Global hepatitis C elimination: an investment framework

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WHO has set global targets for the elimination of hepatitis B and hepatitis C as a public health threat by 2030. However, investment in elimination programmes remains low. To help drive political commitment and catalyse domestic and international financing, we have developed a global investment framework for the elimination of hepatitis B and hepatitis C. The global investment framework presented in this Health Policy paper outlines national and international activities that will enable reductions in hepatitis C incidence and mortality, and identifies potential sources of funding and tools to help countries build the economic case for investing in national elimination activities. The goal of this framework is to provide a way for countries, particularly those with minimal resources, to gain the substantial economic benefit and cost savings that come from investing in hepatitis C elimination.

Introduction

In 2016, the World Health Assembly adopted the WHO Global Health Sector Strategy on Viral Hepatitis 2016–21,¹ which provided a roadmap for the elimination of hepatitis B and hepatitis C and outlined clear elimination targets, including an 80% reduction in new chronic infections and a 65% reduction in mortality compared with 2015. Although 194 countries have endorsed this strategy, far fewer have developed national plans for viral hepatitis elimination,² with only some adopting a public health approach to eliminating viral hepatitis. In many countries, the major barriers to a comprehensive response are leadership and political will, which is exacerbated by competing health-care priorities and scarce resources,³ particularly in highly endemic areas.¹ A Lancet Gastroenterology & Hepatology Commission,⁴ which focused on accelerating the elimination of viral hepatitis, identified 20 heavily burdened countries that account for more than 75% of the global burden of viral hepatitis and highlighted the need for these countries to mobilise domestic funding to address this issue. The Commission outlined innovative financing models to support country-level elimination programmes and called for the development of an investment case for viral hepatitis to show the feasibility of elimination and quantify its health, social, and economic benefits.

An estimated 71 million people are living with hepatitis C infection and at current rates of infection, hepatitis C will cause 0·84 million deaths annually by 2040 due to hepatitis C-related cirrhosis and liver cancer.⁴ However, the advent of direct-acting antivirals has revolutionised hepatitis C care, with cure rates of more than 95% after 8–12 weeks of well-tolerated once-daily tablets, and these drugs have provided a unique opportunity to eliminate hepatitis C as a global public health threat. Since direct-acting antivirals became available in 2013,³ they have been shown to reduce the risk of liver failure and liver cancer⁵ and improve patients’ quality of life.⁶ A full course of generic direct-acting antivirals is now available at a cost of US$105 in 112 low-income and middle-income countries⁷ but are cost-effective even at a much higher price across a range of low-income, middle-income, and high-income country settings.¹⁴¹¹ Nonetheless, treatment coverage remains low globally, with an estimated 5 million people initiating direct-acting antiviral treatment by the end of 2017, leaving most people who are living with a hepatitis C infection untreated.⁶ Emerging data about the productivity losses associated with hepatitis C, and conversely the improvements in productivity after cure,¹²¹⁷ will help quantify the broader economic losses attributable to hepatitis C.¹⁸¹⁹ A WHO costing exercise estimated that a total cost of $16·0 billion was needed for hepatitis C testing and treatment, in addition to $20·5 billion for programme costs to eliminate hepatitis C by 2030 in 67 countries.²⁰ Identifying sources of investment and building the economic case for countries to invest in national hepatitis C-related activities will be crucial to achieve global elimination targets.

In 2011, to capitalise on strong political commitment, an investment approach for an effective response to HIV/AIDS was published, and was seen as a major turning point in the HIV epidemic.²¹ This approach showed how major efficiency gains could be realised through the rapid scale up of HIV/AIDS prevention, treatment, and care programmes by harnessing social mobilisation, increasing synergies between programme elements, and promoting the benefits of treatment as prevention. A similar strategic approach to investment in prevention, testing, and treatment activities for hepatitis B and hepatitis C elimination is needed.

