

INTERIM GUIDANCE FOR COUNTRY VALIDATION OF VIRAL HEPATITIS ELIMINATION

JUNE 2021

TECHNICAL REPORT

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ACRONYMS AND ABBREVIATIONS

ALT	alanine aminotransferase	MCH	maternal and child health
ANC	antenatal care	MSM	men who have sex with men
APRI	aspartate aminotransferase-to-platelet ratio index	MTCT	mother-to-child transmission
ART	antiretroviral treatment	NAT	nucleic acid test
CDAF	Center for Disease Analysis Foundation	NSP	needle–syringe programme
CHB	chronic hepatitis B	NTD	neglected tropical disease
DAA	direct-acting antiviral (drug)	NVS	National Validation Secretariat
DBS	dried blood spot	NVTF	National Validation Task Force
EMTCT	elimination of mother-to-child transmission (of hepatitis B)	OST	opioid substitution therapy
EPI	Expanded Programme on Immunization	PMTCT	prevention of mother-to-child transmission
EQA	external quality assessment	PVST	post-vaccination serological testing
GHSS	Global Health Sector Strategy (on viral hepatitis)	PWID	people who inject drugs
GVAC	Global Validation Advisory Committee	RDT	rapid diagnostic test
GVS	Global Validation Secretariat	RVC	Regional Validation Committee
HBeAg	hepatitis B e antigen	RVS	Regional Validation Secretariat
HBIG	hepatitis B immunoglobulin	RVTF	Regional Validation Task Force
HBsAg	hepatitis B surface antigen	SDGs	Sustainable Development Goals
HBV	hepatitis B virus	SRA	stringent regulation authority
HCC	hepatocellular carcinoma	STI	sexually transmitted disease
HCV	hepatitis C virus	SVR	sustained virological response
HCVAb	HCV antibody	UHC	universal health coverage
HCVcAg	hepatitis C virus core antigen	UN	United Nations
HepB-BD	hepatitis B birth dose	UNAIDS	Joint United Nations Programme on HIV/AIDS
HepB3	three doses of hepatitis B vaccine	UNICEF	United Nations Children's Fund
IHME	Institute for Health Metrics and Evaluation	UNODC	United Nations Office on Drugs and Crime
LMICs	low- and middle-income countries	WHO	World Health Organization
		WUENIC	WHO and UNICEF Estimates of National Immunization Coverage

GLOSSARY

Chronic hepatitis B virus (HBV) infection	Persistence of hepatitis B surface antigen (HBsAg) for at least six months. The persistence of HBsAg in two specimens six months apart is frequently used in clinical practice to confirm chronic hepatitis B infection.
Chronic hepatitis C virus (HCV) infection	The presence of viraemia (HCV RNA or HCV core antigen [HCVcAg]) in association with positive serology for HCV antibody
Cirrhosis	An advanced stage of liver disease characterized by extensive liver scarring secondary to prolonged inflammation of the liver (F4 in the METAVIR scoring system)
Compensated cirrhosis	Cirrhosis without signs or symptoms of decompensation
Decompensated cirrhosis	Cirrhosis with signs or symptoms of decompensation. The main clinical features are portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy), coagulopathy, and liver insufficiency (jaundice).
Elimination as a public health problem	Reduction of disease incidence, prevalence, morbidity or mortality to below a level at which the public health burden is considered negligible as a result of deliberate efforts. The target level is generally defined globally by WHO. When reached, continued action is required to maintain the reduction. Documentation of independent confirmation of elimination as a public health problem/threat is called “validation”. Elimination as a public health threat is considered equivalent to elimination as a public health problem.
Hepatocellular carcinoma (HCC)	Primary cancer of the liver arising from the hepatocytes and may be a complication of chronic hepatitis B or C infection

Hepatitis B surface antigen (HBsAg)	HBV envelope protein often produced in excess and detectable in the blood in acute and chronic HBV infection
Hepatitis B e antigen (HBeAg)	Viral protein found in the high replicative phase of HBV. HBeAg is usually a marker of high levels of replication with wild-type virus but is not essential for viral replication
HBV DNA	HBV viral genomes that can be detected and quantified in serum by nucleic acid testing (NAT)
HCV antibody	Antibody to HCV, which can be detected in the blood usually within two to three months of HCV infection or exposure
HCV core antigen (HCVcAg)	Nucleocapsid peptide 22 of HCV, which is released into the plasma during viral assembly and can be detected from early on and throughout the course of infection
HCV RNA	HCV viral genomes that can be detected and quantified in serum by nucleic acid testing (NAT)
Rapid diagnostic test (RDT)	Immunoassays that detect antibodies or antigens and can give a result in less than 30 minutes. Most RDTs can be performed with capillary whole blood collected by finger-stick sampling, but now also by oral fluid sampling.
Enzyme immunoassay (EIA)	Laboratory-based serological immunoassays that detect antibodies, antigens or a combination of both
Nucleic acid testing (NAT)	A molecular technology, for example, polymerase chain reaction (PCR) or nucleic acid sequence-based amplification (NASBA) that can detect very small quantities of viral nucleic acid (RNA or DNA), either qualitatively or quantitatively
Spontaneous viral clearance	Clearance of HCV infection without treatment
HCV sustained virological response (SVR)	Undetectable HCV RNA in the blood 12 weeks after treatment completion. SVR 12 is considered equivalent to a cure for HCV infection.

EXECUTIVE SUMMARY

In 2016, the World Health Assembly adopted the Global Health Sector Strategy (GHSS) on viral hepatitis. The GHSS called for elimination of viral hepatitis B and C infection as a public health problem (defined as a 90% reduction in incidence [95% for HBV and 80% for HCV] and 65% reduction in mortality by 2030, compared with the 2015 baseline). This target is aligned with similar strategies and elimination plans for HIV and sexually transmitted infections (STIs) to be achieved by 2030. The target is also linked to public health disease elimination targets of the health-related Sustainable Development Goals (SDGs). A broad range of countries have now developed national hepatitis elimination strategies and plans, guided by the GHSS, and have set national targets for elimination of hepatitis. Several countries have now also requested guidance from the World Health Organization (WHO) on the establishment of global criteria for measuring elimination of viral hepatitis and a standardized process for validation of elimination. A new GHSS strategy on viral hepatitis is planned for 2022.

Global commitments have been made for the elimination or eradication of over 30 diseases. WHO has developed global strategies, targets and normative guidance to support elimination efforts across most of these disease areas through a standardized approach to the assessment of country and regional progress and validation of achievement of the elimination targets. The WHO Global Framework for Multi-disease Elimination is now being developed to unify global disease elimination efforts, promote cross-programmatic synergies and efficiencies, and standardize, where possible, definitions of disease elimination, criteria and validation processes. At a regional level, the Pan American Health Organization has also developed an Integrated Framework for the Elimination of Communicable Diseases in the Americas.

In line with the GHSS, WHO has developed this interim guidance and framework for countries and other stakeholders seeking validation of elimination of viral hepatitis as a public health problem, with a specific focus on the hepatitis B virus (HBV) and the hepatitis C virus (HCV). This document provides a global framework for the processes and standards for validation of elimination. Section 1 provides the background to the key WHO guidelines and recommended interventions. Section 2 includes a summary of the key recommended interventions with impact and programmatic targets as well as options for approaches to measuring progress towards these targets for the three main areas for validation of elimination: elimination of mother-to-child transmission (EMTCT) of HBV as well as the path to elimination (Chapter 3), reduction in HCV incidence (Chapter 4), reduction in HBV and HCV mortality (Chapter 5). Chapter 6 summarizes other considerations in assessing a country's progress towards validation of elimination. These include an assessment of the quality of strategic information, laboratory processes, diagnostics and medicines, and health-care programmes, as well as adherence to the principles of equity, human rights and community engagement during the process of validation. In Section 3, Chapter 7 summarizes the governance process for WHO validation of EMTCT of HBV or elimination of viral hepatitis B and/or C as a public health problem.

This interim guidance has the following aims: (i) to place hepatitis elimination efforts within a public health perspective; (ii) to help build national capacity; (iii) to address different country contexts, including differences due to various baseline levels of endemicity and/or profiles of the viral epidemics; (iv) to implement control and elimination programmes efficiently; and (v) to motivate countries to take rapid and appropriate action toward viral hepatitis elimination. This document also emphasizes that all countries should work towards a common goal of viral hepatitis elimination by 2030, regardless of the present burden of hepatitis-related diseases, intensity of transmission, heterogeneity in the epidemiology of hepatitis B and C, and differences in national responses and resources.

The guidance was developed through two consultation meetings with more than 50 external experts, including Ministry of Health representatives from 15 countries: a Part 1 meeting focused on assessing HBV EMTCT in June 2020, and a Part 2 meeting on assessing reduction in HCV incidence, HBV and HCV mortality, and governance in November 2020.

Overall, the guidance suggests the use of absolute impact targets to validate elimination at the national level (instead of, although equivalent to, the relative reduction targets originally defined in the 2016 GHSS) in combination with a set of programmatic targets (Table 1). The main impact indicators and targets for measuring elimination are defined as follows:

- **$\leq 0.1\%$ HBsAg prevalence in those aged 5 years or less***
- **An absolute annual HCV incidence of ≤ 5 per 100 000 persons and of ≤ 2 per 100 people who inject drugs (PWID)**
- **An HBV- and HCV-related annual mortality rate of ≤ 4 and ≤ 2 per 100 000 persons, respectively (combined HBV/HCV ≤ 6 per 100 000 persons).**

This process relies on the availability of high-quality national programmes and a comprehensive system for surveillance, with systematic documentation of reaching the proposed impact and programme targets and maintaining the programme targets for a total of at least 2 years.

Countries are encouraged to pursue elimination of both viral hepatitis B and C together as a public health problem, but may also choose to apply for one of the four certification options (A–D) in a phased approach to be officially recognized by WHO for EMTCT of HBV, or elimination of HBV and/or HCV as a public health problem (see Table 2). A path to elimination that represents the milestones of progress towards EMTCT of HBV is also proposed. This is intended to recognize – mostly at a regional level – clear progression and significant national effort towards implementing key interventions for HBV EMTCT in high-burden countries that may not yet be in a position to achieve the impact targets for elimination.

* For those regions and countries with a long history of high hepatitis B (HepB) vaccination coverage (e.g. Region of the Americas and some parts of the European Region), and that already conduct school-based serosurveys, there could be flexibility in conducting serosurveys in older children >5 years.

TABLE 1 Summary of impact and programmatic targets for country validation of elimination for HBV EMTCT, HCV incidence and HBV/HCV mortality

Elimination targets	Elimination of chronic HBV infection as a public health problem		Elimination of chronic HCV infection as a public health problem	
2030 GHSS relative reduction reference targets (compared to 2015)	Incidence 95% reduction	Mortality 65% reduction	Incidence 80% reduction	Mortality 65% reduction
HBV- and HCV-specific absolute prevalence, incidence and mortality targets	HBV EMTCT ≤0.1% HBsAg prevalence in ≤5 year olds ^{a,b} <i>Additional target:</i> ≤2% MTCT rate (where use of targeted HepB-BD) ^c	Annual mortality^g (HBV) ≤4/100 000	Annual incidence (HCV) ≤5/100 000 ≤2/100 (PWID)	Annual mortality^g (HCV) ≤2/100 000
Programmatic targets^d	Countries with universal HBV vaccine birth dose (BD) ≥90% HepB3 vaccine coverage ≥90% HepB timely hepatitis B BD (HepB-BD) coverage ^e Countries with targeted HBV vaccine birth dose (BD) ≥90% HepB3 vaccine coverage ≥90% coverage of those infants at risk with targeted HepB-BD ≥90% coverage of maternal antenatal HBsAg testing ≥90% coverage with antivirals for those eligible ^f	Testing and treatment ≥90% of people with HBV diagnosed ≥80% of people diagnosed with HBV and eligible for treatment are treated ^h Prevention ≥90% HepB3 vaccine coverage ≥90% HepB-BD coverage	Testing and treatment ≥90% of people with HCV diagnosed ≥80% of people diagnosed with HCV are treated ^g Prevention 0% unsafe injections 100% blood safety 300 needles/syringes/PWID/year	

EMTCT: elimination of mother-to-child transmission; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HepB-BD: hepatitis B birth dose vaccine; HepB3: three doses of hepatitis B vaccine; PWID: people who inject drugs

a Childhood prevalence is a proxy for HBV incidence.

b The ≤0.1% HBsAg prevalence can be measured among either 5 year olds, 1 year olds or those aged 1–5 years, according to existing country surveillance and data collection activities. For those regions and countries with a long history of high Hep B vaccination coverage (e.g. WHO Region of the Americas), and that already conduct school-based serosurveys, there could be flexibility to conduct serosurveys in older children >5 years.

c The ≤2% MTCT rate is an *additional* impact target to the ≤0.1% HBsAg prevalence among ≤5-year-old children in countries that provide targeted HepB-BD.

d All programmatic targets must be achieved and maintained for at least 2 years.

e Timely birth dose (HepB-BD) is defined as within 24 hours of birth.

f In accordance with national policies or WHO 2020 guidelines on use of antiviral prophylaxis on PMTCT of HBV.

g The GHSS defines the reduction of combined mortality for both HBV and HCV to ≤6/100 000/year at a global level. The use of HBV- and HCV-specific mortality target rates will depend on the national epidemiology of viral hepatitis and the relative contributions of HBV and HCV to overall mortality.

h Short-term curative treatment for HCV infection (SVR12), and generally lifelong antiviral therapy for HBV to maintain long-term HBV DNA viral suppression, in accordance with standard guidelines.

A series of country pilots of these elimination criteria across the WHO regions will be undertaken during 2021 to evaluate the feasibility of different approaches to measuring the proposed impact and programmatic targets for elimination and to inform a revised 2022 guidance. Key questions that remain to be addressed during the pilot phase include the following: the need for a path to elimination track for HCV incidence and HBV/HCV mortality in addition to HBV EMTCT; the feasibility of MTCT rate as an additional criterion for validation of EMTCT in settings with use of targeted hepatitis B vaccine birth dose (HepB-BD); the need for additional modelling to support proposed levels of programmatic coverage of HBsAg testing and antiviral prophylaxis in pregnant women; the acceptable age ranges for conduct of HBsAg serosurveys for validation of HBV EMTCT; the feasibility of using combined versus HBV/HCV-specific mortality rates; and the use of reduction in HCV viraemic prevalence as a proxy for direct measurement of reduction in incidence and mortality. This document should be considered provisional until after the pilots are completed.

TABLE 2 Options for validation of elimination of viral hepatitis B and C as a public health problem

Option	Options for validation of elimination	Impact indicators	Programme indicators
Option A	HBV EMTCT (as part of triple elimination of HIV, syphilis and HBV, or HIV/HBV) ^a	Annual HBV incidence ^b and MTCT rate ^c (additional target) in countries with targeted timely HepB-birth dose (BD)	HBV birth dose and infant vaccination coverage for newborns and infants HBV antenatal testing and antiviral prophylaxis coverage
Option B	HCV as a public health problem	Annual HCV incidence and HCV mortality	Coverage of prevention, testing and treatment
Option C	HBV as a public health problem (including HBV EMTCT)	Annual HBV incidence (and MTCT rate) and HBV mortality	Coverage of prevention, testing and treatment
Option D	Elimination of both HBV and HCV as a public health problem (including HBV EMTCT)	A, B and C above	A, B and C above

EMTCT: elimination of mother-to-child transmission; Hep B: hepatitis B; MTCT: mother-to-child transmission

a Countries can choose EMTCT of HIV, or HIV and syphilis, or HIV and syphilis and hepatitis B.

b The prevalence of hepatitis B surface antigen (HBsAg) in children aged ≤5 years is used as a surrogate indicator of the cumulative incidence of chronic hepatitis B.

c The ≤2% MTCT rate is an *additional* impact target to ≤0.1% HBsAg prevalence among ≤5-year-old children in countries that provide targeted timely HepB-BD.

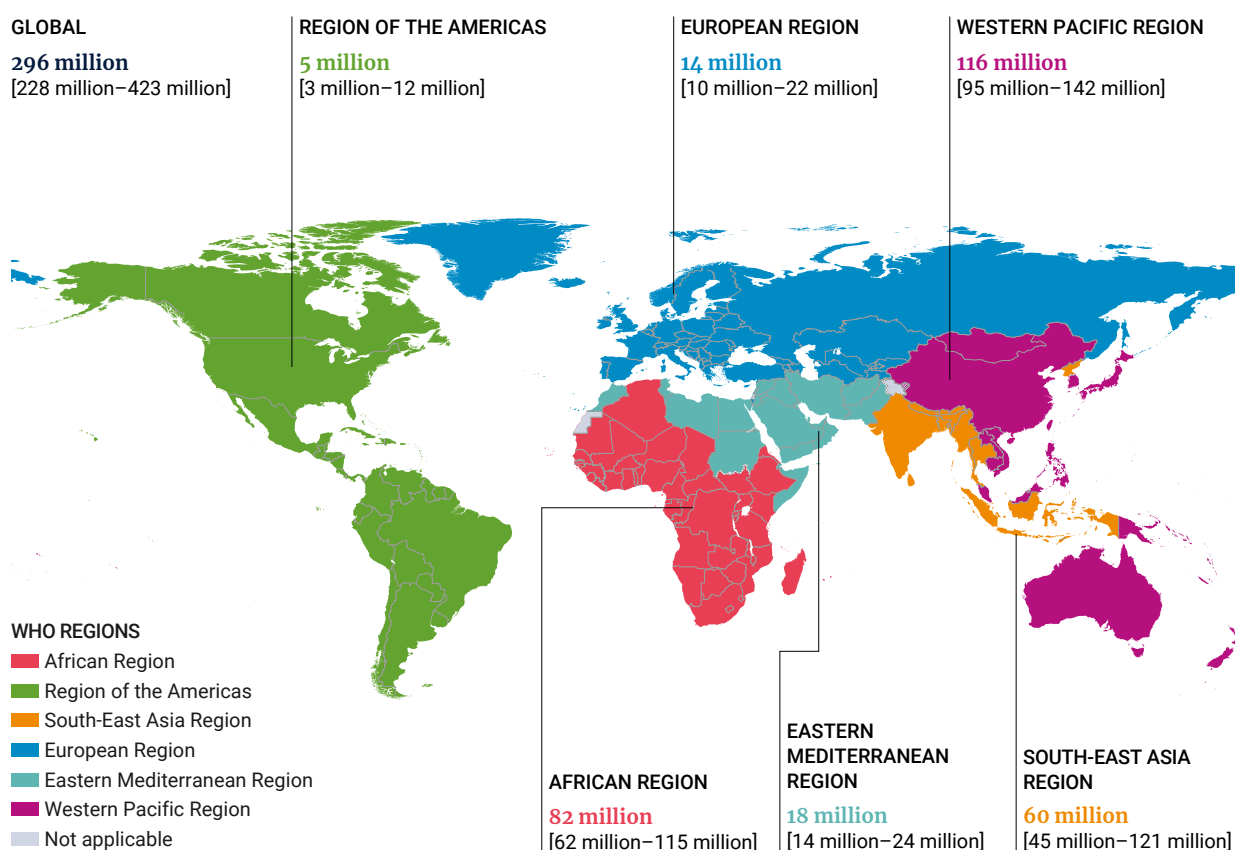
SECTION ONE: BACKGROUND

1. INTRODUCTION AND BACKGROUND

1.1. Epidemiology of viral hepatitis B and C infection

Hepatitis B infection: The World Health Organization (WHO) estimates that in 2019, 296 million persons, or 3.8% of the population, were living with chronic hepatitis B virus (HBV) infection in the world (Fig. 1.1) (1). The African and Western Pacific regions accounted for 67% of those living with HBV. In 2015, the estimated global prevalence of HBV infection in HIV-infected persons was 7.6%, and 2.7 million persons were coinfecting with HBV and HIV (2). Most of the people currently living with HBV infection were born before the hepatitis B vaccine was widely available and used in infancy (1).

FIG. 1.1 Burden of chronic hepatitis B infection (HBsAg positivity) by WHO Region, 2019 (1)

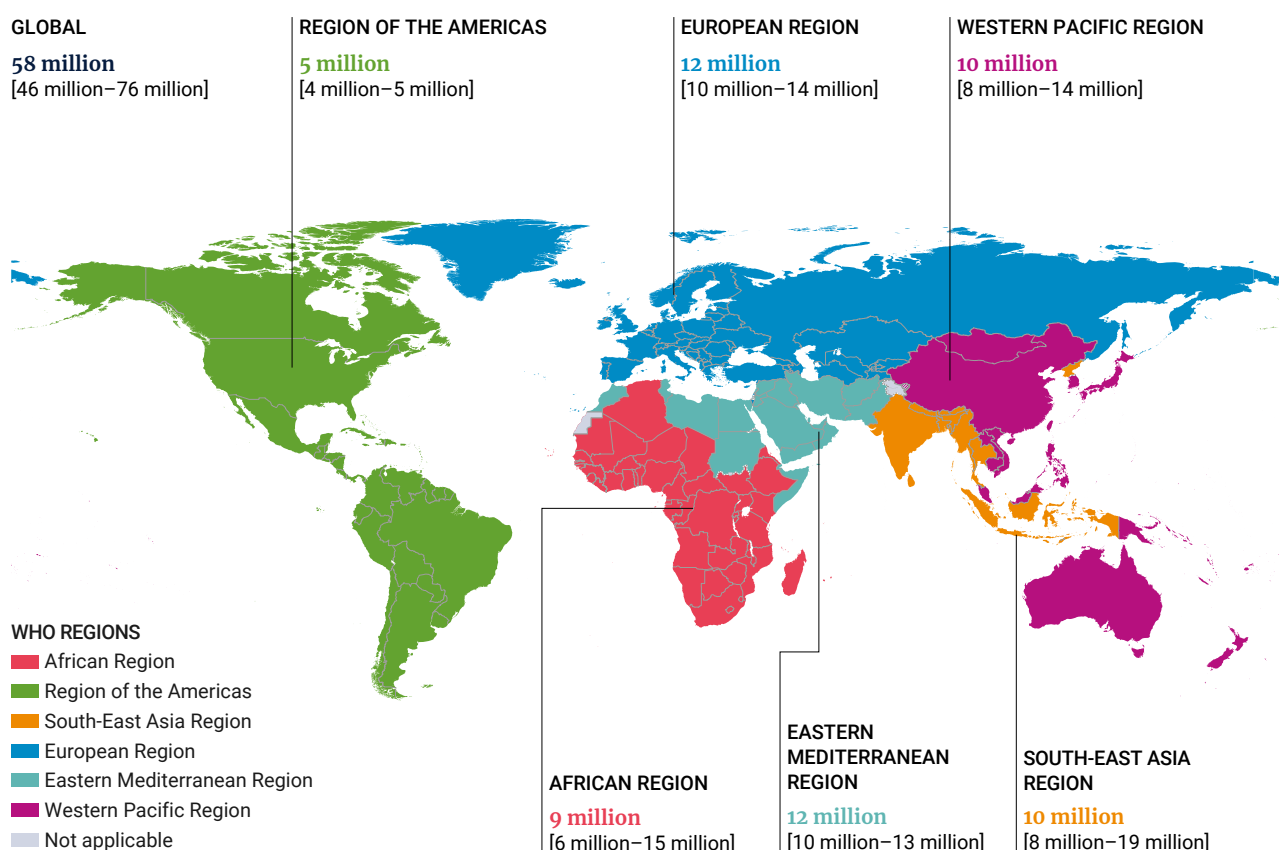


1. Introduction and background

WHO has also estimated that the prevalence of chronic HBV infection among children under 5 years of age fell from 4.7% in the pre-vaccine era (early to mid-1990s) to 0.9% in 2019 (1). The remaining infections are in neonates or infants, which occur through transmission from the mother at birth prior to vaccination or early childhood transmission through close contact with other infected young children and infected adults in the household. New estimates show that about 1.5 million people newly acquire hepatitis B infection each year, despite the availability of a highly efficacious vaccine.

