



## Eliminating hepatitis C

WHO has ambitious global targets, made feasible by new highly effective treatments. But drugs alone are not enough. Talha Burki reports.

The past few years have been an eventful time for those involved with hepatitis C. Direct-acting antivirals, the first of which was approved in 2013, can cure more than 95% of patients in a matter of weeks. In 2016, the 194 member states of WHO agreed to eliminate all forms of viral hepatitis as a public health threat by 2030. WHO's global strategy targets reductions of 65% in mortality from hepatitis C virus (HCV) and 80% in new infections, relative to 2015 levels. "It is certainly achievable, but strong governmental support, both at national and local level, is essential", Marc Bulterys, who leads the WHO Global Hepatitis Programme, told *The Lancet Infectious Diseases*.

Individual countries have made dramatic progress. Egypt has the highest prevalence of HCV in the world. Since 2015, it has treated 2.4 million infected individuals, most of whom have been cured. A publicly funded national hepatitis programme oversees control efforts. Egypt intends to have screened its entire adult population by September, 2019, and

to treat 2.5–3 million people within 6 months of diagnosis.

**"only nine nations are on track to achieve the elimination targets for HCV."**

NHS England has announced its plan to eliminate HCV by 2025. 160 000 people are thought to carry the virus in the country. The NHS has asked the pharmaceutical industry to assist with case-finding. Progress had been delayed by a legal challenge by AbbVie against NHS England's procurement deal for direct-acting antivirals, but the tender resumed after the UK high court ruled in NHS England's favour in January, 2019.

Pakistan has driven down the cost of a course of generic direct-acting antivirals to less than US\$50 and has outlined plans for an ambitious testing programme. But the country has a huge task on its hands. An estimated 8 million Pakistanis are infected with HCV. Unsafe injection practices, both within and outside the official health-care system, unsterilised dental

equipment, reused razor blades by the country's preponderance of roadside barbers, and patchy enforcement of blood-screening procedures contribute to around 150 000 new infections every year.

Mongolia, which has an estimated disease burden of 150 000 infections, has already screened over half its adult population. All those who test positive for HCV are offered treatment under the domestic health insurance programme at the cost of around \$450 for a course of generic drugs, most of which reimbursed by the government.

Nonetheless, only nine nations are on track to achieve the elimination targets for HCV. The size of the challenge can be captured in a handful of statistics. An estimated 71 million people worldwide are chronically infected, 69 million of whom have yet to begin treatment. 80% of those carrying HCV are unaware of the fact. In 2015, around 400 000 people died from HCV-related liver complications, there were 843 000 cures, and 1 750 000 new infections. All of which meant that the global burden grew. Only 39% of countries operate haemovigilance systems and despite the enormous advances in blood safety and infection control since 2000, figures from 2015 suggested that 3% of health-care-related injections are still given with unsterilised, reused needles and syringes.

"There has been this intense focus on direct-acting antivirals, but there is not a straight line from drugs to elimination", explains Timothy Hallett (Imperial College London, UK). "An awful lot of other things need to fall into place if the targets are to be met: screening and outreach and, in particular, harm reduction." Hallett is co-author of a modelling study



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Harm reduction will be essential to eliminate hepatitis C virus

that was published earlier this year in *The Lancet*. The study concluded that a comprehensive package of prevention, screening, and treatment would result in an 81% reduction in incidence of HCV infection by 2030, thus achieving the global strategy target, as well as a 61% reduction in mortality by the same year, slightly below the target, which would instead be attained by 2032. Impressive figures indeed, but the key word here is “comprehensive”.

Two thirds of the global population of injecting drug users (IDUs) are thought to have HCV infection. IDUs account for 23% of new cases, 8% of the total disease burden, and 32% of deaths. Hallett’s modelling study envisaged a situation in which 40% of IDUs worldwide have access to harm reduction services such as needle exchange and opioid substitution therapy. As things stand, only 1% of IDUs live in nations where both these interventions are on offer. 27 clean needles and syringes are currently available for each IDU per year. WHO has targeted increasing this number to 200 by 2020 and 300, generally reckoned to be the ideal, by 2030. But only one-quarter of countries have the kind of data that allows them to assess their progress towards these goals.

Many IDUs are often incarcerated and most prisons do not offer harm reduction services. Prevailing stigma, especially in the ex-Soviet states, mean that policy-makers frequently sideline IDUs. Egypt’s success in combating HCV is at least partly attributable to the fact that the virus is so widely disseminated. “Everyone in Egypt knows someone with hepatitis C; that makes a difference, in contrast to countries who do not prioritise the disease because it is concentrated in injecting drug-using populations”, said Jessica Burry (Médecins Sans Frontières [MSF], Geneva, Switzerland).

WHO’s global strategy will cost an estimated \$11.9 billion from 2016 to 2021. “Countries which have very substantial epidemics are stepping

up”, points out Bulterys. 62% of people living with HCV are in nations which have access to generic direct-acting antivirals, the price of which tends to hover between \$100–200. “If these countries can include the drugs in their basic health insurance programmes, they will be able to treat people at quite a low cost”, said Bulterys. But that still leaves a sizeable proportion of patients reliant on originator brand products. When Gilead released sofosbuvir in 2013, the list price was \$84 000 for a course of treatment. AbbVie and MSD have since entered the market and costs have been driven down. The 2016–17 Australian programme was able to negotiate a price of less than \$8000 per course of treatment. But for most countries, this is still much too expensive.

**“The other big challenge is diagnostics; prices are still quite high and that is a barrier for countries”**

“Middle-income, high-burden countries are having a lot of trouble getting down to a price that would allow governments to scale up treatment”, Burry told *The Lancet Infectious Diseases*. MSF is among six organisations to appeal the European Patent Office’s decision to uphold Gilead’s patent on sofosbuvir in September, 2018. “In some European countries, Gilead charges as much as €43 000 for a 12-week treatment course, when generic versions of the same course can be purchased for less than €75 outside of Europe”, stated MSF.

China has 7–10 million people with HCV infection, most of whom have not been identified, but it has been excluded from all generic licenses. Meeting the WHO targets implies treating over 50 million people with direct-acting antivirals by 2030 and if China, India, or Pakistan do not put into practice a comprehensive package of interventions, the targets will not be met until at least 2047.

“The other big challenge is diagnostics; prices are still quite high and that is a barrier for countries, particularly when they have started to treat the pool of people that they already know are infected”, notes Burry. “You have to screen a lot of people for every diagnosis”. There are heartening signs from Egypt, which managed to cut the cost of each antibody test to around \$0.50.

“Reducing the price of the drugs and diagnostics is a great start, but countries really need to think about how to implement the global strategy”, warns Hallett. This means setting up detailed screening and harm reduction plans and arranging medication for those who test positive for HCV—the Australian HCV programme starts patients on treatment on the same day they are diagnosed. Switching to oral medications more generally would also help; an estimated 90% of injections administered in primary health-care every year could be delivered orally.

Certain countries offer encouraging examples. Rwanda has managed to screen 300 000 people for HCV, by August, 2018, Georgia had started more than 48 000 patients on direct-acting antivirals, and from 2016 to 2017, Australia treated almost a quarter of its estimated 230 000 infected population. But if one country is to act as a model, Burry believes it should be Egypt. “They refused to grant patents on the early oral drugs, so they were able to kickstart local generic production and massively cut the price of treatment; the political will to tackle hepatitis C runs right to the top of the government, and they used this will to make treatment available in the public sector and to set up massive screening programmes”, she said. “Egypt has it all figured out; it would be great if more countries could follow their lead”.

Talha Burki