THE CARTER CENTER

Summary of the Twenty-Sixth Meeting of the International Task Force for Disease Eradication (ITFDE) June 20, 2017

The 26th Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30am to 5:00pm on June 20, 2017 to discuss new World Health Organization (WHO) goals for the elimination of hepatitis B infection (HBV) and hepatitis C infection (HCV) as public health threats. The Task Force members at the time of this meeting were Dr. Stephen Blount, The Carter Center (Chair); Dr. Dirk Engels, World Health Organization; Dr. Peter Figueroa, The University of the West Indies, Jamaica; Dr. Donald Hopkins, The Carter Center; Dr. Julie Jacobson, Bill & Melinda Gates Foundation; Dr. Hamid Jafari, Centers for Disease Control and Prevention (CDC); Professor David Molyneux, Liverpool School of Tropical Medicine (retired); Dr. Patrick Osewe, The World Bank; Dr. Stefan Peterson, UNICEF; Dr. David Ross, The Task Force for Global Health; Dr. Dean Sienko, The Carter Center; Dr. Nilanthi de Silva, University of Kelaniya, Sri Lanka/WHO Strategic and Technical Advisory Group (STAG); Dr. Laurence Slutsker, PATH; Dr. Roberto Tapia, Carlos Slim Foundation; Dr. Ricardo Thompson, National Institute of Health (Mozambique), and Dr. Dyann Wirth, Harvard School of Public Health. Eight Task Force members (Blount, Figueroa, Jafari, Molyneux, Ross, Sienko, Slutsker, Thompson) attended this meeting, and two were represented by an alternate (Dr. Gottfried Hirnschall for Engels; Dr. Anne Detjen for Peterson).

Presenters at the meeting, which was chaired by Dr. Stephen Blount, included Dr. Catharina Boehme, FIND; Dr. Gottfried Hirnschall, World Health Organization; Dr. Olufunmilayo Lesi, University of Lagos Teaching Hospital (Nigeria); Dr. Homie Razavi, Center for Disease Analysis Foundation; the Honorable Dr. David Sergeenko, Ministry of Labor, Health and Social Affairs (Georgia), and Dr. John Ward, Centers for Disease Control and Prevention.

Background

Five types of viral hepatitis are known to cause infection in humans (hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E). Only two types, HBV and HCV, typically cause chronic liver disease, which remains largely asymptomatic until late in the course of illness. Many persons infected with HBV or HCV are unaware they are infected and have clinically silent infections for decades until developing cirrhosis, hepatocellular carcinoma (HCC), and extra-hepatic manifestations of the disease. The World Health Organization (WHO) estimates that in 2015, viral hepatitis was responsible for 1.34 million deaths per year.[1] Worldwide, mortality attributed to viral hepatitis has increased by 22% since 2000 despite declines in deaths caused by other infectious diseases, including HIV, tuberculosis (TB), and malaria. Certain countries and sub-national areas experience disproportionately high rates of viral hepatitis, highlighting the need for strategic information to appropriately target interventions.

[1] World Health Organization. *Global Hepatitis Report 2017*. Available at: http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/.

In 2016, in light of the growing public health burden of viral hepatitis, availability of highly effective and safe therapies and vaccines, and persisting gaps in prevention and response, the World Health Assembly approved WHO's first Global Health Sector Strategy on Viral Hepatitis 2016-2021.[2] This strategy sets the first global targets for eliminating HBV and HCV infections as public health threats by 2030 (defined as a 90% reduction in incidence and a 65% reduction in deaths) and establishes indicators to monitor implementation of necessary interventions to reach these goals. WHO's Global Strategy is based on a public health approach prioritizing implementation of feasible and effective interventions, promoting service delivery approaches that ensure quality and equity for all persons at risk or living with hepatitis B and hepatitis C, taking programs to scale to achieve sustained impact at the population level, and establishing stakeholder responsibility and accountability. The Global Strategy also sets quality indicators to monitor performance of viral hepatitis vaccination, safe injection, harm reduction programs, testing, and treatment programs. As of June 2016, WHO has provided technical capacity to help 42 countries prepare national plans and develop policy recommendations to guide development of national viral hepatitis surveillance, hepatitis B immunization, safe injection, HBV and HCV testing, and treatment policies. The Global Strategy and global elimination targets defined therein are models for national planning. In 2017, the United States' National Academies for Sciences, Engineering, and Medicine (NASEM) published a report titled, "A National Strategy for the Elimination of Hepatitis B and C"[3], that proposes elimination goals for the United States and recommends actions to reach them; U.S. goals closely mirror those set forth by WHO. The feasibility of reaching viral hepatitis elimination goals depends on the capacity to implement effective interventions to prevent transmission (i.e., primary prevention) and morbidity (i.e., secondary prevention) while supporting clinical studies and translational research to bring forward new technologies and models of care that improve prevention effectiveness.

Hepatitis B

Globally, approximately 278 million people are living with HBV infection and, in 2015, this infection resulted in 887,000 deaths. The prevalence of hepatitis B is highest in countries of sub-Saharan Africa and East Asia, where 6% of the adult population is chronically infected.[1] Rates of chronic hepatitis B are also high in the Amazon region of South America, Africa, central Asia and South East Asia. The African and Western Pacific regions accounted for 68% of those infected globally. Country-specific estimates of HBV disease burden are available for more than 100 countries (*Figure 1*) through Polaris, (http://polarisobservatory.org/), a global observatory with the mission of providing data, tools, training, and decision analytics to support the elimination of hepatitis B and C globally by 2030.

