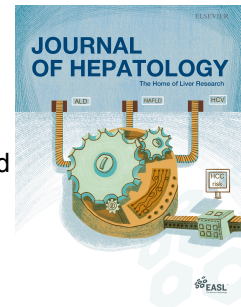


Journal Pre-proof

Barriers to viral hepatitis elimination and new strategies to overcome them in low- and middle-income countries

Erwan Vo-Quang, Maud Lemoine, Jean-Michel Pawlotsky



PII: S0168-8278(26)02887-4

DOI: <https://doi.org/10.1016/j.jhep.2026.08.032>

Reference: JHEPAT 10675

To appear in: *Journal of Hepatology*

Received Date: 10 February 2026

Revised Date: 30 July 2026

Accepted Date: 31 August 2026

Please cite this article as: Vo-Quang E, Lemoine M, Pawlotsky JM, Barriers to viral hepatitis elimination and new strategies to overcome them in low- and middle-income countries, *Journal of Hepatology*, <https://doi.org/10.1016/j.jhep.2026.08.032>.

This is a PDF of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability. This version will undergo additional copyediting, typesetting and review before it is published in its final form. As such, this version is no longer the Accepted Manuscript, but it is not yet the definitive Version of Record; we are providing this early version to give early visibility of the article. Please note that Elsevier's sharing policy for the Published Journal Article applies to this version, see: <https://www.elsevier.com/about/policies-and-standards/sharing#4-published-journal-article>. Please also note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2026 The Authors. Published by Elsevier B.V. on behalf of European Association for the Study of the Liver.

Barriers to viral hepatitis elimination and new strategies to overcome them in low- and middle-income countries

Erwan Vo-Quang^{1,2}, Maud Lemoine^{2,3}, Jean-Michel Pawlotsky^{1,4}

¹Team “Viruses, Hepatology, Cancer”, Institut Mondor, INSERM U955, Université Paris-Est, Créteil, France; ²MRC The Gambia Unit at London School of Hygiene and Tropical Medicine, Fajara, The Gambia; ³Department of Digestion, Metabolism and Reproduction, Imperial College London, London, UK; ⁴National Reference Centre for Viral Hepatitis B, C and D, Department of Virology, Hôpital Henri Mondor (AP-HP), Université Paris-Est, Créteil, France

Short title: Barriers to viral hepatitis elimination in LMICs

The authors received no specific funding for this work.

Corresponding author: Prof. Jean-Michel Pawlotsky, Department of Virology, Hôpital Henri Mondor, 1 Rue Gustave Eiffel, 94010 Créteil, France.

Tel: 33-1-4981-2827; Fax: 33-1-4981-4831

E-mail: jean-michel.pawlotsky@aphp.fr

Keywords: Viral hepatitis elimination; low- and middle-income countries; cascade of care; point-of-care diagnostics; decentralised and integrated care; mother-to-child transmission; hepatitis B and C treatment simplification; hepatocellular carcinoma prevention.

Word count: 9204

Number of Tables: 4

Number of figures: 2

Conflict of interest statement: E.V.-Q. has no conflicts of interest to disclose. M.L. has received consultancy fees from Abbott, Cepheid and GlaxoSmithKline. J.-M.P. has served as an advisor and/or speaker for AbbVie, Diagnostics for the Real World, Gilead and GlaxoSmithKline.

Author contributions: E.V.-Q. wrote the first draft of the article. M.L. and J.-M.P. critically revised the article. J.-M.P. finalised the article and supervised the writing process.

Abstract

Chronic infections with hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis D virus (HDV) are major causes of cirrhosis and hepatocellular carcinoma (HCC) worldwide. The greatest burden is borne by low- and middle-income countries (LMICs). Despite the availability of highly effective preventive tools, simplified diagnostics, and affordable antiviral therapies, progress toward the World Health Organization's (WHO) goal of eliminating viral hepatitis as a public health threat by 2030 is insufficient in most LMICs. Gaps persist throughout the entire care continuum, from vaccination and the prevention of mother-to-child transmission to screening, confirmatory testing, linkage to care, treatment initiation, and long-term follow-up. Structural weaknesses in health systems, limited laboratory infrastructure, centralised models of care, financial constraints, stigma, and fragmented disease-specific programmes continue to hinder large-scale implementation. This article examines the main barriers encountered across the viral hepatitis care cascade, from prevention and testing to treatment and long-term follow-up. It discusses practical approaches to overcoming them, including simplified diagnostic and treatment pathways, point-of-care and near-point-of-care technologies, self-testing, integrated testing platforms, decentralised care, and task sharing. Attention is given to the prevention of mother-to-child transmission, the needs of populations underserved by conventional healthcare systems, and comorbidities that influence liver disease progression. In conclusion, technological advances alone will not be sufficient. Progress will also depend on stronger health systems, decentralised models of care, and the integration of viral hepatitis services into existing healthcare programmes.

Key points

- Low- and middle-income countries account for most of the morbidity and mortality associated with chronic viral hepatitis, yet coverage of diagnosis and treatment remains low.
- Timely administration of the HBV birth dose remains a major bottleneck, owing to delivery constraints, cold-chain requirements, and gaps in policy and financing.
- Multi-step HCV diagnostic and pretreatment pathways contribute to loss to follow-up, whereas simplified and one-step approaches can shorten the care cascade.
- Decentralised care and task sharing can support treatment scale-up, particularly when backed by reliable sample-referral systems and near-point-of-care testing.
- Integrating viral hepatitis services into existing HIV, syphilis, antenatal care, and other disease programmes can increase testing and treatment coverage.
- Expanded harm reduction services, together with policies that reduce criminalisation and stigma, are central to HCV micro-elimination among people who inject drugs.
- Dried blood spots, oral fluid testing, self-testing, multiplex assays, and simplified molecular platforms may reduce the number of steps between screening and treatment if referral and quality-assurance systems are maintained.
- Emphasising the prevention of hepatocellular carcinoma may help to raise the political priority of viral hepatitis and attract additional funding.

Introduction

Nearly 300 million people worldwide are living with chronic viral hepatitis. Of these, 240 million people are infected with the hepatitis B virus (HBV), nearly 5% of whom are also infected with the hepatitis D virus (HDV). Additionally, an estimated 47 million people are infected with the hepatitis C virus (HCV) [1,2]. Chronic viral hepatitis infections are a major cause of cirrhosis and hepatocellular carcinoma (HCC) [3,4]. The World Health Organization (WHO) estimates that approximately 1.3 million people die from viral hepatitis each year [1,2]. Most patients living with HBV and HCV infection reside in low- and middle-income countries (LMICs), where most new infections and hepatitis-related morbidity and mortality occur. This highlights the need to prioritise control efforts in these settings [5]. The WHO has set the goal of eliminating viral hepatitis as a major public health threat by 2030, with defined incidence and mortality targets [6].

Over the past 20 years, effective tools have been developed to control viral hepatitis. Point-of-care (POC) tests for hepatitis B surface antigen (HBsAg) and anti-HCV antibodies are available in areas without access to laboratories [7]. Dried blood spots (DBS) can also be used to detect and quantify viral antigens, antibodies and/or nucleic acids in a central laboratory following shipment. Highly effective vaccines have been available for hepatitis B since the 1980s. Combining HBV vaccination at birth with antiviral prophylaxis significantly reduces mother-to-child transmission (MTCT) of HBV. In addition, nucleoside and nucleotide analogues have been available since the early 2010s to treat chronic HBV infection. For hepatitis C, pangenotypic HCV direct-acting antivirals (DAAs) have more recently transformed the management of chronic infection. Effective treatments for both HBV and HCV are now widely available as

affordable generic medicines. However, these interventions have not yet been scaled up in many LMICs, which are lagging far behind on the path to eliminating viral hepatitis by 2030 [1]. Context-adapted strategies are urgently needed to accelerate progress in these settings.

In 2016, the World Health Assembly adopted the Global Health Sector Strategy with the aim of eliminating viral hepatitis as a public health threat by 2030. Global targets were subsequently set, including reducing the incidence by 90% and mortality by 65% [8]. The WHO identified seven key interventions across the viral hepatitis care cascade, spanning prevention, testing and treatment: (i) hepatitis B vaccination, (ii) preventing hepatitis B MTCT, (iii) ensuring blood safety, (iv) ensuring injection safety, (v) implementing harm reduction strategies, (vi) providing testing services, and (vii) providing antiviral therapy.

Programme targets and global progress are summarised in Tables 1 and 2 [2,9,10]. Although certain interventions, such as hepatitis B vaccination and blood and injection safety, are approaching their targets, significant gaps remain in terms of prevention of MTCT of HBV, testing, and treatment services. Currently, coverage of the HBV vaccine birth dose, diagnosis and treatment is below 50%, 30% and 20%, respectively [1]. However, global averages mask substantial regional disparities. For example, hepatitis B birth dose coverage stood at approximately 17% in the WHO African Region in 2023, compared to 79% in the WHO Western Pacific Region [11].

This review follows the major steps of the viral hepatitis care cascade, from prevention and diagnosis to linkage to care, antiviral treatment, health-system strengthening and HCC prevention. Within each stage, HBV- and HCV-specific barriers and innovations are discussed separately whenever the challenges and interventions differ, whereas common implementation challenges and health-system

approaches are addressed jointly to avoid unnecessary duplication and to emphasise shared solutions. Tables 3 and 4 summarise HBV-specific, HCV-specific and cross-cutting barriers and innovations across the care cascade.

1. HBV vaccination in children

1.1. Barriers to HBV vaccination in children

Approved HBV vaccines, administered in 2 or 3 doses, achieve a response rate of over 90% in non-immunocompromised individuals. With the support of the Global Alliance for Vaccines and Immunisation (GAVI), now known as the Vaccine Alliance, infant vaccination coverage has increased significantly over the past decade, rising from 1% in 1990 to 83% in 2024 [11]. Numerous studies have demonstrated the success of universal HBV vaccination programmes in reducing HBsAg prevalence, as well as cirrhosis and HCC [12,13]. Despite these remarkable achievements, vertical transmission remains the primary route of HBV infection worldwide. Significant regional disparities exist, with coverage exceeding the global average in the Western Pacific (91%), the Americas (85%), Europe (92%), and Southeast Asia (90%), while being lower in the Eastern Mediterranean (79%) and African (74%) regions [14].

Barriers to vaccination exist at the individual, provider, and system levels [15]. Barriers at the individual level include maternal education, caste, socio-cultural background, religion, household wealth, geographical location, infant birth order and birth year, and trust in vaccination [16,17]. Barriers at the provider level include a lack of knowledge regarding vaccine indications and contraindications, inadequately trained medical staff, and an absence of systems to remind patients about missed

vaccinations. Barriers at the system level include the need for robust immunisation delivery systems to manage vaccine costs and ensure proper storage. Maintaining the cold chain remains a major logistical challenge. Intramuscular administration also requires trained staff and safe sharps disposal.

1.2. Innovations in HBV vaccination

These barriers help to explain why uptake of the HBV vaccine remains suboptimal in many LMIC settings despite the availability of safe and effective vaccines. Several innovations could improve delivery and uptake. For example, conditional incentives and opt-out birth-dose approaches could enhance the timeliness of vaccinations.

The scarcity of electronic medical records in LMICs makes it difficult to accurately assess national uptake of the HBV birth dose vaccine. One study used data from the Demographic and Health Survey to map delayed vaccination in The Gambia [18]. Similar geospatial approaches have been applied in South Asia to identify vaccination gaps and optimise resource allocation [17,19]. Such analyses can improve stakeholders' understanding of local immunisation patterns, helping them to target resources effectively at areas of greatest need and strengthen vaccine delivery systems.

A 2016 WHO report highlighted that most WHO-prequalified monovalent HBV vaccines are thermostable, enabling their use outside the traditional cold chain. Storing these vaccines at ambient temperatures (37-45°C) for up to 4 weeks could significantly increase the uptake of the HBV birth dose, particularly in remote areas. Controlled temperature chain strategies have been shown to be both feasible and

cost-effective [20], and could substantially improve the timely administration of the birth dose in settings with limited resources.

The current standard of mono-antigenic HBV vaccines has been shown to be less immunogenic in older adults, people with obesity, people who smoke, and patients with diabetes or chronic kidney disease [21]. Low response rates after only 2 doses have also been reported [22]. Results from the PROTECT trial, which compared tri-antigen HBV vaccines with mono-antigenic vaccines in a randomised controlled trial, indicated higher seroprotection rates with tri-antigen vaccines, particularly in individuals aged 45 years and over [23]. Among patients with HIV and patients with chronic kidney disease undergoing haemodialysis, 3 doses of a vaccine consisting of HBsAg combined with small synthetic immunostimulatory oligodeoxynucleotides provided longer-lasting protection against HBV than 3 to 4 doses of a classical HBV vaccine [24,25]. These vaccines may therefore represent a preferable option for immunocompromised individuals at increased risk of HBV infection, although cost and availability will influence implementation in LMICs.

Although existing HBV vaccines are safe and effective, challenges remain, including the need for three doses, appropriate vaccine storage, and trained healthcare personnel in LMICs. Needle-free vaccination methods, also known as “mucosal vaccines“, could improve the effectiveness and implementation of HBV vaccination programmes. Novel delivery systems are being investigated, including disposable, pre-filled, single-use syringes, as well as intradermal, oral, or nasal prophylactic HBV vaccines. In particular, a 10 µg (birth dose) HBV vaccine delivered via dissolving microneedle patches has been shown to effectively induce protective antibody responses in mice and rhesus monkeys [26]. Ongoing studies are evaluating the immunogenicity and efficacy of these innovative delivery methods in humans.

2. Hepatitis B and C MTCT prevention

Although improving childhood HBV vaccination remains essential, preventing perinatal transmission requires additional interventions during pregnancy and around the time of delivery. MTCT prevention differs substantially between HBV and HCV due to the different preventive tools available. This section therefore discusses HBV and HCV sequentially.

2.1. Barriers to hepatitis B MTCT prevention

2.1.1. Barriers to the hepatitis B birth dose vaccine

The barriers largely mirror those described above, including limited knowledge and awareness among parents and caregivers [27]. Additional barriers relating to delivery, cold chain maintenance, and timely administration have been reported, particularly in rural areas and among infants born outside of health facilities or on non-vaccination days [27,28]. By 2021, only 14 (30%) of the 47 countries in the WHO African Region had introduced the hepatitis B birth dose vaccine, highlighting gaps in policy implementation [29]. Financial and institutional support also played a critical role. Notably, GAVI suspended its support for the introduction of the hepatitis B birth dose in 2020 due to competing demands during the COVID-19 pandemic. This interruption to support was identified as a major barrier in a survey of African stakeholders [30]. GAVI resumed its support for eligible countries in 2024, which may help to address previous implementation gaps.

2.1.2. *Barriers to antiviral HBV prophylaxis in pregnancy*

Since 2019, the WHO has recommended antiviral prophylaxis for HBsAg-positive women with HBV DNA levels of at least 200,000 IU/mL. However, nucleic acid testing requires laboratory infrastructure, reliable supply chains, and sustained operational capacity, all of which may limit access in some settings. Nevertheless, experience from large-scale HIV viral load programmes has demonstrated that such testing can be effectively implemented and decentralised with adequate support. In all WHO regions, except the Americas and the Western Pacific Region (8% and 15%, respectively), the proportion of mothers with high HBV DNA levels receiving antiviral therapy is less than 6% [31].

In this context, the WHO has conditionally recommended qualitative hepatitis B e antigen (HBeAg) testing, either through laboratory-based enzyme immunoassays (which are not widely available in LMICs) or rapid diagnostic tests (RDTs), as an alternative to HBV DNA testing in settings without access to HBV DNA quantification [32]. While HBeAg RDTs can be easily performed at the point of care in LMICs, they are unable to accurately identify pregnant women with HBV DNA levels $\geq 200,000$ IU/mL (sensitivity of less than 70%) due to their poor analytical sensitivity [33,34]. Furthermore, most HBeAg RDTs require plasma or serum, necessitating venipuncture and centrifugation [33].

