Hepatitis B virus (HBV) and hepatitis C virus (HCV) cause 1.3 million deaths annually. To prevent more than 7 million deaths by 2030, the World Health Organization set goals to eliminate HBV and HCV, defined as a 90% reduction in new infections and a 65% reduction in deaths, and prevent more than 7 million related deaths by 2030. Elimination of HBV and HCV is feasible because of characteristics of the viruses, reliable diagnostic tools, and available cost-effective or cost-saving interventions. Broad implementation of infant immunization against HBV, blood safety, and infection-control programs have greatly reduced the burden of HBV and HCV infections. To achieve elimination, priorities include implementation of HBV vaccine-based strategies to prevent perinatal transmission, safe injection practices and HCV treatment for persons who inject drugs, and testing and treatment for HBV- and HCV-infected persons. With sufficient capacity, HBV and HCV elimination programs can meet their goals.

**Goals**

Disease elimination and eradication are public health approaches that aim to improve health for an entire population (health equity) and engage public and private stakeholders in the response. Eradication is the permanent reduction to zero of the worldwide incidence of an infection caused by a specific agent via deliberate efforts. Elimination of infection is the reduction to zero of infection or disease caused by a specific agent in a defined geographic area via deliberate control efforts; interventions must be continued in perpetuity to prevent reemergence of infection. The term elimination also is used with specific levels of control for an infection or a disease (such as reducing incidence of tuberculosis to <1/million population).

In 1997, the WHO introduced the concept of the elimination of diseases as “public health problems.” However, what constitutes a public health problem is subjective and has multiple definitions. As such, elimination goals tailored to meet WHO’s standards vary depending on the circumstances of and resources available within the targeted population. Resolution WHA69.22 of the 2016 World Health Assembly adopted global health strategies on HIV, viral hepatitis, and sexually transmitted infections for the period 2016–2021. The WHO global strategy sets goals for the...
elimination of HBV and HCV as public health threats by 2030. The specific targets are a 90% reduction (over 2015 levels) in new chronic infections to fewer than 1 million new infections per year and 65% reduction in deaths to fewer than 500,000 deaths per year.

Despite the imprecision inherent in WHO’s goals to eliminate HBV and HCV as public health threats, elimination targets are useful and have several purposes. The goals convey a sense of urgency and increase awareness of the opportunities for improving health through HBV and HCV prevention and cure. The acceptance of numerical targets focuses program planning and promotes accountability of program operations.

The WHO encourages nations to develop HBV and HCV elimination goals appropriate for their epidemiologic circumstances and health system capacities. Several countries, including Australia, Egypt, Georgia, and Iceland, have launched national HCV elimination programs with targets selected to meet their specific needs. Countries of the WHO Western Pacific region committed to implementing vaccine-based strategies to reduce the prevalence of HBV to <1% among children. In 2017, the National Academies of Sciences recommended HBV and HCV elimination goals for the United States. The WHO’s flexibility allows for revision of goals as program experience is accrued. As progress toward elimination is achieved, more stringent targets can be defined, potentially leading to an eradication goal.

Criteria for Disease Elimination

HBV and HCV meet accepted criteria for disease elimination based on features of the infectious agents, the magnitude of the health problem, and the effectiveness of interventions to prevent transmission and disease (Table 1). Humans are essential in the life cycle of HBV and HCV. The viruses do not propagate in the environment, and intermediate hosts are not involved in the replicative cycle. HBV and HCV are blood-borne infections that can be reliably detected with widely available assays. HCV transmission is largely constrained to direct contact with contaminated blood among transfusion recipients and persons receiving non-sterile injections in health care and in the community—particularly among persons who inject drugs (PWIDs). HBV is more infectious than HCV after perinatal exposures, needle-stick injuries, and sexual contact. As a result, the reproduction number (R0) (the expected average number of new infections produced directly by an infected individual) is greater for HBV (R0 = 4.9–7.0) than for HCV (R0 = 1.2–2.9). The R0 values of HBV and HCV fall within the range for smallpox (R0 = 4.5), which has been eradicated globally, and polio (R0 = 6.0) and measles (R0 = 14.5), which can be prevented with vaccines and have been eliminated from several regions (26-28). Vaccination against HBV infection and other interventions are necessary to prevent HBV and HCV transmission and related mortality.