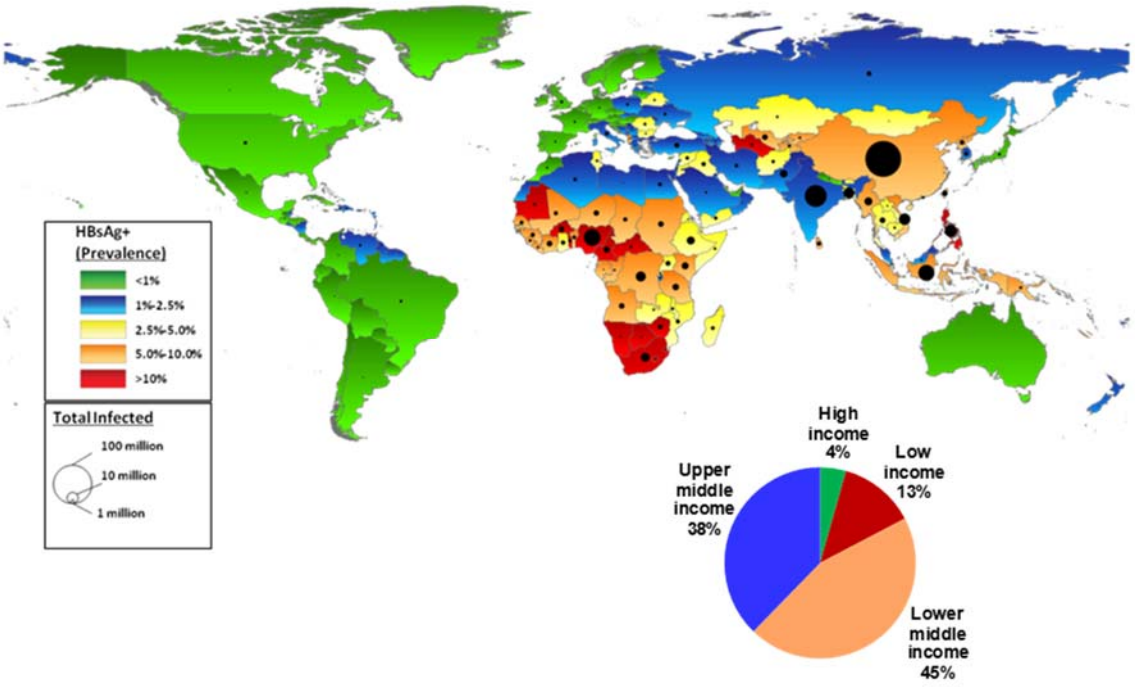
HBV is transmitted by percutaneous or mucosal exposure to blood or body fluids of an infected person, such as from an infected mother to her newborn during childbirth; through close personal contact within households; unscreened blood transfusion or unsafe injections in health-care settings; injection-drug use; and from sexual contact with an infected person. Persons typically remain asymptomatic at the time they are initially infected, not knowing they are infected until decades later when they develop liver disease. Risk for chronic HBV infection is greatest for persons infected at birth or in the first years of life. Of infants who acquire HBV infection from their mothers at birth, as many as 90% become chronically infected compared with 30%–50% of children infected at 1-5 years of age. This percentage is smaller

[2] World Health Organization. *Global Health Sector Strategy on Viral Hepatitis, 2016-2021*. Available at: http://www.who.int/hepatitis/strategy2016-2021/portal/en/.

[3] The National Academy of Sciences, Engineering, and Medicine. *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report.* Available at: http://nationalacademies.org/hmd/reports/2017/national-strategy-for-the-elimination-of-hepatitis-b-and-c.aspx?_ga=2.208536466.1004180495.1501595935-1527997965.1501595935.

among older children, adolescents, and adults, for whom approximately 6%-10% of all acute HBV infections persist as chronic infection. Of persons with chronic HBV infection, 15%–25% will develop chronic liver disease, including cirrhosis, liver failure, or liver cancer.[4] Accordingly, protecting newborns and young children from HBV infection is the priority for HBV prevention.

Figure 1. HBV (HBsAg) Prevalence Distribution



Global efforts to prevent HBV infection are, for the most part, steadily improving. The hepatitis B vaccine, available since 1982, is the cornerstone of HBV prevention. Public health activities to implement hepatitis B vaccine-based strategies have progressively increased over the past 3 decades, beginning with recommendations from WHO in the early 1990s to include the three-dose series of hepatitis B vaccine in routine infant immunization. As a result of this and other global initiatives (e.g., the Global Alliance for Vaccines and Immunizations [GAVI]), reductions in vaccine costs, and the development of pentavalent vaccines, hepatitis B vaccination coverage among infants is high in almost all high-income countries, but vaccination rates remain low in Africa and parts of Asia. Over 90% of children respond to the hepatitis B vaccination series, typically conferring protection for at least 20 years.

WHO recommends that all newborns receive a birth-dose of hepatitis B vaccine.[5] Infants exposed to HBV around the time of birth are at highest risk for chronic HBV and severe liver disease in later life, and a dose of hepatitis B vaccine administered immediately after birth (preferably within 24 hours) can prevent 85% of mother-child transmission of HBV. The addition of hepatitis B immunoglobulin for HBV-exposed infants increases protection to >90%, and recent studies suggest that providing mothers who have high viral loads of HBV with antiviral prophylaxis can prevent breakthrough infections among infants who receive the recommended vaccine strategies at birth. However, global rates of coverage for the birth dose of hepatitis B vaccine are low, with only about 40% of newborns receiving this dose.[1] Coverage can be

[4] van Damme P, Ward J, Shouval D, Wiersma, Zanetti A. *Hepatitis B Vaccines*. In Plotkin SA, Orenstein WA, eds. *Vaccines*, Seventh Edition, London, Elsevier Health Sciences, 2017.
[5] World Health Organization. *Summary of Key Points: WHO Position Paper of Hepatitis B Vaccines, October 2009.* Available at: http://www.who.int/immunization/Hep_B_key_points_summary_sep09.pdf?ua=1.

improved by integrating hepatitis B vaccination with other routine maternal and neonatal health services, which is most readily accomplished when newborns are delivered in birthing facilities under the care of trained attendants.[6] The proportion of children born in such facilities has increased over the last several decades, contributing to increases in hepatitis B vaccination of newborns in China and other countries. Local health-facility policies specifying birth-dose vaccination, standing orders for vaccination, and availability of vaccine in the delivery room are examples of other strategies shown to facilitate high rates of hepatitis B vaccination of newborns in birthing facilities.

Infants born at home face the greatest challenges regarding receipt of a birth-dose of hepatitis B vaccine. In some countries of Asia and Africa, the majority of infants are born at home; as such, countries in WHO's African region have the lowest rates of birth dose coverage in the world. The absence of country-level policies for hepatitis B vaccination at birth in this region compounds the challenge of protecting this vulnerable population. For infants born outside of birthing facilities, certain interventions can facilitate provision of a birth dose of hepatitis B vaccine, including home visits by providers capable of administering vaccine, education of birth attendants, and improved vaccine availability. Vaccination coverage can also be increased in the home setting through availability of vaccine equipment that simplifies vaccine delivery and needle disposal, such as compact, pre-filled, auto-disable injection devices for single-dose vaccine.[6] Other simplified options for vaccine delivery are under investigation; in animal models, patches containing micro-needles coated with HBsAg have been shown to be safe and to deliver sufficient antigen to elicit protective levels of HBV antibody. Continued development of new technologies for vaccine delivery, together with continued assessment and improvements in existing immunization practices, can improve hepatitis B birth-dose coverage to levels necessary to eliminate HBV transmission.