Investment frameworks for viral hepatitis elimination

Building on the work of the WHO Global Health Sector Strategy on viral hepatitis (2016),¹ we developed a strategic investment framework for the global elimination of hepatitis B and hepatitis C by 2030 (figure 1). Although these diseases have different epidemic characteristics, they share many similarities in health system requirements and approaches for effective disease control,¹ including interventions to prevent infections (safety of blood supply and safety of health care-associated injections) and testing and treatment programmes that are delivered through common
platforms (population-based, community-level, health centre, and primary-level, secondary-level, and tertiary-level hospitals) and workforces (specialists, doctors, and nurses). The framework adopts a public health and health-systems strengthening approach to identify national and international activities that would support country-level implementation of viral hepatitis elimination strategies across diverse settings. For the purposes of this Health Policy paper, we focus on hepatitis C elimination to show how policy makers and
Government health expenditure | Increase government health expenditure and increase budget allocation for hepatitis C activities; develop an HCV national plan and investment case to estimate the size of the population living with hepatitis C and the overall costs to the community and government | Australia,26 Egypt,56 and Scotland;41 African Union countries14 committed to allocate at least 15% of their annual budget to improve the health sector in their country

Health insurance and universal health coverage | Increase access and use by making health services more affordable through voluntary or mandatory health insurance and universal health coverage schemes | Thailand24 and South Africa41

Influencing market forces to reduce costs of commodities | Encourage effective price negotiations with pharmaceutical manufacturers for hepatitis treatment and diagnostics; local production of generic drugs; volume or tiered pricing; Medicines Patent Pool; compulsory licences and patent challenges | Australia,32 Mercosur countries,26 Pakistan,26 India,39 Malaysia,10 Affordable Medicines Facility-malaria (AMFM)18 is a pilot project funded by UNITAID and hosted by the Global Fund that negotiates price reductions of malaria treatments with manufacturers and provides a subsidy to buyers through a co-payment; Argentina, Brazil, China, Morocco, the Russian Federation, Ukraine, and Médecins du Monde are challenging the patent applications for sofosbuvir26

Maximising effectiveness of public health spending | Synergistic action creates opportunities to finance substantial improvements in HCV care without further straining health-sector budgets via integration of viral hepatitis into existing services and universal health coverage; adopt an investment case approach to guide investments for maximum impact; reallocation of existing funds towards hepatitis | South Africa13,14 and Scotland;41 Global Fund’s Debt2Health initiative13 helps channel the resources of developing countries away from debt repayment and towards life-saving investments in health

Innovations to reduce costs of commodities or health service delivery | Dried blood sampling to reduce diagnostics costs; non-specialist care models, including task sharing and task shifting; financial transaction tax to generate revenue for health programmes | Australia26 and Scotland;41 UNITAID has raised US$2 billion from a €1 levy on air tickets leaving France and has been applied in 15 countries globally

Private-public partnerships | Formal risk-management mechanism in which public authorities partner with the private sector to provide services. Private-public partnerships aim to share the risks and costs of investment, while enhancing the development of innovation through partnerships | The Gavi Matching Fund25 is a public–private partnership designed to incentivise private sector investments in immunisation; RED24 is a brand created to engage business and consumer power in the fight against AIDS in Africa. Branded products and services, when purchased, activate corporate giving to the Global Fund. RED has generated over US$600 million in funds

Development assistance for health (international donors) | Provision of effective treatment through development assistance for health; low-cost diagnostics | UNITAID14 is partnering with GFID to support the development of better, simpler, point-of-care diagnostic tools for HCV and to introduce HCV testing and treatment into HIV programmes in seven countries

Sharing costs with other strategies | Harm reduction costs can be shared between diseases (eg, HIV and HCV), and therefore can be more cost-effective; immunisation and blood safety; co-infection with HIV and service delivery | Portugal,13 Pakistan, Rwanda,38 Brazil,19 and Georgia;32 for 35 years, the Pan American Health Organization (PAHO) Revolving Fund for vaccines39 has helped member states pool their national resources to procure high-quality life-saving vaccines and related products at the lowest price

Dedicated hepatitis fund | Create a global viral hepatitis fund to use resources and cultivate synergies through innovative public–private partnerships to catalyse action on viral hepatitis; the proposed fund would primarily support the most affected countries and communities where, despite national commitment, national health systems cannot adequately or effectively address hepatitis epidemics | EndHep2030 Fund29 is the only grant-making organisation dedicated exclusively to the mission of ending viral hepatitis

Pooled financing | Bring together development and commercial actors to pool financing and offer opportunities to scale up blended finance models. Blended finance models are the strategic use of development finance and philanthropic funds to mobilise private capital flows to emerging and frontier markets | The Global Procurement Fund (GPRO)24 works with participating countries to pool orders from member countries and uses international competitive bidding to purchase products at negotiated prices. GPRO only works with manufacturers that have freedom to operate with a license from originator companies or those with a licence from the Medicines Patent Pool

