CI: 0.59–1.88), p=0.87 • HBV: aOR: 0.96 (95% CI: 0.45–2.07), p=0.925 Invasive ventilation, n/N (%): AIH: • *OR: 2.17 (95% CI: 1.02-4.62) • AIH: 9/70 (13%) • No CLD: 49/769 (6%) • p=0.049 AIH vs non-AIH CLD: • *OR: 0.72 (95% CI: 0.35-1.48) • AIH: 9/70 (13) • Non-AIH CLD: 147/862 (17) • p=0.504 *ICU admission, n/N (%):* AIH: • *OR: 3.76 (95% CI: 2.12-6.65) • AIH: 20/70 (29%) • Non-CLD: 74/769 (10%) • p<0.001 AIH vs non-AIH CLD:

Study	Population and Setting	Intervention	Definitions	Results
	patient was not aged 16 years or over at the time of SARS-COV-2 positive diagnosis; patients with variant syndromes of PBC and PSC (so-called AIH/PBC or AIH/PSC overlap syndromes) and patients with AIH and coexisting liver disease (e.g. AIH with alcohol-related liver disease)			• *OR: 1.34 (95% CI: 0.78-2.31) • AIH: 20/70 (29%) • Non-AIH CLD: 198/862 (23%) • p=0.240 *Hospitalization, n/N (%):* AIH: • *OR: 1.60 (95% CI: 0.91-2.82) • AIH: 53/70 (76%) • Non-CLD: 508/769 (66%) • p=0.112 AIH vs non-AIH CLD: • *OR: 0.55 (95% CI: 0.31-0.98) • AIH: 53/70 (76%) • Non-AIH CLD: 733/862 (85%) • p=0.060 **Severity of Condition:** *Multivariable logistic regression [aOR] (95% CI)* *Mortality, n/N (%):* CLD without cirrhosis: • AIH: 6/70 (9%) • Non-AIH CLD: 60/862 (7%) • p=0.473 CTP-A: • AIH: 8/70 (12%) • Non-AIH CLD: 164/862 (19%) • p=0.746 CTP-B: • AIH: 38/70 (54%) • Non-AIH CLD: 293/862 (34%) • p=0.225 CTP C: • AIH: 35/70 (50%) • Non-AIH CLD: 448/862 (52%) • p=1.0 Among CLD Cohort: CLD without cirrhosis: ref CTP-A: aOR: 2.18 (95% CI: 1.24–3.84), p=0.007 CTP-B: aOR: 4.79 (95% CI: 2.72–8.45), p<0.001 CTP-C: aOR: 12.41 (95% CI: 6.73–22.88), p<0.001 **Duration of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
				Treatment/ Associated Therapy: NR **Comorbid Conditions:** Among CLD Cohort: Obesity: • aOR: 1.07 (95% CI: 0.69–1.65), p=0.767 • OR: 1.02 (95% CI: 0.71-1.45), p=0.935 • Died: 51/190 (27%) • Survived: 197/742 (27%) Heart Disease: • aOR: 1.41 (95% CI: 0.88–2.26), p=0.151 • OR: 2.02 (95% CI: 1.39-2.95), p<0.001 • Died: 51/190 (27%) • Survived: 114/742 (15%) Diabetes: • aOR: 1.17 (95% CI: 0.77–1.78), p=0.469 • OR: 1.28 (95% CI: 0.93–1.78, p=0.133 • Died: 78/190 (41%) • Survived: 261/742 (35%) Hypertension: • aOR: 1.05 (95% CI: 0.70–1.59), p=0.805 • OR: 1.43 (95% CI: 1.04–1.98), p=0.028 • Died: 87/190 (46%) • Survived: 275/742 (37%) COPD: • aOR: 0.63 (95% CI: 0.3–1.29), p=0.204 • OR: 1.53 (95% CI: 0.93–2.52), p=0.094 • Died: 24/190 (13%) • Survived: 64/742 (9%) Non-HCC Cancer: • aOR: 1.02 (95% CI: 0.48–2.16), p=0.961 • OR: 1.41 (95% CI: 0.89–2.23), p=0.139 • Died: 29/190 (15%) • Survived: 84/742 (11%) HCC: • aOR: 1.11 (95% CI: 0.57–2.15), p=0.761 • OR: 1.42 (95% CI: 0.89–2.23), p=0.224 • Died: 18/190 (10%) • Survived: 51/742 (7%) **Risk Markers:** Among CLD Cohort: Age per 10 years, *median (IQR)*:

Study	Population and Setting	Intervention	Definitions	Results
				• aOR: 1.27 (95% CI: 1.09–1.50), p=0.003 • OR: 1.03 (95% CI: 1.02-1.04), p<0.001 • Died: 63 (53-73) • Survived: 57 (46-67) Sex, male, n/N (%): • aOR: 0.77 (95% CI: 0.51–1.17), p=0.221 • OR: 1.03 (95% CI: 0.74-1.44), p=0.847 • Died: 120/190 (63%) • Survived: 463/742 (62%) Ethnicity, white: • aOR: 1.37 (95% CI: 0.92–2.04), p=0.124 • OR: 2.37 (95% CI: 1.70-3.29), p<0.001 • Died: 122/190 (64%) • Survived: 320/742 (43%) Smoker: • aOR: 0.53 (95% CI: 0.25–1.14); p=0.106 • OR: 0.84 (95% CI: 0.44-1.61), p=0.602 • Died: 12/190 (6%) • Survived: 55/742 (7%) **Long-term Sequelae:** NR
Author: Marjot & Moon[37] **Year:** 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To determine the impact of COVID-19 on patients with pre-existing liver disease. **IVA Score:** 27 (high)	**Population:** N = 1,365 patients **Setting:** 2 open online international registries of 130 institutions across 29 countries and a large hospital network in the UK **Location:** multinational; 29 countries **Study dates:** March 25-July 8, 2020 **Inclusion criteria:** All cases of laboratory-confirmed SARS-CoV-2 infection in patients with CLD aged >16 years old, from any	**Health Condition Category:** Chronic liver disease, Risk factors, Comorbid conditions **Medical Condition, n/N (%):** Chronic liver disease: 745/1365 (54.6%) • Cirrhosis: 386/745 (51.8%) • NAFLD: 322/745 (43.2%) • Alcohol-related liver disease (ARLD): 179/745 (24.0%) • Chronic HBV infection: 96/745 (12.9%) • Chronic HCV infection: 92/745 (12.3%) **Control/Comparison group, n/N (%):** No chronic liver disease: 620/1365 (45.4%) • No liver disease & no cirrhosis: 359/745 (48.2%) • No liver disease & no NAFLD: 423/745 (56.8%)	Data retrieved from 2 registries and electronic medical records **Medical Condition(s):** *CLD*: with or without cirrhosis *Increasing Obesity*: BMI of >30 kg/m2 *NAFLD*: ND *Alcohol-related liver disease*: ND *Chronic HBV infection*: ND *Chronic HCV infection*: ND **Severity Measure(s):** *Child-Turcotte-Pugh (CTP) cirrhosis*: CTP-A, CTP-B, CTP-C **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Hospitalization*: ND *ICU Admission*: ND *Intubation:* invasive ventilation	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI) adjusted for all variables, n/N (%)* **Calculated by ERT* *Mortality, n/N (%):* • *OR: 0.72 (95% CI: 0.56-0.93) • CLD: 150/745 (25%) • Non-CLD: 160/620 (26%), p=0.014 NAFLD among CLD population: • aOR: 1.01 (95% CI: 0.57–1.79), p=0.965 • *OR: 0.19 (95% CI: 0.38-0.81) • Died: 48/150 (32.0%) • Survived: 274/595 (46.1%) ARLD among CLD population: • aOR: 1.79 (95% CI: 1.03–3.13), p=0.040 • *OR: 3.11 (95% CI: 2.12-4.55) • Died: 64/150 (42.7%) • Survived: 115/595 (19.3%) HBV among CLD population: • aOR: 0.96 (95% CI: 0.41–2.23), p=0.926 • *OR: 1.30 (95% CI: 0.78-2.15) • Died: 23/150 (15.3%)

