HIV and hepatitis C



Protesters march to demand treatment for patients with hepatitis C.

KEY POINTS

- 2.3 million people have HIV and hepatitis C co-infection 6.2% of people living with HIV globally.
- Both hepatitis C and HIV are transmitted through shared injecting equipment, so scale up of harm reduction and needle and syringe programmes are key to prevent both HIV and hepatitis C.
- Treatment for HIV is now enabling people to live longer, but liver disease in people with HIV and hepatitis C co-infection is becoming a major cause of illness and death.
- Although treatment for hepatitis C is available, improving access to testing and treatment remains a major concern.

Explore this page to find out more about the epidemiology of co-infection, the impact of HIV on hepatitis C, prevention programmes, treating hepatitis C, treatment programmes and the outlook for HIV and hepatitis C coinfection.

Hepatitis C is a viral, blood-borne infection that damages the liver, one of the body's most important organs. While many people do not have any symptoms, the hepatitis C virus can cause fatigue, loss of appetite, muscle and joint pain, mild cognitive problems and depression. It can range in severity, from a mild illness lasting a few weeks to a serious, lifelong illness.1

Each year, around 1.75 million people newly acquire the hepatitis C virus.2 Between 15 and 45% of those infected will spontaneously clear the virus within six months without any treatment. The remaining 60 to 80% will develop chronic hepatitis C.

In 2015, the World Health Organization (WHO) estimated that 71 million people, or 1% of the world's population, were living with chronic hepatitis C. Of these people, 20% (14 million) knew their diagnosis and 7.4% of those diagnosed (1.1 million) were started on treatment. In 2016, 1.76 million people were additionally treated, bringing the global coverage of hepatitis C treatment to 13%. Much needs to be done in order for the world to achieve the 80% treatment target by 2030. 3

This advanced stage of the disease can cause severe scarring of the liver (cirrhosis), liver cancer (hepatocellular carcinoma) and liver failure. Each year, an estimated 399,000 people die from complications relating to hepatitis C.4

There is considerable overlap between hepatitis C and HIV, as both blood-borne viruses can be transmitted in similar ways and affect some of the same social groups. The most common modes of infection are through unsafe injecting drug use, unsafe healthcare, and the transfusion of unscreened blood and blood products. It can also be transmitted sexually and be transmitted from mother to baby, although these routes are much less common.5 6

As people living with HIV live longer, liver disease in people with HIV and hepatitis C co-infection is becoming a major cause of illness and death.

The epidemiology of HIV/hepatitis C co-infection

It is estimated that 6.2% of people living with HIV also show signs of past or present hepatitis C infection. This equates to 2.3 million people living with HIV, over half of whom (1.36 million) are people who inject drugs.7 Injection drug use accounts for 23% of new hepatitis C infections while 8% of people living with chronic hepatitis C currently inject drugs.8

Global prevalence of HIV-HCV coinfection

An estimated **36.7** million people are living with HIV globally



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Among people living with HIV, the prevalence of hepatitis C is highest in people who inject drugs

(82.4%), followed by men who have sex with men (6.4%) and pregnant women (4%).9 Studies also show very high rates among prisoners living with HIV, although less data has been collected.

As a result, developing models of care that meet the needs of people from these key populations is a vital first step to providing an effective co-infection treatment programme. However, the proportion of people living with HIV and hepatitis C co-infection varies considerably, according to risk group and world region.

In 2016, low- and middle-income countries accounted for about 75% of people living with hepatitis C. China has the largest hepatitis C epidemic (almost 10 million people living with hepatitis C in 2015), followed by Pakistan (7.2 million), India (6.2 million) and Egypt (5.6 million). These four countries account for almost 40% of all people living with hepatitis C.10

Eastern Europe is home to the greatest number of people living with HIV-hepatitis C co-infection, estimated to be around 600,000 people.11 Around 400,000 people in sub-Saharan Africa are also living with HIV/hepatitis C co-infection.12

The impact of HIV on hepatitis C

The interaction between HIV and hepatitis C affects the transmission and natural history of hepatitis C.13 People who do not receive HIV treatment are less likely to spontaneously clear their hepatitis infection, have higher hepatitis viral loads and experience more rapid hepatitis disease progression than HIV-negative people.

They may also belong to groups that are criminalised and stigmatised, meaning they are likely to experience barriers to accessing health services.14On the other hand, antiretroviral treatment taken to treat HIV helps keep hepatitis C under control. Hepatitis outcomes are better in people who receive HIV treatment. Whereas response to the older generation of hepatitis C treatments was poorer in people with HIV, this is not the case with modern therapies.

