

The global campaign to eliminate HBV and HCV infection: International Viral Hepatitis Elimination Meeting and core indicators for development towards the 2030 elimination goals

Stephanie Popping¹, Debora Bade², Charles Boucher^{1,2}, Mark van der Valk³, Manal El-Sayed⁴, Olafsson Sigurour⁵, Vana Sypsa⁶, Timothy Morgan⁷, Amiran Gamkrelidze⁸, Constance Mukabatsinda⁹, Sylvie Deuffic-Burban¹⁰, Michael Ninburg¹¹, Jordan Feld¹², Margaret Hellard¹³ and John Ward^{14,15}

¹Department of Viroscience, Erasmus Medical Center, Erasmus University, Rotterdam, the Netherlands

²Virology Education, Utrecht, the Netherlands

³Amsterdam UMC location Meibergdreef, Amsterdam, the Netherlands

⁴Department of Pediatrics, Ain Shams University, Cairo, Egypt

⁵Division of Gastroenterology, Department of Medicine, Landspítali University Hospital, Reykjavik, Iceland

⁶Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Greece

⁷Gastroenterology Section, VA Long Beach Healthcare System, Long Beach, CA, USA

⁸National Center for Disease Control and Public Health, Tbilisi, Georgia

⁹Kigali University, Kigali, Rwanda

¹⁰Inserm, Université Paris Diderot, UFR de Médecine-site Bichart, Paris, France

¹¹World Hepatitis Alliance, London, UK

¹²Toronto Centre for Liver Disease, Sandra Rotman Centre for Global Health, University of Toronto, Toronto, Canada

¹³Disease Elimination Program, Burnet Institute, Melbourne, Australia

¹⁴National Center for HIV, Viral Hepatitis, STD, and TB, CDC, Atlanta, GA, USA

¹⁵Task Force for Global Health, Decatur, Atlanta, GA, USA

Abstract

Hepatitis B virus (HBV) and hepatitis C virus (HCV) affect more than 320 million people worldwide, which is more than HIV, tuberculosis (TB) and malaria combined. Elimination of HBV and HCV will, therefore, produce substantial public health and economic benefits and, most importantly, the prevention of 1.2 million deaths per year. In 2016, member states of the World Health Assembly unanimously adopted a resolution declaring that viral hepatitis should be eliminated by 2030. Currently, few countries have elimination programmes in place and even though the tools to achieve elimination are available, the right resources, commitments and allocations are lacking. During the fifth International Viral Hepatitis Elimination Meeting (IVHEM), 7–8 December 2018, Amsterdam, the Netherlands, an expert panel of clinicians, virologists and public health specialists discussed the current status of viral hepatitis elimination programmes across multiple countries, challenges in achieving elimination and the core indicators for monitoring progress, approaches that have failed and successful elimination plans.

Keywords: hepatitis C virus, elimination, World Health Organization, hepatitis B virus, viral hepatitis

Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) affect more than 320 million people worldwide, which is more than HIV, tuberculosis (TB) and malaria combined [1,2]. Elimination of HBV and HCV will, therefore, produce substantial health and economic benefits and, most importantly, the prevention of over 1.2 million deaths annually [1].

In 2016, the World Health Assembly (WHA) unanimously adopted the resolution that viral hepatitis should be eliminated by 2030. In addition, the World Health Organization (WHO) published the Global Health Sector Strategy on hepatitis to reach this goal [1]. The International Task Force for Disease Eradication (ITFDE) adapted and endorsed the elimination goals of WHO, and HBV and HCV infections are recognised as feasible targets for elimination. In addition, WHO established a framework to guide implementation of the key interventions at a national level to achieve the global elimination goals. At the start of the elimination era for viral hepatitis, few countries are on track to meet the 2030 elimination goals. Moreover, in 2017, only 28% and 48% of countries are reported to have elimination plans in place for HBV and HCV, respectively [3,4].

HBV and HCV infection meet accepted criteria for disease elimination. However, appropriate resources, commitment and allocation are currently lacking. If the right parties work together, including governments, international organisations, the private sector and civil society, great success can be achieved. Modelling studies have indicated that if core interventions are implemented with sufficient service coverage, elimination could be accomplished. This will require collecting strategic information, planning of programmes with involvement of all stakeholders, engaging civil society, arranging financial support and implementing appropriate strategies for target populations [5]. Key for the viral hepatitis response is to be integrated within countries' efforts to achieve universal health coverage as part of the 2030 Sustainable Development Goals.