Study	Population and Setting	Intervention	Definitions	Results
	location, and with any symptom profile or disease severity; within the same time period, data for non-CLD patients were collected using an identical case report form for consecutive patients testing positive for SARS-CoV-2 **Exclusion criteria:** SARS-CoV-2 infection was not laboratory-confirmed, the submission was a duplicate, if cirrhosis status was unclear, if hospitalization status or mortality outcome was not known or not reported, if the patient had a liver transplant, or if the patient was not aged over 16 years at the time of diagnosis	• No liver disease & no ARLD: 566/745 (76.0%) • No liver disease & chronic HBV infection: 649/745 (87.1%) • No liver disease & chronic HCV infection: 653/745 (87.7%)	*Ventilation*: ND **Comments:** Cirrhosis subset analysis included in paper but not extracted	• Survived: 73/595 (12.3%) HCV among CLD population: • aOR: 1.09 (95% CI: 0.58–2.06), p=0.785 • *OR (95% CI): 0.45 (95% CI: 0.23-0.88) • Died: 10/150 (6.7%) • Survived: 82/595 (13.8%) *Hospitalization, n/N (%):* • *OR (95% CI): 2.84 (2.11-3.83) • CLD: 668/745 (90%) • Non-CLD: 467/620 (75%) • p<0.001 *ICU Admission, n/N (%):* • *OR: 3.48 (95% CI: 2.49-4.85) • CLD: 177/745 (24%) • Non-CLD: 51/620 (8) • p<0.001 *Invasive Ventilation, n/N (%):* • *OR: 4.09 (95% CI: 2.72-6.15) • CLD: 132/745 (18%) • Non-CLD: 31/620 (5%) • p<0.001 **Severity of Condition:** *Mortality, n/N (%):* CLD without cirrhosis: ref • Died: 27/150 (18%) • Survived: 332/595 (55.8%) CTP-A: • aOR: 1.90 (95% CI: 1.03–3.52), p=0.040 • Died: 33/150 (22%) • Survived: 138/595 (23.2%) CTP-A vs CLD without cirrhosis • *OR: 2.94 (95% CI: 1.70-5.08 CTP-B: • aOR: 6.76 (95% CI: 3.95–11.58), p<0.001 • Died: 44/140 (29.3%) • Survived: 80/595 (13.4%) CTP-B vs CLD without cirrhosis • *OR: 6.76 (95% CI: 3.95-11.58) CTP-C: • aOR: 12.57 (95% CI: 7.12–22.18), p<0.001 • Died: 46/150 (30.7%)

Study	Population and Setting	Intervention	Definitions	Results
				• Survived: 45/595 (7.6%) CTP-C vs CLD without cirrhosis • *OR: 12.57 (95% CI: 7.12-22.18) *Hospitalization, n/N (%):* CTP-A: 150/171 (88%) CTP-A vs CLD without cirrhosis • *OR: 0.80 (95% CI: 0.45-1.41) CTP-B: 111/124 (90%) CTP-B vs CLD without cirrhosis • *OR: 0.95 (95% CI: 0.49-1.86) CTP-C: 84/91 (92%) CTP-C vs CLD without cirrhosis • *OR: 1.34 (95% CI: 0.57-3.11) CLD without cirrhosis: 323/359 (90%) *ICU Admission, n/N (%):* CTP-A: 40/171 (23%) CTP-A vs CLD without cirrhosis • *OR: 1.28 (95% CI: 0.83-1.99) CTP-B: 34/124 (27%) CTP-B vs CLD without cirrhosis • *OR: 1.59 (95% CI: 0.99-2.55) CTP-C: 34/91 (37%) CTP-C vs CLD without cirrhosis • *OR: 2.51 (95% CI: 1.52-4.13) CLD without cirrhosis: 69/359 (19%) *Ventilation, n/N (%):* CTP-A: 27/171 (16%) CTP-A vs CLD without cirrhosis • *OR: 0.92 (95% CI: 0.55-1.50) CTP-B: 23/124 (19%) CTP-B vs CLD without cirrhosis • *OR: 1.11 (95% CI: 0.65-1.89) CTP-C: 21/91 (23%) CTP-C vs CLD without cirrhosis • *OR: 1.47 (95% CI: 0.65-1.89) CLD without cirrhosis: 61/359 (17%) **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:**

Study	Population and Setting	Intervention	Definitions	Results
				Mortality: CLD & Obesity: • aOR: 1.27 (95% CI: 0.79–2.02), p=0.319 • *OR: 1.19 (95% CI: 0.81-1.76) • Died: 46/150 (30.7%) • Survived: 161/595 (27.1%) CLD & Hypertension: • aOR: 0.98 (95% CI: 0.62–1.53), p=0.914 • *OR: 1.27 (95% CI: 0.89-1.82) • Died: 68/150(45.3%) • Survived: 235/595 (39.5%) CLD & Diabetes Mellitus: • aOR: 1.19 (95% CI: 0.75–1.90), p=0.459 • *OR: 1.32 (95% CI: 0.91-1.90) • Died: 63/150 (42.0%) • Survived: 211/595 (35.5%) CLD & Heart Disease: • aOR: 1.14 (95% CI: 0.68–1.90), p=0.627 • *OR: 1.76 (95% CI: 1.16-2.66) • Died: 41/150 (27.3%) • Survived: 105/595 (17.6%) CLD & COPD: • aOR: 0.86 (95% CI: 0.40–1.85), p=0.707 • *OR: 1.36 (95% CI: 0.72-2.55) • Died: 14/150 (9.3%) • Survived: 42/595 (7.1%) CLD & Non-HCC Malignancy: • aOR: 1.28 (95% CI: 0.60–2.72), p=0.525 • *OR: 1.64 (95% CI: 0.82-3.28) • Died: 12/150 (8.0%) • Survived: 30/595 (5.0%) CLD & Hepatocellular Carcinoma (HCC): • aOR: 1.46 (95% CI: 0.67–3.18), p=0.346 • *OR: 1.70 (95% CI: 0.89-3.25) • Died: 14/150 (9.3%) • Survived: 34/595(5.7%) **Risk Markers:** *Mortality:* Age, median (IQR): • aOR: 1.02 (95% CI: 1.01–1.04), p=0.011 • Died: 62(54-72) • Survived: 58 (46-67) Sex (male):

