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Review Article

Covid-19 and alcohol associated liver disease

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ABSTRACT

The COVID-19 pandemic is having substantial impacts on the health status of individuals with alcohol use disorder (AUD) and alcohol-associated liver disease (ALD). AUD and ALD have both been impacted throughout the pandemic, with increases in alcohol use during the early stages of the pandemic, reduced access to treatment during the mid-pandemic, and challenges in managing the downstream effects in the post-COVID era. This review will focus on how the COVID-19 pandemic has impacted AUD and ALD epidemiology and access to treatment, and will discuss to address this rising AUD and ALD disease burden.

1. Introduction

The COVID-19 pandemic is having substantial impacts on the health status of individuals with alcohol use disorder (AUD) and alcohol-associated liver disease (ALD). AUD and ALD have both been impacted throughout the pandemic, with increases in alcohol use during the early stages of the pandemic, reduced access to treatment during the mid-pandemic, and challenges in managing the downstream effects in the post-COVID era. This review will focus on how the COVID-19 pandemic has impacted AUD and ALD epidemiology and access to treatment, and will discuss to address this rising AUD and ALD disease burden (Table 1 and 2).

2. Alcohol consumption and alcohol use disorder

Prior to the onset of the COVID-19 pandemic, harmful alcohol consumption and alcohol use disorder were rising in the United States [1]. In 2001–2002, the 12 month prevalence of AUD was 8.5%; a decade later in 2012–2013, this rose to 12.7%, a 49% increase [1]. The reasons underlying these trends are not well understood. While some of the increases may reflect improved screening and diagnosis, they have coincided with increases in ALD mortality, likely reflective of true increase in alcohol consumption [2].

In the first few months of the pandemic starting in March 2020, concerns emerged that the pandemic could exacerbate rising substance use disorders (SUDs) [3,4]. Prior evidence has shown that increasing financial insecurity, unemployment, and psychological distress are associated with increased harmful substance use [5,6]. During the first year of the pandemic, alcohol sales rose substantially within the United States, from $7.1 billion in 2019 to $9.5 billion in 2020 [7]. These trends were mirrored internationally; China witnessed a more than two-fold increase in harmful alcohol consumption [8], and England observed increases in high-risk drinking in particular [9]. As alcohol sales increased, the United States also observed increases in alcohol-related hospitalizations [10] and alcohol-related mortality [11].

Several reasons underlie these trends in alcohol consumption. Previous studies have shown that mass traumatic events/experiences are associated with short-term increases in alcohol use [5]. Although the COVID-19 pandemic was indeed a mass traumatic event, it was not a finite experience, and has now continued for more than two years. During the pandemic, many Americans lost their jobs and experienced financial insecurity, both of which are associated with heavy alcohol consumption and rising prevalence of AUD [6]. Furthermore, the psychological distress and isolation that came with the pandemic and quarantines may have provoked heavier alcohol use [4,12]. In fact, during the pandemic, subjective feelings of distress were associated with increased harmful alcohol use [13].

Another reason alcohol consumption and AUD may have increased is the pandemic's unique impact on SUD treatment. Many AUD/SUD treatment modalities involve group meetings and group settings. During the pandemic, support groups like Alcoholics Anonymous or Narcotics Anonymous and intensive outpatient treatment understandably became less accessible amidst efforts to reduce COVID-19 spread [14]. These impacts were also seen in

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Table 1
COVID-19 and alcohol-associated liver disease.

