Received: 11 August 2022 | Accepted: 11 August 2022

DOI: 10.1002/hep.32741

PUBLIC POLICY CORNER

OPEN

Attacking the public health crisis of hepatocellular carcinoma at its roots

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Abstract

As the third most common cause of cancer-related death worldwide with significant mortality rates in the United States, hepatocellular carcinoma has strong association with cirrhosis and chronic hepatitis B virus (HBV) with a growing at-risk population from the rise in chronic liver disease from alcohol use and nonalcoholic fatty liver disease. Despite this, progress in identifying at-risk individuals and early detection of HCC in these populations have lagged behind treatment advances.The lack of consensus may undermine widespread adoption of surveillance programs, thus preventing HCC detection at a curable stage. This public policy corner piece focuses on opportunities for prevention of HCC by focusing on its principal risk factors: viral hepatitis, NAFLD, and alcohol-related liver disease, and three key action points to reverse the course of this public health crisis: 1) Awareness and education; 2) Screening and diagnosis, and 3) Partnerships and advocacy.

Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death worldwide with significant mortality rates in the United States.[1,2] Its strong association with cirrhosis and chronic hepatitis B virus (HBV) provides a compelling logic for targeted screening and prevention.[3,4] Despite this, progress in identifying at-risk individuals and early detection of HCC in these populations has lagged behind treatment advances.

Currently available tools for HCC screening are imperfect. Although HCC surveillance in high-risk groups is endorsed by the American Association for the Study of Liver Diseases (AASLD),[5] not all organizations share this view. This lack of consensus may undermine widespread adoption of surveillance programs, thus preventing HCC detection at a curable stage. HCC management involves treatments tailored to tumor burden and hepatic reserve, but disparities

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ALD, alcohol-related liver disease; CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus

Potential conflict of interest: The AASLD Public Policy Corner is a regular publication of the AASLD Public Policy Committee highlighting key subject areas of AASLD's public policy agenda. The Public Policy Committee advocates for AASLD members and their patients in front of key decision makers including legislators, regulatory agencies and key opinion leaders within the United States Government.

exist in access to the multidisciplinary teams that should oversee this complex process.

The at-risk population for HCC is growing in response to the rise in chronic liver disease from alcohol use and NAFLD,[3,4] and there is an urgency to address these issues. This will require robust research support, particularly in diagnostics and health services delivery. Stakeholders in government and professional organizations must engage to heighten HCC awareness among health practitioners and the community and to improve linkage to care.

In this public policy piece, we examine opportunities for prevention of HCC by focusing on its principal risk factors: viral hepatitis, NAFLD, and alcohol-related liver disease (ALD). Adoption of the strategies we have highlighted below represents three key action points to reverse the course of this public health crisis:

1. Awareness and education
2. Screening and diagnosis
3. Partnerships and advocacy

Viral hepatitis

Despite the launch in 2016 of the World Health Organization (WHO) global campaign to eliminate the public health burden of viral hepatitis by 2030,[6] millions of Americans remain infected with HBV and hepatitis C virus (HCV). Close to half of Americans infected with viral hepatitis are unaware of their infection.[7,8] Lack of awareness concerning screening and surveillance, both within the community and among health practitioners, also remains a challenge. Marginalized populations, including the homeless, the incarcerated, and people who inject drugs, are at higher risk for HBV and HCV exposure and face disparities in access to care.

We place particular focus on HBV as the incidence of HCC from HCV is decreasing because of the advent of direct acting antivirals for HCV, whereas HBV still has no curative treatments.[9,10] The burden of HBV is the highest globally and is disproportionately high among the foreign-born, in whom HBV screening rates remain lower and liver cancer mortality rates higher than in United States–born individuals.[11] Vertical transmission also account for most of the burden of chronic HBV. In response, the Centers for Disease Control and Prevention (CDC) has launched the National Comprehensive Cancer Control Program (NCCP) to put liver cancer prevention concepts into action through selection of relevant strategies, choosing key partners, and measuring the extent of strategic success.[12] The NCCP has developed and implemented education programs for the general public, high-risk populations, and decision-makers to increase knowledge and awareness of HCC and viral hepatitis.

Updated recommendations from the CDC and Advisory Committee on Immunization Practices endorsing universal HBV vaccination of adults age 59 years and younger provide another opportunity to reduce the extent of HBV infection.[13] Federal efforts are needed to support education and infrastructure to implement these guidelines. Successful application should decrease HBV prevalence, thus reducing the risk of HCC. Much still needs to be done to promote greater awareness about the consequences of viral hepatitis, including HCC.

NAFLD

With prevalence of approximately 25%, NAFLD is positioned to become the leading cause of HCC in America. Despite this, there has been little public health response to the threat posed by NAFLD. Awareness and understanding of this disorder have been limited primarily to the gastroenterology/hepatology community.[14,15] NAFLD is linked to the metabolic syndrome, itself a risk factor for HCC. Like HCC, metabolic syndrome is complex and requires multidisciplinary care. Lifestyle interventions, including weight loss through dietary modification and increased physical activity, are the only known therapies that prevent progression of hepatic fibrosis, the dominant risk factor for NAFLD-related HCC.