Study	Population and Setting	Intervention	Definitions	Results
				• aOR: 0.72 (95% CI: 0.47–1.13), p=0.154 • *OR: 0.94 (95% CI: 0.65-1.36) • Died: 92/150 (61.3%) • Survived: 373/595 (62.7%) Ethnicity (white): • aOR: 1.40 (95% CI: 0.90–2.18), p=0.135 • *OR: 2.52 (95% CI: 1.73-3.68) • Died: 100/150 (66.7%) • Survived: 263/595 (44.2%) Smoker: • aOR: 0.49 (95% CI: 0.21–1.19), p=0.116 • *OR: 0.84 (95% CI: 0.40-1.77) • Died: 9/150 (6%) • Survived: 42/595 (7.1%) **Long-term Sequelae:** NR
Author: McKeigue[25] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Case-control **Study Objective:** To identify risk factors for severe COVID-19 and to lay the basis for risk stratification based on demographic data and health records. **IVA Score:** 19 (moderate)	**Population:** N = 41,220 Analysis, n = 733 **Setting:** NR **Location:** Scotland **Study dates:** NR **Inclusion criteria:** Cases of severe or fatal COVID-19 were defined by either a positive nucleic acid test followed by entry to critical care or death within 28 days or a death certificate with COVID-19 as underlying cause; for each case, the CHI database was used to select up to 10 controls who were matched for sex and 1-year age band, were registered with	**Health Condition Category:** Chronic liver disease **Medical Condition:** Liver disease: 5/733 (0.6%) **Control/Comparison group:** No liver disease: 728/733 (99.3%)	**Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** ND **Clinical marker:** NR **Treatment/ Associated Therapy:** ND **Outcome Definitions:** *Mortality*: Fatal cases **Comments:** None	**Severe COVID-19:** **calculated by ERT* *Mortality: n/N (%)* 250/733 (34.1%) Liver disease: • *OR: 7.83 (95% CI: 0.87-70.5) • Fatal: 4/250 (2%) • Non-fatal: 1/483 (0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	the same primary care practice, and were alive and resident in Scotland on the same day as the first date that the case tested positive **Exclusion criteria:** The 0.6% of cases that were recorded on the CHI database as no longer alive and resident in Scotland on the day that ECOSS recorded them as testing positive			
Author: Mollalo[39] **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	**Health Condition Category:** Chronic liver disease, Risk factors **Medical Condition:** Hepatitis: 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 **Control/Comparison group:** Non-significant (NS): non-significant counties	**Medical Condition(s):** *Hepatitis*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19 case fatality ratio (CFR)*: proportion of recorded death over the confirmed cases *COVID-19 Mortality rate (MR)*: mean COVID-19 mortality rate per 100,000 individuals **Comments:** None	**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:* Hepatitis: • HH: 5.602 (95% CI: 1.265-24.814), p=0.023 • LL: 0.808 (95% CI: 0.187-3.483), p=0.774 **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

Study	Population and Setting	Intervention	Definitions	Results
	excluded from subsequent analyses			
Author: Oh[59] **Year:** 2021 **Data Extractor:** MW **Reviewer:** CS **Study design:** Cohort **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)	**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 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	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Mild liver disease: 13,612/122,040 (10.9%) Moderate or severe liver disease: 146/122,040 (0.1%) **Control/Comparison group, n/N (%):** No mild liver disease: 108,428/122,040 (88.8%) No moderate or severe liver disease: 121,894/122,040 (99.9%)	**Medical Condition(s):** ICD-10 codes were used to evaluate CRDs and other comorbid conditions in the study population: **Severity Measure(s):** *Mild liver disease:* B18.x, K70.0 - K70.3, K70.9, K71.3 - K71.5, K71.7, K73.x, K74.x, 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 **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	**Severe COVID-19:** *aOR: Multivariable Logistic Regression: Multivariable Logistic Regression* **Severity of Condition:** *Mortality:* Mild liver disease: • aOR: 0.80 (95% CI: 0.58-1.10); p=0.170CI: 0.58-1.10); p=0.170 Moderate or severe liver disease: • aOR: 5.12 (95% CI: 1.32-19.90); p=0.018CI: 1.32-19.90); p=0.018 **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Parlak[53] **Year:** 2021	**Population:** N = 343 **Setting:** Hospital	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):**	**Medical Condition(s):** *Fatty liver disease:* If the attenuation of the liver was at least 10 HU less than that	**Severe COVID-19:** *aOR: Multivariable Logistic Regression: Multivariable Logistic Regression*

