Editorial

JOURNAL OF HEPATOLOGY

Achieving hepatitis C elimination in Europe – To treatment scale-up and beyond

M. Hellard[1,2,3,*], N. Scott[1,2], R. Sacks-Davis[1,4], A. Pedrana[1,2]

[1]*Burnet Institute, Melbourne, VIC 3004, Australia;* [2]*Department of Epidemiology and Preventive Medicine, Monash University, Clayton, VIC 3008, Australia;* [3]*Department of Infectious Diseases, The Alfred Hospital and Monash University, Melbourne, VIC 3004, Australia;* [4]*Department of Medicine, University of Melbourne, Parkville, VIC 3010*

See Article, pages 402–411

Fraser and colleagues[1] have used a mathematical model to show that for many European countries, using direct-acting antiviral (DAA) therapy to treat hepatitis C infection is unlikely to have a substantive impact on hepatitis C incidence and prevalence among people who inject drugs (PWID) unless treatment rates are increased substantively beyond current levels. Their model explicitly accounts for the opioid substitution therapy (OST) and needle and syringe program (NSP) coverage of each setting, which is important not only because of the proven effectiveness of the programs in reducing hepatitis C transmission,[2] but because it allows the authors to quantify the benefits of prevention interventions in isolation and when combined with treatment scale-up. Their findings reiterate the importance of high prevention coverage (OST and NSP) as a primary method of reducing incidence and prevalence and also as a method of enhancing the epidemiological impact of treatment, through treatment-as-prevention.

The implication of this work is that for many countries the elimination of hepatitis C as a public health threat is not going to happen by chance. A number of barriers need to be overcome, requiring a focused effort from governments and health services. The first barrier is that widespread treatment scale-up is currently precluded by restricted and inconsistent access policies in many European countries.[3,4] Fraser and colleagues' model predicts that without scaling up universal treatment access, OST and NSP alone can produce notable decreases in hepatitis C prevalence, from approximately 20% to more than 75%, depending on current coverage. However, the greatest and most rapid benefits require a combination of both prevention and treatment scale-up in unison.

Despite the current barriers to treatment access in some countries, continued falling prices and growing evidence for the cost-benefit of elimination efforts means that treatment access is constantly changing. It is difficult to imagine that universal treatment access will not become a reality for these countries eventually. Therefore, while the continued advocacy for unrestricted treatment access continues to be of immediate importance, it should not be allowed to distract from the many other aspects of a comprehensive programmatic response that are required to achieve hepatitis C elimination – activities which represent equally critical pieces of the elimination puzzle.

A second and potentially more complex barrier to treatment scale-up is countries' capacities and health infrastructures to deliver treatment and prevention programs at scale. If Fraser and colleagues' model predictions are correct – that elimination is theoretically achievable by scaling up prevention and treatment –broader questions must now be asked of these settings. How will countries scale up access to treatment, and what additional health system strengthening activities would be required if unrestricted access were granted tomorrow? These activities include training and education for providers, increasing laboratory capacity to ensure appropriate testing and increasing awareness of DAAs among key risk populations. In addition, could these changes to the health system be started now in anticipation of drug prices that will inevitably decrease? Mathematical models suggest that the extent and speed at which treatments are scaled-up are important determinants of reinfection and cumulative treatment costs. Lessons learnt from implementation science must therefore be incorporated into broader hepatitis C strategies. In settings with unrestricted access, such as Australia, evidence is emerging that the additional activities required to achieve and sustain high treatment rates require substantial time and effort to coordinate. This includes addressing staffing capacity constraints, diversifying and decentralising services, addressing stigmatization and discrimination and ensuring geographically and culturally appropriate services are available.[5,6]

Health system limitations form an upper bound on the possible treatment scale-up, since existing services may not have the resources or workforce capacities to support substantive increases in patient numbers. A third barrier to scale-up is effectively engaging key risk populations and their specific needs.[7] Implicit in Fraser and colleagues' study is the well-established message that to achieve hepatitis C elimination in most European countries treatment scale-up needs to happen among PWID, the group at greatest risk of transmission, otherwise treatment-as-prevention will not be effective. However, decades of conservative drug policy in most European countries, leading to stigmatization and discrimination, among other factors, have resulted in low engagement of PWID in care in