Alcohol Consumption and Alcohol Use Disorder	
Epidemiology	- AUD prevalence was rising pre-pandemic [1] - Alcohol sales increased in the first year of the pandemic [7] - Alcohol-related hospitalizations and alcohol-related mortality increased post-pandemic [2,10,11]
Mechanisms	- Mass traumatic events associated with short-term increases in alcohol consumption [5] - Financial insecurity and unemployment associated with increased substance use disorders [6] - Psychological distress and isolation [4,12,13]
Impaction on Substance Use Disorder Treatment	- Group SUD treatment curtailed [14,15] - Residential treatment settings impacted by COVID-19 [15,16]
Alcohol-Associated Liver Disease Epidemiology	
Pre-Pandemic	- ALD prevalence increased prior to the pandemic [17] - Hospitalizations for AC and AH were rising [18,19] - ALD became the leading indication for liver transplantation [20,21]
Post-pandemic	- AH admissions increased more than 50% [24,25] - ALD mortality accelerated during the covid 19 pandemic, increasing more than 20% in males and females [26] - Females and younger adults experienced highest relative increases in ALD [26]
Impact on Alcohol-Associated Liver Disease Outcomes	
Rising Alcohol Consumption	- Alcohol use in cirrhosis associated with increased mortality, infection, and gastrointestinal bleeding [30,31] - Higher prevalence of ALD in ACLF hospital admissions [32] - Alcohol consumption may have a detrimental impact on the immune system [33,34]
COVID-related outcomes	- Patients with ALD have increased risk of severe illness and death from COVID-19 [36–38] - Patients with cirrhosis had a 30% case fatality rate [36,37] - COVID-19 can provoke ACLF [36] - ALD has the highest case-fatality rate of all etiologies of liver disease [38,39]
Impact on ALD Treatment and Liver Transplantation	
ALD Treatment	- Early in the pandemic, cirrhosis and ALD-related hospitalizations declined likely reflecting delays in care [40] - Access to outpatient hepatology treatments and early alcohol treatment may have been impacted by COVID-19
Liver Transplantation	- Transplant candidates have increased risk of severe COVID-19 and death [47] - Transplants for severe AH increased by more than 50% during the COVID era and median MELD-Na at transplant rose [43,44]
Post-Transplant Care	- Concerns regarding immunosuppressed status, however mortality has been similar across LT-recipients and non-LT patients when accounting for other confounders [52]
Demographic Trends and Increasing Inequities	
Pre-pandemic	- AUD and ALD prevalence highest in American Indian/Alaska Native Populations [1] - Racial and ethnic minority groups have worse AUD outcomes compared to White individuals [54] - Among patients hospitalized with cirrhosis, Black patients have the highest mortality [55]
Post-Pandemic	- Black and Hispanic/Latinx patients with CLD were disproportionately impacted by COVID-19 [60] - Highest relative increase in alcohol use in women and Black individuals [62] - Highest relative increase in AH admissions in women and Black patients [61] - Highest relative increase in ALD mortality in women and young adults [26]
**These disparities likely reflect inequitable access to treatment, social and economic exclusion, and other downstream sequelae of structural racism*	
Improving AUD and ALD Care During the COVID-19 Pandemic	
Telemedicine	- Effective for providing specialty hepatology care [68] - Effective in reducing alcohol use [69,70] - Virtual and web-based programs during the pandemic were effective at treating AUD in ALD patients [71,72] - May neglect at-risk populations without stable housing or internet options [73]
Prevention and Treatment of COVID-19	- Vaccination should be emphasized for those with chronic liver disease - Medications for the treatment of COVID-19 need to be understood in the context of liver dysfunction
Response to Rising AUD and ALD	
Prevention	- Improve public health messaging [77] - Higher taxation on alcohol has been associated with reduce alcohol consumption and lower ALD [84–87]
Screening	- Sensitivity in primary care screening is < 50% and evidence-based tools are underused [78–80] - AUDIT-C or SASQ as evidence-based screening tools [81,82]
Treatment	- AUD treatment reduces hepatic decompensations and all-cause mortality in patients with cirrhosis [90] - Patients with ALD are often undertreated for their AUD [92] - Integrated care and team-based approaches should be used [94] - Profound shortage of addiction providers [97,98] - Brief alcohol interventions in primary care [99] - Collaborative care models for AUD in primary care [101]

ACLF; Acute-on-chronic liver failure. AH; Alcohol-associated hepatitis; ALD; Alcohol-associated liver disease. AUD; Alcohol use disorder. AUDIT-C; Alcohol use disorders identification test – consumption. CLD; Chronic liver disease. SASQ; Single alcohol screening question. SUD; Substance use disorder.

Table 2
Studies exploring the impact of the COVID-19 pandemic on alcohol consumption and alcohol-associated liver disease.