Results-based financing | Seek to create market incentives to achieve key social outcomes by only paying when results are achieved. Performance-based financing targets the supply side, whereas conditional cash transfers target the demand side of a given market | Since 2014, the Global Fund has implemented a results-based financing model in Rwanda39 called National Strategy Financing to incentivise results and efficiency

Social impact bonds and development impact bonds | Social impact bonds and development impact bonds draw on elements of impact investing and public-private partnerships and allow outcome funders to pay directly for the achievement of outcomes rather than for inputs. Investors provide the upfront risk capital and play a critical role in helping improve service delivery by bringing private sector discipline into practice | Global Fund24 supports a social impact bond to address HIV in adolescent girls and young women in South Africa. The International Finance Facility for Immunization uses donor pledges to issue vaccine bonds to raise money for Gavi, the Vaccine Alliance

HCV=hepatitis C virus.

Table 1: Financing mechanisms and approaches to support HCV elimination

others can use this framework to support and justify investment in hepatitis C activities.

For hepatitis C elimination, the framework firstly identifies the importance of using multiple financing sources and mechanisms, including domestic, private sector, and intentional sources to generate or access revenue, which policy makers and financiers can then use to galvanise further investment. Secondly, the framework identifies elimination activities that countries and international agencies can implement, as well as identifying key enablers to allow the effective implementation of hepatitis C programmes at scale. Key enablers are a set of complex factors and interventions that are influenced by societal characteristics that make environments conducive to evidence-based practice and policy—these enablers directly impact on health-care system responsiveness. Finally, the framework outlines the economic benefits of achieving hepatitis C
### Activities and key enablers

| National                                                                 | International                                                                 | Tools                                                                 | Examples                                                                 |
|-------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------|--------------------------------------------------------------------------|
| **(1) Weak surveillance systems and inadequate data**                   |                                                                                | WHO hepatitis C continuum of care monitoring and evaluation framework   | Australia, Scotland, Rwanda, Georgia, Scotland, Rwanda, Brazil            |
| National                                                                | International                                                                 | WHO country health statistics and information systems                  | Rwanda, Brazil                                                          |
| **(2) Low awareness and prioritisation among policy makers**            |                                                                                | World Hepatitis Day events and campaigns; policy reports and briefing   | Scotland, Australia, Egypt                                               |
| National                                                                | International                                                                 | meetings with policy makers; national meetings, conferences, and other  | South Africa, Rwanda, Thailand                                           |
| **(3) Insufficient funding, donor support, and investment for elimination activities** |                                                                                | high-level political forums                                              |                                                                        |
| National                                                                | International                                                                 | Burnet-Optima HCV model; Hep C Programme Financing Strategy Template     | Brazil, Rwanda, Pakistan                                                 |
| **(4) Low awareness of treatment within affected communities and the impact of stigma** |                                                                                | Burnet-Optima HCV model; Hep C Calculator; cost-effectiveness analysis   | South Africa, Thailand                                                  |
| National                                                                | International                                                                 | registry database                                                        |                                                                          |
| **(5) Siloed health programmes and poor health infrastructure**         |                                                                                | Global Health Sector Strategy on Viral Hepatitis 2015–20; WHO Model      | Rwanda, Ukraine, Georgia                                                 |
| National                                                                | International                                                                 | Essential Medicines List; WHO Model Essential In Vitro Diagnostics List; |                                                                          |
| **(6) Systemic and structural barriers to progress**                    |                                                                                | hepatitis testing, treatment, and care guidelines; injection-safety and  |                                                                          |
| National                                                                | International                                                                 | blood-safety policies                                                    |                                                                          |
| **(Table 2 continues on next page)**                                    |                                                                                |                                                                        |                                                                          |
elimination, including direct, indirect, and cross-sectoral economic benefits, and the broader benefits that investment can provide through health systems strengthening. In parallel, to show the impact of the investment framework we modelled two investment scenarios for hepatitis C. First, the elimination scenario, where investments in activities were scaled up to meet WHO targets of diagnosing 90% of people living with hepatitis C and 80% of diagnosed individuals started on treatment by 2030. Second, the progress scenario, in which more modest investments in activities were made to implement hepatitis C testing and treatment targets of diagnosing 45% of people living with hepatitis C and 80% of diagnosed individuals started on treatment by 2030. The models estimate the impact, cost, cost-effectiveness, and economic benefits over time of both scenarios globally and across the six WHO regions. The models estimate the economic productivity losses associated with hepatitis C infection because of absenteeism and presenteeism. Details and findings of these models are detailed in the accompanying modelling Health Policy paper.24