Hepatitis C prevention programmes

Both hepatitis C and HIV are readily transmitted through the sharing of equipment used to inject heroin, crack cocaine and other drugs. Therefore, harm reduction services use the same approach to prevent transmission of both viruses in people who inject drugs.

Needle and syringe programmes should make sufficient quantities of sterile injecting equipment available. Opioid substitution therapy for people with drug dependency reduces the transmission of viral infections because it helps people inject drugs less often. It also helps engage people with healthcare.15

WHO also recommends peer interventions for people who inject drugs.16 Research suggests that combined programmes, rather than singular approaches, are more effective.17

Australia, New Zealand and Western Europe offer integrated hepatitis C, HIV and harm reduction services with promising results, leading to increased access to healthcare among people who use drugs, particularly when programmes involve peer outreach workers.18

Despite the scientific evidence in favour of harm reduction strategies, punitive instead of public

health approaches for people who inject drugs are still frequent in many countries. Criminalisation and stigmatisation of people who inject drugs hinders prevention.19 20A scale-up of hepatitis C treatment in people who inject drugs would reduce viral loads and make transmission less likely.21

Harm reduction expansion

An early harm reduction success story comes from Switzerland. Responding to a rapid rise of HIV infections in the late 1980s, needle and syringe programmes and low-threshold opioid substitution therapy, where enrolment criteria is kept to a minimum, were provided in almost all cities. Supervised drug consumption sites were set up in bigger cities.

The country's drug policy is based on four pillars: policing (supply reduction), demand reduction, harm reduction, and prevention of drug use. The measures have kept hepatitis C infections under control and also had a dramatic impact on HIV infections.22

Health professionals and advocates have also been able to implement harm reduction policies in some otherwise conservative countries. For example, there has been a great expansion of methadone maintenance and needle exchange programmes in Malaysia, although overall coverage remains insufficient.23

Kenya has been steadily expanding its harm reduction services since 2013 and is now considered one of the leading harm reduction champions in Africa. Kenya is the only country in the region where hepatitis C treatment is available free of charge for some people who inject drugs.24

Hepatitis C prevention for men who have sex with men

In addition to the 'classic' hepatitis C epidemic associated with sharing injecting equipment, a 'new' epidemic in which the virus is transmitted during sex between men has emerged.25 Evidence from Western Europe, Australia and the USA suggest outbreaks are concentrated in urban areas among gay men and other men who have sex with men living with HIV, with serosorting (sexual networks of HIV-positive men) and recreational drug use likely to be contributing to transmission.26

Prevalence of hepatitis C among men who have sex with men is higher than 8% in Germany and the Philippines, 18% in Uzbekistan, 36% in the Seychelles and 60% in Mauritius.27 However, the number of countries monitoring and reporting on this is extremely limited. Little progress has been made in the development of effective hepatitis C prevention approaches for men who have sex with men.28

A modelling study based on the situation in Victoria, Australia found that major reductions in hepatitis C prevalence can be achieved among HIV-positive men who have sex with men within two years through the implementation of routine hepatitis C monitoring and prompt treatment as a part of HIV care. It found that, if the average time from hepatitis C diagnosis to treatment was six months, an 80% reduction in hepatitis C prevalence could be achieved in 122 weeks. This was reduced to 77 weeks if the average time between hepatitis C diagnosis and starting treatment was decreased to 16 weeks.29

The frequency with which men are re-infected with hepatitis C after successful treatment underlines

Treating hepatitis C

The first treatment for hepatitis C, interferon-alpha, was introduced in 1989. Until 2011, treatment relied on injections of pegylated interferon and ribavirin tablets, a regimen many patients found difficult to take.

But a better understanding of the lifecycle of the virus and important efforts in drug development have propelled significant developments in hepatitis C treatment. The new generation of treatments are known as direct acting antivirals (DAAs): ten different drugs, in four different drug classes are approved by regulators.31

Treatment with DAAs is a vast improvement on the older treatments. Treatment is taken for a shorter period of time, is easy-to-take with oral tablets only, has few side-effects, and results in a sustained virological response (when no hepatitis C virus is found in blood in the 24 weeks after completing treatment, indicating that the infection is cured) for more than 95% of people treated.32

Access to treatment is improving, driven by the effectiveness of DAA, although it remains limited. Between 2015 and 2016, the annual number of people starting treatment rose to from 1 million to 1.5 million. Egypt and Pakistan accounted for about half of all people who started DAA treatment in 2016. Australia, Brazil, China, France, Georgia, Mongolia, Morocco, Rwanda and Spain also expanded the number of people on DAA treatment.33

However, diagnosis rates are still too low. In 2016, only about one in five people living with hepatitis C across the world had been diagnosed. In low-income countries, less than 10% of people with hepatitis C had been diagnosed, compared with over 40% in high-income countries.34

The total, cumulative number of people ever given treatment for hepatitis C reached 5.4 million people in 2015. Most of the people treated before 2015 received older treatments. Of the people that completed treatment in 2015, 80% (843,000) achieved a sustained virological response.35

Hepatitis C treatment guidelines

Guidelines issued by WHO in April 2016 recommend four 'preferred regimens', each including the drug sofosbuvir, in order to simplify treatment decisions for hepatitis C.36 Depending on the regimen, treatment may last 12 or 24 weeks.

