

The availability of next-gen hepatitis C therapies may see the global elimination of the disease - but access to treatment must be stepped up dramatically

2014 will do down as a pivotal year in the fight against hepatitis C virus (HCV), a blood-borne infection that is thought to infect around 2.5% of the world's population - some 170 million people.

The availability of new, more effective therapies for hepatitis C virus have raised the tantalising prospect of being able to eliminate the infection on a global basis, although there are still significant obstacles to overcome.

Viral hepatitis - which generally means hepatitis B and C - "kills more people every year than HIV, malaria and tuberculosis combined, but has not had the same level of resources committed to it," according to Charles Gore, who is chief executive of the Hepatitis C Trust in the UK and president of the World Hepatitis Alliance (WHA).

A resolution passed at the Assembly last year called on the World Health Organization (WHO) to draw up a strategy with targets for the elimination of viral hepatitis, and with milestones on the path to elimination likely to be set for 2020 and 2030.

While the availability of a vaccine for hepatitis B has made elimination of that form of viral hepatitis feasible, for HCV that would have been unthinkable before the development of new directly-acting antivirals - across three drug classes - that have simplified treatment and improved sustained virologic response (SVR) rates, which in HCV can be considered an effective cure.

The launch of drugs such as Gilead's Sovaldi (sofosbuvir) and Harvoni (sofosbuvir and ledipasvir), AbbVie's Viekirax (ombitasvir/paritaprevir/ritonavir) and Exviera (dasabuvir), J&J's Olysio (simeprevir) and Bristol-Myers Squibb's Daklinza (daclatasvir) means that doctors finally have an alternative to lengthy, cumbersome and hard-to-tolerate regimens based on immunostimulating pegylated interferons.

Interferon regimens required months of therapy, saddled patients with debilitating side effects

including fatigue, depression and flu-like symptoms and - even with the addition of an oral antiviral called ribavirin - only cleared the virus in around 60% of recipients.

The launch a few years ago of first-generation protease inhibitors to the pharmacotherapeutic arsenal - Vertex' Incivek (telaprevir) and Merck & Co's Victrelis (boceprevir) - drastically improved success rates in some patients. However, the development of resistance, increases in adverse effects and a lack of activity in some HCV genotypes reduced their impact and initial blockbuster sales fell off dramatically once the new generation of treatments (see figure 1) approached the market.

'Treatment numbers are declining when an increase is urgently needed'

In fact, the Hepatitis C Trust has made a commitment to shutting down no later than 2030, says Gore, "on the ground that HCV will be eliminated as a public health concern and our organisation will no longer be needed".

"There are not very many conditions you can cure in just 12 weeks," he points out.

While there is every reason to be optimistic about the prospects for HCV elimination, there are still massive problems to overcome before that can become a reality.

At the moment, low rates of diagnosis and a sizeable population of carriers of the virus who do not know they are infected means that only around 3% of patients are treated, even in developed countries. Given that around a quarter of people infected with the virus will go on to develop liver cancer or cirrhosis without treatment, its unsurprising that there are deep concerns that the disease could eventually become a public health timebomb.

Public Health England's 2014 report *Hepatitis C in the UK* last year (figure 1) reveals the scale of the problem, even for a country with a sophisticated healthcare system. Hospital admissions from hepatitis C-related end-stage liver disease quadrupled between 1998 and 2012 to reach around 2,400, with deaths rising by the same margin to 428, and that pattern is repeated in many other developed countries around the world.

The latest official data put the number of HCV patients in the UK at around 214,000, with around 11,000 having serious complications such as liver cancer or cirrhosis.

"There is evidence that the number of people being treated each year is levelling off or starting to decline when an increase in the numbers treated is urgently needed," notes the author of the report - hepatitis specialist Dr Helen Harris of Public Health England.

"Part of the problem may be that many of those who are willing and 'easy' to treat have already been treated," she added, whilst acknowledging that another factor may be people waiting for improved treatments rather than undergoing more difficult-to-tolerate regimens with lower rates of sustained viral response (SVR).

People with HCV generally fall into three categories - those who have injected drugs at some point in their lives, those who are exposed to the virus in healthcare settings from contaminated blood or unsanitary equipment, and migrants who are born or brought up in countries with a high prevalence of HCV.