For persons living with chronic hepatitis B, treatment with anti-viral medications suppresses HBV replication, decreasing risks for cirrhosis, liver cancer, and all-cause mortality.[7] At a price of less than U.S. $50 per year of treatment,[8] generic versions of these medications greatly reduce cost-related barriers to treatment. Yet in many countries, most persons with HBV have not been tested and are unaware of their infection status. Rates of HBV treatment coverage are very low worldwide. Of those diagnosed with HBV infection, less than 1 in 10 are currently receiving treatment. Although current therapy for HBV infection is effective, it is not curative. Unlike curative HCV medications, HBV therapy requires a lifelong course of treatment. Stimulated by the successes with HCV drug development, researchers have renewed interest in finding drugs active against new targets in the HBV life cycle that can enhance the immune response to HBV infection, leading to a functional cure for hepatitis B.[9]

Models constructed to determine the economic impact of eliminating HBV reveal that the elimination of HBV can be cost-saving given that targets are met. For instance, modeling has been conducted for Vietnam, where disease burden reduction strategies targeting a 70% scale up (70% Regional Action Plan for Viral Hepatitis[RAPVH]) have been assessed at different future price points in Vietnam.[10] Although the price of HBV therapy has declined to U.S $50 per year in most low and middle income countries,

---

[6] World Health Organization. *Practices to Improve Coverage of the Hepatitis B Birth Dose Vaccine. 2013.* Available at: http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf.

[7] Lok AS, McMahon BJ, Brown RS Jr, et al. Antiviral Therapy for Chronic Hepatitis B Viral Infection in Adults: A Systematic Review and Meta-Analysis. *Hepatology 2016*; 63(1):284-306. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26566246.

[8] World Health Organization. *Global Price Reporting Mechanism*. Available at: http://apps.who.int/hiv/amds/price/hdd/Default0.aspx.

[9] Liang TJ, Block TM, McMahon BJ, Ghany MG, Urban S, Guo JT, Locarnini S, Zoulim F, Chang KM, Lok AS. Present and Future Therapies of Hepatitis B: from Discovery to Cure. *Hepatology 2015*; 62(6):1893-908.

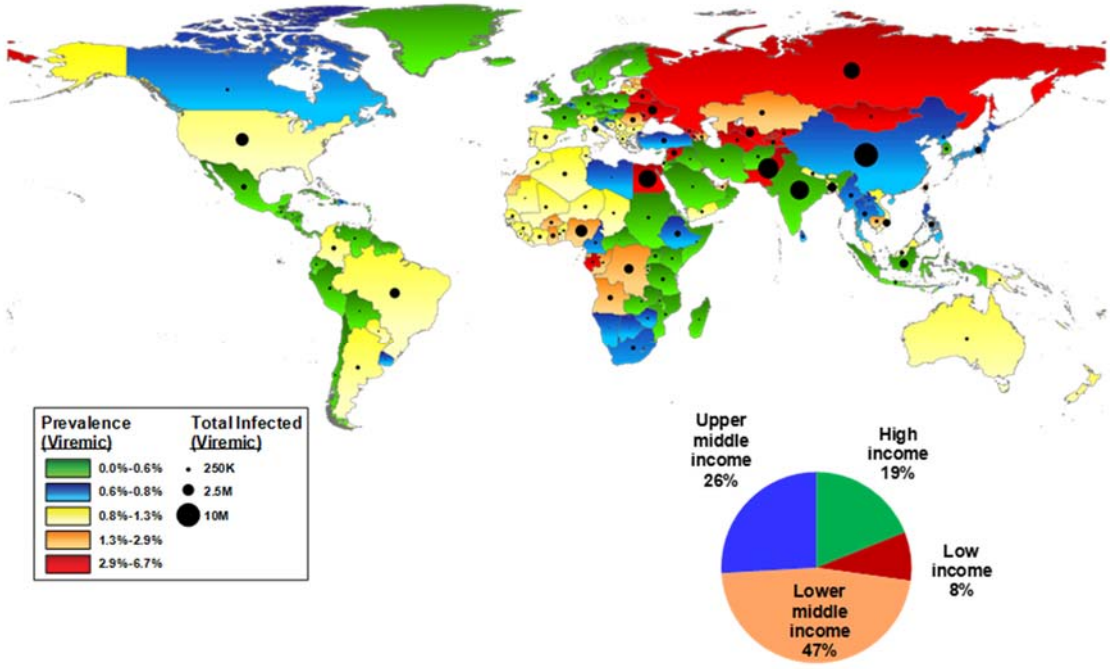
[10] Polaris Observatory, unpublished data.

models indicate that total direct costs of implementing scaled-up interventions would be higher relative to the status quo strategy. However, when longer life expectancy and higher productivity (indirect costs) are considered, the total cost of the elimination strategy is lower than the costs associated with status quo approaches after 2021-2025 (depending on the future drug prices).

Hepatitis C

The global burden of hepatitis C infection is substantial. Worldwide, 71 million (62–79 million) persons are chronically infected with HCV, corresponding to a prevalence of 1.0% (0.8%-1.1%); nearly 400,000 people die each year from hepatitis C, mostly from cirrhosis and HCC. Hepatitis C is found worldwide, the most affected WHO regions are the Eastern Mediterranean and European regions, with prevalence of 2.3% and 1.5%, respectively (*Figure 2*). Prevalence of HCV infection in other WHO regions varies from 0.5% to 1.0%.[1]

Figure 2. HCV Prevalence Distribution



HCV is transmitted primarily through percutaneous exposure that results most commonly from exposures in health-care settings with poor infection control and from injection-drug use. Less often, HCV transmission occurs among HIV-positive persons, especially HIV-infected men who have sex with men (MSM), as a result of sexual contact with an HCV-infected partner, among persons who receive tattoos in unregulated settings, and among infants born to HCV-infected mothers and household contacts. Injection-drug use is a major risk factor for HCV transmission, particularly in high-income countries: an estimated 67% of persons who inject drugs (PWID) worldwide have been infected with HCV.[11] The incidence of HCV is high among PWID beginning soon after they first inject drugs, with the risk for transmission rising