The cost-effectiveness of adding peripartum antiviral prophylaxis to hepatitis B vaccination at birth depends primarily on the cost of diagnosis and monitoring. Assuming these two parameters were to remain stable, the combined strategy would be cost-effective in 26% of countries by 2100 [35]. However, there are still several

research gaps regarding pregnant women, including treatment eligibility based on fibrosis scores, HBV DNA thresholds for antiviral prophylaxis, and the timing of initiating and discontinuing antiviral prophylaxis.

2.1.3. Additional HBV biological challenges

In addition to implementation barriers, viral resistance can result in vaccine failure in infants. A study in Cameroon reported HBV transmission to infants who had received the genotype A2-derived vaccine Engerix-B from mothers with high-level viraemia and genotype E infection [36]. Vaccine-induced neutralising antibodies may be unable to neutralise genotype E strains with a threonine-to-serine substitution at position 140, a mutation commonly observed in this genotype. Although individual vaccine escape mutations are rare, their impact when using a vaccine designed for a different genotype has not been adequately evaluated in most settings [37].

2.2. Innovative approaches to hepatitis B MTCT prevention

Different implementation strategies for preventing MTCT of HBV can be conceptualised along a gradient of complexity and cost. These include: universal antiviral prophylaxis for all HBsAg-positive pregnant women; HBeAg-based strategies; HBV DNA-based strategies; and emerging biomarker-based approaches, such as hepatitis B core-related antigen (HBcrAg). Simpler strategies may facilitate rapid scaling-up in settings with limited resources, whereas more complex approaches may optimise targeting where resources allow. Recently, the WHO recommended a “treat-all” strategy for pregnant women with HBV infection in settings without access to HBV

DNA testing or HBeAg RDTs, despite the low level of evidence [38]. As approximately 20% of pregnant women with HBV infection would otherwise meet conventional eligibility criteria for peripartum antiviral prophylaxis, this strategy is expected to increase treatment uptake [38,39]. Although peripartum antiviral prophylaxis is safe [40], the impact of this strategy remains to be determined. Nevertheless, universal peripartum antiviral prophylaxis may be more cost-effective than other strategies in many countries [35].

The WHO has recommended integrating HBV testing into horizontal HIV and syphilis programmes during antenatal care [32]. This “triple elimination initiative” has been shown to be an acceptable, effective and cost-effective way of reducing HBV MTCT in Asia [41,42]. In the Democratic Republic of the Congo, a study evaluated the feasibility of incorporating HBV MTCT prevention into existing HIV maternal and child healthcare facilities, including providing HBV vaccination at birth [43]. Although only 68% of infants received the birth dose of the vaccine, the high level of acceptance of this approach among pregnant women suggests that integrating HBV testing and treatment into existing HIV services is feasible and acceptable and may reduce concerns related to stigma while increasing uptake of HBV testing. Similar integrated antenatal screening approaches have been successfully implemented in several Asian countries, including China and Vietnam, where triple elimination strategies have contributed to improved HBV MTCT prevention [44,45].

A universal birth-dose strategy could protect infants born to HBsAg-negative mothers from earlier horizontal transmission, as they would otherwise receive their first vaccine at 6-8 weeks of age. However, the risk of infection appears to be minimal, and a systematic review found no clear benefit of birth-dose vaccination in this group. This suggests that the birth-dose vaccination strategy should target infants born to

HBsAg-positive mothers [46]. Overall, screening for HBV during antenatal care, combined with measures to reinforce HBV birth-dose vaccination in exposed children, could improve vaccine uptake and reduce MTCT of HBV. Nevertheless, the effectiveness of the HBV birth-dose vaccine in preventing MTCT remains poorly documented in Africa.

Several studies have suggested that the HBcrAg may effectively identify pregnant women with HBV who are eligible for peripartum antiviral prophylaxis [36,47,48]. Although DBS samples can be used for HBcrAg detection and quantification, the elution technique from DBS and the capacity to perform the assay require a certain level of laboratory expertise [49]. Recently, however, a simple, inexpensive lateral flow assay has been developed for detecting HBcrAg at the point of care. Its ability to diagnose HBV DNA levels $\geq 200,000$ IU/mL was high in a cohort of patients with chronic hepatitis B [50]. The real-world performance of this RDT for identifying pregnant women with high viremia is currently being evaluated in Burkina Faso and The Gambia. HBcrAg has also been extensively evaluated in Asian cohorts, particularly in Japan and Taiwan, where it has demonstrated good performance as a surrogate marker of high HBV DNA levels [47,51]

Currently, there are no true POC, instrument-free rapid molecular tests available for the quantitative detection of HBV DNA. Cartridge-based molecular platforms enable relatively rapid and decentralised quantification of HBV DNA and are being used more and more in certain settings. However, they still require dedicated instruments, a stable electricity supply, and sustained procurement systems, which could restrict their deployment in the least well-resourced areas. A simple, rapid, and less expensive alternative to polymerase chain reaction (PCR), based on loop-mediated isothermal amplification (LAMP), has been developed. This test has a

sensitivity of 98.0% and a specificity of 94.6% for diagnosing HBV DNA levels $\geq 200,000$ IU/mL [52]. Recently, a simple semi-quantitative nucleic acid test, based on DNA extraction, recombinase polymerase amplification (RPA), and lateral flow immunochromatography, with a threshold of 200,000 IU/mL, was developed. This test has an area under the ROC curve of 0.99 and could be useful in LMICs [53].

2.3. Current challenges and innovative approaches to hepatitis C MTCT prevention

Unlike HBV, the prevention of HCV MTCT relies primarily on improved screening strategies and linkage to care, since no vaccine is available and antiviral treatment during pregnancy is not yet routinely recommended.

Routine HCV testing overcomes several limitations of risk-based screening, which often fails due to under-reporting of risk factors by pregnant women. This may be due to fear of stigma or practices such as female genital mutilation [54,55]. Although the WHO has yet to endorse universal HCV screening for all pregnant women, several international societies recommend it [56]. Viraemic HCV status may affect pregnancy outcomes by increasing the likelihood of preterm delivery, intrahepatic cholestasis of pregnancy, and postpartum haemorrhage [57]. A meta-analysis of 25 studies involving 2,017 pregnant women with HCV viremia and no HIV co-infection estimated the rate of HCV MTCT to be 5.8% (95% confidence interval [CI]: 4.2-7.8%) [58]. Identifying women of childbearing age with HCV infection is crucial for preconception diagnosis and treatment. Integrating HCV screening with other disease screening could improve the early detection of HCV before conception. Universal HCV screening could be considered as part of the recommended triple elimination initiative.

Although DAAs are not approved for use during pregnancy, no adverse safety issues have been identified in preclinical or real-life studies [59]. A modelling study showed that universal screening and treatment during pregnancy could potentially improve both maternal and infant outcomes [60]. Further extensive studies in LMICs are required to evaluate the feasibility and cost-effectiveness of these strategies, and to identify any implementation barriers.

3. Prevention of parenteral HBV and HCV transmission

In addition to preventing vertical transmission, eliminating viral hepatitis in LMICs also requires reducing parenteral transmission. This remains a significant cause of new HBV and HCV infections in many settings and can be achieved by implementing safer blood transfusion practices, ensuring safer injections and expanding harm reduction services.

3.1. Barriers to blood safety

In high-income countries, infections with HBV or HCV resulting from blood or blood product transfusions have become exceptional due to the widespread use of serological and nucleic acid testing of donations [61]. In LMICs, donors' blood is generally tested for HBsAg, and in some countries for anti-HBc antibodies too. The prevalence of HBsAg in blood donations ranges from 0.02% in high-income countries to 1.7% and 2.8% in lower-middle-income and low-income countries, respectively [62]. In contrast, anti-HCV antibody testing is not universal in LMICs. HCV is detected in

approximately 0.007% of blood donations in high-income countries, compared to around 0.4% in lower-middle-income countries and 1.0% in low-income countries [62].

A cross-sectional study of the performance of HIV, HBV, and HCV tests in African countries revealed that RDTs performed poorly in blood testing, with a risk of transfusing infected blood units of approximately 5.6% when RDTs are used as the sole screening method [63]. The window periods of HBV and HCV infection can also make it more challenging to detect these viruses during the screening process. On average, anti-HCV antibodies become detectable two months after infection, which makes it difficult to detect the virus when screening is based solely on antibody detection [64].

Occult HBV infection (OBI), characterised by the presence of anti-HBc antibodies and low levels of HBV DNA in plasma or serum without detectable HBsAg, is also a risk factor for HBV transmission. The prevalence of OBI correlates with the endemicity of HBV: prevalence rates of 0.06%, 0.12%, and 0.98% have been reported in countries with low, intermediate, and high endemicity, respectively [65]. A transmission rate of 0.85% from donors with OBI has been reported [66]. Although the combination of HBsAg and nucleic acid testing is effective at preventing most HBV transmissions, access to HBV DNA testing is limited in LMICs. Consequently, a residual risk of transmission remains in blood donors with OBI [67]. Therefore, the significant proportion of OBI cases, particularly in countries with a high level of endemicity, increases the risk of HBV transmission in settings where access to screening tools is limited.

Strengthening post-donation notification systems and linkage to care for individuals identified through blood bank screening represents an underused opportunity to expand access to diagnosis and treatment.

3.2. Barriers to injection safety

In addition to the risks associated with blood transfusion, unsafe medical injections continue to contribute to the ongoing transmission of HBV and HCV. Such unsafe practices include the reuse of injection equipment, accidental needle-stick injuries among healthcare workers, overuse of injections, and unsafe sharps waste management [68]. In 2000, the WHO estimated that 40% of the 16 billion injections administered worldwide were given with reused equipment [69]. Significant progress has been made in reducing the transmission of HBV and HCV through injections since 2000, thanks to safer injection campaigns. In 2016, the WHO updated its guidelines on safe injection practices, recommending the use of syringes with features that protect against sharps injuries and prevent reuse [68]. However, knowledge and practice among public health and healthcare professionals in LMICs remains limited [70].

3.3. Barriers to harm reduction

Outside of healthcare settings, transmission is also sustained by limited access to evidence-based harm reduction interventions, particularly for people who inject drugs (PWID). Despite the existence of effective public health strategies, the transmission of HCV through the use of unsterile injecting equipment continues to drive HCV incidence in many regions [71]. In 2018, 38% of HCV infections were attributed to injecting drug use. Eliminating unsafe injection practices could prevent 43% of new HCV infections between 2018 and 2030 [71]. HCV infection is more

prevalent among PWID than in the general population in many countries [72]. Successful harm reduction programmes in countries such as Vietnam and Ukraine have demonstrated reductions in HCV incidence among PWID when services are scaled up [73,74]. PWID with HCV infection are also at risk of HIV co-infection, which increases the risk of liver disease progression and HCC. HBV infection is also common among PWID [75].

A combination of drug laws, policies, and law enforcement practices, as well as stigmatisation and criminalisation, often hinders the provision and uptake of harm reduction and HCV prevention services [76]. Needle and syringe exchange programmes and opioid substitution therapy have been associated with lower HCV infection rates [77]. Therefore, strategies to scale up opioid agonist maintenance therapy in LMICs represent a public health priority. However, although needle and syringe programmes and opioid agonist therapy are among the most cost-effective interventions for preventing HIV and HCV transmission among PWID, local cost and long-term sustainability data remain limited in many LMICs. More resources are therefore needed to generate context-specific economic evidence to support policy decisions and the long-term implementation of harm reduction programmes [78,79].

3.4. Innovative approaches to reducing parenteral HBV and HCV transmission

Universal screening of all donated blood for transfusion-transmissible infections remains the cornerstone of blood safety. In LMICs, efforts should primarily focus on expanding access to high-quality universal screening while strengthening blood transfusion services. Additional innovations, including pathogen reduction

technologies, automation, and digital quality-management systems, may further improve blood safety where resources permit, although their implementation remains constrained by cost and infrastructure requirements [2].

Innovations in injection safety have focused primarily on preventing reuse of injection equipment and facilitating implementation of WHO recommendations. Auto-disable and reuse-prevention syringes, combined with strengthened procurement policies, healthcare worker training, and safer sharps waste management, can further reduce healthcare-associated HBV and HCV transmission [80,81]. Future efforts are needed to improve access to these technologies, particularly in primary healthcare facilities and other resource-limited settings where unsafe injection practices remain common.

Innovations in harm reduction have primarily focused on improving service delivery rather than developing new interventions. Community-based and peer-led models, integration of harm reduction with HIV and viral hepatitis testing and treatment, and decentralised service delivery have been associated with improved access to testing, treatment and HBV vaccination among PWID in several settings [82–84]. Expanding these implementation strategies, together with policies that reduce stigma, criminalisation and other structural barriers, are likely to be essential to increase coverage of harm reduction services and further reduce HBV and HCV transmission in LMICs.

4. Diagnosis of HBV and HCV infection

If prevention opportunities are missed, progress towards elimination depends on health systems' ability to diagnose infections early and efficiently.

4.1. Barriers to HBV and HCV testing

The WHO recommends a risk- and symptom-based strategy for screening for both HBsAg and anti-HCV antibodies [38,85]. Risk-based HBV screening includes the following groups: household and sexual contacts of people with chronic hepatitis B; people living with HIV; PWID; men who have sex with men (MSM); sex workers; and other groups, such as indigenous people, people in prisons, and transgender people [38]. Risk-based HCV screening is recommended for individuals belonging to populations with high seroprevalence, such as mobile/migrant populations from countries with high-intermediate endemicity, certain indigenous populations, and individuals with a history of exposure to or high-risk behaviour for HCV infection. This includes PWID, people in prisons and other closed settings, MSM, sex workers, individuals with HIV, and children of mothers with chronic HCV infection, especially if they are coinfectd with HIV [85]. Additionally, general population testing is recommended in settings with an HBsAg seroprevalence of $\geq 2\%$ or an anti-HCV antibody seroprevalence of $\geq 5\%$. In many LMICs, viral hepatitis testing relies primarily on serological RDTs because of limited laboratory infrastructure and access to molecular testing. Despite the existence of testing guidelines, HBV and HCV infections remain underdiagnosed in LMICs. In 2019, diagnostic coverage was less than 30% in all WHO regions except the Eastern Mediterranean region [1].

A lack of knowledge, low educational attainment and stigma are common barriers to the uptake of viral hepatitis testing [86,87]. Specific populations, such as PWID or people in prisons, have expressed concerns about confidentiality and experiences of stigma [88,89]. At the provider level, barriers to offering HCV screening

include time constraints, limited knowledge of HCV, and reluctance to discuss behaviours associated with HCV exposure [90]. At the health system level, access to referral hospitals is limited by geographical distance in many LMICs. Fragmented and siloed programme structures, with limited communication between disease-specific programmes (e.g. HIV, tuberculosis, and viral hepatitis), represent an additional barrier, leading to missed opportunities for integrated screening and linkage to care. Integrating viral hepatitis services into existing HIV, tuberculosis, antenatal care, or harm reduction programmes has proven effective in improving testing uptake and linkage to care [78,91,92].

The introduction of POC tests should improve access to testing in LMICs. However, structural barriers, including those related to policy, regulation, the economy, laboratories, training, and infrastructure, must be overcome to improve access to POC testing [93]. Furthermore, LMICs suffer from a lack of funding to establish and strengthen viral hepatitis programmes. The COVID-19 pandemic has exacerbated existing barriers [94].

4.2. Innovative approaches to HBV and HCV testing

These common barriers, together with virus-specific diagnostic constraints, have led to more streamlined and decentralised testing approaches.

4.2.1. Simplification of testing algorithms

HBV testing can be based on simple, inexpensive and reliable HBsAg RDTs. However, simplified diagnostic pathways should also facilitate assessment of

treatment eligibility by improving access to HBV DNA testing. Indeed, the increasing availability of near-POC molecular platforms capable of quantifying HBV DNA, often using the same instruments already deployed for HIV or tuberculosis programmes, offers an opportunity to decentralise HBV care. Further reductions in assay costs and broader implementation of simplified molecular testing strategies will be required to expand access to antiviral treatment in LMICs.