Hepatitis C infection: WHO estimated that in 2019, 58 million persons were living with hepatitis C virus (HCV) infection in the world, accounting for 0.75% of the population (1). Of those living with HIV, 2.3 million persons also had HCV infection, of which 1.4 million were PWID (3). HCV infection is unevenly distributed across the world. The European and Eastern Mediterranean regions are the most affected, but there are variations in prevalence across and within countries. Unsafe health-care procedures and injection drug use were the leading causes of new HCV infections. In 2019, there were 1.5 million new infections (1).

FIG. 1.2 Burden of chronic hepatitis C viraemic infection by WHO Region, 2019 (1)

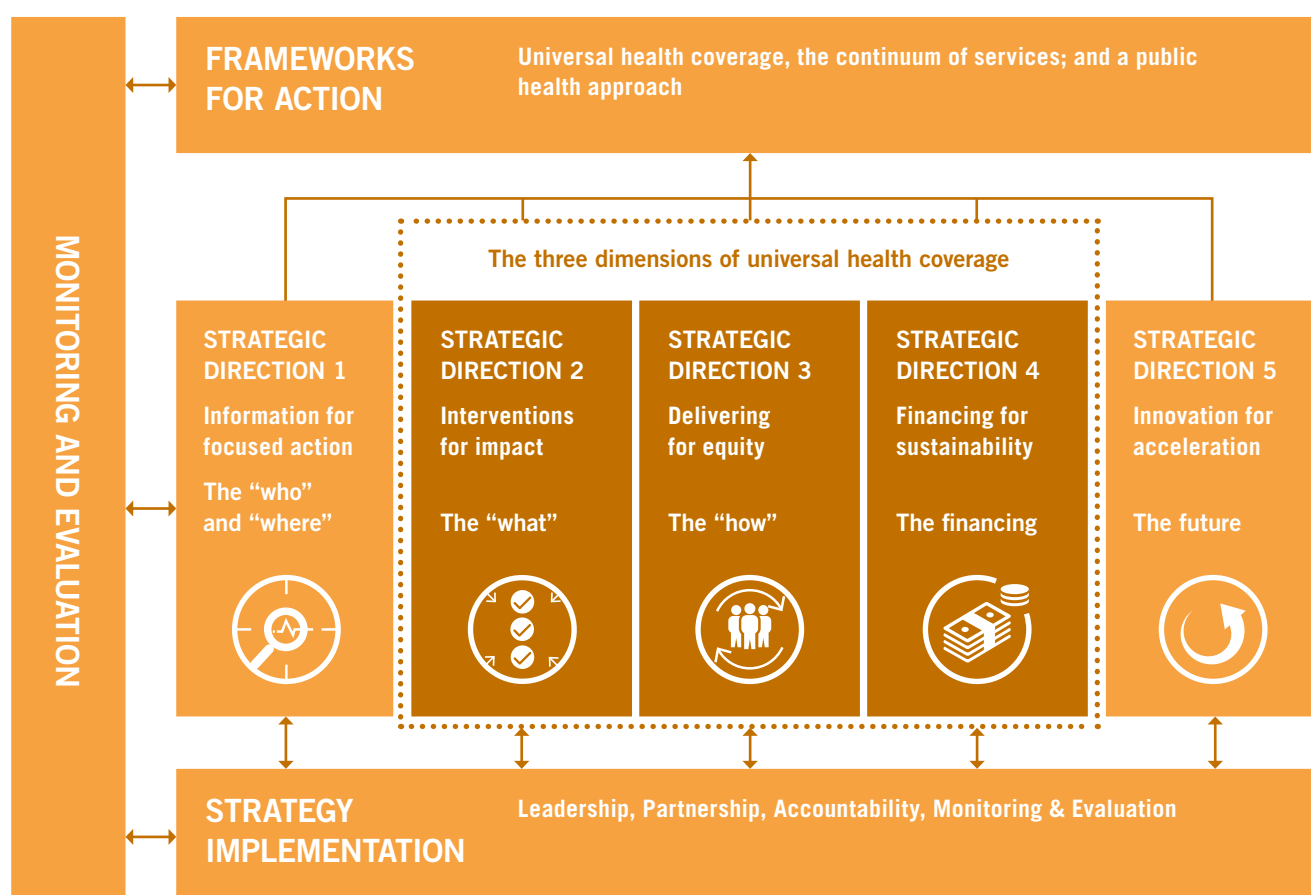


WHO estimated that, in 2019, viral hepatitis B and C were together responsible for 1.1 million deaths mainly due to cirrhosis and hepatocellular carcinoma (HCC) (1). Unless more people with HBV and HCV infection are diagnosed and treated, the number of deaths due to viral hepatitis will continue to increase (1).

1.2. Global Health Sector Strategy on viral hepatitis 2016–2021

The Global Health Sector Strategy (GHSS) on viral hepatitis (4), approved by the World Health Assembly in 2016, has the vision of a world where transmission of viral hepatitis is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, diagnosis, care and treatment. Its goal is to eliminate viral hepatitis as a major public health problem by 2030. As described in Fig. 1.3, this vision could be achieved through five strategic directions; the development of hepatitis B and C impact and programmatic targets; and under the key principle of promoting a public health approach and achieving universal health coverage (UHC).

FIG. 1.3 Framework for the Global Health Sector Strategy on viral hepatitis 2016–2021 (4)



The Strategy’s targets are aligned with the 2030 Agenda for Sustainable Development (5) and relevant World Health Assembly resolutions. Ambitious global impact and programmatic targets have been set for 2020 and 2030, which guide the setting of national targets. These targets apply to everyone at risk of viral hepatitis infection: children, adolescents and adults; rich and poor; women and men; and all populations affected and at risk. An updated WHO global strategy will be developed during 2021, for publication in 2022.

1.3. Key interventions for the prevention, diagnosis, treatment and care of viral hepatitis

The GHSS on viral hepatitis outlines key interventions and their respective targets to achieve elimination by 2030 (4).

This section provides a summary of WHO-recommended key prevention, diagnosis, treatment and care interventions and services (Table 1.1).

TABLE 1.1 Service coverage indicators for the core interventions of the Global Health Sector Strategy (GHSS) on viral hepatitis: 2015 baseline and targets

			Targets	
Interventions	Indicator	2015 baseline	2020	2030
1 Hepatitis B vaccination	HEPB3 coverage	84%	90%	90%
2 HBV PMTCT ^a	HEP vaccine birth dose coverage	39%	50%	90%
3 Blood safety	Donations screened with quality assurance	89%	95%	100%
Injection safety	Proportion of unsafe injections	5%	0%	0%
4 Harm reduction	Syringes & needles distributed/PWID/year	27	200	300
5 Testing services	% HBV-infected diagnosed	9%	30%	90%
	% HCV-infected diagnosed	20%	30%	90%
6 Treatment	% diagnosed with HBV on treatment	8% ^b	— ^c	80% ^d
	% diagnosed with HCV started on treatment	7% ^b	— ^c	80% ^d

HepB: three doses of hepatitis B vaccine; PMTCT: prevention of mother-to-child transmission; PWID: person who injects drugs
Source: WHO, including commissioned work, United Nations, UNICEF and one published in study (73)

a Interventions to prevent the mother-to-child transmission of HBV

b Less than 20% of persons living with HBV infections are eligible for treatment with antinucleosides

c 5 million treated for HBV and 3 million treated for HCV (cumulative targets)

d Of those eligible for treatment

1.3.1 Hepatitis B vaccination and prevention of mother-to-child transmission of HBV

Most of the global burden of chronic hepatitis B (CHB) infection can be attributed to mother-to-child vertical transmission (MTCT) of HBV at the time of, or shortly after, birth or in early childhood from infected children and adults through horizontal transmission. Such perinatal infections lead to a high rate of chronicity, and these individuals may remain viraemic for decades (6).

WHO recommends universal immunization of infants, with at least three doses of the hepatitis B vaccine, and timely hepatitis B birth dose (HepB-BD) vaccination (as soon as possible after birth, preferably within 24 hours) (7). Since 1992, WHO has recommended inclusion of the hepatitis B vaccine in the Expanded Programme on Immunization (EPI) (8). High coverage of the timely HepB-BD, given within 24 hours of birth, and completion of the infant hepatitis B vaccine series are the most important interventions for reducing MTCT of HBV as well as early childhood transmission and achieving the HBV elimination goals.

The **infant hepatitis B vaccine series** should be completed through administration of two or three additional doses of hepatitis B-containing vaccine, each separated by at least four weeks, according to the national infant immunization schedule.^{a,b} Completion of the infant hepatitis B vaccine series leads to immunological protection and prevention of infection in >95% of children (7).

Since 2020, WHO has recommended that hepatitis B surface antigen (HBsAg)-positive pregnant women at high risk of transmitting the virus to their infants due to high HBV DNA level ($\geq 200\ 000$ IU/mL) receive peripartum antiviral tenofovir prophylaxis from the 28th week of pregnancy until at least delivery to prevent mother-to-child transmission (PMTCT) of HBV (9). This recommendation is in addition to the 3-dose hepatitis B vaccination in all infants (starting with timely HepB-BD). In a number of settings (mostly high-income countries), hepatitis B immunoglobulin (HBIG) may also be used to further reduce the risk of MTCT of HBV.

2030 Immunization Agenda (IA2030)

The Immunization Agenda 2030 (10) sets an ambitious, overarching global vision and strategy for vaccines and immunization programmes for the decade 2021–2030. The IA2030 recommends that countries provide vaccination across the life-course – from birth (e.g. HepB-BD) to the elderly. There is also a focus on coverage and equity, with a commitment that everyone everywhere should have equal access to vaccines. This is critical in meeting the timely HepB-BD and HepB3 coverage targets.

1.3.2 Harm reduction interventions

WHO, the United Nations Office on Drugs and Crime (UNODC), Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Bank estimate that globally, there are more than 11 million people who inject drugs (PWID) – 1.4 million PWID are living with HIV, 5.5 million with hepatitis C and 1.2 million are living with both hepatitis C and HIV (11). Further, an estimated 23–39% of new HCV infections occur among people who currently inject drugs (12).

Harm reduction measures recommended by WHO (13,14) include distribution of sterile needles and syringes to PWID and OST for people who are dependent on opiates. Needle and syringe distribution and OST programmes should be provided with high coverage to effectively prevent HCV, HBV and HIV transmission (15,16), but globally coverage remains inadequate (17).

1.3.3 Prevention of hepatitis infections in health-care settings

Unsafe injections within health-care and community settings and transfusion of contaminated blood and blood products continue to be important modes of HBV and HCV transmission in some countries and settings. Infection prevention by improving blood safety and instituting universal safe injection practices are core interventions in the GHSS for control of viral hepatitis. WHO recommends the use of sterile single-use needles and syringes for all medical injections (14) and has published guidance on standard procedures for effective sterilization and decontamination of medical devices (18). WHO also recommends that 100% of donated blood should be screened for bloodborne infections (HBV, HCV, HIV and syphilis) to avoid transfusion-related transmission (19) and has developed a global action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023 (20).

a Three doses of hepatitis B vaccine are sufficient to induce immunity. However, for programmatic reasons, the monovalent BD may be followed by three additional doses in national routine infant immunization schedules:

- i) Three-dose schedule: three doses of hepatitis B vaccine, the monovalent birth BD followed by two doses (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine;
- ii) Four-dose schedule: four doses of hepatitis B vaccine, with the monovalent BD followed by three doses (monovalent or combined vaccine), usually given with other routine infant vaccines.

b The HepB3 vaccination coverage indicator measures the third dose of hepatitis B vaccine whether or not a fourth dose is given.

1.3.4 Testing for hepatitis B and C infection

WHO issued comprehensive testing guidance for hepatitis B and C in 2017 (21). Focused testing for hepatitis B or C infection is recommended for individuals from populations most affected by HBV or HCV infection. These include those who are either part of a population with higher seroprevalence (e.g. some mobile/migrant populations from countries with high/intermediate endemicity, and certain Indigenous populations), or who have a history of exposure to, or high-risk behaviours for, HBV or HCV infection (e.g. PWID, people in prisons and other closed settings, men who have sex with men [MSM] and sex workers, people living with HIV, their partners, family members and children of people living with chronic HBV infection). Routine testing of all pregnant women for HBsAg, HIV and syphilis in antenatal clinics, and all health-care workers is also recommended. In settings with a $\geq 2\%$ or $\geq 5\%$ seroprevalence of HBsAg or anti-HCV (depending on the country context regarding epidemiology or infrastructure), it is recommended that all adults have routine access to and be offered testing (i.e. a general population testing approach) (9,21). Overall, these different testing approaches should make use of existing facility-based services (such as antenatal clinics, refugee or migrant clinics, HIV and TB clinics, or chronic care clinics for diabetes/hypertension) as well as community-based testing opportunities and programmes. In addition, the 2030 global testing target is that 90% of those living with viral hepatitis B or C infection will have been diagnosed – making close to universal screening necessary to reach this target.

Screening for HBsAg and HCV antibody (HCVAb) should be carried out with a serological assay (in either a rapid diagnostic test [RDT] or laboratory-based immunoassay format) that meets minimum quality, safety and performance standards (21). The preferred strategy for confirmation of pre-treatment HBV assessment is evaluation of HBV DNA viraemia and for chronic HCV infection, HCV RNA using a quantitative or qualitative nucleic acid test (NAT) (though qualitative testing is sufficient for HCV viraemia).

1.3.5 Treatment of hepatitis B

Antiviral treatment with tenofovir for HBV infection (often lifelong) aims to reduce morbidity and mortality by reducing the risk of HBV-related complications such as cirrhosis, decompensated liver failure and HCC, especially in those with advanced liver disease through long-term viral suppression. WHO recommendations therefore focus on ensuring treatment of individuals with severe HBV-related liver disease or at high risk for progressive liver disease.

WHO recommends, as a priority, that all adults, adolescents and children with chronic HBV infection and clinical evidence of compensated or decompensated cirrhosis should be treated, regardless of alanine aminotransferase (ALT) levels or hepatitis B e antigen (HBeAg) status or HBV DNA levels (22). Treatment is also recommended for adults with CHB infection who do not have clinical evidence of cirrhosis but have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA $>20\,000$ IU/mL), regardless of HBeAg status, especially in those aged more than 30 years. Where HBV DNA testing is not available, treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status (22). Continued monitoring is necessary in all persons with CHB but, in particular, in those who do not currently meet the above-recommended criteria for who to treat or not treat, to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease.

1.3.6 Treatment of hepatitis C

Treatment of hepatitis C using direct-acting antivirals (DAAs) with attainment of sustained virological response (SVR) after 12 weeks post-treatment (SVR12) – so called “cure” – has been shown to substantially reduce the incidence of HCC by an estimated 85%, liver-related mortality and all-cause mortality by 75% in individuals with cirrhosis (23, 24) and close to 70% in those without cirrhosis (25).

WHO recommends offering treatment to all individuals diagnosed with HCV infection who are 12 years of age or older, irrespective of disease stage, using pangenotypic DAA drug regimens (sofosbuvir/daclatasvir, sofosbuvir/velpatasvir, and glecaprevir/pibrentasvir) (24). The length of treatment varies according to the presence or absence of cirrhosis, although SVR12 is achieved in $\geq 90\%$ of individuals (24). HIV coinfection does not reduce the effectiveness of HCV DAA pangenotypic therapy (24).

1.4. Progress on the global response

The *Progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: accountability for the global health sector strategies, 2016–2021* (1) provides a mid-term assessment of implementation of the GHSS on viral hepatitis, along with the related strategies on HIV and sexually transmitted infections (STIs). It reports the global burden of hepatitis B (296 million) and hepatitis C (58 million) and highlights major gaps and the need for concrete programmatic actions in the response to viral hepatitis. A summary of targets and current status is given in Table 1.2.

TABLE 1.2 Status of the global hepatitis response in 2019 (WHO 2021 global progress report) (1)

Targets (by 2020 and 2030)	Status in 2019
Impact 30% reduction in the number of people newly infected with chronic viral hepatitis B and C infection by 2020, 90% reduction by 2030 10% reduction in the number of people dying from viral hepatitis B and C by 2020, 65% reduction by 2030	1.5 million people were newly infected with chronic hepatitis B infection in 2019 1.5 million people were newly infected with chronic hepatitis C infection in 2019 1.1 million people died from infection with all hepatitis B and C viruses in 2019
Service coverage 90% coverage of hepatitis B virus vaccine (third dose) by 2020 50% coverage of services to prevent mother-to-child transmission of hepatitis B virus by 2020, 90% coverage by 2030 95% of blood donations screened in a quality-assured manner by 2020, 100% screened by 2030 50% of injections administered with safety-engineered devices in and outside health facilities by 2020, 90% by 2030 200 sterile needles and syringes provided per person who injects drugs per year by 2020, 300 by 2030 30% of people with chronic viral hepatitis B and C infection diagnosed by 2020, 90% by 2030 80% each of eligible people with chronic hepatitis B and C infection treated by 2030	85% coverage of hepatitis B vaccine (third dose) in 2019 43% global coverage for timely HepB-BD of hepatitis B vaccine in 2019 - Only baseline data available: 89% of donations screened with quality assurance in 2015 3.9% reuse of injection equipment in 2017 (26) 33 needles and syringes provided per person who injects drugs per year in 2017 (26) 30.4 million (10%) people living with hepatitis B knew their hepatitis B status in 2019 15.2 million (21%) people living with hepatitis C knew their hepatitis C status in 2019 6.6 million (22%) people diagnosed with hepatitis B received treatment in 2019 9.4 million (62%) people diagnosed with hepatitis C infection had been treated using DAAs between 2015 and 2019

DAA: direct-acting antiviral (drug); Hep B-BD: hepatitis B birth dose

1.4.1 Key developments and WHO guidance since the GHSS for viral hepatitis

Since the adoption of the GHSS on viral hepatitis in 2016 (4), there have been major developments in the global hepatitis landscape and response, including national and programmatic expansion, new and revised WHO guidelines, enhanced service delivery platforms and initiatives.

National responses and programmatic initiatives

- **Expansion of the national response.** In 2016, only 15 countries had comprehensive national action plans for viral hepatitis. By 2019, around 124 countries had national action plans or they were in development. WHO encourages countries to cost their national response in order to facilitate resource planning and allocation (1).
- **Expansion of HBV vaccine birth dose coverage.** HepB-BD, with two additional vaccine doses during infancy, is the most important intervention for eliminating MTCT of HBV. Global coverage of BD increased to 43% in 2019 (1).
- **New HCV medicines.** New HCV DAAs have revolutionized treatment since 2016. Cure (SVR12) can be achieved in more than 90% of cases with pangenotypic regimens. There has been great progress in reducing DAA prices, although treatment costs remain a key barrier to treatment expansion in certain countries (27).

WHO guidelines and hepatitis-related global guidance

Since the development of the GHSS on viral hepatitis, WHO has produced a comprehensive portfolio of strategies, policies and guidelines relevant to the elimination of viral hepatitis, covering the full continuum of prevention, diagnosis, treatment and care for hepatitis B and C (9,14,21,22,24).

- **Hepatitis B and C testing guidelines 2017.** This guideline outlines the public health approach to strengthening and expanding current testing practices for HBV and HCV infection, including public health approaches to service delivery and treatment monitoring. Adopting and adapting these recommendations will support improved access, services, and care and progress towards national and international elimination goals for hepatitis (21).
- **WHO “treat all” recommendation for HCV, 2018.** In 2018, WHO recommended that all people living with HCV should receive treatment, which will be essential for countries to achieve the HCV elimination targets (24).
- **Consolidated strategic information guidelines for viral hepatitis, 2019.** This is based on a simplified framework for surveillance, monitoring and evaluation (28,29).
- **Guidance on PMTCT of HBV, 2020** includes the use of antiviral prophylaxis for eligible HBsAg-positive mothers (9).
- **Planned consolidated guidelines on viral hepatitis, 2022.** WHO is currently working on consolidating and updating its viral hepatitis guidance into one modular guideline document for publication in 2022. This will include updated guidance on HCV self-testing, service delivery and eligibility criteria for HBV treatment. WHO is also working on updating their consolidated key population guidelines for publication at the end of 2021, which will be person-centred and consolidated across HIV, viral hepatitis and STIs.
- **Integration into UHC and public health systems.** UHC is the overarching goal of global action to address health inequalities, under which all people have access to the health services and commodities they need, which are of sufficient quality to achieve impact without exposing the user to financial hardship. WHO promotes the integration of all essential hepatitis B and C prevention, diagnosis and treatment interventions into national health services and benefits packages. These interventions are highlighted and fully included in the WHO UHC compendium (30) and will be further updated and improved throughout 2021 and include health workforce and other resource needs.
- **Preventing perinatal hepatitis B transmission: a guide for introducing and strengthening hepatitis B birth dose vaccination (31)**

In addition to the above progress and highlights since the adoption of the GHSS, the following initiatives provide a platform for further integration of elimination of viral hepatitis.

Elimination of mother-to-child transmission of HIV, syphilis and hepatitis B – triple elimination

Since 2016, WHO has promoted an integrated approach to the elimination of mother-to-child transmission (EMTCT) of infectious diseases pioneered by the joint effort of the Pan American Health Organization, the WHO Office for the Region of the Americas, and the Regional Office for the Western Pacific Region (32–36).

In 2017, the Pan American Health Organization published the *Framework for elimination of mother-to-child transmission of HIV, syphilis, hepatitis B, and Chagas – “EMTCT Plus”* (33), which includes region-specific impact and programme targets for all four diseases, followed by a progress report in 2019 and inclusion in the 2019 Integrated Sustainable Framework for the Elimination of Communicable Diseases in the Americas (34). At the same time, the Regional Committee for the Western Pacific endorsed the Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030 (35). This was followed in 2020 with the development of the draft regional operational guidance on the EMTCT of HBV in the Western Pacific (32). Both regional frameworks are aligned with the existing global and regional strategies, action plans and goals for reproductive, maternal, newborn and child health, and control of HIV, hepatitis and STIs. The Framework also includes impact and programme targets for each of the three communicable diseases.

The WHO Global Framework for Multi-disease Elimination (GFME)

Inspired by the initiative of the Pan American Health Organization, WHO is currently developing an overall framework to facilitate elimination of multiple communicable diseases at the same time, including viral hepatitis, in a holistic, coordinated, comprehensive and sustainable manner, and adopting a people-centred approach within the context of achieving UHC. UHC provides the pathway to disease elimination and in itself can be achieved only if there is adequate investment in disease elimination efforts. Achievement of the Sustainable Development Goals (SDGs) and WHO’s “Triple Billion” targets is dependent on the success of disease elimination efforts.

The Framework aims to guide actions at country, regional and global levels to achieve greater efficiency, equity and impact through cross-programme synergies. The Global Framework recognizes that major differences exist across each of the diseases or health conditions targeted for elimination. This includes the interventions that are used and the maturity of different disease elimination programmes. The Framework focuses on those diseases and health conditions where elimination or eradication commitments have been made and provides the rationale for multi-disease elimination, promotes greater standardization of definitions, and criteria and validation processes for disease elimination. It also provides guidance on the integration of disease elimination efforts, including those for viral hepatitis, into broader national health planning and programming. Today, 33 diseases have been assigned global targets for elimination or eradication (Table 1.3). This represents considerable progress over the last 40 years since the eradication of smallpox was certified.