[11] Nelson PK, Mathers BM, Cowie B, et al. Global Epidemiology of Hepatitis B and Hepatitis C in People Who Inject Drugs: Results of Systematic Reviews. *Lancet* 2011;378(9791):571-83.

with the duration of drug injecting behaviors, frequency of injection, and frequency of sharing needles and drug preparation equipment.[12]

For most HCV-infected persons in low and middle income countries, most infections are caused by unsafe medical injections and other medical procedures. Infection control to eliminate exposures to contaminated blood, professional education, development of infection-control programs, and availability of single-use syringes and other safe technologies reduce transmission risk. Education campaigns designed to change social-cultural preferences from injectable medications to equally effective oral therapies reduce risks of HCV transmission, and health systems that monitor infection control provide providers with data to guide quality improvement.[13] Most blood banks around the world screen donated blood for HCV.[14] However, HCV testing in blood banks and other health facilities can be improved by the addition of virologic tests to detect early HCV infection and participation in programs to verify the quality of test technologies and practices.

No hepatitis C vaccine is available, as the genetic diversity of HCV and the lack of immune markers of immunoprotection raise formidable challenges to HCV vaccine development. However, access to clean injection equipment made available through syringe services programs (SSP) and treatment with medication assisted therapy (MAT) each reduce transmission risk by 50%, and if both interventions are available, by 70%.[15] In most countries, two major factors limit the effectiveness of these interventions: a) lack of policies to spur acceptance and implementation of these interventions and b) insufficient capacity to provide a sufficient number of SSP and MAT programs to adequately serve risk populations. The capacity of these programs must be expanded in at least two ways: programs must be sufficient in number to be readily available to persons who inject drugs and must be of sufficient scale to provide enough clean injection equipment (SSPs) and medication to limit injecting behaviors (MAT programs). Public acceptance of SSP (including among law enforcement) and public funds for both services, alone or as part of public-private partnerships, are essential in bringing HCV prevention to scale. Data from health models suggest that integrating HCV testing, care, and treatment into existing programs serving PWID enhances prevention and increases the feasibility of reducing the incidence of HCV by 90%.[16] Of PWID cured of their infection who continue to inject drugs, 2% become reinfected with HCV each year.[17] This risk can be minimized with continued provision of MAT and access to SSP, as needed, following completion of HCV therapy. Demonstration projects integrating SSP, MAT, and HCV testing/treatment into comprehensive programs can provide experience to guide delivery of these services globally.

Persons with chronic HCV can be cured of their infection. An arsenal of all-oral antiviral therapies clear HCV in >90% of persons who complete therapy, have an excellent safety profile, and require only one to several pills per day for 8-12 weeks; newer medications undergoing clinical trial are expected to shorten

---

[12] Wiessing L, Ferri M, Grady B, et al. Hepatitis C Virus Infection Epidemiology among People Who Inject drugs in Europe: A Systematic Review of Data for Scaling Up Treatment and Prevention. *PloS One.* 2014;9(7):e103345.

[13] World Health Organization. *Injection Safety: WHO Best Practices for Injections and Related Procedures Toolkit.* Available at: http://www.who.int/injection_safety/toolbox/9789241599252/en/.

[14] World Health Organization. *Blood Transfusion Safety: Global Database on Blood Safety.* Available at: http://www.who.int/bloodsafety/global_database/en/.

[15] Platt L, Reed J, Minozzi S, et al. Effectiveness of Needle/Syringe Programmes and Opiate Substitution Therapy in Preventing HCV Transmission among People Who Inject Drugs. *Cochrane Database Syst Rev 2016*;2016(1).

[16] Fraser H, Zibbell J, Hoerger T, et al. Scaling Up HCV Prevention and Treatment Interventions in Rural USA - Model Projections for Tackling an Increasing Epidemic. *Addiction 2017*. [Epub ahead of print].

[17] Aspinall EJ, Corson S, Doyle JS, et al. Treatment of Hepatitis C Virus Infection among People Who Are Actively Injecting Drugs: A Systematic Review and Meta-Analysis. *Clinical Infectious Diseases*: an official publication of the Infectious Diseases Society of America. 2013;57(Suppl 2):S80–9.

the duration of therapy.[18] Achieving a sustained virologic response (SVR), the measure of cure, following HCV therapy is associated with a 74% decline in all-cause mortality, 85% reduction in liver cancer, and 93% reduction in liver failure and mortality.[19] Although the initial 2014 U.S. market price of curative HCV medications was high ($86,000-$94,000 per course), drug costs in the United States have declined by at least 50%; HCV therapy is now considered cost saving for treatment of all HCV infected persons.[20,21] With availability of generic formulations for use in low-to-middle income countries, the cost of HCV therapies has also dramatically declined globally, now dropping to less than U.S. $200 per treatment course in some countries. Although quality assurance remains an issue for these generic versions of patent formulations, the large decrease in prices associated with generic drugs greatly reduces cost as an access barrier to HCV treatment in countries where health resources are constrained and for marginalized populations in developed countries.

Scaling up HCV prevention activities to meet elimination goals is cost-effective, reducing future expenditures for care and treatment for persons with HCV-related morbidities. For example, in Saudi Arabia, where about 103,000 people were living with HCV infection in 2015 (prevalence of 0.5%), models indicate that expanded screening and treatment as part of an elimination effort would result in increased health-care expenses. However, the additional costs are offset by the reduced health-care expenditures resulting from fewer cases of HCC and cirrhosis.[10] Indeed, compared with the current level of interventions, the costs of an HCV Elimination Program in Saudi Arabia would be lower than costs associated with the status quo strategy by 2027. After taking the indirect costs into account (e.g., shorter life expectancy and lower productivity), the cost of the elimination strategy would be less than the status quo strategy, starting in 2025.