HBV- and HCV-related morbidities and mortalities are mostly associated with chronic infections, which cause progressive liver fibrosis that can lead to cirrhosis and hepatocellular carcinoma (HCC). The latency period from initial HBV or HCV infection to development of severe liver disease is typically several decades, providing ample time for diagnosis and initiation of antiviral therapy to prevent premature mortality. The risk of chronic HBV infection varies with age of infection: acute HBV infection becomes chronic in approximately 90% of infants infected in the first year of life (primarily through perinatal transmission), 30% of children infected during ages 1–5 years, and <5% of persons infected as older children or adults. Persons with chronic HBV infection have a 15%–25% risk of mortality from cirrhosis and HCC. It is therefore important to vaccinate newborns and children younger than 5 years of age against HBV to eliminate transmission and disease.

Of HCV-infected persons, 25%–30% clear the virus spontaneously. Persons who clear HCV infection have detectable antibodies but remain susceptible to reinfection. Of persons who develop chronic HCV infection, approximately 40% develop cirrhosis by 30 years of infection and there is a 1%–5% annual risk of HCC. The risk of cirrhosis is greatest for persons infected with HCV as adults and for persons with HIV infection, alcoholic liver disease, or other comorbidities. Chronic HCV infection can also cause extrahepatic manifestations, such as non-Hodgkin’s lymphoma.

Table 1. Criteria for Elimination of Hepatitis B Virus and Hepatitis C Virus

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global public health importance</td>
<td>257 million persons are living with chronic HBV and HCV infection; there are 1.28 million deaths from HBV (n = 884,000) and HCV (n = 399,000) infections</td>
</tr>
<tr>
<td>Biologic feasibility</td>
<td>HBV and HCV require humans for replication, have no intermediate hosts, and do not propagate in the environment; HBV and HCV infections can be detected with high sensitivity and specificity; risks of HBV and HCV are highest with parenteral blood exposure; HBV- and HCV-related diseases develop several decades after infection</td>
</tr>
<tr>
<td>Technical feasibility</td>
<td>To prevent HBV or HCV transmission, we have vaccines, tests, removal of contaminated blood products, universal precautions for infection control in health care settings; access to addiction treatment; sterile equipment for PWIDs.</td>
</tr>
<tr>
<td>Global endorsement</td>
<td>World Health Assembly; International Task Force for Disease Eradication</td>
</tr>
</tbody>
</table>
Health Benefits of Elimination

HBV and HCV are large global health problems. The achievement of elimination goals will have large public health benefits, including the prevention of more than 7 million HBV- and HCV-related deaths. \(^2,3\) In 2013, HBV and HCV were responsible for 1.28 million deaths, including 884,000 deaths from HBV and 399,000 deaths from HCV infection; more than three quarters of liver cancer deaths are caused by HBV or HCV infection.\(^2\)

In 2015, the WHO estimated that 257 million and 71 million persons worldwide were living with chronic HBV and chronic HCV infections, respectively.\(^2,3\) The prevalence of chronic HBV infection, defined as positive for the HBV surface antigen (HBsAg) is 3.5% globally and varies geographically. Countries with >6% of population positive for HBsAg are in the Western Pacific region and sub-Saharan Africa; certain indigenous populations in the Americas have high HBV prevalence. Because of infant immunization, HBV prevalence for children younger than 5 years of age is less, <1% and 3% in the Western Pacific and African regions, respectively, and 1.3% globally\(^2\) (Figure 1). The burden of HCV infection is greatest in North Africa, specifically Egypt, and in certain countries of Eastern Europe and Asia (Figure 2). Of 1.7 million new HCV infections in 2015, a total of 40% were attributed to unsafe injection in health care settings and about one third were attributable to injection drug use.\(^2\) An estimated 8.1 million (52%) of PWIDs globally have been infected with HCV.\(^3,4\)

In the United States, based on published surveys, 847,000 to 2.2 million persons are living with HBV infection and 3.5 million persons are living with chronic HCV infection.\(^3,5-7\) HBV prevalence is highest among Asian Americans (3.1%), most of whom were born in countries with high prevalence of HBV infection.\(^5,5\) Of persons living with HCV, 81% were born in the years 1945–1965; they became infected in health care settings (such as transfusions of unscreened blood) or by injection drug use before discovery of the virus in 1989 and implementation of prevention measures.\(^5,5\) In 2014, the number of deaths from HCV infection (n = 19,659) exceeded the number of deaths from the 60 other reportable infectious diseases in the United States.\(^5,5\) In 2016, a total of 1698 HBV-related death and 18,153 HCV-related deaths were reported.\(^5,5\)

Implement Effective Interventions to Prevent Transmission

Effective interventions are available to prevent HBV and HCV transmission and premature mortality.\(^4,5\) Successful implementation of these interventions has advanced progress toward HBV and HCV elimination before goals were established. Interventions to prevent HBV and HCV transmission and disease are highly cost-effective or cost-saving.\(^4,5,5\) The WHO has set indicators to monitor access to priority interventions (Figure 3).\(^2\)