TABLE 1.3 Diseases with global elimination targets

Goal	Diseases targeted
Eradication	Dracunculiasis; malaria; polio; yaws
Elimination of transmission	Human African trypanosomiasis (HAT) (<i>gambiense</i>); leprosy; measles, onchocerciasis, rubella (including congenital rubella syndrome [CRS])
Elimination as a public health problem	Cervical cancer; Chagas disease; cholera; gonorrhoea; hepatitis B & C; HIV; HAT (<i>rhodesiense</i>); leishmaniasis (visceral); lymphatic filariasis; maternal and neonatal tetanus; meningitis; rabies; schistosomiasis; soil-transmitted helminthiasis/strongyloidiasis; syphilis; trachoma; TB; vector-borne diseases (including chikungunya, dengue, Japanese encephalitis and Zika virus disease); yellow fever

1.5. Progress on regional strategies and country programmes

The epidemiology of viral hepatitis B and C across the world is heterogeneous. While in some regions, such as the Western Pacific and Africa, hepatitis B infection accounts for a greater proportion of the disease burden, in Europe and the Eastern Mediterranean Region, hepatitis C infection is more prevalent. In addition, there is marked variability in the hepatitis responses within and across regions, as well as between and within countries, a result of geography, socioeconomics and political will. Nevertheless, the goal of the 2016 GHSS is the elimination of viral hepatitis as a *global* public health problem, and is therefore dependent on concerted and coordinated global action to address viral hepatitis, operationalized at the regional and country levels.

All six WHO regions have developed regional action plans to facilitate the elimination of viral hepatitis (36–41). While the *Global Health Sector Strategy on viral hepatitis 2016–2021* is an overarching framework that provides a series of strategic directions to guide a comprehensive viral hepatitis response (4), these region-specific plans recommend priority areas for action by countries relevant to their respective regional contexts, along with actions to be undertaken by WHO to support countries in achieving elimination targets. The target audience for regional action plans includes ministries of health, policy-makers, programme officers, clinicians, nongovernmental organizations, health planners and those implementing health plans, the private (non-profit and for-profit) sector, donors, patient groups, in addition to community and civil society organizations. These have provided the basis for the rapid growth in a number of countries with national action plans on viral hepatitis. In addition, regional action and country-level support have driven innovations in viral hepatitis responses as well as valuable lessons for improving the global response.

African Region. From three countries with national strategic plans for viral hepatitis in 2015, 29 countries had developed national hepatitis plans by 2020, while five countries had developed investment cases in the context of disease burden and funding needs to support policy development. Innovative approaches to integrated service delivery of hepatitis C interventions within the pre-existing infrastructure of national HIV health programmes have been pioneered in Rwanda, and serve as a model case study for other Member States in the Region. Substantial progress has been made to scale up childhood hepatitis vaccination in all 47 countries in the WHO African Region and regional reported coverage with three doses of HepB (HepB3) increased from 5% in 2000 to 76% in 2015 (42). However, coverage has plateaued at 70–75% since 2009 and currently, only 19 countries have a HepB3 coverage of over 90%. HepB-BD coverage is estimated to be 6% compared to the global coverage of 43%. Improvement in HepB3 coverage and introduction of the HepB-BD is critical for achieving the regional hepatitis B elimination targets and requires strong political commitment to reach both facility-based and home births. In January 2020, the Cairo Declaration on Viral Hepatitis Elimination (43) was signed and endorsed by the African heads of state and presidents of Member States of the African Union, heralding a unique opportunity for high-level political advocacy and commitment to accelerate the regional hepatitis response.

Region of the Americas. More than half of the countries in the Americas (57%) have national strategies or plans for prevention, treatment and control of viral hepatitis. HCV DAAs are readily accessible in 17 countries and recommended as first-line therapy for chronic hepatitis C. In Brazil, there has been an expansion of HCV screening services to the primary health-care level, and testing and treatment are provided free of charge in the public sector for all HCV-infected patients. By the end of 2018, Brazil had treated 78 666 patients, a significant step towards meeting its national targets. Several subregional hepatitis initiatives were launched in 2019, with a particular focus on South America. Ministers of health of Mercosur countries^c signed a declaration on hepatitis elimination at the XLV Meeting of Ministers of Health of Mercosur in São Paulo in November 2019 (44). In July 2019, with the support of the Pan American Health Organization and Organismo Andino de Salud-Convenio Hipólito Unanue (ORAS-CONHU), heads of hepatitis programmes of six Andean countries reached agreement on joint strategies against hepatitis (45) and, in the Caribbean, hepatitis was included in the Caribbean Regional Strategic Framework for HIV/AIDS 2019–2025 (46), providing an entry point for accelerated expansion of diagnosis of hepatitis and its treatment.

The countries of the Americas have vaccinated their populations against hepatitis B for more than 20 years and have achieved the goal of eliminating MTCT of this disease (estimated regional prevalence of hepatitis B in children aged 5 years of <0.1%). Vaccination coverage with the third dose for children under the age of 1 year was 87% and HepB-BD increased from 61% in 2010 to 76% in 2017. Efforts are needed to continue increasing hepatitis B vaccination coverage in children. In 2017, the Framework for the Elimination of Mother-to-Child Transmission of HIV, Syphilis, Hepatitis and Chagas Disease (EMTCT-PLUS) was launched to address persisting inequalities in access to health and lost opportunities that remained between and within countries (33).

European Region. Several innovations in viral hepatitis responses have been implemented, including innovative service delivery models, as featured in a recent compendium of good practices (47), including: integrated multidisciplinary model of care with peer support to ensure continuum of HCV care for PWID in Antwerp, Belgium; Mobile InfoHep Centre that provides comprehensive linkage to care for viral hepatitis in Croatia; hepatitis C treatment integration into harm reduction services and primary health care in Georgia as well as integrated screening and diagnosis of HCV, HIV and TB; the use of point-of-care HCV confirmation testing in OST clinics in Italy; and establishing the National Viral Hepatitis Patient Registry in the Russian Federation. The European Region also established a working group as part of its European technical advisory group of experts in immunization, which is validating the countries for achievement of the regional hepatitis B control target of ≤0.5% HBsAg prevalence among vaccinated cohorts. So far, four countries have been validated to have achieved that target.

Eastern Mediterranean Region. The Eastern Mediterranean Region developed its 2017–2021 action plan on the roadmap and priority actions towards the achievement of national, regional and global targets. The Region also established a regional verification committee for hepatitis B in 2019. Impressive price reductions in testing and treatment for HCV have occurred in the Region and this can be considered a regional success. Furthermore, seven countries have integrated the essential package of viral hepatitis interventions into their national health benefit package. The Region is home to some of the highest HCV-burden countries and testing and treatment have been markedly scaled up in Egypt. Of note is the Egypt Presidential initiative that was launched in October 2018 with the goal of screening the entire adult population of Egypt for HCV (48). By December 2019, a total of 60 million people had been screened, and 4 million with hepatitis C had been treated. Egypt has demonstrated the feasibility of implementing a large-scale elimination programme when there is high-level political commitment.

c Political bloc comprising Argentina, Brazil, Paraguay, Uruguay and Venezuela

1. Introduction and background

Pakistan is now adopting a comprehensive microelimination initiative in high-prevalence districts, with widespread population-based screening, linkage to treatment, and prevention interventions. Pakistan developed its National Hepatitis Strategic Framework for the hepatitis response 2017–2021, aiming at disease elimination by 2030 (49). Significant progress has also been made in reducing the price of DAAs to US\$ 35 for a 3-month course.

South-East Asia Region. Most countries now have national strategic plans for viral hepatitis and are increasingly adopting and implementing testing and treatment guidelines for HBV and HCV. According to available data, the proportion of people living with HBV and HCV who know their status is 2% and 7.3%, respectively, with the proportion of those diagnosed who are initiated on treatment just 11% and 69%, respectively, well short of the regional target of 75% (40). India is tackling hepatitis C through the lens of UHC. The Hepatitis C Relief Fund launched in 2016 in Punjab state in India has enabled 33 000 persons to access free hepatitis treatment and care via a decentralized network of over 22 district hospitals and three government medical colleges. Over 19 000 persons had completed treatment by 2019, with a cure rate of more than 92%. Health workers are trained in the requisite skills for the detection and treatment of viral hepatitis C to promote a primary health care and public health approach to addressing HCV (50). The South-East Asia Region also established in 2019 a regional expert panel for verification of achievement of the regional hepatitis B control target of 1%. So far, four of 11 countries have been verified to have achieved that target (51).

Western Pacific Region. From six countries with national action plans on hepatitis in 2017, 20 countries had developed national comprehensive action plans for hepatitis prevention, care and treatment by 2020. Access to hepatitis medicines with reduction in prices has improved across the Region, with different strategies used by countries to achieve price reduction. Most countries have access to good-quality low-cost generic hepatitis medicines. From a baseline of six countries in 2017, 19 countries had included hepatitis as part of social health insurance and/or government financing by 2020 (52). Of note, China has undertaken an economic analysis and developed an investment case to estimate the hepatitis disease burden and the impact on health and on financing health budgets, providing evidence for strategy and policy-making, and for price negotiations of antivirals to treat chronic hepatitis B infection and DAAs for hepatitis C. The price of HBV medicines reduced from US\$ 3000 to US\$ 10/year, 2015–2019 while the price of HCV medicines reduced from US\$ 10 000 to US\$ 1500–2000/cure, 2016–2019. Additionally, in May 2017, Mongolia launched the Healthy Liver Programme (HLP) 2017–2020, through which hepatitis services are fully financed through social health insurance. As of October 2020, 1.2 million people above 15 years of age had been tested for HBV and HCV (~65% of the national target) and more than 50 000 people were provided treatment. The Western Pacific Region has established a regional verification mechanism for hepatitis B since 2005. Significant progress has been made in hepatitis B vaccination. The HBsAg prevalence has decreased to <1% at the regional level and 21/36 countries have achieved hepatitis B control (53).

2. ELIMINATION OF VIRAL HEPATITIS: PRINCIPLES AND PRACTICE

This chapter focuses on the guiding principles for validation of elimination, key recommended components in the development and implementation of an evidence-based national hepatitis action plan, and summarizes the approaches to country validation of elimination of viral hepatitis as a public health problem.

2.1. Guiding principles in the validation of elimination of viral hepatitis

The overarching guiding principle in achieving elimination of viral hepatitis is that of a public health approach, which aims to provide the maximum health benefit for the largest number of people within the available resources. The approach promotes standardization and simplification of interventions and services, with a focus on decentralization, integration and community engagement. The validation process stresses this approach as central to achieving elimination at the country level. Additional principles include the following:

- **Promotion of universal care adopts a harmonized and integrated approach to EMTCT** of HIV, syphilis and hepatitis B (together with other conditions, such as Chagas disease in the Region of Americas, and hepatitis C in Mongolia), ensuring the health of mothers through comprehensive care of women, quality maternal and child health services, care of infants, reduction in preventable adverse birth outcomes and leveraging existing HBV immunization initiatives. From the HIV experience in the African Region, male partners are attending PMTCT services to be tested for HIV. This approach promotes access to women and household members, which could potentially be explored for provision of HBV/HCV services.
- **Adaptation to the country context** effectively addresses disease epidemics in each unique population, setting and context, reflecting important variations in disease burden and epidemic dynamics across different countries and regions.
- **Country-led: the process places a strong emphasis on country accountability** and promotes country stewardship in setting national targets and designing its own path to elimination.
- **Respects human rights and promotes equity in access:** elimination criteria must be achieved in a manner that protects and respects human rights and promotes equity. It recognizes the central role of civil society and affected communities in implementing community-led and community-owned elimination programmes for viral hepatitis with their involvement in the validation process.

2.2. The national planning process

National planning of the domestic hepatitis response is the building block from which validation of the elimination of viral hepatitis can ultimately be achieved. Therefore, the national planning process should be informed by a comprehensive assessment of the national situation with regard to disease epidemiology and dynamics, population characteristics and country context, health system capacity and multisectoral national response to viral hepatitis. **The process should be guided by setting national impact and programmatic targets that are consistent with the global approach to elimination and targets of the GHSS on viral hepatitis, and are ideally presented as absolute thresholds as set out in this guidance.**

The national strategy should be operationalized through a fully costed national viral hepatitis action plan, which defines the core interventions and resources needed to achieve national elimination targets. A well-developed investment case, which demonstrates the value of taking a disease elimination approach in support of implementation of the national hepatitis elimination strategy, is a powerful tool for advocacy and resource mobilization.

The Ministry of Health should be responsible for implementing the national hepatitis plan, and coordinating efforts across the public, community and private sectors and with other relevant government sectors. A strong civil society is key to an effective national hepatitis response, providing a legitimate and authentic voice to those affected by hepatitis and, also in some cases, providing a range of services, particularly for those vulnerable and marginalized populations. Civil society should be engaged in all aspects of national planning, implementation and accountability.

The WHO *Manual for the development and assessment of national viral hepatitis plans* provides guidance to countries on key components of a national plan and its integration into the broader national health response (54).

In addition, the WHO UHC compendium (30) is a tool that can assist countries in selecting the most appropriate package of interventions and services for inclusion in their national hepatitis elimination plan, as countries plan for leveraging of existing programmes, services and health insurance schemes and expansion of domestic funding as part of their national response.

2.2.1 Monitoring and evaluation

The validation process will require the measurement and documentation of the impact (incidence and mortality) and programmatic targets (prevention and care), and implementation considerations for elimination of viral hepatitis. This process relies principally on the availability of high-quality national programmes and a comprehensive system for surveillance, with systematic documentation of reaching the proposed impact and programme targets and maintaining programme targets for a total of at least 2 years.

National hepatitis action plans should include a monitoring and evaluation framework that describes how the specific programmatic and impact targets and indicators of the national response will be continuously measured and assessed. Most countries have existing arrangements for monitoring and evaluation of the wider national health sector response, which can be modified to also include that for hepatitis.

In 2019, WHO published the *Consolidated strategic information guidelines for viral hepatitis (29)*, which summarizes and simplifies the overall approach proposed by WHO to collect, analyse, disseminate and use strategic information on viral hepatitis at local, subnational, national and international levels.

The data systems needed to report against the core indicators of the monitoring and evaluation framework for viral hepatitis should also capture those data necessary to report progress towards elimination in the validation process. Data sources should include the following:

1. Nationally representative viral hepatitis surveillance (acute and chronic infection), including surveillance for the prevalence of chronic infections ideally through biomarker surveys, data on testing for viraemic infection and treatment, surveillance for incident chronic HCV infections, as well as acute hepatitis (not only acute jaundice), which reflects new acute infections;
2. Vital statistics or surveillance of cause-specific mortality;
3. Programme data or health-care facility surveys; routine data from the EPI and programmes for PMTCT, injection safety and harm reduction for prevention activities; surveillance for infections transmitted in health-care settings (e.g. through surgery, transfusion, dialysis, endoscopy); data from patient registers or databases to monitor the cascade of diagnosis and treatment.

Further details regarding data sources for national programming and validation can be found in *Consolidated strategic information guidelines*, which provide a simplified framework for viral hepatitis surveillance, monitoring and evaluation (29).

2.3. Approaches to the country validation of elimination of viral hepatitis B and C as a public health problem

2.3.1 Introduction

This section summarizes the approaches to country validation of elimination of viral hepatitis as a public health problem. It provides practical guidance on implementation, including the use of targets set out in this guidance and the relevant measurement indicators in the WHO monitoring and evaluation framework for viral hepatitis B and C (29) based on the results framework. In order to be validated, the different criteria and targets, the rationale for their use and the respective approaches to measurement are detailed in Chapters 3–5 and summarized in Table 2.1. The use of **absolute impact targets**, aligned to and as defined by the GHSS on viral hepatitis 2016–2021 (4), allows standardization across all settings.

TABLE 2.1 Summary of impact and programmatic targets for country validation of elimination for HBV EMTCT, HCV incidence and HBV/HCV mortality

Elimination targets	Elimination of chronic HBV infection as a public health problem		Elimination of chronic HCV infection as a public health problem	
2030 GHSS relative reduction reference targets (compared to 2015)	Incidence 95% reduction	Mortality 65% reduction	Incidence 80% reduction	Mortality 65% reduction
HBV- and HCV- specific absolute prevalence, incidence and mortality targets	HBV EMTCT ≤0.1% HBsAg prevalence in ≤5 year olds ^{a,b} <i>Additional target: ≤2% MTCT rate (where use of targeted HepB-BD)^c</i>	Annual mortality^g (HBV) ≤4/100 000	Annual incidence (HCV) ≤5/100 000 ≤2/100 (PWID)	Annual mortality^g (HCV) ≤2/100 000
Programmatic targets^d	Countries with universal HBV vaccine birth dose (BD) ≥90% HepB3 vaccine coverage ≥90% HepB timely hepatitis B BD (HepB-BD) coverage ^e Countries with targeted HBV vaccine birth dose (BD) ≥90% HepB3 vaccine coverage ≥90% coverage of those infants at risk with targeted HepB-BD ≥90% coverage of maternal antenatal HBsAg testing ≥90% coverage with antivirals for those eligible ^f	Testing and treatment ≥90% of people with HBV diagnosed ≥80% of people diagnosed with HBV and eligible for treatment are treated ^h Prevention ≥90% HepB3 vaccine coverage ≥90% HepB-BD coverage	Testing and treatment ≥90% of people with HCV diagnosed ≥80% of people diagnosed with HCV are treated ^g Prevention 0% unsafe injections 100% blood safety 300 needles/syringes/PWID/year	

EMTCT: elimination of mother-to-child transmission; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HepB-BD: hepatitis B birth dose vaccine; HepB3: three doses of hepatitis B vaccine; PWID: people who inject drugs

a Childhood prevalence is a proxy for HBV incidence.

b The ≤0.1% HBsAg prevalence can be measured among either 5 year olds, 1 year olds or those aged 1–5 years, according to existing country surveillance and data collection activities. For those regions and countries with a long history of high Hep B vaccination coverage (e.g. WHO Region of the Americas), and that already conduct school-based serosurveys, there could be flexibility to conduct serosurveys in older children >5 years.

c The ≤2% MTCT rate is an *additional* impact target to the ≤0.1% HBsAg prevalence among ≤5-year-old children in countries that provide targeted HepB-BD.

d All programmatic targets must be achieved and maintained for at least 2 years.

e Timely birth dose (HepB-BD) is defined as within 24 hours of birth.

f In accordance with national policies or WHO 2020 guidelines on the use of antiviral prophylaxis on PMTCT of HBV.

g The GHSS defines the reduction of combined mortality for both HBV and HCV to ≤6/100 000/year at a global level. The use of HBV- and HCV-specific mortality target rates will depend on national epidemiology of viral hepatitis and the relative contributions of HBV and HCV to overall mortality.

h Short-term curative treatment for HCV infection (SVR12), and generally lifelong antiviral therapy for HBV to maintain long-term HBV DNA viral suppression, in accordance with standard guidelines.

2.3.2 Options for validation of elimination of viral hepatitis B and C as a public health problem

Countries will be officially and globally recognized for validation of elimination of hepatitis B and C by WHO for one of the four options (options A–D) given in Table 2.2: elimination of MTCT of HBV, elimination of HBV and/or HCV as a public health problem, and elimination of both HBV and HCV as public health problems. The implementation considerations for elimination (Chapter 6) provide guidance on assessing the quality of strategic information systems and data; laboratory systems, diagnostics and medicines; quality of clinical services and programmes, including vaccination, and the principles of human rights, equity, gender equality and community engagement relevant to the elimination of viral hepatitis (see country-level checklist for implementation considerations in Annex 2) as recommended by WHO.

TABLE 2.2 Options for validation of elimination of viral hepatitis B and C as a public health problem

Option	Options for validation of elimination	Impact indicators	Programme indicators
Option A	HBV EMTCT (as part of triple elimination of HIV, syphilis and HBV, or HIV/HBV) ^a	Annual HBV incidence ^b and MTCT rate ^c (additional target) in countries with targeted timely HepB-birth dose (BD)	HBV birth dose and infant vaccination coverage for newborns and infants HBV antenatal testing and antiviral prophylaxis coverage
Option B	HCV as a public health problem	Annual HCV incidence and HCV mortality	Coverage of prevention, testing and treatment
Option C	HBV as a public health problem (including HBV EMTCT)	Annual HBV incidence (and MTCT rate) and HBV mortality	Coverage of prevention, testing and treatment
Option D	Elimination of both HBV and HCV as a public health problem (including HBV EMTCT)	A, B and C above	A, B and C above

EMTCT: elimination of mother-to-child transmission; Hep B: hepatitis B; MTCT: mother-to-child transmission

a Countries can choose EMTCT of HIV, or HIV and syphilis, or HIV and syphilis and hepatitis B.

b The prevalence of hepatitis B surface antigen (HBsAg) in children aged ≤5 years old is used as a surrogate indicator of the cumulative incidence of chronic hepatitis B.

c The ≤2% MTCT rate is an *additional* impact target to ≤0.1% HBsAg prevalence among ≤5-year-old children in countries that provide targeted timely HepB-BD.

2.3.3 Criteria for elimination of viral hepatitis B and C as a public health problem according to country options for certification

The **criteria for elimination** include the attainment of both the (i) **impact targets** (Table 2.3) and (ii) **programmatic targets**, and the documentation of implementation considerations as set in this guidance (Chapter 6 and Annex 2). Achievement and determination of elimination will require the availability in countries of high-quality programmes and a comprehensive system for surveillance, with systematic documentation of having reached the proposed impact and programme targets and maintaining the programme targets for at least 2 years, and in a manner consistent with international human rights considerations.

In order to be validated for HBV EMTCT (option A), a country must show that the elimination target for HBV incidence has been attained. The prevalence of HBsAg in children aged 5 years or less is a proxy measurement of new hepatitis B infections from vertical and/or early horizontal transmission, and is used as a surrogate indicator of the cumulative incidence of chronic hepatitis B. Achievement of the programmatic targets should also be maintained for at least 2 years. In addition to the attainment of impact and programme targets, countries applying for validation will also be assessed across the various implementation considerations.

The criteria for country validation of elimination of HCV alone, HBV alone or both HBV and HCV as a public health problem (options B, C, D) require the attainment of the relevant **HBV and/or HCV impact targets (incidence and mortality)** and the **programme targets**, as well as the documentation of implementation considerations (Chapter 6), as set in this guidance. It is recognized that attainment of the incidence and mortality targets may occur at different times, as it may take much longer for mortality to drop, following an incidence reduction.

TABLE 2.3 Indicators and data sources for impact targets and proposed data sources

Targets	Preferred measurement indicators	Alternative (proxy) measurement indicators	Data sources and approaches to measurement
i. HBV incidence: impact target and measurement indicators			
≤0.1% prevalence of HBsAg in ≤5 year olds ^a	% HBV infections in ≤5 year olds ^a	MTCT rate ≤2% ^b	See Box 3.6 • National serosurvey • Post-vaccination serological testing (PVST) survey for MTCT rate • Programmatic data
ii. HCV incidence: impact target and measurement indicators			
Annual incidence of new HCV infections <5/100 000 persons AND ≤2/100 people who inject drugs (PWID)	No. of new HCV cases per 100 000 persons AND No. of new HCV cases per 100 PWID	Reduction in HCV viraemic prevalence by 80% from baseline (in general population and PWID)	See section 4.2 • Prospective cohort studies • Surveillance for acute HCV • Repeat cross-sectional surveys assessing HCV viraemic prevalence • Modelled estimates using serial serosurveys and programmatic data
iii. HBV and/or HCV mortality: impact target and measurement indicators			
Annual incidence of HBV-related deaths <4/100 000 Annual incidence of HCV-related deaths <2/100 000	No. of deaths caused by HCV and/or HBV infection per 100 000 population	Reduction in HCV viraemic prevalence by 80% from baseline ^c	See section 5.2 • Data from vital registration of deaths and cancer registries (HCC reporting) • Surveillance for sequelae (cirrhosis) • Repeat cross-sectional surveys assessing trends in HCV viraemic prevalence

HCC: hepatocellular carcinoma; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission; PWID: people who inject drugs

a The ≤0.1% HBsAg prevalence can be measured among either 5 year olds, 1 year olds or those aged 1–5 years, according to existing country surveillance and data collection activities. For those regions and countries with a long history of high Hep B vaccination coverage (e.g. Region of the Americas), and that already conduct school-based serosurveys, there could be flexibility in conducting serosurveys in older children >5 years.

b The ≤2% MTCT rate is an *additional* impact target to ≤0.1% HBsAg prevalence among ≤5-year-old children in countries that provide targeted HepB-BD, where vertical transmission remains in specific populations of pregnant women with high HBsAg (see Chapter 3).

c Can be used as an alternative measurement only with regard to HCV mortality

Data systems that are needed to inform strategic information on viral hepatitis for validation of elimination include (i) serosurveys; (ii) surveillance for acute hepatitis, chronic hepatitis infections and sequelae; and (iii) programme data documenting prevention, testing and treatment, which include the cascade of care (29). However, mathematical models can usefully complement the empirically collected data in several areas to determine attainment of the country elimination target.