During the fifth International Viral Hepatitis Elimination Meeting (IVHEM), 7–8 December 2018, Amsterdam, the Netherlands, an expert panel of clinicians, virologists and public health specialists discussed what progress is needed to achieve elimination, what major challenges are still to be faced and, in addition, the core indicators for monitoring progress. IVHEM brought together current or proposed HBV and HCV prevention and elimination programmes to share local experiences in planning and implementation of the key interventions recommended by WHO. Through information sharing, the goals of the meeting were to help programmes improve performance and guide development of new elimination programmes.

Corresponding author: Stephanie Popping, Viroscience department, Erasmus MC, Postbus 2040, 3000CA, Rotterdam, the Netherlands
Email: s.popping@erasmusmc.nl

The investment challenges

A major barrier towards elimination is the lack of funding. Viral hepatitis is significantly underfunded compared to HIV, TB and malaria. Currently, there is no significant support from the Global Fund, PEPFAR, the Gates Foundation or other similar international funders outside of the setting of HIV co-infection. Without some support from these, or similar organisations it is unlikely that the 2030 elimination targets will be achieved [4].

Several reasons have been postulated as to the lack of funding for viral hepatitis. First, there is limited knowledge about the high cost of the viral hepatitis epidemic that will continue to grow in future years if current trends in testing and treatment continue. Reaching the 2030 elimination targets by increasing testing and treatment can, however, stop these increasing costs. In fact, achieving viral hepatitis elimination will produce a positive return on investment by 2028 from savings due to the removal of indirect cost associated with viral hepatitis [4]. Additionally, some countries are likely to obtain an even greater health benefit with their current investment. Egypt for instance is currently undertaking massive screening programmes for HCV, but has built into this screening for multiple diseases including HBV, obesity, diabetes and hypertension. In the first 20 days in October, over 4 million people were screened with 140,000 HCV cases detected; as well as more than 1 million cases of obesity and 20,000 diabetic patients were identified.

A second likely reason for the lack of investment is that, viral hepatitis infects many minorities who are often highly vulnerable and underrepresented at a political level. Due to their vulnerability these groups are often not in position to advocate for support and funding. HIV is an example where involvement of civil society drove the HIV movement and resulted in awareness, political support and funding. Work needs to be done to support civil society and community organisations to be engaged and advocating for funding. Only with enough community advocacy will the political leadership start to support the matter and the pledge for a global fund can begin.

Whilst the viral hepatitis response would benefit from the support of international funding organisations, it is key that individual countries take responsibility for supporting the investment in elimination. China is a good example. Sustainable HBV programmes were established with support from private partnerships and leadership [4]. GAVI was one of the organisations that supported universal hepatitis B immunisation of infants in China. In addition, organisations such as GAVI, which recently announced prioritised investment in HBV birth-dose vaccines, can make a tremendous difference with raising awareness particularly through immunisation campaigns, especially in low- and middle-income countries. Georgia's HCV response is another example where a strong government leadership, combined with private investment from Gilead Sciences and technical support from the US Centers for Disease Control and Prevention and FIND/Unitaid led to successes.

The lack of national and international investment in viral hepatitis programmes, especially in low- and middle-income countries, means that national hepatitis programmes are underfunded. As a result, testing programmes are hampered and only small numbers of individuals therefore have access to treatment [6]. In order to establish a strong hepatitis response and strengthen healthcare systems, especially in low- and middle-income countries, financial support is needed to lay the groundwork for elimination by providing essential research and support [6].

Strategic information of successful countries on track towards the elimination goals

There are several countries that have developed elimination plans [3,4]. One of the most successful countries is Egypt, where many are already cured, and mass testing programmes are identifying the millions of individuals who are unaware of their infection [7]. Not only adults are included in these programmes: Egypt is also including children and adolescents. By testing and treating the young population, parents are also engaged in testing. In addition, adolescents tend to strengthen the community by raising awareness and advocacy. During the testing programme, stigma in schools or when parents were asked for consent for testing of their child has been identified. By working together with organisations such as the national mother and child organisation, knowledge is gained regarding the protection of children from discrimination and stigma. This approach can be an example for other countries, since worldwide over 11 million children (under the age of 15) have HCV infection [8].

Georgia is another country that has successes in eliminating viral hepatitis. There is a high prevalence of HCV infection (5.4% of adults have HCV) [9]. Since 2015, an HCV elimination programme has been in place, based on six main principles: (1) advocacy, awareness and education, and partnerships for HCV-associated resources; (2) HCV transmission reduction; (3) identification of those with HCV; (4) HCV laboratory diagnostics; (5) HCV care and treatment; and (6) HCV surveillance. The programme receives funding from the Global Fund, and is constantly evolving to meet the beneficiaries' needs. Georgia uses an integrated approach by combining testing protocols and care for HIV, TB and HCV. By integrating viral hepatitis care into existing platforms, costs are reduced. To improve coverage and maximise the number of the target population, Georgia decentralises HCV-related services. This improves accessibility for persons living in rural areas. In addition, primary healthcare workers and non-specialised settings near patients' homes are involved in the management of uncomplicated HCV cases.