A similar analysis for Ethiopia,[10] a low-income country with an HCV prevalence of 0.6% and 611,000 infections in 2015, showed that in that country, the total number of HCV infections is expected to remain constant over the next 15 years under the status quo strategy, with HCV-related morbidity and mortality expected to double over the same period. The current number of HCV patients treated in Ethiopia is low (30 patients per year), and patients pay for their own treatment. To achieve HCV elimination targets, Ethiopia must treat 50,000 patients per year and newly diagnose 42,000 patients per year by 2025. Although this represents a significant increase in screening and treatment, the country has access to generic therapies that cost $1,300 per patient. Modeling revealed that expanded screening, treatment, and other health-care services will cost more initially. Because most HCV infections in Ethiopia are not diagnosed and patients die of HCC and cirrhosis without ever knowing the cause, expanded screening will initially lead to diagnosis of patients with advanced liver disease who need hospitalization. However, over time, the elimination strategy will cost less as patients are diagnosed early, treated, and cured before progressing to advanced liver disease. Analysis indicates that, in Ethiopia, health-care spending will be less than costs associated with the status quo strategy after 2031, while achieving substantial health benefits.

---

[18] AASLD/IDSA. *HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C.* Available at: http://www.hcvguidelines.org/.

[19] van der Meer AJ, Veldt BJ, Feld JJ, et al. Association between Sustained Virological Response and All-Cause Mortality among Patients with Chronic Hepatitis C and Advanced Hepatic Fibrosis. *JAMA* 2012;308(24):2584-93.

[20] Chhatwal J, He T, Hur C, Lopez-Olivo MA. Direct-Acting Antiviral Agents for Patients with Hepatitis C Virus Genotype 1 Infection Are Cost-Saving. *Clin Gastroenterol Hepatol* 2017;15(6):827-837.

[21] Hill A, Simmons B, Gotham D, Fortunak J. Rapid Reductions in Prices for Generic Sofosbuvir and Daclatasvir to Treat Hepatitis C. *J Virus Erad* 2016;2(1):28–31. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946692/.

Examples of Elimination Efforts in Countries with High Viral Hepatitis Burden

Nigeria

Many countries are beginning to explore ways to reduce disease transmission and HBV-related morbidity and mortality with the goal of achieving HBV elimination, including Nigeria. As the most populous nation in Africa, Nigeria has an average national prevalence of HBV and HCV of 12% and 2%, respectively, as shown in a pilot study conducted by the Federal Ministry of Health and corroborated by other researchers. The key drivers of HBV transmission are childhood transmission and unsafe injection practices, including in settings providing tattoos or scarification marks. An estimated 20 million Nigerians are currently infected, and up to 5 million HBV infected people, in the absence of testing and treatment, will die prematurely from complications of liver cirrhosis or HCC. These complications of long-term chronic viral hepatitis are often the first clinical presentation and tend to occur in middle-age, the most productive part of adult life. This adversely impacts human productivity and national economy and is a direct cause of personal financial calamity, suffering, and death.

Prior to 2013, infant hepatitis B vaccination and treatment of the complications of chronic viral hepatitis by medical specialists (e.g., hepatologists) were the mainstay of hepatitis activity. The individualized fee-for-service model and the high cost of screening and care left the vast majority of infected persons with no access to care. In light of increasing global advocacy, the call for scaling-up hepatitis prevention and care formally commenced in Nigeria with the establishment of the National Viral Hepatitis Control Program and a National Hepatitis Technical Working Group (TWG) in 2013. The TWG is a multi-stakeholder committee that encourages momentum for hepatitis policy development and has successfully formulated and costed a national hepatitis plan, established key national priorities in line with the WHO goals and targets, and developed HBV and HCV policy and treatment guidelines. In early 2015, early government advocacy culminated in the partnership with the former Head of State, retired General Yakubu Gowon, as the Goodwill Ambassador for the elimination of viral hepatitis in Nigeria.[22] In 2016, collaborations with the Clinton Health Access Initiative (CHAI) and pharmaceutical organizations subsidized anti-viral therapy and commencement of access programs for hepatitis C. A pilot study of diagnostic integration with pre-existing programs involving leveraging on the GeneXpert (tuberculosis) Platform and Roche PCR (HIV/AIDS) platforms to improve HCV and HBV Viral Load access, respectively, is on-going at selected sites. Such integration may provide the strategic leverage to rapidly scale-up hepatitis control by enhancing synergy and decreasing costs. Additionally, collaboration of civil society with the World Hepatitis Alliance rapidly expanded and unified civil society with the potential of deepening public and political awareness and advocacy.

Despite this progress, much work lies ahead to achieve viral hepatitis elimination in Nigeria. A multi-faceted approach is needed to achieve large-scale implementation of the national hepatitis prevention plan. Strengthening of primary prevention with expansion of birth dose and childhood hepatitis B immunization are needed, along with improvements in injection and blood safety. Government commitment and leadership is pivotal to implementing the national hepatitis prevention plan and requires additional resources from domestic sources and international partners. The priorities for capacity building include employing a simplified funded public-health approach to screening and care, strengthening the fragmented health-care system, training health-care workers (all cadres, especially middle- and community-level), and developing public health surveillance infrastructure. Collaborations and partnerships with the private sector, international partners, non-governmental organizations, professional medical associations, the civil society, and other stakeholders are integral to scaling up hepatitis prevention and treatment in Nigeria.

[22] Nigerian Federal Ministry of Health. *FG Plans to Eliminate Viral Hepatitis by 2021*. Available at: http://health.gov.ng/index.php/78-featured/404-fg-plans-to-eliminate-viral-hepatitis-by-2021.

Georgia

The country of Georgia has one of the highest burdens of hepatitis C in the world, with an estimated 5% of the adult population, or 150,000 people, living with HCV.[23] The burden of HCV infection is greatest among men aged 30–59 years. Risks associated with HCV infection in Georgia include receipt of contaminated blood products, other exposures in health-care settings, and injection-drug use, the latter being an important driver of the current epidemic. Prevalence is high in the estimated 50,000 PWID living in Georgia.