Path to elimination for HBV EMTCT

A path to elimination for HBV EMTCT that represents milestones of progress towards elimination is also proposed. This is intended to recognize, mostly at a regional level, clear progression and significant national effort towards implementing key hepatitis interventions for HBV EMTCT in high-burden countries that may not yet be in a position to achieve the impact targets for elimination. The process for being on the path to elimination of viral hepatitis as a public health problem is completed at the regional level, unless a region specifically requests global-level engagement for higher-level advocacy.

The path to elimination of HBV EMTCT is a single set of criteria based **only on programmatic targets**. See section 3.2.3 in Chapter 3 for gold, silver and bronze criteria on the path to elimination. The path to elimination of HBV EMTCT therefore seeks to recognize high-burden countries with an HBsAg prevalence >1% among ≤5 year olds and/or with a general population prevalence >5%, which have made significant progress in implementing key hepatitis B vaccination interventions and some progress with antenatal HBV testing and antiviral prophylaxis for eligible women, but which may not yet be in a position to achieve the impact targets for HBV incidence. It is anticipated that criteria for the path to elimination of HCV and HBV as a public health problem will be further developed during 2021/2022 using interim programme targets for HBV and/or HCV testing and treatment (≥50% of infected persons diagnosed; ≥50% of persons diagnosed initiated on treatment) and a combination of prevention targets.

2.3.4 Governance approaches to elimination

Governance of the elimination of hepatitis B and/or C as a public health problem as well as EMTCT of HBV will be guided by relevant validation committees, task forces and secretariats at the national, regional and global levels as proposed in the “multi-disease elimination” route illustrated in Fig. 7.1. This route is aimed at the efficient use of human resource capacity at the national and regional levels for assessing the validation of all conditions slated for elimination. To assess country reports for validation, regions should have the required expertise in relevant disease areas, including immunization, viral hepatitis and health systems strengthening.

Countries that have been validated for achieving the elimination of viral hepatitis as a public health problem will be assessed every 5 years for maintenance of validation.

If a country opts to be validated only for the HBV EMTCT component of its viral hepatitis strategy, applications could be channelled through the triple MTCT elimination route using existing regional and global processes (Global Validation Advisory Committee [GVAC]) originally designed for dual validation of EMTCT of HIV and syphilis, which is currently being strengthened to address triple elimination.

2.3.5 Country pilots

A series of country pilots for assessing these elimination criteria will be undertaken during 2021/2022 to evaluate the different approaches to measuring the proposed incidence and mortality targets, as well as the programmatic indicators, and will inform a revised version of this interim guidance in 2022. The pilots will be implemented through desk reviews, virtual and hybrid meetings, and field visits in selected countries using standardized WHO protocols and tools.

The overall goal of the pilots will be to assess the feasibility, accessibility and acceptability of the use of the various targets, criteria and processes for validation of elimination and path to elimination for HBV EMTCT – as set out in this guidance, in collaboration with several countries. Specific objectives will include the assessment of existing national data systems and their capability to generate data to measure the required indicators for validation of hepatitis elimination; identification of gaps in national elimination efforts (including surveillance, laboratory and coverage of core interventions) and concurrent piloting of the standardized tools and checklists (including the checklist for implementation considerations).

2. Elimination of viral hepatitis: principles and practice

The country pilots will also evaluate the feasibility of different approaches to measuring the proposed impact and programmatic targets for elimination and to inform a revised 2022 guidance. Key questions that remain to be addressed during the pilot phase include the following: the need for a path to elimination track for HCV incidence and HBV/HCV mortality in addition to HBV EMTCT; the feasibility of MTCT rate as an additional criterion for validation of EMTCT in settings with targeted hepatitis B vaccine birth dose (HepB-BD); the need for additional modelling to support proposed levels of programmatic coverage of HBsAg testing and antiviral prophylaxis in pregnant women; the acceptable age ranges for conduct of HBsAg serosurveys for validation of HBV EMTCT; the feasibility of using combined versus HBV-/HCV-specific mortality rates; and the use of reduction in HCV viraemic prevalence as a proxy for direct measurement of reduction in incidence and mortality.

At the country level, the expected results would include: (a) a country situation analysis and assessment of readiness for validation of elimination; and (b) a country report with recommendations for preparing for national validation of elimination for use by the government and stakeholders. At the global level, the collective results from the country pilots will include a standardized template for a dossier on country validation of elimination, and a global readiness and preparedness planning tool to support country planning towards elimination of viral hepatitis, alongside enhanced advocacy and engagement of key national government and other stakeholders at country and regional levels. It will also include revised standardized evaluation protocols and tools that will ultimately inform the revision and completion of the final 2022 guidance.

SECTION TWO:
IMPACT AND PROGRAMME
CRITERIA FOR ELIMINATION AND
MEASUREMENT APPROACHES

3. VALIDATION OF ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B: TARGETS, INDICATORS AND MEASUREMENT

3.1. Background

In the absence of preventive interventions, MTCT at the time of or shortly after birth and early childhood transmission account for most of the burden of CHB infection, because the majority of perinatal infections lead to chronic infection. The risk of developing CHB decreases from around 90% of infected neonates born to HBeAg-positive mothers to 30% among children infected between the ages of 1 and 4 years, and is less than 5% among those infected as adults (55). Considerable progress has been made towards achieving elimination of mother-to-child and early horizontal transmission of hepatitis B through universal infant hepatitis B immunization, including the BD, which has been highly effective in reducing new infections in children. In addition to childhood vaccination and timely HepB-BD vaccination, WHO recommends the screening of pregnant women and assessing their eligibility for antiviral prophylaxis and/or antiviral treatment (9) in order to further reduce the perinatal transmission rates of HBV.

The GHSS impact target for elimination of viral hepatitis is defined as a 90% reduction in the incidence of chronic hepatitis infection (95% for hepatitis B and 80% for hepatitis C) alongside a 65% reduction in mortality, compared with the 2015 baseline absolute measure (4). The prevalence of HBsAg in children aged 5 years is a proxy for new hepatitis B infections from vertical and/or early horizontal transmission, and is used as a surrogate target of the cumulative incidence of CHB infections. The GHSS on viral hepatitis includes an HBsAg prevalence target in children of $\leq 1\%$ by 2020 and $\leq 0.1\%$ by 2030. In addition, most WHO regions have established regional targets (38,56–58). The GHSS also established coverage targets for HBV preventive interventions (three or more doses of HBV vaccine for 90% of infants, and timely HepB-BD vaccination for at least 90% of neonates, i.e. within 24 hours of birth, as well as those common to HBV/HCV prevention – safe injections and blood products, and harm reduction measures), diagnosis (diagnosis of 90% of people infected with HBV) and treatment (antiviral treatment of 80% of people who are diagnosed and eligible for treatment) (9).

3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

3.1.1 Triple elimination of mother-to-child transmission of HIV, syphilis and hepatitis B infection

Over the past decade, WHO policy recommendations have increasingly integrated health-care interventions to support person-centred care. In 2014, WHO first launched criteria and processes for validation of EMTCT of HIV and syphilis, known as “dual elimination” (59), and established the GVAC for EMTCT of HIV and syphilis the following year. In 2020, WHO launched the first guidelines on PMTCT of hepatitis B and use of antiviral prophylaxis (9). Triple elimination has now started in WHO regions with more developed health-care systems and expertise (regions of the Americas, Europe and Western Pacific). Updated guidance on validation of elimination of HIV, syphilis and hepatitis B will be issued in 2021. In May 2016, the World Health Assembly endorsed three new WHO global health sector strategies (2016–2021) on HIV, STIs and viral hepatitis. These included global targets for 2030 of zero new HIV infections in infants, elimination of congenital syphilis as a public health problem, and $\leq 0.1\%$ prevalence of HBsAg among children aged 5 years. The three strategies will be updated in 2021 and include EMTCT of hepatitis B in addition to HIV and syphilis, thereafter referred to as “triple elimination”.

Triple elimination targets can be achieved only when access to quality reproductive, maternal and child health-care services is ensured and used by all women, children and their families. Mother-to-child or vertical transmission of HIV, hepatitis B and syphilis can be effectively prevented and eliminated by similar strategies among people of reproductive age, including antenatal screening for HIV, syphilis and HBV, syphilis treatment of mothers and their infected infants, HBV and HIV antiviral treatment or HBV prophylaxis for eligible mothers, and HBV infant prophylaxis (including birth dose vaccination). The funding and organization of antenatal care (ANC) services and programmes at global and national levels provides an opportunity for integrated service delivery to optimize programme efficiencies, deliver quality patient-centred care and improve outcomes.

This chapter defines targets as well as indicators and provides measurement tools for use in the assessment and validation of EMTCT of hepatitis B within the triple elimination framework. It also outlines a process for recognition of a country’s progress on a “Path to Elimination” in settings where, because of a particularly high HBsAg prevalence, the country may not yet be able to achieve the impact targets for HBV EMTCT.

3.2. Indicators and targets for validation of EMTCT of hepatitis B

The goal of hepatitis B EMTCT programmes is to ensure that MTCT of hepatitis B is prevented or reduced to a very low level. The GHSS on viral hepatitis defined HBV EMTCT as a 95% reduction in hepatitis B incidence by 2030 compared to 2015 levels, such that it ceases to be a public health problem. This follows the same principle that has been applied to existing elimination programmes for MTCT of HIV and syphilis, as well as for elimination of several neglected tropical diseases (NTDs) such as Chagas disease.

3.2.1 Impact targets for validation of EMTCT of HBV

To achieve validation of the elimination of MTCT of HBV, it is necessary to demonstrate the attainment of a set of impact and programmatic targets, as shown in Box 3.1.

BOX 3.1 Impact targets for validation of elimination of MTCT of HBV

Countries that provide **universal HepB-BD** to all neonates should have achieved the following **impact target** for validation of EMTCT of hepatitis B:

- $\leq 0.1\%$ HBsAg prevalence among the ≤ 5 -year-old birth cohort (and older children)^a

Countries that provide targeted timely HepB-BD only should have achieved an additional **impact target** for validation of EMTCT of hepatitis B:^b

- $\leq 0.1\%$ HBsAg prevalence among the ≤ 5 -year-old birth cohort (and older children)

AND

- Maternal–child transmission rate of $\leq 2\%$

a The $\leq 0.1\%$ HBsAg prevalence can be measured among either 5 year olds, 1 year olds or those aged 1–5 years, according to existing country surveillance and data collection activities. For those regions and countries with a long history of high Hep B vaccination coverage (e.g. Region of the Americas), and that already conduct school-based serosurveys, there could be flexibility to conduct serosurveys in older children >5 years.

b Countries that provide targeted timely HepB-BD, and where vertical transmission continues due to specific populations of pregnant women with a high HBsAg prevalence, e.g. Indigenous populations or other higher-risk vulnerable populations, are required to show both $\leq 0.1\%$ HBsAg prevalence among ≤ 5 -year-old children *and* an MTCT rate of $\leq 2\%$.

EMTCT: elimination of mother-to-child transmission; HepB-BD: hepatitis B birth dose; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission

BOX 3.2 Rationale for impact targets**Universal HepB-BD – HBsAg prevalence $\leq 0.1\%$ in ≤ 5 year olds (and older children)**

In the absence of preventive interventions, MTCT at the time of, or shortly after, birth accounts for most of the global burden of CHB infection, because a large proportion of these perinatal infections lead to chronic infection. The prevalence of HBsAg in ≤ 5 year olds captures new infections from both these transmission routes and is therefore a proxy of true CHB incidence. It is recognized that the measurement of HBsAg prevalence in 5 year olds only reflects the impact of an intervention from five years earlier. Therefore, there is flexibility for countries to include a broader age grouping of those 1–5 years of age or 1 year olds to measure this indicator using representative serosurveys. It is also recognized that conducting surveys in <5 year olds may be challenging in certain countries. Since many countries already conduct school-based hepatitis B serosurveys (e.g. in the Western Pacific Region), or among vaccinated cohorts across a wider age range (e.g. in the European Region), there could be flexibility to use these existing serosurveys in older children >5 years (as well as ≤ 5 years), especially if there is a long history and programmatic evidence of high infant vaccination coverage maintained over several years (e.g. Region of the Americas). This will also capture the impact on both vertical and horizontal transmission.

3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

BOX 3.2 Rationale for impact targets (continued)

The GHSS on viral hepatitis proposes the elimination of viral hepatitis as a public health problem by 2030 (4), defined as a 90% reduction in the incidence of new cases (95% for hepatitis B) and a 65% reduction in deaths compared with the 2015 baseline. The GHSS 2030 targets of 95% reduction in new chronic HBV infections is equivalent to $\leq 0.1\%$ prevalence of HBsAg in ≤ 5 year olds based on modelled outputs (global and from China) (60).

Attainment of this impact target is feasible: in 2020, for example, based on modelled data from the Center for Disease Analysis, 52/119 countries (61,62) were estimated to be already at $\leq 0.1\%$ HBsAg prevalence (one country in the WHO African Region, 10 in the Eastern Mediterranean, 23 in Europe, 13 in the Americas, five in the Western Pacific, but none yet in the South-East Asia Region (53,62,63)) and are therefore candidates for validation of achieving the HBsAg prevalence impact target for EMTCT of hepatitis B. Based on actual serosurvey data, there are eight countries/territories in the Western Pacific Region that have an HBsAg prevalence $\leq 0.1\%$ and one country in South-East Asia with a prevalence of 0.05% (63). This guidance expands the cohort for measurement of this indicator to ≤ 5 year olds or 1 year olds, as well as to older children >5 years to provide countries (especially those with a long history and programmatic evidence of high sustained coverage of HepB-BD and infant vaccination) with greater flexibility in validation of elimination.

Targeted HepB-BD – HBsAg prevalence $\leq 0.1\%$ in ≤ 5 year olds and mother-to-child transmission rate of $\leq 2\%$

The MTCT rate $\leq 2\%$ is an **additional** target in countries that provide targeted timely HepB-BD, or for those countries with a low HBsAg prevalence but where it is recognized that there is still continuing vertical transmission due to specific subpopulations of pregnant women with high HBsAg (e.g. among Indigenous populations or migrant populations from high HBsAg-prevalence countries).

The MTCT rate measures the proportion of HBsAg-positive infants (numerator) among those infants exposed (denominator), i.e. infants of HBsAg-positive mothers. Calculation of this transmission rate requires both high-level coverage ($>95\%$) of antenatal HBsAg testing to identify positive mothers, and post-vaccination serological testing (PVST) of exposed infants at 9–12 months of age to identify infected infants. It is recognized that some countries providing targeted timely HepB-BD, which do not currently have the required data collection systems and linkages between programmes in place to capture this target, will need to develop this capacity.

The MTCT target threshold of $\leq 2\%$ is based on a modelled output MTCT rate from one country, China, predicting attainment of $\leq 0.1\%$ HBsAg prevalence in 5 year olds by 2030 using the combined strategy of targeted timely HepB-BD plus at least two additional doses of hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) at very high coverage ($>95\text{--}99\%$) (64). The relationship between MTCT rate and HBsAg prevalence requires confirmation through modelling in other countries during the piloting phase in 2021/2022. Although the MTCT target of $\leq 2\%$ was not specified in the GHSS targets for 2030 (4), it was included in the WHO Regional Action Plan for Viral Hepatitis in the Western Pacific (38).

CHB: chronic hepatitis B infection; EMTCT: elimination of mother-to-child transmission; HepB-BD: hepatitis B birth dose; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission; PVST: post-vaccination serological testing

3.2.2 Programmatic targets for validation of EMTCT of HBV

BOX 3.3 Programmatic targets for validation of EMTCT of HBV

UNIVERSAL HEPB-BD

Countries that provide **universal HepB-BD** to all neonates should have achieved and maintained both of the following programmatic targets for at least 2 years.

- **≥90% coverage of HepB3 vaccination**
- **≥90% coverage of HepB-BD**

Note: a target of ≥80% coverage of HepB-BD and HepB3 in all provinces or subnational areas can support evidence of equity of EMTCT of HBV in those countries with universal timely HepB-BD but is not essential for validation of elimination.

TARGETED TIMELY HEPB-BD

Countries that **provide targeted timely HepB-BD only to offspring of HBsAg-positive mothers** should have achieved and maintained the following programmatic targets for at least 2 years.

- **≥90% HepB3 vaccine coverage**
- **≥90% coverage of infants at risk with targeted timely HepB-BD**
- **≥90% coverage of HBsAg antenatal testing among pregnant women**
- **≥90% coverage with antivirals for those eligible HBsAg-positive pregnant women with high viral loads (plus coverage of HBV-exposed babies with HBIg, if available)**

BOX 3.4 Rationale for programmatic targets

The GHSS on viral hepatitis sets programme coverage targets for the most important preventive interventions (≥90% of infants with three or more doses of vaccination and ≥90% of neonates who receive HepB-BD vaccination within 24 h of birth), but also for diagnosis of 90% of people infected with HBV, and antiviral treatment of 90% of people who are diagnosed and eligible for treatment, especially for countries using targeted timely HepB-BD. Global models have estimated that achievement of these programme coverage levels in vaccination, testing and treatment targets in the applicable birth cohort would likely result in a country achieving the impact targets.

A minimum period of 2 years for attainment of the indicators for vaccination coverage is required to ensure continuous programme performance. Of note, generally for vaccination, a five-year period of sustainability is required to be able to measure the impact by serosurveys (65).

3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

BOX 3.4 Rationale for programmatic targets (*continued*)

UNIVERSAL HEPB-BD

Achievement of $\geq 90\%$ hepatitis B third-dose infant vaccination coverage and $\geq 90\%$ hepatitis B-BD vaccination coverage are aligned with the GHSS global programmatic targets (4) based on modelling of coverage required to reach the impact targets. These targets are also consistent with the Global Vaccine Action Plan ending in 2020, but a new Immunization Action Plan is in development (10,66). These vaccine coverage indicators are annually estimated by WHO and the United Nations Children's Fund (UNICEF) in assessment of the Joint Reporting Form (67) and as a hepatitis core indicator (29). By 2019, 51 of 95 countries (where data are available) were estimated to have $\geq 90\%$ timely HepB-BD coverage, and 117 of 186 countries (where data are available) were estimated to have coverage of the HepB3 vaccine dose of $\geq 90\%$, and 75 at $\geq 95\%$ (68). It is noted that the WHO regions of the Americas and the Western Pacific have set regional coverage of HepB-BD and HepB3 targets at $\geq 95\%$.

$\geq 80\%$ coverage of HepB3 vaccination in all provinces or subnational areas is consistent with the Global Vaccine Action Plan coverage for 2020 (66). Because of heterogeneity in coverage and population distribution, a country can achieve 90% nationally, but fail to reach remote populations. By ensuring 80% coverage at subnational levels, the immunization programme aims to achieve equity throughout the country.

TARGETED TIMELY HEPB-BD

If there is targeted timely HepB-BD, then indicators with coverage targets are needed, which address interventions in both the newborns of HBsAg-positive mothers (HepB3 and HepB-BD) as well as in the mothers (HBsAg testing in mothers and antivirals for those eligible).

For the offspring of HBsAg-positive mothers, the same 90% coverage of HepB3 and HepB-BD as for universal HepB-BD applies.

The $\geq 90\%$ coverage of HBsAg testing of pregnant women is an essential programmatic target only in countries that offer targeted timely HepB-BD to infants of high-risk mothers. The high coverage serves to ensure the identification of high-risk mothers and exposed infants for interventions and to be broadly consistent with the $>95\%$ testing coverage required for EMTCT of HIV and syphilis, in which testing and treatment of infected mothers is the only intervention to prevent MTCT.

The $\geq 90\%$ coverage of use of antivirals in eligible HBsAg-positive pregnant women and with a high HBV DNA level ($>200\,000$ IU/mL) or HBeAg positivity (plus **HBIg in HBV-exposed infants, if available**) is an additional indicator based on the 2020 WHO PMTCT recommendations for the use of antivirals in HBsAg-positive pregnant women (9). This is lower than the coverage levels set for antiretroviral therapy (ART) and syphilis treatment for HIV and syphilis elimination, respectively, because for hepatitis B, the availability of vaccines (BD and infant vaccination) is the most effective intervention for PMTCT of hepatitis B. Therefore, maternal testing and the use of antivirals are additional interventions. Further confirmation is required of this proposed threshold based on modelling.

CHB: chronic hepatitis B infection; EMTCT: elimination of mother-to-child transmission; HepB3: three doses of hepatitis B vaccine; HepB-BD: hepatitis B birth dose; HBIg: hepatitis B immune globulin; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission; PMTCT: prevention of mother-to-child transmission

3.2.3 Criteria for the path to elimination: recognizing progress towards EMTCT of hepatitis B

There is considerable heterogeneity in the epidemiology of hepatitis B across different countries and in the implementation and coverage of key interventions for PMTCT, especially HepB-BD and infant vaccination interventions. Many high-burden countries have made considerable progress in scaling up infant hepatitis B vaccination for PMTCT of hepatitis B, with or without HepB-BD vaccination. However, there are other countries that have faced challenges in making progress towards achieving the 2020 target of $\leq 1\%$ HBsAg prevalence in 5 year olds. For example, the WHO African Region is characterized by high endemicity of hepatitis B infection, suboptimal coverage of routine infant vaccination, low coverage of HepB-BD, and limited availability of in vitro diagnostic infrastructure and commodities (including HBIg). In addition, as recently as 2019, only 59.5% of pregnant women delivered in a health-care facility, compounding challenges in delivering the BD (69). A number of Pacific Island countries of the Western Pacific Region also have a high hepatitis B prevalence, a general lack of health infrastructure and supply chain issues, including challenges in cold chain management.

In 2017, in order to recognize the challenges in achieving EMTCT of HIV and syphilis in high-burden countries, particularly those in the African Region, and the considerable progress made in some countries, the GVAC established a set of criteria for countries as they progress along the “path to elimination”. Given the considerable heterogeneity in the epidemiology of hepatitis B and the viral hepatitis response in countries, we propose a similar approach to the validation of elimination for HIV and syphilis, which includes the options of full *elimination* of transmission as well as a *path to elimination*. The path to elimination is particularly applicable to high HBsAg-prevalence countries that are still improving coverage of hepatitis B infant and BD vaccination, such as in the African Region. This is important, given the opportunity for low-income countries to access funding for introduction of HepB-BD through the investment strategy of Gavi, the Vaccine Alliance (70). An overview of the approach for hepatitis B can be found in Fig. 3.1.

The path to elimination involves a three-tier system (gold, silver and bronze), which recognizes different stages of progress toward elimination. Each tier is defined by attainment of increasing levels of service coverage of key interventions for PMTCT of hepatitis B through infant and childhood vaccination and testing of pregnant women (Table 3.1). Moving to a higher tier brings a country progressively closer to the ultimate elimination target of $\leq 0.1\%$ HBsAg prevalence in 5 year olds, given that achievement of HepB-BD and HepB3 vaccination coverage, together with antenatal testing and antiviral prophylaxis, will ultimately result in the elimination of MTCT of HBV.

A country seeking validation for being on the path to elimination will have the opportunity of being recognized for significant efforts towards PMTCT of hepatitis B, and organize a consultative process to further develop its national strategy to reach elimination in the coming years. The validation should be initiated through a desk review and will also review four key areas (data quality; laboratory and programme quality; equity and human rights; and community engagement) (Table 3.1). It will follow the same procedure as a country requesting validation for EMTCT of hepatitis B, and generally be completed at the regional level. A consultative process should involve community-led organizations and, where local capacity is suboptimal, efforts to empower and strengthen the community should be included in the plan.