HDV testing should also be integrated into the diagnostic pathway for individuals who test positive for HBsAg. The true global burden of HDV infection is unclear due to a lack of surveillance data, particularly in LMICs. In addition, prevalence estimates differ substantially according to the populations studied, with population-based screening studies generally reporting lower prevalence than hospital- or hepatology clinic-based cohorts [95]. The exact prevalence of HDV infection among people with chronic HBV infection therefore varies by region [96]. Reflex testing for anti-HDV antibodies in all HBsAg-positive individuals, followed by HDV RNA testing in those who are anti-HDV positive, could improve diagnosis and linkage to care [97]. However, access to both anti-HDV antibody testing and HDV RNA quantification remains limited in many LMICs.

HCV testing involves two steps: first, screening for anti-HCV antibodies to detect exposure; and second, detecting HCV RNA to confirm viremia. New sampling approaches, such as the use of oral fluids or DBS, have the potential to simplify the HCV screening process. The performance of oral fluid testing as an alternative to finger-prick or venipuncture whole blood testing is equivalent to that of current laboratory-based enzyme immunoassays for anti-HCV antibody testing [98]. Simplification also requires minimising the number of phlebotomy visits throughout the HCV care process. DBS enables the high-performance detection of anti-HCV

antibodies and the quantification of HCV RNA from the same sample [99]. Additionally, qualitative nucleic acid testing would suffice for diagnosing active HCV infection. In Thailand, a simplified test-and-treat strategy using qualitative nucleic acid testing reduced costs from USD 65.7 to USD 48.6 [100]. Similar simplified testing strategies have been evaluated in South Asia, particularly in Pakistan, with encouraging results in large-scale screening programmes [101,102].

Access to and affordability of HCV confirmatory RNA testing remain challenging in LMICs. Recently, a novel 15-minute near-POC qualitative PCR assay demonstrated a limit of detection of 200 IU/mL, broad genotype coverage (genotypes 1 to 6), and excellent preliminary diagnostic performance, supporting same-day molecular confirmation of active HCV infection in decentralized settings [103]. HCV core antigen testing provides an alternative method of detecting viraemic HCV infection. Advantages of HCV core antigen testing include high performance [104], lower cost per test, and faster turnaround time [105]. However, the most widely used HCV core antigen assay requires a floor-standing immunoassay analyser. Further large-scale implementation studies are needed to assess the relative utility, cost-effectiveness, and challenges of using HCV core antigen testing instead of HCV RNA testing. Combined antigen-antibody assays reduce the duration of HCV seronegativity compared to current anti-HCV enzyme-linked immunosorbent assays during acute infection [106], but their cost-effectiveness remains to be established. They may be useful in populations at increased risk [107].

Qualitative HCV RNA testing from blood samples or DBS, as well as HCV core antigen assays, require specialised infrastructure, which limits their use in LMICs. Ideally, a POC diagnostic test for active HCV infection would provide results in less than 20 minutes, enabling patients to receive their results while they are still present.

This type of technology is essential for implementing test-and-treat care models. Adopting one-step diagnostic approaches based on either HCV core antigen or HCV RNA testing in settings with high HCV seroprevalence, or in specific subpopulations (e.g. PWID and MSM), could simplify the care cascade and reduce loss to follow-up.

Overall, lessons from HIV programmes suggest that universal, opt-out screening strategies could improve both case detection and linkage to care [2,78]. In settings with a high prevalence of HBV infection, modelling studies suggest that one-time universal HBsAg screening combined with linkage to vaccination and antiviral treatment is likely to be cost-effective [108,109]. For HCV, integrating opt-out testing into existing services, including emergency departments, primary care, and harm reduction programmes, has been shown to increase testing uptake and linkage to care [110,111]. However, implementation should be adapted to local epidemiology and health system capacity.

4.2.2. Self-testing

Self-testing, in which individuals collect their own sample, perform a simple RDT, and interpret the results, has the potential to increase uptake of viral hepatitis screening, particularly among underserved and hard-to-reach populations [112]. Evidence supporting HCV self-testing has expanded substantially, whereas evidence for HBV self-testing remains limited. Two systematic reviews have demonstrated the feasibility and acceptability of HCV self-testing in various populations and settings [112,113]. However, implementation studies have shown that, although self-testing increases uptake, substantial losses can occur at the stage of confirmatory RNA testing, highlighting the need to strengthen linkage to care and access to virological

testing. Modelling studies also suggest that HCV self-testing is likely to be a cost-effective strategy to support HCV elimination [114].

WHO recommends HCV self-testing as an additional testing approach, and the first WHO-prequalified product became available in 2024, with at least four additional HCV self-tests currently in development. The 2026 WHO consolidated guidance also incorporates HBV self-testing, although evidence remains insufficient to support large-scale implementation [115].

4.2.3. New POC technologies

Recent advances in POC and near-POC nucleic acid testing have the potential to transform the diagnosis and care pathways of viral hepatitis in LMICs. Cartridge-based molecular systems, which are already widely used for HIV and tuberculosis, can provide relatively rapid detection of HCV RNA and HBV DNA. This enables same-day diagnosis and facilitates “test-and-treat” approaches. These technologies could reduce loss to follow-up associated with multi-step diagnostic algorithms, particularly in decentralised settings. Integrating them into existing multi-disease platforms could further improve efficiency by leveraging established laboratory networks. However, challenges remain, including cost, infrastructure requirements, and competition with other disease programmes.

For HBV, the availability of cartridge-based HBV DNA assays on existing multi-disease molecular platforms represents an important advance. By leveraging laboratory infrastructure already established for HIV and tuberculosis, these assays could facilitate decentralised assessment of treatment eligibility while reducing the need for referral to specialised laboratories.

A rapid POC lateral-flow assay for the detection of anti-HDV antibodies in serum or plasma was developed several years ago and showed promising preliminary performance, with pan-genotypic reactivity and results available within 20 minutes [116]. However, this assay has not progressed to widespread commercial availability. Affordable, fully validated anti-HDV RDTs suitable for decentralised use remain an important unmet need.

For HCV, an RDT detecting HCV core antigen is being developed as a simplified alternative to the conventional two-step strategy based on anti-HCV antibody screening followed by HCV RNA confirmation. The performance and cost-effectiveness of the RDT are encouraging [117].

Several populations, such as PWID and MSM, are at increased risk of both viral hepatitis and HIV. It is also crucial to detect these infections in women of childbearing age due to the risk of MTCT. Multiplex POC assays based on blood or oral samples allow simultaneous testing for HIV, HBV, and HCV from a single sample, with satisfactory sensitivity and specificity [118].

Although no instrument-free platforms are currently available, several technologies show potential for the simplified detection of HCV RNA. These include RT-PCR and isothermal nucleic acid amplification technologies, some of which are combined with CRISPR technologies [119]. In parallel, integrated multi-pathogen testing platforms are also being developed.

4.2.4. Integrated, centralised and decentralised multi-disease testing platforms

At the health system level, these advances are increasingly being incorporated into integrated multi-disease platforms, whether centralised or decentralised, which could improve efficiency and expand access. However, robust collaboration between national disease programmes and public health laboratories is required for this integration to be successful. Mapping health facilities and their catchment areas is therefore essential for the effective design and implementation of these platforms.

5. Treatment of HBV and HCV infection

5.1. Barriers to HBV and HCV treatment

Although several barriers to treatment are common to both HBV and HCV in LMICs, there are key differences, particularly regarding lifelong therapy for HBV and curative, short-course therapy for HCV. These barriers arise at various stages of the treatment process, from initial eligibility assessment to long-term follow-up and successful treatment outcomes.

5.1.1. Barriers to treatment implementation

Unlike HIV infection, for which antiretroviral therapy is recommended for all individuals with confirmed infection, patients who test positive for HBsAg or anti-HCV antibodies generally require additional evaluation before treatment initiation. This includes HBV DNA quantification (although some simplified guidelines now recommend treatment based on HBsAg positivity alone in selected settings) or confirmation of active HCV infection by HCV RNA or HCV core antigen testing,

together with an assessment of liver disease severity. This two-step diagnostic and staging strategy complicates the viral hepatitis care cascade. Furthermore, as these treatment criteria are laboratory-based, it is challenging to assess liver disease in remote areas. The WHO has recently recommended a simplified strategy for settings with limited resources that does not require an assessment of HBV DNA, instead relying on ALT levels to indicate treatment. While broader treatment eligibility criteria simplify treatment pathways, they also increase the number of patients eligible for treatment. Currently, access to viral hepatitis treatment in LMICs is limited to large cities, where it is provided by specialists in national hospitals or private clinics. The time and cost of travelling to these cities is considered a major barrier to accessing treatment [120].

5.1.2. Barriers to treatment access

Even when patients can be identified and staged correctly, access to antiviral therapy is uneven across LMICs. Although prices have decreased, largely owing to the availability of generic formulations, affordable HCV DAAs remain inaccessible in several countries. [121]. Furthermore, despite being included in the Medicines Patent Pool, access to certain regimens, such as glecaprevir/pibrentasvir, remains limited in many LMICs due to the lack of widely available generic formulations.

Although some barriers, including drug affordability, limited healthcare infrastructure and weak linkage to care, affect both HBV and HCV infection, other barriers are virus-specific. In LMICs, limited access to HCV DAA therapy is partly due to a lack of government and international funding. Furthermore, delays in or lack of regulatory approval for antiviral therapies pose an additional barrier. The perception

that PWID are less likely to adhere to treatment remains an important barrier to care, despite evidence showing high adherence to both lifelong HIV therapy and short-course HCV treatment [76,122]. Modelling analyses suggest that treating HCV in PWID is both effective and cost-effective [122,123]. Furthermore, the requirement to abstain from alcohol in order to access HCV DAAs is not based on scientific evidence, thereby restricting access to care [122].

5.1.3. Barriers to treatment follow-up

For HBV in particular, access to treatment must also be considered in the context of the long-term follow-up required for lifelong therapy. High rates of loss to follow-up have been reported in longitudinal cohorts, particularly in sub-Saharan Africa [124–126]. The main barriers to long-term follow-up include out-of-pocket costs, transportation difficulties, and limited access to viral hepatitis care.

5.1.4. Barriers to successful treatment

The effectiveness of treatment may also be compromised by several virological and behavioural factors.

HBV antiviral therapy with nucleoside/nucleotide analogues requires lifelong treatment. Viral resistance is now very rare with the third generation of antiviral agents, such as entecavir and tenofovir. However, because these drugs are not universally available as generics in LMICs, older nucleos(t)ide analogues are still used in some settings, increasing the risk of antiviral resistance [127,128].

HCV DAAs have been developed against the HCV genotypes most prevalent in high-income countries. Recent studies have shown that a substantial proportion of people with HCV infection in parts of Asia and Africa harbour HCV subtypes that are “unusual” in the populations in which most DAA regimens were originally developed. Some of these subtypes may carry polymorphisms that reduce susceptibility to HCV DAAs, resulting in treatment failure [129–133].

HCV reinfection may occur among PWID and people living with HIV due to several factors, including the expansion of HIV pre-exposure prophylaxis (PrEP) and continued high-risk behaviours. Strengthening the prospective surveillance of individuals who have achieved SVR and who have risk factors for reinfection is important, as high reinfection rates can hinder viral micro-elimination in harm reduction settings [134–136].

5.1.5. Barriers related to comorbidities and associated liver diseases

Comorbid conditions and complications also influence long-term outcomes in chronic viral hepatitis. Metabolic-associated steatotic liver disease (MASLD) is becoming increasingly prevalent worldwide because of the global increase in diabetes and obesity. MASLD has been associated with liver disease progression in people with chronic HBV infection [137,138]. The presence of steatotic liver disease should not preclude consideration of HBV antiviral therapy according to current treatment recommendations. However, identifying patients with MASLD can be difficult due to limited access to reliable steatosis markers (e.g., elastography). Diabetes and obesity are also associated with liver disease progression in people who have achieved HCV

cure with DAA therapy [139]. Alongside viral hepatitis, managing diabetes is essential, as simple interventions can influence the progression of liver disease [140].

Approximately 4.5% of HBsAg-positive individuals and 16.4% of patients attending hepatology clinics are estimated to be infected with HDV [95]. HDV infection is particularly prevalent in Mongolia, the Republic of Moldova, and countries in West and Central Africa. Populations at increased risk include PWID, haemodialysis patients, MSM, sex workers, and people living with HIV or HCV. Access to HDV RNA quantification remains limited and costly in many LMICs, complicating confirmation of active infection and treatment monitoring. Recent studies from Catalonia, the United States, and Sweden have similarly highlighted major gaps throughout the HDV cascade of care, including low rates of anti-HDV testing among HBsAg-positive individuals, limited access to HDV RNA testing, and substantial attrition before specialist assessment and treatment [141–143]. The recent approval of bulevirtide in the United States, following its approval in Europe and other regions, further strengthens the need to systematically screen HBsAg-positive individuals for HDV infection, so that eligible patients can be identified and linked to treatment. Final results from a phase 3 trial confirmed the efficacy and acceptable safety of prolonged bulevirtide monotherapy for up to 144 weeks, although its cost, daily subcutaneous administration, need for prolonged treatment, and virological monitoring requirements will probably continue to limit access in many LMICs [144,145].

Treatment of HBV and HCV does not eliminate the risk of HCC, particularly in patients with cirrhosis. Surveillance for liver cancer requires an abdominal ultrasound every 6 months, which can be challenging in remote areas where there is no access to radiologists or sonographers. The survival rate for HCC patients in LMICs is poor,

highlighting the need for strategies that can be implemented at a local level to deliver HCC surveillance and provide early treatment [124,146].

5.2. Innovations in antiviral therapy

These barriers have prompted a variety of innovations across the care cascade, including simplified treatment eligibility assessments and monitoring, decentralised care models, and new antiviral agents.

5.2.1. Innovations addressing barriers to treatment eligibility

Determining eligibility for anti-HBV treatment remains challenging, particularly in LMICs. Simplified approaches that omit HBV DNA quantification have therefore been introduced. The Treatment Eligibility in Africa for the Hepatitis B Virus (TREAT-B) score considers only the ALT level and HBeAg serostatus [147]. This score has been evaluated in several regions and has demonstrated moderate to high performance in determining treatment eligibility among treatment-naïve patients with chronic hepatitis B [147]. The Hepatitis B in Africa Collaborative Network (HEPSANET) score uses platelet count, AST, and ALT levels, achieving a sensitivity and specificity of 78% and 87%, respectively, in identifying treatment-eligible individuals [148].

Inspired by the “treat all” strategy used for HIV, a similar approach has been recommended for chronic HBV infection. However, this could potentially overburden health facilities when antiviral therapy is only required by certain patient groups to prevent cirrhosis, its complications, and HCC. Comprehensive algorithms, such as the EASL 2025 criteria [149], or simplified algorithms, such as the TREAT-B [148] or WHO

2024 criteria [38], may be more effective than the “treat all” strategy in reducing the burden of HBV-related disease. However, their cost-effectiveness remains uncertain [150].

For HCV, the availability of pangenotypic DAA regimens has eliminated the need for routine pretreatment genotyping, greatly simplifying treatment delivery in LMICs. Shifting care tasks to non-specialists is recommended, as treatment outcomes are comparable to those provided by specialists [83].

5.2.2. Innovations simplifying treatment delivery and monitoring

For HBV, decentralisation of care and task shifting to non-specialist healthcare providers are increasingly recognised as effective strategies to expand treatment coverage in LMICs. Simplified follow-up algorithms and integration of HBV care into existing HIV and primary healthcare programmes may further improve long-term retention in care while reducing the burden on specialist services.

The feasibility of simplified HCV treatment monitoring has been assessed in a clinical trial. A phase 3, open-label, randomised, controlled trial compared a simplified approach involving two clinic visits and two telephone consultations with the study nurse to a control approach involving three clinic visits and two telephone consultations. The simplified strategy did not demonstrate non-inferiority [151]. The MINMON approach, which included no pre-treatment HCV genotyping and the administration of the entire treatment course at once (with no scheduled visits or laboratory monitoring) and two points of remote contact, resulted in 95% of enrolled patients achieving a sustained virological response [152]. This approach appears particularly well suited to HCV treatment in LMICs.