The 3-dose series of the HBV vaccine is >95% effective in preventing infection and protects against chronic infection for at least 30 years.\(^2,5,4\) In 1992, the WHO recommended that all countries incorporate the hepatitis B vaccine into their national childhood immunization services.\(^5,5\) By 2015, 84% of all infants globally received the vaccine, approaching the 2020 coverage target of 90%.\(^5,5\)
For all countries, development of HBV-containing combination vaccines simplified vaccine administration for infants.56 Gavi, The Vaccine Alliance, supports Hepatitis B vaccine purchase and administration to increase infant immunization in low-income countries. By 2020, successful introduction of the vaccine in all 73 Gavi-eligible countries is projected to prevent 4.8 million HBV-related deaths.58 Compared to children born before routine hepatitis B immunization, cohorts of vaccinated children have significantly lower rates of chronic HBV infection, HCC, and related mortality in later life.24,30,59–63 For example, in China, HBV immunization has reduced proportion of HBsAg-positive individuals by 90%, to 1% among vaccinated cohorts of children. Among children born in China from 1992 through 2006, vaccination averted 16–20 million chronic HBV infections and 2.8–3.5 million future HBV-related deaths.61

Globally, the great challenge to the elimination of chronic HBV infection is vaccination of newborns. A birth dose of hepatitis B vaccine, preferably within 24 hours of birth, followed by 2 doses of infant immunizations, decreases risk of perinatal HBV transmission by 90%.56,64 Maternal testing for HBV and administration of HBV immunoglobulin to newborns of HBsAg⁺ mothers, and antiviral prophylaxis for mothers with high viral loads, essentially eliminates transmission risks.56,64,65 The integration of hepatitis B vaccination with other services provided by maternal and child programs is necessary to achieve high vaccination coverage. In 2015, only 39% of newborns received the HBV vaccine.
Vaccination coverage is highest for children born in birthing facilities with reliable supplies of hepatitis B vaccine and attendants trained to vaccinate newborns.\textsuperscript{64} Vaccination is lowest among children born at home, where these services are not available—particularly for home births in sub-Saharan African countries.\textsuperscript{24,56,64} Although considered an off-label use, hepatitis B vaccines are heat stable and can be stored for 1 month at 37°C and for 1 week at 45°C without a loss of potency.\textsuperscript{56} Storage and distribution of hepatitis B vaccine outside the typical cold chain for vaccines can improve hepatitis B vaccination coverage in rural areas. To increase birth dose coverage, Gavi is considering extending support for the purchase, typically $0.18–0.40 per dose, and administration of the hepatitis B vaccine to newborns in eligible countries. A decision is expected in June 2019.\textsuperscript{66}

In the absence of a vaccine, the prevention of blood-borne exposures is key for the elimination of HCV transmission. Successful prevention programs have greatly reduced new infections associated with two major routes of HCV transmission. Routine HCV screening of donated blood has significantly reduced transmission risk for transfusion recipients, from 7% to 14% in the 1980s to 1 in 1,900,000 donations in 2002.\textsuperscript{42,43,50} As a result of the WHO Blood Transfusion Safety Program (http://www.who.int/bloodsafety/en/) and other initiatives, 97% of all donations globally are screened for HBV and HCV, exceeding the 2020 performance targets.\textsuperscript{57,67} Adoption of recommended HBV and HCV screening by blood banks remains a priority—particularly for low-income countries.\textsuperscript{68}

Globally, improvements in infection control have resulted in an 88% decrease in the proportion of injections administered with non-sterile equipment and an 83% decrease in HCV infection attributed to unsafe injections.\textsuperscript{15,69,70} However, globally, 8% of injections continue to be given with unsterilized equipment.\textsuperscript{71} Further improvements in injection safety and HCV prevention will require education of providers to follow infection control procedures, and providers and the public to change their preferences for injected medications when equally effective oral therapies are available.\textsuperscript{69,70}

With sustained improvements in blood safety and infection control, the successful elimination of HCV transmission is contingent on the effectiveness of HCV prevention among PWIDs. For PWIDs, adequate access to opioid substitution therapy (OST) and syringe services programs (SSPs) reduces HCV transmission risk by 74%.\textsuperscript{56,57,71} Globally, these prevention services are in short supply. In 2017, of 179 countries, only 93 and 86 countries reported having SSP and OST programs, respectively.\textsuperscript{57,72} Thirty-three sets of needles/syringes were distributed per PWID annually—for below the WHO targets of 200 and 300 distributions for 2020 and 2030, respectively.\textsuperscript{72} Studies in Australia and the Netherlands have associated decreases in HCV incidence with expansion in access to SSP and OST.\textsuperscript{71} These countries’ experiences demonstrate the feasibility of implementing the strategies needed to eliminate transmission for PWID.