3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

TABLE 3.1 Path to elimination for MTCT of hepatitis B

Indicators for the assessment of progress on the path to elimination of MTCT of hepatitis B in countries with an HBsAg prevalence >1% among ≤5 year olds and/or with general population prevalence exceeding 5% ^a		
	Impact targets	Programme targets
GOLD TIER	Not necessary	≥90% coverage of hepatitis B 3rd dose infant vaccination ≥90% coverage of universal timely hepatitis B birth dose - Antenatal hepatitis B surface antigen (HBsAg) testing coverage >30%
SILVER TIER	Not necessary	≥90% coverage of hepatitis B 3rd dose infant vaccination ≥50% coverage of universal timely hepatitis B birth dose - Antenatal HBsAg testing available in public sector
BRONZE TIER	Not necessary	≥90% coverage of hepatitis B 3rd dose infant vaccination - Implementation of universal timely hepatitis B birth-dose policy

a Programme targets should be achieved for 2 years.

Requirement for high coverage at the district level: e.g. ≥80% coverage in all districts for HepB3 in all tiers and ≥80% coverage in all districts for HepB-BD in gold tier and ≥50% for timely targeted HepB-BD in all districts for the silver tier.

BOX 3.5 Rationale for the path to elimination

The path to elimination seeks to recognize high-burden countries that have made significant progress in implementing key hepatitis B vaccination interventions alongside antenatal testing and antiviral prophylaxis for eligible women, but that may not yet be in a position to achieve the elimination impact target of ≤0.1% HBsAg prevalence in ≤5 year olds. This may be because of a current high HBsAg prevalence and limited implementation of universal HepB-BD vaccination. Countries with an estimated HBsAg prevalence in 5 year olds of ≥1% are eligible to seek validation for the path to elimination as it is recognized that it takes time to expand programmatic coverage to an extent that it will move prevalence from >1% to ≤0.1%.

A key principle is that each tier of the path to elimination represents a *milestone of progress* towards elimination, where validation of elimination is the ultimate goal.

The cost of measurement of the impact indicator of HBsAg prevalence in ≤5 year olds through a national survey may be an impediment to monitoring and achieving progress towards elimination. Hepatitis B vaccination is highly efficient in preventing MTCT of hepatitis B and if the coverage levels in the gold, silver and bronze tiers were attained then this would result in countries being able to achieve elimination in future years. For these reasons, the path to elimination criteria only require achieving programmatic coverage targets as countries progress to measuring impact targets.

The indicators for the path to elimination reflect the critical role of HepB-BD and infant vaccination in eliminating MTCT of HBV.

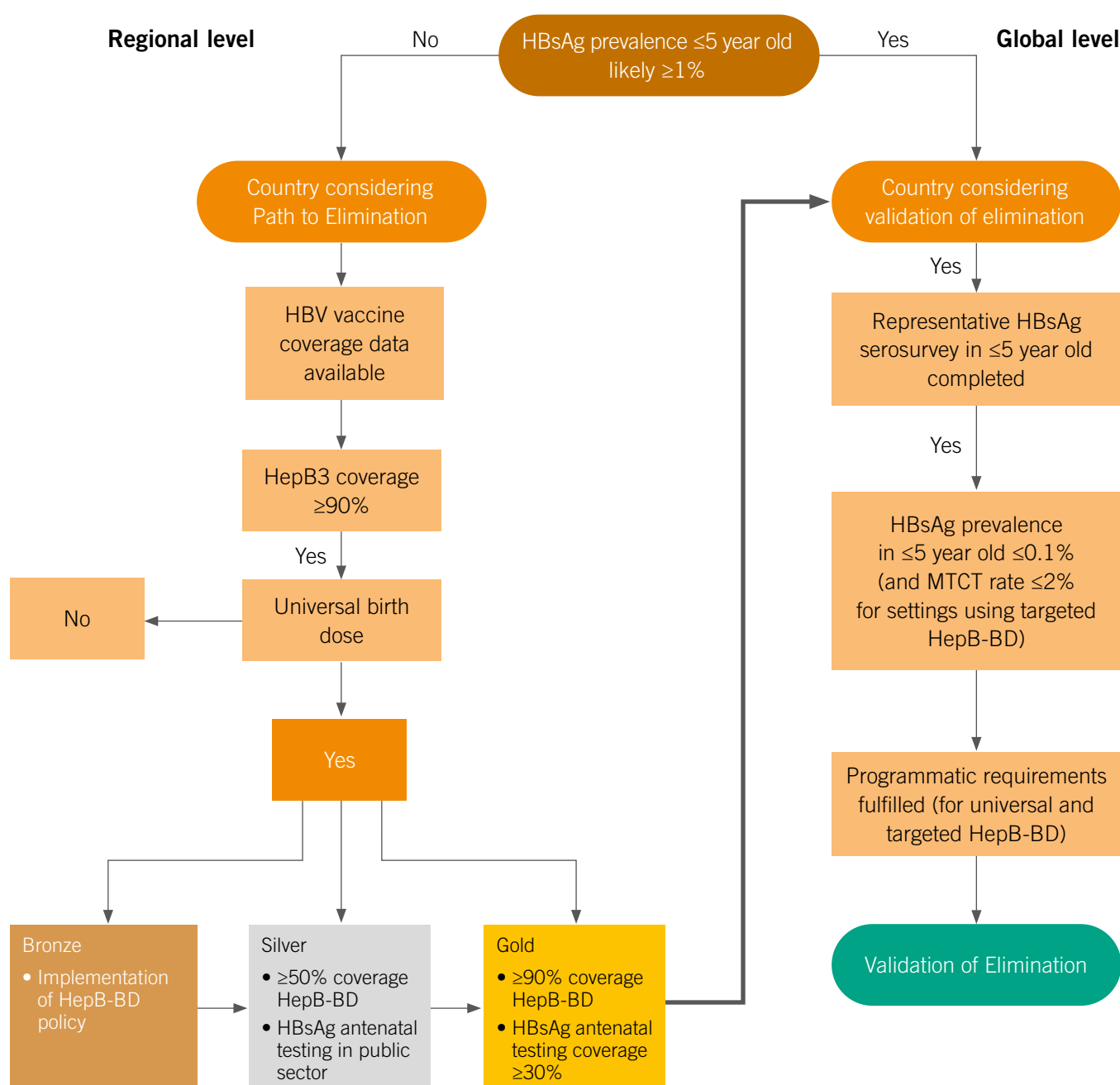
- The bronze level recognizes where a country has implemented a universal BD policy as a first critical step towards EMTCT.
- The silver level of BD coverage of ≥50% recognizes the attainment of the 2020 milestone target for BD coverage in the GHSS (4).
- The gold level of BD coverage of ≥90% recognizes the attainment of the 2030 service coverage target for BD coverage in the GHSS (4); it further introduces the importance of HBsAg testing in pregnant women within the triple elimination framework.

BOX 3.5 Rationale for the path to elimination (continued)

Other programmatic indicators are not included in the path to elimination process, as the aim is to use a set of simplified indicators that are routinely measured in the majority of countries. Other measures such as the use of tenofovir and/or HBIG are not routinely captured in many countries (Fig. 3.1).

BD: birth dose; EMTCT: elimination of mother-to-child transmission; GHSS: Global Health Sector Strategy (on viral hepatitis); HepB-BD: hepatitis B birth dose; HBIG: hepatitis B immune globulin; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission; PMTCT: prevention of mother-to-child transmission

FIG. 3.1 Summary schematic of approach to validation of hepatitis B EMTCT and path to elimination for countries



3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

3.3. Approaches to measuring indicators for validation of EMTCT of hepatitis B

3.3.1 Measurement of the impact indicator for validation of EMTCT of hepatitis B

The preferred approach is for countries to collect empirical data, i.e. a national survey on HBsAg seroprevalence (single or multiphase) in children aged ≤ 5 years (and also older children, as appropriate) (Box 3.6). If this is not feasible, a mathematical modelling process of the impact indicator, using available representative empirical data, may be considered. Triangulation of methods is recommended.

3.3.2 Empirical data for measuring the impact target

BOX 3.6 Measurement of childhood prevalence of HBsAg in ≤ 5 year olds

A. Preferred approach: measurement of childhood HBsAg prevalence in ≤ 5 year olds

The preferred approach is to directly measure a proxy for chronic HBV incidence (i.e. childhood HBsAg prevalence in ≤ 5 year olds) with national-level biomarker surveys among young children. This is the recommended gold standard by WHO in ≤ 5 year olds for monitoring progress towards hepatitis B control targets, but requires large sample sizes in settings that have a low prevalence (65). The focus should be on obtaining the best possible representative prevalence estimates with narrow confidence intervals in the 0–5-year-old age cohort. The advantage of measuring hepatitis B surface antigen (HBsAg) prevalence in ≤ 5 year olds is that it captures the effects of interventions on mother to child as well as early horizontal transmission, but a limitation is that it only reflects the impact of an intervention from five years ago. There is therefore flexibility for countries to include the convenience of an age group of 1–5 years or a narrower age range such as 1 year of age (to capture the impact of recent interventions, although this would not reflect sustainability) to measure this indicator using representative serosurveys. However, there are logistical and cost constraints in undertaking serosurveys in a younger cohort aged 1 year, with requirement for household surveys and venous sampling. It is also recognized that conducting surveys in ≤ 5 year olds may be challenging in certain countries. Since many countries already conduct school-based hepatitis B serosurveys or among vaccinated cohorts across a wider age range, there could be flexibility to use these existing serosurveys in older children >5 years (as well as ≤ 5 years), especially if there is a long history and programmatic evidence of high sustained birth dose and infant vaccination coverage (e.g. Region of the Americas) or in western Europe. This will also capture the impact on both vertical and horizontal transmission.

The technical challenges of conducting a nationally representative biomarker survey can be minimized through complementing it with other focused surveys targeting high-risk geographical areas or subpopulations likely to have a higher prevalence (e.g. children from particular racial/ethnic groups or migrant communities) or based on programmatic indicators such as HepB3 and HepB-BD and prevalence in pregnant women or women of reproductive age, multiphase methodology serosurveys (71,72) (to reduce the required sample size and increase the power of the serosurvey to confirm elimination) or integrating into existing national surveys for other disease areas, which are often performed using dried blood spot (DBS) testing, such as the Demographic and Health Surveys and AIDS Indicator Surveys.

For countries with a small population size such as the islands in the Pacific, this need not be a hindrance to conducting a serosurvey to verify elimination. Indeed, because of their small population size, it may be actually easier to do the survey and validate elimination. A finite population correction (FPC) factor can be calculated when estimating the required sample size. Even for verification of control, an FPC factor was applied to generate the sample size due to the small size of the population in those islands (73,74).

BOX 3.6 Measurement of childhood prevalence of HBsAg in ≤5 year olds (continued)

B. Additional approach: measurement of the MTCT rate through follow up of HBV-exposed infants in settings using Hep B targeted timely birth dose vaccination (Box 3.2)

Measurement of the additional indicator and target of an MTCT rate of $\leq 2\%$ may be indicated in low-HBsAg prevalence countries (both in the overall population and in ≤ 5 year olds), and in countries using targeted timely HepB-BD where there are subpopulations with still high prevalence and so continuing vertical MTCT of hepatitis B (e.g. among Indigenous populations or migrant populations from high-HBsAg prevalence countries). It may also be considered in settings where population-based serosurveys may not be feasible.

Note (Box 3.2): The MTCT rate is calculated as the proportion of infants with CHB infection, i.e. HBsAg-positive infants (numerator) of those infants exposed (denominator), i.e. infants of HBsAg-positive mothers. Calculation of this transmission rate requires both high-level coverage ($>90\%$) of antenatal HBsAg testing to identify positive mothers, and post-vaccination serological testing (PVST) of exposed infants at 9–12 months of age to identify infected infants. *Note:* some countries such as China recommend PVST at 7–9 months of age. The WHO policy on hepatitis B vaccination recommends that PVST^a should be carried out at least 1–2 months after administration of the last dose of the hepatitis B vaccine series when the antibody response is greatest (7). Several scenarios are possible. The exposed infant may be: (i) infected with HBV; (ii) uninfected and have responded adequately to the hepatitis B vaccine series; or (iii) uninfected but may not have responded to the hepatitis B vaccine and needs to be revaccinated.

It is recognized that some countries providing targeted timely HepB-BD, which do not currently have the required data collection systems and linkages between programmes in place to capture this target, will need to develop this capacity.

^a Routine PSVT testing for immunity is not necessary, but is recommended in the context of HBV elimination in low-prevalence settings where it serves as a tool to estimate EMTCT of HBV (7).

BD: birth dose; CHB: chronic hepatitis B infection; EMTCT: elimination of mother-to-child transmission; GHSS: Global Health Sector Strategy (on viral hepatitis); HepB3: three doses of hepatitis B vaccine; HepB-BD: hepatitis B birth dose; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission

3.3.3 Measurement of programmatic indicators

Indicators for hepatitis B vaccination coverage are based on routinely collected programme data, which are collated through the WHO and UNICEF Estimates of National Immunization Coverage (WUENIC). While the final estimates are informed by data from national authorities and may differ from the reported data, they constitute an independent technical assessment by WHO and UNICEF of the likely true coverage (68). For district-level coverage (where necessary), vaccine administrative coverage data can be used or available data from immunization coverage surveys that are powered to provide district-level estimates.

Timely HepB-BD estimates are produced for vaccination given within 24 h after birth. The timeliness component of HepB-BD administration is required; however, previous surveys and administrative data either do not appropriately collect or report on the strict timing for administration. As a result, WHO and UNICEF estimates for HepB-BD have been overestimated historically, especially for countries with low rates of “institutionalized” births in health facilities (68).

3. Validation of elimination of mother-to-child transmission of hepatitis B: targets, indicators and measurement

Testing coverage of pregnant women can be captured through national data reporting systems for the maternal and child health programme. While many countries collect and report antenatal HIV and syphilis testing data, national surveillance of hepatitis B testing and reporting on pregnant women and their viral loads lags behind. Countries are encouraged to include hepatitis B testing in HIV and syphilis testing programmes and follow this up with integrated data collation and reporting.

Data on the use of antivirals and HBIg during pregnancy should be collected and reported through national data collection systems for maternal and child health and antenatal programmes.

3.3.4 Using mathematical modelling alongside empirical data to determine attainment of the elimination targets

Modelling is not a substitute for the collection of data but can be a tool with which existing data can be used to offer new insights and identify data gaps. Where national empirical data are of sufficient quality and coverage, mathematical models^d using existing in-country data as well as previously published literature may be useful to assess the progress of countries towards the achievement of the impact targets for perinatal and horizontal hepatitis B elimination. They can also be used to project the potential impact of additional preventive (including immunization) and treatment interventions for CHB infections towards the 2030 targets.

To determine if a country has achieved elimination, modelling could be used in the following specific applications:

- to set country-specific targets for programmatic coverage that can be used to guide a strategic response;
- to utilize programmatic data to determine whether it is likely that elimination has been reached in any particular place. This could also inform the commissioning of a biomarker survey. The general assumption is that where global targets for programmatic coverage indicators have been reached then elimination is also likely to have been reached. However, this relies on assumptions made in the course of various modelling exercises that may not apply to all epidemiological contexts. In addition, there would need to be assurance of high-quality programmatic data and robust reporting systems if this methodology was to be adopted;
- to establish whether measurement of MTCT rate may alone be sufficient to establish whether elimination has been reached, and to “convert” a measurement of MTCT to an estimate of the likely incidence rate for the whole population;
- to establish the necessary design of a biomarker survey and to “convert” a measure of HBV prevalence into an estimate of the likely incidence rate for the whole population. The standards for the calculation of these indicators for HBV EMTCT, comparable to the approach used for the Spectrum model for HIV (75), remain to be determined.

^d Mathematical models employed in the process should be independent and peer reviewed, as inputs, assumptions, analysis and outputs will be reviewed in detail during the process of review of the national validation report by the Regional Validation Task Force. In addition, the models used might vary across countries.

4. VALIDATION OF REDUCTION IN HCV TRANSMISSION AND INCIDENCE: TARGETS, INDICATORS AND MEASUREMENT

4.1. Background

A key goal of national hepatitis C elimination programmes is to reduce HCV transmission to very low levels, as well as liver-related mortality, such that HCV infection ceases to be a public health problem. The GHSS on viral hepatitis defines this level as an 80% reduction in global HCV incidence (new cases) in 2030 compared to 2015 levels (4). At the country level, reduction of HCV incidence by 80% can occur only where there is high coverage of evidence-based prevention interventions, including safe injection in health-care settings, harm reduction for PWID, as well as access to high coverage of testing, treatment and cure, especially in populations with ongoing high rates of transmission.

The epidemiology and drivers of new HCV infections vary markedly between countries and regions, and are not well defined in some countries. In some settings, epidemics are predominantly driven by sharing of needles, syringes and drug paraphernalia among PWID and occur among men who have sex with men (MSM), while others have more generalized epidemics that affect the general population and often in particular older age groups, as a result of poor injection safety and infection control in both formal and informal health-care settings (1). Nevertheless, most countries have epidemic profiles that show mixed HCV transmission. As an example, a modelling analysis undertaken in 2019 assessed the degree to which injecting drug use contributes to HCV transmission in different settings (12). Based on these modelled estimates, 31% of countries globally are estimated to have more than 90% of their new infections among PWID; 63% have mixed epidemic dynamics with new infections occurring largely through unsafe health-care procedures but also from risk behaviours related to injecting drug use; and 6% of all countries were estimated to have more than 90% of all new infections originating in health-care settings (12).^e

This chapter outlines simplified criteria for validation of elimination of HCV transmission at the country level, which includes an “absolute” incidence target derived from the GHSS 2030 impact target of an 80% reduction in incidence. It also provides a range of options for countries to measure this impact target according to available surveillance data and capacity.

4.2. Indicators and targets for validation of the elimination of HCV transmission

To achieve validation of elimination of HCV transmission, it is necessary to demonstrate that HCV incidence rates are below a specified absolute threshold at the national level (Box 4.1.). Countries also need to demonstrate achievement of the core programmatic targets, as shown in Box 4.3.

^e Note that these country estimates are associated with some uncertainty due to limitations in data availability and quality, and representativeness.

BOX 4.1 Impact targets for validation of HCV transmission

Countries should have achieved the following impact targets for validation of HCV transmission:

- ≤ 5 new annual HCV infections/100 000 persons

*This HCV incidence should be **representative** of the adult population at country level.*

AND

- ≤ 2 new annual HCV infections/100 PWID

*This HCV incidence should be **representative** of the adult PWID population at country level.*

BOX 4.2 Rationale for absolute incidence impact targets

Absolute incidence targets are proposed on the basis of the Global Health Sector Strategy (GHSS) target of 80% relative reduction in HCV incidence for the following reasons (4):

- They enable direct comparison of progress towards elimination across countries.
- In many countries, baseline estimates of incidence (in 2015) are either unavailable or likely to be inaccurate, with wide confidence intervals. This would mean that relative reduction measures would be rather unreliable. Thus, setting absolute incidence targets reduces the burden on the country for the validation process.
- An absolute incidence impact target has a more direct relationship with the public health burden of HCV in a country, and therefore the goal of elimination of viral hepatitis as “a public health problem”.
- An absolute incidence impact target aligns better with absolute validation targets for mortality and elimination of mother-to-child transmission (EMTCT) of HBV.

The calculation of the absolute global incidence rate of **≤ 5 new annual HCV infections/100 000 persons** is based on the 80% reduction in the HCV incidence target (when compared to a 2015 baseline), as outlined in the GHSS (4). Using the WHO-estimated global annual HCV incidence in 2015 (26) of **23.7 per 100 000 people**, the global annual incidence rate would need to **decrease in the adult population to ~ 4.7 new annual HCV infections per 100 000 people** to meet this target of 80% reduction. To allow for uncertainty in this estimate, this figure has been rounded off to a target of **annual incidence of ≤ 5 new HCV infections/100 000 persons**.

The rationale behind the specific absolute global target of **≤ 2 new annual HCV infections/100 PWID** is based on modelled estimates indicating **an annual incidence in 2015 of 8.6 per 100 PWID** (which varies by region from an estimated 4.3 to 12.5 per 100 PWID) (12). An 80% reduction in the annual incidence rate of 8.6 per 100 PWID accounts thus for a global annual HCV incidence of 1.7 per 100 PWID for validation of elimination, **rounded off to ≤ 2 new annual HCV infections/100 PWID to account for uncertainty**.

Countries that are able to clearly **demonstrate that injecting drug use is not present** in any community across the country need to document only the incidence rate in the general adult population.

BOX 4.2 Rationale for absolute incidence impact targets (continued)

There was initial consideration of a proposal for different HCV incidence impact targets for different epidemic scenarios (i.e. concentrated [among PWID], mixed and generalized epidemics [among the general population]). However, two impact targets among PWID and the general population were adopted instead for all countries regardless of their epidemic profile for the following reasons: the importance of a unified set of indicators across all countries; the challenges in categorizing countries according to HCV epidemic profiles; and the fact that the majority of low- and middle-income countries (LMICs) globally have a mixed epidemic profile with a contribution from both unsafe health-care practices and sharing of needles, syringes and drug paraphernalia among PWID. Demonstrating achievement of both these targets is the optimal approach to achieving and maintaining elimination of HCV transmission as a public health problem. However, it is important for all countries to fully understand the underlying drivers and dynamics of their epidemic, and appropriate monitoring and evaluation as they develop their elimination strategy. Absolute HCV incidence measures should be used where a country is able to measure incidence in a representative sample in the major population groups that are affected by HCV transmission and are contributing to new HCV infections.

4.2.2 Programmatic targets for validation of reduction in HCV incidence

In addition to the above impact targets for validation, countries must demonstrate overall high-level achievement of programmatic targets. These targets are not specific to HCV incidence alone but reflect the targets for eliminating HCV as a public health problem overall. Countries must demonstrate that they have achieved and maintained **for at least 2 years** the following programmatic targets for validating the elimination of HCV as a public health problem (Box 4.3):^f

BOX 4.3 Programmatic targets for validation of reduction in HCV incidence**Testing and treatment**

- ≥90% of persons with chronic hepatitis C virus (HCV) infection diagnosed
- ≥80% of persons diagnosed with chronic HCV infection treated

Prevention

- 100% blood safety
- Injection safety: 0% unsafe injections in health-care settings
- ≥300 syringes and needles distributed/person who injects drugs (PWID)/year^{a,b}

*Note: Countries that are able to clearly **demonstrate that injecting drug use is not present** in any community across the country need to document only the programmatic prevention target for health care-based injection safety.*

a The numerator is the number of sterile needles and syringes distributed in the past 12 months by needle-syringe programmes (NSPs), and the denominator the number of PWID in a country (or subnational geographical entity).

b In addition to this target, it is highly relevant to also document the coverage of opioid substitution therapy and achievement of high coverage (defined as ≥40% of people who inject opioids on opioid substitution therapy at census) as an additional programmatic target.

^f For all programmatic targets, countries need to document availability and coverage in diverse subnational areas and among marginalized and most-affected populations.

BOX 4.4 Rationale for the programmatic targets

The 2016 GHSS on viral hepatitis established programme coverage targets for both preventive interventions (infants with three or more doses of vaccination, neonates who receive birth-dose vaccination within 24 hours of birth, as well as blood and injection safety and harm reduction), diagnosis (diagnosis of people with chronic HBV or HCV infection), and treatment (antiviral treatment of people who are diagnosed with chronic HBV or HCV infection and eligible for treatment). This was partially based on global mathematical models, which showed that achievement of these coverage levels in treatment interventions would result in a country achieving the impact targets for incidence and mortality (4).

Demonstrating these programme coverage levels, in addition to the impact targets, allows country validation of reduction in HCV incidence.

4.3. Approaches to measuring indicators for validation of elimination of HCV transmission

4.3.1 Measurement of impact targets of absolute incidence for validation of elimination of HCV transmission

The optimal approach to measuring the absolute HCV incidence target for validation of elimination will be determined by whether the general or specific population incidence can be assessed directly and generate reliable estimates.

