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REVIEW

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Health disparities in chronic liver disease

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Abstract

The syndemic of hazardous alcohol consumption, opioid use, and obesity has led to important changes in liver disease epidemiology that have exacerbated health disparities. Health disparities occur when plausibly avoidable health differences are experienced by socially disadvantaged populations. Highlighting health disparities, their sources, and consequences in chronic liver disease is fundamental to improving liver health outcomes. There have been large increases in alcohol use disorder in women, racial and ethnic minorities, and those experiencing poverty in the context of poor access to alcohol treatment, leading to increasing rates of alcohol-associated liver diseases. Rising rates of NAFLD and associated fibrosis have been observed in Hispanic persons, women aged > 50, and individuals experiencing food insecurity. Access to viral hepatitis screening and linkage to treatment are suboptimal for racial and ethnic minorities and individuals who are uninsured or underinsured, resulting in greater liver-related mortality and later-stage diagnoses of HCC. Data from more diverse cohorts on autoimmune and cholestatic liver diseases are lacking, supporting the need to study the contemporary epidemiology of these disorders in greater detail. Herein, we review the existing literature on racial and ethnic, gender, and socioeconomic disparities in chronic liver diseases using a social determinants of health framework to better understand how social and structural factors cause health disparities and affect chronic liver disease outcomes. We also propose potential solutions to eliminate disparities, outlining health-policy, health-system, community, and individual solutions to promote equity and improve health outcomes.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; AI/AN, American Indian and Alaskan Native; AIH, autoimmune hepatitis; AiLD, autoimmune liver diseases; ALD, alcohol-associated liver disease; aOR, adjusted OR; APC, annual percent change; AUD, alcohol use disorder; CDC, Centers for Disease Control and Prevention; CHB, chronic Hepatitis B; CLD, chronic liver disease; DAA, direct-acting antiviral; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; NHANES, National Health and Nutrition Examination Survey; NIS, Nationwide Inpatient Sample; PAF, population attributable fraction; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis; PWID, people who inject drugs; QI, quality improvement; RR, relative risk; SSDOH, social and structural determinants of health; UDCA, ursodeoxycholic acid; UNOS, United Network for Organ Sharing.

INTRODUCTION

Health disparities occur when plausibly avoidable health differences are experienced by socially disadvantaged populations.[1] These disparities occur in the context of structural and social determinants of health (SSDOH) or the social policies, laws, and structures that govern access to education, employment, housing, and health care.[2,3] These macrolevel system and social forces can together create and reinforce inequity in living conditions and unmet social needs, contributing to disease risk factors and ultimately poor outcomes in marginalized groups (Figure 1).[4,5] Specifically, structural racism, or the legacy of systematic discrimination in housing, education, employment, and the legal system, has led to profound differences in health care access and health outcomes among racial and ethnic minorities and is at the root of many observed health inequities.[6] Categories of race and ethnicity are socially constructed and have changed over time and place.[7] Nevertheless, this categorization has consequences on health outcomes. Specific to liver disease, racial disparities have led to delays in diagnosis, unequal access to therapy for viral hepatitis and liver transplantation (LT), and unequal health outcomes.[8,9]

Gender is defined as social relationships between men, women, and those who identify as transgender or nonbinary in terms of their roles, behaviors, activities, attributes, and opportunities, which are based on different levels of power.[10,11] Systematic gender inequality in health care, or structural sexism and its relationship to health outcomes, is being increasingly explored.[12] In liver disease, disparities in access to treatment for alcohol-associated liver disease (ALD) and NASH have been identified in women with adverse clinical consequences.[13,14]

Finally, although the body of literature is still growing, the close relationship between lived environment and socioeconomic factors, including insurance status and food insecurity, and liver disease outcomes is being increasingly recognized.[15,16]

The burden of liver disease continues to rise and is a leading cause of disability and premature mortality. Therefore, understanding health disparities, their sources, and consequences in chronic liver disease (CLD) is fundamental to improving public health and achieving health equity. We focused this review primarily on chronic and advanced liver disease, with less emphasis on HCC and LT given recent comprehensive reviews published in these areas.[17–19] We also did not describe in detail health differences related to genetic ancestry or biologic sex given our focus on health disparities. Finally, we completed the review by providing actionable recommendations to reduce health disparities in liver disease.

ALD

Disease burden–alcohol consumption

Alcohol consumption has increased dramatically in the last two decades.[20,21] Unfortunately, the COVID-19

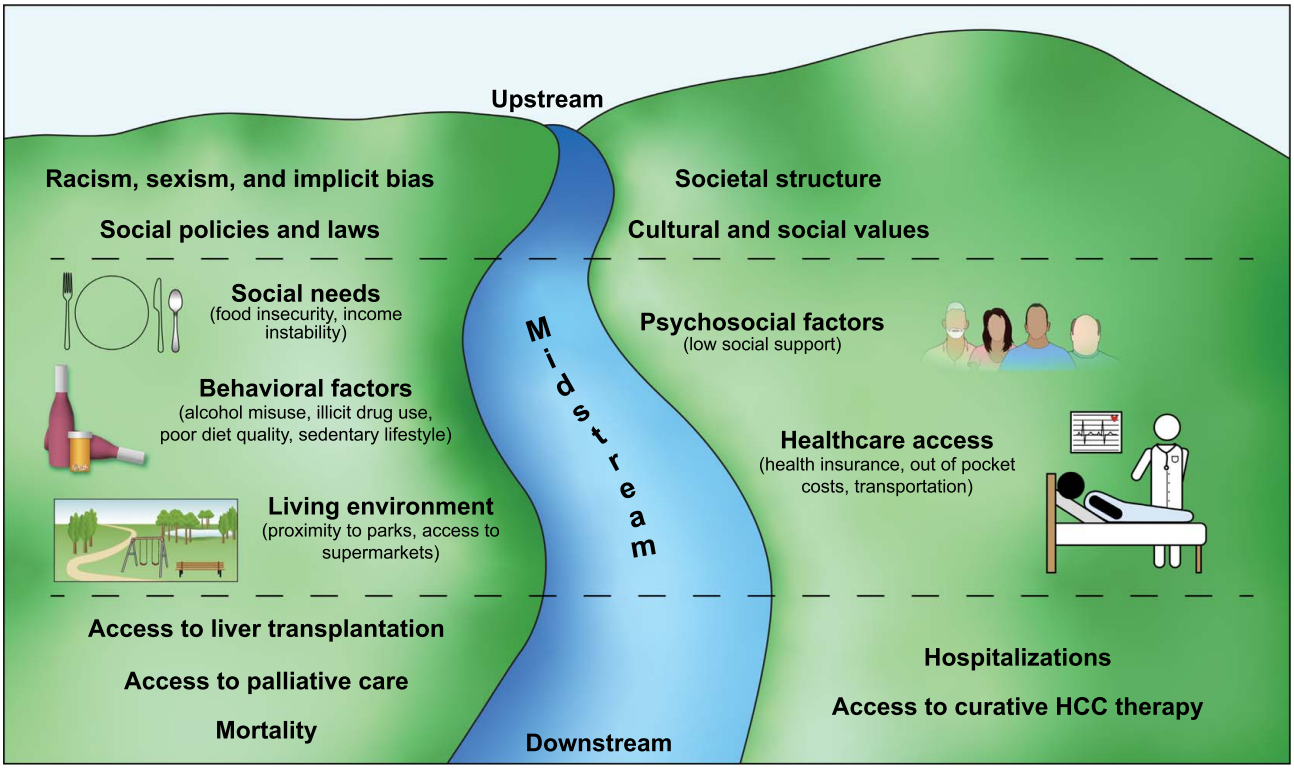

FIGURE 1 Conceptual framework for the contribution of SSDOH to disparities in liver disease outcomes.[4,5]

pandemic has resulted in even greater increases in high-risk alcohol consumption, with a recent study reporting a 54% increase in national sales of alcohol for the week ending March 21, 2020, compared to 1 year prior.[21] These increases in alcohol consumption have disproportionately impacted socially disadvantaged populations. A cross-sectional national survey evaluating drinking patterns before and after the pandemic found increases in alcohol consumption in Black participants and women.[22] In an international survey of 37,206 women taken during the pandemic, higher educational attainment, living with children, working from home, and psychological distress were all independently associated with increased alcohol consumption.[23]

There are no postpandemic data on gender minority groups; however, in a survey of 452 transgender adults in Massachusetts, factors associated with substance use treatment included male-to-female identity (adjusted OR [aOR], 3.03; 95% CI, 1.95–4.67), high educational attainment (aOR, 3.59; 95% CI, 2.35–5.50), discrimination (aOR, 1.90; 95% CI, 1.22–2.95), gender-affirming medical care (aOR, 1.99; 95% CI 1.32–3.00), low income (aOR, 0.58; 95% CI, 0.39–0.86), and unstable housing (aOR, 1.80; 95% CI, 1.21–2.67).

The data on the relationship between alcohol consumption and the SSDOH have been mixed. In a study including 15,981 participants in the National Health and Nutrition Examination Survey (NHANES) from 2006 to 2016, lower socioeconomic status (poverty index category > 1.85; OR, 0.69; 95% CI, 0.59–0.81) was a risk factor for harmful drinking.[24] However, in other data sets there has been a positive relationship between alcohol consumption and socioeconomic status. In a population-based study of 457,677 adults, people who did not graduate from high school or who had incomes $<$ $25,000 a year had the lowest prevalence of binge drinking, with rates of 13.7% and 16.2%, respectively. In fact, binge drinking prevalence increased with household income and was highest among those with a household income $>$ $75,000 a year (20.2%).[25,26] Neighborhood-level deprivation has been shown to be inversely associated with or to have no association with alcohol consumption in two US-based studies.[27,28] Importantly, lower socioeconomic status has been associated with negative alcohol-related consequences, including alcohol-related mortality.[26]

Disease burden

In regard to racial and ethnic differences in ALD disease burden, the prevalence of the full spectrum of ALD was 4.1% in White, 3.4% in Black, 9.3% in Hispanic, and 2.7% in other participants. In a recent analysis of Explorys Inc. data which aggregates electronic health records from multiple US health systems, among 8,445,720 patients, Black patients (OR, 2.63; 95% CI, 2.46–2.81) and women (OR, 1.14; 95% CI, 1.08–1-20) were found to be more likely than White patients and men, respectively, to be diagnosed with alcohol-associated hepatitis.[29] While this study provided a snapshot of a large population, the analysis did not adjust for other demographic, clinical, or socioeconomic variables; and other racial and ethnic groups were not included.