In the United States, access to SSPs (30 needle/syringes/PWID/y) and OST (19 treatments per PWID/y) is low, despite a 3-fold increase in HCV incidence related to increases in injection of prescription opioids and heroin.\textsuperscript{40,72,73} Increases in HCV incidence are greatest in states with no or few SSP\textsuperscript{74,75} In 2018, a total of 318 SSPs were operating in the United States and Puerto Rico;\textsuperscript{76} the Centers for Disease Control and Prevention estimates 2200 SSPs are needed to adequately serve the current number of PWID.\textsuperscript{74} States are responding to the opioid epidemic by permitting establishment of additional SSPs.\textsuperscript{7} Increases in access to OST are also needed; 89% of PWID cannot obtain treatment for their addiction despite a desire to stop using drugs.\textsuperscript{76} Access to drug treatment and clean injection equipment must be extended to prisons—these interventions are scarce for incarcerated persons, among whom an estimated prevalence of HCV infection is high. Globally, 26% of incarcerated persons have been infected with HCV.\textsuperscript{78}

Reducing the morbidities and mortality of HBV and HCV infections requires HBV and HCV testing to identify infected persons with linkages to recommended care and treatment.\textsuperscript{9,80} Long-term antiviral treatment suppresses HVB replication, lowering the risk of HCC by 50% and all-cause mortality by 40%.\textsuperscript{79,80} An 8- to 12-week regimens of all-oral antiviral medications cures >90% of HCV infections, reducing the risk of HCC and all-cause mortality by 80% and 75%, respectively.\textsuperscript{58,69,81,82} HCV cure also produces a 56% decrease in mortality from extrahepatic manifestations.\textsuperscript{71} HCV treatment outcomes for PWID are comparable to those for other HCV-infected persons, and the risk of reinfection is low (0.0–6.4/100 person-years).\textsuperscript{34} Models indicate that the addition of HCV treatment as prevention strategies to OST and SSP are more effective in stopping HCV transmission than access to OST and SSP alone.\textsuperscript{83}

Expand Testing and Treatment Access to Prevent Mortality

Although recommendations are available to guide testing, care, and treatment, HBV and HCV infections are underdiagnosed and undertreated.\textsuperscript{2,57,79–82} In 2015, only 22 million (9%) HBV-infected persons had been diagnosed and only 1.7 million (8%) of those diagnosed were receiving treatment; approximately 5%–30% of HBsAg-positive persons met the criteria for HBV treatment.\textsuperscript{57} Of the 71 million estimated persons infected with HCV globally, only 14 million (20%) have been diagnosed, and only 7% of those diagnosed have received treatment.\textsuperscript{57} To promote early diagnosis of infection, WHO recommends routine HBV and HCV testing of certain populations based on risk exposures (such as injection drug use), persons in certain settings (incarceration facilities), and populations with ≥2% or ≥5% seroprevalence of HBsAg or HCV antibody.\textsuperscript{57,80,81}

In the United States, persons are selected for HBV and HCV tests based on behavioral risks for infection (such as injection drug use), health care exposures (such as receipt of unscreened blood donations), and medical features (such as evidence of liver disease).\textsuperscript{79,84,85} HCV testing is also recommended for persons born in countries with a 2% or higher prevalence of HBsAg-positivity.\textsuperscript{55} For HCV, a
one-time test for HCV is recommended for all persons born from 1945 through 1965.\textsuperscript{84} Recent health models indicate that HCV testing of all adults in the United States is cost-effective and should be considered when national HCV testing recommendations are revised.\textsuperscript{86}

There are strategies to increase HBV and HCV testing and linkage to care. Culturally appropriate education of target populations increases awareness of the importance of HBV testing, lessens stigma, and overcomes misconceptions about the severity of infection and benefits of treatment.\textsuperscript{87–89} Community-based case managers can help migrant populations and other marginalized populations access services.\textsuperscript{87} Within health settings, professional education, electronic reminders, and standing orders prompt HBV and HCV testing.\textsuperscript{88,89} In the laboratory, reflex RNA testing of specimens positive for HCV antibody improves detection of individuals with HCV infection.\textsuperscript{86} Point-of-care testing can expand access to HBV and HCV testing for marginalized populations.\textsuperscript{90} With availability of safe, all-oral therapies, HCV testing and treatment can now be co-located in primary care settings with appropriate training of clinicians, including pharmacists and other mid-level providers. Gastroenterologists, hepatologists, and other specialists continue to have essential roles providing consultative services to other providers and managing HCV-infected persons with advanced disease and other complications.