The target incidence rates to document elimination of HCV transmission (≤ 5 new annual HCV infections/100 000 persons; ≤ 2 new annual HCV infections/100 PWID) are ideally generated from empirical data, which are critical for accuracy in estimating the elimination of new HCV infection.

For countries where incidence **cannot** be measured empirically, viraemic prevalence trends of HCV over time can be used as an alternate measurement (Boxes 4.5 and 4.6.).

BOX 4.5 Measuring indicators for validation of elimination of HCV transmission**A. Preferred approaches****Measuring incidence in the general adult population**

Method of choice: direct estimation based on a prospective cohort design (HCV antibody [Ab] retesting of persons who initially tested negative)

Suitable only if: (i) HCV incidence is sufficiently high to balance sample size requirements (suggested threshold: ≥ 0.1 per 100 person-years), and (ii) financial and logistical resources are available to conduct nationwide surveillance among a representative cohort.

Alternative method: monitoring incidence trends based on surveillance for acute HCV infection.

Applicable if: (i) nationwide surveillance system collects high-quality data on acute HCV infection; and (ii) the monitoring system remains constant over time.

BOX 4.5 Measuring indicators for validation of elimination of HCV transmission (continued)

Measuring incidence in specific populations with ongoing risk behaviour and HCV exposure

Method of choice: direct estimation through a prospective cohort design (HCVAb or RNA retesting of persons who initially tested negative for HCVAb or RNA).

Suitable only if: financial and logistical resources are available to conduct surveillance among a representative cohort (no threshold on baseline incidence because it is generally high).

Alternative method A: indirect estimation based on tests for recent HCV infection

Suitable only if: (i) baseline HCV incidence is sufficiently high to balance sample size requirements (suggested threshold: ≥ 10 per 100 person-years); (ii) nationwide repeated cross-sectional studies measuring HCVAb and/or RNA can be conducted.

Alternative method B: direct estimation based on a retrospective cohort design (HCVAb or RNA retesting of persons who initially tested negative for HCVAb or RNA).

Applicable if: (i) high-quality and representative data collected through medical records are available and (ii) testing frequency and population targeted remained consistent over time.

B. Alternative approach: Using trends in reduction in HCV viraemic prevalence over time as a proxy measure for reduction in HCV incidence

It is recognized that, due to resource constraints and limited strategic information infrastructure, the necessary data points for the above methods to measure HCV incidence may not be available in many low- and middle-income countries (LMICs), where the majority of new HCV infections continues to occur. In addition, incomplete surveillance may produce an underestimate of incidence rates, and many LMICs may not have sufficiently robust surveillance for estimating annual incidence rates.

If countries are unable to measure absolute incidence directly through relevant representative population samples, the measurement of reduction in HCV viraemic prevalence can be used as an alternate measure (Box 4.6). This alternative measurement approach assesses a relative reduction in viraemic prevalence as a proxy for an absolute incidence target. Further country pilots and potential additional modelling will establish whether an absolute measure of viraemic prevalence is feasible and preferred.

In this case, countries should demonstrate achievement of $>80\%$ reduction in viraemic prevalence among the adult population (when compared to baseline) *and* among people who inject drugs (PWID) as a proxy for 80% reduction in HCV incidence and is an alternate to direct measurement of the HCV transmission impact targets (≤ 5 new annual HCV infections/100 000 persons; ≤ 2 new annual HCV infections/100 PWID).

As with measuring incidence rates directly, the reduction in viraemic prevalence over time should be representative of the adult population and PWID at country level.

Viraemic prevalence trends over time can be documented through repeat cross-sectional studies that are representative of the respective population groups. These include biobehavioural surveys among PWID and men who have sex with men (MSM) (if RNA testing is incorporated) and general population household surveys.

BOX 4.6 Rationale for reduction in HCV viraemic prevalence as a proxy measure for reduction in HCV incidence

Although incidence is a standard surveillance indicator, it is recognized that many low- and middle-income countries (LMICs) will be challenged to obtain complete and timely annual incidence measures. If countries are unable to measure absolute incidence directly in **relevant** representative population samples, the measurement of reduction in viraemic prevalence can be used as an alternate measure.

≥80% reduction in viraemic prevalence in a representative sample of the adult population and in a representative sample of people who inject drugs (PWID) is proposed as an alternate measure.

Modelling suggests that changes in viraemic prevalence closely track changes in HCV incidence over time with scale up of treatment, where there have not been significant changes in the coverage of prevention interventions (76). This means that if the ≥80% reduction in prevalence of HCV viraemia (chronic HCV infection) in the general population and in specific subpopulations that drive transmission (e.g. PWID) has been achieved, then an 80% reduction in HCV incidence is also likely to have been met.

Nevertheless, an increase in the prevalence of high-risk practices (e.g. in injecting drug use) as well as in the scale up of prevention interventions will also have an impact on HCV incidence and the correlation with HCV viraemic prevalence. For example, if there is a notable increase in health-care-related safe injection practices and/or harm reduction for PWID over the same time period – the target of 80% reduction in HCV viraemic prevalence may need to be adjusted.

This method of measuring reduction in HCV viraemia trends over time can be used if a country does not have representative absolute incidence data from the main population groups for HCV transmission, but does have good ongoing chronic HCV prevalence estimates in these population groups. This method needs a well-established baseline measurement of viraemic prevalence. Further country pilots and potential additional modelling will establish whether an absolute measure of viraemic prevalence is preferable and more adapted.

4.3.2 Measurement of programmatic indicators

The GHSS target for diagnosis is that 90% of people living with hepatitis B or C have been diagnosed by 2030 (4). The numerator for this indicator in terms of HCV diagnosis is the number of persons with chronic HCV infection who have been diagnosed, and the denominator is the estimated number of persons with chronic HCV infection. Disaggregation should be done by sex, age, high-risk/-burden population for viral hepatitis B and C, pregnant women and HIV infection (77). Proposed methods include counting the number of persons reported with chronic infection (clinical and laboratory notification systems with deduplication) and dividing this number by the estimated size of the population infected, or using survey data where persons are asked if they are aware of their viral hepatitis infection status in population surveys.

The GHSS target for treatment coverage is 80% of people diagnosed with hepatitis B or C and eligible for treatment are treated with recommended antivirals (4). For HCV, treatment coverage is defined as the proportion of persons diagnosed with chronic HCV infection (i.e. HCV RNA or HCV core antigen [HCVcAg] positive) and started on treatment during a specified time frame (e.g. 12 months) over the number of persons diagnosed with chronic HCV infection (defined as positive for HCV RNA or positive for HCVcAg) for the specified time period (12 months).

The WHO *Consolidated strategic information guidelines for viral hepatitis* (29) determined that a 0% proportion of unsafe health-care injections in health-care facilities is one of the essential prevention targets for viral hepatitis elimination. Data for this programmatic target are best taken from health facility surveys or can be alternatively derived from population surveys (e.g. Demographic and Health Surveys). This programmatic indicator is expressed as the proportion of injections given with new, sterile syringes.

The GHSS target for harm reduction as a core prevention intervention for elimination of viral hepatitis is set at 300 sterile syringe/needle sets distributed per person per year for PWID. For this programmatic indicator, the numerator is the number of sterile needles/syringes distributed in the past 12 months by needle–syringe programmes (NSPs) and the denominator the number of PWID in a country. While it is recognized that many countries will have challenges in collecting these data, data sources include those from harm reduction programmes, population size estimation exercises or national hepatitis programmes. Additional disaggregation can be done by sex, age and type of setting (community, prison/closed setting).

4.3.3 Using mathematical modelling alongside empirical data to determine attainment of the elimination targets

Modelling is not a substitute for the collection of data but can be a tool whereby existing data can be used to offer additional insights and help with estimations. Mathematical modelling may be used to integrate measurements of HCV viraemic prevalence, coverage of prevention, testing and treatment interventions and potentially mortality data to estimate absolute HCV incidence and establish whether the targets defined here have been met.

5. VALIDATION OF MORTALITY REDUCTION FROM HBV AND HCV: TARGETS, INDICATORS AND ASSESSMENT

5.1. Background

Viral hepatitis is a leading cause of death, causing an estimated 1.1 million deaths annually (1). Around 96% of deaths due to viral hepatitis are attributable to complications of chronic HBV (66%) infection and chronic HCV (30%) infection from decompensated cirrhosis and HCC (78). Highly effective treatments are available for both infections, with short-course DAA curative treatment for hepatitis C infection (24), and long-term antiviral treatment with tenofovir or entecavir for people with chronic HBV infection (22). Without treatment, an estimated 20–30% of people with chronic HBV or chronic HCV will develop cirrhosis and are at risk of decompensated cirrhosis and HCC (79,80). People with chronic HBV may develop HCC in the absence of cirrhosis, but such cases are rare in those with chronic HCV (81,82).

WHO impact targets for elimination in the GHSS for viral hepatitis include a 65% reduction in global HBV-related and HCV-related mortality compared to the 2015 baseline, alongside a reduction in HCV and HBV incidence. To accelerate global progress towards elimination, accurate surveillance data are required for mortality and country-level programme monitoring indicators (4). It is recognized that the impact of prevention and treatment interventions will take a much longer time to have an impact on mortality compared to incidence, especially for hepatitis B, due to the large number of infected adults who were born before introduction of the hepatitis B vaccine.

This chapter outlines criteria for the validation of reduction in liver-related mortality due to HBV and/or HCV to meet the targets for elimination of viral hepatitis at the national level. It also provides options for countries to measure or estimate mortality rates according to specific country contexts, given the significant differences in the HBV and HCV epidemics across WHO regions, and in available surveillance data and capacity for gathering accurate and adequate data.

5.2. Indicators and targets for validation of reduction in HBV and HCV mortality for elimination

5.2.1 Impact targets for validation of HBV and HCV mortality

To validate a reduction in hepatitis B and C mortality to support elimination of viral hepatitis as a public health problem, it is necessary to demonstrate attainment of a specific absolute threshold for mortality from viral hepatitis B and C of $\leq 6/100\ 000$ per year (HCV-related and HBV-related mortality rate of $\leq 2/100\ 000$ and $\leq 4/100\ 000$ per year, respectively) at the country level by 2030 (Box 5.1). In addition, countries need to demonstrate achievement of the core programmatic targets, as shown in Box 5.3.

BOX 5.1 Impact targets for validation of reduction in mortality due to HBV and/or HCV

Countries should have achieved the following impact targets for validation with regard to hepatitis B and/or hepatitis C mortality:^a

- **A combined mortality rate of $\leq 6/100\ 000$ per year**
- **Absolute HBV-related mortality rate of $\leq 4/100\ 000$ per year**
and
- **Absolute HCV-related mortality rate of $\leq 2/100\ 000$ per year**

a The calculation of these targets for HCV and HBV alone is based on the global relative contribution of HBV and HCV to global mortality.

At the country level, for the documentation of reduction in mortality from viral hepatitis, countries should have achieved a combined mortality rate of $\leq 6/100\ 000$ per year. Based on global contributions of HBV and HCV to mortality, this equates to an HCV-related mortality rate of $\leq 2/100\ 000$ per year. Similarly, for the documentation of reduction in mortality from HBV only, countries should have achieved an HBV-related mortality rate of $\leq 4/100\ 000$ per year.^g The adoption of these proposed differential mortality rates for HBV and HCV at country level will depend on the national epidemiology of HBV and HCV, and their relative contribution to overall mortality, and will require further evaluation during the pilot phase (Box 5.2). It is recognized that attainment of the incidence and mortality targets may occur at different times, as it may take much longer for mortality to drop, following an incidence reduction.

BOX 5.2 Rationale for absolute mortality indicators for HBV and HCV

In the Global Health Sector Strategy (GHSS) for viral hepatitis, elimination of viral hepatitis as a public health problem by 2030 is defined as a 90% reduction in incidence (95% for HBV and 80% for HCV) and a 65% reduction in mortality from HBV and HCV, compared with the 2015 baseline (4). In addition, the GHSS states that global HBV- and HCV-related mortality should be reduced from 1.4 million deaths in 2015 to less than 500 000 by 2030 (i.e. 65% for both viral hepatitis B and C). Global population projections for 2030 are ~8.6 billion, and so the absolute 2030 mortality rate that would equate to the 500 000 deaths is calculated as 5.9/100 000 for HBV and HCV combined, rounded to 6/100 000 population. The relative contribution of HBV and HCV to liver-related global mortality is 66% and 30%, respectively), which is equivalent to 4/100 000 for HBV and 2/100 000 for HCV per year.

Overall, the use of absolute targets for annual mortality is the preferred indicator for validation of elimination versus a relative reduction in mortality for the following reasons:

- It enables direct comparison of progress towards elimination across countries.
- A direct measurement or an indirect estimate of liver-related mortality for 2030 obviates the need to establish viral hepatitis-related mortality in 2015, and so reduces the burden on the country validation process.

g The calculation of these targets for HCV and HBV alone is based on the global relative contribution of HBV and HCV to global mortality.

BOX 5.2 Rationale for absolute mortality indicators for HBV and HCV (continued)

- Baseline estimates of mortality in 2015 are unavailable in many countries or likely to be inaccurate, with wide confidence intervals. This would mean that even if estimates of mortality were available in 2030, relative reduction measures would also be unreliable.
- Absolute mortality targets have a more direct relationship with the public health burden of HBV and HCV in a country, and therefore the goal of elimination of viral hepatitis as “a public health problem”.

Potential limitations of the absolute target are as follows:

- For those countries with HCV and HBV mortality rates already below 6/100 000 per year, there may be a disincentive to take measures to further reduce mortality.
- The absolute HCV- and HBV-specific mortality rates lack precision, and since HBV and HCV are often undiagnosed infections, their associated mortality may be undercounted. With a relative change, the bias is likely to be similar at both time points.
- Some countries, notably those with a high burden and high liver-related mortality rates in 2015 at baseline, may find it easier to achieve the relative mortality target (65% reduction) because of the larger disease burden at baseline. This is corroborated by modelled estimates (Center for Disease Analysis Foundation [CDAF]) (61). The use of a relative mortality target in high-burden countries requires further evaluation.
- In addition, since the relative reduction in mortality of 65% is a widely recognized global target from the 2016 GHSS, many countries have already adopted this in their national strategies or action plans.

5.2.2 Programmatic targets for validation of HBV and HCV mortality

In the near- to medium term, mortality relating to hepatitis is determined by the proportion of people living with HBV or HCV diagnosed and treated (Box 5.3). These targets can be used in relation to the diagnosis and treatment of HCV or HBV, depending on which validation option is requested by the country (HBV and/or HCV) (see section 2.3.2).

BOX 5.3 Programmatic targets for validating the elimination of HBV and HCV mortality

Countries should have achieved and maintained for at least 2 years the following programmatic targets for validating the elimination of HBV and HCV mortality:

- ≥90% of persons with chronic hepatitis B or C virus infection diagnosed
- ≥80% of eligible persons diagnosed with chronic hepatitis B virus infection treated
- ≥80% of persons diagnosed with chronic hepatitis C virus infection treated

BOX 5.4 Rationale for programmatic targets

The 2016 GHSS on viral hepatitis established programme coverage targets for preventive interventions, diagnosis (diagnosis of 90% of people with chronic HBV or HCV infection), and treatment (antiviral treatment of 80% of people who are diagnosed with chronic HBV or HCV infection and eligible for treatment). This was based on global mathematical models, which showed that achievement of these coverage levels would result in a country achieving the impact targets for incidence and mortality (4).

National and cohort data showing the impact on mortality of attainment of high coverage of testing and treatment interventions. The most important determinant of mortality, in the short- to medium term, is access to early diagnosis and effective antiviral treatment to prevent disease progression to cirrhosis and reduce development of HCC and liver-related deaths. For HBV, this is long-term antiviral treatment with tenofovir (or entecavir) to achieve sustained suppression of HBV DNA below detectable levels (22), and for HCV, short-course curative treatment with DAA regimens (24).

Over the past five years, data have emerged of the impact of scale up of testing and treatment for HBV and HCV on mortality from study cohorts as well as national datasets. Attainment of cure (sustained virological response [SVR]12) with DAA treatment for HCV is associated with a near-90% reduction in liver-related mortality, an 80% reduction in the incidence of HCC, and a 75% reduction in all-cause mortality (23,25,83). Similarly, long-term suppressive antiviral therapy with tenofovir or entecavir for HBV infection has been shown to reduce cirrhosis, progression to decompensated cirrhosis and the risk of HCC and liver-related deaths (84–87).

DAA: direct-acting antiviral (drug); HCC: hepatocellular carcinoma

5.3. Approaches to measuring indicators for hepatitis B and C mortality

There is a paucity of quality data on liver-related mortality due to HBV and HCV, particularly in low- and middle-income countries, and challenges in generating complete country-specific empirical datasets for HBV- and/or HCV-related mortality (among deaths due to HCC and decompensated cirrhosis).

There are several potential approaches and methodologies that can be used for measuring and monitoring mortality due to HBV- and HCV-related liver conditions in countries. Countries should review and identify the most appropriate option according to their epidemiological profile, health system context, and availability and quality of surveillance data. The advantages and disadvantages of the different options are summarized in the boxes on their rationale. Where possible, a relatively standardized methodology should be used across multiple countries.

The different approaches are as follows:

- direct measurement of liver-related mortality due to HBV and/or HCV;
- indirect estimates of liver-related mortality due to HBV and/or HCV using
 - a) HCC incidence as a proxy for liver-related mortality;
 - b) estimation of the attributable fraction using sentinel site surveillance, and application of these estimates to vital statistics data on cirrhosis/HCC;
 - c) reduction in HCV viraemic prevalence for HCV-related mortality;
 - d) estimation of trends in mortality by mathematical modelling using data from a), b) or c).

The capacity for assessing mortality rates varies widely across the world: some countries (or jurisdictions within countries) have good HCV and HBV testing levels, sophisticated public health surveillance systems, and notification registries that allow data linkage with, for example, hospitalizations, cancer and death registries. These settings, such as in some European countries, Australia and Canada, can both closely monitor trends in HBV- and HCV-related mortality, and use empirical data to validate and adjust mathematical models to estimate and project the impacts of interventions. At the other end of the spectrum, many countries, particularly low-income ones, have low screening levels, and lack the capacity to monitor liver-related deaths, even from HCC, at the population level (88).

5.3.1 Direct measurement of liver-related mortality due to HBV and/or HCV

The optimal approach to measuring the absolute mortality indicator is to do so through direct measurement.

The measurement of an absolute decline in mortality requires the capacity to estimate and monitor the number of liver-related deaths among people with HBV and/or HCV infection. Options for empirical data-based or direct mortality monitoring include death certifications, cancer registries and sentinel clinics. However, for many settings, this would require a significant change in coding practices, and even the format of the death certificate, not just mining death certificate data.

5.3.2 Indirect measurement of liver-related mortality due to HBV and/or HCV

There are several different methodologies that can support the estimation of a national mortality rate based on alternative approaches to measurement, where direct measurement of the national mortality rate is not possible.

A. Use of HCC incidence as a surrogate for liver-related mortality

This approach consists of identifying new HCC cases that can be attributed to either HBV or HCV, and is therefore a country-level proxy of liver-related mortality due to HBV and HCV. This approach requires the availability or establishment of population-based surveillance systems for monitoring people with HBV and HCV infection, as well as linkage between databases of diagnoses and cancer registries for viral hepatitis or hospitalization records of HCC diagnosis (Box 5.5) (89–92).

BOX 5.5 Rationale for the use of HCC incidence as a proxy for HBV- and HCV-related mortality

Worldwide, primary liver cancer, which is mostly hepatocellular carcinoma (HCC), is the fifth leading type of cancer and the third leading cause of cancer-related deaths (93). The relative contribution of HBV and HCV infections to HCC varies across different regions. For example, HBV-related HCC is more dominant in Asian (except for Japan) and African countries (94). Poor survival following HCC means that trends in HCC incidence correlate well with trends in HCC mortality (92,95).

The major advantage of using HCC incidence as a surrogate indicator for liver-related mortality is that new HCC cases are often more reliably recorded than decompensated cirrhosis. This is because there is more reliable surveillance for both clinical diagnostic events and deaths due to HCC. The focus for such an indicator and measurement mechanism would be to optimize surveillance mechanisms for monitoring cancer diagnoses and deaths, including those that are HCC related, rather than a broader focus on viral hepatitis liver-related mortality. Limitations include: the need for considerable resources to optimize data collection; lack of cancer registries as well as access to histological data in many countries, as well as data on attributable causes such as limited access to data on HBV and HCV; and that trends in HCC incidence do not always reflect trends in liver-related mortality, particularly in settings where HCC management is improving. In addition, there are concerns that a focus on HCC would underestimate hepatitis-related mortality – for example, in the European Union, HCC-related deaths account for 55% of the mortality burden due to viral hepatitis.

B. Use of sentinel networks of clinical sites for estimation of attributable fraction

The use of clinic-based sentinel networks in countries provides a mechanism for monitoring cases of HCC as well as decompensated cirrhosis in the absence of a formal registry, and the attributable fraction of cases due to HBV and HCV. This population-specific caseload can then be extrapolated to the national level to provide a national estimate of HBV- and HCV-related mortality (Box 5.6).

BOX 5.6 Rationale for measuring and monitoring the HBV-/HCV-attributable fraction of HCC and cirrhosis among all cases with HCC and cirrhosis

WHO has developed a protocol to assist sentinel centres (e.g. hepatology or gastroenterology units) to estimate the proportion of people with HBV- and HCV-related cirrhosis and HCC. This proportion can be used to estimate the fractions of these sequelae attributable to HBV and HCV infection and to then generate national HBV and HCV mortality rates. The WHO protocol provides detailed methodology on sampling procedures and data collection, as well as guidance on data analysis, data ownership and ethical considerations (96).

A major advantage of the use of clinic-based sentinel networks is that this information is already utilized by the Institute for Health Metrics and Evaluation (IHME) as part of their global burden of disease modelling approach (97). A further advantage is that a relatively small number of representative sites could be utilized to provide an ongoing surveillance mechanism. Limitations include the fact that the characteristics of cases at larger tertiary centres may not be representative of community caseloads, and referral patterns may vary based on local patterns of comorbidities and primary health care capacity.

C. Reduction in HCV viraemia as alternative impact indicator for reduction in HCV-related mortality

It is recognized that, due to resource constraints and limited infrastructure for collection of strategic information, the necessary data to measure HCV mortality may not be available in many low- and middle-income countries. If countries are unable to measure absolute mortality directly and are not using any of the other indirect measurements outlined here, they can consider using the decline over time in viraemic HCV prevalence as an alternate measure for validation of HCV elimination.^h This is used also as an alternative impact indicator for reduction in HCV incidence (Box 5.7).

BOX 5.7 Reduction in HCV prevalence as an impact target for reduction in HCV-related mortality

In this case, countries should have achieved the following impact target for validation with regard hepatitis C mortality:

- $\geq 80\%$ reduction in viraemic prevalence in the adult population when compared to baseline

*As with measuring mortality rates directly, the reduction in viraemic prevalence over time should be measured in a sample that is **representative** of the adult population at country level.*

Viraemic prevalence trends over time can be documented through repeat cross-sectional studies that are representative of the respective population groups; these include biobehavioural surveys among PWID and MSM (if RNA testing is incorporated) and general population household surveys.

MSM: men who have sex with men; PWID: people who inject drugs

BOX 5.8 Rationale for the proxy measure of $\geq 80\%$ decline in prevalence of HCV viraemia

Modelling by the Center for Disease Analysis Foundation (CDAF) for selected countries – including the United Kingdom, Egypt, United States of America and Mongolia – demonstrates a relationship between HCV treatment coverage, declines in HCV viraemic prevalence and mortality (61) (Dore G, Alavi M, Valerios H, Janjua NZ, Hutchinson S, Dirac M et al. Monitoring HBV- and HCV-related mortality: a background paper [unpublished observations]).