Author (Year)[Ref.]	Primary outcome	Study Design	Study Population	Main Study Findings
Alcohol Consumption and Alcohol-Related Complications				
Jackson et al. (2021) [9]	High-risk alcohol consumption	Cross-sectional survey	Adults ≥ 16 years old living in England (N = 20,558)	High-risk alcohol use increased from 25% in April 2019-February 2020 to 38% in April 2020, and use of evidence-based treatment declined (4.0% to 1.2%).
Lee et al. (2021) [7]	Alcohol sales	Nielsen National Consumer Panel prospective cohort study	Households in the contiguous United States (N = 144,704 households)	Alcohol sales from April-June increased from $7.1 billion in 2018 to $9.55 billion in 2020.
Sharma et al. (2021) [10]	Alcohol-related hospitalizations	Retrospective Cohort	Hospitalizations for alcohol withdrawal at a tertiary hospital in Delaware (N = 847)	34% increase in hospitalizations for alcohol withdrawal at the end of stay-at-home orders in 2020 compared to 2019.
White et al. (2022) [11]	Alcohol-related deaths	Cross-sectional	United States mortality data from the National Center for Health Statistics	Alcohol-related deaths increased 26% from 2019 to 2020, largest increases in adults aged 35 to 44 years (40%) and 25 to 34 years (27%).
Alcohol-Associated Liver Disease Burden				
Deutsch-Link et al. (2022) [27]	ALD mortality	Cross-sectional	United States mortality data from the National Center for Health Statistics	From 2019 to 2020, ALD-related mortality increased 21% in males and 27% in females. Highest relative increases observed in those under age 45.
Gonzalez et al. (2022) [24]	AH hospitalizations	Retrospective cohort	Hospitalizations for AH at a tertiary hospital in Michigan (N = 337)	AH admissions increased 50% in 2020 from 2016 to 2019.
Görgülü et al. (2022) [32]	ICU admissions for ACLF	Retrospective cohort	ICU admissions for ACLF in Germany (N = 237)	From 2017–2019, 24–27% of ICU admissions for ACLF were from AH; in 2020, 57% of ACLF admissions were from AH.
Julien et al. (2021) [23]	ALD Burden	Microsimulation modeling study	US adults born between 1920 and 2012	Increased alcohol use during the pandemic is projected to result in 8000 additional ALD deaths and 18,7000 additional cases of decompensated cirrhosis between 2020 and 2040.
Shaheen et al. (2022) [28]	AH and AC hospitalizations	Retrospective cohort	Adult hospitalizations for AH or AC in Alberta, Canada. (N = 6642)	Average monthly admissions for AH increased from 11.6/10,000 admissions before March 2020 to 22.1/10,000 admissions after. AC hospitalizations were stable.
Sohal et al. (2022) [25]	AH hospitalizations	Retrospective cohort	Hospitalizations for AH at 2 community hospitals in California (N = 329)	AH admissions increased 51% between 2019 and 2020, 100% increase in patients < 40 years, and 125% increase in female patients.
COVID-19-related Outcomes				
Belli et al. (2021) [47]	COVID-19 outcomes in LT candidates and post transplant outcomes	Prospective cohort study	Adult patients listed for LT who contracted COVID-19. Multi-center study at 149 transplant centers across Europe. (N = 113)	Mortality in LT candidates from COVID-19 was 33% (45% in decompensated cirrhosis). Prior COVID-19 infection did not impact early post-transplant survival.
Iavarone et al. (2020) [36]	Cirrhosis and COVID-19 outcomes	Multi-center retrospective cohort study	Hospitalized patients with cirrhosis and COVID-19 across 9 hospitals in Northern Italy from March 1st-31st 2020 (N = 50)	Out of 50 patients with cirrhosis and COVID-19, 28% of patients developed ACLF and the 30-day mortality was 34%.
Kulkarni et al. (2021) [52]	COVID-19 outcomes in LT recipients	Systematic Review and Meta-Analysis	Meta-analysis of 18 studies with 1522 LT recipients infected with COVID-19 (December 2019-May 2020)	Mortality in LT recipients was 17.4%. Mortality in LT recipients was similar to non-LT recipients after adjusting for age and comorbidities.
Marjot et al. (2021) [39]	CLD and COVID-19 outcomes	Multi-center international cohort study	Patients with CLD > 16 years old with COVID-19 (N = 745)	Case fatality rate for patients with ALD was 36%, the highest of any CLD etiology. Case fatality rate for CP-A, B, and C cirrhosis was 24%, 35%, and 54%, respectively.
Wang et al. (2021) [35]	SUD and risk of COVID-19	Retrospective case control study	US EHR data from IBM Watson Health Explorys (N = 73,099,850)	History of AUD in the past year was associated with an increased risk of contracting COVID-19 (AOR=7.75). Patients with any SUD had increased risk of death (9.6% vs 6.6%) and hospitalization (41% vs 30%) compared to general COVID-19 patients.
ALD Treatment and Liver Transplantation				
Anderson et al. (2021) [45]	Liver Transplantation for AH	Retrospective cohort study	Adults registered in the UNOS database	From June 2020 to January 2021, wait-list registrations for AH increased by 60% and transplants for AH increased by 62%.
Bittermann et al. (2021) [43]	Liver Transplantation for AH	Retrospective cohort study	Adults registered in the UNOS database	From March 2020 to February 2021, AH listing increased by 107% and AHD liver transplants increased by 210%.
Cholankeril et al. (2021) [43]	Liver Transplantation for ALD	Retrospective cohort study	Adults registered in the UNOS database	ALD listing increased by 7.3% and ALD transplants increased by 10.7% during the pandemic, with ALD accounting for more listings (40.1%) than HCV (12.4%) and NASH (23.4%) combined.

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Table 2 (*continued*)