Iceland is also leading in elimination and, according to mathematical models, could potentially reach the WHO elimination targets by 2020 [10]. A nationwide programme has been established, Treatment as Prevention for Hepatitis C (TraP HepC), where universal access to direct-acting antivirals (DAAs) is combined with intensified screening and harm-reduction efforts. One central virology laboratory serves the entire country and reports all new HCV infections directly to a national HCV registry. Emphasis is on early case finding and treatment of high-risk groups such as persons who inject drugs (PWID) and prisoners, as well as patients with advanced liver disease. Using the treatment-as-prevention (TasP) approach, previously described as a good tool for HIV prevention and described as effective for HCV, the aim is to not only offer a cure to patients but also to reduce the domestic HCV incidence by 80% prior to the WHO elimination goals for 2030 [11–13]. The programme has already resulted in a major decrease of HCV prevalence among key risk groups such as PWID and prisoners.

In Athens (Greece), a fast-track intervention to seek-test-link-treat PWIDs has been established, based on a programme established during an outbreak of HIV among persons who inject drugs [14,15]. Athens accounts for 8700 high-risk drug users, of whom 2450 had actively injected in the past 30 days [16]. Harm-reduction programmes with opioid substitution therapy (OST) and needle syringe programmes (NSP) are in place, but waiting times are long. In addition, DAAs have been available without restriction since September 2018. However, they are only accessed by a small percentage of PWIDs. The current programme is used

to increase diagnosis and treatment for HCV and HIV infection among PWIDs. Chain-referral sampling is used to bring individuals into care (a single individual from a target population is invited and requested to invite three other recruits from their network) [17]. A combination of rapid identification, fibroscans and biochemical testing are used in a single visit to avoid losing individuals in the care cascade (Table 1). Specially trained clinicians visit the study site, to improve linkage to care. In addition, PWIDs are assigned a peer-navigator, who accompanies them to their first liver or infectious diseases clinic appointment. Similarly to Iceland,

a national HCV treatment registry is used to monitor progress and to improve linkage to care.

In the United States the Veterans Administration (VA) uses Lean as a strategic methodology to improve HCV care (Table 1). Lean is a business methodology that promotes the flow of value (care) to the customer (patient), through continuous improvement, and increases access to information to ensure responsible decision-making. Currently, 8.9 million veterans receive VA care, and the VA leadership has identified HCV as a priority. ‘Hepatitis Innovation

Table 1. The challenges, failures, lessons learned and solutions from different countries in efforts to eliminate viral hepatitis

Country	Challenge and/or failures	Solutions and lessons learned
Egypt	High HCV prevalence, treated all patients and screening programmes were running behind, cost of diagnosis, number of PCR tests was a bottleneck	<ul style="list-style-type: none"> • Before 2014: established data networking centre and political will to eliminate HCV. Since, 2016 pledge from the president to eliminate HCV [7] • National plan since 2014 including HCV treatment centres • Generic DAAs • Decentralising the screening project by using mobile units and different testing sites • Negotiated for a lower PCR price given number of tests required • Loan from the World Bank and private sector cooperation • Companies helped to develop dried blood spot test • Simplify the monitoring strategy
Georgia	High HCV prevalence, need to identify the missing millions, reaching the younger population, cost, linkage to care	<ul style="list-style-type: none"> • Integrated hepatitis care into HIV, TB and malaria care • Scaling-up advocacy for hepatitis, HIV and TB • Decentralisation of healthcare (screening and treatment) using primary healthcare • Massive screening programmes, focusing on affected age group of males (30–60 years) and high-risk groups • Universal screening in harm-reduction networks • Used medical university students as extra help in these harm-reduction networks • When elimination was feasible the authorities were on board • Strengthen the healthcare system through the support of Global Fund • More enrolment of public health specialists for linkage-to-care process
Australia	Reaching the younger population, decline in number of people accessing treatment [18]	<ul style="list-style-type: none"> • Decentralising care and bringing care to the community where patients access services (community care/primary care) [19] • Point-of-care test in needle and syringe programmes (RAPID-EC) • Increase awareness about new HCV treatments • Increase coordination between services, for example community and prisons • Support enhanced data management
France	Prioritisation of treatment, high drug cost, high HCV prevalence and HCV transmission among PWIDs [20]	<ul style="list-style-type: none"> • Established mathematical models to gain further insight into the best treatment strategies and harm-reduction programmes [21–23] • Price negotiations allowing the significant decrease in drug costs
United States	High HCV prevalence, optimising HCV in the VA	<ul style="list-style-type: none"> • System redesign using LEAN methodology [26,27]
Netherlands	Linkage to care of the high-risk group, retention in care	<ul style="list-style-type: none"> • Involving target group in establishing linkage-to-care strategies • Using affected community in building online and offline information platform [28] • Development of play-safe chemsex toolkit
Canada	Projects stalled due to constant data gathering required by health authorities, screening programmes were successful but the labs could not process the numbers	<ul style="list-style-type: none"> • Not everything has to be perfect • Negotiating is power, important to get all the major players in the room. The leadership must push the agenda forward; in addition, the industry must also understand the needs and can support the gaps in care
Myanmar	Low general awareness and in key populations, rural areas hard to reach, low vaccine coverage	<ul style="list-style-type: none"> • Aiming for high advocacy by increasing the political will • Decentralisation of healthcare
Rwanda	Receiving funding	<ul style="list-style-type: none"> • Government acknowledged viral hepatitis as a major health problem and sought funding • Strengthening of the programme by the Global Fund
Greece	Small numbers of PWIDs accessed care, waiting lists for harm-reduction programmes are long	<ul style="list-style-type: none"> • Established a fast-track intervention to seek-test-link-treat PWIDs [14,15] • Used previous HIV programmes as an example • Chain-referral sampling to engage individuals into care [17] • Rapid identification, fibroscans and biochemical testing all in a single visit • Peer-navigators to improve linkage to care
Iceland	Some actively injecting drug users remain difficult to engage in treatment and maintain on treatment; visitors from abroad, such as asylum seekers and foreign prisoners with pre-existing chronic HCV infections; patients at an increased risk of infection and re-infection (MSM, persons sharing needles)	<ul style="list-style-type: none"> • Incentives (including financial) for difficult patients. Adherence support • Screening of immigrants and asylum seekers. Collaboration with the chief epidemiologist and immigration authorities. • Scale-up of HCV testing and harm-reduction efforts, including increased access to needles and syringes (NSP)