Financing hepatitis C elimination activities

Hepatitis C elimination will require considerable leadership, political will, and financial investment. Global financing sources, such as the Global Fund, Gavi,25 and Unitaid26 have successfully brought together elements of the financing value chain to mobilise, pool, and invest in or replenish health programmes.27 As of July, 2018, the Global Fund had disbursed more than $38 billion for HIV/AIDS, tuberculosis, malaria, and health systems; however, its global strategy for 2017–22 did not mention hepatitis C.28 Since 2013, Unitaid has invested $60 million in programmes that aim to develop better, simpler, point-of-care diagnostic tools and programmes and support countries in gaining access to cheap hepatitis C medicines, as well as in integrating hepatitis C testing and treatment into HIV programmes.26,29 However, with shrinking aid budgets and reduced development assistance for health,30 new funding to support a global response to hepatitis C elimination is unlikely. For most countries, funding for hepatitis C programmes will be reliant on domestic and innovative financing sources and blended finance instruments to sustain and scale up health programmes.27 Blended finance is the strategic use of development finance and philanthropic funds to mobilise private capital flows to emerging and frontier markets in developing countries that can support sustainable development. Domestic sources already account for most of the funding for the development of country-level responses to hepatitis C,24 highlighting the need for clear strategies to enable countries to support intervention scale up and delineate stakeholder responsibility, accountability, and funding models. In 2016, a report on innovative financing of hepatitis B and hepatitis C prevention and treatment in low-income and middle-income countries outlined how a combination of funding mechanisms, adapted to the country, payers, and patients, will be needed to accurately target country-specific challenges.31 This report promoted public–private partnerships with a focus on non-infrastructure interventions and a shared value approach to enable countries to partner with pharmaceutical and diagnostic companies where there are clear synergies between public health programmes and companies’ commercial activities. In 2018, the UN secretary-general launched the strategy for financing the 2030 Agenda for Sustainable

Table 2: Challenges and activities to support investment in hepatitis C elimination

| Activities | Tools | Examples |
|------------|-------|----------|
| (Continued from previous page) | | |
| (6) Restricted access to affordable prevention, diagnostics, and medicines | | |
| National | Negotiate access to affordable diagnostics, prevention, and medicines to ensure population coverage and equitable access to treatments; negotiate prices with pharmaceutical companies; include hepatitis C drugs on the national Essential Medicines List and Essential In Vitro Diagnostics List; use TRIPS flexibilities and patent challenges; simplify clinical guidelines for cost reduction and testing, and treatment decentralisation; comprehensive prevention or harm-reduction service packages | | |
| International | Fund and facilitate access to affordable prevention, diagnostics, and medicines and invest in new technologies: support generic competition to drive prices down; promote mechanisms for affordable medicines acquisition; accelerate regulatory approval for WHO (or equivalent) prequalified products; capacity-building for regulatory authorities’ pre-market assessments and registration of new medicines and diagnostics; encourage private investment funding through innovative blended financing models for low-cost prevention, medicines, and diagnostics’ research and development | | |
Panel: Common challenges to hepatitis C elimination

1 Weak surveillance systems and inadequate data
   • Low-quality surveillance systems and an absence of reliable cause-specific mortality data for liver cancer and liver failure
   • Scarce data of good quality means the true economic impact of viral hepatitis, including health-care costs, reduced quality of life, workforce participation, and productivity, is substantially underestimated
   • As a consequence, insufficient resources are allocated to the issue

2 Low awareness among policy makers and little political will to prioritise hepatitis C elimination
   • Often driven by inadequate data and weak surveillance systems, competing health priorities, and small health budgets
   • Compounded by an absence of awareness in the general population and at-risk communities, who then do not demand action from their governments

