

State of the Hepatitis C Virus Care Cascade

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Hepatitis C virus (HCV) infection can nearly always be cured. The care cascade asks how often cure occurs in the population, not only how often those treated are cured but also how often those diagnosed are treated, how often those infected are diagnosed, and how often those at risk for HCV infection (or reinfection) receive preventive services. The care cascade is the public health perspective on the hepatitis C epidemic. Naturally, the care cascade varies over time and especially from setting to setting based on the dynamics of public health policies and practices. This review considers the hepatitis C care cascade globally, in the United States, and in select settings.

GLOBAL CASCADE

Worldwide, an estimated 71 million persons were infected with HCV in 2015.¹ An estimated 14 million (20%) were diagnosed, and 5 million (7%) had been treated successfully (Fig. 1).² In 2019, there were still 71 million infected because the number of new infections (~1.74 million per year) has been roughly the same as successful treatments. In fact, Hill and coworkers³ estimate that in 2016 the number of cures outnumbered new infections by 5:1 in

just 10 countries, and that there were more new infections than treated infections in more than half. Clearly, there are multiple challenges across the cure cascade, including preventing new infections, diagnosing existing infections, and providing curative treatment to those diagnosed.

ICELAND CASCADE

The care cascade varies regionally, reflecting variability in the burden of infection and vigor of public health response. For example, Iceland is a high-income country where the burden of infection is low and the public health response is strong.⁴ In 2015, the total number of HCV-infected persons was thought to be less than 1,000. All residents are medically insured, treatment is free (provided by Gilead), reporting is mandatory, and there was a registry of HCV-infected persons going back to 1991. A campaign to test and treat began in January 2016: 741 HCV RNA-positive persons were diagnosed through November 2018, 720 were linked to care, 703 started on treatment, and 633 were cured (Fig. 2). There remain threats, such as reinfection of persons who use drugs and small pockets of infection in hard-to-reach

Abbreviations: HCV, hepatitis C virus; WHO, World Health Organization.

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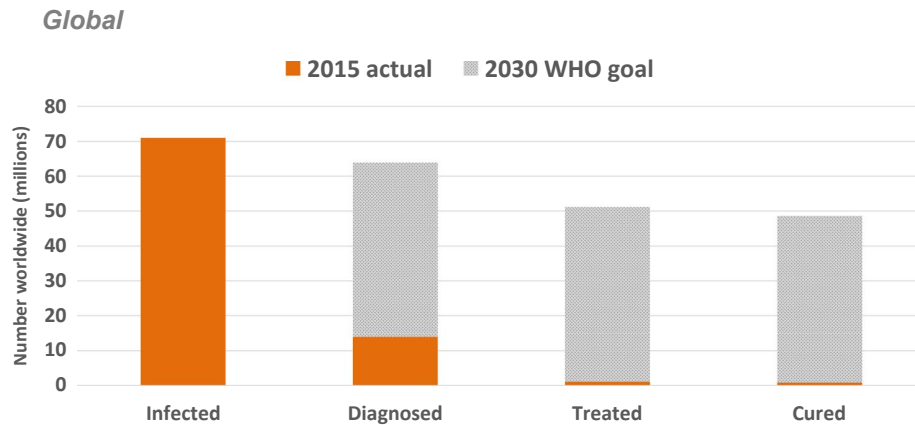


FIG 1 Global HCV treatment cascade, 2015. Among an estimated 71 million persons infected with HCV worldwide, approximately 20% were diagnosed and 7% successfully treated by 2015. WHO targets to eliminate HCV for 2030 are shown with 95% treatment efficacy assumed. The number cured is cumulative. Adapted with permission from *New England Journal of Medicine*.² Copyright 2019, Massachusetts Medical Society.

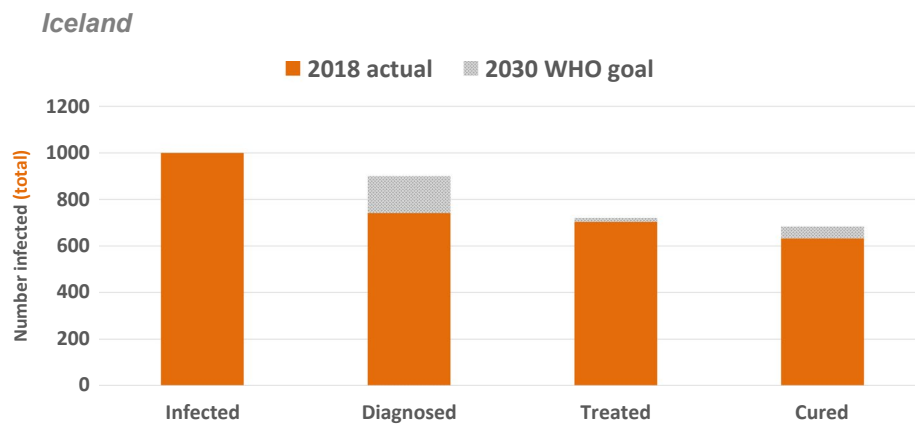


FIG 2 Iceland HCV treatment cascade, 2018. Among an estimated 1,000 persons infected, nearly all have been diagnosed and cured, demonstrating high likelihood of achieving WHO targets to eliminate HCV for 2030.⁴ The number cured is cumulative.

homeless populations; however, Iceland is on track to eliminate HCV by 2020.