Box 1. Essential components of HCV elimination programmes

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

Teams' (HIT) were installed at each hospital, comprising doctors, pharmacists, nurse practitioners, physician assistants, research nurses, clerks and system redesign personnel. Their aim is to improve HCV care by redesigning care and the delivery processes with the lean methodology, which makes it feasible to measure improvements in variability, access, quality of HCV care and problems with HCV screening. Each year, the HIT leadership teams set national goals for HCV testing rates and treatment rates. In addition, they have constructed HCV dashboards, where providers have clear 'real-time' access to patient data. Moreover, HITs established different testing interventions such as: clinical reminders; reflex HCV-RNA testing; performance indicators for healthcare executives; and multimedia marketing. Special programmes are focused on at-risk groups by educating and partnering with mental health and substance use treatment providers and homeless stand-downs. Challenges are that many of the remaining untreated patients have barriers to receiving treatment, such as homelessness, substance use, refusal of treatment, other comorbidities (e.g. cancer), or do not use VA services at this time.

Gaps in the treatment cascade

Finding the missing millions

Care-cascade analysis is an essential evaluation tool for the challenges on the way to cure. The cascade of care for HBV and HCV showed that one of the major difficulties on the road to elimination is finding the missing millions affected by the illnesses. While Egypt was very successful in treating all known individuals with HBV and HCV, there were many who were undiagnosed and massive testing programmes were needed to identify the missing millions [7]. With major support from the president, successful negotiations with several companies saw reduced prices for *in vitro* diagnosis tests. By simplifying diagnostics and the costs of follow-up programmes, the cost for each case of HCV elimination declined. Subsequently, the lack of polymerase chain reaction machines created the next bottle neck, limiting the number of specimens that could be tested. To solve the capacity problem, a change to diagnosis and screening using point-of-care tests was made. This allowed decentralised testing using mobile units and local testing sites, tackling the issue region by region rather than the whole country at once.

In Rwanda, there is a strong political will to eliminate hepatitis, due to the higher mortality from viral hepatitis than from HIV. The Rwandan government supported hepatitis elimination programmes by allocating \$9 million and obtained support from the Global Fund. HBV and HCV prevalence is estimated to vary around 3.1–4.5% and 4.6–8.9%, respectively (total population of 12 million) [29]. HIV programmes form a successful model for service delivery and platforms for testing (viral load and genotyping). Therefore, hepatitis screening services have been successfully integrated into existing HIV care. In addition, DAAs are freely

available. In Rwanda, 280,000 individuals were tested, 9000 patients were treated, and television and radio were used to target individuals aged 45 and older for hepatitis testing to reach the missing millions.