5.2.3. *Emerging antiviral strategies*

Tenofovir alafenamide (TAF) is now available to treat chronic hepatitis B and is as effective as tenofovir disoproxil fumarate, but has a more favourable renal and bone safety profile [153,154]. To date, no TAF resistance has been reported [155]. Despite the lack of high-quality safety data in LMICs, adverse events related to tenofovir disoproxil fumarate or entecavir appear to be rare. This raises questions about the value of expanding access to TAF in LMICs [156].

New HBV therapies currently in late-stage clinical development may enable some patients to achieve sustained HBsAg loss after finite treatment. Recent phase III data with the antisense oligonucleotide bepirovirsen represent the first demonstration that this strategy can achieve functional cure in a proportion of patients with low baseline HBsAg level [157,158]. However, participation in phase 2 or 3 clinical trials for new chronic hepatitis B therapies is almost non-existent among patients in sub-Saharan Africa. Only 1.0% of clinical trials involve the WHO African region [159].

Beyond current oral therapies, long-acting antiviral technologies are being developed for both HBV and HCV [160–163]. However, important considerations include the costs associated with their more complex manufacturing process and the time required for approval. Additionally, drug resistance at the end of long dosing intervals is a potential concern [163]. Long-acting regimens have the potential to transform the “test and treat” approach to HCV. They have demonstrated the capacity to suppress HBV replication for several months in experimental models [164–166]. Their ability to reduce cccDNA is still under investigation. It is unclear whether a long-

acting anti-HBV drug could facilitate the scaling up of anti-HBV treatment in LMICs [167].

However, technological and therapeutic innovations alone are unlikely to succeed without broader changes to the health system that facilitate the delivery, uptake and retention of care.

6. Improving health systems

6.1. Simplification, decentralization, and task-sharing

Many of the barriers described above stem not only from limitations in tools, but also from the organisation of health services. Strengthening health systems is therefore essential to translate innovation into impact.

Several studies have evaluated the effectiveness of public health strategies aimed at improving HBV and HCV testing and linkage to care. Community-based interventions, patient navigation, decentralisation, and task sharing can improve testing and linkage to care [168,169]. Recent global modelling analyses also suggest that maintaining treatment scale-up requires sustained case finding as the pool of previously diagnosed untreated individuals becomes depleted [170]. Interventions involving community-based organisations, peer mentoring, and financial incentives can also enhance the HCV care continuum [171,172]. Decentralising viral hepatitis care, particularly in rural areas, is essential for improving access to HCV testing. A simplified HCV care model involving RDTs, HCV RNA detection using a near-care assay, and non-specialist clinical staff has been demonstrated to be feasible within a rural Cambodian public health system [173]. Similar decentralised care models have

been implemented in Southeast Asia, including in Myanmar and Vietnam [73,174,175]. A systematic review highlighted that the decentralisation and integration of HCV care into harm reduction sites or primary care settings is associated with improved access to testing and linkage to care [83]. Building on these approaches, micro-elimination strategies targeting populations at increased risk, such as PWID, using integrated “one-stop” models that combine testing, treatment, and harm reduction services at the point of care, have shown promising results in settings with limited resources [176,177]. Fingerstick whole blood DBS sampling is recognised as a valuable tool for increasing access to HCV testing and linkage to care [178].

6.2. Integration of viral hepatitis with other programs

In many WHO regions, programmes for viral hepatitis, HIV, and tuberculosis tend to operate as separate vertical structures, reflecting differences in the history of diagnostic development, funding mechanisms, and diagnostic sample types. Integrating viral hepatitis care into these programmes is a promising strategy for improving the viral hepatitis care cascade. Advances in POC molecular diagnostics for tuberculosis, HIV and HCV infection offer several opportunities for integrated, multiplexed POC testing. These new technologies also enable non-specialist staff to perform tests that would previously have required specialists. Integrating these services could improve both the uptake and retention rates in target populations [179].

PWID face substantial structural barriers to accessing conventional healthcare services despite a high burden of HIV, tuberculosis, and viral hepatitis. Integrated and low-threshold screening and treatment services are therefore particularly important for this population. Furthermore, the growing burden of non-communicable diseases,

driven by the global increase in obesity and diabetes, suggests that patients with these conditions could benefit from HCV screening at district hospitals. [180]. Women of childbearing age are also at significant risk of transmitting HIV, HBV, and/or HCV to their newborns [181]. In countries with high prevalence rates of these infections, integrated multi-testing strategies could identify women of childbearing age with HIV, HBV, and/or HCV and link them to care, thereby preventing MTCT. Further integration efforts to increase adult HBV vaccination uptake could build on existing adult vaccination platforms. However, integration strategies must be adapted to local contexts, and careful implementation is essential for success.

6.3. Implementation

The effectiveness of the above strategies may be limited by cultural and structural barriers. Incorporating an acceptability component into implementation research is essential for identifying barriers and facilitators associated with potential interventions and mitigating risks. Qualitative research exploring patient and provider perspectives on testing strategies, including sampling methods and testing locations, is also needed. Furthermore, training healthcare workers in viral hepatitis is crucial to maximising the impact of these strategies [182].

7. Prevention and treatment of HCC

To prevent hepatitis-related mortality in LMICs, it is necessary to scale up antiviral interventions and improve strategies for HCC prevention, surveillance, and early diagnosis. Although the introduction of antiviral therapies has reduced the

incidence of HCC, the risk remains, particularly among patients with cirrhosis and/or other risk factors. The burden of HCC is particularly high in LMICs, where access to curative and palliative therapies is limited, resulting in high mortality rates and a substantial impairment of quality of life [124,146].

7.1. Primary prevention

Several prognostic scores have been developed in Asia and Europe to identify people with chronic HBV infection who are at risk of HCC, but none have been developed and validated in African populations [183–185]. Beyond viral hepatitis prevention, primary HCC prevention also relies on education and reducing exposure to aflatoxin B1. Efforts to prevent exposure to this carcinogen are critical, yet awareness remains low [186]. Mobile technologies may represent an effective approach to delivering educational messages, particularly in sub-Saharan Africa, where 27% of adults (202 million people) are illiterate. Using biopesticides and implementing comprehensive agricultural practices can limit aflatoxin contamination and reduce HCC incidence by 10-29%, as demonstrated in China and Taiwan [187]. The Partnership for Aflatoxin Control in Africa aims to promote these practices [188]. Similar efforts to reduce exposure to environmental carcinogens are being explored in Latin America.

7.2. Secondary prevention

In addition to reducing risk factors upstream, efforts are also needed to strengthen secondary prevention by detecting HCC earlier. A prospective cohort study

of patients with chronic hepatitis B, conducted at a tertiary referral centre in Senegal, demonstrated high uptake of HCC surveillance. This included the use of abdominal ultrasounds and advanced imaging techniques, such as four-phase computed tomography, magnetic resonance imaging, or liver biopsies for lesions measuring at least 1 cm in diameter [189]. However, decentralised strategies are essential to extend HCC surveillance to eligible patients in remote areas. POC ultrasound is simple, portable, and widely accepted. With appropriate training and validation, it could improve access to HCC surveillance in rural areas [190]. Nevertheless, ultrasound depends heavily on operator skill and machine quality, despite being safe and inexpensive.

Several urinary metabolites have been validated as diagnostic markers for HCC in the PROLIFICA project in Nigeria and The Gambia. However, their applicability outside of these settings is limited due to the requirement for advanced analytical techniques and ultra-low temperature storage [191]. The GALAD score, which is based on serum biomarkers, has shown promise in improving the early detection of HCC in patients with liver fibrosis and cirrhosis. However, its cost may hinder its implementation at scale [192]. Prospective validation of the GALAD score for HCC surveillance is currently underway in Vietnam and Saudi Arabia [193].

Overall, reframing elimination messaging around liver cancer prevention may help increase political commitment, advocacy, and public engagement.

8. Lessons from successful elimination strategies in LMICs

Successful elimination efforts depend on a combination of simplified care models, integration within existing health systems, sustainable financing, and robust

political commitment. Despite ongoing challenges, several LMICs have shown that it is possible to make rapid progress towards eliminating viral hepatitis. Egypt provides one of the most compelling examples of successful large-scale hepatitis C elimination. Through a government-led initiative combining mass screening, simplified diagnostic algorithms, and widespread access to low-cost DAAs, more than 60 million individuals were screened and millions treated within a few years [194]. In Rwanda, a national programme integrating hepatitis services into primary healthcare and leveraging existing HIV platforms has contributed to a substantial expansion in hepatitis B and C testing and treatment [195,196]. Decentralisation of care, use of non-specialist providers, and integration of laboratory services have been critical to improving access in rural areas.

Mongolia has implemented a comprehensive national strategy targeting both HBV and HCV, including population-based screening, linkage to care, and subsidised antiviral treatment. Supported by strong public-private partnerships and innovative financing mechanisms, the programme has been associated with substantial increases in diagnosis and treatment coverage [197]. In Pakistan, the large-scale implementation of hepatitis C screening, including pilot programmes using self-testing and community-based approaches, has shown high acceptability and encouraging levels of uptake [198]. However, these programmes also emphasised the importance of strengthening confirmatory RNA testing and linkage to care to maximise the impact of expanded screening. Overall, experiences from Asia, Latin America, and Eastern Europe suggest that many successful elimination strategies can be adapted across diverse LMIC settings, while acknowledging that implementation must remain context-specific.

Conclusion

Despite the availability of promising and increasingly accessible innovations, this review highlights that major barriers to viral hepatitis elimination persist at every step of the care cascade in LMICs. The WHO has set the ambitious goal of eliminating viral hepatitis as a public health threat worldwide by 2030. At first glance, this goal seems achievable, given the effective tools that have been developed (Figure 3). However, significant gaps remain throughout the viral hepatitis care cascade, and high rates of new infections and deaths are undermining the likelihood of achieving this target.

While technological advancements are promising, sustained political commitment and dedicated public funding are crucial to ensuring that people with viral hepatitis have access to appropriate services. Communication around viral hepatitis elimination could also be reframed through the lens of HCC prevention to attract greater attention from stakeholders and funders. Such an approach may be particularly relevant because chronic viral hepatitis often remains asymptomatic for many years, whereas HCC is a severe and widely recognised complication that may resonate more strongly with policy makers and funders. Integrating dedicated funding within existing international financing mechanisms, such as the Global Fund, could help countries address this challenge more effectively. Without targeted investments to improve access to viral hepatitis screening and treatment tools in LMICs, the disparity between high-income countries and LMICs is likely to continue to widen.

Abbreviations: HBV : hepatitis B virus ; HDV : hepatitis D virus ; HCV : hepatitis C virus ; HCC : hepatocellular carcinoma ; WHO : World Health Organization ; LMIC: low- and middle-income country; POC: point-of-care; HBsAg: hepatitis B surface antigen; DBS: dried blood spot; MTCT: mother-to-child transmission; DAA: direct-acting antiviral; GAVI: Global Alliance for Vaccines and Immunisation; HBeAg: hepatitis B e antigen; RDT: rapid diagnostic test; HBcrAg: hepatitis B core-related antigen; PCR: polymerase chain reaction; LAMP: loop-mediated isothermal amplification; RPA: recombinase polymerase amplification; OBI: occult B infection; PWID: people who inject drugs; MSM: men who have sex with men; PrEP: pre-exposure prophylaxis; MASLD: metabolic-associated steatotic liver disease; TREAT-B: Treatment Eligibility in Africa for the Hepatitis B Virus ; HEPSANET : Hepatitis B in Africa Collaborative Network; TAF: tenofovir alafenamide.

Acknowledgments: The authors would like to thank Dr Elvire Desjonquères for her help with designing the figures.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process: During the preparation of this work, the authors used DeepL Write to improve the syntax of the text in English and ChatGPT to help reorganise the flow of the revised article and generate Tables 3 and 4 and the graphical abstract. The authors then reviewed and edited the content as needed, taking full responsibility for the published article.

References

- [1] Cui F, Blach S, Manzenigo Mingiedi C, Gonzalez MA, Sabry Alaama A, Mozalevskis A, et al. Global reporting of progress towards elimination of hepatitis B and hepatitis C. *Lancet Gastroenterol Hepatol* 2023;8:332-42.
- [2] <https://www.who.int/publications/i/item/9789240122383>
- [3] Maucourt-Boulch D, de Martel C, Franceschi S, Plummer M. Fraction and incidence of liver cancer attributable to hepatitis B and C viruses worldwide. *Int J Cancer* 2018;142:2471-7.
- [4] Alberts CJ, Clifford GM, Georges D, Negro F, Lesi OA, Hutin YJ-F, et al. Worldwide prevalence of hepatitis B virus and hepatitis C virus among patients with cirrhosis at country, region, and global levels: a systematic review. *Lancet Gastroenterol Hepatol* 2022;7:724-735.
- [5] Cooke GS, Flower B, Cunningham E, Marshall AD, Lazarus JV, Palayew A, et al. Progress towards elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission update. *Lancet Gastroenterol Hepatol* 2024;9:346-65.
- [6] <https://www.who.int/publications/i/item/9789240053779>
- [7] Chevaliez S, Pawlotsky J-M. New virological tools for screening, diagnosis and monitoring of hepatitis B and C in resource-limited settings. *J Hepatol* 2018;69:916-26.
- [8] <https://www.who.int/publications/i/item/9789240028395>
- [9] <https://www.who.int/publications/i/item/9789241565455>
- [10] <https://www.who.int/publications/i/item/9789240039360>
- [11] <https://www.who.int/news-room/fact-sheets/detail/immunization-coverage>

- 1082 [12] Chiang C-J, Yang Y-W, You S-L, Lai M-S, Chen C-J. Thirty-year outcomes of
1083 the national hepatitis B immunization program in Taiwan. *JAMA* 2013;310:974-
1084 6.
- 1085 [13] Peto TJ, Mendy ME, Lowe Y, Webb EL, Whittle HC, Hall AJ. Efficacy and
1086 effectiveness of infant vaccination against chronic hepatitis B in the Gambia
1087 Hepatitis Intervention Study (1986-90) and in the nationwide immunisation
1088 program. *BMC Infect Dis* 2014;14:7.
- 1089 [14] <https://immunizationdata.who.int>
- 1090 [15] Kimmel SR, Burns IT, Wolfe RM, Zimmerman RK. Addressing immunization
1091 barriers, benefits, and risks. *J Fam Pract* 2007;56:S61-69.
- 1092 [16] de Figueiredo A, Simas C, Karafillakis E, Paterson P, Larson HJ. Mapping global
1093 trends in vaccine confidence and investigating barriers to vaccine uptake: a
1094 large-scale retrospective temporal modelling study. *Lancet* 2020;396:898-908.
- 1095 [17] Khan J, Shil A, Mohanty SK. Hepatitis B vaccination coverage across India:
1096 exploring the spatial heterogeneity and contextual determinants. *BMC Public*
1097 *Health* 2019;19:1263.
- 1098 [18] Wariri O, Utazi CE, Okomo U, Metcalf CJE, Sogur M, Fofana S, et al. Mapping
1099 the timeliness of routine childhood vaccination in The Gambia: a spatial
1100 modelling study. *Vaccine* 2023;41:5696-705.
- 1101 [19] Khan J, Shil A, Puri P. Population and sub-national (district) level diversity in
1102 missed and dropout of different doses of hepatitis-B vaccine among Indian
1103 children aged 12-59 months. *PLOS Glob Public Health* 2022;2:e0000243.
- 1104 [20] Scott N, Palmer A, Morgan C, Lesi O, Spearman CW, Sonderup M, et al. Cost-
1105 effectiveness of the controlled temperature chain for the hepatitis B virus birth