When these guidelines were issued, the choice of drug regimen was dependent on which of the six genotypes the patient had. Different genotypes, each with its own genetic composition of the virus, are more common in different parts of the world. Each patient therefore required genotype testing before treatment could be provided.

In July 2018, WHO updated these treatment guidelines to reflect certain key developments. It recommended that the use of DAA regimens for all people with chronic hepatitis C infection, rather than reserving DAA treatment for people with more advanced disease as had previously been done. In part, this is linked to the continued substantial reduction in the price of DAAs, which has enabled treatment to be rolled out rapidly in a number of low- and middle-income countries. In addition, as several new pangenotypic DAA medicines have now been approved, the need for genotyping to guide treatment decisions has been reduced.37

Treating hepatitis C in people with HIV co-infection

DAAs have good outcomes for people previously considered 'hard-to-treat'. This includes people with HIV co-infection. The outcomes of treatment in people with co-infection are comparable to those in people with hepatitis C alone - rates of sustained virological response are over 95%, even in individuals who have not responded to previous treatment and people with cirrhosis.38"There is no longer a need to consider HIV/HCV- co-infected patients as a special, difficult-to treat patient population," WHO states in its 2016 guidance.39

The key issue that remains, WHO emphasises, is the potential for drug-drug interactions between medications for HIV and hepatitis C. When these may occur, the regimens for either infection may need to be altered.40 However, modern HIV medications rarely have the harmful effects on the liver that characterised some older drugs. Hepatitis C treatment is generally provided to people who are already taking HIV treatment.41

A 2018 evidence review assessed data from seven studies of people with HIV and hepatitis C coinfection. Most of these were based in high-income countries. Four were focused on mainly gay and bisexual men, while three included a combination of people who inject drugs, gay and bisexual men and other people living with HIV. It found that, although the uptake of treatment for hepatitis C has increased since DAA treatment has become available, approximately half of those in need remain untreated. Among those people who have initiated treatment, completion and sustained virological response rates were promising.42

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Hepatitis C treatment programmes

An important first step to providing treatment for people with hepatitis C and HIV co-infection is to diagnose infections. HIV services should routinely screen all patients for hepatitis C.

However, guidelines recommending screening are often poorly implemented, especially in low and middle-income countries. Hepatitis C testing may not be systematically provided to groups which have elevated rates of hepatitis C, such as people who inject drugs, prisoners, sex workers, and men

who have sex with men.43

Improving access for key populations

For people from key populations, stigma and structural barriers continue to hinder access to diagnosis, treatment and care for hepatitis C.44 .

To ensure equitable access and engage key populations, clinical services for hepatitis C will need to better adapt their models of care. They may need to provide outreach services, be flexible around appointment requirements, train staff, and consult civil society- and community-led organisations (particularly organisations led by people who use drugs and men who have sex with men).45

Buyers' clubs

Buyers' clubs pool resources to buy DAA medicines via the internet. There are many buyers' clubs around the world enabling people to access treatment who would otherwise be unable to receive it. They exist as a stopgap response to the failure of public health systems to ensure equitable access to hepatitis C treatment.

However, there are concerns that compromise other important aspects of treatment, including treatment monitoring and management of co-infection.46

Data for planning

Epidemiological data are needed to plan hepatitis C treatment services. It is important to know the number of people with hepatitis C and with co-infection, the proportion diagnosed, the distribution of disease stages (patients with advanced disease will require more monitoring and will require treatment urgently) and the distribution of genotypes (influencing the drugs required).47

Despite this, there is a severe lack of data on hepatitis C. Information on access to hepatitis care disaggregated by population subgroups is limited and mostly only available from high-income countries.48

Co-ordinated care for people with hepatitis C and HIV co-infection

People with hepatitis C and HIV co-infection may have other health issues that require additional care. For example, opiate dependency is common in people who inject drugs. Integrating opioid substitution therapy and harm reduction services with provision of hepatitis C and HIV treatment can improve health outcomes.49 People may also have needs in relation to excessive alcohol use (which can accelerate hepatitis disease progression).