The adverse effects of alcohol consumption uniquely burden minority communities. Explanations for higher ALD in Hispanic and Black populations compared to White populations include SSDOH. Specifically, denser alcohol outlet densities and closer proximity to alcohol outlets as a result of the multigenerational effects of zoning and redlining, neighborhood disinvestment, and reduced access to health care contribute to higher disease burden.[30] In addition, the patatin-like phospholipase domain-containing-3 (PNPLA3) gene has been determined by genome-wide association studies to be associated with hepatic fat content and hepatocyte damage[31] and has been strongly associated with ALD.[32] This allele is more common in Hispanic persons, is thought to contribute to higher rates of NAFLD, and may in part explain the higher prevalence of ALD.[32,33]

Women have been demonstrated to be more susceptible to liver disease with less alcohol consumption in the setting of a smaller volume of distribution, reduced gastric alcohol dehydrogenase compared to men, and sex differences in hepatic alcohol metabolism.[34,35] In addition, targeted alcohol advertising in television, print, and social media conflating the women's liberation movement with heavy drinking alongside male peers and the “wine mom” persona has contributed to normalizing heavy drinking among women.[36] This greater biological susceptibility coupled with increases in alcohol consumption as reflected in these cultural trends have likely contributed to rising rates of ALD in women. In an NHANES study from 2015 to 2016, the prevalence of ALD among those with Stage 2 or greater fibrosis more than doubled in women, from 0.5% to 1.3%.[37] In a study of a privately insured population the prevalence of alcohol-associated cirrhosis increased by 50% from 2009 to 2015 among women compared to only a 30% increase in men.[38] Finally, hospital admissions for alcohol-associated hepatitis have dramatically increased for women; among three community hospitals in California, there was a 125% increase in women hospitalized for severe acute alcohol-associated hepatitis during the COVID-19 pandemic.[39]

Access to care

Studies have identified racial and ethnic disparities in accessing specialty alcohol and substance use disorder

treatment services.[40] In an analysis from the National Survey on Drug Use and Health from 2015 to 2017 of 12,070 participants, access to alcohol and substance use treatment between insured Black and White participants was similar (OR, 0.86; 95% CI, 0.65–1.16), but a disparity between insured Hispanic and White participants (OR, 0.72; 95% CI, 0.53–0.97) was seen, suggesting that insurance status may explain some of the racial and ethnic disparities in access to such care. However, in a cohort of 35,682 veterans with cirrhosis and alcohol use disorder (AUD) receiving Veterans Health Administration care, in which access to care is not dependent on insurance status, only 14% received pharmacotherapy and behavioral AUD treatment,[41] highlighting that provider or system barriers may contribute to lack of access. Importantly, in socially disadvantaged populations, including those of Black race, being unsheltered and having a diagnosis of HCV, an opioid use disorder, a high AUD identification test score, substance use disorders, and a diagnosis of posttraumatic stress disorder were all associated with receiving behavioral therapy or pharmacotherapy.[41]

Data suggest that there are disparities in access to alcohol and substance use treatment for women. In a study of a commercial claims database of privately insured patients, women were less likely to receive face-to-face counseling visits (HR, 0.84; $p < 0.001$) or Food and Drug Administration–approved relapse prevention medications (e.g., disulfiram, naltrexone, and acamprosate) (HR, 0.85; $p < 0.001$) than men.[13] Gender-specific barriers to participation in alcohol and substance use treatment have been explored and include failed identification of substance use problems in women who may present differently from men. In addition, women are more likely to have partners, friends, and family members who support their substance use and less likely to receive mandated treatment through employers or the criminal justice system. They also may face greater financial burdens associated with seeking treatment and need for child care. Finally, women are particularly susceptible to stigma associated with seeking treatment.[42]

LT has recently become an accepted treatment for select patients with severe acute alcohol-associated hepatitis.[43] However, evidence of disparities in access to LT for this indication is emerging. Multicenter cohort studies have shown that patients accepted for LT have been largely male (83%), White (73%), and privately insured (66%).[44] Despite data demonstrating growing rates of alcohol-associated hepatitis among Black patients and women during the COVID-19 pandemic, these groups are underrepresented among transplant recipients, suggesting that groups most affected by alcohol-associated liver disease do not have commensurable access to LT.[45] Importantly, a recent study showed that Medicaid policies resulted in lower proportions of LT for alcohol-associated hepatitis.[46]

Outcomes

ALD has been identified as a contributor to reduced life expectancy in Americans.[47] In 2017, mortality from ALD was higher than in any other year since 1999, with age-adjusted rates of 13.1 per 100,000 (95% CI, 12.9–13.3) in men and 5.6 per 100,000 (95% CI, 5.4–5.7) in women.[47] Furthermore, ALD mortality increased in every race and ethnicity except Black men. Absolute increases in mortality were particularly pronounced in Native American women (2005–2017 annual rate difference [ARD], 0.8; 95% CI, 0.6–0.9) and White women (2013–2017 ARD, 0.4; 95% CI, 0.3–0.5).[47] In a study using the Nationwide Inpatient Sample (NIS) from 2007 to 2014, Native American (OR, 1.88; 95% CI, 1.06–3.34) and Asian Pacific Islander (OR, 2.02; 95% CI, 1.00–4.06) patients with alcohol-associated hepatitis had higher inpatient mortality relative to White patients, whereas Black patients with alcohol-associated cirrhosis were found to have higher inpatient mortality than White patients (OR, 1.13; 95% CI, 1.04–1.24). Additionally, a study using multiple cause of death data found that having a college degree was associated with increased mean age at death from ALD among all racial and ethnic groups except Hispanic women.[48] The exploration of the impact of education and other social determinants on ALD outcomes warrants further study.

NAFLD

Disease burden

There are significant racial and ethnic disparities in NAFLD prevalence. Specifically, Hispanic persons are disproportionately affected by NAFLD. Perhaps the most compelling data come from a systematic review and meta-analysis[49] of 34 studies that revealed a pooled relative risk (RR) of NAFLD in Hispanic persons of 1.36 (95% CI, 1.08–1.73) compared to White persons. Black individuals had a lower risk of NAFLD compared to White individuals, with a pooled RR of 0.68 (95% CI, 0.54–0.84). Hispanic persons had the highest rates of severe disease, reflected by the highest prevalence of NASH (pooled RR, 1.24; 95% CI, 1.02–1.52), followed by White, then Black persons (pooled RR of NASH compared to Whites, 0.72; 95% CI, 0.60–0.87). There were no significant differences in the risk of biopsy-proven fibrosis among patients with NAFLD between racial and ethnic groups.[49] Limitations of this meta-analysis included the lack of data on other socioeconomic factors in several of the included studies and heterogeneity in the method of NAFLD diagnosis, which ranged from liver histology or magnetic resonance spectroscopy to *International Classification of Diseases*, Ninth Revision, codes and laboratory tests. Genetic factors play a role in variations between

groups; for example, the PNPLA3 variant, which is strongly associated with hepatic fat content, more commonly occurs among Hispanic persons,[50] particularly in those of American ancestry.[51] Lifestyle factors (e.g., physical inactivity, sedentary behavior) are known to modulate the associations of genetic factors with NAFLD,[52] but the racial and ethnic differences in these behaviors have not been thoroughly investigated. There are increasing data, however, that racial and ethnic minorities are more likely than White persons to live in food swamps, or neighborhoods saturated with unhealthy food choices; to be the target of unhealthy food and beverage marketing; and to have cultural practices that contribute to disparities in obesity, a principal risk factor for NAFLD.[53,54]

Gender differences in NAFLD prevalence have been described, with men having a 19% higher prevalence than women in a recent systematic review and meta-analysis.[55] However, while women have a similar risk of NASH compared to men (RR, 1.00; 95% CI, 0.88–1.14), they are more likely to have advanced fibrosis (RR, 1.37; 95% CI, 1.12–1.68). Age seems to modify the effect of sex, with women aged > 50 having a higher risk of NASH and advanced fibrosis; and the sex effect is attenuated among younger populations, except in females with polycystic ovarian syndrome. This is likely due to decreases in estrogen during the menopausal transition, resulting in the loss of estrogen's protective antifibrotic effects on the liver.[56]

Lastly, socioeconomic disparities also exist in NAFLD disease burden. In particular, food insecurity, or the limited or uncertain access to nutritionally adequate foods,[57] is associated with higher odds of developing NAFLD (OR, 1.38; 95% CI, 1.08–1.77) and NAFLD-associated advanced fibrosis (OR, 2.20; 95% CI, 1.27–3.82) independent of poverty status, education level, race, and ethnicity.[58] Potential explanations for this association include poorer diet quality and higher prevalence of metabolic disease among adults in food-insecure households as well as competing demands between food and medical care.

