ISSUE BRIEF

MÉDECINS SANS FRONTIÈRES ACCESS CAMPAIGN

HEPATITIS C: THE HIDDEN EPIDEMIC

The treatment of people infected with hepatitis C virus (HCV) in developing countries has long been neglected. Now, an abundance of new drugs in the pipeline is set to transform and simplify treatment of the disease with effective oral medicines. But potentially sky-high prices – together with a lack of political commitment to confront the real burden of the HCV pandemic and overcome access barriers – threaten to prevent these promising medicines from reaching people who need them in developing countries.

HEPATITIS C – A PUBLIC HEALTH PRIORITY IGNORED FOR TOO LONG

It is estimated that 180 million people[1] are chronically infected with HCV, with the disease killing an estimated 350,000 people each year[2]. The vast majority of these people live in developing countries where there is little or no provision to diagnose or treat the disease. Although treatable and curable, millions of people in developing countries do not even know they are infected with HCV because of severely limited screening. For this reason, it has not been possible to build up an accurate picture of the scale of the epidemic and the medical need. This in turn has sapped political incentive to prioritise access to treatment.

In addition, the lack of success with today's most widely used treatment has kept demand and use of this treatment low: the currently available medicines are not very effective, are administered through one injection per week plus daily pills – a burden to patients and caregivers alike – and cure people an average of just 50 percent of the time.[3, 4] They can also cause side effects such as flu-like symptoms, anaemia and depression. Finally, the treatment can last as long as 48 weeks (depending on the disease genotype) and is very expensive, with prices* ranging from US$10,000 to $20,000 per treatment course.[5] Even in wealthy countries, doctors and patients choose to forego treatment, or to wait for the release of promising treatment, which is currently still in the drug development pipeline.

> *"There's no national treatment programme in India, so patients who have a bit of money, who can sell property and gold, are able to somehow access treatment but those who do not are simply not treated."*
>
> **Leena Menghaney, Médecins Sans Frontières Access Campaign, India.**

NEW TOOLS PROMISE TO TRANSFORM TREATMENT

Hepatitis C treatment is on the verge of being critically transformed, with the development of new, more effective and better-tolerated all-oral regimens that will potentially treat all genotypes of the disease. At the same time, newer and increased simplification of laboratory technologies will allow the development of reliable and simple tests to diagnose and monitor HCV both through point-of-care devices and laboratory-based tests that will be suitable for district-level laboratories.

These advances offer the potential to move from complex treatment requiring specialised centres to simplified protocols that will allow treatment to be offered in ever more remote settings, opening the door for many more people to receive life-saving treatment. The challenge is to make sure both these transformative drugs and the improved diagnostic tests are made available and affordable for people living in developing countries.

* Treatment course consisting of pegylated interferon alpha and ribavirin.

ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

MSF Access Campaign
Médecins Sans Frontières, Rue de Lausanne 78, CP 116, CH-1211 Geneva 21, Switzerland
Tel: + 41 (0) 22 849 89 02 Fax: +41 (0) 22 849 8902 Email: access@msf.org

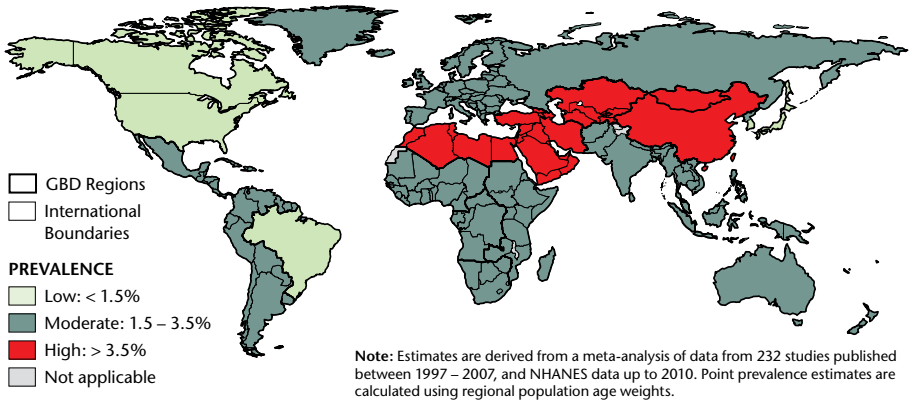
www.msfaccess.org facebook.com/MSFaccess twitter.com/MSF_access

WHAT IS HEPATITIS C AND WHO IS AFFECTED?

Hepatitis C is a virus that can cause liver disease and liver inflammation. People infected often do not show symptoms for many years. The disease is treatable with antiviral drugs, but if untreated, HCV can be fatal, with many people dying of liver cirrhosis and/or liver cancer.

HCV infection is found worldwide. There are a number of different ways in which the infection spreads; it may happen through blood transfusions from unscreened donors or injection with contaminated equipment, with injecting drug users who share injection equipment a particularly high-risk population. Transmission through contaminated healthcare equipment in hospitals and other health care facilities is also responsible for the high prevalence of HCV in some countries.