Study	Population and Setting	Intervention	Definitions	Results
Data Extractor: MW **Reviewer:** CS **Study design:** Cohort **Study Objective:** To retrospectively evaluate the chest CT of PCR-confirmed COVID19 cases and classify lung involvement by location, extension, and type, and to investigate the relationship between this classification and whether the patient had steatosis or not. **IVA Score:** 24 (moderate)	**Location:** Turkey **Study dates:** March 15 - April 30, 2020 **Inclusion criteria:** COVID-19 suspected patients with chest CT examinations admitted to the emergency department were included. **Exclusion criteria:** Patients under the age of 18 years, those with image artifacts, those that received an intravenous contrast agent for examinations, such as CT angiography, and those with chronic liver disease were excluded.	Fatty liver disease: 55/343 (16%) **Control/Comparison group, n/N (%):** No fatty liver disease: 288/343 (84.0%)	of the spleen or if the attenuation of the liver was less than 40 HU **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	*OR: Univariable (Univariate) Logistic Regression* *Mortality, n/N (%)* Fatty liver: • aOR: 4.522 (95%CI: 1.443-14.173); p=0.010: 4.522 (95%CI: 1.443-14.173); p=0.010 • OR: 3.915 (95%CI: 1.519-10.088); p=0.005 • Died: 8/20 (40.0%) • Survived: 47/323 (14.5%) • p=0.007 *ICU admission, n/N (%)* Fatty liver: • ICU: 19/54 (35.1%) • Non-ICU: 36/289 (12.4%) • p<0.001 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Peng[34] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To investigate the clinical features of critically ill SARS-CoV-2 patients with and without diabetes and	**Population:** N = 49 **Setting:** 2 hospitals designated for hospitalization of COVID-19 patients **Location:** China **Study dates:** February 1 - March 25, 2020 **Inclusion criteria:** Critically ill patients with COVID-19	**Health Condition Category:** Chronic liver disease **Medical Condition:** Chronic liver disease: 5/49 (10%) **Control/Comparison group:** No chronic liver disease: 44/49 (89.7%)	**Medical Condition(s):** *Chronic liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Ventilation*: non-invasive ventilation and invasive ventilation **Comments:** None	**Severe COVID-19:** *Odds ratios [OR] (95% CI); n/N (%)* ** calculated by ERT* Mortality, n/N (%): 16/49 (32.6%) Chronic liver disease: • *OR: 0.48 (95% CI: 0.05-4.7) • Died: 1/16 (6%) • Survived: 4/33 (12%) • p=1.000 *Ventilation*: 45% of all patients received non-invasive ventilation and 55% received invasive ventilation **Severity of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
identified risk factors for death of these patients. **IVA Score:** 24 (moderate)	admitted to study hospitals **Exclusion criteria:** NR			**Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Rubio-Rivas[9] **Year:** 2020 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To assess the characteristics and risk factors for mortality in patients with severe COVID-19 treated with tocilizumab (TCZ), alone or in combination with corticosteroids (CS). **IVA Score:** 23 (moderate)	**Population:** N = 186 **Setting:** Tertiary care public university hospital **Location:** Spain **Study dates:** March 17-April 7, 2020 **Inclusion criteria:** All consecutive patients aged ≥18 years admitted to study hospital with laboratory-confirmed COVID-19 via PCR of nasal or pharyngeal swabs and given TCZ due to severe COVID-19 pneumonia and systemic hyperinflammation; according to hospital guidelines, in order for TCZ to be used patients had to meet a Pa02/Fi02 × 100 <300 (or its surrogate Sat02/Fi02 × 100 <315) and at least 2 of the following criteria: ferritin >1000 ng/ml, C-	**Health Condition Category:** Chronic liver **Medical Condition:** Chronic liver disease: 7/186 (3.8%) **Control/Comparison group:** No chronic liver disease: 179/186 (96.2%)	**Medical Condition(s):** *Chronic liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: all-cause in-hospital mortality **Comments:** None	**Severe COVID-19:** *Univariable cox proportional hazards regression; hazard ratio [HR] (95%CI), n/N (%)* *Multivariable cox proportional hazards regression includes age, sex, chronic heart failure, atrial fibrillation, chronic liver disease, cancer, and use of CS in combination with TCZ; hazard ratio [HR] (95%CI), n/N (%)* **calculated by ERT* *Mortality*: 39/186 (20.9%) Chronic liver disease: • aHR: 4.69 (95% CI: 1.62–13.59), p=0.004 • *OR: 5.48 (95% CI: 1.17-25.63) • Non-survivors: 4/39 (10.3%) • Survivors: 3/147 (2%) • p=0.036 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	reactive protein >1000 mg/l, interleukin-6 >70 ng/l, D-dimer >1000 mcg/l, or lactate dehydrogenase >400 U/l; patients admitted to either conventional hospital wards, semi-critical (noninvasive mechanical ventilation), or critical care units (invasive mechanical ventilation) **Exclusion criteria:** NR			
Author: Schonfeld[22] **Year:** 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To describe the clinical characteristics and severity of disease at the time of their initial evaluation of a large cohort of patients diagnosed with COVID-19 and to report on patient outcomes while assessing for potential underlying risk factors associated with admission to an ICU or with death. **IVA Score:** 21 (moderate)	**Population:** 207,079 patients **Setting:** nationwide **Location:** Argentina **Study dates:** March 3-October 2, 2020 **Inclusion criteria:** Patients with suspected COVID-19 (≥2 of the following symptoms: fever ≥37.5°, cough, odynophagia, shortness of breath, anosmia or dysgeusia) that was subsequently laboratory confirmed through sequencing or RT-PCR assay of nasal and pharyngeal swab with complete datasets	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 914/207079 (0.4%) **Control/Comparison group, n/N (%):** No comorbidities: 122163/207079 (59.0%)	Data retrieved from COVID-19 database **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *ICU Admission*: ND *Hospitalization*: general ward **Comments:** None	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Mortality, n/N (%)*: 10913/207079 (5.3%) Liver disease: • *OR: 0.17 (95% CI: 0.14-0.19) • 185/10913 (1.7%) *ICU Admission, n/N (%):* 5652/207079 (2.7%) Liver disease: • *OR: 0.09 (95% CI: 0.07-0.12) • 84/5652 (1.5%) *Hospitalization*, n/N(%): 41703/207079 (20.1%) Liver disease: • *OR: 0.02 (95% CI: 0.02-0.02) • 397/41703 (1.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR

Study	Population and Setting	Intervention	Definitions	Results
	Exclusion criteria: Patients missing data for age or sex, not reporting symptoms, or missing data on comorbidities			**Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Shao [35] **Year:** 2021 **Data Extractor:** MW **Reviewer:** ECS **Study design:** Cohort **Study Objective:** To explore the implication of liver injury and chronic liver diseases in patients with COVID-19. **IVA Score:** 21 (moderate)	**Population:** N = 1,520 **Setting:** Single university hospital **Location:** China **Study dates:** February 4 - April 10 **Inclusion criteria:** Patients diagnosed with severe or critical COVID-19 and admitted to hospital from February 4 to March 30, 2020 **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition:** Chronic liver disease: 127/1520 (8.3%) • Chronic hepatitis B: 64/127 (50.4%) • Chronic hepatitis C: 20/127 (15.7%) • Fatty liver disease: 37/127 (29.1%) • Cirrhosis without documented etiological factors: 6/127 (10.2%) **Control/Comparison group:** No chronic liver disease: 1393/1520 (91.6%) • No chronic hepatitis B: 63/127 (50.6%) • No chronic hepatitis C: 107/127 (84.2%) • No fatty liver disease: 90/127 (70.8%) • No cirrhosis without documented etiological factors: 121/127 (95.2%)	Medical condition data extracted from electronic health records **Medical Condition(s):** *Pre-existing Chronic Liver Disease*: Chronic Hepatis B, chronic hepatitis C, fatty liver disease; all diagnosed by consensus diagnostic criteria **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: in hospital death *ICU Admission*: ICU admission during hospitalization **Comments:** None	**Severe COVID-19:** *Mortality, n/N (%):*5/121 (4.13%) *[numerators and denominators do not total 100% because some patients were not discharged at study end]* *Among CLD comorbidities population (n = 121):* CHB • Died: 4/64 (6.25%) • Discharged: 57/64 (89.06%) • *OR: 3.78 (0.41-34.9) CHC • Died: 1/20 (5%) • Discharged: 19/20 (95%) • *OR: 1.21 (0.12-11.4) FLD • Died: 0/37 (0%) • Discharged: 35/37 (94.59%) • *OR: 0.19 (0.01-3.64) • p= 0.535 *Among CLD population:* *ICU Admission, n/N (%):* 9/127 (7.08%) • Cirrhosis: 2/13 (15.38%) • No cirrhosis: 7/114 (6.14%) • *OR: 2.78 (0.51-15.05) • p=0.231 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
Author: Singh[23] **Year:** 2020 **Data Extractor:** CO **Reviewer**: MW/DOS **Study design:** Cohort **Study Objective:** To study the impact of preexisting liver disease on outcomes in a large cohort of patients with COVID-19 in the United States. **IVA Score:** 23 (moderate)	**Population:** N = 2,780 patients **Setting:** 34 health care organizations **Location:** USA **Study dates:** January 20-April 12, 2020 **Inclusion criteria:** Patients ≥10 years age diagnosed with ICD-10 codes U07.1, B34.2, B97.29, J12.81 after January 20,2020 **Exclusion criteria:** Patients with ICD-10 code 079.89 (other specified viral infection)	**Health Condition Category:** Chronic liver disease **Medical Condition:** Liver disease: 250/2780 (9%) Cirrhosis: 50/2780 (1.8%) **Control/Comparison group:** No liver disease: 2530/2780 (91%)	Data retrieved from electronic medical records **Medical Condition(s):** *Liver disease*: diagnosis of chronic liver disease, cirrhosis, or related complications either at the time of COVID-19 diagnosis or any time before that; defined according to the ICD-10-CM codes alone or in combination **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Hospitalization*: ND **Comments:** none	**Severe COVID-19:** *Risk ratio [RR] (95% CI)* *^1:1 propensity score matched risk ratio [RR] (95% CI) using greedy nearest-neighbor matching algorithm* **Odds ratio [OR] (95% CI) calculated by ERT* *Mortality, n/N (%)*: Liver Disease: • RR: 2.8 (95% CI: 1.9-4.0), p<0.001 • *OR: 3.0 (95% CI: 1.96-4.60) • Liver disease: 30/250 (12.0%) • No liver disease: 110/2530 (4.3%) • ^RR: 3.0 (1.5-6.0); p=0.001 • Liver disease: 30/250 (12.0%) • No liver disease: 10/250 (4.0%) Cirrhosis: • RR: 4.6 (95% CI: 2.6-8.3), p < 0.001 *Hospitalization, n/N (%):* Liver disease: • RR: 1.7 (95% CI: 1.2-2.0), p<0.001 • *OR: 2.52 (95% CI: 1.94-3.28) • Liver disease: 130/250 (52.0%) • No liver disease: 760/2530 (30.0%) • ^RR: 1.3 (1.1-1.6), p=0.006 • Liver disease: 120/250 (48.0%) • No liver disease: 90/250 (36.0%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Sterling[42] **Year:** 2020	**Population:** N = 256 patients	**Health Condition Category:** Chronic liver disease **Medical Condition:**	Data retrieved from electronic medical records **Medical Condition(s):**	**Severe COVID-19:** *Multivariable logistic regression [aOR] (95% CI)* *Ventilation*: 18%