People needing hepatitis C treatment may have unmet needs in relation to depression or other mental health issues. Meeting these needs may enhance patients' adherence and engagement with care.

In the UK, an integrated hepatitis C and harm reduction programme, in which 69% of participants were drug users and 47% had mental illness, found 98% complied with treatment and 87% achieved a sustained virological response. Other studies suggest there are potential benefits in integrating

pharmacy-based opioid substitution therapy with hepatitis C care models, as this can increase hepatitis C screening, follow-up and treatment. compliance.50

Some populations at risk of hepatitis C are also at risk of tuberculosis (TB), especially people who inject drugs and prisoners.51 As well as TB screening, for programmes to be effective the side-effects and drug-drug interactions of HIV, TB and hepatitis therapies must be considered.

Drug prices

The excessively high price of DAAs has prompted debates about pricing, affordability and limited access. In high-income countries, the cost to treat a single patient can reach US\$83,000. As a result, health systems in even the richest countries have rationed or restricted the provision of hepatitis C treatment to the sickest patients.52

The price paid varies significantly between countries. When countries' wealth is taken into account, drug prices are considerably higher in middle-income countries, especially those in central and eastern Europe.53 Some countries have used legal tools such as compulsory licenses and patent oppositions in order to permit generic versions of the drugs. The low price of generics has enabled a handful of countries such as Egypt and India to scale up treatment of hepatitis C.]

For example, a generic DAA has been produced by Pharco Pharmaceuticals in Egypt and the not-forprofit Drugs for Neglected Diseases initiative (DNDi). Successful trials have been conducted in Malaysia, where treatment is expected to cost US\$300 for 12 weeks, or \$3.50 per day, and is likely to be available by 2020. DNDi has also signed deals in Latin America where initially a 12-week course will cost \$500, reducing to \$300 over time.54 This is a fraction of the cost of DDAs produced by major pharmaceuticals. For instance, although Gilead has lowered the price of its hepatitis C treatment (Harvoni), in 2018 it cost around US\$48,000 for a 12-week course in Malaysia.55

Despite these advances, legal manoeuvring by pharmaceutical companies and a lack of political will has meant that very few countries can access generic DAAs. However, a major step forward came in November 2018 when it was announced that the Medicines Patent Pool had signed a royalty-free licence agreement with pharmaceutical company AbbVie. The license will permit the development and sale of affordable generic DAAs in 99 low- and middle-income countries and territories.56

In addition, as currently practiced, the clinical management of hepatitis C requires sophisticated laboratory capacity to diagnose infection, identify the genotype, assess fibrosis and monitor response to treatment. However in many countries, the costs of these tests is prohibitive or there are few laboratories that can perform them.

Linkage to care in New York City

The Check Hep C programme, hosted by four community-based organisations in neighbourhoods of New York where hepatitis C infection is relatively common, gave a key role to 'patient navigators' – people who supported patients to seek antiviral therapy for hepatitis C, adhere to treatment and connect with subsidised healthcare and medications.

More than half of the participants who were eligible for care began treatment during the project, 91% of whom were successfully cleared of the virus. The results demonstrate the important part navigators can play in improving outcomes for people with hepatitis C infection.57

The outlook for hepatitis C and HIV coinfection

Hepatitis C treatment is currently provided in specialised centres by hepatologists. To expand access, treatment will need to be provided by non-specialists in primary-care clinics. Large numbers of healthcare workers will need training in the clinical management of hepatitis C.

Shifting to this public health approach is one of several ways in which simplified and standardised procedures could help bring hepatitis C treatment to scale – provided the costs of drugs and monitoring is reduced.

There remains a long way to go before the world will be on track to reach the WHO target of eliminating hepatitis C as a major public health threat by 2030. Reaching this goal means diagnosing 90% of people living with hepatitis C and putting 80% on treatment, while drastically reducing new hepatitis C infections.58 For this to happen, efforts in each of these areas will need to be greatly accelerated. But until political and financial support for integrated hepatitis C, harm reduction and HIV diagnosis, treatment and care becomes a global health priority these targets may remain unreachable.

The huge strides being made on the prices of DAAs suggests many more countries will soon be in a position to provide effective treatment. But, as with HIV treatment, reaching the people most affected by hepatitis C will remain challenging as long as these people are criminalised and stigmatised. Friendly, non-judgemental testing and treatment services, designed, led and implemented by people from the communities they are intended to serve, must be implemented if the millions of people living with hepatitis C are to get the treatment to which they are entitled.

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