One major barrier in finding the missing millions is the lack of awareness of viral hepatitis. Globally, 9-out-of-10 individuals are unaware of their infection status, as most have no well-defined symptoms and many do not classify themselves as belonging to at-risk groups [1]. In addition, millions of people have been, and continue to be, infected, accidentally and unnoticed, by unscreened blood transfusions and unsterilised equipment [30]. Although certain countries have established massive testing programmes, there is still limited experience on how to engage with large numbers of undiagnosed individuals, and it is likely to vary between countries and regions depending on which risk behaviours are driving the epidemic.

A good insight into country-specific epidemics is essential as a baseline for the development of testing approaches. The HCV epidemic in Canada, for instance, is concentrated around birth cohorts and most people are unaware of their risk. Targeted testing in birth cohorts, therefore, would be a perfect strategy, although this would be an insufficient strategy in Egypt, where HCV exists among the whole population. Solely testing the birth cohort results in many undiagnosed infections, so screening programmes should be implemented more widely. By contrast, in Australia, former and current PWIDs are aware of their infection but unaware of the availability of curative DAAs. This does not require a testing programme but linkage to care. Mathematical models can help to identify the most cost-effective testing strategy [23].

Improving linkage to care

Linkage to care is crucial and an important precursor to retention. Cascade analysis with recent data is fundamental to improve linkage to care. As an example, in African countries, cascade analysis pointed to a more pronounced treatment gap compared to other regions [1,10,31]. A common reason for delaying health services among people living with HIV/AIDS was 'medical pluralism', the use of multiple health systems including traditional healers in sub-Saharan Africa [32,33]. Many lessons can be learned from HIV care, which can be used in determining viral hepatitis linkage-to-care programmes. In particular, viral hepatitis testing can be integrated into the already existing delivery models for HIV and primary care.

Several minorities also face linkage-to-care issues, often due to stigmatisation and low political commitment. This results in limited service penetration and a lack of engagement of healthcare providers. In the UK for example, homeless persons, are estimated to be 50 times more likely to have chronic HCV infection, but only 3% receive treatment [34]. PWIDs also have difficulties in finding health care, which is a significant barrier in linkage to care. There is also a lack of specialised services and programmes for younger people who would particularly benefit from earlier treatment and care. Currently, only Egypt has a testing and treatment programme for adolescents, and more countries should advocate for treatment programmes among this age group. Calling attention to marginalised populations is appropriate since HBV and HCV are often the result of poor healthcare and a problem for civil society as a whole. Public education can build awareness of the burden of disease and linkage to liver cancer to promote greater advocacy by civil society to call on political leaders to commit national resources to HCV and HBV elimination.

In the Netherlands, linkage to care for high-risk groups was one of the major challenges (Table 1) and the community generated

innovative ideas. New HCV infections are concentrated among men who have sex with men (MSM) [35,36] while new cases of HCV among PWIDs are very low: in 2016 there were 44 cases in MSM with fewer than five associated with injection drug use [37]. Since 2015, DAAs have become available without restriction, which resulted in a decline in incidence of 70% among MSM [11,38]. However, re-infections are still high and predominantly related to the involvement of MSM in high-risk sexual activities (including chemsex). MSM are, therefore, the key group for interventions. Currently, innovative harm-reduction strategies are used in close collaboration with the community to achieve HCV elimination. NoMoreC is a good example of a community platform where MSM educate other MSM on HCV and safe sex. In addition, play-safe toolboxes can be ordered as well as free HCV home tests, based on dry bloodspot testing [28]. The aim of this platform is to increase awareness and knowledge, encourage regular and timely testing, and offer tailored advice to MSM to reduce their risk of acquiring HCV [28].

HCV treatment uptake in Australia was initially high, but has begun to fall over the past 12 months [39]. Several barriers for linkage to care were identified, such as: a shortage of healthcare practitioners in some area (particularly rural and regional Australia), lack of coverage services; stigma and discrimination; accessing tertiary care services; and HCV being not a priority [18] (Table 1). As a solution, Australia redefined linkage to care models towards the community, where patient access to services and care was decentralised. Several studies, for example, the PRIME study and RAPID-EC, showed that patients were more likely to engage in care when DAAs were given in primary care compared to tertiary hospitals [19,40]. Prescribing rules were changed and, by 2018, most DAAs were prescribed by general practitioners.

HBV care is neglected compared to HCV

HBV care is 'neglected' compared to HCV in terms of treatment and, in addition, there is still limited recognition of the illness. There are several reasons why. First, the greatest HBV morbidity and mortality is found in low- and middle-income countries. In many of these countries HIV had been a major contributor to morbidity and mortality until the development of good coverage of antiretroviral therapy. Additionally, with the advent of DAAs, HCV has become a treatable condition; however, HBV has been left behind. Second, there is no community movement, as there was with HIV, to bring the condition into the spotlight. Civil society is very important for creating advocacy and raising awareness. With the availability of DAAs, this awareness has increased for HCV, although mostly led by drug company treatment campaigns rather than by the affected community. Third, HBV testing needs to be more accessible and cost barriers need to be reduced. HBV monitoring is also difficult with many different steps. Additionally, the timely use of HBV vaccination at birth is a challenge in certain countries, particularly in sub-Saharan Africa where coverage is around 10%.