The costs of HCV medications, a major barrier to treatment in the United States, have decreased from an initial price range in 2014 of $84,000–$96,000 per treatment course to about $25,000.\textsuperscript{91,92} HCV therapeutic regimens costing <$60,000 per curative course are cost-saving.\textsuperscript{81} With reductions in drug costs, states are easing policies that limited HCV treatment to patients with advanced liver disease, those receiving specialty care, and patients with sobriety from alcohol and other drugs. Although at least 18 state Medicaid programs have removed all restrictions to treatment,\textsuperscript{12} states continue to deny HCV treatment until patients develop severe liver fibrosis.\textsuperscript{93} Persons with cirrhosis when cured of HCV infection have a 1.5% annual risk of HCC, requiring continued clinical surveillance for signs of liver cancer.\textsuperscript{95} Early treatment of HCV infection, before development of severe liver disease, is in the best interest of patients and global elimination of HCV-related mortality.

More than 100 countries can now access generic medicines for $200 or less per curative treatment; at these expenditures, HCV treatment is cost-saving.\textsuperscript{57,94,95} Of HCV-infected persons, 62% live in countries where generic HCV medications are available.\textsuperscript{57} However, in 2016, only 10 countries (Australia, Egypt, France, Germany, Iceland, Japan, the Netherlands, Qatar, Spain, and the United States) had treated $\geq 7\%$ of their HCV-infected population; 44 countries had treated $< 1\%$. As a result, in 2017, the global population of HCV-infected persons decreased by only 300,000 (0.4%) persons, to an estimated 69.55 million.\textsuperscript{96}

In the United States during 2013–2016, at least 673,000 persons received HCV treatment contributing to a decrease in national prevalence of current HCV infection from 3.5 million to 2.4 million.\textsuperscript{90} The number treated is reflected in a decrease in the proportion of anti-HCV+persons positive for HCV RNA, indicative of current infection, falling to 57% in 2013–2016 compared to 72% in earlier years. This proportion of infected persons receiving treatment contributed to the 7% decrease in HCV-related mortality.\textsuperscript{90} The proportion of HCV-infected persons reporting treatment, declines in HCV prevalence, and trends in HCV-related deaths, indicate the feasibility of the United States reaching elimination goals for HCV-related mortality. To do so, HCV testing and linkage to care must be implemented on a large scale and sustained over time to find and treat 250,000 HCV-infected persons annually.\textsuperscript{20,32}

### Develop, Implement, and Evaluate Elimination Programs

The experience gained from previous disease eradication and elimination initiatives reveals the essential components of effective programs\textsuperscript{7–13,160} (see list of essential components of HCV elimination programs). Strategic data are needed to assess the burden of HBV and HCV disease and health-system capacities, as well as to monitor progress toward elimination goals. However, in 2016, only half of countries with national prevention plans had the data needed to estimate HCV prevalence.\textsuperscript{22} A plan of action establishes time-limited numerical targets, prioritizes activities, and helps engage partners in specific roles. However, in 2017, only 82 of 132 countries had action plans in place for viral hepatitis prevention, and few include elimination targets and strategies.\textsuperscript{57}

The following are essential components of HCV elimination programs:

- Data are used to assess HCV disease burden and health system capacity
- Plan of action with time-limited numerical targets
- Civic and political support for implementing partners and target populations
- Capacity to deliver appropriate interventions to target populations
- Sustainable models for financing programs
- Integration of services in existing health systems
- Strategic data to monitor program performance and progress toward elimination goals
- Participation in operational research

Support of civil society is as important as technical proficiency for HBV and HCV elimination. Civic organizations can increase acceptance of community-based interventions (such as SSPs), stimulate health systems to improve delivery of clinical care services for HBV and HCV infection, and build political support for financing programs until elimination goals are achieved.\textsuperscript{7–13} International philanthropic organizations provide funds to help countries plan and implement elimination programs.\textsuperscript{101,102}

The services needed to eliminate HBV and HCV must be available to all persons at risk for infection and disease.
Strategic information and local plans guide distribution of resources to support delivery of services in community and clinical settings. HBV and HCV prevention services can be integrated with HIV and cancer prevention, reproductive health, drug treatment, and other appropriate programs. Sustainable and innovative models for financing are needed for programs to have sufficient capacity to achieve elimination targets. Approaches are needed to incorporate hepatitis prevention, care, and treatment services within existing health systems with no undue costs for target populations. Integration of viral hepatitis–related services into existing programs and public–private partnerships facilitates cost sharing. Development of investment cases inform implementation of care models, and negotiations for purchase of diagnostics and therapies at costs appropriate for health systems.