Author (Year)[Ref.]	Primary outcome	Study Design	Study Population	Main Study Findings
Mahmud et al. (2020) [40]	CLD Hospitalizations	Retrospective cohort study	VA patients ≥ 18 years of age hospitalized for any reason between January 1st-April 15 in 2019 and 2020 (N = 12,467 hospitalizations)	During the first few weeks of the pandemic, cirrhosis-related hospital admissions declined by more than 50%. Hospitalizations had significantly higher MELD-Na.
Demographic Trends and Disparities				
Adeniji et al. (2021) [60]	COVID-19 in and socioeconomic factors in patients with CLD	Retrospective cohort study	Adults ≥ 18 years old and a diagnosis of CLD diagnosed with COVID-19 across 21 medical centers in the US from March-May 2020. (N = 909)	Black and Hispanic patients with CLD were more likely to contract COVID-19 compared to White patients with CLD. Black and Hispanic patients were less likely to have private insurance, and were more likely to experience poverty and overcrowding.
Barbosa et al. (2021) [62]	Disparities in alcohol consumption	Cross-sectional study	Online survey of US adults (≥21 years old) (N = 993) in February 2020 and April 2020.	Compared to February 2020, in April 2020, average drinks per day was 29% higher, risky drinking was 20% higher, and binge drinking was 21% higher. The increases were larger for women than men, and Black patients.
Damjanovska et al. (2021) [61]	Disparities in ALD	Retrospective cohort study	Claims data from the US (N = 8445,720)	Prevalence of AH treatment more than doubled from pre-covid to during the COVID era. Black patients were more likely to be diagnosed with AH (OR 2.63) or alcohol-associated pancreatitis (OR 2.17).
Deutsch-Link et al. (2022) [27]	ALD mortality	Cross-sectional study	United States mortality data from the National Center for Health Statistics	From 2019–2020, the highest relative increase in ALD mortality was observed in American Indian/Alaska Native and Asian men, and American/Indian Alaska Native and Hispanic/Latina women. Women had a higher relative increase (27%) than men (21%).
Devoto et al. (2022) [65]	Mental health and alcohol consumption	Prospective cohort study	US online survey of adult women as part of a larger longitudinal study (N = 499)	30% of women reported worsening intimate partner violence, and 17% of women reported using drugs or alcohol to cope with relationship problems after the onset of the pandemic. Risky alcohol consumption was associated with anxiety and depression.
Lee et al. (2021) [7]	Alcohol sales	Nielsen National Consumer Panel prospective cohort study	Households in the contiguous United States (N = 144,704 households)	Asian (55%), Black (42%) and Hispanic/Latinx (40%) individuals had a higher relative increase in alcohol purchases from 2019 to 2020 compare to White people (34%) or Other (25%); the absolute increase was highest in White individuals.
Rodriguez et al. (2020) [4]	Alcohol consumption	Cross-sectional survey	Adults living in the United States (N = 754)	Psychological distress from COVID-19 was associated with higher alcohol consumption in women, but not men.
Sohal et al. (2022) [25]	AH hospitalizations	Retrospective cohort	Hospitalizations for AH at 2 community hospitals in California (N = 329)	Between 2019 and 2020, relative AH admissions increased more in female patients (125%) than male patients (35%). Higher increases were seen in those < 40 years (100%), than 40–60 years (28%).
Improving Care Delivery and the Incorporation of Telemedicine				
Bossi et al. (2020) [71]	Web-based program for group treatment of ALD	Intervention/Case-series. 10 patients enrolled into 3 weeks of web-based group treatment.	Ten adult ALD patients included starting in March 2020	Adherence was high (7/10 patients attended over 90% of group meetings). 2/10 dropped out, and 2/10 experience a relapse.
Kaner et al. (2017) [70]	Digital interventions for AUD	Cochrane Review	57 studies included with 34,390 participants	No difference in outcomes comparing digital and face-to-face interventions. Majority of studies demonstrated some reduction in binge-drinking (moderate-quality evidence), with an average reduction of 3 standard drinks per week.
Kruse et al. (2020) [69]	Telemedicine for AUD	Systematic review	Systematic review of 22 studies examining the impact of telemedicine on treatment of AUD	16 studies (73%) reported a statistically significant reduction in alcohol consumption.
Yau et al. (2021) [72]	Multidisciplinary virtual clinic for patients with AUD and ALD	Experimental cohort study	Adults ≥ 18 years of age with ALD at receiving care through a multidisciplinary virtual clinic for AUD and ALD in Canada (N = 61)	Clinic retention rate was 75%. 70% of patients were started on anti-craving medications and 45% of patients remained abstinent from alcohol during the study period.
Response to Rising Alcohol Consumption and Burden of Alcohol-Associated Liver Disease				
Aslam et al. (2021)	Impact of alcohol taxes on waitlisting for liver transplantation	Retrospective Cohort Study	UNOS adult liver transplant waitlist additions for ALD from 2007 to 2016 (N = 24,316)	Associated between lower beer tax and higher ALD transplant waitlisting.

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Table 2 (*continued*)

Author (Year)[Ref.]	Primary outcome	Study Design	Study Population	Main Study Findings
Bush et al. (1998) [81]	Evaluation of AUDIT and AUDIT-C screening tools	Cross-sectional study	Veterans Affairs patients from 3 general medicine clinics were administered with AUDIT and AUDIT-C ($N = 243$)	AUDIT-C outperformed full AUDIT for detecting heavy drinking. A cutoff of ≥3 had a sensitivity of 98% and specificity of 57%, and ≥4 had a sensitivity of 91% and specificity of 70% for heavy drinking.
Elder et al. (2010) [84]	Impact of tax policies on alcohol consumption and related harms	Systematic Review	72 papers and technical reports included	Nearly all studies found an inverse relationship between tax/price of alcohol on heavy alcohol use and harmful alcohol-related outcomes.
O'Donnell et al. (2014) [99]	Brief alcohol interventions in primary care	Systematic review of reviews	24 systematic reviews included	Brief alcohol interventions were consistently effective and reducing hazardous and harmful drinking in primary care.
Ponicki et al. (2006) [86]	Impact of alcohol taxes on cirrhosis mortality	Retrospective population-based study	30 U.S. states from 1971 to 1998 ($N = 840$ state-by-year observations)	Cirrhosis mortality was significantly related to taxes on distilled spirits, but not to taxation of wine and beer.
Rogal et al. (2020) [90]	Impact of AUD treatment of ALD outcomes	Retrospective cohort study	Adults receiving care in the VA health system with cirrhosis and AUD ($N = 35,682$)	12% of patients received behavioral treatment alone, 1% received pharmacotherapy and behavior treatment, and 0.4% received pharmacotherapy alone. Treated was associated with lower risk of hepatic decompensation and lower short and long-term mortality.
Rush et al. (1986) [85]	Impact of alcohol tax policy on alcohol consumption mortality from cirrhosis	Retrospective population-based study	Alcohol sales data and state-wide mortality data	In Michigan, from 1955 to 1982, the relative price of alcohol decreased by more than 50%, and per capita consumption and death due to cirrhosis increased substantially.
Vickers Smith et al. (2019) [83]	Trajectories associated with AUDIT-C scores	Prospective cohort study	Million Veteran Program cohort who were administered the AUDIT-C ($N = 495,178$)	Successful implementation of AUDIT-C for yearly alcohol use screening. Higher-risk AUDIT-C score groups were associated with increased prevalence of AUD, cirrhosis and hepatitis C.
Watkins et al. (2017) [101]	Collaborative care models in primary care for treatment of AUD and opioid use disorder	Randomized clinical trial	377 primary care patients in 2 federally qualified health centers in the US.	Patients randomized to collaborative care model were more likely to receive treatment for their AUD, report abstinence and higher engagement.