Access to care

Few studies have examined disparities in diagnosis and access to care. A mixed-methods study of 194 women of Mexican decent with and without NAFLD[59] revealed low awareness of risk factors for NAFLD and a common misperception that liver disease was only caused by alcohol use. Despite the high disease burden of NAFLD among Hispanic persons, they remain underrepresented in clinical trials for NASH. A recent systematic review and meta-analysis of 38 clinical trials for NAFLD, NASH, or cirrhosis showed that only 45% of clinical trials included information regarding patient ethnicity and that only 12% of clinical trial enrollees were Hispanic persons.[60]

Within the United States, gender disparities have been identified among patients with NASH awaiting LT. In a retrospective analysis from the United Network for Organ Sharing (UNOS) database of 5492 patients listed for NASH between 2005 and 2012, women were more likely to experience death on the LT waitlist or removal for clinical deterioration compared to men (17.1% vs. 11.4%, $p < 0.001$).[14] Rates of LT were also lower for women with NASH (adjusted HR, 0.81; 95% CI, 0.75–0.88) after adjustment for sociodemographic, metabolic, and liver-related factors.[14] In general, women experience greater disadvantage on the waitlist than men due to their smaller stature and lower serum creatinine levels; therefore, it is not clear that this gender disparity is unique or more pronounced among those with NASH.

Outcomes

A cross-sectional analysis of the NIS evaluated trends in hospitalization-related outcomes among adults with NAFLD from 2007 to 2014 hospitalized for a wide range of diagnoses (e.g., septicemia, pancreatitis, obesity, chest pain, renal failure, hepatic coma, pneumonia).[61] There was a greater rate of increase in hospitalizations among men compared to women and for Hispanic compared to White persons, followed by Black persons. However, despite lower hospitalization rates, Black persons had longer hospital stays and lower likelihood of discharge to home or an inpatient rehabilitation hospital (i.e., favorable discharge disposition). Uninsured or publicly insured patients had higher rates of admissions, higher inpatient mortality, greater length of stay, and unfavorable discharge dispositions.[61] Few studies have examined disparities in long-term complications of NAFLD, such as the risk of developing cirrhosis or HCC. However, in a recent analysis of the Surveillance, Epidemiology, and End Results-Medicare data from 2000 to 2011, metabolic disorders had the largest population attributable fraction (PAF) among Hispanic (39%) and White (35%) persons, reflecting racial and ethnic differences in the contribution of NAFLD to HCC.[62] In an epidemiological cohort study of the global burden of NASH across 195 countries from 1990 to 2017, the age-standardized global disability-adjusted life years rate of liver cancers was negatively associated with poorer socioeconomic status (Pearson r coefficient, −0.41; $p < 0.001$).

Data on disparities in long-term prognosis and mortality among NAFLD populations are sparse. In the NHANES survey, food insecurity was associated with greater risk of all-cause mortality and greater outpatient health care use among patients with NAFLD, even after controlling for other socioeconomic conditions including poverty and education level.[15] Whether NAFLD-related prognosis differs by race and ethnicity, however, is unclear because the data characterizing prognosis are discordant.[49] Research is needed to evaluate for potential disparities in long-term health outcomes in NAFLD.

HCV

Disease burden

There are significant disparities in HCV prevalence by race and ethnicity (Figure 2). The age-adjusted incidence rate of acute HCV is higher in American Indian and Alaskan Native (AI/AN) persons than any other racial and ethnic group in the United States and was 3.6 per 100,000 in 2018 compared to 1.3 per 100,000 in non-Hispanic White persons.[63] Chronic HCV incidence rates remain highest in Black populations, with persons aged 20–59 years (OR, 1.6; 95% CI, 1.1–2.3) and ≥ 60 years (OR, 10; 95% CI, 4.9–20.1) being more likely to have chronic HCV compared to the same age groups from all other races and ethnicities.[64]

The burden of HCV is highest among socioeconomically disadvantaged groups and where SSDOH are barriers to people getting educated, tested, and treated, contributing to spread of the disease.[63] A higher burden of disease is seen in those experiencing poverty because HCV prevalence among Medicaid enrollees is 7.5 times higher than the prevalence in the commercially insured population.[65] Importantly, the interaction between two or more poor social determinants can drive higher disease prevalence rates. In a study evaluating HCV antibody positivity rates in an HIV and sexually transmitted disease testing site in Los Angeles located in a high-poverty, high–substance use area, 43.9% of Hispanic participants and 44.2% of White participants tested screened positive.[66] This is in contrast to an HCV prevalence rate of only 1.5%–2% in the NHANES and Hispanic Community Health Study of Latinos taken in the general community.[67] It should also be noted that there is heterogeneity within ethnic groups; in this same study of Hispanic participants, HCV prevalence was 11.6% in Puerto Rican men versus only 0.4% in South American men.[67]

HCV prevalence among people who inject drugs (PWID) is 60%–70%,[68] forming an important at-risk population for ongoing virus transmission. Other SSDOH are present among PWID, potentially compounding disparities in HCV care. In a meta-analysis of 32,000 PWIDs, women, Hispanic persons, and Black persons were less likely to be employed. An estimated 38% of PWID in the cohort reported being homeless.[69] Being unemployed and unstably housed are risk factors for untreated disease.[70] Incarcerated persons are another vulnerable group who possess a significant risk for HCV infection, with data from Perry County, a rural county in Appalachian Kentucky, demonstrating that PWID are often incarcerated repeatedly (10 short incarcerations, average 3.4 months) and that incarceration could increase the risk of HCV infection 2.8-fold.[71]

As a result of the opiate epidemic, there has also been an increase in HCV infection among US women of

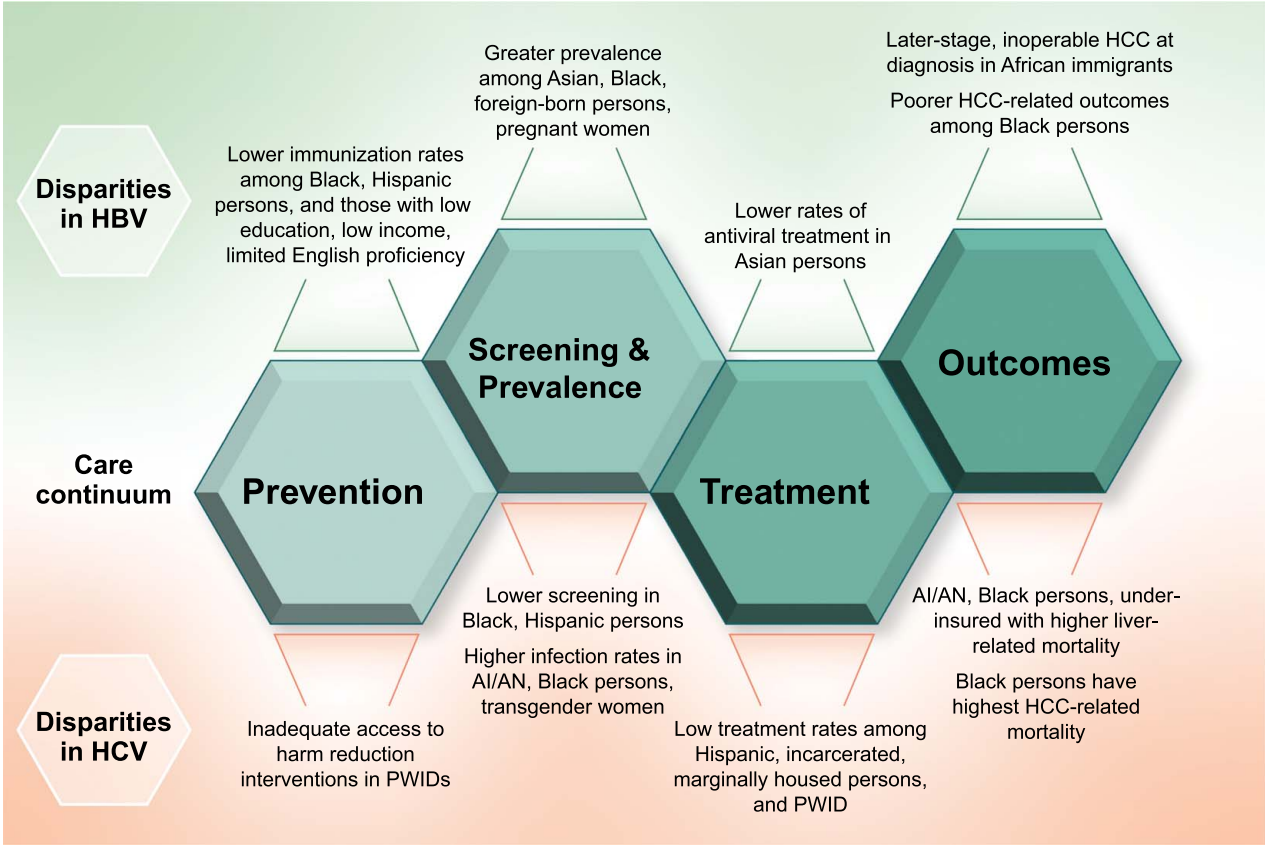

FIGURE 2 Disparities in the viral hepatitis care cascade.

childbearing age.[72] Commercial laboratory data from 2011 to 2016 demonstrated a significant increase in HCV antibody positivity by 36% (from 4.4% to 6.0%).[72] This epidemiologic shift increases the risk for maternal to child transmission and makes this demographic the focus of viral elimination efforts.[63,72] Transgender women have been historically understudied in the HCV epidemic, but in a recent Centers for Disease Control and Prevention (CDC) National HIV Behavioral Surveillance survey study of 201 transgender women, 24% were HCV-seropositive. Risks were higher among those with a history of injection drug use (adjusted prevalence ratio, 4.44; 95% CI, 2.15–9.18).[73] In a study of sexually transmitted infections among patients testing at a Los Angeles lesbian, gay, bisexual, transgender and queer testing center, the proportion of HCV in a small sample of transgender women was 4% among HIV-negative and 15% among HIV-positive women.[74] Finally, in a Medicare data set of 7454 transgender beneficiaries, the prevalence of viral hepatitis was 8.6% compared to 1.7% in cisgender beneficiaries.[75]

