Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 and Cirrhosis: A Combination We Must Strive to Prevent

See "Outcomes of SARS-CoV-2 infection in patients with chronic liver disease and cirrhosis: a national COVID cohort collaborative study" by Ge J, Pletcher MJ, Lai JC, N3C Consortium, on page 1487.

Since the first cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were reported in late 2019, coronavirus disease 2019 (COVID-19) has claimed the lives of more than 4 million people worldwide.[1] In the hepatology community, there has been recognition that patients with chronic liver disease, especially cirrhosis, may be among those at highest risk of a severe clinical course. In addition to the risk incurred by cirrhosis-related immune dysfunction,[2] patients with cirrhosis often have comorbid conditions that predispose to severe COVID-19, such as diabetes, chronic kidney disease, and heart disease. Moreover, a wide spectrum of socioeconomic and ethnic backgrounds are represented in patients with chronic liver disease; among these are groups disadvantaged by inequities in social determinants of health who have shouldered a disproportionate burden of COVID-19–related morbidity and mortality.[3]

In this issue of *Gastroenterology*, Ge and colleagues[4] conduct a retrospective cohort study to evaluate the outcomes of patients with cirrhosis and COVID-19 using electronic health record data from the National COVID Cohort Collaborative Data Enclave, or N3C.[4] The N3C is a novel, centralized, curated, national repository of harmonized electronic health record data from clinical sites across the United States, with the National Center for Advancing Translational Sciences at the National Institutes of Health serving as data steward. It was formed in response to the need for rapid accrual of large-scale data on COVID-19. Such efforts have traditionally been challenging due to the disparate data management systems across health care sites. At the time of the study, 57 sites were included in the N3C, with more than 6 million unique patients.

The 220,727 patients included in Ge et al's study[4] were adults with chronic liver disease who underwent testing for SARS-CoV-2 via nucleic acid amplification testing or culture between January 1, 2020 and July 1, 2021. Among patients with cirrhosis, COVID-19 was associated with a 2.38-fold (95% CI, 2.18–2.59) increased risk of 30-day mortality after adjusting for age, race and ethnicity, chronic liver disease etiology, comorbidities as quantified by a modified Charlson Comorbidity Index, and geographical region. Among patients with COVID-19 and chronic liver disease, the presence of cirrhosis was associated with a 3.31-fold (95% CI, 2.91–3.77) higher risk of 30-day mortality. Demographic and clinical factors associated with increased mortality among patients with cirrhosis and COVID-19 included older age, identification as "other" or unknown race or ethnicity, underlying alcohol-associated liver disease, and a greater burden of comorbidities.

Results of this study are largely consistent with observations made in previous studies based on registry data,[5] multicenter consortia,[6,7] research network data,[8] and the Veterans Health Administration.[9] Although these studies have been limited by issues of selection bias, generalizability, and imperfect control groups, they have been critical in establishing cirrhosis as a major risk factor for poor

outcomes from COVID-19. The study by Ge and colleagues[4] confirms the main findings of these studies using a larger and nationally representative patient cohort with more recent follow-up data.

An obvious strength of the study by Ge and colleagues[4] is the size of the patient sample, enabling stratified analyses that yielded interesting observations. One observation was that, among patients with cirrhosis, the magnitude of the association between COVID-19 and mortality decreased with more advanced liver disease. COVID-19 was associated with a 5-fold greater risk of death among patients with compensated cirrhosis, but a 2.2-fold greater risk of death among patients with decompensated cirrhosis. With the caveat that no test of interaction was performed to determine whether these hazard ratios are statistically different, these results do underscore the high baseline risk of poor outcomes among patients with advanced liver disease. To some extent, this reflects the choice of controls in this study, which included patients with negative COVID-19 tests, but who had an indication for testing and, as such, may have had higher than average baseline mortality. However, these results also caution us to remain vigilant in caring for patients with decompensated cirrhosis in the face of challenges to health care delivery due to COVID-19.

There seems to be little residual doubt that concerns about the impact of COVID-19 on patients with cirrhosis are well-founded. Our next task in the hepatology community is to turn our attention to risk mitigation. Although COVID-19 vaccinations have been remarkably effective in the general population, the efficacy in patients with cirrhosis is only beginning to be evaluated.[10] Existing clinical trials of vaccines included only a small number of patients with liver disease, so we will need to rely on real-world observational data for guidance. The vaccination rate among patients with cirrhosis is unknown; such information is necessary to inform efforts to improve vaccine uptake. We will also need to determine whether patients with cirrhosis are among those who benefit from booster doses. Lastly, it would be useful to know whether patients with cirrhosis benefit from early treatment to prevent progression to severe COVID-19, whether there is a role for post-exposure prophylaxis, and whether treatments shown to improve outcomes of COVID-19 are similarly effective in patients with cirrhosis. The resurgence of COVID-19 in recent months adds urgency to addressing these questions.