3 Insufficient funding, donor support, and investment in hepatitis C elimination activities
   • Insufficient funding from global donors such as the Global Fund and the Bill & Melinda Gates Foundation
   • Countries need to generate domestic revenue for elimination activities

4 Low awareness of hepatitis C treatment within affected communities and the impact of stigma
   • Only 20% of the estimated 71 million people living with hepatitis C are aware of their infection
   • Widespread stigma and discrimination, combined with a lack of understanding that hepatitis C is now easily curable, contributes to low testing and treatment coverage

5 Siloed health programmes and poor health infrastructure
   • Inadequate laboratory capacity
   • Absence of reliable supply chains and quality assurance programmes for vaccines, medicines, and diagnostics
   • Inadequate capacity and skills in the health workforce reduce the effectiveness of viral hepatitis programmes
   • Over-reliance on centralised specialist services or tertiary hospitals, particularly in low-income and middle-income countries, despite clear evidence of the effectiveness of primary-care systems for viral hepatitis service delivery

6 Restricted access to affordable prevention, diagnostics, and medicines
   • Despite major reductions in the cost of treatments over the past few years, major discrepancies in prices exist across low, middle, and high-income countries
   • Many countries are missing opportunities to access cheaper medicines through voluntary licences that allow the production and supply of generic antiviral medicines to 112 low-income and middle-income countries
   • Access to affordable diagnostics is a key barrier for many countries, with diagnostics often costing more than treatment in low-income and middle-income countries, where inadequate laboratory capacity and access to reliable and low-cost diagnostics prevent rapid scale up of testing and treatment programmes

Common challenges to hepatitis C elimination

Development, which identified actions to support countries to accelerate the financing of the Sustainable Development Goals. This strategy included aligning global economic policies and financial systems with the 2030 agenda, enhancing sustainable financing strategies and investments at the regional and country levels, and seizing the potential of financial innovations, new technologies, and digitisation to provide inclusive and more equitable access to finance.

Positioning national hepatitis C responses within a framework of universal health coverage and the broader Sustainable Development Goals can enable policy makers to leverage the roll out of universal health coverage for investment in hepatitis C programmes while facilitating the prevention, diagnosis, and early management of other major health conditions (eg, liver cancer, hepatitis B, HIV, and tuberculosis) and chronic diseases, (eg, diabetes and hypertension). Many of the strategies and infrastructure required for hepatitis C elimination can be effectively added to existing HIV (and potentially tuberculosis and other universal health coverage) programmes at little additional cost, with examples underway in Georgia, Rwanda, and Ukraine. Multiple policy and economic mechanisms can be used to improve the affordability of hepatitis C elimination. These mechanisms have been used to finance various health-related issues and approaches and have been implemented successfully in some countries (table 1).

Key elimination activities

Our investment framework identifies national and international activities that would support the elimination of hepatitis C, along with key enablers to allow hepatitis C programmes to be implemented effectively at scale (table 2). These activities were framed to address existing challenges that underpin the lack of investment and action in many countries, which are often interlinked and have cascading effects that perpetuate each other in a negatively reinforced cycle (panel; figure 2). For example, many low-income and middle-income countries with a
Growing hepatitis C disease burden do not have a formally costed hepatitis C elimination programme. This issue can arise from an absence of awareness among policy makers about the burden of hepatitis C-related disease and the potential benefits of prioritising hepatitis C elimination. This lack of awareness about disease burden is often driven by inadequate data and weak surveillance systems. These limitations in turn reduce governments’ capacity to prioritise resource allocation for national viral hepatitis elimination action plans and reduce public sector-optimised procurement of medicines or diagnostics. Countries then have fragmented procurement, rather than national pooled procurement; this situation can lead to a high mark-up in drug prices from pharmaceutical companies, and the perception that direct-acting antivirals are expensive. In turn, national programme managers might be missing opportunities to appropriately invest in hepatitis C elimination activities.