To address this epidemic, the country of Georgia took the first steps towards HCV elimination in early 2011 by establishing the Global Fund project for HIV co-infected patients, providing HCV treatment in prisons, and offering discounts for medicines for members of the civil sector. In 2013, Georgia engaged the United States Centers for Disease Control and Prevention (CDC) to develop a national serologic survey to assess the national HCV burden and assist with the development of a national plan for addressing the country's HCV epidemic. This synergy prompted Gilead Sciences to join the collaborative response to HCV elimination in Georgia, making available HCV medications free-of-charge to Georgians identified as having HCV infection. These efforts culminated in the launch of the world's first HCV Elimination Program in April 2015.[24]

Implementation of Georgia's HCV Elimination Program has resulted in establishment of two management and screening centers, one in the capital of Tbilisi and one in the west Georgian city of Zugdidi. Although only four clinics were capable of providing care and treatment to HCV-infected persons at the start of the Program, the number of clinics has expanded to 30, increasing availability of testing and treatment services throughout the country. Key activities of the HCV Elimination Program include public awareness campaigns, provider training, blood safety, infection control, and improving implementation of screening activities with linkage to care and treatment. To date, 650,000 people have been tested as part of Georgia's HCV Elimination Program, almost 30,000 of whom have completed treatment. A total of 98% of persons completing treatment have achieved SVR, or virologic cure of HCV. Georgia's HCV Elimination Program model can provide important lessons for future initiatives to control HCV infection worldwide, particularly as testing is simplified, treatment becomes more affordable, and more countries seek to address the growing prevalence of HCV infection. The HCV Elimination Program will remain a priority activity for the government of Georgia for at least the next 5 years.

Strategies and Tools for Reaching Viral Hepatitis Elimination Goals

Access to HCV and HBV therapy begins with testing to identify infected persons, followed by referral to a skilled provider; together, these essential prevention steps are known as the HBV care cascade and the HCV cure cascade. For settings in which testing is implemented, ample evidence supports the utility of at least eight interventions in improving access to testing care and treatment for HBV and HCV.[25] These interventions include creating local testing policies appropriate for local epidemiologic circumstances; educating providers; implementing clinical decision tools that prompt testing; testing the same specimen

[23] Centers for Disease Control. The Role of Screening and Treatment in National Progress toward Hepatitis C Elimination — Georgia, 2015–2016. *MMWR* 2017;66:773–776.

[24] Kvaratskhelia V. *National-Level Elimination of Hepatitis C: The Republic of Georgia Experience.* Available at: http://www.viralhepatitisaction.org/sites/default/files/Valeri%20Kvaratskhelia_National-level%20Elimination%20of%20Hepatitis%20C%20%28Country%20of%20Georgia%29.pdf.

[25] Ward JW. Strategies for Expanding Access to HBV and HCV Testing and Care in the United States: The CDC Hepatitis Testing and Linkage to Care Initiative, 2012-2014. *Public Health Rep* 2016;131 Suppl 2:1-4.

for HCV antibody and, if positive, testing for HCV RNA; tracking performance indicators; providing financial incentives for best practices; conducting case management; and co-localizing HCV and primary care. Although additional models are needed to identify ways to optimize provision of HCV and HBV therapy, Project ECHO (a telehealth approach for bringing specialty support to front-line clinicians managing patients with HCV) has demonstrated in formal evaluations to prepare primary-care providers to care for HCV-infected patients at a level comparable to that of specialists. Project ECHO supported HCV programs are currently operating in 11 countries.

A single test to detect current HCV infection, as a replacement for the current two-test process, would greatly simplify testing to diagnose HCV infection and monitor response to therapy. As more persons are treated and achieve SVR yet continue to have HCV antibody, the first-line antibody test will be less useful, increasing the need for a front-line test for current HCV infection adaptable for use in primary-care settings.

Guided by public health surveillance, the United States has developed plans and policies to target HBV and HCV testing to those populations at risk for transmission and disease.[26] Target populations are defined by risk behaviors (e.g., injection-drug use), place of birth (i.e., migrants from HBV endemic countries), setting (e.g., corrections facilities), birth cohort (e.g., HCV testing for persons born during 1945-1965 in the United States), and even entire populations (e.g., HCV testing for all adults 18-60 years of age in the U.S. Cherokee Nation). Yet the target populations for HBV and HCV testing in the United States are unique to that country. Other countries must also collect strategic information, viral hepatitis surveillance information, and health system data to direct interventions to their own target populations, monitor implementation of interventions, and measure progress toward elimination goals.

For most countries, public health surveillance systems and other sources of strategic data are scant or nonexistent. Indeed, only 30% of countries collect HCV data rated as "moderate to good" in quality.[27] Deficits in data can be corrected by building support for serologic surveys to estimate HBV and HCV prevalence at the country level. CDC has assisted in the conduct of surveys in Georgia and plans to do so in Punjab, India and Vietnam. Other countries (i.e., China[28] and Egypt[29]) have supported national surveys. Yet survey costs, lack of expertise in survey design, and poor-quality laboratory services limit the number of countries capable of conducting these surveys. Improving availability of resources to support national serologic surveys is a priority. Costs can be reduced by integrating HBV and HCV testing into existing surveys, including USAID demographic and health surveys and HIV impact assessments (conducted by 15 countries).[30,31] Another opportunity to improve the availability of strategic data is supporting development of HBV and HCV case surveillance to identify sources of ongoing transmission. WHO recommends countries develop systems to collect clinical and programmatic data to monitor performance, particularly regarding hepatitis B vaccination coverage, HBV and HCV testing results, access to syringe

[26] World Health Organization. *Division of Viral Hepatitis (DVH) Strategic Plan, 2016–2020: Bringing Together Science and Public-Health Practice for the Elimination of Viral Hepatitis.* Available at: https://www.cdc.gov/hepatitis/pdfs/dvh-strategicplan2016-2020.pdf.

[27] Polaris Observatory HCV Collaborators. Global Prevalence and Genotype Distribution of Hepatitis C Virus Infection in 2015: A Modelling Study. *Lancet Gastroenterol Hepatol.* 2017 Mar;2(3):161-176.

[28] Yonghao G, Jin X, Jun L, et al. An Epidemiological Serosurvey of Hepatitis B Virus Shows Evidence of Declining Prevalence Due to Hepatitis B Vaccination in Central China. *Int J Infect Dis* 2015;40:75-80.

[29] Guerra J, Garenne M, Mohamed MK, Fontanet A. HCV Burden of Infection in Egypt: Results from a Nationwide Survey. *J Viral Hepat* 2012;19(8):560-7.

[30] ICAP. *Population-Based HIV Impact Assessments.* Available at: http://icap.columbia.edu/global-initatives/the-phia-project/.

[31] United States Agency for International Development. *The Demographic and Health Surveys (DHS) Program.* Available at: http://dhsprogram.com/.

services, treatment eligibility, and number of starts and completions for therapy. Data to evaluate laboratory services are particularly important, because high quality data are essential for diagnosis and surveillance. Data from vital records and cancer registries are useful for detecting trends in severe morbidity and mortality.