PAKISTAN CASCADE

In contrast, Pakistan is a low-income country with one of the highest national burdens of HCV and relatively low public health capacity to respond.⁵ In 2015, it was estimated that there were 8.2 million HCV-infected persons; 1 million (12%) were aware of their infection, a total of 400,000 had been cured cumulatively, and there were 281,000 new infections (Fig. 3).⁶ Pakistan has a national hepatitis elimination plan and heavily discounted treatment costs (\$60/course). However, there are many challenges. To achieve elimination, more than 25 million

persons would need to be tested to diagnose 900,000 new infections and cure 700,000.⁶ That expanded testing and treatment would need to be repeated annually until about 2026.⁶ Capacity to provide that treatment at traditional medical facilities is limited, and the costs are considerable. Under the status quo, the total cost of HCV management from 2018 to 2030 would be \$8.2 billion.⁶ However, 97% of those costs are for the late consequences of infection (cirrhosis and hepatocellular cancer) and do not necessarily produce as many quality years as if funds were spent on elimination by shifting resources to testing and treatment. Interestingly, with heavily discounted treatment, testing costs dominate. For example, in one scenario, expanded testing and treatment cost \$10 billion, with half on HCV testing and only 5% on antiviral treatment.⁶ That strategy

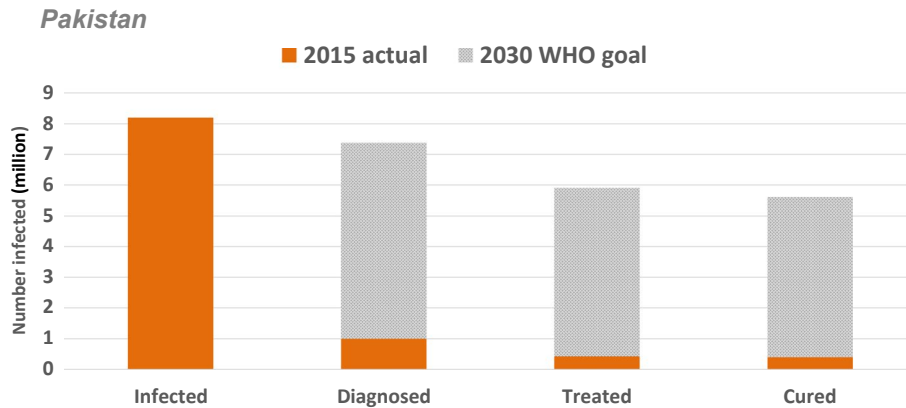


FIG 3 Pakistan HCV treatment cascade, 2015. Among an estimated 8.2 million HCV-infected persons, in 2015, 1 million (12%) were aware of their infection and 400,000 had been cured cumulatively, demonstrating challenges of achieving WHO targets to eliminate HCV by 2030.^{5,6} The number cured is cumulative.

raises total costs but reduces the proportion (40%) spent on consequences and, most importantly, saves lives.

US CASCADE

The United States is a high-income country with a modest disease burden, access to curative oral treatments since 2014, no hepatitis C elimination plan, an opioid epidemic, and little public health response. With the approval of safe oral treatments in 2014, HCV treatment uptake rose sharply in the United States and was associated with a decline in the number of persons with viremia and HCV-related mortality.⁷ Moreover, HCV elimination appears to be likely in some subpopulations, such as veterans and within some Native American settings where uniform

testing and treatment was implemented and funded. However, by the end of 2018 in the United States, one review projected that there were still 2.71 million persons with ongoing HCV infection out of a total of 4.29 million who were once infected; 50% to 60% were aware of their diagnosis, and 1.58 million had already been successfully treated (Fig. 4).⁷⁻¹⁰

There remain many impediments to HCV elimination in the United States, where HCV treatment has declined since 2016. Low treatment uptake reflects a spectrum of residual challenges, including limited testing and awareness of infection, lack of concern about HCV infection among some already diagnosed, and obstacles to receiving treatment, including refusal of some states to pay for treatment for Medicaid recipients. The price of

