Report from the International Viral Hepatitis Elimination Meeting (IVHEM), 17–18 November 2017, Amsterdam, the Netherlands: gaps and challenges in the WHO 2030 hepatitis C elimination framework

Stephanie Popping1*, Manal El-Sayed2, Jordan Feld3, Angelos Hatzakis4, Margaret Hellard5, Olufunmilayo Lesi6, Michael Ninburg7, John Ward8 and Charles Boucher9

1 Department of Viroscience, Erasmus University, Rotterdam, the Netherlands
2 Department of Paediatrics, Ain Shams University, Cairo, Egypt
3 Toronto Centre for Liver Disease, University of Toronto, Toronto, Canada
4 Department of Hygiene and Epidemiology and Medical Statistics, Medical School of National and Kapodistrian University of Athens, Athens, Greece
5 Disease Elimination Program, Burnet Institute, Melbourne, Australia
6 Department of Medicine, College of Medicine, University of Lagos, Lagos, Nigeria
7 Hepatitis Education Project, Seattle, WA, USA
8 Division of Viral Hepatitis, US Centers for Disease Control and Prevention, Atlanta, GA, USA
9 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

Abstract

The current global burden of hepatitis C (HCV) is estimated at 71 million people. The World Health Organization (WHO) has stated that HCV could be eliminated as a public health threat by 2030. A key recommendation to reach this elimination goal is to reduce new infections by 90% and liver-related mortality by 65%. Countries are encouraged by the WHO to develop their own national elimination programmes in order to reach these goals. However, various gaps and challenges, such as the lack of high-quality epidemiological data, stigmatisation, and optimisation of the cascade of care, have arisen in the WHO strategic framework. The International Viral Hepatitis Elimination Meeting (IVHEM) has therefore established an expert panel made of clinicians, virologists, and public health specialists to discuss and address these challenges. This review highlights the outcome and proposed solutions to attempt at facilitating HCV elimination.

Keywords: hepatitis C, elimination, people who inject drugs

The World Health Organization (WHO) has stated that viral hepatitis could be eliminated as a public health threat by 2030. Currently, the global burden of hepatitis C virus (HCV) is estimated at 71 million people [1,2]. Key recommendations in the WHO elimination goals are to reduce new infections by 90% and HCV-related liver mortality by 65% [2].

Various gaps and challenges, however, have arisen on the path towards achieving the WHO elimination goals. The International Viral Hepatitis Elimination Meeting (IVHEM), held on 17–18 November 2017 in Amsterdam gathered an expert panel of clinicians, virologists and public health specialist to discuss key gaps and challenges to achieve HCV elimination. This report highlights the conclusions drawn from this meeting and the important milestones that need addressing in relation to the WHO framework.

A major gap in the response to the epidemic remains the lack of reliable epidemiological data in many countries and regions. While improved data has led to revised estimates in the global HCV burden, dropping from 170 million to 71 million affected people [1], prevalence figures are frequently based on rough estimates, with many countries having no or limited seroprevalence data. Accurate global and regional estimates are imperative, since they allow the establishment of a baseline from which to monitor progress and the impact of interventions aimed at reducing the disease.

Data gaps are considerable in some subpopulations. For example, there is not only a lack of available data in the paediatric field, but also of awareness regarding the infection. Although, an approximate 11 million children (<15 years) worldwide are living with HCV, they are rarely tested [3]. Diagnosis of HCV infection in children remains difficult due to the asymptomatic nature of the disease and lack of liver enzyme elevations [3]. Currently, no direct-acting antiviral (DAA) treatment is approved for children under the age of 12 years [4], despite the fact that they could derive considerable benefit from treatment as they will achieve a high gain in quality-adjusted life years. In addition, if left untreated, there is the possibility of onward HCV transmission due to high-risk behaviour during adolescence [4,5]. Therefore, appropriate epidemiological data and awareness of the infection must be improved in order to allow children access to DAAAs. Furthermore, children and adolescents with HCV infection often face discrimination at school or when playing sports at a stage of life that is highly susceptible to stigma as social interaction and peer acceptance are among their among top priorities. In addition, stigma can also contribute as a primary barrier to accessing care as seen in youths with HIV infection [6]. Therefore, it is important to address this issue and to find ways to fight stigmatisation, not only for adults but also for children and adolescents.