AC; alcohol-associated cirrhosis. ACLF; acute-on-chronic liver failure. AH; alcohol-associated hepatitis. ALD; alcohol-associated liver disease. AOR; adjusted odds ratio. AUD; alcohol use disorder. AUDIT-C; Alcohol Use disorders Identification test – Consumption. CLD; chronic liver disease. CP; Childs-Pugh. EHR; electronic health record. ICU; intensive care unit. OR; odds ratio. SUD; substance use disorder.

residential treatment settings, which are also vital components of SUD treatment [15]. Patients with SUDs even reported decreased use of residential treatment and decreased access to SUD treatment overall in the earlier stages of the COVID-19 pandemic [16]. Increased barriers to care may have both increased risk of relapse of those in recovery, and prevented early intervention among those with harmful alcohol use.

3. Impact on epidemiology of alcohol-associated liver disease

With increasing trends in alcohol consumption, the prevalence of ALD was also increasing prior to the onset of the COVID-19 pandemic. National data on privately insured patients indicated that the prevalence of alcohol-associated cirrhosis (AC) increased 43% between 2009 and 2015 [17]. These increases were higher in women and in adults < 45 years old.

Rising prevalence of ALD prior to COVID-19 translated into increased healthcare utilization. Hospitalizations for AC and alcohol-associated hepatitis (AH) increased by approximately 20% from 2007 to 2014 [18]. In fact, between 2002 and 2014, total inpatient charges for AC in the United States doubled, and AC accounted for more than half of all inpatient charges related to cirrhosis [19]. The United States also observed marked increases in liver transplantation (LT) for ALD and AH [20,21]. While some of this may reflect expanding criteria for LT for AH in recent years [22], this likely also reflects true increases in burden of disease as the ALD mortality increased substantially over the same time period [2].

The COVID-19 pandemic has exacerbated these trends in ALD disease burden and mortality. Early in the pandemic, one modeling study predicted significant increases in ALD disease burden and mortality based on short term increases in alcohol consumption [23]. Subsequent observational data confirmed many of the predictions in this model. In a large health system in Michigan, AH admissions increased over 50% after May 2020 [24]. Another study from California witnessed a 51% increase in AH hospital admissions from 2019 to 2020, with the highest relative increases observed in women and adults younger than the age of 40 years [25]. US mortality data coincided with increases in hospitalizations. From 2019 to 2020, ALD-related mortality increased by 21% in males and 27% in females, with highest increases also in females and young adults [26]. Similar trends were also observed in other countries outside the US. For example, hospitalizations for alcohol-associated liver disease and alcohol-related pancreatitis in Japan increased by 20% during the pandemic [27]. Studies from Canada and England also reported a near doubling of hospital admissions for AH after the onset of the COVID-19 pandemic [28,29].

4. Impact on outcomes of alcohol-associated liver disease

Alcohol consumption, particularly heavy use, has a detrimental impact on ALD-related outcomes. Among patients with AC, heavy alcohol use is associated with increased mortality and hepatic decompensation [30]. In another study, heavy alcohol consumption in patients with cirrhosis was associated with about two folds risk of death, upper gastrointestinal bleeding, and infection [31]. In 2020, after the onset of the pandemic, Görgülü and colleagues [32] observed a modest increase in intensive care unit admissions for acute on chronic liver failure (ACLF), from 12 to 13% in 2017–2019

to 15.9% in 2020. However the distribution of underlying etiologies for ACLF changed more dramatically; in 2017–2019 24–27% of intensive care unit admissions for ACLF were precipitated by AH, whereas in 2020, this increased by over 100% to 57% of ACLF admissions contributed by AH [32].

Heavy alcohol consumption also has a detrimental impact on the immune system [33]. One network meta-analysis suggested that ethanol exposure augments SARS-CoV2 induced inflammation [34]. A large observational study also demonstrated that individuals with AUD have a higher risk of COVID-19 infection, and presence of any SUD was associated with increased COVID-19 mortality [35].

Patients with ALD and particularly decompensated cirrhosis are more likely to experience severe illness and death from COVID-19 [36–38]. Early studies on COVID-19 in cirrhosis demonstrated over a 30% case fatality rate, with over a 50% case fatality rate in decompensated cirrhosis [36,37]. About a third of patients with cirrhosis can develop acute on chronic liver failure when infected with COVID-19 [36]. Among patients with chronic liver disease (CLD), patients with ALD have the highest risk of COVID-19-related mortality compared to other etiologies of CLD, with a case-fatality rate of around 30–35% [38,39]. After adjusting for several covariates, Kim et al. found that ALD was associated with more than double the odds of COVID-19-related mortality compared to other etiologies of CLD [38].