Access to care

HCV screening is the cornerstone of elimination efforts, and it is estimated that 49% of Americans are unaware of their disease status.[76] In National Health Interview Surveys from 2013 to 2015 that explored HCV screening rates in a baby boomer cohort, Black (OR, 0.81; 95% CI, 0.69–0.94) and Hispanic (OR, 0.79; 95% CI, 0.66–0.95) participants were less likely to be screened than White participants[77]; women (OR, 0.79; 95% CI, 0.66–0.95) also had decreased odds of screening. The use of other preventive health services was positively associated with HCV screening, including ever having been tested for HIV (aOR, 4.17; 95% CI, 3.70–4.70) and having a colon cancer screening test in the prior 12 months (aOR, 1.43; 95% CI, 1.25–1.62). In a multicomponent intervention to improve HCV screening in a safety-net health system that included provider and patient education, an electronic medical record–enabled best practice alert, and increased HCV treatment capacity, the number of eligible baby boomers screened increased from 10% to 35%.[78] Notably, the demographics of the screened population remained stable preintervention and postintervention.[78] Birth cohort–specific screening has yielded suboptimal results.[79] Newer screening guidelines recommend at least once-in-lifetime screening for all adults to move the United States closer to viral hepatitis elimination goals.[80]

Gaining access to direct-acting antiviral (DAA) therapy has been challenging for racial and ethnic minorities and socioeconomically disadvantaged groups. In an analysis of adults with chronic HCV from four health systems including 29,544 adults across four states, the treatment rate at the end of 2017 was similar between men and women at 25% and lowest among Hispanic persons at 18% compared to non-Hispanic persons at 28%.[81] Treatment rates were also lowest among uninsured (6%) compared to Medicaid-insured (9%) and privately insured (34%), persons.[81] In a Kaiser Permanente cohort, living in the lowest neighborhood deprivation index category (i.e., a more deprived neighborhood; RR, 0.8; 95% CI, 0.7–0.8), having maximum annual out-of-pocket health care costs $>$ \$3000 compared with $\leq$ \$3000 (adjusted RR , 0.9; 95% CI, 0.8–0.9), and having Medicaid (adjusted RR, 0.7; 95% CI, 0.6–0.8) compared with private health insurance were associated with a lower likelihood of DAA initiation, highlighting the importance of SSDOH in access to DAA treatment.[82]

National and state health care policy changes and local initiatives have enhanced efforts to improve access to DAA therapies for socially disadvantaged populations. Removal of Medicaid restrictions on DAA therapy including fibrosis, sobriety, and prescriber requirements led to increased treatment rates in a large Indiana cohort; however, patients with Medicaid still had less access than those with private insurance, suggesting that additional efforts at the policy level will be needed to promote health equity.[83]

Outcomes

Without appropriate access to the HCV care continuum, morbidity and mortality disparities will persist. In 2019, AI/AN persons had an age-adjusted HCV-related mortality rate of 8.63 and Black persons a rate of 6.33 compared to 3.33 per 100,000 for the overall population.[84] While other racial and ethnic groups have higher HCC incidence rates, Black persons have the highest HCC-related mortality, driven by the high burden of untreated HCV.[85] Overall, HCV-related mortality has decreased after introduction of DAA agents in late 2013, from 1.21 per 100,000 persons in 2014 to 1.05 per 100,000 persons in 2018. Unfortunately, these changes are not reported by race or ethnicity.[86]

HCV mortality is higher in those who are uninsured or underinsured. In an NHANES analysis of 19,452 participants, adults with HCV and Medicaid had a higher mortality rate than those who were privately insured (Medicaid OR, 6.31; 95% CI, 1.22–29.94), even after controlling for other socioeconomic variables including income and education.[87]

There are few data comparing HCV-related mortality by gender; however, in a CDC WONDER database analysis of a San Francisco County cohort from 1999 to 2019, age-adjusted mortality rates were significantly higher for men compared to women (13.7 per 100,000 for men vs. 5.2 per 100,000 for women).[88]

CHRONIC HEPATITIS B

Disease burden

Chronic hepatitis B (CHB) remains a major public health concern in the United States, despite being highly preventable and treatable, with fewer than half of US adults aware of their infection.[76] A large burden of disease disproportionately impacts Asian and, to a lesser extent, Black persons, and the majority are foreign-born individuals (Figure 2).[89,90] The US prevalence rates of CHB are markedly variable by racial and ethnic groups, with 2.74% of Asian individuals, 0.64% of Black individuals, and only 0.15% of non-Asian/non-Black individuals being infected.[89] The explanation for the greater prevalence of CHB in Black persons remains poorly understood, though high rates of exposure and low rates of immunization in those with high-risk behaviors have been hypothesized. Rates of vaccination-induced immunity are lowest in socioeconomically disadvantaged groups.

Rates of CHB infection may be even higher among Asian persons than reported in national, population-based cohorts such as the NHANES. In a retrospective study of over 25,000 adults receiving care at a federally qualified health center in New York City primarily serving low-income Asians, 13.4% were infected with CHB, and risk factors for infection included being born in China (OR, 40.4; 95% CI, 12.1–134.8), having limited English proficiency (OR, 1.67 for Mandarin as preferred language; 95% CI, 1.33–2.10), or being uninsured (OR, 1.74; 95% CI, 1.42–2.12).[91] There is marked heterogeneity in CHB prevalence among different Asian ethnicities. Data from the 2014–2015 US birth rate population revealed that Chinese and Vietnamese American mothers are 10 times more likely to experience HBV infection than are Asian Indian and Japanese mothers.[92] Such data emphasize the importance of screening immigrant populations and treating ethnic groups as distinct rather than as one category, which can mask heterogeneity within groups.

Rates of CHB infection in the general population have remained stable overall over the past two decades, likely due to multifaceted efforts to reduce HBV infection, though are significantly higher among foreign-born persons.[70] Data from the NIS revealed a near doubling of rates of HBV infection from 1998 to 2011 among pregnant women, resulting in an annual increase of 5.5% (95% CI, 3.8–7.3), though this trend may have been due to increases in prenatal testing.[93] The highest rates of CHB were in PWID and HIV-positive women. Additionally, compared to pregnant White women, Black women and those of "other" races, which includes Asian women, experienced a 5-fold and 12-fold increased odds of CHB, respectively, during that time period. The authors hypothesized that the increased likelihood of CHB among Black pregnant women may be due to lower vaccination rates and higher exposures (e.g., from high-risk sexual activity or drug use). Additionally, the higher prevalence in the "other" women may reflect the endemicity in their country of origin because this group was made up of predominantly Asian women.

Access to care

Rates of CHB screening and vaccination are lowest in socioeconomically disadvantaged groups. Asian persons have the highest rates of vaccine-associated immunity (34.1%; 95% CI, 32.0–36.2), and Black (25.5%; 95% CI, 24.0–27.0) and Hispanic (22.2%; 95% CI, 21.3–23.3) persons have the lowest,[89] though notably rates of immunity are low across all racial and ethnic groups. Immunity rates are also inversely correlated with education and income levels because individuals with an education level above high school, a high household income, or an insurance plan (in particular, private insurance) have higher rates of immunity.[89]

Immunization rates are suboptimal in high-risk individuals, such as Black and foreign-born Asian persons born before the era of universal vaccination. Among 20,574 Asian adults who received care at an urban, safety-net hospital, only 62% underwent HBV testing, and 47% of HBV-susceptible patients were vaccinated.[94] There are many potential barriers to screening and vaccination, including patients' lack of knowledge about CHB and its complications, lack of English fluency, stigma associated with the disease, and financial and institutional barriers.[95–97] Gaps in provider knowledge also represent a significant barrier to screening. A survey of primary care providers practicing in an urban, safety-net hospital setting revealed that 43% were unfamiliar with HBV guidelines,[94] highlighting the need for provider education in improving screening rates. Expansion of routine HBV vaccination recommendations by the Advisory Committee on Immunization Practices in 2021 to all adults between the ages of 19 and 59 may simplify guidelines for providers and reduce barriers to both screening and vaccination.[98]

Rates of linkage to care also remain suboptimal in certain ethnic groups. For example, only 29% of Korean Americans with CHB who were aware of their diagnosis were currently seeing physicians for management of their hepatitis B; the remaining 71% were not seeing a physician or linked to any health care services.[95] In another study of 4350 Asian patients (including Chinese, Vietnamese, and Hmong) who were tested for CHB between September 2014 and September 2017, Hmong patients with CHB had the lowest linkage to care compared to other Asian groups; only 64% received an HBV DNA level and alanine aminotransferase (ALT), 57% were referred to a hepatologist, and 8.5% were treated with antiviral therapy.[99] These

findings underscore the need for culturally appropriate and multilingual health education and risk reduction programs for CHB, to increase screening and vaccination efforts.