HBV and HCV elimination programs are in various stages of planning and implementation at the national, subnational, facility-, and risk-population levels. Some programs were started before the global elimination goals were established and serve as field studies that demonstrate how these essential components can be applied to HBV and HCV elimination.

### Countries of the World Health Organization Western Pacific Region

In 2005, the 35 countries of the WHO Western Pacific Region committed to implementing HBV vaccine-based strategies and reducing HBsAg seroprevalence from ≥8% to <2% in 5-year-old children by 2012. To reach these goals, the Western Pacific Region countries monitored data from vaccine registries to assure that vaccination coverage among infants was sustained. To prevent perinatal HBV transmission, countries integrated birth-dose vaccination into routine obstetrical services provided by birthing facilities. To meet the large unmet vaccination needs for home births, China and other countries built additional facilities to increase the number of mothers delivering in facilities, as well community-based interventions to vaccinate infants born at home. To verify achievement of the regional targets, countries conducted national serologic surveys of target populations. In 2016, a total of 24 countries and the region overall had reduced HBsAg prevalence to <1%. Current activities involved assisting other countries in the region to achieve this goal and developing regional plans to achieve further reductions in HBV prevalence.

### Georgia

In April 2015, with the assistance of the US Centers for Disease Control and Prevention, the country of Georgia conducted a national HCV serologic survey, which found the prevalence of HCV infection to be 5.4% among the adults; PWID and previous recipients of blood transfusions had the highest rates of HCV infection. The government proposed a program to reach a goal of HCV elimination, defined as a 90% reduction in HCV prevalence by 2020. A national elimination plan was developed to guide and evaluate program implementation. Through a public–private partnership, Gilead Sciences agreed to donate medications to treat HCV-infected persons. From April 2015 through December 2016, of 30,046 persons tested and found to be infected with HCV, 27,595 (92%) began treatment; 98% of persons who received all-oral therapies were cured of HCV infection. Co-localization of HCV testing and treatment in primary care is underway to sustain the level of HCV testing and treatment needed to achieve the national elimination goal. To prevent HCV transmission, program activities include improvements in blood banking and injection safety in the community and health care settings.

### Egypt

More than 6 million persons in Egypt are living with HCV infection, largely resulting from the poor injection control associated with a national, community-based campaign against schistosomiasis conducted from 1950 through 1980. In 2006, the Egyptian government set goals for a reduction in HCV prevalence to <2% within 10 years and approaching disease elimination (prevalence <1%) by 2030. From 2006 through 2017, a total of 60 HCV treatment centers were established, a national patient registry was developed, and testing and treatment services were made available at low cost to patients. In 2011, a comprehensive national plan of action was developed to include all aspects of HCV prevention. Approximately 1 million patients have received HCV treatment with 1 antiviral medication produced in country. To meet the 2030 goal, approximately 350,000 persons will need to be diagnosed and treated annually. A major challenge to program sustainability is the scale-up of HCV testing for broader segments of the population.

### Iceland

Based on data from national surveillance registries, an estimated 880–1300 persons (0.3% prevalence) were living with HCV in Iceland, most of whom had a history of injection drug use. In 2015, a coalition of stakeholders developed an elimination plan with a goal for an 80% reduction in HCV incidence by 2025. PWID have access to syringe services and receive 430 sets of sterile injection equipment per year. Program strategies include active recruitment of previously diagnosed persons for HCV treatment, expanded HCV testing in homeless shelters and other outreach settings, and expansion of preventive services for PWID. The national government provided financial support for the HCV elimination campaign augmented by a public–private partnership with Gilead Sciences to obtain donations of HCV medications. In the first 15 months of the program, 557 persons with HCV were identified, and 526 started treatment, comprising 40%–60% of the HCV-infected population. If this number of persons treated per year can be sustained, the program is on track to eliminate HCV.

### Australia

Since 2000, Australia has developed HCV prevention plans in collaboration with public health authorities, clinicians, and civil society. Australia has long-standing
political support for SSPs and HCV testing for PWID. The national government, in collaboration with civil society, committed a budget of AUS$1 billion to purchase HCV medications in 2016–2020 and negotiated with industry for an acceptable purchase price for antiviral medications. The government capped the amount of funds going to purchase treatments each year to ensure that as more persons are treated, the cost per patient treated decreases. This financing plan creates incentives for testing and linking infected persons to care. In 2016–2017, an estimated 69,000 persons (26% of the total infected population) were treated for HCV infection; out-of-pocket costs per patient were AUS $3–$7. Despite this progress, the number of persons treated is decreasing, as the persons diagnosed in previous years are treated and cured. In addition to a sound financing plan, Australia will need to develop explicit national elimination goals and coupled with continued outreach to target populations with appropriate and effective strategies for HCV testing and linkage to care.

