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**Title of Initiative:** Interventions to Address Disparities in Liver Diseases and Liver Cancer

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**Objective:** This initiative will support community engaged, multilevel, and multidomain intervention research to reduce disparities in liver diseases and liver cancer among populations who experience health disparities in the United States.

**Background:** Liver diseases and liver cancer have greater prevalence and mortality among all racial and ethnic minority and low socioeconomic status (SES) populations. Race and ethnicity-based disparities in prevalence and severity of liver diseases include chronic hepatitis B (HBV) and chronic hepatitis C (HCV) viral infections, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), and liver cirrhosis (LC). Chronic HBV disparities are significant, with non-U.S.-born (70% of U.S. cases) and Asian American, Native Hawaiian, and Pacific Islander (AANHPI) persons at highest risk. American Indian/Alaska Native (AI/AN) persons are at highest risk for HCV. Men are typically at higher risk for all liver diseases and liver cancer, yet chronic HCV burden among women of reproductive age has increased recently (with the greatest increase in AI/AN women), also increasing overall risk of maternal-to-child transmission. Hepatitis infection risk is elevated among sexual and gender minority (SGM) populations, although data are largely limited to men who have sex with men. NAFLD prevalence is highest among Mexican-origin Latinos (42.8%), followed by non-Hispanic Whites (NHWs) (30.6%), all Latinos (27.6%), non-Hispanic Blacks (21.6%), and Asian Americans (18.4%). NASH prevalence is similar, and highest in Latinos (45.4%). Chronic liver disease (CLD) and/or LC mortality is twice as high (and rising) in AI/ANs compared to Latinos. Available Native Hawaiian and Pacific Islander (NHPI) data indicates these persons have over twice the CLD and/or LC mortality rate of Asian Americans (7.9 versus 3.4 per 100,000). All racial and ethnic minority populations also have a higher burden of liver cancer (e.g., hepatocellular carcinoma [HCC]) that is increasing. Liver cancer incidence is highest among AI/AN persons (21.2 per 100,000), followed by Latino (15.3), AANHPI (12.5), non-Hispanic Black (10.8), and NHW (7.7) populations, with similar mortality disparities. Importantly, populations that have been marginalized experiencing liver disease and liver cancer disparities are often unaware of this risk and live with undiagnosed, preventable, and curable conditions of progressive liver damage, developing LC, end-stage liver disease, or HCC before receiving appropriate care.

Common risk factors (e.g., evitable toxin exposure, substance use) for and conditions often comorbid (e.g., viral hepatitis, obesity, Type 2 diabetes [T2D]) with CLD and HCC are well-

established in the literature. Risk and protective factors vary by population and influence liver disease and liver cancer susceptibility and progression. Disparities in the incidence and progression of preventable and curable liver diseases (i.e., HBV, HCV, NAFLD, NASH) also correspond to disparities in CLD with advanced disease progression (i.e., LC, liver failure, HCC). For instance, obesity, metabolic disorder, and T2D are risk factors for NAFLD, NASH and liver cancer, and these conditions also disproportionately impact Latinos and non-Hispanic Blacks. CLD and HCC trends by geographic regions further reflect disproportionate concentrations in risk factors shaped by sociocultural and historical factors.

Liver disease and liver cancer disparities are shaped by systemic and structural influences (e.g., structural racism, discrimination, economic disparities, quality education, public safety), that impact access to resources, or social determinants of health (SDoH). Poverty and low SES at the individual and neighborhood levels, food insecurity, and exposure to environmental pollutants are among the SDoH linked to adverse liver disease outcomes in minoritized populations. Along with experiencing greater susceptibility to established risk factors, persons of racial and ethnic minority, SGM, non-U.S.-born, and/or low SES populations are also more likely to experience inequities in healthcare access (i.e., screening, surveillance, and treatment) and literacy. Immigration status, language and cultural barriers, and mistrust among these populations have significant influence on healthcare literacy and access. Limited or no healthcare access significantly contributes to liver health disparities and often results in late diagnosis, limited treatment options, and poor survival rates. For instance, HBV is vaccine-preventable, yet U.S. HBV vaccination uptake is low, with the lowest uptake among racial and ethnic minority populations. Greater post-pandemic increases in liver diseases and liver cancer among women and racial and ethnic minority populations indicate disparities are worsening and are related to collateral effects on liver health disparities, such as adverse economic effects, limited or delayed access to health care, psychosocial strain, and health behavior pattern changes, that are forecasted to worsen without intervention.