The global prevalence of HCV infection by region, 2005



Note: Estimates are derived from a meta-analysis of data from 232 studies published between 1997 – 2007, and NHANES data up to 2010. Point prevalence estimates are calculated using regional population age weights.

Countries with high rates of chronic infection are Egypt (22%), Pakistan (4.8%) and China (3.2%).[3] The main mode of transmission in these countries is likely to be unsafe injections using contaminated equipment. Reproduced from Mohd Hanafiah K, et al.[2]

HCV: A LEADING CO-INFECTION WITH HIV

HCV is a leading co-infection affecting people living with HIV/AIDS, who are more vulnerable because of their weaker immune systems and HIV and HCV often share a common mode of transmission. It's estimated that worldwide between four and five million people with HIV are also co-infected with HCV.[6] Morbidity and mortality is higher for patients co-infected with HIV and HCV, and the incidence of HCV is not affected by antiretroviral treatment (ART). In fact, where ART has decreased HIV mortality in high-coverage contexts, liver disease, often associated with HCV, is becoming the predominant cause of death for people living with HIV.[7, 8] It has been shown that chronic HCV infection is independently associated with a 50% increase in mortality among patients with a diagnosis of AIDS.[9]

HEPATITIS C in NUMBERS

- 180 million people worldwide are estimated to be living with HCV.[1]
- Over 350,000 people die each year from HCV.[2]
- Taken together, chronic viral hepatitis B and C are the main cause of hepatocellular cancer worldwide.[1]
- End-stage liver disease most commonly caused by viral hepatitis is also rising to the top of the non-AIDS causes of death in people living with HIV in countries where ART coverage is relatively high.[10]

MSF and Hepatitis C

Through its work, MSF has seen high rates of HCV seroprevalence among blood donors in Africa: 7.1% in the Central African Republic; 8% in the Democratic Republic of Congo; and 7.2% in Nigeria. MSF has also seen HCV prevalence in Pakistan's east Balochistan of 6.1%.

MSF in 2013 started providing HCV treatment to several patients in India, and is preparing to offer treatment to more individuals in the country. MSF is also considering starting treatment in several additional countries. For more detailed information about MSF Access Campaign activities on hepatitis C, please visit: www.msfaccess.org/content/diagnosis-and-treatment-hepatitis-c-technical-landscape.

REFERENCES

1. El-Serag H. Epidemiology of Viral Hepatitis and Hepatocellular Carcinoma. Gastroenterology. 2012; 142:1264–1273.
2. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to hepatitis C virus seroprevalence. Hepatology.2012 Nov 21.doi:10.1002/hep.26141.
3. Ford N, Kirby C, Singh K, Mills EJ, Cooke G, Kamarulzaman A, du Cros P. Chronic hepatitis C treatment outcomes in low and middle income countries: a systematic review and meta-analysis. Bull World Health Organ 2012;90:540-550.
4. Davies A. Singh KP, Shubber Z, du Cros P, Mills E, Cooke G, Ford N. Treatment outcomes of treatment–naïve hepatitis C patients co-infected with HIV: A systematic review and meta analysis of observational cohorts. PloS One 2013;8(2):e55373.
5. MSF HCV landscape analysis available at: http://www.msfaccess.org/content/diagnosis-and-treatment-hepatitis-c-technical-landscape
6. Easterbrook P, Sands A, Harmanci H. Challenges and priorities in the management of HIV/HBV and HIV/HCV coinfection in resource-limited settings. Sem Liver Dis 2012;32(2):147-157.
7. Lo Re V, Tate J, Kallan M, Lim J, Goetz M, Klein M, Rimland D, Rodriguez-Barradas M, Butt A, Gibert C, Brown S, Kostman J, Strom B, reddy R, Justice A, Localio R.Increased risk of hepatic decompensation and hepatocellular carcinoma in HIV/HCV-co-infected patients compared to HCV-mono-infected patients despite combination antiretroviral therapy [Oral Abstract number 17867]. 19th International AIDS Conference. Washington DC, USA: July 22-27, 2012.
8. Deng LP, Gui XE, Zhang YX, Gao SC, Yang RR. Impact of human immunodeficiency virus infection on the course of hepatitis C virus infection: A meta-analysis. World J Gastroenterol 2009;15(8):996-1003.
9. Branch AD, Van Natta ML, Vachin ML, Dieterich DT, Meinert CL, Jabs DA, Studies of the Ocular Comlications of AIDS research group. Mortality in HCV-infected patients with a diagnosis of AIDS in the era of combination anti-retroviral therapy. Clin Infect Dis 2012;55:137-144.
10. Lewden C, Salmon D, Morlat P, Bévilacqua S, Jougla E, Bonnet F, Héripret L, Costagliola D, May T, Chêne G, and the Mortality 2000 study group. Causes of death among human immunodeficiency virus (HIV)–infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS. Int J Epidemiol 2005; 34:121–30.
11. Shivkumar S, Peeling R, Jafari Y, Joseph L., &Pant Pai N. (2012). Accuracy of Rapid and Point-of-Care Screening Tests for Hepatitis C. Ann Intern Med, 157, 558–566.
12. Lawitz E, Mangia E, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. NEJM. April 23,2013. Available at: http://www.nejm.org/doi/full/10.1056/NEJMoa1214853?viewType=
13. Gilead press release. Data from phase 3 studies of Gilead's Sofosbuvir for hepatitis C presented at 48th annual EASL meeting: findings published in the New England Journal of Medicine. Available at: http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle&ID=1809511&highlight=
14. Gane E et al. Nucleotide Polymerase Inhibitor Sofosbuvir plus Ribavirin for Hepatitis C. NEJM. 2013; 368(1): 34-44.