- 1106 dose vaccine in various global settings: a modelling study. *Lancet Glob Health*
1107 2018;6:e659-67.
- 1108 [21] Yang S, Tian G, Cui Y, Ding C, Deng M, Yu C, et al. Factors influencing
1109 immunologic response to hepatitis B vaccine in adults. *Sci Rep* 2016;6:27251.
- 1110 [22] Centers for Disease Control and Prevention. Use of hepatitis B vaccination for
1111 adults with diabetes mellitus: recommendations of the Advisory Committee on
1112 Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2011;60:1709-
1113 11.
- 1114 [23] Vesikari T, Langley JM, Segall N, Ward BJ, Cooper C, Poliquin G, et al.
1115 Immunogenicity and safety of a tri-antigenic versus a mono-antigenic hepatitis
1116 B vaccine in adults (PROTECT): a randomised, double-blind, phase 3 trial.
1117 *Lancet Infect Dis* 2021;21:1271-81.
- 1118 [24] Marks KM, Kang M, Umbleja T, Cox A, Vigil KJ, Ta NT, et al. HepB-CpG vs
1119 HepB-Alum vaccine in people with HIV and prior vaccine nonresponse: the BEE-
1120 HIVe randomized clinical trial. *JAMA* 2025;333:295-306.
- 1121 [25] Girndt M, Houser P, Manllo-Karim R, Ervin JE, Charytan C, Chow S, et al. Long-
1122 term immunogenicity and safety of the hepatitis B vaccine HepB-CpG
1123 (HEPLISAV-B) compared with HepB-Eng (Engerix-B) in adults with chronic
1124 kidney disease. *Vaccine* 2023;41:3224-32.
- 1125 [26] Choi Y, Lee GS, Li S, Lee JW, Mixson-Hayden T, Woo J, et al. Hepatitis B
1126 vaccine delivered by microneedle patch: immunogenicity in mice and rhesus
1127 macaques. *Vaccine* 2023;41:3663-72.
- 1128 [27] Freeland C, Kanu F, Mohammed Y, Nwokoro UU, Sandhu H, Ikwe H, et al.
1129 Barriers and facilitators to hepatitis B birth dose vaccination: perspectives from

- healthcare providers and pregnant women accessing antenatal care in Nigeria. PLOS Glob Public Health 2023;3:e0001332.
- [28] Thanh Thi Le X, Ishizumi A, Thi Thu Nguyen H, Thi Duong H, Thi Thanh Dang H, Manh Do C, et al. Social and behavioral determinants of attitudes towards and practices of hepatitis B vaccine birth dose in Vietnam. Vaccine 2020;38:8343-50.
- [29] Kabore HJ, Li X, Alleman MM, Manzenigo CM, Mumba M, Biey J, et al. Progress toward hepatitis B control and elimination of mother-to-child transmission of hepatitis B virus: World Health Organization African region, 2016-2021. MMWR Morb Mortal Wkly Rep 2023;72:782-7.
- [30] Njuguna HN, Hiebert L, Gupta N, Ward JW. Status of HBV birth dose vaccination in Africa: the impact of COVID-19 and GAVI support on policy development. Lancet Gastroenterol Hepatol 2023;8:502-3. -
- [31] Polaris Observatory Collaborators. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. Lancet Gastroenterol Hepatol 2023;8:879-907.
- [32] <https://www.who.int/publications/i/item/978-92-4-000270-8>
- [33] Seck A, Ndiaye F, Maylin S, Ndiaye B, Simon F, Funk AL, et al. Poor sensitivity of commercial rapid diagnostic tests for hepatitis B e antigen in Senegal, West Africa. Am J Trop Med Hyg 2018;99:428-34.
- [34] Stockdale AJ, Meiring JE, Shawa IT, Thindwa D, Silungwe NM, Mbewe M, et al. Hepatitis B vaccination impact and the unmet need for antiviral treatment in Blantyre, Malawi. J Infect Dis 2022;226:871-80.
- [35] Nayagam S, de Villiers MJ, Shimakawa Y, Lemoine M, Thursz MR, Walsh N, et al. Impact and cost-effectiveness of hepatitis B virus prophylaxis in pregnancy:

- 1155 a dynamic simulation modelling study. *Lancet Gastroenterol Hepatol*
1156 2023;8:635-45.
- 1157 [36] Shimakawa Y, Veillon P, Birguel J, Pivert A, Sauvage V, Le Guillou-Guillemette
1158 H, et al. Residual risk of mother-to-child transmission of hepatitis B virus
1159 infection despite timely birth-dose vaccination in Cameroon (ANRS 12303): a
1160 single-centre, longitudinal observational study. *Lancet Glob Health*
1161 2022;10:E521-9.
- 1162 [37] Mokaya J, Vasylyeva TI, Barnes E, Ansari MA, Pybus OG, Matthews PC. Global
1163 prevalence and phylogeny of hepatitis B virus (HBV) drug and vaccine
1164 resistance mutations. *J Viral Hepat* 2021;28:1110-20.
- 1165 [38] <https://www.who.int/publications/i/item/9789240090903>
- 1166 [39] Delamare H, Ishii-Rousseau JE, Rao A, Cresta M, Vincent JP, Ségéral O, et al.
1167 Proportion of pregnant women with HBV infection eligible for antiviral
1168 prophylaxis to prevent vertical transmission: a systematic review and meta-
1169 analysis. *JHEP Rep* 2024;6:101064.
- 1170 [40] Funk AL, Lu Y, Yoshida K, Zhao T, Boucheron P, van Holten J, et al. Efficacy
1171 and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child
1172 transmission of hepatitis B virus: a systematic review and meta-analysis. *Lancet*
1173 *Infect Dis* 2021;21:70-84.
- 1174 [41] Loarec A, Nguyen A, Molino L, Chissano M, Madeira N, Rusch B, et al.
1175 Prevention of mother-to-child transmission of hepatitis B virus in antenatal care
1176 and maternity services, Mozambique. *Bull World Health Organ* 2022;100:60-9.
- 1177 [42] Nguyen VTT, Trang HTQ, Ishikawa N, Anh Nguyen L, Anh LAK, Minh TB, et al.
1178 Feasibility, benefits, and cost-effectiveness of adding universal hepatitis B and

- 1179 syphilis testing to routine antenatal care services in Thai Nguyen province,
1180 Vietnam. *Int J STD AIDS* 2021;32:135-43.
- 1181 [43] Thompson P, Morgan CE, Ngimbi P, Mwandagaliwa K, Ravelomanana NLR,
1182 Tabala M, et al. Arresting vertical transmission of hepatitis B virus (AVERT-HBV)
1183 in pregnant women and their neonates in the Democratic Republic of the Congo:
1184 a feasibility study. *Lancet Glob Health* 2021;9:e1600-9.
- 1185 [44] Zhang L, Tao Y, Woodring J, Rattana K, Sovannarith S, Rathavy T, et al.
1186 Integrated approach for triple elimination of mother-to-child transmission of HIV,
1187 hepatitis B and syphilis is highly effective and cost-effective: an economic
1188 evaluation. *Int J Epidemiol* 2019;48:1327-39.
- 1189 [45] Bell L, Van Gemert C, Allard N, Brink A, Chan PL, Cowie B, et al. Progress
1190 towards triple elimination of mother-to-child transmission of HIV, hepatitis B and
1191 syphilis in Pacific Island Countries and Territories: a systematic review. *Lancet*
1192 *Reg Health West Pac* 2023;35:100740.
- 1193 [46] Ansari A, Vincent JP, Moorhouse L, Shimakawa Y, Nayagam S. Risk of early
1194 horizontal transmission of hepatitis B virus in children of uninfected mothers in
1195 sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Glob Health*
1196 2023;11:e715-28.
- 1197 [47] Yoshida K, Desbiolles A, Feldman SF, Ahn SH, Alidjinou EK, Atsukawa M, et al.
1198 Hepatitis B core-related antigen to indicate high viral load: systematic review and
1199 meta-analysis of 10,397 individual participants. *Clin Gastroenterol Hepatol*
1200 2021;19:46-60.
- 1201 [48] Shimakawa Y, Ndow G, Njie R, Njai HF, Takahashi K, Akbar SMF, et al.
1202 Hepatitis B core-related antigen: an alternative to hepatitis B virus DNA to
1203 assess treatment eligibility in Africa. *Clin Infect Dis* 2020;70:1442-52.

- 1204 [49] Shimakawa Y, Vernoux L, Gabassi A, Mercier-Delarue S, Vincent JP, Simon F,
1205 et al. Analytical validation of hepatitis B core-related antigen (HBcrAg) using
1206 dried blood spots (DBS). *J Viral Hepat* 2021;28:837-43.
- 1207 [50] Shimakawa Y, Ndow G, Kaneko A, Aoyagi K, Lemoine M, Tanaka Y, et al. Rapid
1208 point-of-care test for hepatitis B core-related antigen to diagnose high viral load
1209 in resource-limited settings. *Clin Gastroenterol Hepatol* 2023;21:1943-1946.
- 1210 [51] Hu H-H, Liu J, Chang C-L, Jen C-L, Lee M-H, Lu S-N, et al. Level of hepatitis B
1211 (HB) core antibody associates with seroclearance of HBV DNA and HB surface
1212 antigen in HBe antigen-seronegative patients. *Clin Gastroenterol Hepatol*
1213 2019;17:172-181.
- 1214 [52] Vanhomwegen J, Kwasiborski A, Diop A, Boizeau L, Hoinard D, Vray M, et al.
1215 Development and clinical validation of loop-mediated isothermal amplification
1216 (LAMP) assay to diagnose high HBV DNA levels in resource-limited settings.
1217 *Clin Microbiol Infect* 2021;27:1858.
- 1218 [53] Mayran C, Foulongne V, Van de Perre P, Fournier-Wirth C, Molès J-P,
1219 Cantaloube J-F. Rapid diagnostic test for hepatitis B virus viral load based on
1220 recombinase polymerase amplification combined with a lateral flow read-out.
1221 *Diagnostics (Basel)* 2022;12:621.
- 1222 [54] Waruingi W, Mhanna MJ, Kumar D, Abughali N. Hepatitis C virus universal
1223 screening versus risk based selective screening during pregnancy. *J Neonatal*
1224 *Perinatal Med* 2015;8:371-8.
- 1225 [55] El-Kamary SS, Hashem M, Saleh DA, Ehab M, Sharaf SA, El-Mougry F, et al.
1226 Reliability of risk-based screening for hepatitis C virus infection among pregnant
1227 women in Egypt. *J Infect* 2015;70:512-9.

- 1228 [56] AASLD-IDSA HCV Guidance Panel. Hepatitis C guidance 2018 update: AASLD-
1229 IDSA recommendations for testing, managing, and treating hepatitis C virus
1230 infection. Clin Infect Dis 2018;67:1477-92.
- 1231 [57] Kushner T, Djerboua M, Biondi MJ, Feld JJ, Terrault N, Flemming JA. Influence
1232 of hepatitis C viral parameters on pregnancy complications and risk of mother-
1233 to-child transmission. J Hepatol 2022;77:1256-64.
- 1234 [58] Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of
1235 hepatitis C virus: systematic review and meta-analysis. Clin Infect Dis
1236 2014;59:765-73.
- 1237 [59] Abdallah M, Alboraie M, Abdel-Razek W, Hassany M, Ammar I, Kamal E, et al.
1238 Pregnancy outcome of anti-HCV direct-acting antivirals: real-life data from an
1239 Egyptian cohort. Liver Int 2021;41:1494-7.
- 1240 [60] Hachicha-Maalej N, Collins IJ, Ades AE, Scott K, Judd A, Mostafa A, et al.
1241 Modelling the potential effectiveness of hepatitis C screening and treatment
1242 strategies during pregnancy in Egypt and Ukraine. J Hepatol 2023;78:937-46.
- 1243 [61] Dahl V, Majeed A, Wikman A, Norda R, Edgren G. Transmission of viral hepatitis
1244 through blood transfusion in Sweden, 1968 to 2012. Euro Surveill
1245 2020;25:1900537.
- 1246 [62] <https://www.who.int/news-room/fact-sheets/detail/blood-safety-and-availability>
- 1247 [63] Laperche S, Francophone African Group for Research in Blood Transfusion.
1248 Multinational assessment of blood-borne virus testing and transfusion safety on
1249 the African continent. Transfusion 2013;53:816-26.
- 1250 [64] Kucirka LM, Sarathy H, Govindan P, Wolf JH, Ellison TA, Hart LJ, et al. Risk of
1251 window period hepatitis C infection in high infectious risk donors: systematic
1252 review and meta-analysis. Am J Transplant 2011;11:1188-200.

- 1253 [65] Im YR, Jagdish R, Leith D, Kim JU, Yoshida K, Majid A, et al. Prevalence of
1254 occult hepatitis B virus infection in adults: a systematic review and meta-
1255 analysis. *Lancet Gastroenterol Hepatol* 2022;7:932-42.
- 1256 [66] Seed CR, Maloney R, Kiely P, Bell B, Keller AJ, Pink J, et al. Infectivity of blood
1257 components from donors with occult hepatitis B infection: results from an
1258 Australian lookback programme. *Vox Sang* 2015;108:113-22.
- 1259 [67] Candotti D, Boizeau L, Laperche S. Occult hepatitis B infection and transfusion-
1260 transmission risk. *Transfus Clin Biol* 2017;24:189-95.
- 1261 [68] <https://www.who.int/publications/i/item/9789241549820>
- 1262 [69] Hauri AM, Armstrong GL, Hutin YJF. The global burden of disease attributable
1263 to contaminated injections given in health care settings. *Int J STD AIDS*
1264 2004;15:7-16.
- 1265 [70] Chao J, Chang ET, So SKS. Hepatitis B and liver cancer knowledge and
1266 practices among healthcare and public health professionals in China: a cross-
1267 sectional study. *BMC Public Health* 2010;10:98.
- 1268 [71] Trickey A, Fraser H, Lim AG, Peacock A, Colledge S, Walker JG, et al. The
1269 contribution of injection drug use to hepatitis C virus transmission globally,
1270 regionally, and at country level: a modelling study. *Lancet Gastroenterol Hepatol*
1271 2019;4:435-44.
- 1272 [72] Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al.
1273 Global prevalence of injecting drug use and sociodemographic characteristics
1274 and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage
1275 systematic review. *Lancet Glob Health* 2017;5:e1192-207.

- 1276 [73] Nagot N, Binh NT, Hong TT, Vinh VH, Quillet C, Vallo R, et al. A community-
1277 based strategy to eliminate hepatitis C among people who inject drugs in
1278 Vietnam. *Lancet Reg Health West Pac* 2023;37:100801.
- 1279 [74] Stone J, Trickey A, Walker JG, Bivegete S, Semchuk N, Sazonova Y, et al.
1280 Modelling the impact and cost-effectiveness of non-governmental organizations
1281 on HIV and HCV transmission among people who inject drugs in Ukraine. *J Int*
1282 *AIDS Soc* 2023;26:e26073.
- 1283 [75] Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al.
1284 Global epidemiology of hepatitis B and hepatitis C in people who inject drugs:
1285 results of systematic reviews. *Lancet* 2011;378:571-83.
- 1286 [76] Csete J, Kamarulzaman A, Kazatchkine M, Altice F, Balicki M, Buxton J, et al.
1287 Public health and international drug policy. *Lancet* 2016;387:1427-80. -
- 1288 [77] Platt L, Minozzi S, Reed J, Vickerman P, Hagan H, French C, et al. Needle
1289 syringe programmes and opioid substitution therapy for preventing hepatitis C
1290 transmission in people who inject drugs. *Cochrane Database Syst Rev*
1291 2017;9:CD012021.
- 1292 [78] <https://www.who.int/publications/i/item/9789240052390>
- 1293 [79] Killion JA, Magana C, Cepeda JA, Vo A, Hernandez M, Cyr CL, et al. Unit costs
1294 of needle and syringe program provision: a global systematic review and cost
1295 extrapolation. *AIDS* 2023;37:2389-97.
- 1296 [80] Pépin J, Abou Chakra CN, Pépin E, Nault V, Valiquette L. Evolution of the global
1297 burden of viral infections from unsafe medical injections, 2000-2010. *PLoS One*
1298 2014;9:e99677.