Monitoring progress

Monitoring progress is an important element in the elimination effort to ascertain if interventions, such as vaccination programmes and other prevention efforts are being effective, whether testing is increasing, and if those testing positive are being linked to care as necessary. Without monitoring, progress cannot be measured, and the impact of the epidemic cannot be understood. WHO recommend three elements for surveillance and 10 core indicators [30]. For surveillance: (1) enhanced case reporting of acute hepatitis describes incidence trends and identifies who

acquire hepatitis; (2) biomarker surveys generate reliable population-based estimates of the prevalence, preferably by age; and (3) sequelae surveillance captures mortality from viral statistics and the attributable fraction describes mortality trend [30]. Cascade monitoring relies on aggregated or individual data. If it is not possible to obtain new data, existing data can be extrapolated to provide working estimates to allow the establishment of elimination programmes.

WHO plans to monitor progress towards elimination by requesting countries to report on their progress by core indicators [30]. WHO is to publish new simplified, consolidated guidelines on hepatitis strategic information that will propose a simplified approach for conducting rapid data extraction to report progress towards elimination in the Global Reporting System for Hepatitis (GRSH) [30]. WHO will monitor what is new, policy uptake, cascade of care and sequelae. With this information, WHO will provide a global system of centralised data.

What further steps are needed

Hepatitis B vaccination of infants, blood safety programmes and universal precautions in healthcare settings have already greatly reduced HBV and HCV incidence. However, morbidity and mortality are still increasing. What is further needed is to prioritise the full implementation of timely HBV vaccinations, drug addiction therapies, safe injection equipment and HCV treatment for persons who inject drugs, and assured access to testing, care and treatment for those with HBV and HCV.

In addition, countries should establish elimination programmes with action plans that have time-limited numerical targets and the capacity to deliver appropriate interventions to target populations, with Egypt and Australia as good examples. Moreover, services should be integrated in existing health systems, as successfully achieved in Georgia, and strategic data should be used to monitor programme performance and progress towards elimination goals with Iceland and the VA as examples. Countries should also participate more in operational research.

Furthermore, a global coalition, as recommended by the ITFDE, can help by building the capacity and advocacy towards elimination [41]. Large elimination campaigns are often supported by coalitions of implementing programmes, funding organisations, technical experts, and even international organisations such as WHO. A global coalition, guided by the ITFDE and experiences of other elimination programmes can provide the knowledge and experience, and can establish dynamic evidence-based meetings such as IVHEM, which can provide assistance from technical experts and opportunities for generating new knowledge.

Conclusion

During IVHEM, key elements, such as linkage to care, finding the missing millions, awareness, stigma, cost, and lack of funding were discussed as challenges to elimination programmes. The experience gained from previous and current disease elimination initiatives revealed the essential components of effective elimination programmes, including action plans, building capacity, integrated services, collecting strategic data, and monitoring progress.

Examples from several countries were given on how costs were lowered and existing healthcare systems were used. For example, the VA fully integrated HBV and HCV care into existing services and Georgia integrated and decentralised towards primary care. Other methods for lowering costs were discussed, such as in Egypt, where negotiations with companies reduced the cost of

testing due to the large volume required and generic DAAs were manufactured locally. In addition, Australia more affordable interventions and diagnostics were negotiated and primary care services are being used to deliver treatment.

In order to establish elimination, collection of strategic information, involvement of all stakeholders, engagement with civil society, and arrangement of financial support were considered important elements. Iceland was given as a good example of where public and private partnership, in combination with a HCV registry, led to a successful nationwide elimination programme.

To improve linkage to care, appropriate strategies for the target population should be established as for example in the Netherlands where the community was engaged in creating a programme.

Most importantly, in order to achieve elimination, we need more involvement from the community, and bring the right parties together because only the voice of millions can really drive the movement forward.

Acknowledgements

Conflict of interest

SP: an unrestricted education grant from Gilead Sciences and further receives funding from Gilead, MSD, ViiV Healthcare and Jansen.

CB: grants from Gilead Sciences, MSD, ViiV Healthcare and Janssen.

MvdV: participated in ad boards with fees paid to his institution for: Abbvie, Gilead, J&J, MSD, ViiV; received independent research grants from: Abbvie, Gilead, MSD, J&J.

MES: PI in a Gilead Sciences-sponsored investigator-initiated trial (received no PI fees).

OS: Speakers fees: MSD, Gilead Sciences.