There are national and international activities and key enablers of hepatitis C elimination, tools to support the implementation of these activities, and examples of countries that have successfully implemented these activities (table 2). National activities include purchased commodities and programmes that have a direct effect on reducing hepatitis C transmission, morbidity, and mortality. These outcomes should be informed by surveillance data and local epidemiology, and scaled up according to the size of the affected population. Supporting governments to develop national plans and local investment cases will help to raise the profile of hepatitis C elimination and build political commitment through global, regional, national, and local forums to catalyse action and financing. Strengthening and integrating viral hepatitis surveillance and monitoring systems within national information systems can aid national and local governments to assess the nature of the epidemic, the true burden of disease, and the attributable cost to the country. This support enables improvement of resource allocation for services and workforce training. A roadmap for such an approach can be found in the WHO viral hepatitis C continuum of care monitoring and evaluation framework.15 In many settings, the effectiveness of viral hepatitis programmes is limited by poor health infrastructure, including low laboratory capacity and an absence of reliable supply chains for vaccines, medicines, and diagnostics.16 Investing in health systems to strengthen approaches that deliver public programmes that address multiple diseases, with an emphasis on task shifting and task sharing,27,28 could increase cost-efficiency and ensure sustainability.29 Promoting the standardisation, simplification, and decentralisation of hepatitis C services to reach and actively involve those populations most affected will help drive demand for such services and ensure population coverage. Supporting community sector advocacy and civil society engagement to highlight inadequate hepatitis C funding and to demand access to testing and treatment will help support all national activities for hepatitis C elimination.

Despite major reductions in the cost of hepatitis C treatments over the past few years,30,31 the high costs of treatment and diagnostics mean that many countries cannot support the scale up of the testing and treatment programmes that are needed to achieve elimination. Countries should explore TRIPS (trade-related aspects of intellectual property rights) flexibilities and licensing agreements and be encouraged to employ voluntary licenses that allow the production and supply of generic antiviral medicines. Voluntary licences are increasingly being used to expand access to patented essential medicines in low-income and middle-income countries.32 Since 2014, Gilead and Bristol-Myers Squibb have issued non-exclusive voluntary licences for key hepatitis C drugs to 112 low-income and middle-income countries (home to 65-4% of the people living with hepatitis C).33 Generic pharmaceutical manufacturers that hold voluntary licenses might also sell generic drugs to countries outside the list of 112 countries if no granted patent is being infringed. Additionally, if a government authority declares a state of emergency, they could issue a compulsory licence to make use of a patent during the patent term without the authorisation of the patent holder to address a public health need.34 For example, compulsory licenses by the government can allow the local production or importation of generic products from other countries for the domestic market without the consent of the patent holder,35 and against royalty payments; however, this route has only been used twice for hepatitis drugs.36 Direct negotiations with pharmaceutical and diagnostic companies has reduced prices in Australia,37 Egypt,38,39 and other countries. Ensuring hepatitis C medicines and diagnostics are included in the WHO Essential Medicines List® and WHO Essential In Vitro Diagnostics List® will be crucial as many

Figure 2: Challenges to investment in hepatitis C virus elimination
HCV=hepatitis C virus.
countries continue to expand their universal health coverage packages.

International activities are implemented by development agencies and related agencies that affect global policy engagement and are designed to create the necessary environment for countries to achieve elimination and encourage financial investment. Helping countries to identify and support priority activities for elimination promotes the prioritisation of these activities on the basis of the country’s epidemiology and context. This support will be important because local technical expertise and capacity might be absent. For example, Georgia’s technical advisory group, composed of both local and international hepatitis C experts to enable country ownership, has adopted a multi-stakeholder-participatory approach to develop strategies, objectives, and actions to help eliminate hepatitis C in Georgia. Promoting simplified clinical pathways and models of care that are integrated across related diseases and platforms, including HIV, tuberculosis, and viral hepatitis, will help to reduce the overall costs of programmes and increase programme coverage.

Key enablers can facilitate the rapid scale up of national hepatitis elimination activities and can be classified into three categories. First, social enablers are factors that can influence the acceptability of hepatitis C investment and make environments conducive to supporting the uptake of hepatitis C elimination activities. This includes political leadership and advocacy to build public support for funding hepatitis C elimination activities, community mobilisation to reduce stigma and increase awareness, and engagement in health services. For example, harnessing opportunities for publicity through World Hepatitis Day, conferences, and other high-level meetings can increase the profile of viral hepatitis elimination and advocate directly to governments to reprioritise budgets to scale up hepatitis C activities. Second, policy enablers support the scale up of hepatitis activities and investment approaches by providing a regulatory environment (laws, policies, and guidelines) to attract investment, strengthen coordination with other health programmes, and identify opportunities for the strengthening of health systems and for cost-savings. For example, the integration of hepatitis C activities into universal health coverage country packages enables hepatitis C drugs to be included on the WHO Essential Medicines List and supports their pooled procurement. Finally, programme enablers are factors that directly impact on the delivery of health programmes, and can enhance the quality, coverage, and effect of hepatitis C elimination activities through a public health approach, for example, by ensuring that clinical guidelines and legislation can support universal access to hepatitis C testing and treatment.