Goals for the elimination of HBV and HCV transmission and disease are feasible. The available interventions are highly effective: hepatitis B vaccination of infants beginning at birth, infection control in health-care settings, harm reduction among PWID, and HBV and HCV testing and treatment. Yet the effectiveness of these interventions can be improved through advances in technology. For instance, micro-needle patches and other vaccine technologies can improve delivery of hepatitis B vaccine for infants born at home. The health benefits of hepatitis B therapies can be enhanced by drug discovery that yields therapies that achieve a functional cure for HBV infection. A single test to detect current HCV infection can expand access to testing and promote receipt of curative therapies. Although these therapies can have a tremendous impact on transmission, a hepatitis C vaccine could play an important preventive role in countries with high rates of HCV transmission and among certain populations, such as PWID and other marginalized populations with limited access to HCV testing and treatment. Finally, standard tools and information technology (IT) applications can help target and evaluate interventions.

In addition to new technologies, new strategies can improve delivery of effective interventions. Countries with high prevalence for HBV infection can implement national policies and programs for hepatitis B birth-dose vaccination. To improve the care cascade, countries can develop national policies and associated programs for HBV and HCV testing. Care models are needed to simplify HBV and HCV management, a critical step in expanding access to lifesaving therapies. Data are needed to guide use of therapies to prevent HBV (e.g., maternal prophylaxis for women with high viral loads) and HCV (e.g., HCV treatment of PWID); both strategies hold great promise for meeting the goals of eliminating transmission. Finally, a cadre of experts is needed to assist conduct of local HCV and HBV serologic surveys and gather data from clinical and public health sources, both of which are critical to monitoring program performance and the progress being made toward reaching elimination goals.

Conclusions and Recommendations

Although the global HBV and HCV elimination goals are ambitious, ITFDE views the global elimination goals as the minimum progress to be achieved. Dependent on resources, disease burden, and other considerations, WHO regions and member countries can adopt more ambitious targets. HBV and HCV Elimination Programs will lead to large scale benefits in the number of new infections prevented and premature deaths averted. ITFDE has reached the following conclusions and developed recommendations to assist countries to achieve viral hepatitis elimination.

1. ***ITFDE endorses the WHO goals for the elimination of HBV and HCV as global health threats by 2030.*** The vast majority of members agreed that both conditions meet standard criteria for disease elimination. First, cost-effective interventions are available to interrupt transmission of these virologic agents, including hepatitis B vaccination, establishment of syringe-service programs, and infection-control programs. HBV and HCV testing and treatment are cost effective and for some populations, cost-saving interventions to prevent HBV and HCV related mortality. Both hepatitis viruses also meet another criterion for elimination: availability of practical diagnostic tools with sufficient sensitivity and specificity to detect infection. Further, humans are essential for the life-cycle of the agent, which has no other vertebrate reservoir and does not amplify in the environment. The success of global HBV and HCV Elimination Programs is dependent on the capacity to deliver

effective interventions, prevention research that can improve effectiveness, and data to monitor progress toward elimination goals. WHO's Global Health Sector Strategy on Viral Hepatitis focuses resources on the most affected populations, while seeking to ensure well-functioning health services for viral hepatitis prevention, sustain a supply of affordable medicines and diagnostics, train the health workforce to deliver viral hepatitis preventive services, leverage public funding for essential viral hepatitis interventions and services, and actively involve affected communities. This strategy can be a model for WHO regional offices and member countries.

2. ***ITFDE recommends development of comprehensive elimination programs tailored for the WHO region, national, or sub-national level, with appropriate attention given to innovative strategies tailored to align with local epidemiologic circumstances, health system capacities, and cultures.*** Certain aspects of hepatitis B and hepatitis C elimination distinguish these efforts from those to eliminate NTD or vaccine-preventable diseases (e.g., polio and measles), and as such require different approaches. High burdens of hepatitis B and hepatitis C are found not only in low income countries, where global health initiatives often concentrate their resources, but in middle-income countries as well as among certain communities and marginalized populations in high-income countries. Efforts to develop elimination programs benefit from advocacy, strategic data regarding disease burden, models of costs and benefits, national planning, and stakeholder engagement. ITFDE agrees with the WHO recommendation for development of comprehensive viral hepatitis prevention programs. Too often at a national level, the programs responsible for these interventions, if they exist at all, are fragmented with little coordination of effort. ITFDE views development of hepatitis B and hepatitis C elimination goals as a prime opportunity to stimulate national planning and program coordination. Comprehensive programs can coordinate the implementation of effective interventions (vaccination, safety of the blood supply, infection-control practices in health-care settings, prevention of blood exposures among persons who inject drugs [PWID], testing, and antiviral therapies). These program activities also prevent other infections, providing an opportunity for program integration and cost sharing. Program coordination will lower the costs of hepatitis prevention, as some interventions have multiple benefits (e.g., infection control) while increasing impact by making interventions more widely available.

3. ***ITFDE recommends development of model elimination programs and demonstration projects, particularly in WHO priority countries.*** Model programs implemented within defined settings (including community settings, clinics [e.g., migrant health], and facilities [e.g., corrections]) can inform program scale-up at the national and sub-national level to illustrate the proof-of-concept for viral hepatitis elimination. Such projects can a) validate the feasibility and cost-effectiveness of simple testing and treatment models at scale, b) drive policy change, c) build country testing and treatment capabilities and support implementation; d) evaluate diagnostic algorithms, and e) inform national policy. Additionally, demonstration projects should be implemented to assess the feasibility of training all health-care staff providing in-home care for infants to assist in the delivery of a timely birth dose of hepatitis B vaccine. Certain health-care workers serving rural areas routinely make home visits to care for mothers and their newborns, creating opportunities for administration of a birth dose of hepatitis B vaccine. For instance, many field staff working for Neglected Tropical Disease (NTD) programs reside and work in remote areas, where home births are most common and hepatitis B vaccination coverage low. An evaluation of how these workers can assist and improve hepatitis B vaccination of newborns represents a keen opportunity for synergy among disease-elimination initiatives.

4. ***ITFDE recommends health equity be a guiding principle for countries and organizations seeking to provide hepatitis B vaccination, hepatitis C treatment, and other effective interventions.*** HBV

and HCV elimination programs can bring immediate benefits to those at risk for these diseases. The advocacy organization proposed by ITFDE can play a key role in directing resources to programs that assure key populations have equal opportunities for elimination of hepatitis B and hepatitis C.