Study	Population and Setting	Intervention	Definitions	Results
Data Extractor: CO **Reviewer:** MW/ECS **Study design:** Cohort **Study Objective:** To determine if FIB-4, a simple tool available to front line providers, would be associated with the need for mechanical ventilator support, and 30-day mortality among hospitalized patients with COVID-19. **IVA Score:** 22 (moderate)	**Setting:** University medical center **Location:** Virginia, USA **Study dates:** February-May 2020 **Inclusion criteria:** All patients admitted to the University Medical Center from February-May 2020 with COVID-19 (confirmed by polymerase chain reaction (PCR) **Exclusion criteria:** NR	Liver disease: 6% **Control/Comparison group:** NR Data were presented by mean and standard deviation (SD) or median and interquartile range (IQR) or frequency and percent	*Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: 30 day mortality in hospitalized patients *ICU Admission*: ND *Ventilation*: ND **Comments:** None	Liver disease: • Ventilation: (6.7%) • No ventilation: (5.7%) • p=0.8 • Multivariable OR p= 0.7 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Vaughan[44] **Year:** 2021 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To explore the patterns of sociodemographic, co-morbid conditions, and symptomatology of COVID-19 to further understanding of the disease. **IVA Score:** 21 (moderate)	**Population:** N = 257 patients **Setting:** Academic health care system (outpatient clinics, hospital, ER) **Location:** CA, USA **Study dates:** March 4, 2020- April 29, 2020 **Inclusion criteria:** Patients with laboratory-confirmed SARS-CoV-2 infection via nasopharyngeal swab RT-PCR assay from March 4-31, 2020 **Exclusion criteria:** Patients whose test specimens were sent	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver condition: 6/257 (2%) **Control/Comparison group, n/N(%):** *Calculated by ERT:* No liver condition: 251/257 (98%)	Data retrieved from electronic medical records *Liver condition*: Hepatitis B, Hepatitis C, Hepatic steatosis, cirrhosis, and other **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Hospitalization*: ND **Comments:** none	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT; n/N (%)* *Hospitalization, n/N (%):* 34/257 (13%) Liver condition: • *OR: 3.42 (95% CI: 0.60-19.45) • Liver condition: 2/6 (33%) • No liver condition: 32/251 (13%) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Intervention	Definitions	Results
	from a non-Stanford facility or had insufficient outcome data			
Author: Wang L [24] **Year:** 2020 **Data Extractor:** CS **Reviewer:** ECS/DOS **Study design:** Cohort **Study Objective:** To investigate the clinical characteristics and prognostic factors in the elderly patients with COVID-19. **IVA Score:** 24 (moderate)	**Population:** N = 339 **Setting:** Single center (designated hospital capable of receiving severe COVID-19 patients) **Location:** China **Study dates:** January 1- March 5, 2020 **Inclusion criteria:** All lab confirmed cases over 60 years old admitted to an isolation ward of a single hospital from January 1 to February 6, 2020 **Exclusion criteria:** NR	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Chronic liver disease: 2/339 (0.6%) **Control/Comparison group, n/N (%):** *Calculated by ERT No chronic liver disease: 337/339 (99.4%)	All data extracted from medical records; patient history was collected for comorbidities **Medical Condition(s):** *Chronic liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** *Cardiac Injury*: serum level of cardiac troponin I (cTnI) was above the 99th percentile upper reference limit **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *COVID-19*: diagnosis confirmed by real-time PCR and according to Interim guidance for novel coronavirus pneumonia published by National Health Commission of the People's Republic of China. *Death*: until March 5, four weeks from last admission. **Comments:** None	**Severe COVID-19:** *Multivariable cox regression/hazard ratio [HR] 95%CI; n/N (%)* *Univariable cox regression/ hazard ratio [HR] 95%CI; n/N (%)* **Odds ratio [OR] (95% CI) calculated by ERT* *Mortality, n/N (%)*: 65/339 (19.2%) Chronic liver disease: • HR: 2.902 (95% CI: 0.402-20.943), p=0.291 • *OR: 4.27 (95% CI: 0.26-69.12) • Dead: 1/65 (1.6%) • Survival: 1/274 (0.4%) • p=0.065 **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Wang QQ[36] **Year:** 2021 **Data Extractor:** MW **Reviewer:** DOS **Study design:** Case-control **Study Objective:** To analyze whether people with CLD are at increased	**Population:** N = 62,266,410 n = 16,530 analyzed **Setting:** 360 hospitals **Location:** USA **Study dates:** 1999 - October 1, 2020 **Inclusion criteria:** Age >18 years old),	**Health Condition Category:** Chronic liver disease, Risk factors **Medical Condition, n/N (%):** CLD, recent encounter (& COVID-19): 390/16530 (2.3%) Recent encounter defined as past year, but prior to their COVID-19 encounter **Control/Comparison group, n/N (%):** No CLD (& COVID-19): 15710/16530 (95%)	**Medical Condition(s):** *Chronic liver disease*: hepatitis B, hepatitis C, alcohol-related liver disease, non-alcoholic fatty liver disease, and cirrhosis **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: rates of death	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT* *Mortality, n/N (%):* CLD, recent encounter (& COVID-19): • 40/390 (10.3%) No CLD (& COVID-19): • 890/15710 (5.6%) • *OR: 1.9 (95% CI: 1.36-2.65) *Hospitalization, n/N (%):* CLD, recent encounter (& COVID-19): • 160/390 (41.0%) No CLD (& COVID-19): • 3850/15710 (23.9%)