Outcomes

Delays in HBV and cirrhosis diagnosis, which may be more common among underserved populations, contribute to more severe disease at presentation and poorer long-term health outcomes.[100] In a retrospective evaluation of adults with CHB from July 2014 to May 2016 at a community-based safety-net hospital, of whom 67% were Asian, nearly 30% of patients had cirrhosis at initial presentation. There were no racial or ethnic disparities identified in the risk of cirrhosis among this cohort, though differences between non-Asians (which included White, Black, other persons) were not evaluated.[100] Men were more likely than women to have cirrhosis (35% vs. 19%) and variceal bleeding (5.6% vs. 1.4%) at presentation.[100]

Racial and ethnic differences in HCC-related outcomes among adults with CHB have been observed. In a multicenter study of 1023 adults with HBV-related HCC from three US and one Spanish center, Black patients had larger tumors at diagnosis (6.2 vs. 4.6 cm) and were younger (55 vs. 65 years) compared to White patients.[101] While this study did not distinguish between Black Americans and African immigrants, recent data suggest that African immigrants with CHB may have even worse outcomes. In a retrospective cohort study of 4400 patients with HCC, of whom 33 were identified as African immigrants, 64% presented with late-stage, inoperable HCC and 77% died within 1 year of HCC diagnosis.[102] Over 70% of patients were unaware of their HBV diagnosis when they presented with HCC, and zero patients were diagnosed through a screening exam. The early age at onset of HCC among African persons with CHB was also recently demonstrated in a large, multicenter retrospective study from the Africa Liver Cancer Consortium in which 59% of HBV-associated HCCs developed before the age of 40 years.[103] These data have led to society-driven recommendations to begin screening for HCC at younger ages among African-born persons.[104,105] Interethnic differences among Asians are also present, with poorer 10-year survival among Southeast Asians (Vietnamese, Laotians, Cambodians) compared to East Asians (Chinese, Korean, Japanese) (23% vs. 35%), possibly due to lower income and limited English proficiency leading to delays in access to timely care.[101]

Recent data on racial and gender disparities in LT among patients with CHB are sparse. Among 1023 patients with HBV-associated HCC, non-Asian persons (compared to Asians) were more likely to be waitlisted for LT (38% vs. 19%) and or receive curative HCC treatment.[101] LT data on Black persons with CHB are more discordant. Among 274 patients with CHB from 15 centers in the United States, including 116 White, 135 Asian, and 23 Black patients, no differences were seen between racial and ethnic groups.[106] However, in a study of 738 patients from 10 academic centers undergoing LT, Black patients had worse posttransplant survival compared to non-Black patients with CHB.[107] Gender disparities have been described in LT outcomes, though few recent studies have evaluated HBV. In one multicenter study, women with HBV had poorer posttransplant outcomes than men, which was hypothesized to be due to higher Model for End-Stage Liver Disease (MELD) scores at transplant as a result of the smaller size of women and fewer graft offers.[107]

AUTOIMMUNE AND CHOLESTATIC LIVER DISEASES

Disease burden

Most studies describing disease burden in autoimmune liver diseases (AiLD) have focused on predominantly White populations. However, emerging epidemiological data suggest a high prevalence of AiLD and more advanced disease at diagnosis among racial and ethnic minorities, which may be due to poorer socioeconomic conditions. In an analysis from 2002 to 2017 at a safety-net outpatient clinic in San Francisco serving underserved communities, among 63 adults with autoimmune hepatitis (AIH) and 2049 non-AIH controls, Black (OR, 9.6; 95% CI, 1.8–178), Hispanic (OR, 25; 95% CI, 5.3–448), and Asian (OR, 10.8; 95% CI, 2.2–196) adults had increased odds of an AIH diagnosis compared to White adults.[108] Additionally, Black individuals had the most severe disease on presentation with higher median ALT levels compared to Hispanic and Asian groups.[108] Despite the high prevalence of primary biliary cholangitis (PBC) among White patients,[109,110] Hispanic persons with PBC are more likely to have overlap syndrome with AIH compared to White persons (31% vs. 13%, $p = 0.002$) and higher rates of ascites and variceal bleeding.[111] The study authors hypothesized that these disparities may be in part due to lack of health insurance, leading to delayed diagnosis and more severe disease at presentation.[111]

Primary sclerosing cholangitis (PSC) has almost exclusively been described in White populations. However, a recent cross-sectional study of 13 North American centers in the Consortium for Autoimmune Liver Disease identified unique clinical features of Black patients with PSC.[112] Black patients had lower rates of concurrent inflammatory bowel disease and more isolated intrahepatic bile duct involvement compared to White patients but similar disease severity.[112,113]

Notably, the analysis also revealed that the prevalence of PSC in Black patients is likely not as rare as what would be interpreted based on published data. While exact prevalence rates were not described, the proportional representation of PSC in Black patients compared to each study center's metropolitan service area was ≥ 0.7 in half of the centers. These findings suggest an underrepresentation of Black patients in clinical trials rather than a disease largely restricted to White persons.

Access to care

In a retrospective analysis of 4241 patients with PBC between 2003 and 2014, Black patients were less likely to receive ursodeoxycholic acid (UDCA) treatment than White patients (OR, 0.5; 95% CI, 0.4–0.7), but there were no differences in treatment rates between Asian compared to either White or Black patients.[109] A follow-up study from the same cohort revealed that untreated Black or Asian patients had significantly higher mortality than their White counterparts (HR, 1.34; 95% CI, 1.08–1.67; and HR, 1.40; 95% CI, 1.11–1.76, respectively).[114] Additionally, Black patients who received UDCA treatment had lower mortality (HR, 0.67; 95% CI, 0.51–0.86), highlighting a lack of access to timely therapy that is effective in curbing disease progression.[114]

Disparities in access to LT among patients with AiLDs have been identified. A study from UNOS of adults waitlisted with PSC but without HCC from 2005 to 2017 found that Hispanics had a lower probability of receiving LT compared to White persons (HR, 0.73; 95% CI, 0.54–0.98), even after controlling for insurance status.[115] Minority patients with cholestatic liver diseases, including Black, Hispanic, and Asian, were also less likely to receive living donor LTs (LDLTs) compared to White patients,[116] potentially related to fewer liver organ donation inquiries in these groups.[116] LDLT recipients were more likely to have private health insurance and less likely to reside in areas of high poverty. Thus, the financial burden of donating (i.e., lost wages from time off work) may be an important barrier to living liver donation and may exacerbate racial and ethnic disparities.

Outcomes

Among patients with AiLD, racial and ethnic minorities and those of a lower socioeconomic status have poorer health outcomes. Hospitalizations for AIH were 69% higher (95% CI, 1.58–1.81) for Black and 20% higher (95% CI, 1.12–1.28) for Hispanic than for White patients ($p < 0.001$ for each comparison) but 64% lower for Asian patients (95% CI, 0.29–0.43).[117] Women with AIH were more likely to be hospitalized than men (OR, 3.09; 95% CI, 2.69–3.56). Black patients with AIH who were hospitalized had a significantly higher odds of inpatient mortality (OR, 2.81; 95% CI, 1.43–5.47) compared to White patients.[117] Among 8460 hospitalizations for PBC from 2007 to 2014, hospitalization rates were 12% higher among Hispanic persons (RR, 1.12; 95% CI, 1.09–1.16) and 53% lower in Black persons (RR, 0.47; 95% CI, 0.45–0.49) compared to White persons.[118]

The data on long-term outcomes, including mortality, in AiLD are discordant. In a single-center retrospective study of 204 Hispanic and non-Hispanic patients with PBC between 2000 and 2011, there were no differences in mortality between Hispanic and non-Hispanic patients despite more severe presentations of PBC and greater likelihood of AIH overlap among Hispanic patients.[111] Studies from UNOS demonstrate worse outcomes among Black and Hispanic patients with AiLD on the LT waitlist, including death or waitlist removal due to clinical deterioration (HR, 1.26; 95% CI, 1.00–1.58) and greater posttransplant mortality.[119] However, given that Black and Hispanic patients have higher waitlist mortality across most etiologies of cirrhosis, it is not known whether this disparity is unique to AiLD.

In a single-center cohort of 449 patients with PSC from 1988 to 2019, of whom 404 were White and 45 were Black, the hazard of liver-related death was higher in Black compared to White individuals (HR, 1.80; 95% CI, 1.25–2.61) despite similar disease severity.[113] There was a significant interaction between Black race and community socioeconomic factors, including education, income, and community safety that attenuated the effect of Black race on mortality (HR, 1.01; 95% CI, 0.99–1.04), suggesting that the difference in mortality was, in large part, mediated by socioeconomic factors.[113]

CIRRHOSIS

Disease burden

The incidence of cirrhosis in the United States continues to increase, but the underlying etiologies have shifted, reflecting the success of treatment for viral hepatitis and the increasing prevalence and lack of effective therapies for ALD and NAFLD.[120] There are notable racial and ethnic differences in the distribution of risk factors, with a high prevalence of metabolic syndrome and NAFLD in Hispanic persons and a high prevalence of alcohol-related liver disease in Black persons, portending a disproportionate burden of chronic liver disease in Hispanic and Black persons.[120] The Global Burden of Disease database from 2007 to 2017 showed an estimated 30% increase in incident HCC and a 34% increase in incident cases of CLD.[121] In 2014, the attributable etiologic fractions for cirrhosis in the United

States were diabetes/NAFLD (15%), ALD (17%), and viral hepatitis (47%).[122] While US data remain limited, a population-based cohort from Ontario, Canada, highlighted the changing epidemiology of cirrhosis by gender, with a 26% increase in incident cirrhosis from 2000 to 2017 and higher rates in women (2.5% per year; 95% CI, 2.0–2.9) than men (1.3% per year; 95% CI, 1.4–2.1) and increased incidence for all etiologies except for ALD and AiLD. Incident cirrhosis cases were projected to continue to increase through 2040, driven primarily by NAFLD-associated cirrhosis in all birth cohorts but with ALD-associated cirrhosis also increasing slightly, primarily among younger (born after 1980) ages and women.[123] While accurate US population-based estimates of cirrhosis by racial and ethnic groups are lacking, cirrhosis-related mortality highlights the disparity in complications of cirrhosis leading to death. A recent analysis revealed a reversal of prior declines in cirrhosis mortality in 2009 with increases in cirrhosis-related mortality across most racial and ethnic groups and in both genders.[124]