5. Impact on treatment of alcohol-associated liver disease and liver transplantation

During the first two months of the pandemic, cirrhosis and ALD-related hospitalizations declined, likely due to fear of contracting COVID-19 from visiting emergency rooms [40]. Patients requiring hospitalization had higher MELD-Na scores suggesting delays in presenting to the hospital. These delays in care may have impacted disease trajectory and the ability to intervene earlier in the course of AUD and ALD.

Early in the pandemic there were also significant concerns regarding use of corticosteroids for AH [41]. Although, real world data on use of recommended treatment with corticosteroids for AH is unavailable during the Covid-19 pandemic, dexamethasone emerging as an evidence-based treatment for severe COVID-19 may have mitigated these concerns [42]. Access to outpatient hepatology clinics and early alcohol treatment may have also been impacted, preventing early detection of decompensation and disease.

The pandemic also appeared to have a profound impact on LT. Very early in the pandemic access to living donor transplantation was more limited, however this was mitigated fairly quickly [43]. Throughout the pandemic, the prevalence of ALD patients on LT waitlists have been approximately 40%, higher than non-alcoholic fatty liver disease (NAFLD) and HCV combined [43]. Transplants for severe AH increased by more than 50% during the COVID era and the median MELD-Na at listing and transplant also increased [43,44]. The increases in waiting list registrations and deceased donor liver transplantation for AH surpassed previously forecasted trends (pre-COVID 19 by more than 50%), whereas trends for non-ALD transplants remained more stable [45]. Although some of these changes reflect a changing landscape in LT for AH/ALD [46], epidemiological data on disease burden, hospitalizations, and mortality suggest changing criteria isn't the only underlying factor behind this trend.

COVID-19 infection presents unique challenges to pre and post-LT care. Pre-transplant patients with end-stage liver disease appear to have markedly worse outcomes after COVID-19 infection, though vaccination has certainly improved these outcomes [47]. Further, current infection delays transplant until recovery from COVID-19, though very limited data exists on transplant outcomes shortly after COVID-19 infection. LT after recovery from COVID-19 has been reported in individual cases in the literature and has been successful in some cases [48,49], however another case reported severe complications including extensive thrombosis [50].

Post-transplant care may also be impacted by COVID-19. Patients who are post-LT have better outcomes from COVID-19 infection than patients with decompensated cirrhosis, however they are still immunocompromised compared to the general population and may experience more severe infection manifestations. An early case series evaluated 24 LT recipients who were hospitalized for COVID-19 in 2020 who had a high prevalence of metabolic comorbidities [51]. In this case series, 79% of patients had their immunosuppression decreased empirically, and overall, 29% died. However this was later evaluated in a systematic review by Kulkarni et al. [52] who found that mortality was similar across LT recipients and non-LT patients (17.4%) when accounting for age and other comorbidities. There was no significant difference in mortality between those infected within one year versus after one year from LT.

Post-transplant care should focus on evidence-based preventive care. Vaccination is recommended for all adults in the United States, however there has been concern that immunocompromised individuals may not mount the same protective response to vaccination. Therefore, full-dose boosters have been recommended for solid-organ transplant recipients [53].

6. Demographic trends and increasing inequities

Racial and social inequalities in AUD and ALD existed prior to the COVID-19 pandemic. Prevalence of AUD continues to be highest in American Indian/Alaska Native populations [1], likely due to a long history of oppression, isolation, and social and economic exclusion. Although White Americans have had the second highest prevalence of AUD [1,54], the gap between White Americans and Black and Hispanic/Latinx Americans seems to be narrowing while all racial and ethnic demographics experience increases in AUD [1]. Among individuals at risk of developing ALD, racial and ethnic minority groups tend to have higher severity and worse overall outcomes, likely due to various inequities in social environments, treatment opportunities, and the criminal justice system [54].

ALD outcomes have also demonstrated marked inequality across race, ethnicity, and socioeconomic status before the pandemic began. For instance, a study examining cirrhosis hospital admissions from the National Inpatient Sample found that in-hospital mortality was highest for Black patients [55]. This study also examined ALD burden in cirrhosis admissions, and the authors demonstrated that ALD was disproportionately prevalent in American Indian/Alaska Native individuals (64%) compared to other racial and ethnic groups (44–53%). Social and racial disparities also impact access to transplant. Patients with higher psychosocial risk profiles are more likely to be declined for transplant wait-listing [56], and Medicaid insurance has the most restrictive alcohol abstinence policies [57].

The COVID-19 pandemic uncovered and magnified existing inequities in health, housing, job security, and countless other social and economic resources. Racial and ethnic minority groups, individuals without access to housing, immigrants, those who were incarcerated, and essential workers experienced a disproportionate burden of disease from COVID-19 [58]. Black, Hispanic/Latinx, and American Indian individuals experienced a higher risk of infection and mortality from COVID-19 [59]. Patients with substance use disorders were also at higher risk of COVID-19 infection, hospitalization, and death [35]. And among the SUD population, Black patients had a higher risk of infection with COVID-19 compared to White patients, as well as worse outcomes with significantly higher risk of death and hospitalization [35].