Study	Population and Setting	Intervention	Definitions	Results
risk for getting COVID-19 or having severe COVID-19. **IVA Score:** 23 (moderate)	including patients who had encounters with healthcare systems for their diagnosis of chronic liver disease (CLD), patients with COVID-19 based on concept "Coronavirus infection (disorder)", and patients with both COVID-19 and CLD **Exclusion criteria:** NR		*Hospitalization*: admission to hospital **Comments:** Number of COVID-19 only is misreported in paper; should be 16530-820 = 15710	• *OR: 2.14 (95% CI: 1.74-2.63) **Severity of Condition:** NR **Duration of Condition:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality, %:* CLD, recent encounter (& COVID-19): • African American: 12.5% • Caucasian: 9.5% • p=0.457 No CLD (& COVID-19): • African American: 7.0% • Caucasian: 4.9% • p< 0.001 *Hospitalization, %:* CLD, recent encounter (& COVID-19): • African American: 43.8% • Caucasian: 38.1% • p=0.321 No CLD (& COVID-19): • African American: 32.6% • Caucasian: 19.9% • p< 0.001 **Long-term Sequelae:** NR
Author: Williamson[6] **Year:** 2020 **Data Extractor:** CS **Reviewer:** DOS **Study design:** Cohort **Study Objective:** To determine factors that are	**Population:** N = 17,278,392 patients **Setting:** Electronic health record system from participating GP surgeries across England; approximately 40% of the English population	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Liver disease: 100,017/17,278,392 (0.6%) **Control/Comparison group, n/N (%):** *Calculated by ERT No liver disease: 17,178,375/17,278,392 (99.4%)	All data retrieved from electronic medical records **Medical Condition(s):** *Liver disease*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:**	**Severe COVID-19:** *Kaplan-Meier hazard ratio [aHR] (95% CI) adjusted for age, sex, and other covariates; n/N (%)* **Odds ratio [OR] (95% CI) calculated by ERT* *COVID-19 related mortality, n/N (%):* 10,926/17,278,392 (0.06%) Liver disease • aHR: 1.75 (95% CI: 1.51–2.03) • *OR: 2.90 (95% CI: 2.50-3.36) • Died: 181/100,017 (0.18%) **Severity of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
associated with COVID-19-related death in England. **IVA Score:** 25 (moderate)	**Location:** England **Study dates:** February 1 – May 6, 2020 **Inclusion criteria:** Adults ≥18 years old currently registered as active patients with a general practice using TPP software with ≥1 year prior follow-up in the GP practice; patients had to have recorded sex, age, and deprivation score **Exclusion criteria:** Patients with less than one year of prior follow-up, <18 years old on February 1, 2020, or missing demographic information		*COVID-19*: suspected or laboratory confirmed *Mortality*: ND **Comments:** Author's note: included clinically suspected (non-laboratory confirmed) cases of COVID-19 since testing was not always carried out	**Duration of Condition:** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Wu[51] **Year:** 2021 **Data Extractor:** CO **Reviewer:** MW/DOS **Study design:** Cohort **Study Objective:** To analyze the risk factors for delayed recovery of COVID-19 among combined SARS-CoV-2 and HBV infection. **IVA Score:** 23 (moderate)	**Population:** N = 620 patients **Setting:** 7 hospitals **Location:** China **Study dates:** January 20- March 20, 2020 **Inclusion criteria:** COVID-19 patients recruited from study hospitals **Exclusion criteria:** All COVID-19 patients with other concomitant viral	**Health Condition Category:** Chronic liver disease **Medical Condition, n/N (%):** Hepatitis B Virus (HBV): 70/620 (11.3%) **Control/Comparison group, n/N (%):** No HBV: 550/620 (88.7%)	Data retrieved from medical records **Medical Condition(s):** *HBV*: ND **Severity Measure(s):** NR **Clinical marker:** NR **Treatment/ Associated Therapy:** NR **Outcome Definitions:** *Mortality*: ND *Ventilation*: ND **Comments:** None	**Severe COVID-19:** **Odds ratio [OR] (95% CI) calculated by ERT* *Mortality, n/N (%):* 14/620 (2.26%) HBV: • *OR: 0.26 (95% CI: 0.02-4.44) • HBV: 0/70 (0%) • No HBV: 14/550 (2.55%) • p=0.356 *Invasive ventilation, %:* • HBV: 11.43% • No HBV: 5.64% • p>0.05 **Severity of Condition:** NR **Duration of Condition:** NR

Study	Population and Setting	Intervention	Definitions	Results
	infections, drug-induced liver injury, and/or with underlying diseases, such as cardiovascular disease and diabetes mellitus, and COVID-19 patients with incomplete data			**Treatment/ Associated Therapy:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

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

Table 13. Internal Validity Assessments of Extracted Studies Reporting the Association between Chronic Liver Diseases and Severe COVID-19 Outcomes

	Author Year	Alizadehsani 2021[28]	Bahardoust 2021[11]	Bajaj 2021[61]	Bennett 2021[12]	Berenguer 2020[62]	Bergman 2021[8]	Butt 2021[52]	Campos-Murguia 2021[60]
	Outcome	Mortality	Mortality; Readmission	Mortality	Mortality; Intubation	Mortality	Mortality, ICU admission, hospitalization	Mortality; ICU admission; hospitalization	Mortality, ICU admission, Intubation
Domain	**Signaling question**	all clinical data including medical history	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from registries	Data retrieved from ERCHIVES database from VAMC	NR
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	1	1	1	1	1	1	0
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	0	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 and Misclassification	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	1	1
	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	0	1	1	1	1
	Adequately powered to detect result	0	0	0	0	0	1	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	0	1	0	1	1	1	1	1

	Author Year	Alizadehsani 2021[28]	Bahardoust 2021[11]	Bajaj 2021[61]	Bennett 2021[12]	Berenguer 2020[62]	Bergman 2021[8]	Butt 2021[52]	Campos-Murguia 2021[60]
	Outcome	Mortality	Mortality; Readmission	Mortality	Mortality; Intubation	Mortality	Mortality, ICU admission, hospitalization	Mortality; ICU admission; hospitalization	Mortality, ICU admission, Intubation
Domain	**Signaling question**	all clinical data including medical history	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from registries	Data retrieved from ERCHIVES database from VAMC	NR
	Data collection methods appropriate	0	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	0	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	0	0	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	0	0	1	1	1	1	1
	Confidence interval is narrow	0	0	0	0	1	1	0	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
	Adjustment for confounders in data analysis phase	0	0	0	1	1	1	0	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	0	1	1	1	1	1
SCORE	Threat to internal validity	20	21	19	23	25	26	22	24
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Moderate