Received 29 November 2017; accepted 3 December 2017
☆ DOI of original article: http://dx.doi.org/10.1016/j.jhep.2017.10.010.
* Corresponding author. Address: Burnet Institute, Melbourne, VIC 3004, Australia. Tel.: +61 3 9282 2163.
E-mail address: margaret.hellard@burnet.edu.au (M. Hellard).

many communities.[8–10] This must be addressed, since improvements in all aspects of the care cascade,[11] including increased testing frequency well beyond current practice,[12] are required to achieve and sustain high treatment uptake among PWID.

The establishment of flexible and culturally acceptable models of care for patients, in particular PWID, has been shown to improve both capacity and engagement. The simplicity of treatments means they can be administered in primary healthcare settings, rather than confined, as in the era of pegylated interferon and ribavirin, to hospital settings. There is increasing evidence that community-based treatment approaches are highly effective in engaging PWID in care and treatment.[13,14] In Australia, a policy enabling non-specialist prescribing of hepatitis C treatments has been in place since DAAs became available in 2016. As a result, over the first 14 months 46% of treatments were prescribed by non-specialists,[13] with particularly high rates of non-specialist prescribing among indigenous, immigrant and regional communities. This policy also facilitates the use of peer-led[15] and nurse-led models of care,[16] which are able to use community-based services[17,18] as primary contact points for diagnosis and treatment.

Fraser and colleagues also touch on the importance of robust surveillance systems for monitoring and evaluating any hepatitis response. In addition to the capacity to monitor chronic HCV prevalence and treatment rates among PWID, these systems will need to monitor newly acquired infection, including reinfection after treatment.[19] These systems are also critical to ensure services are appropriately located. For example, transmission occurring through injecting drug use is geographically heterogeneous and related to drug market characteristics, yet while health services are also often geographically heterogeneous, they are often distributed according to different coverage objectives. Therefore, it is important that effective resource planning is undertaken to ensure appropriate hepatitis C-related services are located in areas of greatest demand and where unmet need is greatest. This should be guided by evidence and appropriate data, and again, it requires time and planning to put suitable systems in place.[20]

In summary, Fraser *et al.* demonstrate that substantive gains can be made towards hepatitis C elimination in Europe if increases in treatment rates and harm reduction coverage are achieved. Universal access to DAAs is required to achieve the WHO 2030 elimination targets and ultimately this will happen in the region. However, while waiting for this to occur, countries should act now to improve their health services infrastructure and ensure the platforms required are in place to successfully deliver scaled-up DAA treatment in a timely manner when universal access does arrive. A comprehensive elimination program requires more than just DAAs, and depending on the starting point it can take many years to set up sufficient service diversity, infrastructure capacity and surveillance systems to facilitate the increases in testing and retention in care that are required. Lessons should be learnt from other settings on the most effective models of care to maximize treatment uptake.

Financial support

MH, RSD and AP are the recipients of National Health and Medical Research Council fellowships. The Burnet Institute receives financial support from the Victorian Government Operational Infrastructure Support Program.

Conflict of interest

The Burnet Institute receives funding for investigator initiated research for hepatitis C from Gilead Science, Abbvie, Merck and GSK. These projects are led by MH.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhep.2017.12.004.