People who inject drugs (PWIDs) represent another group of highly stigmatised individuals [7]. As a result, they often do not acknowledge themselves as PWID or as previous PWID (for example, individuals who have occasionally injected drugs when younger). When wanting care, these individuals often cannot find appropriate healthcare services that are prepared to engage with them, and owing to non-evidence-based rules, adequate treatment is not provided. Stigmatisation represents one of the primary barriers to achieving the WHO elimination goals.

HCV prevalence is high in correctional settings in many countries because of the high numbers of incarcerated PWIDs [8]. More epidemiological data is however needed to assess global epidemiology in this population [9]. While the HCV epidemic in this setting represents an excellent opportunity for
Micro-elimination, overall there is little political support. Stigmatisation results in a shortage of programme funders, harm-reduction programmes and appropriate health monitoring systems [10]. In addition, the prevalence of criminalised risk behaviour, injection drug use, risk factors for the acquisition of HCV such as tattooing and unprotected intercourse, is high in prisons. This further enhances stigmatisation and barriers towards accessing appropriate support [11,12].

Despite clear evidence that harm-reduction programmes, such as needle and syringe exchange programmes and opioid substitution therapy, are effective in reducing HIV and HCV incidence and are highly cost effective, many countries have limited harm-reduction programmes due to ongoing concerns (despite evidence to the contrary) that such initiatives may boost drug use [10,13].

These concerns are particularly relevant when considering the incarcerated population. Only a few countries implement adequate preventative measures or provide HCV treatment for detainees. Currently, 90 countries have needle and syringe exchange programmes in place outside prison settings as compared to only eight countries that do so in at least one prison setting [14]. Healthcare providers and non-governmental organisations need to collaborate to overcome these barriers and establish harm-reduction and monitoring programmes in order to attain the WHO elimination goals.

A further barrier towards the WHO elimination goals remains the lack of identification of HCV-infected individuals and the high number who are unaware of their infection. In a number of countries where DAA therapy is widely available and affordable, such as Portugal and Australia, the number of people being treated has been falling owing to difficulties in diagnosing individuals with HCV. Increasing the awareness of HCV is, therefore, vital. Generally speaking, most individuals have no well-defined symptoms and many do not classify themselves as part of a risk group, and only presenting to care with complications and advanced disease. In 2015, an estimated 20% (14 million) of the individuals living with HCV were aware of their infection and among these, only one quarter had received treatment [2]. There is still limited experience on how to engage with this large number of undiagnosed individuals and this is likely to vary between countries and regions, and depend on what type of risk behaviour is driving the epidemic. It will be important to share experiences in the forthcoming years in order to understand what type of intervention does or does not work in order to upscale treatment.

In addition to raising HCV risk awareness, it is also important that screening/testing programmes are optimised. To date there is limited data on the effectiveness of various testing programmes among key populations. Currently HCV testing programmes lack coverage, are often costly, with some countries reporting higher prices for testing than for treatment. Negotiations with diagnostic companies may help to lower the costs of screening programmes. Furthermore, development of diagnostic and treatment monitoring with point-of-care testing, and novel cheaper tests should be encouraged.

There are successful testing programmes that can be used as examples for other countries and different settings. One of them is ‘network-based testing’ among PWIDs [15]. Another example is opt-out testing within the incarcerated population. This ensures a more timely diagnosis and, when combined with treatment, also acts as treatment as prevention [16]. The final example, among people living with HIV and HCV, involves more frequent testing in order to diagnose reinfection early, which is a cost-effective prevention approach when HCV PCR tests are used [17]. It will be very important in the future for testing strategies to be evaluated for their efficiency and whether they lead to a higher treatment uptake in a cost-effective manner.