VS: Gilead, Abbvie.

TM: received funding for clinical trials performed by: Abbvie, BMS, Genfit, Gilead and Merck.

AG: no conflict of interest.

CM: no conflict of interest.

SDB: received grants from ARHEL and MSD; served on advisory boards for Abbvie, BMS, Gilead and MSD; lecture fees from Abbvie, BMS and Gilead, outside the submitted work.

MN: grant support from Gilead Sciences, MSD and Abbvie.

JF: grant funding from Abbvie, Abbott, Gilead, Janssen and Merck, and scientific consulting from Abbvie, Contravir, Gilead and Merck.

MH: funding from Gilead Sciences, Abbvie and GSK for investigator-initiated research.

JW: no conflict of interest.

The IVHEM meeting, organised by Virology Education, received financial support from Gilead.

References

- World Health Organization. *Global Hepatitis Report 2017*. Geneva: 2017. Available at: www.who.int/hepatitis/publications/global-hepatitis-report2017/en/ (accessed January 2019).
- Stanaway JD, Flaxman AD, Naghavi M *et al*. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet* 2016; **388**: 1081–1088.
- Lazarus JV, Stumo SR, Harris M *et al*. Hep-CORE: a cross-sectional study of the viral hepatitis policy environment reported by patient groups in 25 European countries in 2016 and 2017. *J Int AIDS Soc* 2018; **21** Suppl 2: e25052.
- Pedrana A, Howell J, Schröder S *et al*. Eliminating viral hepatitis: the investment case. *World Innovation Summit for Health*. November 2018. Doha, Qatar.
- Ward JW, Hinman AR. What is needed to eliminate hepatitis B virus and hepatitis C virus as global health threats? *Gastroenterology* 2018; epub ahead of print.
- Gore C, Hicks J, Deelder W. Funding the elimination of viral hepatitis: donors needed. *Lancet Gastroenterol Hepatol* 2017; **2**: 843–845.
- El-Akel W, El-Sayed MH, El Kassas M *et al*. National treatment programme of hepatitis C in Egypt: hepatitis C virus model of care. *J Viral Hepat* 2017; **24**: 262–267.
- Sokal E, Nannini P. Hepatitis C virus in children: the global picture. *Arch Dis Child* 2017; **102**: 672–675.
- Baliashvili D, Kasradze A, Kuchukhidze D *et al*. Prevalence and genotype distribution of hepatitis C virus in Georgia: a 2015 nationwide population-based survey. *J Hepatol* 2017; **66** Suppl 1: S277.
- Scott N, Olafsson S, Gottfrethsson M *et al*. Modelling the elimination of hepatitis C as a public health threat in Iceland: a goal attainable by 2020. *J Hepatol* 2018; **68**: 932–939.
- Boerekamps A, van den Berk GE, Lauw FN *et al*. Declining hepatitis C Virus (HCV) incidence in dutch human immunodeficiency virus-positive men who have sex with men after unrestricted access to HCV therapy. *Clin Infect Dis* 2018; **66**: 1360–1365.
- Martin NK, Thornton A, Hickman M *et al*. Can hepatitis C Virus (HCV) direct-acting antiviral treatment as prevention reverse the HCV epidemic among men who have sex with men in the united kingdom? Epidemiological and modeling insights. *Clin Infect Dis* 2016; **62**: 1072–1080.
- Olafsson S, Tyrfinngsson T, Runarsdottir V *et al*. Treatment as prevention for hepatitis C (TraP Hep C) – a nationwide elimination programme in Iceland using direct-acting antiviral agents. *J Intern Med* 2018; **283**: 500–507.
- Sypsa V, Psychogiou M, Paraskevis D *et al*. Rapid decline in HIV Incidence among persons who inject drugs during a fast-track combination prevention program after an HIV outbreak in Athens. *J Infect Dis* 2017; **215**: 1496–1505.
- Hatzakis A, Sypsa V, Paraskevis D *et al*. Design and baseline findings of a large-scale rapid response to an HIV outbreak in people who inject drugs in Athens, Greece: the ARISTOTLE programme. *Addiction* 2015; **110**: 1453–1467.
- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). *European drug report, trends and developments*. 2015. Available at: www.emcdda.europa.eu/system/files/publications/974/TDAT15001ENN.pdf (accessed January 2019).
- Broadhead RS, van Hulst Y, Heckathorn DD. The impact of a needle exchange's closure. *Public Health Rep* 1999; **114**: 439–447.
- Grebely J, Bruneau J, Lazarus JV *et al*. Research priorities to achieve universal access to hepatitis C prevention, management and direct-acting antiviral treatment among people who inject drugs. *Int J Drug Policy* 2017; **47**: 51–60.