Implementation of a national NAFLD public health agenda will require its recognition across disciplines as a major issue, the development of consensus guidelines for prevention, screening, and management, and an action plan to deploy them. Such a plan should empower health practitioners with a comprehensive model of care that includes pathways for screening and diagnosis as well as risk stratification tools to guide specialty referral.[16] The plan should also include robust support to promote lifestyle interventions that reduce NAFLD progression and consequent HCC risk.

ALD

Currently the highest cause of liver-related mortality worldwide, ALD has received little attention compared with other liver diseases because of the stigmata associated with alcohol use disorders, despite its significant negative health and economic impact.[17,18] The recent precipitous increase in alcohol misuse in America has been paralleled by a rise in ALD-related complications, including HCC.[19] In order to offset this trend, expanded public health efforts in ALD prevention and diagnosis will be necessary.

Prevention of alcohol misuse or consumption beyond recommended maximum levels should be a critical part of a strategy to reduce the extent of ALD. There is a

wealth of information in the WHO's Global Alcohol Database on alcohol use from every country, with eight categories of existing policies that span a broad spectrum of regulatory measures to curb excessive alcohol use.[20] The goal is to develop a comprehensive picture of alcohol consumption and attributable disease burden and to provide global public health strategies and action plans to reduce harmful use of alcohol, such as sales restrictions and price and tax controls.[21–23] Regulations can be customized locally, based on analysis of patterns of alcohol intake and socioeconomic and cultural factors. We call for consideration of tailored regional policies, instituted on a state-by-state basis, to prevent adverse outcomes of alcohol use, including the development of HCC.

Partnership and advocacy

Addressing the burden of HCC will require multilevel engagement from grassroots to governmental bodies and partnerships with private institutions and patient advocacy groups. Insights of those living with liver disease and their personal stories can influence and help guide the development of effective public policy interventions, incorporating patient-centered care, to improve disease-related outcomes.

Leading the way is the patient-created Global Liver Institute. Their Liver Cancer Council works with committed stakeholders, including patients, caregivers, and professionals, to develop programs directed toward the needs of the liver cancer community. Their 2021 policy agenda has promoted the development of patient centric legislation, for example, the Liver Illness, Visibility, Education, and Research (LIVER) Act, introduced by US Senator Tammy Duckworth and Representative Nydia M. Velázquez. This proposed legislation would increase funding at the National Institutes of Health and CDC for liver cancer research, for expansion of HBV vaccination, and for screening and treatment for chronic liver disease and HCC.[24]

Like the patient-led World Hepatitis Alliance, which pushed for the World Health Assembly Resolution for global elimination of viral hepatitis, we need groups to advocate for a public health agenda for NAFLD and ALD. We call for collaboration and engagement with noncommunicable disease (NCD) community organizations, such as the NCD Alliance, to work in concert to address these areas of unmet need.

Lessons from the COVID pandemic

The pandemic has had significant adverse economic and sociopolitical effects, diverting resources from non-COVID-related public health issues (e.g., viral hepatitis) and amplifying pre-existing health disparities within the population.[25] The pandemic has also catalyzed efforts to strengthen healthcare systems already in place, which can be leveraged in the future for programs in viral hepatitis, NAFLD, and ALD. The speed with which new systems in health care delivery have been built should serve as a model to provide government agencies better insight on how to prioritize resources to combat HCC and the liver diseases that drive its development.

AASLD actions

The AASLD is committed to advocacy for legislation and funding to tackle HCC and its upstream risk factors. Its efforts are spearheaded by its Public Policy Committee, which has expanded to include members of patient advocacy organizations. In partnership with government relations consultants CRD Associates, AASLD influences legislative and regulatory policies that will achieve meaningful progress, for example, the expansion of the Recalcitrant Cancer Research Act of 2012. A particularly important activity is Capitol Hill Day, open to all AASLD members, which provides face-to-face opportunities to convey to Congressional representatives the importance of reducing the burden of liver disease.

SUMMARY

There are multiple opportunities to reduce the negative impact of HCC. Strengthening advocacy and support from a broad spectrum of stakeholders is critical in this endeavor. Although we have focused on prevention and management of chronic liver diseases, the precursors to HCC, we acknowledge the importance of advancing technology for HCC detection and the ongoing development of effective treatments. Additional information on AASLD's public policy activities, which are relevant to these issues, can be found online.

CONFLICT OF INTEREST

Lisa J. Townshend-Bulson received grants from Gilead. Steven D. Lidofsky received grants from Gilead, Intercept, and Target.

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How to cite this article: Lee HM Lidofsky SD Taddei TH Townshend-Bulson LJ. Attacking the public health crisis of hepatocellular carcinoma at its roots. Hepatology. 2023;77:1456–1459. https://doi.org/10.1002/hep.32741