

 VIRAL HEPATITIS IN 2020

# Hepatitis C virus elimination: laying the foundation for achieving 2030 targets

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The World Health Organization's targets for hepatitis C elimination by 2030 are ambitious, but, in 2020, global leadership demonstrated by Egypt, innovative strategies to improve linkage to treatment for marginalized populations and the broadened capacity of direct-acting antiviral therapy have been promising for enhanced global elimination efforts.

a patient with active HCV infection was US\$85, and the cost per cure was \$130.

Key elements outlined for the success of the Egyptian HCV screening and treatment programme were political will (including considerable support from the president), social pressure from affected communities, no-cost testing and treatment, mass procurement through a single negotiating body of cheap diagnostics and DAA therapy, and simplified management, including task shifting to primary care physicians.

Despite this incredible success, the report<sup>6</sup> does include some areas of either concern or need for further population-level evidence of efficacy. Only a minority of patients (36.6%) commenced on DAA therapy had information on virological outcome, so although documented cure was extremely high (98.8%), the overall treatment success might be somewhat lower. Characterization of population-level effects of this rapid DAA scale-up will be crucial for Egypt, but, equally importantly, it would provide evidence needed to advocate for investment and action in global HCV elimination efforts. These impact assessments should include evaluation of trends in hepatocellular carcinoma, liver-related mortality, population-level HCV viraemic prevalence and incidence of new HCV infections.

A potential impediment to HCV elimination is that in many countries/regions, highly marginalized individuals such as people who inject drugs (PWID) are the predominantly affected populations. Innovative strategies are therefore required to enhance screening and linkage to care for so-called 'hard-to-reach' populations. A cluster-randomized trial reported in 2020 undertaken in Scottish community pharmacies involved in opiate agonist therapy (OAT) delivery for PWID randomly assigned pharmacies (1:1) to refer patients with positive HCV antibodies to conventional care or care in the pharmacy (known as

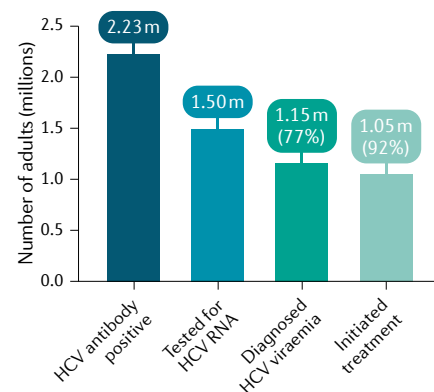


Fig. 1 | **Cascade of HCV care in Egypt.** Oct 2018–Sep 2019. HCV, hepatitis C virus. Data from REF.<sup>6</sup>.

Any review of 2020 needs to acknowledge the global health challenge that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has created. A key concern regarding the all-consuming nature of the community and public health response to COVID-19 is its effect on other public health issues. However, 2020 should also be remembered as a major milestone on the pathway towards elimination of hepatitis C virus (HCV) as a global public health threat. The awarding of the 2020 Nobel Prize in Physiology or Medicine 2020 to Harvey J. Alter, Michael Houghton and Charles M. Rice “for the discovery of Hepatitis C virus”, approximately three decades after their initial work<sup>1</sup>, has balanced concerns that 2020 would be a major setback for HCV elimination efforts. This Year in Review will cover three key contributions to HCV science and public health, including the promise they hold for enhanced global elimination efforts.

The World Health Organization (WHO)'s 2030 global elimination targets<sup>2</sup> for HCV are 80% of those eligible treated, 90% reduction in incidence of new infections and 65% reduction in liver-related mortality. However, the estimated 71 million people living with chronic HCV infection worldwide, an escalating liver disease burden resulting in approximately 400,000 deaths per year from liver failure and liver cancer<sup>3</sup>, a minority (possibly only 20%) of people with chronic HCV diagnosed<sup>4</sup> and an estimated 1.75 million people newly infected with HCV each year<sup>2</sup> demonstrate the enormous task ahead. The development of direct-acting antiviral (DAA) therapy for chronic HCV infection is one of the great advances in clinical medicine in the

past few decades<sup>5</sup>, but massive screening and treatment implementation programmes are required to translate the potential of DAA therapy into population-level benefits.

The exemplar for HCV screening and treatment delivery in recent years is Egypt. In a *New England Journal of Medicine* Special Report, the key elements of the Egyptian HCV elimination programme were outlined<sup>6</sup>. Over the period 2014–2017, the Egyptian National Committee for Control of Viral Hepatitis had overseen a national hepatitis C strategy that provided no-cost DAA-based HCV treatment to more than 2 million people. Rather than continuing this already impressive strategy, declining treatment numbers led the committee to introduce a national HCV screening initiative in 2018.