An additional responsibility we must not neglect is preparing for the indirect toll of the pandemic on patients with cirrhosis. Multiple studies have described pandemic-related declines in routine care, such as surveillance imaging for liver cancer and procedures such as upper endoscopies.[11,12] Whether these changes will translate into worse liver cancer–related outcomes or increased liver-related mortality remain to be seen. A study using Veterans Health Administration data showed lower rates of hospitalizations for cirrhosis during the pandemic, but higher Model for End-Stage Liver Disease score on admission.[13] Although a number of factors could account for this observation, it is certainly conceivable that delays or gaps in care have resulted in patients presenting to the hospital with more decompensated disease. Moving forward, clinicians, patients, and health care systems might need to recalibrate their risk-to-benefit calculations to ensure that patients with liver disease have timely access to the care they need, while minimizing the risk of COVID-19 exposure.

In the early phases of this unprecedented pandemic, members of the scientific and medical communities raced to share information and disseminate knowledge about a rapidly spreading disease. Our collective efforts are still needed to ensure that our most vulnerable patients are protected, and to prepare for the direct and indirect effects of COVID-19 on patients with liver disease.

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COVID-19 and Social Determinants of Health in Gastroenterology and Hepatology

See "Outcomes of SARS-CoV-2 infection in patients with chronic liver disease and cirrhosis: a National COVID Cohort Collaborative Study" by Ge J, Pletcher MJ, Lai JC, N3C Consortium, on page 1487.

The coronavirus disease 2019 (COVID-19) pandemic laid bare the structural inequities in health care, with Black, Latino (LatinX/Hispanic) and American Indian/Alaska Native (AI/AN) populations in the United States experiencing disproportionately higher rates of infection, hospitalization, and death than White populations. The National Academy of Science, Engineering, and Medicine report on health equity identified social determinants of health (SDOH) as fundamental causes of racial inequities in health.[1] Although underlying comorbidities like cardiovascular diseases, diabetes, obesity, and cancer are risk factors for COVID-19 outcomes, the role of SDOH in disparities by race and ethnicity is undeniable.[2] In a cohort study of 44,000 Medicare beneficiaries hospitalized with COVID-19 across 1188 US hospitals, racial disparities in mortality and discharge to hospice were explained by differences in the hospitals to which Black and White patients were admitted after adjusting for age, sex, ZIP code–level income, and underlying comorbidity.[3] The negative impact of neighborhood deprivation for those residing in low socioeconomic conditions on the disparate COVID-19 outcomes in minoritized populations,[4] and the disproportionately higher rates of COVID-19 hospitalizations and mortality reported in ZIP codes with predominantly Black and Latino populations irrespective of socioeconomic status,[5] are the backdrop and context within which the findings by Ge et al[6] should be interpreted.

Although the primary aim of Ge et al[6] was to describe COVID-19 outcomes for individuals with chronic liver disease (CLD), the results of their secondary analyses by race and ethnicity are also noteworthy. The authors identified an association between Latino ethnicity and increased mortality among patients with COVID-19 and CLD. For the subgroup of Latino patients with cirrhosis, there was no statistical relationship between COVID-19 and mortality. The findings are consistent with studies that demonstrate an association between CLD and poor COVID-19 outcomes.[7–9] However, the results are in contrast to a recent multi-institutional study that found an association between Latino ethnicity and severe COVID-19 disease among patients with decompensated cirrhosis, but no association between Latino ethnicity and COVID-19–related mortality.[7]

There are several possible explanations for an association between Latino ethnicity and mortality in COVID-19. Given the higher prevalence of CLD, cirrhosis, and poorer CLD outcomes among Latino populations in the United States compared to other racial and ethnic groups,[10,11] the presence of CLD can confound or amplify the relationship between COVID-19 and mortality. In addition, Latino patients might have higher mortality in the setting of COVID-19 and comorbid CLD due to overall higher incidence of COVID-19,[2] high prevalence of chronic conditions, and/or poor access to health care, all of which are consequences of adverse SDOH. The profound ethnic disparities in incidence of CLD, other chronic illnesses, and COVID-19 reflect the pervasiveness of adverse SDOH in Latino communities and their harmful impact on broader health outcomes.

Of note, despite high incidence and mortality from COVID-19 among Black and AI/AN people in the United States, the authors' findings did not extend to these groups. Although unadjusted analysis found a statistically significant association between COVID-19 and mortality for Black patients, there was no significant association in controlled models. Findings for AI/AN patients were not reported. The reasons for a lack of association in these subgroups is unclear. Improved CLD outcomes in Black compared with