5. ***ITFDE recommends improving the quality of public health surveillance and other strategic information sources, particularly for low and middle income countries.*** Data are needed for at least three purposes. First, data are essential for raising governmental and public awareness, identifying priorities, and guiding elimination program planning. Data from representative serologic surveys, disease burden, other epidemiologic information, and cost-effectiveness analyses presented in a compelling manner are key in persuading decision-makers to invest in eliminating viral hepatitis. Secondly, data are needed to monitor indicators of access to recommended vaccination, testing, treatment, and other prevention interventions. These data can be used for program improvement and to call attention to resource needs. Lastly, data are needed to monitor progress toward elimination targets: reductions in HBV and HCV incidence and mortality. Data from well-designed hepatitis surveillance programs, health systems, cancer registries, and vital records can be employed to monitor progress toward elimination targets.

6. ***ITFDE recommends HBV and HCV Elimination Programs engage communities for awareness, planning, and implementation.*** A transparent planning process that openly seeks input from the community increases support for the program, builds trust in the program, and increases demand for viral hepatitis prevention services. Engagement of communities can also help secure and sustain political commitment and stakeholder involvement. Community engagement can promote identification of locally appropriate strategies to assure program accountability (e.g., steering committees with community representatives and annual reports), along with strategies for program implementation, increasing program effectiveness. Social and cultural issues affecting uptake of HBV and HCV preventive services are most effectively identified through engagement of the community. One such issue is stigma. Because the source of stigma can vary locally (from fear of an association between hepatitis B and liver cancer to an association with substance abuse for hepatitis), feedback from and action taken at the community level promotes implementation of those elimination strategies that reduce rather than reinforce stigma in a particular setting.

7. ***ITFDE recommends establishing collaborations with multiple partners to finance HBV and HCV Elimination Programs.*** It is unlikely that a single major source of funding will be tapped to support all aspects of a hepatitis elimination program. Rather, decisions regarding engaging potential financing partners will be based on an assessment of the gaps in prevention interventions, health system capacity, political commitment, and available internal and external resources. Options for financing are diverse. Global partners can be engaged in securing funding for HBV and HCV Elimination Programs. For instance, support received from the Global Alliance for Vaccines and Immunization (GAVI) for immunization of young children with multi-antigen vaccinations resulted in large increases in hepatitis B vaccination in this population. Further gains in prevention can be made with additional GAVI support for the purchase of single antigen hepatitis B vaccine, which is necessary for the vaccination of newborns. As a start, GAVI should be encouraged to align its goals with those in the Global Vaccine Action Plan and to extend support for additional hepatitis B vaccination initiatives in GAVI-eligible countries. Similarly, the World Bank should be engaged to determine novel mechanisms for funding HCV treatment among HIV-infected persons. The diversity of populations at risk among countries in different income strata requires diverse approaches to planning and financing. For example, many middle- and high-income countries have internal resources that can be directed to support viral hepatitis prevention; in this case, external resources can support epidemiologic assessments, technical reviews of health-care capacity, and local planning

to catalyze development of internally funded HBV and HCV Elimination Programs. Low-income countries have the greatest need for external resources during all phases of program planning, implementation, and evaluation. For countries of any income level, public-private partnerships should be actively pursued, as they are important in supporting testing, case management, and access to high-quality diagnostics and therapies.

Hepatitis elimination requires active participation of other health programs and initiatives – e.g., immunization programs and coalitions, maternal and newborn care groups, HIV diagnosis care and treatment, infection control and blood safety communities, etc. The hepatitis control programs in WHO, or CDC and national programs alone will find it very challenging to achieve elimination without the support of implementing partners.

8. ***ITFDE recommends innovative use of new communication and information technologies.*** For example, smart phone technology can be used to educate at risk populations, inform them of prevention options (e.g., locations of syringe service programs), and monitor the role of social media in community engagement. Data collection for key hepatitis B and hepatitis C program indicators and elimination targets should be priorities for national eHealth initiatives and improvements in information technologies for public health surveillance, vital registries, and clinical services.

9. ***ITFDE recommends a research agenda that can accelerate program development, improve effectiveness, and increase the feasibility of HBV and HCV elimination.*** Research can improve prevention technologies as well as improve delivery of effective interventions. For hepatitis B, research priorities include development of new technologies (e.g., micro-needles and auto-disposable hepatitis B syringes) and implementation strategies for providing a timely (preferably within 24 hours of birth) hepatitis B vaccine to newborns. Current hepatitis B therapies effectively suppress viral replication but require lengthy treatment regimens to reduce morbidity/mortality risks. Discovery of medications providing a functional cure for HBV infection can overcome this challenge, increasing the feasibility of HBV elimination. For hepatitis C, the research agenda seeks to develop a single test for current HCV infection. New care models can simplify the "test and treat" process for both HBV and HCV. Research also calls for a better understanding of how to access at risk populations (e.g., PWID), identify transmission early, and intervene quickly with a set of recommended interventions to limit the introduction and dissemination of HCV in a community**.**

10. ***ITFDE recommends establishment of a global coalition charged with building the capacity and advocacy needed to achieve the WHO targets for global viral hepatitis elimination.*** Potential members of the coalition include national governments, civil society and non-governmental organizations, international organizations, donor agencies, foundations, and corporations. The capacity supported by a coalition can take many forms tailored to meet local epidemiology and health system capabilities. The most immediate need is catalytic funding for epidemiological assessment, modeling, and education activities that raise awareness and build interest in HBV and HCV elimination within countries and communities. Building on that interest, the coalition can support development of elimination plans. To assist plan implementation, a coalition can increase availability of technical experts to assist with program development and evaluation. A coalition that fosters public-private partnerships can also provide much needed advocacy, playing a key role in financing and strengthening the diverse initiatives undertaken as part of an elimination program. These activities include a) strengthening the investment case for elimination; b) recognizing the significance of elimination as a pillar for sustainable development, a public health and social movement, and an issue of equity; c) linking HBV and HCV to other global health initiatives (e.g., the U.S Global Health Security agenda); d) establishing a robust strategy to communicate the opportunities and

urgency of elimination to decision makers; e) establishing a coalition or partnership to advance the elimination agenda; and f) identifying champions for elimination, particularly from countries bearing the greatest disease burden.