- 1299 [81] Heffernan A, Cooke GS, Nayagam S, Thursz M, Hallett TB. Scaling up
1300 prevention and treatment towards the elimination of hepatitis C: a global
1301 mathematical model. *Lancet* 2019;393:1319-29.
- 1302 [82] Litwin AH, Lum PJ, Taylor LE, Mehta SH, Tsui JI, Feinberg J, et al. Patient-
1303 centred models of hepatitis C treatment for people who inject drugs: a
1304 multicentre, pragmatic randomised trial. *Lancet Gastroenterol Hepatol*
1305 2022;7:1112-27.
- 1306 [83] Oru E, Trickey A, Shirali R, Kanter S, Easterbrook P. Decentralisation,
1307 integration, and task-shifting in hepatitis C virus infection testing and treatment:
1308 a global systematic review and meta-analysis. *Lancet Glob Health* 2021;9:e431-
1309 45.
- 1310 [84] Tressler S, Bhandari R. Interventions to increase completion of hepatitis B
1311 vaccination in people who inject drugs: a systematic review and meta-analysis.
1312 *Open Forum Infect Dis* 2019;6:ofz521.
- 1313 [85] <https://www.who.int/publications/i/item/9789241550345>
- 1314 [86] Tan SHS, Wang D, Tan WJ, Allameen NA, Fong NP. Facilitators and barriers of
1315 hepatitis B screening and vaccination. *Vaccine* 2020;38:5447-53.
- 1316 [87] Mazhnaya A, Geurts B, Brigida K, Bakieva S, Sadirova S, Witzigmann A, et al.
1317 Barriers and facilitators to viral hepatitis testing in Uzbekistan: scoping
1318 qualitative study among key stakeholders, healthcare workers, and the general
1319 population. *BMC Public Health* 2024;24:1482.
- 1320 [88] Crowley D, Van Hout MC, Lambert JS, Kelly E, Murphy C, Cullen W. Barriers
1321 and facilitators to hepatitis C (HCV) screening and treatment-a description of
1322 prisoners' perspective. *Harm Reduct J* 2018;15:62.

- 1323 [89] Balsom CR, Farrell A, Kelly DV. Barriers and enablers to testing for hepatitis C
1324 virus infection in people who inject drugs: a scoping review of the qualitative
1325 evidence. BMC Public Health 2023;23:1038.
- 1326 [90] Shehata N, Austin T, Ha S, Timmerman K. Barriers to and facilitators of hepatitis
1327 C virus screening and testing: a scoping review. Can Commun Dis Rep
1328 2018;44:166-72.
- 1329 [91] <https://www.who.int/publications/i/item/9789240096394>
- 1330 [92] <https://www.who.int/publications/i/item/9789240124233>
- 1331 [93] Pai NP, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-care testing for
1332 infectious diseases: diversity, complexity, and barriers in low- and middle-
1333 income countries. PLoS Med 2012;9:e1001306.
- 1334 [94] Kaufman HW, Bull-Otterson L, Meyer WA, Huang X, Doshani M, Thompson
1335 WW, et al. Decreases in hepatitis C testing and treatment during the COVID-19
1336 pandemic. Am J Prev Med 2021;61:369-76.
- 1337 [95] Stockdale AJ, Kreuels B, Henrion MYR, Giorgi E, Kyomuhangi I, de Martel C, et
1338 al. The global prevalence of hepatitis D virus infection: systematic review and
1339 meta-analysis. J Hepatol 2020;73:523-32.
- 1340 [96] Razavi-Shearer D, Child H, Razavi-Shearer K, Voeller A, Razavi H, Buti M, et
1341 al. Adjusted estimate of the prevalence of hepatitis delta virus in 25 countries
1342 and territories. J Hepatol 2024;80:232-42.
- 1343 [97] Razavi HA, Buti M, Terrault NA, Zeuzem S, Yurdaydin C, Tanaka J, et al.
1344 Hepatitis D double reflex testing of all hepatitis B carriers in low-HBV- and high-
1345 HBV/HDV-prevalence countries. J Hepatol 2023;79:57-80.

- [98] Lee SR, Kardos KW, Schiff E, Berne CA, Mounzer K, Banks AT, et al. Evaluation of a new, rapid test for detecting HCV infection, suitable for use with blood or oral fluid. *J Virol Methods* 2011;172:27-31.
- [99] Prabdhial-Sing N, Gaelejwe L, Makhathini L, Thaver J, Manamela MJ, Malfeld S, et al. The performance of hepatitis C virus (HCV) antibody point-of-care tests on oral fluid or whole blood and dried blood spot testing for HCV serology and viral load among individuals at higher risk for HCV in South Africa. *Health Sci Rep* 2021;4:e229.
- [100] Wasitthankasem R, Wanlapakorn N, Pimsing N, Posuwan N, Poovorawan Y. Simplified test-to-treat strategy for hepatitis C in Thailand: the Phetchabun model. *J Infect Dis* 2023;228:S198-203.
- [101] Chhatwal J, Chen Q, Wang X, Ayer T, Zhuo Y, Janjua NZ, et al. Assessment of the feasibility and cost of hepatitis C elimination in Pakistan. *JAMA Netw Open* 2019;2:e193613.
- [102] Mazzilli S, Aslam MK, Ahmed M, Wailly Y, Miazek M, Ashraf S, et al. Decentralised hepatitis C management: a simplified, integrated model of care in a primary health centre in Pakistan, August 2022-June 2023. *J Viral Hepat* 2026;33:e70103.
- [103] Reed JL, Butzler MA, Hawkins CA, Manabe YC, Holden J, Thomas DL, et al. Development of a rapid automated point-of-care test for hepatitis C vViral RNA on the DASH Rapid Polymerase Chain Reaction System. *J Infect Dis* 2026;233:823-30.
- [104] Lamoury FMJ, Soker A, Martinez D, Hajarizadeh B, Cunningham EB, Cunningham P, et al. Hepatitis C virus core antigen: a simplified treatment monitoring tool, including for post-treatment relapse. *J Clin Virol* 2017;92:32-8.

- 1371 [105] Peeling RW, Boeras DI, Marinucci F, Easterbrook P. The future of viral hepatitis
1372 testing: innovations in testing technologies and approaches. *BMC Infect Dis*
1373 2017;17:699.
- 1374 [106] Schnuriger A, Dominguez S, Valantin M-A, Tubiana R, Duvivier C, Ghosn J, et
1375 al. Early detection of hepatitis C virus infection by use of a new combined
1376 antigen-antibody detection assay: potential use for high-risk individuals. *J Clin*
1377 *Microbiol* 2006;44:1561-3.
- 1378 [107] Rouet F, Deleplancque L, Mboumba BB, Sica J, Mouinga-Ondémé A, Liégeois
1379 F, et al. Usefulness of a fourth generation ELISA assay for the reliable
1380 identification of HCV infection in HIV-positive adults from Gabon (Central Africa).
1381 *PLoS One* 2015;10:e0116975.
- 1382 [108] Toy M, Hutton D, Harris AM, Nelson N, Salomon JA, So S. Cost-effectiveness
1383 of 1-time universal screening for chronic hepatitis B infection in adults in the
1384 United States. *Clin Infect Dis* 2022;74:210-7.
- 1385 [109] Su S, Wong WC, Zou Z, Cheng DD, Ong JJ, Chan P, et al. Cost-effectiveness
1386 of universal screening for chronic hepatitis B virus infection in China: an
1387 economic evaluation. *Lancet Glob Health* 2022;10:e278-87.
- 1388 [110] Sperring H, Ruiz-Mercado G, Yun BJ, Twitchell D, Shah B, Schechter-Perkins
1389 EM. Automated opt-out hepatitis C testing to reduce missed screening
1390 opportunities in the emergency department. *Am J Public Health* 2024;114:1228-
1391 31.
- 1392 [111] Evans H, Balasegaram S, Douthwaite S, Hunter L, Kulasegaram R, Wong T, et
1393 al. An innovative approach to increase viral hepatitis diagnoses and linkage to
1394 care using opt-out testing and an integrated care pathway in a London
1395 emergency department. *PLoS One* 2018;13:e0198520.

- 1396 [112] <https://www.ncbi.nlm.nih.gov/books/NBK572750/>
- 1397 [113] Perazzo H, Castro R, Villela-Nogueira C, Torres M, Silva SL, Cardoso SW, et
1398 al. Acceptability and usability of oral fluid HCV self-testing for hepatitis C
1399 diagnosis: a systematic review and meta-analysis. *J Viral Hepat* 2023;30:838-
1400 47.
- 1401 [114] Shin G, Kim BK, Bae S, Lee H, Ahn SH. Self-testing strategy to eliminate
1402 hepatitis C as per World Health Organization's goal: analysis of disease burden
1403 and cost-effectiveness. *Clin Mol Hepatol* 2025;31:166-78.
- 1404 [115] <https://www.who.int/publications/i/item/9789240119529>
- 1405 [116] Lempp FA, Roggenbach I, Nkongolo S, Sakin V, Schlund F, Schnitzler P, et al.
1406 A rapid point-of-care test for the serodiagnosis of hepatitis Delta virus infection.
1407 *Viruses* 2021;13:2371.
- 1408 [117] Adeeb M, Zhong H, Reipold EI, Zhuo Y, Shilton S, Chhatwal J. Cost-effectiveness
1409 of a core antigen-based rapid diagnostic test for hepatitis C. *Value Health*
1410 2022;25:1107-15.
- 1411 [118] Fisher DG, Hess KL, Erlyana E, Reynolds GL, Cummins CA, Alonzo TA.
1412 Comparison of rapid point-of-care tests for detection of antibodies to hepatitis C
1413 virus. *Open Forum Infect Dis* 2015;2:ofv101.
- 1414 [119] Ivanova Reipold E, Shilton S, Donolato M, Fernandez Suarez M. Molecular
1415 point-of-care testing for hepatitis C: available technologies, pipeline, and
1416 promising future directions. *J Infect Dis* 2024;229:S342-9.
- 1417 [120] Kelly C, Hulme C, Farragher T, Clarke G. Are differences in travel time or
1418 distance to healthcare for adults in global north countries associated with an
1419 impact on health outcomes? A systematic review. *BMJ Open* 2016;6:e013059.

- 1420 [121] Tordrup D, Hutin Y, Stenberg K, Lauer JA, Hutton DW, Toy M, et al. Additional
1421 resource needs for viral hepatitis elimination through universal health coverage:
1422 projections in 67 low-income and middle-income countries, 2016-30. *Lancet*
1423 *Glob Health* 2019;7:e1180-8.
- 1424 [122] Grebely J, Haire B, Taylor LE, Macneill P, Litwin AH, Swan T, et al. Excluding
1425 people who use drugs or alcohol from access to hepatitis C treatments: is this
1426 fair, given the available data? *J Hepatol* 2015;63:779-82.
- 1427 [123] Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ, et al.
1428 Treatment of hepatitis C virus infection among people who are actively injecting
1429 drugs: a systematic review and meta-analysis. *Clin Infect Dis* 2013;57(Suppl.
1430 2):S80-9.
- 1431 [124] Ndow G, Vo-Quang E, Shimakawa Y, Ceesay A, Tamba S, Njai HF, et al. Clinical
1432 characteristics and outcomes of patients with cirrhosis and hepatocellular
1433 carcinoma in The Gambia, west Africa: a prospective cohort study. *Lancet Glob*
1434 *Health* 2023;11:e1383-92.
- 1435 [125] Ndow G, Shimakawa Y, Leith D, Bah S, Bangura R, Mahmoud I, et al. Clinical
1436 outcomes of untreated adults living with chronic hepatitis B in The Gambia: an
1437 analysis of data from the prospective PROLIFICA cohort study. *Lancet*
1438 *Gastroenterol Hepatol* 2024;9:1133-46.
- 1439 [126] Desalegn H, Orlie SMS, Abera H, Mamo E, Grude S, Hommersand K, et al.
1440 Five-year results of a treatment program for chronic hepatitis B in Ethiopia. *BMC*
1441 *Med* 2023;21:373.
- 1442 [127] Marcellin P, Buti M, Krastev Z, de Man RA, Zeuzem S, Lou L, et al. Kinetics of
1443 hepatitis B surface antigen loss in patients with HBeAg-positive chronic hepatitis
1444 B treated with tenofovir disoproxil fumarate. *J Hepatol* 2014;61:1228-37.

- [128] Lumley SF, Delphin M, Mokaya JF, Tan CCS, Martyn E, Anderson M, et al. A systematic review and meta-analysis of the risk of hepatitis B virus (HBV) resistance in people treated with entecavir or tenofovir. *J Clin Virol* 2024;174:105711.
- [129] Childs K, Davis C, Cannon M, Montague S, Filipe A, Tong L, et al. Suboptimal SVR rates in African patients with atypical genotype 1 subtypes: implications for global elimination of hepatitis C. *J Hepatol* 2019;71:1099-105.
- [130] Fourati S, Rodriguez C, Hézode C, Soulier A, Ruiz I, Poiteau L, et al. Frequent antiviral treatment failures in patients infected with hepatitis C virus genotype 4, subtype 4r. *Hepatology* 2019;69:513-23.
- [131] Vo-Quang E, Soulier A, Ndebi M, Rodriguez C, Chevaliez S, Leroy V, et al. Virological characterization of treatment failures and retreatment outcomes in patients infected with “unusual” HCV genotype 1 subtypes. *Hepatology* 2023;78:607-20.
- [132] Vo-Quang E, Pawlotsky J-M. “Unusual” HCV genotype subtypes: origin, distribution, sensitivity to direct-acting antiviral drugs and behaviour on antiviral treatment and retreatment. *Gut* 2024;73:1570-82.
- [133] Gupta N, Mbituyumuremyi A, Kabahizi J, Ntaganda F, Muvunyi CM, Shumbusho F, et al. Treatment of chronic hepatitis C virus infection in Rwanda with ledipasvir-sofosbuvir (SHARED): a single-arm trial. *Lancet Gastroenterol Hepatol* 2019;4:119-26.
- [134] Yeung A, Palmateer NE, Dillon JF, McDonald SA, Smith S, Barclay S, et al. Population-level estimates of hepatitis C reinfection post scale-up of direct-acting antivirals among people who inject drugs. *J Hepatol* 2022;76:549-57.

- [135] Hosseini-Hooshyar S, Hajarizadeh B, Bajis S, Law M, Janjua NZ, Fierer DS, et al. Risk of hepatitis C reinfection following successful therapy among people living with HIV: a global systematic review, meta-analysis, and meta-regression. *Lancet HIV* 2022;9:e414-27.
- [136] Lens S, Miralpeix A, Gálvez M, Martró E, González N, Rodríguez-Tajes S, et al. HCV microelimination in harm reduction centres has benefits beyond HCV cure but is hampered by high reinfection rates. *JHEP Rep* 2022;4:100580.
- [137] Huang S-C, Su T-H, Tseng T-C, Chen C-L, Hsu S-J, Liao S-H, et al. Distinct effects of hepatic steatosis and metabolic dysfunction on the risk of hepatocellular carcinoma in chronic hepatitis B. *Hepatol Int* 2023;17:1139-49.
- [138] Cheng Y-M, Hsieh T-H, Wang C-C, Kao J-H. Impact of HBV infection on clinical outcomes in patients with metabolic dysfunction-associated fatty liver disease. *JHEP Rep* 2023;5:100836.
- [139] Ciancio A, Ribaldone DG, Dotta A, Giordanino C, Sacco M, Fagoonee S, et al. Long-term follow-up of diabetic and non-diabetic patients with chronic hepatitis C successfully treated with direct-acting antiviral agents. *Liver Int* 2021;41:276-87.
- [140] Tsai P-C, Kuo H-T, Hung C-H, Tseng K-C, Lai H-C, Peng C-Y, et al. Metformin reduces hepatocellular carcinoma incidence after successful antiviral therapy in patients with diabetes and chronic hepatitis C in Taiwan. *J Hepatol* 2023;78:281-92.
- [141] Palom A, Rando-Segura A, Calatayud-Samper L, Fernández-Rivas G, Sellés-Sanchez A, Mormeneo-Bayo S, et al. Real-world outcomes of Opti-Hep-D: an innovative, multicentre and multidisciplinary program improving hepatitis D cascade of care. *Liver Int* 2026;46:e70672.