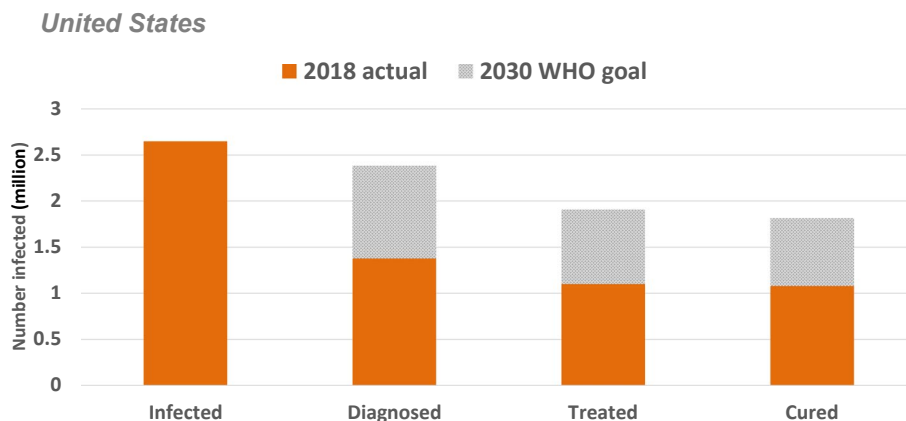


FIG 4 US HCV treatment cascade, 2018. By the end of 2018, it has been estimated there were 2.71 million persons with ongoing HCV infection; 50% to 60% were aware of their infection, whereas 1.58 million had already been cured.^{5,6} The number cured is cumulative.

treatment in the United States has dropped significantly but remains the reason that many barriers to treatment are sustained. Chief among those is corrections, where 10% to 20% of the remaining infected persons may be at any one time. Individual states are responsible for those costs, as well as the cost of treating persons with low income. Solutions such as the “Netflix” subscription plan that fixes the total cost and incentivizes (rather than punishes) states to test and treat are being tested. Individual factors, such as competing priorities and distrust of traditional medical providers, cannot be overestimated as well, because studies have shown that even free same-day treatment is occasionally not accepted.

In addition, HCV incidence in the United States continues to increase due to the opioid epidemic, which occurs in rural regions of the country where public health outreach is limited.¹¹ Thus, although harm reduction services prevent HCV infection, there is no obvious way to distribute them (the way they are currently provided) to all of the areas where they are needed.

SUMMARY

HCV treatment is an incredible tool, but one that is effective only when coupled with testing, linkage, and preventive services. This situation is not unlike what exists with malaria, tuberculosis, and HIV. With each of those, well-funded global public health responses have been necessary to deliver treatment to those in need and to achieve elimination. It will be the same for HCV.

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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) Thomas DL. Global elimination of chronic hepatitis. *N Engl J Med* 2019;380:2041-2050.
- 3) Hill AM, Nath S, Simmons B. The road to elimination of hepatitis C: Analysis of cures versus new infections in 91 countries. *J Virus Erad* 2017;3:117-123.
- 4) Olafsson S, Fridriksdottir RH, Tyrfinngsson T, et al. Iceland may already have reached the WHO 2030 targets for diagnosis and treatment of hepatitis C virus infection. Results from the Treatment as Prevention for Hepatitis C (TrapHepC) program. EASL; April 10-14, 2019; Vienna, Austria. Available at: http://www.natap.org/2019/EASL/EASL_116.htm
- 5) Mahmud S, Al Kanaani Z, Abu-Raddad LJ. Characterization of the hepatitis C virus epidemic in Pakistan. *BMC Infect Dis* 2019;19:809.
- 6) Chhatwal J, Chen Q, Wang X, et al. Assessment of the feasibility and cost of hepatitis C elimination in Pakistan. *JAMA Netw Open* 2019;2:e193613.
- 7) Hofmeister MG, Rosenthal EM, Barker LK, et al. Estimating prevalence of hepatitis C virus infection in the United States, 2013-2016. *Hepatology* 2019;69:1020-1031.
- 8) Chhatwal J, Chen Q, Bethea ED, et al. The impact of direct-acting anti-virals on the hepatitis C care cascade: Identifying progress and gaps towards hepatitis C elimination in the United States. *Aliment Pharmacol Ther* 2019;50:66-74.
- 9) Kim HS, Yang JD, El-Serag HB, et al. Awareness of chronic viral hepatitis in the United States: An update from the National Health and Nutrition Examination Survey. *J Viral Hepat* 2019;26:596-602.
- 10) Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of hepatitis C virus infection in US States and the district of Columbia, 2013 to 2016. *JAMA Netw Open* 2018;1:e186371.
- 11) Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged \leq 30 years—Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep* 2015;64:453-458.