The key advantage of this indicator is that it removes the need for ascertaining deaths due to HBV- or HCV-related liver conditions and the same proxy measure can also be adopted for a reduction in incidence. However, it would require incorporation into national surveillance programmes and systems for monitoring population-level viraemic prevalence through population-level surveys.

^h There is a less convincing argument for the role of viraemic prevalence in HBV-related mortality measurement.

BOX 5.8 Rationale for the proxy measure of $\geq 80\%$ decline in prevalence of HCV viraemia (continued)

The use of this measure should be applied only where there are significant treatment programmes, as otherwise a reduction in prevalence could be due to increased mortality (and/or other prevention measures like a reduction in unsafe injections).

An important limitation is that this proxy measure relates only to HCV infection. Since only a limited number of people with chronic HBV infection (12–25%) are eligible for antiviral therapy (98) and treatment is rarely curative, a measure that incorporates an estimation of the eligible population that was on suppressive antiviral therapy would need to be established. Such a measure would be more complex to estimate and monitor than one for a change in the prevalence of HCV viraemia.

Estimation of trends in mortality by mathematical modelling

Modelling is not a substitute for the collection of data but can be a tool whereby existing data can be used to offer new insights and help with estimations. While the preferred approach is for countries to collect mortality data directly, i.e. a national death registry, if this is not feasible, a mathematical modelling process of the impact indicator, using available existing representative empirical data or proxy measures, e.g. HCC incidence, attributable fraction of HCC cases due to HBV/HCV and HCV viraemic prevalence, may be considered. Modelling-based mechanisms have the potential for calibration using epidemiological data and would be suitable whether the target was absolute mortality or relative reduction. Such modelling could be used to model mortality on the basis of sequential measurement of prevalence, or estimation of viraemic prevalence or empirical data from HCC incidence or attributable fraction. These modelling approaches allow comparison with empirical data, if available, and could serve as the primary method in settings where there are limited mortality data but sufficient other epidemiological and programmatic data, as has been undertaken in Pakistan (99).

Modelling data could also be used to predict the impact of testing and treatment programme coverage or other service delivery data on mortality. This option, however, requires access to and ongoing monitoring of primary data for service delivery interventions (particularly antiviral therapy coverage) and then development of models to incorporate these parameters as well as data on other relevant comorbidities (e.g. alcohol use disorder) that affect progression of liver disease.

At present, there are several reasonable approaches to mathematical modelling of viral hepatitis mortality. The use of mathematical modelling to complement empirical data for the estimation of country-level mortality should therefore be clearly described and justified, the important sources of uncertainty reported and model validity addressed (Box 5.9). Additionally, assumptions should be stated, ascertained and discussed, and sources of parameters and empirical data communicated prior to request for WHO validation.

BOX 5.9 Rationale for indirect estimation of HBV- and HCV-related mortality using mathematical modelling

Data on death registration or cancer registration is inadequate or of low quality in most countries. The lack of systematic and cause-specific death registries in most countries means that a reliance on direct monitoring of trends in HBV- and HCV-related death notifications would be problematic. In many high- and some middle-income countries, dynamic models of transmission using available programmatic data are commonly used to understand the HBV and HCV epidemics and project the impact of prevention, diagnosis and treatment scale up (61,100). Bayesian meta-regression and cause of death ensemble models (CODEm) have also been used to triangulate between data on multiple indicators and produce estimates of the incidence and prevalence of HBV and HCV and their sequelae, including mortality, and to gauge the impact of interventions (101).

The major strength of using mathematical modelling is that there are at least two well-established international modelling groups involved in country-level estimation of HBV- and HCV-related mortality for many years. A potential limitation is the diversity of modelling methodologies that have been used by different countries. The options are for countries to use their own in-country established groups or adapt a preferred international model. In the case of disease progression models, with co-factor (such as alcohol) and treatment impact parameters within the models that are not specific to individual countries, additional country-specific data will be needed to provide context-specific estimates of impact. Likewise, country-level estimates from meta-regression and CODEm provide uncertain estimates for locations where data for one or more indicators are scarce, and would need country-specific data for at least some model inputs to obtain sufficient certainty to validate elimination.

5.3.3 Measurement of programmatic coverage indicators for HBV and HCV mortality

The GHSS target for diagnosis is that 90% of people living with hepatitis B and/or C have been diagnosed by 2030. The numerator is the number of persons with chronic HBV and/or HCV infection who have been diagnosed and the denominator is the estimated number of persons with chronic HBV and/or HCV infection (4). Disaggregation should be done by sex, age (adults/children, more than 15 and less than 15 years of age), high-risk/-burden population for viral hepatitis B and C, pregnant women and HIV coinfection (102). Proposed methods are to count persons reported with chronic HBV and HCV infection (clinical and laboratory notification systems with deduplication) and dividing this number by the estimated size of the population infected or using survey data where persons are asked if they are aware of their viral hepatitis infection status in population surveys.

The GHSS target for treatment is 80% of people diagnosed with hepatitis B or C and eligible for treatment are treated with recommended antivirals. For hepatitis B, this is calculated as the number of persons with chronic HBV infection (defined by HBsAg-positive serological status) who are currently receiving treatment of the estimated 12–25% of the population living with chronic hepatitis B eligible for treatment (98) (based on modelled estimates or prevalence data from population-based serosurveys). These programme data should be disaggregated by sex, age, high-risk or high-burden populations and HIV status.

For HCV, treatment coverage is defined as the proportion of persons diagnosed with chronic HCV infection (i.e. HCV RNA or HCVcAg positive) started on treatment during a specified time frame (e.g. 12 months) over the number of persons already diagnosed with chronic HCV infection (defined as positive for HCV RNA or for HCVcAg) for the specified time period (12 months). All individuals already diagnosed to date but treated and cured would be excluded from this calculation.

6. IMPLEMENTATION CONSIDERATIONS FOR VALIDATION OF ELIMINATION

Implementation considerations for validation of elimination are those health systems and related criteria that can be used to determine the feasibility of achieving or sustaining the elimination of viral hepatitis, including for the pathway to elimination.

- The national report and dossier for assessment of validation of viral hepatitis elimination should include a chapter on implementation considerations, as described below (see the overall template for a national report in Annex 1).
- A checklist is provided for countries in Annex 2 to facilitate the systematic writing of the chapter on implementation considerations in the national hepatitis elimination report. It is suggested that a country highlights key findings from this checklist in the report's narrative, and that the full checklist is provided in an annex to the report.
- The regional validation process will review and provide feedback on the implementation considerations chapter in the national hepatitis elimination report as part of the Regional Validation Task Force (RVTF) report.
- Implementation considerations should not be considered essential criteria for validation of elimination. However, these will be considered during revalidation, and a country should be able to demonstrate that it has addressed the recommendations relating to implementation considerations made during the initial validation process.

Development of the national hepatitis elimination report should be integrated into the overall review process of the national hepatitis programme and, as appropriate, into the broader national health system and/or programme reviews for other diseases, including those for multidisease elimination programmes, national health information, national immunization strategy, laboratory services and human resources. The aim is to improve efficiencies, reduce costs and ensure inter-programme synergies and consistency.

6.1. Ensuring the quality of strategic information systems and data

Countries should have a national health management information system that can generate and analyse reliable data necessary for monitoring and assessing progress against the hepatitis elimination criteria and impact and programme targets. Where possible, these data should be collected routinely through the national health management information system, in line with WHO guidance on viral hepatitis strategic information (29,103,104) and the global reporting system for hepatitis (105), but with consideration also for data collection from sentinel sites where the national system is weak.

Evidence of data quality in the national hepatitis elimination report will be assessed through a review of the national system capacity to provide quality, disaggregated and representative data, particularly related to impact indicators for the incidence and mortality of HBV and HCV.

6. Implementation considerations for validation of elimination

Evidence of data of high quality in the national hepatitis elimination report will be assessed through a review of the national system capacity to provide robust and representative data (and, where appropriate, disaggregated by geographical area and risk groups), particularly related to assessment of the impact indicators for the incidence and mortality of HBV and HCV. It is recognized that while national surveys can provide data of high quality on impact indicators, this may be a challenge for programme-level data, as it is based on routine data collection and sometimes limited geographical coverage.

The assessment should be based on the WHO *Comprehensive monitoring and evaluation framework for viral hepatitis B and C* (102) and the WHO *Consolidated strategic information guidelines for viral hepatitis: planning and tracking progress towards elimination* (29) that summarizes the overall approach to collecting, analysing, disseminating and using strategic information on viral hepatitis at local, subnational, national and international levels. It describes the use of strategic information at various stages of the response in the context of strengthening broader health information systems and highlights the 10 core programmatic indicators for elimination of viral hepatitis.

National hepatitis elimination reports should focus on detailing evidence to support the quality of data sources that provide proof of achievement of elimination. These data points relate specifically to the impact and programmatic indicators described in this guidance. Countries are encouraged to utilize existing data infrastructure on national surveillance and hepatitis (and other diseases) and, where necessary, engage in obtaining additional specific information required for the validation process.

In addition to standard viral hepatitis surveillance data points for impact indicators or programmatic goals, as well as health-care facility surveys, quality data should also be sourced from the EPI for hepatitis B vaccination, alongside HBsAg testing in pregnant women and antiviral prophylaxis in those eligible. In addition, data on prevention interventions, and testing and treatment for hepatitis B and C should be obtained from programme data. These should be able to capture service delivery and outcome data from both the public and private health sectors.

The validation assessment should also consider the national capacity to undertake or commission mathematical modelling for viral hepatitis to model incidence, prevalence or mortality into the future. For example, national surveillance and programmatic data as well as data from the published literature (e.g. systematic reviews and meta-analysis of prevalence studies) on the coverage of interventions such as vaccination, testing, diagnosis and treatment as well as seroprevalence, liver cancer cases and mortality may provide inputs into the model. Through this process, it is possible to estimate progress towards or achievement of the impact indicators for hepatitis elimination, as indicated in the previous sections, where the specific data points are available and nationally representative. The report also provides an opportunity to include reflections on potential limitations of the outputs.

The modelling process is highly technical and requires both empirical data and national consensus on key data inputs and assumptions. In addition to reviewing data inputs, analysis and outputs of the model, the mathematical model and its assumptions used to generate the data for the national validation report should also be subject to a thorough independent peer review by modelling experts.

The checklist provided in Annex 2 provides further details on key elements that should be assessed in the area of data quality.

6.2. Ensuring the quality of diagnostics, laboratory services and medicines

Meeting laboratory standards is an important requirement for validation of hepatitis elimination. Laboratories that contribute data points to the surveillance system and for validation, including serosurveys, and for clinical diagnosis and programme implementation should:

- verify that RDTs (for HBsAg and for HCV antibodies or other serological tests) and hepatitis molecular tests are verified in accordance with international standards by stringent regulation authorities (SRAs), or the WHO Prequalification Programme;
- apply a quality assurance mechanism routinely and consistently to laboratories and verify that they participate in a domestic external quality assessment (EQA) programme (106). EQA allows testing conducted by a laboratory, testing site or individual user to be compared to that of a source outside the laboratory, in addition to internal quality assurance;
- put in place a laboratory quality management system to ensure that hepatitis tests are procured, stored and used in accordance with manufacturers' protocols;
- verify that personnel with proficiency in the performance of diagnostic tests have been trained in accordance with the manufacturers' instructions and nationally recommended algorithms.

In terms of ensuring that quality standards are met for medicines, it is important that national testing and treatment guidelines specify which medicines and diagnostic assays should be used. Furthermore, it is important to ensure that medicines used for the treatment of viral hepatitis have been approved and registered by a stringent national authority and included in the national essential medicines list. The checklist provided in Annex 2 provides further details on the key elements that should be assessed in the area of data quality of laboratories and medicines.

6.3. Ensuring the quality of prevention, diagnosis and treatment services, including that of the vaccination programme

A programme quality assessment is part of the validation process and is an in-country exercise.

The programme components assessed are only those relevant to the elimination of hepatitis B and C as public health problems. These include the **provision of quality-recommended prevention, diagnostic and treatment services for viral hepatitis**, liver cirrhosis and liver cancer, accompanied by laboratory and data systems targeted at affected populations for viral hepatitis in both the public and private sectors.

To achieve validation of EMTCT of hepatitis B, HCV incidence and the mortality targets for hepatitis B and C, countries must demonstrate the achievement of the programmatic targets that are outlined in the document *and* provide evidence that high-quality services for hepatitis exist in both the public and private health sectors in both urban and rural areas. These aspects of programme quality will be addressed in the national hepatitis elimination report under the chapter on implementation considerations.

6. Implementation considerations for validation of elimination

For **EMTCT of hepatitis B**, strengthening of the maternal and child health (MCH) and vaccination programmes, coordinated and linked to the HIV, viral hepatitis and STI programmes, is key (107). The national programme should include comprehensive ANC services, including hepatitis B testing and treatment prophylaxis, preferably integrated with HIV and syphilis testing and treatment programmes, treatment and care for hepatitis B-infected pregnant and postpartum women, with timely birth-dose vaccination of their newborns. Immunization stakeholders, such as ministries of health and Gavi, should regularly assess the quality of the national immunization programme, including for hepatitis B birth dose and infant vaccination. Priority should be placed on leveraging these existing efforts and assessments of the national immunization programme to inform about the performance of hepatitis B immunization-related activities and so avoid duplication. Interprogrammatic relationships at the national level should be further developed. This should include an assessment of equity in HBV vaccine access, with evidence that high-quality services for HBV PMTCT are being delivered at the lower-performing subnational administrative units (e.g. municipalities) and underserved communities (e.g. migrant populations). In addition, there should be evidence that health workers are considered a priority population for HBV vaccination.

Programmatic assessment of **interventions to prevent HCV and HBV transmission** in adolescents and adults should include availability and quality assessments of safe injection policies and practices in health facilities, safe blood products, effective harm reduction interventions, such as high coverage of NSPs (potentially with low dead-space needles and syringes) and OST, and accessible HCV treatment to populations with high HCV incidence and/or prevalence (e.g. PWID and those in closed settings such as prisons).

Hepatitis testing and treatment assessment should include the availability of quality screening (HBsAg and HCVAb), confirmatory testing (e. g. HBV DNA and HCV RNA) and disease staging (APRI [e.g. aspartate aminotransferase-to-platelet ratio index], elastography) for the general population as well as vulnerable groups – as per the WHO testing and treatment guidelines (21,22,24). There should be evidence of health-sectorwide linkage to hepatitis care and treatment for all individuals testing positive, including blood donors and high-risk populations. Recommended antiviral treatment for hepatitis B should be limited to those effective medicines with a high barrier to resistance. Highly effective DAAs that include pangenotypic combination therapy for hepatitis C and treatment for hepatitis B should be registered, included in the national guidelines, on the national list of essential medicines, and available through public health systems. Cost should not be a barrier to care and treatment for people living with chronic hepatitis. **Liver cancer screening** using recommended practices should be available to those with cirrhosis, and detection and treatment programmes for liver cancer should be included in the public health system.

Countries are encouraged to work with the RVTF or Regional Validation Secretariat (RVS) to determine an appropriate selection process to ensure that the assessment accurately reflects the lowest-performing subnational administrative unit. To be eligible for validation, a country does not have to meet the programmatic targets for elimination in all subnational units, but there must be evidence that performance in subnational units has been reviewed and that substantial efforts are being made to address low-performing units. These efforts should include outreach to impoverished, migrant, remote or key populations and those in closed settings. There should be evidence that hepatitis services are being offered, accessed and have achieved success that can be maintained.

The checklist provided in Annex 2 provides further details on the key elements that should be assessed in the area of programme quality.

6.4. Ensuring community engagement, human rights and equity in access to services

Equity, human rights, gender equality and community engagement principles are relevant to the elimination of viral hepatitis. The validation assessment needs to take these principles into consideration.

The concepts of **no one left behind and health equity** are central to the WHO GHSS (4), and the broader WHO mission (103,108). WHO hepatitis guidance reflects equity, human rights, gender equality and community engagement as fundamental principles that impact on countries' effective implementation of action to address viral hepatitis (21,22,24,109).

With regard to **"triple elimination"**, a key requirement for country validation of EMTCT of HIV, syphilis and HBV is that the interventions to reach impact and programme targets have been implemented in a manner consistent with international, regional and national human rights standards, have engaged the community of women living with HIV and HBV and have taken gender equality into consideration. These same principles apply to the elimination of viral hepatitis in general.

Many individuals with chronic HBV and HCV infection are from **marginalized or stigmatized** populations such as PWID, MSM, people in prison, migrants, Indigenous peoples, and have poor access to health care. WHO guidance recommends specific focus on these populations regarding access to health care, including to hepatitis services (13).

Concerns that mandatory or coercive approaches might be used among highly affected and vulnerable populations highlight the importance of adequate information, informed consent, appropriate health worker training and rights-based legal frameworks to facilitate access to testing and treatment services (21,22, 24). Stigma and discrimination among key and vulnerable populations at high risk of HIV, HBV and HCV have been well documented (110). Despite increased access to highly effective HCV treatment, stigma, discrimination and criminalization continue to persist in many parts of the world. For hepatitis B, although there is substantial variation in stigma and discrimination, as well as human rights violations across regions and countries, criminalization is less common than with HIV (111–113).

Additionally, gender equality is a very important aspect of public health and viral hepatitis elimination. Gender equality considerations are particularly relevant in the context of vertical transmission of HIV, HBV and syphilis, as gender norms and practices implicitly shape sexual and reproductive health (SRH) and the rights of women, as well as the health outcomes of their children. Promoting and ensuring gender equality can improve the opportunities for women and girls to access the necessary information and services. In addition, providing the opportunity for engagement of young women in health services and offer testing to establish hepatitis B status during or before pregnancy is a critical first step to preventing further MTCT.

The relationship between hepatitis C and gender is complex. In most countries, population prevalence of hepatitis C is higher in males, and increases with age. In addition, there is also a predominance of men among people who use or inject drugs, MSM (by definition), as well as residents of closed settings, such as prisons. Nevertheless, women who use drugs and women in closed settings are especially vulnerable for a variety of reasons – in many countries, sociocultural and economic inequality means that women living with hepatitis C may have poorer access to hepatitis C prevention, diagnosis and treatment services.

National responses should be cognisant of the hepatitis prevention, diagnosis and treatment needs of gender-diverse groups, including transgender populations, and support active measures to include this high-risk and marginalized population in accessing these services.

6. Implementation considerations for validation of elimination

Fundamentally, the goal of the **GHSS is to save lives** through global attainment of the incidence and mortality impact targets. Saving lives requires the active participation of people living with and at risk for hepatitis B or C in recommended interventions for prevention, diagnosis and treatment of hepatitis. The following implementation considerations have been identified as potential barriers to achieving these mortality and incidence reductions and should be assessed and included in national validation reports.

The checklist provided in Annex 2 provides further details on key elements that should be assessed in the area of equity, human rights, gender equality and community engagement.

6.4.1 Human rights

The important issues to be considered in reviewing hepatitis B and C in the context of human rights obligations in law and practice are as follows:

1. availability of voluntary and accessible viral hepatitis testing and treatment;
2. evidence of confidentiality and privacy of hepatitis B and C testing and treatment;
3. evidence of absence of legal discrimination (for employment status, access to education, housing, social benefits);
4. documentation of stigma-free access to health care, testing and treatment for HBV and HCV in policy and practice;
5. evidence that people living with hepatitis are informed of their status and educated about their medical care;
6. evidence of the absence of drug use, sexual orientation status, incarceration experience, immigration status or profession as a criterion for exclusion from hepatitis testing and treatment;
7. evidence of the possibility of health-care access without disclosure of or discrimination against key population status;
8. decriminalization of populations at risk or most affected by viral hepatitis, including people who use drugs, sex workers, MSM.

6.4.2 Equity

The goal for delivering for equity – the absence of inequalities in health that are avoidable by reasonable means – is Strategic direction 3 of the GHSS (4). It has a focus on strengthening health and community systems to deliver high-quality services to achieve equitable coverage and maximum impact.

Assessment of the equity principles of hepatitis elimination during the validation process includes the following:

1. evidence that national hepatitis elimination targets and interventions include populations that are most affected;
2. evidence of service decentralization, especially with regard to access to prevention, testing and treatment for vulnerable populations and communities, including outside major urban centres;
3. evidence of the integration of hepatitis services in general health service provision and other services as appropriate – which may include services for HIV, STIs, other infectious diseases, MCH, vaccination, migrant health, reproductive health, harm reduction and OST;

4. evidence of care linkages at different levels of the health system with clear definition of the relative contribution and roles of community services, primary health care peer workers, referral care and hospital care;
5. evidence of cultural responsiveness in the health-care system and efforts to reduce cultural and language barriers;
6. evidence of disaggregation of data by key variables such as gender, geography and risk groups to enable detection of differences across population groups;
7. evidence of inclusion of core essential hepatitis interventions, medicines, diagnostics and vaccines within the national health benefit package to promote equity of access.

6.4.3 Gender equality

Gender equality is an additional important aspect of public health and elimination of viral hepatitis.

Assessment of gender equality that supports elimination during the validation process includes the following:

1. evidence of the availability of epidemiological data disaggregated by gender;
2. evidence of disaggregation of programmatic data on hepatitis prevention, diagnosis and treatment services by gender;
3. evidence of the presence of a national policy that includes specific reference to addressing the gender needs of those living with or at risk for viral hepatitis, including transgender populations;
4. evidence of accessible hepatitis testing and treatment services for women;
5. evidence of efforts to address stigma/discrimination for both men and women living with hepatitis.

6.4.4 Community engagement

The meaningful participation of people living with hepatitis B and C and their families and communities is of critical importance in determining and developing national and subnational policies for affected communities, and should be actively promoted. Community engagement is also important and highly relevant for supporting and implementing service delivery.

Community engagement can be assessed through evidence of formal and active national-level participation of affected persons in the development, implementation and evaluation of the national hepatitis responses.

Assessment of community engagement supporting elimination during the validation process includes the following:

1. evidence of affected community representatives in the national hepatitis task force;
2. national hepatitis policy documents explicitly state the active participation of the affected community in hepatitis prevention, diagnosis and treatment services;
3. evidence of peer-led or peer navigation interventions for hard-to-reach, rural and marginalized populations;
4. government funding for representative groups of the hepatitis-affected community.