- 1494 [142] Mageras A, Rodriguez N, Katzenstein C, Lee F, Alpert L, Branch AD, et al. Novel
1495 implementation of hepatitis B to hepatitis Delta reflex testing in a US healthcare
1496 system. *Am J Gastroenterol* 2026;121:1650-8.
- 1497 [143] Kamal H, Lindahl K, Ingre M, Gahrton C, Karkkonen K, Nowak P, et al. The
1498 cascade of care for patients with chronic hepatitis delta in Southern Stockholm,
1499 Sweden for the past 30 years. *Liver Int* 2024;44:228-40.
- 1500 [144] Wedemeyer H, Aleman S, Brunetto MR, Blank A, Andreone P, Bogomolov P, et
1501 al. A phase 3, randomized trial of bulevirtide in chronic hepatitis D. *N Engl J Med*
1502 2023;389:22-32.
- 1503 [145] Wedemeyer H, Aleman S, Blank A, Andreone P, Bogomolov P, Chulanov V, et
1504 al. 144 weeks of bulevirtide monotherapy for chronic hepatitis D: final and post-
1505 treatment results from a phase III randomized trial. *J Hepatol* 2026; online ahead
1506 of print.
- 1507 [146] Yang JD, Mohamed EA, Aziz AOA, Shousha HI, Hashem MB, Nabeel MM, et
1508 al. Characteristics, management, and outcomes of patients with hepatocellular
1509 carcinoma in Africa: a multicountry observational study from the Africa Liver
1510 Cancer Consortium. *Lancet Gastroenterol Hepatol* 2017;2:103-11.
- 1511 [147] Shimakawa Y, Njie R, Ndow G, Vray M, Mbaye PS, Bonnard P, et al.
1512 Development of a simple score based on HBeAg and ALT for selecting patients
1513 for HBV treatment in Africa. *J Hepatol* 2018;69:776-84.
- 1514 [148] Minier N, Guingané AN, Okeke E, Sinkala E, Johannessen A, Andersson MI, et
1515 al. Development and evaluation of a simple treatment eligibility score
1516 (HEPSANET) to decentralise hepatitis B care in Africa: a cross-sectional study.
1517 *Lancet Gastroenterol Hepatol* 2024;9:323-32.

- 1518 [149] European Association for the Study of the Liver. EASL Clinical Practice
1519 Guidelines on the management of hepatitis B virus infection. *J Hepatol*
1520 2025;83:502-83.
- 1521 [150] Nguyen LBL, Lemoine M, Ndow G, Ward ZJ, Hallet TB, D'Alessandro U, et al.
1522 Treat-all versus targeted strategies to select HBV-infected people for antiviral
1523 therapy in The Gambia, west Africa: a cost-effectiveness analysis. *Lancet Glob*
1524 *Health* 2024;12:e66-78.
- 1525 [151] Dore GJ, Feld JJ, Thompson A, Martinello M, Muir AJ, Agarwal K, et al.
1526 Simplified monitoring for hepatitis C virus treatment with glecaprevir plus
1527 pibrentasvir, a randomised non-inferiority trial. *J Hepatol* 2020;72:431-40.
- 1528 [152] Solomon SS, Wagner-Cardoso S, Smeaton L, Sowah LA, Wimbish C, Robbins
1529 G, et al. A minimal monitoring approach for the treatment of hepatitis C virus
1530 infection (ACTG A5360 [MINMON]): a phase 4, open-label, single-arm trial.
1531 *Lancet Gastroenterol Hepatol* 2022;7:307-17.
- 1532 [153] Buti M, Gane E, Seto WK, Chan HLY, Chuang W-L, Stepanova T, et al.
1533 Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of
1534 patients with HBeAg-negative chronic hepatitis B virus infection: a randomised,
1535 double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*
1536 2016;1:196-206.
- 1537 [154] Agarwal K, Brunetto M, Seto WK, Lim Y-S, Fung S, Marcellin P, et al. 96 weeks
1538 treatment of tenofovir alafenamide vs. tenofovir disoproxil fumarate for hepatitis
1539 B virus infection. *J Hepatol* 2018;68:672-81.
- 1540 [155] Chan HLY, Buti M, Lim Y-S, Agarwal K, Marcellin P, Brunetto M, et al. Long-
1541 term treatment with tenofovir alafenamide for chronic hepatitis B results in high

- 1542 rates of viral suppression and favorable renal and bone safety. *Am J*
1543 *Gastroenterol* 2024;119:486-96.
- 1544 [156] Woldemedihnn GM, Aberra H, Desalegn H, Berhe N, Belay DB, Rueegg CS, et
1545 al. Renal safety of long-term tenofovir disoproxil fumarate treatment in patients
1546 with chronic hepatitis B. *Open Forum Infect Dis* 2023;10:ofad404.
- 1547 [157] Yuen MF, Lim SG, Plesniak R, Tsuji K, Janssen HLA, Pojoga C, et al. Efficacy
1548 and safety of bepirovirsen in chronic hepatitis B infection. *N Engl J Med*
1549 2022;387:1957-68.
- 1550 [158] Hou J, Lim SG, Buti M, Yuen MF, Gane E, Lampertico P, et al. Phase 3 results
1551 of bepirovirsen treatment for chronic hepatitis B virus infection. *N Engl J Med*
1552 2026;394:2395-406.
- 1553 [159] Delphin M, Mohammed KS, Downs LO, Lumley SF, Waddilove E, Okanda D, et
1554 al. Under-representation of the WHO African region in clinical trials of
1555 interventions against hepatitis B virus infection. *Lancet Gastroenterol Hepatol*
1556 2024;9:383-92.
- 1557 [160] Winner B, Peipert JF, Zhao Q, Buckel C, Madden T, Allsworth JE, et al.
1558 Effectiveness of long-acting reversible contraception. *N Engl J Med*
1559 2012;366:1998-2007.
- 1560 [161] Swindells S, Andrade-Villanueva J-F, Richmond GJ, Rizzardini G, Baumgarten
1561 A, Masiá M, et al. Long-acting cabotegravir and rilpivirine for maintenance of
1562 HIV-1 suppression. *N Engl J Med* 2020;382:1112-23.
- 1563 [162] Fobelo Lozano MJ, Sánchez-Fidalgo S. Adherence and preference of
1564 intravenous zoledronic acid for osteoporosis versus other bisphosphonates. *Eur*
1565 *J Hosp Pharm* 2019;26:4-9.

- 1566 [163] Flexner C, Thomas DL, Clayden P, Swindells S. What clinicians need to know
1567 about the development of long-acting formulations. Clin Infect Dis
1568 2022;75:S487-9.
- 1569 [164] [https://www.unmc.edu/newsroom/2023/01/06/study-shows-proof-of-concept-
1570 efficacy-for-a-long-acting-hepatitis-b-treatment/](https://www.unmc.edu/newsroom/2023/01/06/study-shows-proof-of-concept-
1570 efficacy-for-a-long-acting-hepatitis-b-treatment/).
- 1571 [165] [https://www.croiconference.org/wp-
1572 content/uploads/sites/2/posters/2022/CROI2022_Poster_545.pdf](https://www.croiconference.org/wp-
1572 content/uploads/sites/2/posters/2022/CROI2022_Poster_545.pdf)
- 1573 [166] Higashi-Kuwata N, Hayashi S, Kumamoto H, Ogata-Aoki H, Das D, Venzon D,
1574 et al. Identification of a novel long-acting 4'-modified nucleoside reverse
1575 transcriptase inhibitor against HBV. J Hepatol 2021;74:1075-86.
- 1576 [167] Durantel D, Dousson CB, Lampertico P. Is there any need for new, long-acting
1577 nucleos(t)ide analogues for the treatment of hepatitis B infection? J Hepatol
1578 2021;74:1011-4.
- 1579 [168] Harris AM, Link-Gelles R, Kim K, Chandrasekar E, Wang S, Bannister N, et al.
1580 Community-based services to improve testing and linkage to care among non-
1581 U.S.-born persons with chronic hepatitis B virus infection: three U.S. programs,
1582 October 2014-September 2017. MMWR Morb Mortal Wkly Rep 2018;67:541-6.
- 1583 [169] Palom A, Almandoz E, Madejón A, Rando-Segura A, Pérez-Castaño Y, Vico J,
1584 et al. Community strategy for hepatitis B, C, and D screening and linkage to care
1585 in Mongolians living in Spain. Viruses 2023;15:1506.
- 1586 [170] Razavi HA, Waked I, Qureshi H, Kondili LA, Duberg A-S, Aleman S, et al.
1587 Number of people treated for hepatitis C virus infection in 2014-2023 and
1588 applicable lessons for new HBV and HDV therapies. J Hepatol 2025;83:329-47.
- 1589 [171] Ward KM, Falade-Nwulia O, Moon J, Sutcliffe CG, Brinkley S, Haselhuhn T, et
1590 al. A randomized controlled trial of cash incentives or peer support to increase

- 1591 HCV treatment for persons with HIV who use drugs: the CHAMPS study. Open
1592 Forum Infect Dis 2019;6:ofz166.
- 1593 [172] Laureillard D, Binh NT, Vinh VH, Hong TT, Quillet C, Thanh NTT, et al. High
1594 efficiency and safety of hepatitis C treatment among people who inject drugs in
1595 Vietnam. J Viral Hepat 2025;32:e70090.
- 1596 [173] Zhang M, O'Keefe D, Craig J, Samley K, Bunreth V, Jolivet P, et al.
1597 Decentralised hepatitis C testing and treatment in rural Cambodia: evaluation of
1598 a simplified service model integrated in an existing public health system. Lancet
1599 Gastroenterol Hepatol 2021;6:371-80.
- 1600 [174] Draper BL, Htay H, Pedrana A, Yee WL, Howell J, Pyone Kyi K, et al. Outcomes
1601 of the CT2 study: A 'one-stop-shop' for community-based hepatitis C testing and
1602 treatment in Yangon, Myanmar. Liver Int 2021;41:2578-89.
- 1603 [175] Nyein P, Tillakeratne S, Phyu S, Yee M, Lwin M, Htike K, et al. Evaluation of
1604 simplified HCV diagnostics in HIV/HCV co-infected patients in Myanmar. Viruses
1605 2023;15:521.
- 1606 [176] Boke J, Monroe-Wise A, Umutesi G, Mbogo L, Sambai B, Bukusi D, et al.
1607 Experience and challenges delivering hepatitis C virus treatment for people who
1608 inject drugs in Kenya. Front Med 2024;11:1429516.
- 1609 [177] Saayman E, Hechter VB, Sishwili NS, Sonderup MW. A decentralized point of
1610 service triple prevention and treatment model for hepatitis B, C and HIV in people
1611 who inject drugs in South Africa. Int J Drug Policy 2025;143:104894.
- 1612 [178] Grebely J, Applegate TL, Cunningham P, Feld JJ. Hepatitis C point-of-care
1613 diagnostics: in search of a single visit diagnosis. Expert Rev Mol Diagn
1614 2017;17:1109-15.

- 1615 [179] Dara M, Ehsani S, Mozalevskis A, Vovc E, Simões D, Avellon Calvo A, et al.
1616 Tuberculosis, HIV, and viral hepatitis diagnostics in eastern Europe and central
1617 Asia: high time for integrated and people-centred services. *Lancet Infect Dis*
1618 2020;20:e47-53.
- 1619 [180] Musafiri T, Kamali I, Kayihura C, de la Paix Gakuru J, Nyirahabihirwe F,
1620 Nizeyimana E, et al. Prevalence of hepatitis B and C infection and linkage to
1621 care among patients with non-communicable diseases in three rural Rwandan
1622 districts: a retrospective cross-sectional study. *BMC Infect Dis* 2024;24:247.
- 1623 [181] Dugan E, Blach S, Biondi M, Cai Z, DePaola M, Estes C, et al. Global prevalence
1624 of hepatitis C virus in women of childbearing age in 2019: a modelling study.
1625 *Lancet Gastroenterol Hepatol* 2021;6:169-84.
- 1626 [182] Wang J, Feng Q, Tam A, Sun T, Zhou P, So S. Evaluation of the first open-
1627 access hepatitis B and safe injection online training course for health
1628 professionals in China. *BMC Med Educ* 2016;16:81.
- 1629 [183] Yang HI, Yuen MF, Chan HLY, Han KH, Chen PJ, Kim DY, et al. Risk estimation
1630 for hepatocellular carcinoma in chronic hepatitis B (REACH-B): development
1631 and validation of a predictive score. *Lancet Oncol* 2011;12:568-74.
- 1632 [184] Papatheodoridis G, Dalekos G, Sypsa V, Yurdaydin C, Buti M, Goulis J, et al.
1633 PAGE-B predicts the risk of developing hepatocellular carcinoma in Caucasians
1634 with chronic hepatitis B on 5-year antiviral therapy. *J Hepatol* 2016;64:800-6. -
- 1635 [185] Kim JH, Kim YD, Lee M, Jun BG, Kim TS, Suk KT, et al. Modified PAGE-B score
1636 predicts the risk of hepatocellular carcinoma in Asians with chronic hepatitis B
1637 on antiviral therapy. *J Hepatol* 2018;69:1066-73.

- 1638 [186] Afum C, Cudjoe L, Hills J, Hunt R, Padilla LA, Elmore S, et al. Association
1639 between aflatoxin M1 and liver disease in HBV/HCV infected persons in Ghana.
1640 Int J Environ Res Public Health 2016;13:377.
- 1641 [187] Liu Y, Chang C-CH, Marsh GM, Wu F. Population attributable risk of aflatoxin-
1642 related liver cancer: systematic review and meta-analysis. Eur J Cancer
1643 2012;48:2125-36.
- 1644 [188] <https://www.aflatoxinpartnership.org>
- 1645 [189] Ramírez Mena A, Thiam M, Ka D, Niang I, Tine J, Fortes L, et al. Hepatocellular
1646 carcinoma surveillance among people living with hepatitis B in Senegal (SEN-
1647 B): insights from a prospective cohort study. Lancet Gastroenterol Hepatol
1648 2024;9:539-49.
- 1649 [190] Tappata M, Ford J, Kayandabila J, Morrison J, Seth S, Lyimo B, et al.
1650 Community-based point-of-care screening for hepatitis B virus and
1651 hepatocellular carcinoma in rural Tanzania. Am J Trop Med Hygiene
1652 2025;112:167-72.
- 1653 [191] Ladep NG, Dona AC, Lewis MR, Crossey MME, Lemoine M, Okeke E, et al.
1654 Discovery and validation of urinary metabotypes for the diagnosis of
1655 hepatocellular carcinoma in West Africans. Hepatology 2014;60:1291-301.
- 1656 [192] Singal AG, Tayob N, Mehta A, Marrero JA, El-Serag H, Jin Q, et al. GALAD
1657 demonstrates high sensitivity for HCC surveillance in a cohort of patients with
1658 cirrhosis. Hepatology 2022;75:541-9.
- 1659 [193] Truong TN, Pham TND, Hoang LB, Nguyen VT, Dao HV, Dao DVB, et al.
1660 Surveillance and treatment of primary hepatocellular carcinoma (aka. STOP
1661 HCC): protocol for a prospective cohort study of high-risk patients for HCC using
1662 GALAD-score. BMC Cancer 2023;23:875.