During the COVID era, we have also witnessed accelerating disparities in ALD-related outcomes. Among patients with CLD, Black and Hispanic/Latinx individuals represented a disproportionate number of COVID-19 infections compared to the general CLD population [60]. A large study of United States claims data found that the prevalence of AH and alcohol-associated pancreatitis increased substantially during the COVID-pandemic, with a higher relative increase in women and Black patients [61]. National mortality data from The Centers for Disease Control Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) demonstrated a marked acceleration in ALD-related deaths after the onset of the COVID-19 pandemic, with the highest relative increase in American Indian/Alaska Native and Asian men, and among American Indian/Alaska Native and Hispanic/Latina women [26]. Alcohol consumption patterns aligned with ALD mortality patterns. In a study examining post-pandemic alcohol purchases, (American Indian/Alaska Native individuals not included), Asian, Black, and Hispanic/Latinx individuals experienced the highest relative increase in alcohol purchases, however the absolute increase was still highest amongst White individuals [7]. Reports of alcohol consumption during the pandemic revealed the highest relative increases in alcohol use in women and Black individuals [62].

Trends in ALD disease burden and mortality have also indicated significant gender inequities. Historically, AUD and ALD have been more prevalent in men, however the gender gap is currently closing [63]. During the COVID-19 pandemic, women have experienced higher relative increases in alcohol consumption compared to men [4,62] and higher reported stress [64]. Women reported increased loneliness and exposure to intimate partner violence, both of which were associated with higher alcohol consumption [65]. Among working individuals, women are disproportionately prevalent among essential workers [66], and women in jobs involving non-essential work were more likely to lose jobs than men during the pandemic [67]. All of these factors contribute to covid-related psychological distress, which has been associated with disproportionately heavier alcohol consumption in women [4].

Differential impact on alcohol consumption may explain some of the higher relative increases in ALD observed in women compared to men during the COVID pandemic. Women experienced higher relative increases in hospital admissions due to AH [25,61], overall ALD admissions [29], and alcohol-associated pancreatitis [61]. Women also experienced a higher relative increase in ALD mortality from 2019 to 2020 compared to men, and experienced a higher monthly rate of increase in mortality after the onset of the COVID pandemic [26].

7. Improving AUD and ALD care during the COVID-19 pandemic: novel technologies and care delivery

The COVID-19 pandemic has substantially impacted AUD and ALD in the United States. Rising disease burden and mortality warrants coordinated efforts to mitigate these troubling trends. Several aspects of AUD and ALD care can be targeted in the context of the pandemic and its aftermath in order to reduce disease burden and improve disease-related outcomes.

First, during surges of COVID-19 cases, telehealth programs should be leveraged to continue providing care for patients while reducing risk of infection. Previous studies have shown that telehealth is effective in providing specialty hepatology care [68], and helps patients reduce alcohol consumption [69]. In a Cochrane review, digital interventions were shown to be helpful in reducing harmful alcohol consumption [70]. During the COVID-19 pandemic, one web-based therapy program was effective in treating patients with AUD and ALD [71]. Although this study was small, it reported excellent adherence to treatment and high rates of alcohol abstinence. Another intervention delivered during the pandemic reported by Yau et al. [72] offered a virtual multi-disciplinary clinic for AUD and ALD patients. The authors found that during the study period, 70% of patients were started on anti-craving medications and 45% of patients remained abstinent from alcohol during the follow-up period.

While telemedicine programs represent important advances in care delivery models and expand access to patients with geographic challenges, transportation issues, or who are at risk of severe COVID-19, they may neglect at-risk populations who may not have stable housing or internet access [73]. As such, in-person treatment and residential care (when appropriate) should remain available to those in need. Identifying patients that need resources and who may be unable to fully engage in virtual-based treatment can be assessed using socioeconomic screening tools. The PRAPARE (Protocol for Responding to and Assessing Patients' Assess, Risks, and Experiences) screening tool has been used during the COVID-19 pandemic to screen for socioeconomic insecurity [74]. This tool assesses patients on 4 domains (personal characteristics, family and home life, money and resources, and social and emotional health) with structured and validated questions. This tool could be used in the evaluation of patients with AUD and ALD to better identify types of care that may meet their current psychosocial needs circumstances.

Other aspects of ALD care that should be considered include prevention and treatment of COVID-19 infection. As mentioned above, patients with ALD are at higher risk for severe COVID-19 and COVID-19-related mortality. Healthcare providers should counsel patients with ALD about this risk and strongly recommend vaccinations and boosters. It appears that vaccine uptake in ALD patients may be excellent, with one Italian study reporting extremely high vaccine adherence (99.1%), higher than the general public [75], however, this study may not be generalizable to the United States. Medications and treatment for COVID-19 need to be considered and understood in the context of liver dysfunction, as they may be metabolized differently [76]. The impact of COVID-19 treatments in patients with liver dysfunction should be investigated in future studies.

8. Response to rising alcohol consumption, alcohol use disorder, and alcohol-associated liver disease

AUD and ALD were certainly rising before COVID-19 and have continued to do so at an even faster rate after the pandemic [7,26]. Even short-term increases in alcohol consumption seen at the beginning of the pandemic are projected to have a substantial impact on ALD disease burden and mortality in the coming years [23]. Continued increases in alcohol consumption and projections like these necessitate urgent efforts to curtail this troubling trend.

One important intervention includes addressing early heavy and harmful alcohol consumption before patients develop AUD or ALD. This can encompass various intervention modalities including public health messaging, changes in tax policies, and improved outpatient screening. Some experts reported that during the COVID-19 pandemic public health messaging in the United States on healthy alcohol use lagged behind cultural messages promoting alcohol as a way to cope with pandemic-related stress [77]. Public health messaging should be leveraged to education the public about unhealthy alcohol consumption.