References

[1] Fraser H, Martin NK, Brummer-Korvenkontio H, Carrieri P, Dalgard O, Dillon J, et al. Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe. J Hepatol 2018;68:402–411.
[2] Turner KM, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction 2011;106:1978–1988.
[3] Marshall AD, Cunningham EB, Nielsen S, Aghemo A, Alho H, Backmund M, et al. Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe. Lancet Gastroenterol Hepatol 2017. https://doi.org/10.1016/S2468-1253(17)30284-4.
[4] Lazarus J, Safreed-Harmon K, Stumo S, Jauffret-Roustide M, Maticic M, Reic T, et al. Restrictions on access to direct-acting antivirals for people who inject drugs: The European Hep-CORE study and the role of patient groups in monitoring national HCV responses. Int J Drug Policy 2017;47:47–50.
[5] Wong E, Pedrana A, Draper B, Gold J, Richmond J, Stoove M, Doyle J, Thompson A, Hellard M, on behalf of the EC Partnership investigator team. Models of Care – exploring different clinical models of care for hepatitis C treatment scale up. AVHEC, Cairns 2017.
[6] Richmond J, Pedrana A, Crooks L, Di Giacomo D, Doyle J, Thompson A, Hellard M, on behalf of the EC Partnership investigator team. Many hands make light work: upskilling the workforce for hepatitis C elimination. AVHEC, Cairns 2017.
[7] Jones S, Murray J, Gold J, Henderson C, Kelsell J, Crawford S, et al. On behalf of the EC Partnership Health Promotion Working Group. Redefining preparedness for hepatitis C treatment from the peer perspective. New Jersey: INHSU; 2017.
[8] Dillon JF, Lazarus JV, Razavi HA. Urgent action to fight hepatitis C in people who inject drugs in Europe. Hepat Med 2016;8:21–26.
[9] Lazarus JV, Sperle I, Maticic M, Wiessing L. A systematic review of hepatitis C virus treatment uptake among people who inject drugs in the European Region. BMC Infect Dis 2014;14:S16.
[10] Grebely J, Bruneau J, Bruggmann P, Harris M, Hickman M, Rhodes T, et al. Users INoHiS. Elimination of hepatitis C virus infection among PWID: the beginning of a new era of interferon-free DAA therapy. Int J Drug Policy 2017;47:26–33.
[11] Scott N, Doyle J, Wilson DP, Wade A, Howell J, Pedrana A, 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.
[12] Scott N, Sacks-Davis R, Pedrana A, Doyle J, Thompson A, Hellard M. Eliminating hepatitis C: the importance of frequent testing of people who inject drugs in high prevalence settings. World Hepatitis Summit; São Paulo, Brazil 2017.
[13] Scott N, Hainsworth S, Sacks-Davis R, Pedrana A, Doyle J, Hellard M. Heterogeneity in hepatitis C virus treatment prescribing and uptake in Australia: a geospatial analysis of a year of unrestricted treatment access. In preparation 2017.
[14] Radley A, Tait J, Dillon JF. DOT-C: A cluster randomised feasibility trial evaluating directly observed anti-HCV therapy in a population receiving opioid substitute therapy from community pharmacy. Int J Drug Policy 2017;47:126–136.
[15] Morris L, Smirnov A, Kvassay A, Leslie E, Kavanagh R, Alexander N, et al. Initial outcomes of integrated community-based hepatitis C treatment for people who inject drugs: findings from the Queensland injectors' health network. Int J Drug Policy 2017;47:216–220.

[16] von Bibra S, Doyle J, Higgs P, Dietze P, Desmond P, Stoove M, et al. Feasibility of recruiting people who inject drugs into a nurse-led model of care trial: the TAP study. J Hepatol 2016;64:S817–S818.
[17] Read P, Lothian R, Chronister K, Gilliver R, Kearley J, Dore GJ, et al. Delivering direct acting antiviral therapy for hepatitis C to highly marginalised and current drug injecting populations in a targeted primary health care setting. Int J Drug Policy 2017;47:209–215.
[18] Grebely J, Alavi M, Micallef M, Dunlop AJ, Balcomb AC, Phung N, et al. Treatment for hepatitis C virus infection among people who inject drugs attending opioid substitution treatment and community health clinics: the ETHOS Study. Addiction 2016;111:311–319.
[19] Sacks-Davis R, Van Gemert C, Bergeri I, Stoove M, Hellard M. Identifying newly acquired cases of hepatitis C using surveillance: a literature review. Epidemiol Infect 2012;140:1925–1934.
[20] Monnet E, Collin-Naudet E, Bresson-Hadni S, Minello A, Di Martino V, Carel D, et al. Place of residence and distance to medical care influence the diagnosis of hepatitis C: a population-based study. J Hepatol 2006;44:499–506.