**SECTION THREE:
GOVERNANCE AND PROCESS
FOR VALIDATION**

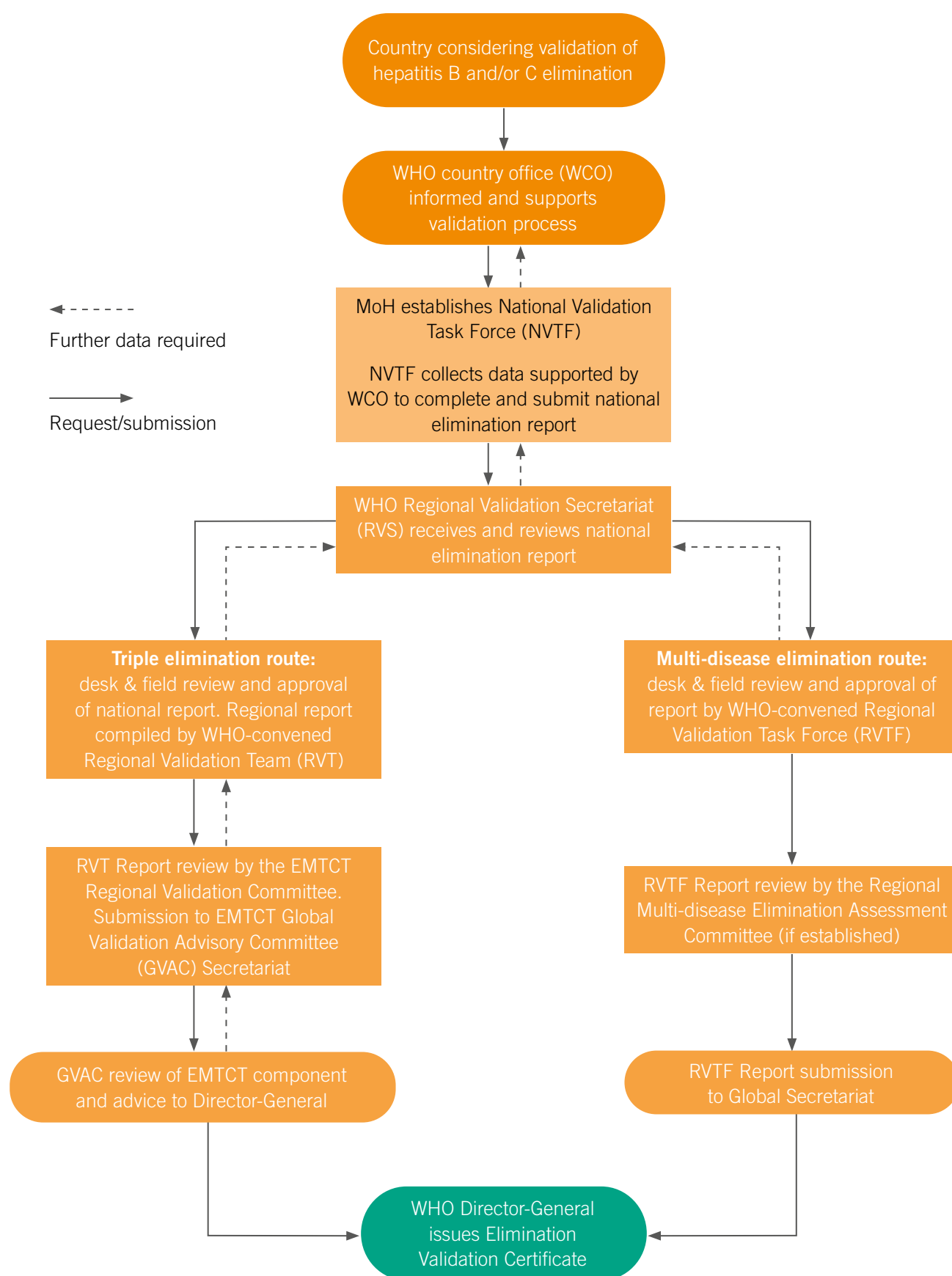
7. VALIDATION OF ELIMINATION: THE PROCESS OF GOVERNANCE

7.1. Overview

The process of validation of the elimination of viral hepatitis as a public health problem aims to confirm the attainment of the impact targets of hepatitis B and C incidence and mortality as detailed in the GHSS, with supporting evidence of adequate programmatic coverage and quality through an inclusive and effective national implementation response. Important principles to be considered by any country before application for validation include the following:

- The process is country led.
- Achieving elimination targets for viral hepatitis has been prioritized within the national health strategy and immunization development plans, and will contribute to reducing the overall national disease burden.
- Achieving elimination targets is feasible and adequate resources are available or could be mobilized.
- There is support and commitment from key stakeholders, including populations most affected and the broader community.
- The process, achievement and maintenance of validation will act as an incentive for accelerated and intensified action. It will also serve as a strong advocacy tool to generate broad support in addressing the burden of viral hepatitis.
- Validation is meaningful to the country and adds to other national accountability mechanisms to monitor progress against national strategies and commitments.

A schematic representation of the overall process of governance of validation is shown in Fig. 7.1.

FIG. 7.1 Governance process flowchart for the validation of viral hepatitis B and/or C as a public health problem

7.2. Process of governance and integration within the existing infrastructure for validation of elimination

The validation process for the elimination of viral hepatitis should be integrated as far as possible with existing national monitoring, validation and certification processes, and infrastructure for disease elimination, including that of other communicable diseases (e.g. malaria, vaccine-preventable diseases, and EMTCT of HIV and syphilis (59)) and approaches proposed by the Global Framework for Multi-disease Elimination, which aims to promote greater programme integration, alignment and efficiency (personal communication from Richard Carr on Global Framework for Multi-disease Elimination [GFME]).

Countries electing to be validated for all components of the elimination of hepatitis B and/or C as a public health problem will focus on the whole strategy. Governance of the process will be guided by relevant committees and secretariats at the national, regional and global levels in the “multi-disease elimination” route, as illustrated in Fig. 7.1. This approach aims to make efficient use of human resources and regional capacity. To assess for validation, regions should have the required expertise in those disease areas and health systems aspects, including viral hepatitis. Of note, the process for assessing attainment of the targets on the “path to elimination” of viral hepatitis as a public health problem is completed at the regional level, unless a region specifically requests global-level engagement for higher-level advocacy.

If a country elects to be validated only for the EMTCT component of its viral hepatitis strategy, applications will be channelled through the triple MTCT elimination route, which involves independent assessment of regional reports by the GVAC and Regional Validation Committee (RVC), where available, for EMTCT (114). This route uses the existing process designed for dual validation of EMTCT of HIV and syphilis, which is now being strengthened to address triple elimination. Notably, this route is currently available to countries opting to be validated for one, two or three conditions of the “Triple Elimination Initiative”, which seeks to promote integrated validation of EMTCT of HIV, syphilis and HBV. Furthermore, if a country that has been validated for all components of the elimination of hepatitis B as a public health problem and later chooses to seek validation for triple elimination, its validated status for EMTCT of HBV will be recognized (if still valid) without the need for a reassessment.

In addition, countries that are validated as having achieved EMTCT of HBV by universal HepB-BD and childhood immunization alone (on account of the longstanding nature of their response programmes and resulting low background prevalence of viral hepatitis) will be recognized as having achieved the “elimination of MTCT of HBV by immunization”. Countries with targeted timely HepB-BD interventions as well as those with a higher burden of HBV as a result of delayed implementation of immunization interventions will need to demonstrate and achieve elimination with adequate coverage of maternal HBsAg testing and treatment of eligible women, and will be recognized through the triple EMTCT validation route.

The resources (human and financial) required to support the validation process for hepatitis elimination should be integrated into the national health plan, optimizing the use of existing resources and maximizing interprogrammatic efficiencies.

7.3. The submission process

Six steps are required for recognition of the elimination of viral hepatitis through validation by WHO.

1. **Request sent to WHO.** Once the national government has reviewed its programmes and is confident that it can meet the qualifying criteria, the national government takes the decision to be assessed for validation of elimination and informs the WHO Representative in the country office, who then relays the request to the WHO regional office. In the absence of a WHO country office, the initial step would be to go directly to the regional office. WHO responds by formally communicating the elimination criteria and processes for validation, including the documents necessary to provide clear, convincing evidence that the specific impact and process targets have been met.
2. **Formulation and implementation of a validation plan of action, preparation and submission of the national hepatitis elimination report.** The national Ministry of Health coordinates the planning and development of a detailed national hepatitis elimination report based on criteria provided by WHO. The Ministry of Health convenes a task force for validation of national hepatitis elimination, as part of the broader national Multi-disease Elimination Assessment Committee (where one exists), and consistent with WHO guidance. The task force is responsible for synthesizing, reviewing and analysing documentation and other information submitted by the Ministry of Health and other sources in order to prepare a draft national elimination report. A broad national consultative process should enable inputs into the report from all key stakeholders. The task force submits the report to the Ministry of Health, which then formally submits it to WHO. Throughout the process, WHO provides technical support and facilitates the coordination function of the Ministry of Health. WHO's support is managed through the WHO country office.
3. **Evaluation by RVTF experts supported by the WHO Secretariat through the regional validation report.** The national hepatitis elimination report is submitted by the respective Ministry of Health through the WHO country office to the respective WHO regional office to the regional WHO Multi-disease Elimination Secretariat, if relevant.
4. The WHO Secretariat convenes a regional task force for validation of hepatitis elimination (as part of a broader regional Multi-disease Elimination Assessment Committee). The RVTF is responsible for reviewing the national report, gathering additional information if required, analysing all relevant inputs and preparing a regional validation report on hepatitis elimination. The WHO Secretariat facilitates the work of the RVTF, including organization of country site visits or virtual review meetings with country counterparts to verify the content of the national report and related documents. The regional report is submitted to the WHO Regional Secretariat, with recommendations as to whether validation of elimination should be granted.
5. **Report review by the Regional Multi-disease Elimination Assessment Committee (if established) for the final decision on approval to be taken.** The WHO Secretariat shares the report with WHO and non-WHO experts on the Regional Multi-disease Elimination Assessment Committee for critical review. Committee members vote on the outcome of the assessment, which is shared with the WHO Secretariat (regional and global). The final regional-level decision to validate the elimination of viral hepatitis as a public health problem is taken by the respective WHO Regional Director.

6. **The approval decision is conveyed to WHO headquarters for further action.** The WHO Global Hepatitis Programme Secretariat reviews the regional report, recommendations and decisions to determine what further action might be required, and to inform global accountability and reporting on hepatitis elimination. The respective WHO Regional Director and the WHO Director-General communicate the final decision to the national government through an official letter.
7. **Optional publication of validation in the WHO *Weekly Epidemiological Record*.** The WHO Secretariat publishes positive decisions in the *Weekly Epidemiological Record*.

While validation of elimination is documented at the global level, recognition of the path to elimination is completed at the regional level only, unless a region specifically requires that this be escalated to the global level for higher-level advocacy purposes.

7.4. Decisions on the maintenance of validation, revalidation and reversal of validation

Countries that have been validated for achieving the elimination of viral hepatitis as a public health problem will be assessed every five years for maintenance of validation. Consideration should be given to synchronizing revalidation with relevant national programme reviews and revalidation of other related diseases. To be assessed for maintenance of validation, the Ministry of Health is asked to submit a brief report to the respective Regional Multi-disease Elimination Assessment Committee, which includes the following information:

- Executive summary
- Brief description of changes, if any, in the overall health system, including financing, since validation
- Brief description of changes, if any, to the viral hepatitis programme since validation
- Key findings for the five years after the last validation review
- Provision of data, sources and methodology for the required impact and programmatic indicators sufficient to demonstrate continued maintenance of elimination targets
- Provision of responses to all WHO recommendations made at the time of validation to show progress
- Outline of the potential risks to sustaining elimination of viral hepatitis.

The WHO Secretariat will work with the Regional Multi-disease Elimination Assessment Committee to reach one of the following conclusions: maintain validation without recommendations; maintain validation with recommendations; defer maintenance of validation pending requests for clarification or more information from the country or do not maintain validation.

7.5. National level

7.5.1 The national hepatitis elimination report

The national hepatitis elimination report should have the following elements:

- Executive summary
- Brief description of the overall health system, including financing
- A description of the national viral hepatitis programme

7. Validation of elimination: the process of governance

- Provision of data, sources and methodology for the required impact and programmatic indicators sufficient to demonstrate proof of achievement of these indicators
- Provision of a response to all implementation considerations for elimination of viral hepatitis detailed in the implementation considerations document. Reference is made to the national elimination report template in Annex 1.
- Outline of the potential risks and accompanying strategies for sustaining elimination of viral hepatitis.

A full description of and template for the national hepatitis elimination report can be found in Annex 1.

7.5.2 National Validation Secretariat

The WHO country office's role is to support the National Validation Task Force (NVTF) in preparing a national hepatitis elimination report detailing evidence of elimination. The National Validation Secretariat (NVS) is hosted by the WHO country office and supports the Ministry of Health in its overall coordination function. It serves as the first point of contact for national stakeholders and as an intermediary between the Ministry of Health, the NVTF and the regional secretariat. It convenes other key national partners contributing to efforts at hepatitis elimination and associated health issues, including United Nations (UN) agencies. It provides technical support to the Ministry of Health and the NVTF, together with relevant UN and other partners, to assist with assessing the programme for the elimination of hepatitis B or C or both, and then developing and preparing the national validation report.

7.5.3 National Validation Task Force

The NVTF is established by the Ministry of Health and is responsible for writing the national elimination report and submitting it on behalf of the Ministry of Health through the NVS, and addressing any queries or clarifications regarding the report, including from the NVTF. NVTF members should have the technical expertise to contribute to the national validation report. The following considerations should inform the establishment of the NVTF:

- The NVTF may in the future be a task force of a broader National Multi-disease Elimination Assessment Committee that coordinates/oversees assessment of the efforts to eliminate all diseases targeted for elimination in the country.
- The NVTF is a multidisciplinary team comprising a wide cross-section of professionals from various services and programmes, such as reproductive, MCH, laboratory, health systems, health information (including epidemiology/surveillance/monitoring), immunization, hepatology, and relevant legal and civil society representatives. If the report includes EMTCT (of HBV), at least one individual with expertise in coinfection of HIV or syphilis with HBV should be included to provide linkage and integration to these areas. The Multi-disease Elimination Assessment Committee should provide broader health systems expertise and link the NVTF with other relevant national disease elimination efforts (i.e. for assessing laboratory, disease surveillance and human resources capacity).
- Preference should be given to members with more than one skill set to ensure that all areas are covered, and the group is close to the minimum size. It is expected that the majority of NVTF members would be national experts, but external experts may be considered, particularly from neighbouring countries that have already completed an elimination validation process.
- All NVTF members should sign statements of confidentiality and declarations of interest reviewed by the Ministry of Health or the Secretariat, as necessary, to identify any real or perceived conflicts of interest. Participation should be voluntary and not remunerated by WHO or the Ministry of Health.

7.6. Regional level

7.6.1 Regional Validation Secretariat

The role of the WHO regional office is twofold: to support the NVTF and NVS, as well as the RVTF in their assessment of the national elimination report; and to act as a conduit for submission of the report to the Regional Director or the Regional Multi-disease Elimination Assessment Committee, where it exists, through the global Secretariat to facilitate ultimate final approval and confirmation of the validation of elimination of viral hepatitis. Where validation ends at the regional level, the Regional Validation Secretariat (RVS) is responsible for facilitating congratulatory or other communication from the WHO Regional Director to the country.

The role of the RVS is as follows:

- establishing, convening and coordinating the RVTF;
- coordinating regional and supporting the coordination of national validation processes and activities;
- approving and submitting the final elimination reports from the RVTF to the WHO Regional Director or the Regional Multi-disease Elimination Assessment Committee through the Global Validation Secretariat (GVS);
- providing communication between regional and national stakeholders and the global level, including communicating the decision of the Regional Director regarding validation or maintenance of validation to the NVS and any request for clarification;
- collaborating with the country to ensure that reports on maintenance of validation are completed every five years and that the report addresses the recommendations made by the RVTF.

7.6.2 Regional Validation Task Force

The RVTF oversees the validation processes in the region and the establishment of teams or working groups dedicated to the validation process for a specific country. It is responsible for submitting a complete and accurate regional validation report to the RVS, which in turn submits it to the Regional Multi-disease Elimination Assessment Committee, where it exists. Where the validation process ends at the regional level, the RVTF is responsible for making a recommendation to the Regional Director for communication to the country. The responsible RVTF should be fully integrated as part of the Regional Multi-disease Elimination Assessment Committee, where it exists.

Steps in the tasks of the RVTF are as follows:

- Review national hepatitis elimination reports from candidate countries, make an assessment of compliance with global-/region-specific minimum criteria, request additional information or clarification.
- Collaborate with the RVS.
- Conduct an in-country or virtual validation visit for an in-depth assessment, supporting the NVTF (joint visit led by WHO, but which includes members of the RVTF).
- Consider the country visit report on hepatitis elimination and assessment of the national elimination report.
- Thereafter, the full RVS will advise whether a country candidate (i) has successfully achieved hepatitis B or C elimination (or both) and can be recommended for validation to the GVS; or (ii) is on the hepatitis B or C path to elimination (or both) and can be recommended for validation to the Regional Secretariat and subsequently the Regional Director.
- Provide recommendations to a country to support ongoing monitoring and maintenance of validation in coordination and aligned with those of regional advisory bodies.

7.7. Global level

7.7.1 Global Validation Secretariat

The GVS is hosted by WHO headquarters and is staffed by the Department of Global HIV, Hepatitis and Sexually Transmitted Infections Programmes. The GVS provides coordination, leadership and oversight to the global validation process. The GVS includes representatives from other relevant departments, especially in the areas of blood and injection safety; reproductive, maternal, neonatal, child and adolescent health; and immunization/vaccine-preventable diseases across the communicable and noncommunicable disease spectrum. It works in collaboration with external partners, including other UN agencies (e.g. UNAIDS, UNICEF, United Nations Population Fund [UNFPA], UNITAID and UNODC).

7.7.1.1 Global Multi-disease Elimination Framework

The Global Multi-disease Elimination Framework (GMEF) seeks to harmonize and standardize elimination concepts, terminology and validation processes in planning for future elimination strategies and plans, and promotes greater standardization, alignment and coordination across existing disease elimination processes. This includes identifying opportunities to advance disease elimination efforts across multiple diseases through people-centred services, with a focus on integrated primary health care, optimizing resources for multi-disease elimination, defining essential interventions and service packages for multi-disease elimination, promoting cross-programme efficiencies and implementing common structures and processes for validation and certification of achievement of disease eradication and elimination targets.

7.7.1.2 Global Validation Advisory Committee

The GVAC is an independent advisory body that provides technical assistance and supports oversight of the validation process for EMTCT of HIV, syphilis and hepatitis B to determine whether countries' efforts towards achieving EMTCT of HIV, syphilis and hepatitis B, as well as the corresponding pathways to elimination meet the global validation criteria.

The GVAC will provide a global-level and WHO Secretariat review of regional hepatitis elimination reports submitted in the context of triple elimination. Specifically, this would occur only where a country is requesting validation of EMTCT of hepatitis B outside validation of elimination of hepatitis B as a public health problem and concurrently with either HIV or syphilis EMTCT validation. Where a country requests validation for HBV EMTCT alone, or elimination of viral hepatitis as a public health problem (HBV and/or HCV), the GVAC will not be required to review for validation of the HBV EMTCT component, and the validation process will remain solely within that for validation of hepatitis.

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ANNEXES

ANNEX 1. NATIONAL ELIMINATION REPORT TEMPLATE

The following template can be helpful in structuring the national elimination report.

- Executive summary
- Country context
 - Description of the NVTF and summary of goals of the review
 - Demography, basic health indicators
 - Country epidemiological profile for hepatitis (trends, drivers of infection)
 - Brief description of all levels of the health system, including financing, special group needs and access where applicable.
- A description of the viral hepatitis policies and programme, including laboratory services, data management, equity
- Provision of data, sources, representativeness of data and methodology for the required impact and programmatic indicators sufficient to demonstrate proof of achievement of these indicators
- Provision of a response to all implementation considerations for elimination of viral hepatitis detailed in the chapter on implementation considerations and demonstration of key findings, including consistency of achievements across geographical areas
- Outline of the potential risks and accompanying strategies for sustaining elimination of viral hepatitis.

ANNEX 2. CHECKLIST FOR SUPPORTING EVIDENCE OF IMPLEMENTATION CONSIDERATIONS FOR VALIDATION OF ELIMINATION

Note: This checklist is provided to facilitate the writing and documentation of the implementation considerations in the national hepatitis elimination report; it is suggested that the full checklist be filled in and used as an annex to the main national elimination report. Depending on the option that is chosen for validation of elimination or path to elimination, not all items of the checklist apply (e.g. when applying for validation of elimination of HCV as public health problem only, the items limited to HBV do not apply).

Implementation component	Present (Y/N)	Detailed information on component (e.g. when developed/updated, etc.)	Evidence of statement and references
1. Data quality			
1.1 Country has a standard mechanism/system in place to collect and report on the WHO 10 core programmatic indicators			
1.2 Programmatic indicators are well defined at the country level and data inputs regularly checked			
1.3 National information system is able to provide disaggregated and representative data relating to hepatitis impact indicators			
1.4 National information system is able to capture service delivery and outcome data from both the public and private health sector			
1.5 National capacity to undertake or commission mathematical modelling using country data for viral hepatitis is available			
1.6 Viral hepatitis case reporting is included in the national surveillance system			
1.7 Surveillance system can differentiate between acute and chronic viral hepatitis cases			
1.8 Attributable fraction of HCC and cirrhosis are estimated on a national level			
1.9 Registry for liver cancer in place			
1.10 Registry for cirrhosis and/or decompensated cirrhosis in place			
1.11 National registry for chronic hepatitis patients established			

Implementation component	Present (Y/N)	Detailed information on component (e.g. when developed/updated, etc.)	Evidence of statement and references
2. Laboratory and medicines quality			
2.1 Laboratory quality management system is in line with existing WHO laboratory guidance			
2.2 Internal and external quality assessment (EQA) programme present			
2.3 National hepatitis reference laboratory oversees the domestic laboratory network and laboratory quality management (including procurement, staff proficiency, etc.)			
2.4 Hepatitis tests and molecular diagnostics are quality assured and WHO prequalified or approved by a relevant regulatory authority			
2.5 Hepatitis B antivirals for treatment are domestically registered and are WHO prequalified or approved by a relevant regulatory authority			
2.6 Hepatitis C direct-acting antivirals are domestically registered and WHO prequalified or stringent regulatory authority (SRA) approved			
3. Quality hepatitis programming, policy and practice			
3.1 National infection control and blood safety policies are consistent with WHO recommendations and implemented accordingly			
3.2 National vaccination programme is consistent with WHO recommendations and implemented accordingly (including assessment of rationale if targeted timely birth dose)			
For elimination of mother-to-child transmission (EMTCT) of hepatitis B, there is evidence of comprehensive antenatal care (ANC) services and timely birth-dose vaccination of their newborns as well as hepatitis B testing and treatment prophylaxis, preferably integrated with HIV and syphilis testing			
3.3 Evidence-based harm reduction interventions (including needle and syringe programming) are implemented in consistence with WHO recommendations			
3.4 National hepatitis testing and diagnosis algorithms are consistent with WHO recommendations and implemented accordingly			
3.5 National hepatitis B and C treatment protocols are consistent with WHO recommendations and implemented accordingly			
3.6 Hepatitis B vaccination is available for health workers and high-risk and vulnerable populations			
3.7 Hepatitis B testing and treatment are available across the country (all regions and districts) and to vulnerable and high-risk populations (including in prisons) through public health systems			
3.8 Hepatitis C testing and treatment are available across the country (all regions and districts) and to vulnerable and high-risk populations (including in prisons) through public health systems			
3.9 There is evidence of liver cancer screening for eligible persons living with chronic viral hepatitis			
3.10 Hepatitis workforce training (in person/online training, curriculum and mentorship) is included in national health policies			
3.11 Programmatic indicators and programme quality have been reported from the lowest-performing subnational unit			

Implementation component	Present (Y/N)	Detailed information on component (e.g. when developed/updated, etc.)	Evidence of statement and references
4. Human rights			
4.1 Evidence of voluntary viral hepatitis B and C testing and treatment			
4.2 Evidence of confidentiality and privacy of hepatitis B and C status and treatment			
4.3 Evidence of absence of legal discrimination (for employment status, access to education, housing, social benefits)			
4.4 Evidence of stigma-free access to health care and treatment for those with HBV and HCV			
4.5 Evidence that people living with hepatitis are informed of their status and provided adequate counselling			
4.6 Evidence of the absence of drug use, sexual orientation status, incarceration experience, immigration status or profession as a criterion for exclusion from hepatitis treatment			
5. Equity			
5.1 Evidence of testing and treatment service decentralization and integration			
5.2 Evidence of disaggregation of programme and epidemiological data by gender and other equity stratifiers ⁱ			
6. Gender equality			
6.1 Evidence of the presence of national policy that includes specific reference to addressing the gender needs of those living with or at risk for viral hepatitis, including access and stigma/discrimination			
6.2 Evidence of efforts to address stigma/discrimination of men and women living with hepatitis			
7. Community engagement			
7.1 Evidence of affected community representatives in the national hepatitis task force			
7.2 National hepatitis policy documents explicitly state the active participation of affected community in hepatitis prevention, diagnosis and treatment services			
7.3 Evidence of peer-led navigation in hepatitis service delivery for hard-to-reach, rural and marginalized populations			
7.4 Evidence of government support or funding for representative groups of the hepatitis-affected community			

ⁱ Equity stratifiers are those variables that can be measured to identify population subgroups having poorer health or health-care access.

**Interim guidance for country validation
of viral hepatitis elimination**

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