Testing for HCV alone without a high proportion of those diagnosed being linked to care will limit progress towards elimination. Currently not all individuals with diagnosed HCV access care and receive treatment. The HCV care continuum can be very complex and people fall out of the care cascade [18]. There is an urgency to simplify testing for improved linkage to care. Reflex testing by immediately performing an HCV-RNA assay on the same sample after a positive hepatitis C antibody test could help to provide a timely diagnosis. Furthermore, the HCV core antigen assay can represent both a cheaper and faster alternative for diagnosing HCV infection [19,20]. In many countries, for example those in Africa, the HCV and HIV cascades of care could be linked. Such an approach is likely to improve the care cascade for both diseases and save costs.

Micro-elimination is possible among certain subpopulations if treatment is upscaled in the forthcoming years. An example is the HCV epidemic among men who have sex with men (MSM) who are living with HIV. These individuals are seen regularly in care and modelling studies show optimism about the micro-elimination perspectives when DAA use is unrestricted [21]. In addition, in high-income countries micro-elimination among subpopulations of HIV co-infected MSM, haemophiliacs and incarcerated individuals are successful and the WHO 2030 target has almost been reached [22–24].

Data gaps remain in the long-term results from patients who have been cured from HCV; these include reinfection rates and the likelihood of individuals with previously diagnosed cirrhosis to develop hepatocellular carcinoma. It will be important to monitor key populations at high risk of reinfection (PWID and MSM) [25] and, whenever possible, to ensure the availability of high-quality harm-reduction programmes. Similarly in some jurisdictions, it will be vital to strengthen healthcare systems, both formal and informal, to prevent onward transmission of HCV. Therefore, innovative surveillance models and identifying reinfection are needed for at-risk populations [26].

Conclusion

While 2030 may still seem far away, there are many challenges and barriers that need to be overcome if we are to successfully achieve HCV elimination by then. IVHEM is providing a platform to discuss the gaps, barriers, and needs so that further research can be tailored and collaborations established. Currently, key barriers are: the lack of high-quality epidemiological data; need for optimisation of the treatment cascade; improvement of screening programmes and affordable diagnostic tools; and gathering insights regarding successful approaches in different populations.

Acknowledgements

Authors’ contributions

SP, CABB, MES, JF, AH, MH, OL, MN, JW contributed to the writing of the manuscript. SP, CABB, MES, JF, AH, MH, OL, MN, JW read and approved the final manuscript.

Conflicts of interest

SP has an unrestricted education grant from Gilead sciences.

CB has received grant support from Gilead Sciences, MSD, Viiv Healthcare and Janssen.
MES was a Principal investigator in a Gilead Sciences-sponsored investigator-initiated trial (no PI fees).

JF received a grant from Abbvie, Abbott, Gilead Sciences, Janssen, MSD; scientific consulting from Abbvie, ContraVir, Gilead and MSD.

AH has research grants from AbbVie, Gilead Sciences and MSD; unrestricted grants from AbbVie, BMS, Gilead, MSD and Novartis; advisor/lecturer for BMS, Gilead Sciences, MSD, AbbVie; co-chair of the Hepatitis B and C Public Policy Association funded by AbbVie, BMS, Gilead Sciences and MSD.

MH has received funding from Gilead Sciences, Abbvie and GSK for investigator-initiated research. MN has grant support from Gilead Sciences, MSD and Abbvie.

The remaining authors declare no conflicts of interests. The IVHEM meeting, organised by Virology Education, received financial support from Gilead, AbbVie and Mylan.