Investment case
Other than life-threatening complications, individuals infected with hepatitis C experience a reduction in quality of life, decreased health and wellbeing, and substantial social stigma. These factors can reduce workforce participation and personal financial security, and lead to direct costs to health systems. Most of these health-care costs typically occur 10–20 years after initial infection with the onset of hepatitis C-induced cirrhosis and liver cancer, which can be very costly and challenging to manage. To gain support and traction from financiers, a strong investment case is essential for country elimination programmes. Epidemic and economic models have been used to support investment cases by quantifying the effect, resource requirements, and return on investment of changes in viral hepatitis disease control strategies. However, much of the work on viral hepatitis elimination explores the cost-effectiveness of scaling up hepatitis C treatment by only taking into account direct costs. Many of these analyses underestimate the cost of chronic viral hepatitis to the community because they do not consider decreased workforce participation or reduced quality of life among people living with hepatitis. Analyses that do not include indirect economic productivity losses do not capture the longer-term economic benefits of increased workforce participation among people who are cured and will not die prematurely, and people who will never become infected. Advancements in diagnostics and the discovery of a cure for hepatitis C mean that major gains are now possible over short time periods, provided investment can be catalysed.

To show the use of the investment framework, we have produced model-based epidemic and economic projections to assess the impact of two investment strategies for hepatitis C: an elimination strategy and a progress strategy. In the elimination strategy, efforts were scaled up to meet the WHO 2030 elimination targets of having 90% of people with hepatitis C diagnosed and 80% of diagnosed patients on treatment by 2030. In the progress strategy, a more modest investment in hepatitis C testing and treatment was modelled to assess the cost-effectiveness of increased investments in hepatitis C without achieving elimination targets. The status quo and the two investment scenarios were assessed for each of the WHO’s six regions in a modelling paper that accompanies this Health Policy.

Epidemiological and economic impact of investment in hepatitis C
On the basis of estimates of the total number of people living with hepatitis C across the six WHO regions, application of the elimination strategy would substantially reduce the overall number of people living with this infection. According to the model projections for elimination, there would be an 85% (95% credible interval [CrI] 70–92) reduction in annual hepatitis C incidence by 2030, and 10 million (95% CrI 4–14 million) new hepatitis C infections globally would be prevented between 2018 and 2030. Elimination would become cost-saving by 2027, with a net economic benefit of
$22·7 billion (95% CrI $17·1–27·9 billion) by 2030. A detailed model description and findings are reported in the modelling paper.\textsuperscript{24}

Cross-sectoral economic benefits and synergies with other development sectors

Achieving the Sustainable Development Goals target 3.8 for universal health coverage requires global investment in infrastructure, and many countries have already commenced major investments in health.\textsuperscript{96} Integrating hepatitis C services within these investment approaches and systems can considerably reduce costs compared with implementing disease-specific programmes. The simplicity and safety of hepatitis C treatment means that most services can be delivered through the primary care sector in many countries, making integration highly achievable. A recent cost-saving study estimated that adding viral hepatitis elimination activities (hepatitis B and C) to universal health coverage would only increase the total costs of this service by 1·5%.\textsuperscript{20} This observation is an important consideration because the human resource costs associated with testing, treatment, and cure can be more than double the commodity costs in many settings, and adequate human resources might already exist and be financed in health systems.\textsuperscript{20} In the accompanying modelling study, once additional human resources costs were removed, investment in hepatitis C elimination became cost saving by 2019, rather than 2027.\textsuperscript{24}

