COMMENT



HCV elimination — lessons learned from a small Eurasian country, Georgia

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In April 2015, in partnership with the US Centers for Disease Control and Prevention and Gilead Sciences, the country of Georgia launched the world's first national HCV elimination programme, aiming to reduce HCV prevalence by 90% by 2020. After 2 years of progress, how can the Georgia experience inform global approaches to eliminating HCV?

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy on Viral Hepatitis 2016–2021, which calls for the elimination of viral hepatitis as a public health threat by 2030 (a 90% reduction in new infections caused by HBV and HCV infections and a 65% reduction in deaths from these infections)¹. An estimated 71 million people have HCV globally, resulting in ~400,000 deaths annually; most mortality is caused by hepatocellular carcinoma and end-stage liver disease². The WHO estimates that 1.75 million new HCV infections occurred worldwide in 2015, with wide variations in incidence; transmission mode also varies by country, but the most common modes globally are associated with unsafe health-care practices, followed by injection drug use².

The absence of a known non-human reservoir and latent cellular reservoir, coupled with availability of highly effective, direct-acting antiviral agents (DAAs) capable of curing >90% of HCV infections3, sets the stage for population-wide HCV elimination. All-oral DAAs are simple to administer (typically requiring single daily dosing regimens of 8-12 weeks), are less costly than they were when first introduced because of availability of generic formulations, have increased tolerability and efficacy over interferon-based therapy, and require less patient monitoring^{3,4}. Programmes equipped with improved cost-effective diagnostics required to identify individuals infected with HCV, such as HCV core antigen testing, along with national policies that facilitate testing services in high-risk populations have the potential to enhance the linkage to care and treatment. All-oral DAA regimens require minimal patient monitoring, enabling decentralization of HCV care and treatment services, and are safe and effective³. Together, these advancements, coupled with prevention strategies including improved infection control, blood safety and provision of harm reduction services to people who inject drugs, make elimination of HCV possible.

Elimination of HCV is feasible in Georgia for several reasons, including: a highly motivated government and civil society that was demanding action (many people from all social strata had family or friends dying of end-stage liver disease or liver cancer); a highly skilled and inspired core group of clinicians with a passion for treating HCV infection; a large burden of disease in a relatively small country (3.7 million population); and a complex epidemiology, including varying modes of transmission and genotypes. The country engaged the US Centers for Disease Control and Prevention (CDC) in 2013 to provide technical assistance and subsequently secured a commitment from Gilead Sciences to provide DAAs for treatment, free of charge, to all Georgians living in the country with HCV infection. To set the stage for a HCV elimination programme, Georgia conducted a national serological survey to estimate HCV prevalence. The survey found a high prevalence of HCV infection: 5.4% of adults, meaning that ~150,000 people are living with HCV infection. Prevalence was higher among men and those aged 30-59 years (Georgia Ministry of Labour, Health, and Social Affairs (MOLHSA), unpublished data, 2016). The seroprevalence survey identified injection drug use and receipt of blood products as risk factors associated with HCV infection (MOLHSA, unpublished data, 2016). Georgia embarked on the world's first HCV elimination programme in April 2015 and set a very ambitious elimination target: a 90% reduction in HCV prevalence by 2020 (REF. 5).

Following the launch of the programme, Georgia initiated key activities and implemented programmes to achieve the elimination target (FIG. 1). The initial phase of the elimination programme focused on providing HCV treatment to persons who were infected and had advanced liver disease (F3 or F4 by METAVIR fibrosis score and/or FIB-4 score >3.25), because these persons are at highest risk of HCV-associated morbidity and mortality⁵. In June 2016, the country expanded the eligibility criteria to treat all HCV-infected individuals. From programme launch through 31 December 2016, nearly 28,000 people initiated treatment, and of those who completed treatment and received PCR testing for HCV at least 12 weeks after completion of treatment, nearly 5,400 (84%) had achieved cure (that is, had no detectable virus). Through

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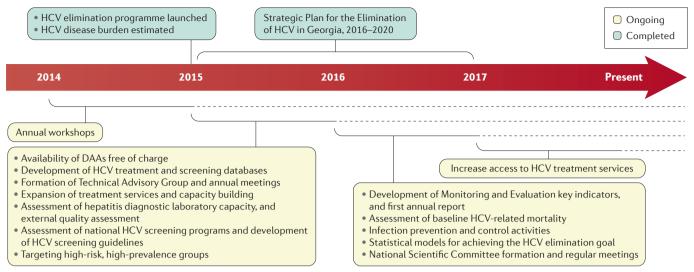


Figure 1 | Key activities for the nationwide HCV elimination programme in Georgia. Full details of all activities are described in <u>Supplementary information S1</u> (table).

December 2016, an estimated 2,500 premature HCV-related deaths and 5,200 new infections were averted⁶.

Although the Georgia HCV elimination programme has made substantial progress since initiation, with rapidly scaling-up care and treatment services, after a 20 month project period only ~20% of the Georgian population living with HCV have received treatment. During the last 3 months of 2016, the number of persons entering the treatment programme declined steadily, suggesting that the first-tier, readily achievable programme initiative providing treatment to those who know they are infected and are motivated to seek treatment — is nearing completion. In response, Georgia is ramping up screening and linkage to care and treatment services. Outreach and provision of services for the most at-risk populations, including people who inject drugs, is also a priority. The next few years are an opportunity for Georgia to demonstrate how to tackle these more complex elimination activities.

Much of Georgia's success can be attributed to the country's openness to working with partners providing technical assistance and support. CDC was the first international partner, with Gilead Sciences coming on board soon thereafter. Since the launch of the programme in April 2015, additional partners (see Acknowledgment section) are now contributing to the HCV elimination efforts in Georgia. Through statistical modelling, countries like Belgium⁷ and Greece⁸ are gauging whether they, too, can achieve the WHO's HCV elimination goals and are assessing the measures needed to curtail incidence and lower prevalence of HCV. In 2017, the National Academies of Science, Engineering, and Medicine set goals for the elimination of HBV and HCV as public health threats in the USA9. DAA costs are decreasing globally and the cost-effectiveness of elimination has been documented10, developments that promote achievement of HCV elimination goals. Nonetheless, Georgia is the only real-world setting in which a comprehensive HCV elimination programme has been launched.

A key lesson from this experience is that availability of curative treatment alone is not enough to achieve

HCV elimination; instead, a comprehensive approach to elimination must be taken, to include screening and linkage to care and treatment policies and programmes, high-quality diagnostics, surveillance, provision of services to high-risk and marginalized populations, and measures to prevent transmission. Although formidable challenges exist, lessons from this model elimination programme can inform similar initiatives in other countries, regardless of income level. The Georgia HCV elimination programme will continue to evolve as innovative screening strategies, diagnostics, and prevention and treatment options are implemented, providing valuable lessons for the world.

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Competing interests statement

The authors declare no competing interests.

SUPPLEMENTARY INFORMATION

See online article: <u>S1</u> (table)

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