Rates of HCC have significantly declined for most racial and ethnic groups in recent years (annual percent change [APC] –5.6% for 2015–2018) with the exceptions of Black persons (no significant change, APC –0.7%) and AI/AN persons (significantly increased, APC 4.8%; 95% CI, 3.4–6.2).[125] AI/AN and Hispanic persons have the highest incidence of HCC,[125,126] with risk of HCC higher in US-born than foreign-born Hispanic individuals (RR, 1.85; 95% CI, 1.25–2.73).[126] A rural–urban disparity in HCC incidence has been identified also, particularly among Hispanic persons and AI/AN.[127] This trend highlights the crucial role of geography and physical proximity to high-quality services for screening, detection, and cancer care in exacerbating HCC disparities among rural populations. The contribution of differing risks for cirrhosis partially explains the racial and ethnic differences in incidence. Using Surveillance, Epidemiology, and End Results-Medicare data from 2000 to 2011, metabolic disorders had the largest PAF among Hispanic (39%) and White (35%) persons, whereas HCV had the largest PAF among Black (36%) and Asian (30%) persons. Alcohol was the third greatest contributor to HCC among all groups except Asian persons (PAF, 13%–20%).[62] Socioeconomic factors are relevant as suggested by late-stage cancer geographic hot-spots which highlight areas overrepresented by racial and ethnic minorities, foreign-born, underinsured or uninsured, and those of lower socioeconomic status.[128]

Not all epidemiologic studies on cirrhosis acknowledge the multiplicity of liver insults that lead to cirrhosis. Accounting for all the contributing causes to cirrhosis may help explain the racial and ethnic differences currently observed. In a study of newly diagnosed patients with HCV, obesity, and diabetes, the aOR of advanced liver disease was nearly 8-fold higher for Hispanic (aOR, 7.89; 95% CI, 3.66–17.01) versus Black persons and 12-fold higher versus White persons (aOR, 12.49; 95% CI, 3.24–48.18).[129] While accounting for these metabolic factors attenuated the disparity, Hispanic persons still had an ~2-fold higher rate of advanced disease than Black and White persons, suggesting the contribution of other unmeasured factors. There remains a need to better characterize disease in more detail by ethnicity, acknowledging substantial heterogeneity within groups that have been historically analyzed as one (e.g., Asian Americans). For example, ALD-related mortality was trending upward in Asian persons in 2016 but with a 6-fold difference in age-standardized mortality when comparing Japanese Americans (highest, 5.48 per 100,000 persons) to Chinese (lowest, 0.93 per 100,000 persons).[130]

Access to care

To prevent cirrhosis and its complications, the first step is awareness of cirrhosis. An NHANES study from 2014 showed that 69% of persons with cirrhosis are unaware of their diagnosis, and compared to the general population, there were higher rates of unawareness among males than females, Black and Hispanic than White persons, and those in poverty.[122] Advanced liver disease at initial presentation suggests lack of awareness or limitations in access to hepatology care. For example, in an NIS study of transjugular intrahepatic portosystemic shunt (TIPS) procedures from 2012 to 2014, higher inpatient mortality during admission for TIPS was seen with Black (vs. White) persons, but adjustment of cirrhosis severity attenuated the mortality difference, suggesting that late presentation may be a contributing factor.[131] A disparity in timely variceal screening among Black persons versus White persons is well recognized.[132,133]

Telehealth has been viewed as a means of increasing access to hepatology care among specific populations, especially those living in rural or remote areas. However, the COVID-19 experience highlights disparities in the quality of such care. A 2020 study from Duke University found that higher rates of incomplete or telephone visits versus video visits were associated with being older, being Black, and having Medicaid/Medicare.[134] Similarly, early COVID telehealth experience at the University of Pennsylvania showed similarly lower video (vs. phone) visits and less patient portal use (as surrogate for digital literacy) among Black (vs. White) and older patients.[135] Because telehealth is likely to remain part of health care beyond COVID, understanding patient-level versus facility-level factors responsible for this digital disparity and ensuring equitable access to “high-quality” virtual exchange are needed.[134]

In a US study of admissions for cirrhosis complications in hospitals that treated minorities in higher proportions (termed *minority hospitals*) versus non-minority hospitals, mortality was higher in minority hospitals. However, this disparity was independent of race,[136] leading the authors to argue that lower resources, busier emergency rooms (leading to delays in initial treatment), and less access to specialized services were the main drivers of the disparity in outcomes. Several studies of admissions for cirrhosis to safety-net hospitals reported that hospital mortality and readmissions were related to severity of disease and comorbidities but did not differ significantly by race and ethnicity or gender.[137]

Disparities in access to LT remain, despite efforts to reduce these disparities through prioritization and redistricting policies.[18] Hispanic and Black persons continue to have lower rates of listing for LT despite a high burden of liver complications.[138] Distance from an LT or academic center[139] and lack of commercial insurance status can limit access to LT. The proportion of uninsured Americans varies considerably by race and ethnicity; in 2020, among adults aged 16–64 years, 29% of Hispanic, 14% of Black, 9% of White, and 9% of Asian persons were uninsured.[140,141] Early evidence suggests that Medicaid expansion has mitigated this disparity, as shown in a recent study that reported higher likelihood of LT waitlisting among Black and Hispanic candidates in states with Medicaid expansion.[142] Gender disparities in LT waitlist mortality are also well established because women are waitlisted with equal frequency to men but have a higher waitlist mortality, in part due to small stature and underestimation of renal dysfunction by serum creatinine. Recently, MELD 3.0 has been proposed as a new model for LT allocation that attempts to mitigate gender disparities in access by crediting extra points to women.[143]

Outcomes

Trends in liver-related mortality from 2003 to 2018 show a 3.4% annual percent increase overall, with significantly higher rates in for men than for women (3.7% vs. 3.2%) and among those of Asian, AI/AN, and White race (5.4%, 5.1%, and 3.4%, respectively) compared to Blacks (2.1%).[144] In a study using the CDC WONDER platform to evaluate cirrhosis mortality trends from 1999 to 2016, declines in cirrhosis-related mortality from 1999 to 2008 were followed by a reversal of this trend in 2009.[124] A significant annual percent increase in cirrhosis mortality was evident. White, AI/AN, and Hispanic persons had the highest age-adjusted cirrhosis mortality, which was largely attributed to ALD and AUD. In a prospective multiethnic cohort with follow-up to 18 years, Hispanic persons had the greater risk of CLD death (1.6 times higher), while rates in Black and Native Hawaiian persons were similar to that in White persons.[145] Among AI/AN persons, cirrhosis is the fifth most common cause of mortality, ranking higher than in any other racial or ethnic group.[146]

Among patients presenting with decompensated cirrhosis from 2005 to 2014, independent predictors of in-hospital mortality were male gender, older age, and being of Black or Asian race. Having insurance or a third-party payer, having a higher household zip code income, and being of Hispanic ethnicity were associated with a lower risk for in-hospital mortality.[147] In a multicenter Chicago-based study of 11,277 patients with compensated cirrhosis from 2006 to 2012, Black persons had the highest mortality, with a 29% higher liver-related mortality and 35% higher overall mortality than White persons, while Hispanic persons had a lower rate of mortality than White persons.[148] This survival advantage associated with Hispanic ethnicity with cirrhosis is observed across cirrhosis etiologies (viral, ALD, and NAFLD)[148] as well as with HCC.[149]

Gender differences in cirrhosis-related mortality were evaluated in several studies. In a cohort of 20,045 patients from six large health systems in Chicago, women had lower all-cause mortality and similar liver-related mortality compared to men despite lower rates of LT waitlisting and subsequent LT.[150] However, a more detailed evaluation by gender, race and ethnicity, and etiology of cirrhosis over time reveals important trends. Liver-related and alcohol-associated mortality from 1999 to 2014 have increased more in Hispanic versus White men, but the opposite was true for women, where mortality was stable among Hispanic but increased among White women.[151] Using death certificate data, an ~2-fold higher mortality from CLD was seen among AI/AN compared to White persons. There was a strikingly higher risk of death among AI/AN women, with rates 4.3–11 times greater than those for White women across various age categories.[152]

SUMMARY

Here, we summarize the most notable findings in this scoping review of health disparities in CLD.

While high-risk drinking and AUD are rising for all demographic groups, women, racial and ethnic minorities, and the socioeconomically marginalized have seen the largest increases in AUD in recent years.[20] These drastic increases in the face of inadequate access to pharmacotherapy and behavioral therapy for alcohol and substance use have translated into increasing burden of ALD and ultimately higher mortality in these groups.[47] In parallel with the increases in alcohol consumption, there have been rising rates of metabolic syndrome and NAFLD in the United States, with Hispanic persons and those experiencing food insecurity or socioeconomic

disadvantage being disproportionately impacted.[15,58] While women over 50 have a higher risk of NASH with advanced fibrosis, women with NASH are less likely to be transplanted and more likely to die on the LT waitlist.[14]

The ongoing success of US viral hepatitis elimination campaigns depends on mitigating disease in marginalized populations.[63] Access to HCV screening remains an issue for racial and ethnic minorities, women, and the poor; and HBV screening is suboptimal in Black and immigrant populations. Failed access to the HCV care continuum has led those insured by Medicaid to have a 6-fold greater risk of death compared to those who were privately insured even when controlling for comorbidity, race, education, and income.[87] Failed treatment access for HCV and HBV contributes to HCC-related mortality for racial and ethnic minorities.[101,103] Data from diverse cohorts on autoimmune and cholestatic liver diseases reveal that Black patients with PBC have the most severe disease at presentation but more limited access to UDCA treatment.[109] Black patients with PSC also have higher mortality, partially accounted for by socioeconomic factors.[113] Taken together, the relationship between disease severity, care access, and outcomes in autoimmune and cholestatic liver disease warrants further study.