Scaling up elimination activities

Eliminating the public health threat of hepatitis C is achievable. The challenge to eliminate hepatitis C as a public health threat by 2030 is not prevented by targets that are too ambitious, but because most countries globally are not investing sufficient funds and political effort to achieve these targets. This investment framework provides a clear pathway for achieving the financing mechanisms and activities required to reach viral hepatitis elimination and highlights the substantial long-term health and financial benefits of meeting the 2030 elimination targets. Countries need to first identify their specific challenges (panel), and using this investment framework and modelling paper,\textsuperscript{24} these countries can begin to build political commitment with the development of a national hepatitis plan that includes an investment case for hepatitis C elimination. Although mobilising considerable amounts of domestic funding for all low-income and middle-income countries with high hepatitis C prevalence might not be realistic in the short term, there are cost-neutral and low-cost strategies that can build momentum and support elimination (figure 3). For countries with lower hepatitis C prevalence and little funding for hepatitis C treatment programmes, the productivity gains and cost savings shown in our models will be less. However, these countries can make considerable advances in hepatitis C elimination at a low cost by adopting synergistic and cost-sharing strategies, such as the integration of hepatitis C services into other health programmes (eg, HIV and tuberculosis programmes) with existing infrastructure, which includes a skilled workforce and robust surveillance systems.

All countries, regardless of hepatitis C prevalence and burden, can leverage the expansion of universal health coverage to ensure hepatitis C services (testing and treatment) are included in their minimum package of health services, which will substantially reduce costs.\textsuperscript{20}
Our models showed that $41·5 billion is required between 2018 and 2030 to achieve global elimination, but that this expense is likely to be recovered in cost savings by 2027, beyond which considerable additional economic returns are possible.22 Rapidly reducing new infections and death from hepatitis C should also have a profound benefit on future disease burden,8 while generating major savings in health-care costs associated with managing severe liver disease and other health-related consequences of viral hepatitis. Unlike in other diseases, highly effective treatments that cure hepatitis C enable the prevention of deaths and new infections without ongoing costs. Moreover, early investment can lead to substantially greater long-term economic benefits,19,31,79 and as the costs of diagnostics and treatments decline through advocacy, international support, private partnerships, and community mobilisation, these benefits will increase.19

Most countries will need to increase their domestic financing and create fiscal space to invest in hepatitis elimination programmes. As such, greater emphasis will need to be placed on the economic benefits of hepatitis programmes. Investment plans to support national policies are needed to ensure evidence-informed decision making regarding which interventions will provide the greatest public health returns. If domestic efforts to provide funding are unsuccessful, new streams of finance—including innovative financing mechanisms—to support national programmes should be explored (table 1).

Similar global economic modelling for hepatitis B has shown how scaling up the coverage of vaccination (to 90% of infants), birth-dose vaccination (to 80% of neonates), use of peripartum antivirals (to 80% of HBeAg-positive mothers), and population-wide testing and treatment (to 80% of eligible people) could achieve hepatitis B elimination by 2030.19 As with global hepatitis C elimination, positioning hepatitis B elimination activities within countries’ universal health coverage packages will help to ensure sustainable funding for vaccines, diagnostics, and medicines. China was an early adopter of a health-system strengthening approach to rapidly scale up hepatitis B immunisation to reach population coverage.19 The country negotiated local manufacturing for treatments and vaccines that have considerably reduced prices and guaranteed supply while generating a new revenue stream. Such investments have also stimulated national drug and vaccine production, ensuring sustainability of the programme and the development of new country industries and technology markets.

Conclusion

Any elimination activity requires resources and considerable investment at a country level, as identified in the Global Health Sector Strategy on viral hepatitis. This investment framework identifies potential funding sources for investing in elimination activities and highlights the substantial long-term health and financial benefits of scaling up activities to achieve the 2030 elimination targets. This is the first global investment framework to show a substantial economic benefit of investing in hepatitis C elimination, demonstrating how such investments would become cost saving by 2027.

Leveraging global support and political will for the expansion of universal health coverage, and ensuring hepatitis services are integrated into these substantial new investments, will enable new funding sources for viral hepatitis elimination activities as well as opportunities to strengthen health systems. Encouragingly, in September, 2019, the UN General Assembly included viral hepatitis in its political declaration on universal health coverage, demonstrating commitment by heads of state, political leaders, health leaders, and policymakers globally to begin integrating hepatitis B and hepatitis C elimination programmes into universal health coverage programmes.

Countries should use the investment case and existing evidence to raise the profile of viral hepatitis elimination and build political commitment through global, regional, national, and local forums that engage affected communities, health care professionals, and other key stakeholders.
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