- Burnet Institute. The Prime study: treating hep C in primary healthcare setting. 2018. Available at: https://www.burnet.edu.au/projects/230_the_prime_study_treating_hep_c_in_primary_healthcare_setting (accessed January 2019).
- Weill-Barillet L, Pillonel J, Semaillé C *et al*. Hepatitis C virus and HIV seroprevalences, sociodemographic characteristics, behaviors and access to syringes among drug users, a comparison of geographical areas in France, ANRS-Coquelicot 2011 survey. *Rev Epidemiol Sante Publique* 2016; **64**: 301–312.
- Deuffic-Burban S, Schwarzingler M, Obach D *et al*. Should we await IFN-free regimens to treat HCV genotype 1 treatment-naïve patients? A cost-effectiveness analysis (ANRS 95141). *J Hepatol* 2014; **61**: 7–14.
- Deuffic-Burban S, Obach D, Canva V *et al*. Cost-effectiveness and budget impact of interferon-free direct-acting antiviral-based regimens for hepatitis C treatment: the French case. *J Viral Hepat* 2016; **23**: 767–779.
- Deuffic-Burban S, Huneau A, Verleene A *et al*. Assessing the cost-effectiveness of hepatitis C screening strategies in France. *J Hepatol* 2018; **69**: 785–792.
- Cousien A, Tran VC, Deuffic-Burban S *et al*. Hepatitis C treatment as prevention of viral transmission and liver-related morbidity in persons who inject drugs. *Hepatology* 2016; **63**: 1090–1101.
- Cousien A, Tran VC, Deuffic-Burban S *et al*. Effectiveness and cost-effectiveness of interventions targeting harm reduction and chronic hepatitis C cascade of care in people who inject drugs: The case of France. *J Viral Hepat* 2018; **25**: 1197–1207.
- Park A, Gonzalez R, Chartier M *et al*. Screening and treating hepatitis C in the VA: achieving excellence using Lean and system redesign. *Federal Practitioner* 2018; **35**: 24–29.
- Belperio PS, Chartier M, Ross DB *et al*. Curing hepatitis C virus infection: best practices from the US Department of Veterans Affairs. *Ann Intern Med* 2017; **167**: 499–504.
- NoMoreC. Available at: <https://nomorec.nl/home> (accessed January 2019).
- National Institute of Statistics of Rwanda. RPHC4: population projections 2014. Available at: www.statistics.gov.rw/publication/rphc4-population-projections (accessed January 2019).
- World Health Organization. Global reporting system for hepatitis 2018. Available at: www.who.int/hepatitis/reporting-database/en/ (accessed January 2019).
- Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol* 2017; **2**: 161–176.
- Audet CM, Hamilton E, Hughart L, Salato J. Engagement of traditional healers and birth attendants as a controversial proposal to extend the HIV health workforce. *Curr HIV/AIDS Rep* 2015; **12**: 238–245.
- Audet CM, Blevins M, Rosenberg C *et al*. Symptomatic HIV-positive persons in rural Mozambique who first consult a traditional healer have delays in HIV testing: a cross-sectional study. *J Acquir Immune Defic Syndr* 2014; **66**: e80–e86.
- Editorial. Microelimination could be a big deal for HCV and HIV services. *Lancet HIV* 2018; **5**: e605.
- Hoorenberg E, Achterbergh RCA, Schim van der Loeff MF *et al*. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. *AIDS* 2017; **31**: 1603–1610.
- Hulleger SJ, van den Berk GE, Leyten EM *et al*. Acute hepatitis C in the Netherlands: characteristics of the epidemic in 2014. *Clin Microbiol Infect* 2016; **22**: 209 e201–203.

37. Visser M, van Aar F, van Oeffelen A *et al*. Sexually transmitted infections including HIV in the Netherlands in 2016. Available at: www.rivm.nl/publicaties/sexually-transmitted-infections-including-hiv-in-netherlands-in-2016 (accessed January 2019).
38. Boerekamps A, Newsum AM, Smit C *et al*. High treatment uptake in human immunodeficiency virus/hepatitis C virus-coinfected patients after unrestricted access to direct-acting antivirals in the Netherlands. *Clin Infect Dis* 2018; **66**: 1352–1359.
39. Kirby Institute. *Monitoring hepatitis C treatment uptake in Australia*. The Kirby Institute; 2018. Available at: <https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-9-july-2018> (accessed January 2019).
40. Williams B, Pedrana A, Howell J *et al*. The Rapid-EC study – a feasibility study of point-of-care testing in community clinics targeted to people who inject drugs in Melbourne, Australia. *J Hepatol* 2018; **68 Suppl 1**: S313–S314.
41. Meeting of the International Task Force for Disease Eradication, June 2017. *Wkly Epidemiol Rec* 2017; **92**: 537–556.