Screening for harmful alcohol consumption should be expanded and improved in primary care settings. Historically, screening for AUD has been inaccurate in primary settings, with a sensitivity of less than 50% based on current practices [78]. Screening is also highly variable across clinic settings [79], and evidence-based screening tools are under-utilized [80]. Screening tools like the AUDIT-C (Alcohol Use Disorders Identification Test – Consumption), can be short and efficient (i.e. the AUDIT-C is comprised of 3 ques-

tions), with good sensitivity and specificity, and should be more widely adopted [81]. In fact, the US Preventive Services Task Force (USPSTF) recommends that all adults over the age of 18 receive screening for alcohol use disorder in primary care settings, and recommend either the AUDIT-C or the Single Alcohol Screening Question (SASQ), though recommendations on screening frequency have yet to be determined [82]. The U.S. Veterans Affairs Health System has successfully implemented an AUDIT-C based screening program, in which all primary care patients receive the AUDIT-C yearly and are referred for further evaluation and treatment if they screen positive [83].

Alcohol taxation policies may also have an important role in prevention of AUD and its associated harms. A previous study showed that higher maximum unit price and taxes on alcohol purchase is effective in reducing alcohol consumption in the general population [84]. A systematic review by Elder et al. [84] reported significant elasticity in alcohol consumption with tax increases across all age groups including adolescents. Elder and colleagues also observed consistent reductions in motor-vehicle crashes and decreased overall mortality with increasing alcohol taxes [84]. Alcohol taxation may also have a substantial impact of the prevalence of cirrhosis. Rush and colleagues reported almost a doubling of the prevalence of cirrhosis in Michigan as the relative alcohol price declined over the course of three decades [85]. More recent studies have confirmed these relationships, though with conflicting data on which specific type of alcohol (beer, wine, spirits) may be more impactful [86,87]. Palatability for alcohol taxes is an area of concern, as they are often not supported by the public, however public support does increase when revenues are specifically directed toward prevention and treatment programs [88]. Given broad evidence that taxation may reduce alcohol consumption and alcohol-related harms, consideration should be given to updated tax policies that could mitigate increasing population alcohol consumption.

Once a person develops ALD, treating AUD or other harmful alcohol consumption is essential. Alcohol cessation can slow down progression of liver disease and even reverse it [89,90]. In a large retrospective cohort study of veterans with AUD and cirrhosis, treatment of AUD reduced incident hepatic decompensation and decreased long-term all cause mortality [90]. However, a disturbing treatment gap persists in the United States; only 9% of Americans with substance use disorders receive SUD treatment [91]. Among VA patients with AUD and cirrhosis, only 14% received any form of AUD treatment, and national data indicates that only 19.8% of all adults with AUD receive any treatment for AUD in their lifetime [92]. While some of this gap in care may reflect patient disinterest [93], barriers to receiving treatment currently exist and should be addressed [94].

Patients with dual ALD and AUD require complex, multidisciplinary care. Treatment of AUD can be challenging in the setting of liver dysfunction given hepatic metabolism of several AUD medications and lack of good data for their use in patients with cirrhosis [95]. Gastroenterologists and hepatologists are well-suited to provide medication management to patients with liver dysfunction, however comfort specifically around prescribing pharmacotherapy for AUD is low among providers [96]. As such, integrated care may be helpful, with a team-based approach to ALD and AUD care [94].

There is a profound shortage of mental health and SUD treatment providers in the United States. One study noted that only 15% of Americans had an outpatient mental health specialty practice in their community [97]. Rural communities had near half the access of urban or suburban communities. Thomas and colleagues have reported severe shortages of mental health providers in 75% of US counties [98]. While we need to expand training of specialists in addiction medicine and addiction psychiatry, this could take years or decades, but we need to act sooner. One potential option is to expand SUD treatment in the context of primary care delivery. A systematic review and meta-analysis demonstrated that standardized screening, brief interventions or advice, referral to treatment (SBIRT) [99] in primary care can be highly effective, however in practice, SBIRT has been under-utilized in primary care settings for several reasons including lack of education, lack of financial reimbursement, lack of time, and fear of losing patients [100]. One could conceive of a similar model in gastroenterology office settings. Addressing barriers to implementation of SBIRT in primary care and gastroenterology office settings could help improve integration into primary care workflow.

Collaborative care models for AUD in primary care have also been effective in treating AUD. The SUMMIT trial compared collaborative care models for AUD and opioid use disorder treatment to standard care, and demonstrated improve abstinence in the collaborative care group [101]. These models offload some of the burden on specialty providers in addiction medicine or addiction psychiatry and allow their expertise to reach higher numbers of patients. These models can be integrated into primary care offices to improve access to SUD treatment for those in need.

9. Conclusion

The COVID-19 pandemic has had a substantial impact on AUD and ALD outcomes. The early stress and isolation led to increased alcohol use and exacerbated already present AUD. The pandemic burdened healthcare delivery and treatment, which impacted access to AUD and ALD care. The infection itself disproportionately harmed the AUD and ALD population. The continued rise in AUD and ALD disease burden portends a troubling rise in prevalence of end-stage liver disease. In the US, we need a united and collaborative effort to prevent harmful alcohol use and treat prevalent alcohol use disorder in patients with and without liver disease.

Conflict of interest

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