	Author Year	Cao 2020[26]	Chen 2020[49]	Chishinga 2021[4]	Chow 2020[43]	Cui 2020[29]	Ding 2020 [38]	Dong 2021[13]	Eshrati 2020[7]
	Outcome	mortality, ICU admission, ventilation	Mortality; Severe COVID-19	Mortality, ICU admission, hospitalization	ICU admission, hospitalization	Mortality	Mortality; ventilation; ICU admission; hospitalization	Mortality, ventilation	Mortality
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from statewide database	data reported to CDC by states and territories	Data retrieved from medical records	Data retrieved from electronic medical records	Data was extracted from medical records	Data retrieved from medical records
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	1	1	1	1	1	1	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	0	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 and Misclassification	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	1	1
	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	0	1	1	1	1	1	1
	Adequately powered to detect result	0	0	0	0	0	0	0	0
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	0	1	1	1	1	1	1	1

	Author Year	Cao 2020[26]	Chen 2020[49]	Chishinga 2021[4]	Chow 2020[43]	Cui 2020[29]	Ding 2020 [38]	Dong 2021[13]	Eshrati 2020[7]
	Outcome	mortality, ICU admission, ventilation	Mortality; Severe COVID-19	Mortality, ICU admission, hospitalization	ICU admission, hospitalization	Mortality	Mortality; ventilation; ICU admission; hospitalization	Mortality, ventilation	Mortality
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from statewide database	data reported to CDC by states and territories	Data retrieved from medical records	Data retrieved from electronic medical records	Data was extracted from medical records	Data retrieved from medical records
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	0	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	0	1	1	1	1
	Confidence interval is narrow	0	1	0	0	0	0	0	0
Confounding	Potential confounders identified	1	1	1	0	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	0	1	1	0	1	0	0	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	22	23	24	20	24	23	23	24
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Year	Espana 2021[57]	Fisman 2020[14]	Forlano 2020[54]	Frager 2020[27]	Fried 2020[15]	Galiero 2020[1]	Gorgulu 2020[16]	Gottlieb 2020[63]
	Outcome	Mortality	Mortality	Mortality, ICU admission	Mortality, intubation	Mortality, mechanical ventilation	Mortality	Mortality, ICU admission, ventilation	Hospitalization
Domain	**Signaling question**	Data retrieved from electronic medical records	Data retrieved from electronic medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from hospital claims	Data retrieved from medical records	Data retrieved from electronic health records	Data retrieved from medical records
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	0
	Well described control/ comparator	1	1	1	1	1	1	1	0
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	0
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	0
	Attrition <10-15% of population	1	1	1	1	1	1	1	0
	Attrition appropriately analyzed	1	1	1	1	1	1	1	0
Information Bias: Measurement and Misclassification	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	1	1
	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	0	1	1	1	1	0
	Adequately powered to detect result	1	1	0	0	1	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	0
	Data collection methods appropriate	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	0	1	1

	Author Year	Espana 2021[57]	Fisman 2020[14]	Forlano 2020[54]	Frager 2020[27]	Fried 2020[15]	Galiero 2020[1]	Gorgulu 2020[16]	Gottlieb 2020[63]
	Outcome	Mortality	Mortality	Mortality, ICU admission	Mortality, intubation	Mortality, mechanical ventilation	Mortality	Mortality, ICU admission, ventilation	Hospitalization
Domain	**Signaling question**	Data retrieved from electronic medical records	Data retrieved from electronic medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from hospital claims	Data retrieved from medical records	Data retrieved from electronic health records	Data retrieved from medical records
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	1	0	0	0	1	0	0	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
	Adjustment for confounders in data analysis phase	1	1	1	0	1	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	0	0	1	1	1	1
SCORE	Threat to internal validity	26	25	22	22	26	23	24	17
	Low, Moderate, High	Low	Moderate	Moderate	Moderate	Low	Moderate	Moderate	High

	Author Year	Grasselli 2020[30]	Guan 2020[47]	Gude-Sampedro 2020[17]	Guerra Veloz 2020[18]	Halalau 2021[45]	Harrison 2020[58]	Hashemi 2020[2]	He 2020[31]	Higuera-de la Tijera 2021[41]
	Outcome	Mortality	Mortality; ICU admission; Mechanical ventilation	Mortality; ICU admission; hospitalization	Mortality; hospitalization; ICU admission; ventilation	Hospitalization	Mortality	Mortality, ICU admission, mechanical ventilation	Mortality, ICU admission, ventilation	Intubation
Domain	**Signaling question**	Retrieved from database of prescription of the general practitioners	Retrieved from medical records, self-reported underlying conditions	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from reports of electronic medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1	1
	Well described population	1	1	1	1	1	1	1	1	1
	Well described setting	1	1	1	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	1	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	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	1
	Attrition <10-15% of population	1	1	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	0	1	1	1	1	1	1	1
	Measure of outcome is valid	1	1	1	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0	0	0

	Author Year	Grasselli 2020[30]	Guan 2020[47]	Gude-Sampedro 2020[17]	Guerra Veloz 2020[18]	Halalau 2021[45]	Harrison 2020[58]	Hashemi 2020[2]	He 2020[31]	Higuera-de la Tijera 2021[41]
	Outcome	Mortality	Mortality; ICU admission; Mechanical ventilation	Mortality; ICU admission; hospitalization	Mortality; hospitalization; ICU admission; ventilation	Hospitalization	Mortality	Mortality, ICU admission, mechanical ventilation	Mortality, ICU admission, ventilation	Intubation
Domain	**Signaling question**	Retrieved from database of prescription of the general practitioners	Retrieved from medical records, self-reported underlying conditions	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from reports of electronic medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records
	Prospective study	1	0	1	1	1	1	1	1	1
	Adequately powered to detect result	0	1	1	0	0	0	0	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1	0	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1	1	1	0
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1	1	1	0
	Confidence interval is narrow	0	0	0	0	0	1	0	0	0
Confounding	Potential confounders identified	1	1	1	1	1	1	1	1	0
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	1	1	0	0	1	1	0	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	0	1	1	1	1	1

	Author Year	Grasselli 2020[30]	Guan 2020[47]	Gude-Sampedro 2020[17]	Guerra Veloz 2020[18]	Halalau 2021[45]	Harrison 2020[58]	Hashemi 2020[2]	He 2020[31]	Higuera-de la Tijera 2021[41]
	Outcome	Mortality	Mortality; ICU admission; Mechanical ventilation	Mortality; ICU admission; hospitalization	Mortality; hospitalization; ICU admission; ventilation	Hospitalization	Mortality	Mortality, ICU admission, mechanical ventilation	Mortality, ICU admission, ventilation	Intubation
Domain	**Signaling question**	Retrieved from database of prescription of the general practitioners	Retrieved from medical records, self-reported underlying conditions	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from reports of electronic medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records
Other Bias	No other sources of bias	1	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	1
SCORE	Threat to internal validity	24	23	25	22	23	25	23	23	20
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Year	Huang 2020[55]	Jiang Y 2020[32]	Killerby 2020[46]	Kim D 2020[56]	Kim SR 2020[40]	Kokturk 2021[19]	Li C 2020[20]	Li G 2020[21]
	Outcome	ICU admission, Mortality	Mortality, ventilation	Mortality, hospitalization	Mortality	ICU admission	Mortality	Mortality, Intubation	Mortality
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from national database	Data extracted from medical records	Data retrieved from medical records	Data retrieved from medical records
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	0
	Well described setting	1	1	1	1	1	1	1	0
	Well described intervention/ exposure	1	1	0	1	1	1	1	1
	Well described control/ comparator	1	1	0	0	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	0	0	1	1	1	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	0	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	0	1	1	1	1	1
	Attrition appropriately analyzed	1	1	0	1	1	1	1	0
Information Bias: Measurement and Misclassification	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	1	1
	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	0	0	1	1	1	1
	Adequately powered to detect result	0	0	1	1	0	0	0	0
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	0	0	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