Knowledge gaps and limitations of available data

Through this literature review we identify gaps in our understanding of liver disease disparities. While much of our understanding of existing disparities comes from large population-based data sets (i.e., UNOS, NIS, NHANES), these cohorts are inherently limited for several reasons. For example, when evaluating transplant access and outcomes, data sources such as the UNOS lack detailed socioeconomic information about income, education, social support, and health behaviors. Also, while many data sets are beginning to include information about neighborhood quality and deprivation, these factors are not accounted for in most disparities analyses. Such data also do not reflect individual-level determinants, which may be unique from the built environment.

Additionally, the NIS and NHANES lack reliable methods for diagnosing liver disease and assessing severity; the NIS contains no laboratory data to assess liver disease severity, and the NHANES has relied on the use of noninvasive risk scores (i.e., aspartate aminotransferase to platelet ratio score or Fibrosis-4 index) to identify liver fibrosis (until 2017 when transient elastography data became available), which may lead to misclassification bias. As transient elastography becomes more widespread, improved measurements of steatosis and fibrosis will help to better characterize the relationship between race, gender, socioeconomic factors, and liver health outcomes in these larger cohorts. Further, increasing use of electronic health record data sets will result in the collection of more granular, high-quality data.

Another major limitation we observed was the lack of stratification by race or ethnicity in studies examining liver outcomes. In one of the largest retrospective analyses of US trends in HCC-related and cirrhosis-related mortality after DAA treatment of HCV, stratification by race and ethnicity was notably missing.[86] Other examples include the underrepresentation of Black persons in prevalence studies of autoimmune/cholestatic liver diseases and lack of inclusion of Black and Hispanic populations in NAFLD therapeutic clinical trials, despite the high disease burden of NAFLD among Hispanic populations.[60,153]

Finally, we echo recent calls within the gastroenterology community for greater scrutiny of the use of broad racial and ethnic categories in research studies[154] because these categories do not account for the high degree of ancestral heterogeneity and differences in cultural practices within racial and ethnic groups. For example, in our review of community-based studies of HBV, we found marked ethnic differences in linkage to care, liver disease severity, and timely HCC diagnosis among Asian persons. These groups may have different disease risks and socioeconomic conditions based on their country of origin that are not captured well in the current literature. Greater knowledge of these differences by more precise measurement may more accurately inform future clinical recommendations.

Health disparity solutions

Syndemic hazardous alcohol consumption, opioid use, and obesity have led to important changes in liver disease epidemiology, exacerbating health disparities. To achieve health equity, solutions that account for the role of the SSDOH in liver disease are most likely to be successful. Specific evidence-informed recommendations across policy, practice, and research are summarized in Figure 3.[155]

Income inequality and structural racism are upstream determinants of downstream outcomes (Figure 1) and will require large-scale policy reform. However, there are also many actions that can be taken from within the health care system to target the SSDOH. Here, we will discuss health policy, health system, and community-level solutions.

Health policy solutions

A multilevel policy approach is needed to curb alcohol consumption (Figure 4). Data from the World Health Organization have highlighted that tax increases

on alcohol-containing beverages, comprehensive restrictions and bans on alcohol marketing, and restrictions on the availability of retailed alcohol curb liver cirrhosis death rates.[9] A recent study showed that each 10–percentage point increase in the restrictiveness of alcohol policy was associated with a decrease in ALD mortality.[156]

Recent data have highlighted the negative impacts of food insecurity on obesity, diabetes, and NAFLD among socioeconomically disadvantaged populations, independent of poverty.[15,58] Expansion of existing large-scale food assistance programs, including the Supplemental Nutrition Assistance Program and the Women, Infants, and Children Program, could improve diet quality for low-income patients with NAFLD who may not otherwise have access to adequate and/or nutritious food (Figure 5). Such measures have been demonstrated to improve medication adherence,[157] reduce health care use,[158] and improve health[159] in the general population and may be even more beneficial in those with chronic diseases, such as NAFLD and advanced liver disease.

The negative contribution of being uninsured or underinsured on liver-related outcomes is significant, as highlighted in HCV with lower treatment rates and higher mortality in those who are not privately insured. While several state Medicaid programs have loosened their treatment restrictions for HCV as global elimination efforts have intensified, many states continue to restrict access to HCV treatment based on fibrosis stage or history of recent drug use.[160] Indeed, Medicaid expansion and leniency of HCV coverage were recently shown to improve cirrhosis mortality.[161] These data highlight the importance of removing payer restrictions and implementing more widespread health insurance at the state and federal levels to expand access to lifesaving therapies and improve liver-related outcomes.

Health systems solutions

Unmet social needs are a barrier to care for racial and ethnic minorities and are being increasingly targeted by health systems for intervention.[162] Social needs screening and referral should be performed in our nontransplant populations to identify populations in need of social work referral early in their disease course so that they might be able to better prioritize their liver health. Similarly, patients who live in communities and neighborhoods that put them at risk for poor liver disease outcomes should be identified early, with closer monitoring by providers as indicated, care navigation programs, and social work referrals.

The above measures assume that patients enter into hepatology care early in their disease course. However, racial and ethnic minorities have been shown to be waitlisted with higher MELD scores and to have larger HCC tumors at presentation, suggesting later access in their disease course to the health care system.[149,163] Wide dissemination of clear clinical care pathways, such as the one designed for NAFLD, to primary care providers can help to identify patients earlier in their disease

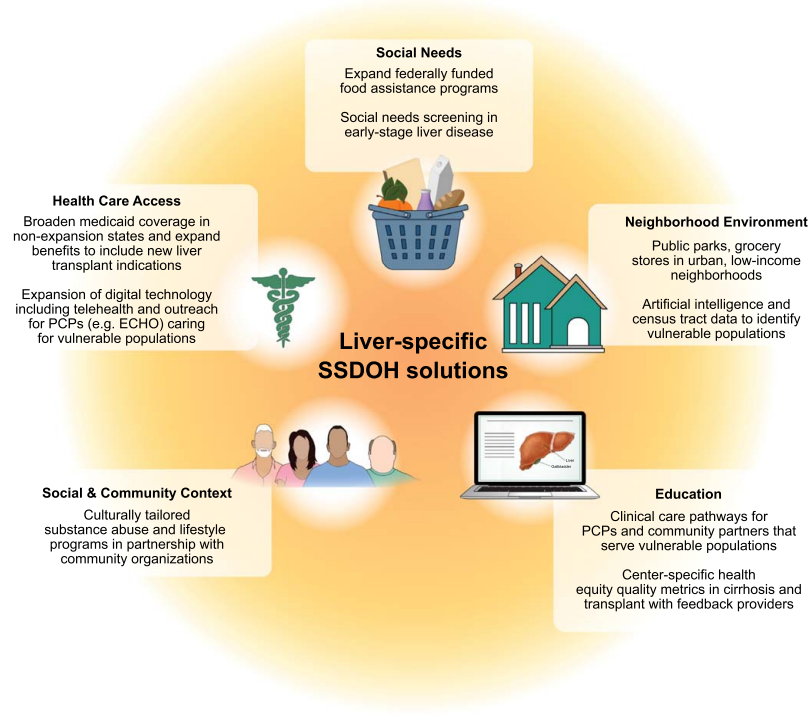

FIGURE 3 Potential policy, practice, and research solutions to address health disparities and improve liver health in CLD.[155] ECHO, Extension for Community Healthcare Outcomes; PCP, primary care provider.

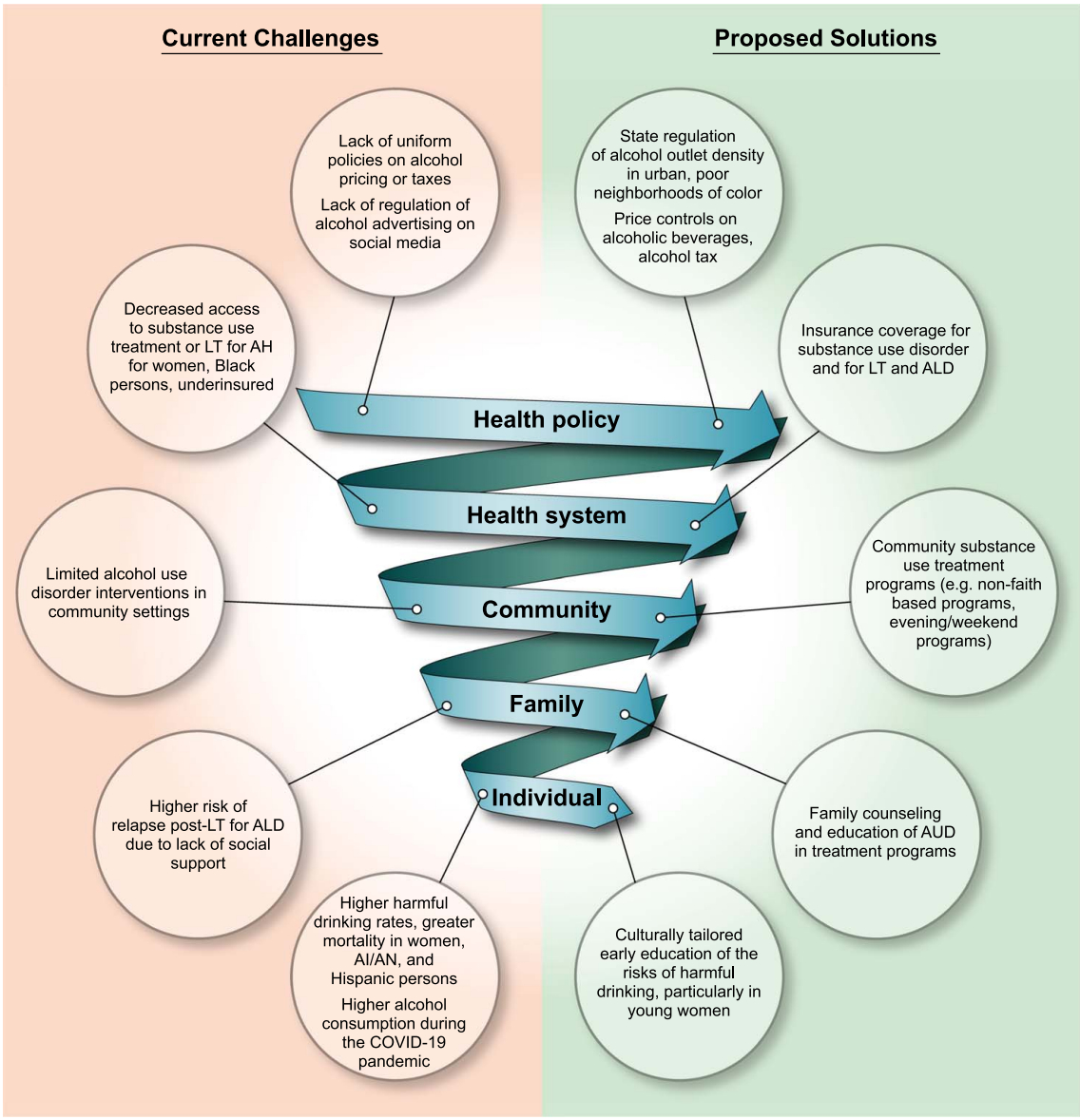

FIGURE 4 Current challenges and proposed solutions to disparities in ALD care. AH, alcoholic hepatitis.