Cherokee Nation of Eastern Oklahoma

In the United States, rates of HCV incidence and mortality are highest for American Indians and Alaskan Natives. The Cherokee Nation is a large American Indian tribe that operates its own health system. In October 2015, the tribal leadership launched the Path Toward Elimination of HCV program, with the goal of screening 80,000 patients and treating 85% of HCV-infected patients during a 3-year period. Principal Chief Bill John Baker expressed the civic hope “to eliminate this disease entirely within the Cherokee population.” The Cherokee nation health system implemented routine testing and trained primary care providers, including pharmacists, to test and treat patients for HCV. The tribal health system manages the costs of HCV testing, care, and treatment; a case registry was created for patient referrals and to monitor trends in service delivery. Through October 2017, the Cherokee Nation screened 23,000 patients. Of 760 persons with HCV infection, 605 have started treatment. The Cherokee Nation expanded routine HCV testing in dental and other clinics within the health system and are developing prevention services for PWID in the community.

Research to Hasten Progress Toward Elimination Goals

Operational and technical research is an essential component of disease elimination programs. Demonstration projects and program evaluations provide data that are used to improve delivery of preventive and clinical care services. Technical studies can develop new vaccines, diagnostics, and therapies. The need for operational and technical research is ongoing—successful implementation of a disease elimination program will reveal needs for difficult-to-reach populations and unrecognized shortcomings of interventions. For examples of research priorities, see Table 2.

Strategic Information

National HBV and HCV seroprevalence surveys are the preferred method to estimate prevalence. However, these can be cost-prohibitive for low- and middle-income countries. Researchers can identify the best strategies for integrating HBV and HCV testing in surveys for HIV or other diseases, and for the use of administrative data and/or surveys of at-risk and hard-to-reach subpopulations. Practical methods are needed for registries to receive surveillance reports of HBV and HCV infections and to serve as resources for referring infected persons to preventive care and treatment services, and for monitoring temporal trends in access to services. Health models based on surveillance data can estimate the number needed to vaccinate or treat, to reach elimination goals, and to guide development of financing strategies for HBV and HCV prevention, testing, and treatment.

Models of Testing, Care, and Treatment

Studies can identify effective strategies for expanding HBV and HCV testing and linkage to care into new settings. An array of proven strategies will facilitate integration of HBV birth-dose vaccination into maternal and child health

### Table 2. Research Agenda for Hepatitis B Virus and Hepatitis C Virus Elimination

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Strategic information</td>
<td>Serologic surveys and use of administrative data to estimate disease burden</td>
</tr>
<tr>
<td></td>
<td>Registries to monitor HBV vaccination and HBV and HCV tests, care, and treatment</td>
</tr>
<tr>
<td></td>
<td>Public health surveillance methods to monitor incidence, prevalence, and mortality</td>
</tr>
<tr>
<td></td>
<td>Health models of cost-effectiveness of interventions</td>
</tr>
<tr>
<td>Models of care</td>
<td>Tools to facilitate HBV and HCV testing, linkage to care and treatment</td>
</tr>
<tr>
<td></td>
<td>HBV and HCV simplified test, care, and treatment procedures for integration in primary care settings</td>
</tr>
<tr>
<td></td>
<td>HCV cure as prevention strategies for PWIDs</td>
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<tr>
<td></td>
<td>Maternal antiviral prophylaxis to prevent perinatal HBV transmission</td>
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<tr>
<td>Technologies</td>
<td>Delivery systems to increase timely HBV vaccination of home births</td>
</tr>
<tr>
<td></td>
<td>A single test to detect current HCV infection</td>
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<tr>
<td></td>
<td>Point-of-care tests to diagnose HBV and HCV infection and monitor response to therapy</td>
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<tr>
<td></td>
<td>Analyses of data to detect networks of transmission and emergence of antiviral resistance</td>
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<tr>
<td></td>
<td>HBV therapies effective in producing a functional cure of infection</td>
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<td></td>
<td>HCV vaccine</td>
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</table>


New Technologies for Testing, Treatment, and Vaccination

Precise, affordable, virus detection assays simplify the testing process and can expand the settings where testing is available for screening and monitoring. Point-of-care tests can expand outreach and access in resource-constrained settings. HCV core antigen tests reliably document viremia and can be a cost-saving alternative to polymerase chain reaction–based tests.