	Author Year	Huang 2020[55]	Jiang Y 2020[32]	Killerby 2020[46]	Kim D 2020[56]	Kim SR 2020[40]	Kokturk 2021[19]	Li C 2020[20]	Li G 2020[21]
	Outcome	ICU admission, Mortality	Mortality, ventilation	Mortality, hospitalization	Mortality	ICU admission	Mortality	Mortality, Intubation	Mortality
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from national database	Data extracted from medical records	Data retrieved from medical records	Data retrieved from medical records
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	0	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	0	1	1	1
	Confidence interval is narrow	0	0	0	0	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1	0	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	0	1	1	1	0	1	0	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	23	24	17	21	20	24	23	21
	Low, Moderate, High	Moderate	Moderate	High	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Year	Li Y 2020	Liu J 2020[50]	Liu R 2020[48]	Maestre-Muniz 2021[33]	Magro 2021[5]	Mallow 2020[3]	Marjot & Buescher 2021[64]	Marjot & Moon 2021[37]
	Outcome	Mortality	Mortality	Mortality	Mortality	Mortality, ICU admission, ventilation	Mortality; ICU admission	Mortality, hospitalization, ICU, ventilation	Mortality, hospitalization, ICU, ventilation
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data extracted from medical records	Data retrieved from medical records/data base	Data retrieved from electronic medical records	Data retrieved from registries	Data retrieved from registries and electronic medical records
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	1	1	1	0	1	1	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 and Misclassification	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	1	1
	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	1	1
	Adequately powered to detect result	0	0	0	0	0	1	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	1
	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

	Author Year	Li Y 2020	Liu J 2020[50]	Liu R 2020[48]	Maestre-Muniz 2021[33]	Magro 2021[5]	Mallow 2020[3]	Marjot & Buescher 2021[64]	Marjot & Moon 2021[37]
	Outcome	Mortality	Mortality	Mortality	Mortality	Mortality, ICU admission, ventilation	Mortality; ICU admission	Mortality, hospitalization, ICU, ventilation	Mortality, hospitalization, ICU, ventilation
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data extracted from medical records	Data retrieved from medical records/data base	Data retrieved from electronic medical records	Data retrieved from registries	Data retrieved from registries and electronic medical records
	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	0	0	0	0	1	0	1
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
	Adjustment for confounders in data analysis phase	1	1	1	1	1	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	0	1	1	1	1	1	1	1
SCORE	Threat to internal validity	23	24	24	24	23	26	24	27
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Low

	Author Year	McKeigue 2020[25]	Mollalo 2021[39]	Oh 2021[59]	Peng 2020[34]	Parlak 2021[53]	Rubio-Rivas 2020[9]	Schonfeld 2021[22]
	Outcome	Mortality	Association between COVID-19 mortality and mortalities for other diseases	Mortality	Mortality, Ventilation	Mortality, ICU admission	Mortality	Mortality, hospitalization, ICU admission
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from USAFacts and UW Global Health Data Exchange	Data retrieved from database	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from COVID-19 database
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1
	Well described population	1	1	1	1	1	1	1
	Well described setting	0	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	1	1	1	1	1
	Well described control/ comparator	1	1	1	1	1	1	1
	Well described outcome	1	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	0	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	1	1	1	1
	Measure of outcome is valid	1	0	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0	0
	Prospective study	1	0	1	1	1	1	0
	Adequately powered to detect result	0	0	1	0	0	0	1
	Outcome assessor blinded	0	0	0	0	0	0	0

	Author Year	McKeigue 2020[25]	Mollalo 2021[39]	Oh 2021[59]	Peng 2020[34]	Parlak 2021[53]	Rubio-Rivas 2020[9]	Schonfeld 2021[22]
	Outcome	Mortality	Association between COVID-19 mortality and mortalities for other diseases	Mortality	Mortality, Ventilation	Mortality, ICU admission	Mortality	Mortality, hospitalization, ICU admission
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from USAFacts and UW Global Health Data Exchange	Data retrieved from database	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from medical records	Data retrieved from COVID-19 database
Information Bias: Performance & Detection	Study participant blinded	0	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	0	1	1	1	1	0	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	0	1	1	1	1	1	0
	Appropriate statistical analyses are conducted correctly	0	1	1	1	1	1	0
	Confidence interval is narrow	0	1	0	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	0	1	1	1	1	1	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1	1
SCORE	Threat to internal validity	19	22	25	24	24	23	21
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Year	Shao 2021[35]	Singh 2020[23]	Sterling 2020[42]	Vaughan 2021[44]	Wang L 2020[24]	Wang QQ 2021[36]	Williamson 2020[6]	Wu 2021[51]
	Outcome	Mortality, ICU admission	Mortality, Hospitalization	Mortality, ICU admission, ventilation	Hospitalization	Mortality	Hospitalization, Mortality	Mortality	Mortality, Ventilation
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Retrieved from medical records	Retrieved from medical records	Extracted from medical records; patient history collected for comorbidities	Retrieved from medical records	Retrieved from medical records	Retrieved from medical records
Study Elements	Design appropriate to research question	1	1	1	1	1	1	1	1
	Well described population	1	1	1	1	1	0	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	1	1	1	1	1	1	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 and Misclassification	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	1	1
	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	1	1
	Adequately powered to detect result	0	0	0	0	1	0	1	0
Information Bias:	Outcome assessor blinded	0	0	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0	0	0

	Author Year	Shao 2021[35]	Singh 2020[23]	Sterling 2020[42]	Vaughan 2021[44]	Wang L 2020[24]	Wang QQ 2021[36]	Williamson 2020[6]	Wu 2021[51]
	Outcome	Mortality, ICU admission	Mortality, Hospitalization	Mortality, ICU admission, ventilation	Hospitalization	Mortality	Hospitalization, Mortality	Mortality	Mortality, Ventilation
Domain	**Signaling question**	Data retrieved from medical records	Data retrieved from medical records	Retrieved from medical records	Retrieved from medical records	Extracted from medical records; patient history collected for comorbidities	Retrieved from medical records	Retrieved from medical records	Retrieved from medical records
Performance & Detection	Investigator/ data analyst blinded	0	0	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	0	1	0	1
	Data collection methods appropriate	1	1	1	1	1	1	1	1
	Sufficient follow up to detect outcome	0	1	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	0	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	0	1	1	1	1
	Confidence interval is narrow	0	0	0	0	0	0	1	0
Confounding	Potential confounders identified	0	1	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	0	1	1	0	1	1	1	0
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	0	1	1	1	1	1	1
SCORE	Threat to internal validity	21	23	24	21	24	23	25	23
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

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