Of a target population of 62.5 million (18 years of age or older), over a 7 month period (October 2018 to April 2019) involving three phases of screening with each phase including 5,800 to 8,000 teams (each consisting of a physician, nurse and a data-entry person), a remarkable 49.6 million (79.4%) people were screened<sup>6</sup>. Initial screening was by rapid point-of-care HCV antibody, with confirmatory HCV RNA testing of those positive, and subsequent linkage to DAA treatment. Among the 2.23 million people who initially screened as HCV-antibody positive, complete evaluation and follow-up data were available by September 2019 for 1.50 million (67%) people, of whom 1.15 million (77%) were HCV RNA positive (FIG. 1). Among those with confirmed active HCV infection, 92% commenced treatment (sofosbuvir plus daclatasvir with or without ribavirin), with commencement usually 10 days following screening (range: 6 to 30 days). The estimated cost of identifying

## Key advances

- A massive national hepatitis C screening and treatment programme in Egypt has demonstrated the feasibility of major progress towards elimination in a high-prevalence lower–middle income country setting<sup>6</sup>.
- A cluster-randomized trial in Scottish pharmacies found higher linkage to treatment for people on opiate agonist therapy using a pharmacist-led model of care compared with a conventional model of care<sup>7</sup>.
- An ultra-short (7 day) antiviral regimen was highly effective (100%) for prevention of hepatitis C virus (HCV) infection in HCV-uninfected recipients of solid organ transplants from donors with HCV infection<sup>9</sup>.

pharmacist-led care)<sup>7</sup>. Screening was undertaken with dried-blood-spot testing; patients eligible to receive pharmacist-led DAA therapy were HCV RNA positive and stable on OAT (having received therapy for 3 months or longer). Patients with surrogate-marker-suspected cirrhosis, history of decompensated cirrhosis, or HIV or chronic hepatitis B virus infection were not eligible. Conventional care was provided in community treatment centres by an experienced multidisciplinary team. In the pharmacist-led care group, prescription of DAA therapy was undertaken by pharmacists, who along with other non-specialist groups — nurses and primary care physicians — can prescribe in Scotland.

Among those patients estimated as infected with HCV in pharmacist-led care ( $n = 341$ ) and conventional care ( $n = 338$ ), rates of diagnosis and treatment agreement (64% versus 41%), treatment initiation (33% versus 17%), treatment completion (32% versus 17%) and assessment for cure (29% versus 13%) were higher in the pharmacist-led care population<sup>7</sup>. Among the 108 patients treated in the pharmacist-led care group, there were only two treatment failures and six non-attenders for cure assessment, with non-attendance lower than in the conventional care group (6% versus 21%). Among all people on OAT in

the randomized pharmacies (including those who were uninfected and non-screened), DAA therapy cure was achieved in 7% (98 out of 1,365) of patients in pharmacist-led care versus 3% (43 out of 1,353) in the conventional care population ( $P < 0.0001$ ). Thus, a pharmacy-led model of care enhanced HCV screening, linkage to care and successful treatment.

A third paper, also published in 2020, highlights the capacity of DAA therapy to prevent transmission of HCV. The escalating opioid epidemic in North America has produced an increasing number of potential organ donors with HCV infection<sup>8</sup>. A single-arm trial was undertaken to evaluate short-course prophylactic therapy in patients uninfected with HCV ( $n = 30$ ) receiving solid organ transplants (13 lung, ten kidney, six heart and one kidney–pancreas) from donors with HCV infection<sup>9</sup>.

Prophylactic therapy consisting of a DAA regimen of glecaprevir plus pibrentasvir combined with the HCV entry blocker ezetimibe was commenced 6–12 hours pre-transplantation and continued for 7 days post-transplantation. The primary end point of prevention of chronic HCV infection 12 weeks following therapy completion was achieved in all 30 (100%) transplant recipients. Interestingly, low-level transient HCV viraemia was detected in 21 (67%) recipients during the initial 14 days post-transplantation including the initial 7 day post-treatment period. This observation is not unexpected, given that low-level HCV viraemia can be observed at chronic HCV treatment completion in patients who subsequently clear virus<sup>9</sup>.

Ethical concerns regarding transplanting HCV-infected organs into recipients without HCV infection should be diminished with the findings from this highly innovative study. The remaining moral dilemma in relation to this setting is the continued high levels of opioid drug overdose and death, particularly in the United States, in the context of inadequate provision of opioid drug treatment and other overdose prevention strategies<sup>10</sup>. This dilemma is a reminder of the importance

of broad public health strategies to improve access to care for vulnerable and marginalized populations with and at-risk of HCV infection.

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## Competing interests

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