There are very few interventions that address liver diseases or liver cancer disparities. Current liver disease and liver cancer interventions are largely treatment, secondary or tertiary prevention, and often involve pharmacological or weight loss treatments for persons with disease processes already in place. Limited research aims to address SDoH or involves the scientific inquiry of minority health or populations with health disparities. However, targeted, community-based interventions to improve HBV and HCV vaccination and screening in AANHPIs have significantly improved liver cancer incidence and mortality since 2007. Additionally, policy-level interventions have eliminated race and ethnicity-based HCV treatment disparities, indicating a need for interventions on upstream SDoH. However, few interventions target upstream SDoH or assess the direct impact on disparate disease progression and clinical outcomes. Thus, to advance health equity in this area, multilevel interventions that address upstream social barriers, identify and support social protective factors, and extend beyond modifying individual-level health behavior are needed. Such interventions are designed with the needs of a target community, recognizing the diversity of disproportionately affected

populations, addressing food insecurity, health literacy, including cultural sensitivity with awareness and resources intended to overcome language and immigration status barriers. SDoH, while not well-studied, require multilevel and multidomain inquiry and intervention, as these determinants have multilevel and multidomain influences on liver diseases and liver cancer disparities. Finally, the COVID-19 pandemic may have placed additional groups at increased liver disease and liver cancer risk, and these interventions may best serve to mitigate new and worsening disparities, as upstream SDoH have wide-ranging impact.

NIMHD has led programmatic efforts to stimulate research on reducing CLD and liver cancer disparities with the purpose of supporting projects conducting multidisciplinary research on etiologic factors and mechanisms of CLD and liver cancer disparities (Mechanisms of Disparities in Chronic Liver Diseases and Cancer; [PAR-20-088/PAR-20-081](#)). While NIMHD also leads in supporting the extremely limited primary prevention intervention research, there is now a need to stimulate strategic intervention research, particularly in the areas of HBV vaccination uptake and HCV treatment access, conducted in a variety of settings that promotes prevention, addresses pathways of upstream SDoH throughout the life course, and is designed with the needs of populations experiencing liver disease and liver cancer disparities as their foundation.

**Description of Initiative:** This proposed initiative would support community-engaged multilevel, multidomain intervention research in liver diseases and liver cancer to promote prevention, address the impact of upstream determinants throughout the lifespan, and emphasize reducing U.S. population-level disparities in screening, prevention, and treatment of liver diseases before they progress to chronic conditions.

Intervention research topics of interest include, but are not limited to:

- Developing and testing HBV and HCV screening uptake methods and approaches, including appropriate screening recommendations and methods for populations with multiple identities that have been marginalized.
- Strategies promoting HBV vaccination acceptance, reducing barriers to uptake, and improving successful series completion.
- Approaches improving HBV and HCV treatment access, disease management resources, linkage to timely care, adherence, and completion.
- Non-invasive and accessible NAFLD, NASH, and/or CLD screening strategies that improve and facilitate risk detection and/or accelerated disease progression to determine early onset in disproportionately affected populations.
- Culturally appropriate, primary prevention interventions of risk reduction and/or health promotion in underserved geographical areas and populations with multiple identities that have been marginalized, including adaptations of existing evidence-based intervention strategies across cultures and contexts.

- Approaches addressing multilevel, intergenerational risk and/or protective factors and potential sensitive periods over the life course when interventions may be most effective, such as maternal-to-child transmission and/or family-level interventions.
- Strategies to address structural factors and institutional discrimination/racism that affect liver disease incidence and progression, including measuring the impact of the addition or removal of treatment eligibility requirements and resources.
- Community-engaged approaches that promote equitable partnerships and consider infrastructure, resources, and sustainability of programs in context.