References
1. 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.
2. World Health Organization. Global Hepatitis Report 2017. Geneva. Available at: www.who.int/hepatitis/publications/global-hepatitis-report2017/en/ (accessed June 2018).
3. Sokal E, Nannini P. Hepatitis C virus in children: the global picture. Arch Dis Child 2017; 102: 672–675.
4. Indolfi G, Thorne C, El Sayed MH et al. Challenge of treating children with hepatitis C virus infection. J Pediatr Gastroenterol Nutr 2017; 64: 851–854.
5. Barritt AS, Lee B, Runge T et al. Increasing prevalence of hepatitis C among hospitalized children is associated with an increase in substance abuse. J Pediatr 2018; 192: 159–164.
6. Lee S, Yamazaki M, Harris DR et al. Social support and human immunodeficiency virus-status disclosure to friends and family: implications for human immunodeficiency virus-positive youth. J Adolesc Health 2015; 57: 73–80.
7. Grebely J, Bruene 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.
8. Dolan K, Moazen B, Noon A et al. People who inject drugs in prison: HIV prevalence, transmission and prevention. Int J Drug Policy 2015; 26: 512–515.
9. Larney S, Kapiris K, Beckwith CG et al. Incidence and prevalence of hepatitis C in prisons and other closed settings: results of a systematic review and meta-analysis. Hepatology 2013; 58: 1215–1224.
10. Sander G, Murphy F. The furthest left behind: the urgent need to scale up harm reduction in prisons. Int J Prison Health 2017; 13: 185–191.
11. Kinner SA, Jenkinson R, Gouillou M, Milloy MJ. High-risk drug-use practices among a large sample of Australian prisoners. Drug Alcohol Depend 2012; 126: 156–160.
12. Post JJ, Dolan KA, Whybin LR et al. Acute hepatitis C virus infection in an Australian prison inmate: tattooing as a possible transmission route. Med J Aust 2001; 174: 183–184.
13. Kamarulzaman A, Reid SE, Schippers A et al. Prevention of transmission of HIV, hepatitis B virus, hepatitis C virus, and tuberculosis in prisoners. Lancet 2016; 388: 1115–1126.
14. International HR. 2016. The global state of harm reduction 2016 London. Available at: www.hri.global/global-state-of-harm-reduction-reports (accessed June 2018).
15. Hellard M, Rolls DA, Sacks-Davis R et al. The impact of injecting networks on hepatitis C transmission and treatment in people who inject drugs. Hepatology 2014; 60: 1861–1870.
16. Morris MD, Brown B, Allen SA. Universal opt-out screening for hepatitis C virus (HCV) within correctional facilities is an effective intervention to improve public health. Int J Prison Health 2017; 13: 192–199.
17. Popping S, Nichols BE, van Kampen JJA et al. 2016. Persistence hepatitis C monitoring in previously HCV infected HIV-positive MSM is a cost-saving method to reduce the HCV epidemic Netherlands Conference on HIV. 22 November 2016. Amsterdam, the Netherlands.
18. Scott N, Doyle JS, Wilson DP et al. Reaching hepatitis C virus elimination targets requires health system interventions to enhance the care cascade. Int J Drug Policy 2017; 47: 107–116.
19. Chevaliez S, Feld J, Cheng K et al. Clinical utility of HCV core antigen detection and quantification in the diagnosis and management of patients with chronic hepatitis C receiving an all-oral, interferon-free regimen. Antivir Ther 2016. [Epub ahead of print].
20. Reckstroh JK, Feld JJ, Chevaliez S et al. HCV care antigen as an alternate test to HCV RNA for assessment of virologic responses to all-oral, interferon-free treatment in HCV genotype 1 infected patients. J Viral Methods 2017; 245S: 14–18.
21. Martin NK, Vickerman P, Dore GJ, Hickman M. The hepatitis C virus epidemics in key populations (including people who inject drugs, prisoners and MSM): the use of direct-acting antivirals as treatment for prevention. Curr Opin HIV AIDS 2015; 10: 374–380.
22. Borembamps A, Van den Berk GE, Fanny LN et al. Declining HCV incidence in Dutch HIV positive men who have sex with men after unrestricted access to HCV therapy. Clin Infect Dis 2017.
23. Oldsson S, Tyrfingsson T, Runarssonott C et al. 2017 PS–129-Treatment as prevention for Hepatitis C in Iceland (TRAP HEP C). A real-world experience from a nationwide elimination program using direct acting antiviral agents 52nd European Association for the Study of the Liver 19–23 April, Amsterdam, the Netherlands.
24. Fitzgerald C. Hepatitis C ‘effectively eradicated’ in haemophilia patients who were given contaminated blood. The Journal, 2016.
25. Ingliz P, Martin TC, Rodger A et al. HCV reinfection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe. J Hepatol 2017; 66: 282–287.
26. Falade-Nwulia O, Sulkowski M. The HCV care continuum does not end with cure: A call to arms for the prevention of reinfection. J Hepatol 2017; 66: 267–269.