course.[164] Partnerships with the National Hispanic Medical Association and other community organizations could be developed to disseminate culturally tailored clinical care pathways to minority groups. Care pathways should include descriptions of high-risk and minority populations.

While early diagnosis of CLD is important, some patients will still need specialty liver disease care. Telehealth has been successful at improving access to care and survival for rural populations with CLD and reducing evaluation time for listing on the LT waitlist.[165,166] However, telehealth may further exacerbate health disparities due to language barriers,[167,168] inequities in access to internet services,[169] or challenges faced in using telemedicine platforms.[170] Strategies to mitigate digital disparities include providing telemedicine education to patients, ensuring language and interpreter access in telehealth platforms, and designing user-friendly patient portals.

To promote equitable access to LT, culturally tailored navigation programs that address literacy, distrust, and social needs, such as the African American Transplant Access Program and the Hispanic Transplant Program at Northwestern, are needed.[171] Additionally, transplant equity working groups through UNOS or the American Association for the Study of Liver Diseases (AASLD) should be formed to develop health equity metrics that could be made publicly available to encourage program initiatives that combat liver health disparities.

Implementation of quality improvement (QI) measures in cirrhosis care is another potential strategy to help health systems mitigate existing health disparities. QI initiatives in patients with cirrhosis have been shown to reduce hospital readmissions[172] and increase HCC surveillance,[173] though the impact on reducing disparities has not been explored. The AASLD has developed

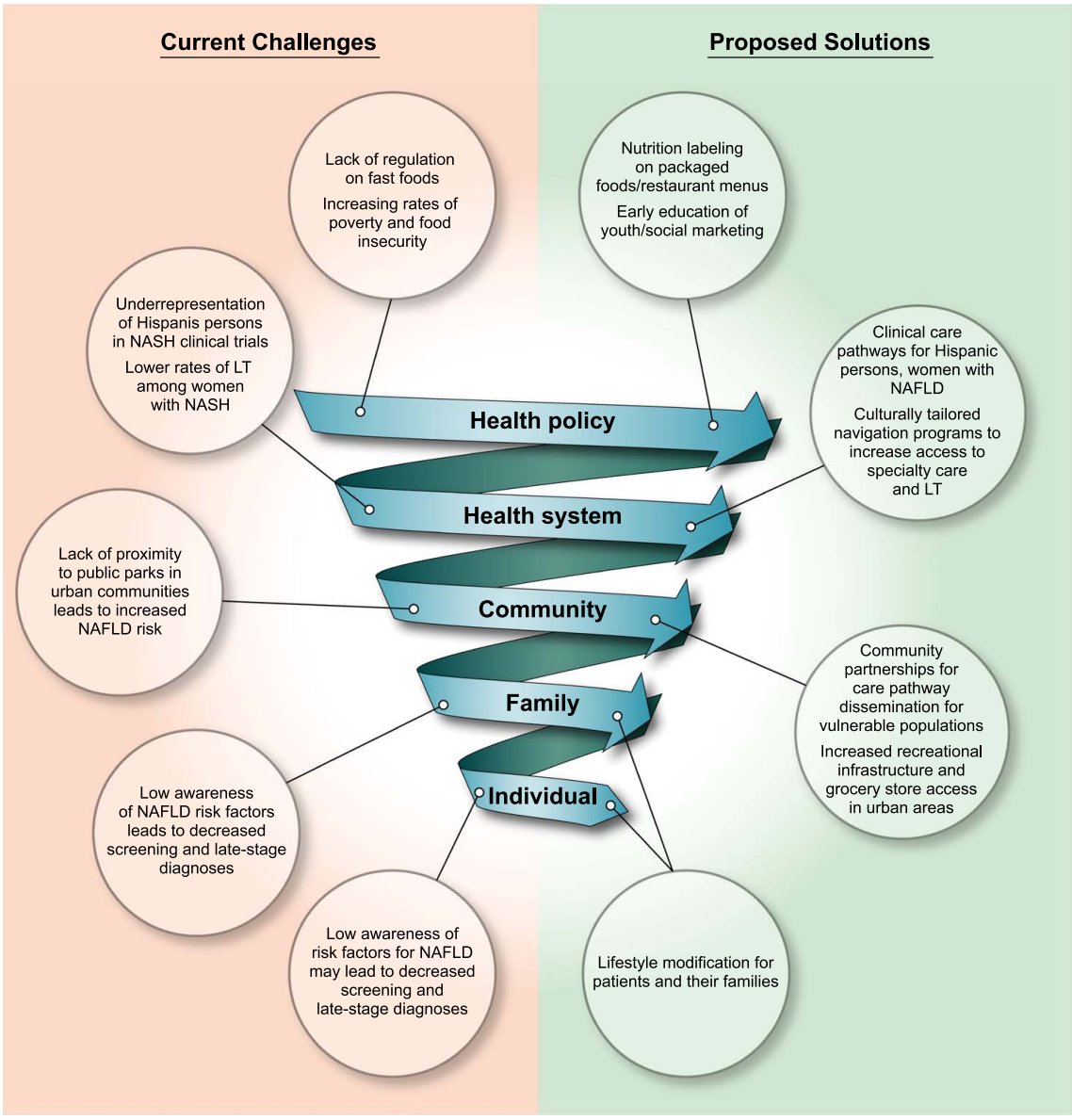

FIGURE 5 Current challenges and proposed solutions to disparities in NAFLD care.

a standard set of QI metrics, including both process-based measures and patient-reported outcomes, for cirrhosis and HCC,[174–176] which have been demonstrated to improve mortality.[177] Assessment of differences in these metrics by gender and race and ethnicity may identify groups that would benefit the most from QI interventions. Application of a QI framework offers a solutions-based approach to potentially reduce liver disease disparities by targeting modifiable aspects of care delivery and then refining the approach over time.

Community-level solutions

In addition to health policy–level and health systems–level solutions, interventions at the community level may be effective in mitigating disparities and improving health outcomes in minority and socioeconomically disadvantaged populations. One example of this is implementation of community-based screening programs for viral hepatitis in high-risk groups, such as people who experience homelessness. The University of California San Francisco's DeLIVER Care Van, a mobile unit that provides HCV testing and treatment to PWID or who experience homelessness in San Francisco, is an example of a grassroots effort to deliver services to underserved communities and meet patients where they are.[178] The Cherokee Nation Hepatitis C Virus Elimination Program is another example of a community-based, multilevel intervention that has been effective at improving the cascade of care, including screening, linkage to care, treatment, and cure.[179] Expansion of treatment programs for alcohol and substance use, including non-faith-based programs, family-based AUD counseling and education, and tailored

support groups for young women, are potential community-level solutions to address the rising tide of AUD in the United States.

In conclusion, we identify significant disparities in CLD burden, access to care, and outcomes in the United States, with racial and ethnic minorities, women, and socioeconomically disadvantaged individuals being disproportionately impacted. Rising rates of ALD and NAFLD and suboptimal viral hepatitis screening and treatment strategies among those at greatest risk are contributing to these disparities. Given that our understanding of liver-related disparities largely comes from population-based retrospective cohorts, the development of prospectively maintained cohorts with granular neighborhood and individual social determinant and liver disease characteristics is needed to examine the root causes of liver health disparities. Ultimately, however, we must move beyond simply reporting disparities to implementing multilevel health equity solutions that acknowledge the relationship between the SSODH and health care disparities.

AUTHOR CONTRIBUTIONS

Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data: Ani Kardashian, Marina Serper, Norah Terrault, Lauren D. Nephew. *Drafting the article or revising it critically for important intellectual content*: Ani Kardashian, Marina Serper, Norah Terrault, Lauren D. Nephew. *Final approval of the version to be published*: Ani Kardashian, Marina Serper, Norah Terrault, Lauren D. Nephew.

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CONFLICT OF INTEREST

Marina Serper consults for Gilead. Norah Terrault consults for EXIGO Management Consultants LLC, ENYO, Entourage Pharma, PPD Pharma-Moderna, Dova Pharmaceuticals, Intercept, and Moderna. She received grants from Gilead, Glaxo-Smith-Kline, Roche-Genentech, Allergan Pharmaceuticals, DURECT Corp, and Helio Health. She provides continuing medical education for Focus Medical Communications.

ETHICS STATEMENT

This review was exempt from IRB review. There were no human subject involved or consent needed for this review. All authors read and agreed to publication of the compiled material.

DATA AVAILABILITY

All references for data cited in this review article are provided in the references section. Any figures that were adapted from existing figures were also cited in the references section.

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