- 1663 [194] Waked I, Esmat G, Elsharkawy A, El-Serafy M, Abdel-Razek W, Ghalab R, et
1664 al. Screening and treatment program to eliminate hepatitis C in Egypt. *N Engl J*
1665 *Med* 2020;382:1166-74.
- 1666 [195] Zhong H, Aaron A, Hiebert L, Serumondo J, Zhuo Y, Adey M, et al. Hepatitis C
1667 elimination in Rwanda: progress, feasibility, and economic evaluation. *Value*
1668 *Health* 2024;27:918-25.
- 1669 [196] Makuza JD, Tuyishime A, Janjua N, Gupta N. HBV elimination in sub-Saharan
1670 Africa: Rwanda's approach to health system integration. *Lancet Gastroenterol*
1671 *Hepatol* 2022;7:511-2.
- 1672 [197] Dashdorj ED, Sereenendorj K, Ochirsum B, Bat-Ulzii P, Renchindorj B, Dashdorj
1673 AN, et al. Progress towards elimination: hepatitis B and C among children and
1674 young adults in rural Mongolia. *J Viral Hepat* 2026;33:e70145.
- 1675 [198] Lim AG, Walker JG, Mafirakureva N, Khalid GG, Qureshi H, Mahmood H, et al.
1676 Effects and cost of different strategies to eliminate hepatitis C virus transmission
1677 in Pakistan: a modelling analysis. *Lancet Glob Health* 2020;8:e440-50.

Table 1. WHO 2030 targets for viral hepatitis elimination. Adapted from WHO reports.

Domain	HBV	HCV
Impact targets		
Incidence reduction (vs. 2015)	95%	80%
Mortality reduction (vs. 2015)	65%	65%
Incidence target	≤2 per 100,000 population	≤5 per 100,000 population
Mortality target	≤4 per 100,000 population	≤2 per 100,000 population
Service coverage targets		
Infant hepatitis B vaccination	90%	—
Timely hepatitis B birth-dose vaccination	90%	—
Diagnosis	90%	90%
Treatment coverage among eligible individuals	80%	80%
Blood safety	100% screening of blood donations	
Injection safety	100% safe injections	
Harm reduction	300 sterile needles/syringes per PWID per year	

Table 2. Current global coverage of key interventions required to achieve WHO 2030 viral hepatitis elimination targets. Adapted from the 2026 Global Hepatitis Report [2]. *Values correspond to the latest WHO global estimates (2024 unless otherwise indicated). Blood safety is based on the latest available global data (2018), and injection safety on the latest available global estimates (2011-2015).

Intervention	Indicator	Global status (2024)*	WHO target (2030)
HBV prevention	Timely hepatitis B birth-dose vaccination	45%	90%
	Three-dose infant hepatitis B vaccination	84%	90%
HBV care cascade	People with chronic HBV infection diagnosed	27%	90%
	Eligible people with chronic HBV infection receiving antiviral treatment	4%	80%
HCV care cascade	People with HCV infection diagnosed	36%	90%
	Eligible people with HCV infection treated	20%	80%
Blood safety	Blood donations screened for transfusion-transmissible infections	98%	100%
Injection safety	Safe injections in health-care settings	96%	100%
Harm reduction	Needles and syringes distributed per person who injects drugs per year	35	300

1690 **Table 3.** Barriers to viral hepatitis elimination across the care cascade in LMICs.

1691

Step of care cascade	Barrier	HBV-specific aspects	HCV-specific aspects	Cross-cutting/system-level aspects	Consequences
Prevention (vaccination, harm reduction)	Limited access to prevention tools	• Birth dose delivery challenges • Cold/controlled temperature chain • Suboptimal vaccine coverage	• No vaccine available	• Health system constraints • Funding gaps • Policy barriers • Limited harm reduction coverage	Ongoing transmission
MTCT prevention	Gaps in antenatal screening and prophylaxis	• Limited HBV DNA testing • Suboptimal HBeAg-based strategies • Low antiviral prophylaxis uptake • Vaccine escape mutations (HBV genotype E)	• Limited systematic HCV screening in pregnancy • No approved treatment during pregnancy	• Fragmented maternal health services • Limited integration	Continued vertical transmission
Testing	Limited access to testing	• Reliance on HBsAg RDTs • Limited access to HBV DNA quantification	• Two-step diagnosis (antibody + RNA) • Limited access to HCV RNA testing	• Rural access barriers • Stigma • Low awareness • Funding constraints	Low diagnosis rates
	Complex diagnostic pathways	• Treatment eligibility requires staging	• Multi-step cascade leading to loss to follow-up	• Weak linkage systems • Siloed programmes	Drop-off across cascade
Across cascade	Loss to follow-up	• Occurrence at testing, staging • Sustained engagement required by lifelong therapy	• Amplified by multi-step diagnosis	• Weak referral systems • Limited patient navigation	Low treatment initiation and retention

	Stigma and criminalisation	• Stigma around HBV testing • Impact on pregnant women and antenatal care uptake	• Criminalisation and stigmatisation of PWID • Barrier to harm reduction and DAA access	• Discrimination • Legal barriers	Reduced access to services
Linkage to care	Weak linkage systems	• Limited follow-up after diagnosis	• Particularly affects key populations • Exacerbated by diagnostic complexity	• Poor referral systems • Limited integration with other programmes	Low treatment uptake
Treatment access	Limited access to antivirals	• Lifelong therapy • Variable access to TDF/TAF	• Limited access to DAAs • Lack of availability of some regimens (e.g. glecaprevir/pibrentasvir) • Unnecessary alcohol abstinence requirements • PWID exclusion policies	• Cost • Regulatory barriers • Centralised care	Low treatment coverage
Treatment and follow-up	Retention challenges	• Lifelong monitoring required	• Reinfection risk in key populations	• Transport costs • Health system constraints	Poor long-term outcomes
Comorbidities and complications	Limited management capacity	• HDV underdiagnosis • Limited access to HDV treatment	• Persistent HCC risk post-SVR in patients with cirrhosis	• Limited access to diagnostics (e.g. elastography, imaging) • HCC risk • MASLD impact	Increased morbidity and mortality

Table 4. Innovations to overcome barriers across the viral hepatitis care cascade in LMICs.

Step of care cascade	Innovation	HBV-specific applications	HCV-specific applications	Cross-cutting/system-level innovations	Expected potential impact
Prevention	Improved vaccine delivery	• Birth dose optimization • Controlled temperature chain • Novel delivery systems (microneedle patches, mucosal vaccines) • Conditional incentives • Tri-antigen vaccines for immunocompromised patients	-	• Integration into maternal and child health services	Increased vaccine coverage
	MTCT prevention strategies	• Treat-all approaches • HBeAg-based and HBV DNA-based strategies • POC HBcrAg lateral flow assay	• Universal HCV screening in pregnancy • DAA treatment during pregnancy	• Integration with HIV/syphilis antenatal programmes	Reduced MTCT
	Harm reduction scale-up	• HBV vaccination in PWID	• Micro-elimination one-stop models for PWID (testing, treatment, and harm reduction at point of care)	• Policy reform • Decriminalisation • Needle and syringe programmes • OST/OAT	Reduced transmission
Testing	Simplified diagnostic algorithms	• HBsAg RDT-based strategies	• One-step diagnosis (core antigen or RNA)	• Streamlined care pathways	Reduced loss to follow-up

	Universal/opt-out screening	One-time HBsAg screening in high-prevalence settings	Integrated opt-out testing in healthcare and community settings	Linkage to vaccination and care	Increased case detection
	Self-testing	Self-test HBsAg kits	First WHO-prequalified HCV self-test	- Improved acceptability - Reduced stigma	Increased testing uptake
	Alternative sampling methods	DBS-based HBV testing	DBS and oral fluid testing	Easier sample collection and transport	Expanded access
	POC and near-POC molecular testing	- Cartridge-based platforms - LAMP and RPA isothermal assays	- POC HCV RNA and core antigen platforms - CRISPR-based technologies	Integration with HIV/TB diagnostic platforms	Same-day diagnosis
	Multiplex testing	HBV/HIV integration	HCV/HIV integration	Multi-disease testing platforms	Improved efficiency
Linkage to care	Integrated care models	Integration into HIV and maternal care	Integration into harm reduction services	- Patient navigation - Community-based approaches - Integration with noncommunicable disease screening (diabetes, obesity) at district level	Improved retention
Treatment	Simplified treatment eligibility	- TREAT-B - Simplified WHO criteria	- Pan-genotypic DAAs - No genotyping	Task-shifting to non-specialists	Increased treatment uptake
	Decentralised care	Primary care-based HBV management	Community-based HCV treatment	- Task-sharing - Decentralisation	Improved access
	Long-acting therapies (future)	Long-acting HBV agents in development	Long-acting DAAs (concept)	- Reduced visit frequency - Potential for “test and treat” models	Improved adherence
Monitoring and outcomes	Simplified monitoring	ALT-based monitoring	MINMON approach	- Digital tools - Remote follow-up	Improved retention

		• Reduced HBV DNA testing frequency in stable patients			
Health systems	Integration across programmes	• Integration of HBV vaccination into SARS-CoV-2/noncommunicable disease platforms • HBsAg screening in blood banks	• Integration of HCV screening into tuberculosis • noncommunicable disease, and emergency programmes	• National programme integration • Sustainable financing within Global Fund mechanisms • Healthcare worker training	System strengthening

Figure legends

Figure 1. Barriers to achieving viral hepatitis elimination targets through key interventions. This figure illustrates the primary obstacles to achieving the key pillars of the WHO's viral hepatitis elimination strategy. The percentages describe the estimated global coverage for each intervention, based on data from the WHO's 2026 Global Hepatitis Report [2]. The identified barriers include structural, technical and social factors that hinder progress towards elimination in LMICs. HBV: hepatitis B virus; HCV: hepatitis C virus; MTCT: mother-to-child transmission; HBeAg: hepatitis B e antigen; RDT: rapid diagnostic test; GAVI: Global Alliance for Vaccines and Immunisation. *2024 estimation.

Figure 2. Key innovations and strategies to accelerate viral hepatitis elimination. The figure summarises current and emerging approaches that support the WHO viral hepatitis elimination agenda. The interventions are organised according to three complementary domains: cascade of care (orange); public health interventions (pink); and comorbidities and complications (purple). Innovations include point-of-care technologies, simplified treatment pathways, decentralised testing platforms and the integration of hepatitis programmes. HBV: hepatitis B virus; HCV; hepatitis C virus; HDV; hepatitis D virus; HCC: hepatocellular carcinoma; MTCT; mother-to-child transmission; POC: point-of-care; RDT: rapid diagnostic test; HBcrAg; hepatitis B core-related antigen. Created with BioRender.com.

1720 **Figure 3.** Simplified and decentralised care to overcome barriers and accelerate viral
1721 hepatitis elimination in LMICs.

Individual

Maternal education; socio-cultural background; religion; household wealth; geographical location; birth order; birth year; individual trust in vaccination

Provider

Lack of knowledge regarding vaccine indications and contraindications; inadequately trained medical staff; lack of reminder systems for missed vaccinations

System

Weak immunisation delivery systems; issues with the cold chain and storage

Birth dose vaccine

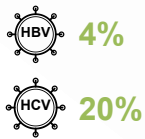
Similar challenges to those of the 3-dose HBV vaccine; timely administration in rural areas, among infants born outside of health facilities, and on non-vaccination days; paused GAVI support

Antiviral prophylaxis in pregnancy

Expensive HBV DNA testing; low sensitivity of HBeAg RDTs; limited access

INTERVENTION

Blood safety / 98%
Injection safety / 96%
Harm reduction / 35

Treatment /**Implementation**

Complex eligibility criteria; time and cost of travelling to centralised care provision

Access

Drug cost; marginalised populations, including migrants; lack of government and international funding; lack of a registration process for antiviral therapies; abstinence requirement for access to HCV DAAs; centralised services

Follow-up

Out-of-pocket costs; transportation

Unsuccessful treatment

Drug resistance with older generations of HBV therapy and with HCV DAAs in "unusual" HCV subtypes

Comorbidities

Identification of patients with MAFLD and HDV infection; surveillance for liver cancer

Blood safety

Window periods of HBV and HCV infection; RDTs used as the sole screening method; limited availability of nucleic acid testing; occult infection

Injection safety

Access to syringes with sharps injury protection and reuse prevention; knowledge and practice among professionals

Harm reduction

Restrictive drug laws; limited needle and syringe programmes and opioid substitution

**Testing /****Individual**

Lack of knowledge; low educational attainment; stigma and confidentiality concerns

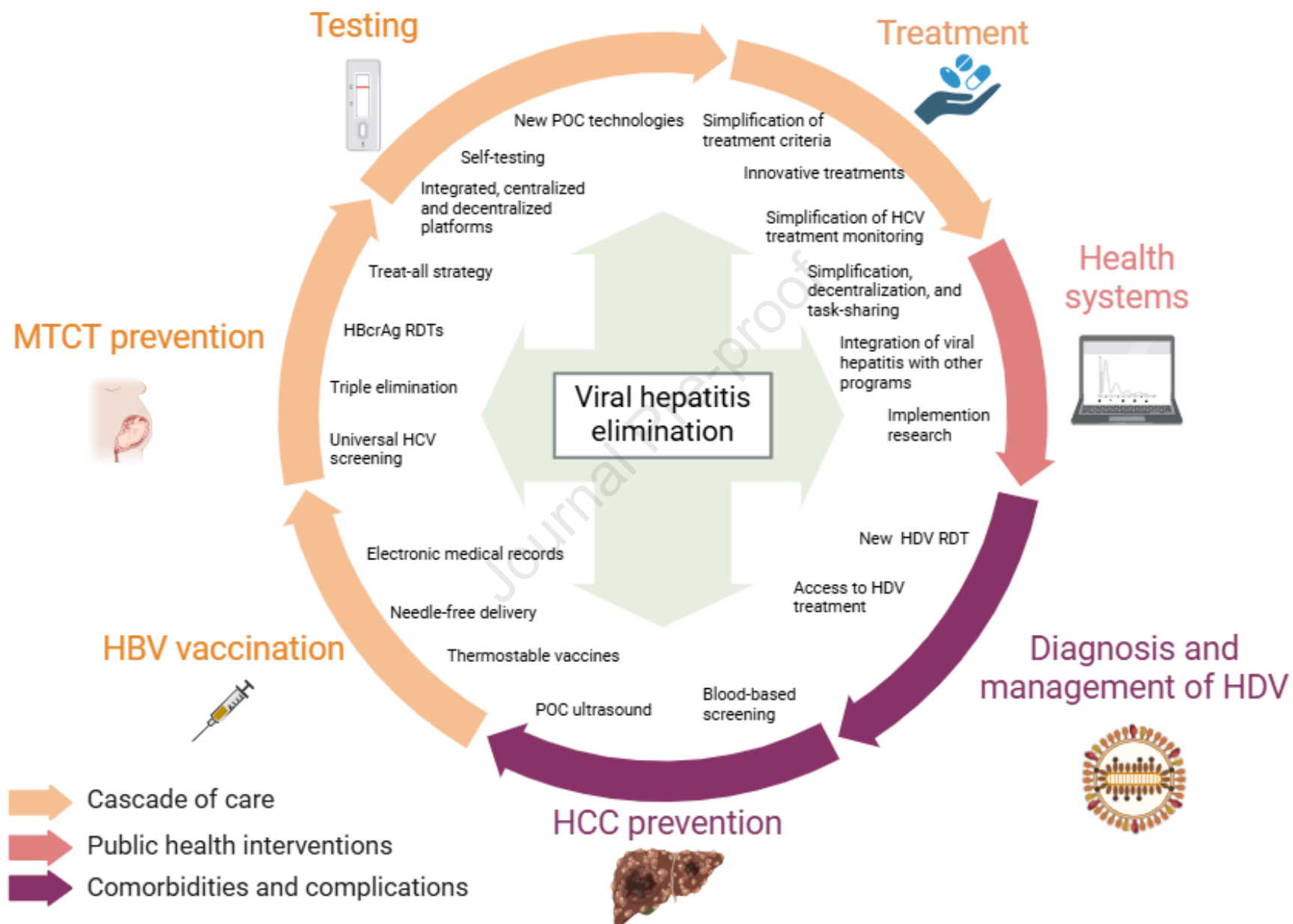
Provider

Time constraints; lack of specific knowledge about HCV; discomfort in asking about risk behaviours

System

Policy and funding gaps; weak laboratory capacity in rural areas

Figure 2



Simplified and decentralized care to overcome barriers and accelerate viral hepatitis elimination in LMICs