Next-generation sequencing can detect the relatedness of HCV quasi-species among patient populations and identify cases with similar genetic sequences, indicative of shared patterns of transmission. Studies are needed to determine how this new technology can be deployed to guide HCV treatment as prevention strategies for PWIDs.

HBV treatments reduce virus replication and mortality. However, patients often require long-term therapy. To improve treatment adherence and outcomes, new models of care tailored for low and middle income countries are needed. Treatment outcomes can also be improved with new therapeutic options that can produce a functional cure of HBV infection, defined as the loss of HBsAg and the absence of virus replication. Compounds that target different phases of the replicative cycle of HBV are in development.

Studies are needed to assess safety and efficacy of treating HCV infection in pregnant women, to interrupt perinatal transmission. Studies can assess outcomes of shorter HCV treatment regimens and other strategies. As more people are treated for HCV infection, elimination programs should remain vigilant for the emergence of virus strains resistant to therapeutic agents—particularly in populations at risks for reinfection. Strategies to guide vaccine storage and distribution outside of the cold chain can improve birth-dose coverage. New delivery systems for the hepatitis B vaccine could be particularly helpful in assuring timely immunization of infants born at home.

A safe and effective vaccine could help prevent new HCV infections and be particularly important in eliminating transmission among PWID. Health models indicate an HCV vaccine, even of low efficacy, is a cost-effective approach for preventing HCV among PWID. One trial is underway to assess safety and effectiveness of a candidate vaccine. In this study, a chimpanzee adenoviral vector (prime) and modified vaccinia virus Ankara (boost) vector were given to persons to induce HCV-specific T-cell responses (NCT01436357; https://clinicaltrials.gov). Results from this study are expected in 2019. Research from public and private sectors is needed to support studies of this and perhaps other vaccine candidates.

Build a Coalition to Assist Elimination Programs

Global public health campaigns are typically by coalitions of implementing programs, funding organizations, technical experts, international health organizations (such as WHO), and other stakeholders. Examples include the Differentiated Care for HIV support center http://www.differentiatedservicedelivery.org/home, Global Polio Eradication Initiative (http://polioeradication.org/) and The Task Force for Global Health Neglected Tropical Diseases Support Center (http://www.ntdsupport.org/) and International Trachoma Initiative (http://www.trachoma.org/). The coalitions operate as technical hubs providing a forum for programs to share information about local plans, strategies, and progress they also receive technical assistance and have research opportunities that can improve program performance. A technical hub can improve collaborations and coordination among HBV and HCV elimination programs. Currently, most viral hepatitis elimination programs, work in relative isolation. Information about programs, when publicly available, are often presented or published in multiple locations over time, complicating and delaying access to others to benefit from this experience.

HBV and HCV elimination programs have limited access to technical experts or research opportunities that can help overcome barriers to implementation. In their endorsement for HBV and HCV elimination, the ITFDE recommended development of a global coalition that would build the capacity and advocacy needed to eliminate viral hepatitis worldwide. Guided by the ITFDE recommendation and the experience of other elimination programs, a global coalition for viral hepatitis elimination will bring programs together to share knowledge and experience, provide technical assistance to overcome barriers, generate new knowledge through research, and advocate for the resources to eliminate viral hepatitis.

Future Directions

Elimination of HBV and HCV infections by 2030 will produce substantial benefits for public health and prevent more than 7 million deaths. Much of what is needed to reach these goals is already in place. The WHO’s goals of elimination have been established and endorsed by World Health Assembly and ITFDE. HBV and HCV infections are recognized as feasible targets for elimination. HBV vaccination of infants, blood safety programs, and universal precautions in health care settings have already produced large-scale reductions in HBV and HCV incidence, morbidity, and mortality. We must now make full use of hepatitis B vaccine base strategies for newborns including HBsAg testing for pregnant women, treat individuals with drug addiction, provide safe injection equipment and treatment of
HCV infection for PWID, and provide HBV and HCV testing with linkages to treatment. Model programs demonstrate how the essential components of disease elimination initiatives—collecting strategic information, planning of programs with involvement of all stakeholders, engaging civil society, arranging financial support, and implementing appropriate strategies for target populations—can be brought together to achieve HBV and HCV elimination. These experiences can guide development and implementation of other programs at the national and sub-national level. A global coalition can help implementing programs share their knowledge and experience and receive technical assistance and research opportunities to improve program performance. With sufficient capacity, national HBV and HCV elimination programs will successfully meet and ultimately exceed goals for global elimination of HBV and HCV as public health threats.

References


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Conflicts of interest
The authors disclose no conflicts.