DIAGNOSTIC ADVANCES CAN HELP REVEAL THE 'HIDDEN EPIDEMIC'

Until now, a lack of reliable epidemiological data has hidden the scale of the HCV epidemic, especially in sub-Saharan Africa, compounding its neglect even further. However, with more affordable diagnostic tools becoming available that are better adapted to performing epidemiologic surveillance and screening, the important knowledge gaps can begin to be filled and more people can be diagnosed.

In addition to antibody tests used to screen for HCV, confirming the presence of the virus with an HCV viral load test is required, because approximately 20-30% of patients with HCV antibodies have actually cleared the virus and do not have active chronic infection. Fortunately, a number of point-of-care options for HCV viral load monitoring are in the pipeline. 'Piggy backing' on the implementation of HIV molecular testing in resource-limited settings, it is now possible to use many of the same instruments used in HIV for measuring HCV viral load for both diagnosis and treatment monitoring in the most remote health care settings.

In addition, there are many rapid and point-of-care serological antibody tests now available for HCV screening. As they are quick and can be performed on finger-prick capillary blood (or sometimes oral fluid), these tests can streamline clinical decision making. They also mostly tolerate heat up to 30°C, which simplifies transportation and storage.

The price of both the rapid serological tests and viral load tests remains a concern, however, with prices of up to $18 for serological tests and up to $50 for viral load tests.

IMPROVING ACCESS TO TODAY'S NON-OPTIMAL TREATMENT IS STILL CRITICAL

While not optimal, current treatment can still cure more than half of patients, and for some genotypes cure rates are even higher. HCV therapy is about to experience a critical transformation, the medicines in the pipeline are still likely to be at least several years away for people living in lower- and middle-income countries. For people in need of treatment now, improved access to the effective, although not optimal, current standard treatment – pegylated interferon alfa (PEG IFN α) and ribavirin – remains critical.

The cost of the originator versions of PEG IFN α in many lower- and middle-income countries is however extremely high, ranging from $10,000 to $20,000 for a 48-week treatment course (based on $200–400 for one vial that is needed each week, in combination with daily oral ribavirin).

Unfortunately, the WHO pathway for assessing the quality of more affordable 'biosimilar' versions of biologic lmedicines does not support access to quality PEG IFN α. WHO should consider establishing a prequalification scheme in order to enable countries and organisations to procure quality biosimilar versions of PEG INF α.

In Egypt, competition from local manufacturers producing an alternative PEG IFN α product has led to a substantial price reduction for both originator products, with the price of a 48-week treatment course of PEG IFN α and ribavirin falling to less than $2,000.

> *"The problem we know from HIV, is that just because drugs are in the pipeline doesn't mean that they get to where they're needed. We still see examples where good HIV drugs are not available in our settings and patients suffer, and we know that that could be the potential for hepatitis C."*
>
> **Dr. Philipp Du Cros,**
> **Head of Manson Unit,**
> **Médecins Sans Frontièrs**

TRANSFORMATIVE DRUGS IN THE PIPELINE ARE LIKELY TO BE PRICED OUT OF REACH

Oral drugs in the pipeline, some of which can be taken once daily, will dramatically improve treatment of HCV: treatment will be more effective. Various short-course (12–16 weeks) combinations of *directly acting antivirals* (DAAs) have been shown to be at least as effective, and in many cases lead to much higher levels of cure, as compared with standard care with PEG-IFN and ribavirin.[12, 13, 14] It will be more convenient for patients and caregivers alike because it will no longer require injections; and it will be much shorter – down to 12 weeks compared to 24–48 weeks on the current treatment with pegylated interferon and ribavirin.

In addition, some of these new oral DAAs are effective against all genotypes of the virus, and several pharmaceutical companies are developing all-oral fixed-dose combination treatments for HCV.[5] These advances will make it simpler both to diagnose the disease and to streamline treatment, which will help pave the way for scale up and decentralisation of care.

But the price of DAAs remains a major concern – it's thought that the price will be comparable to the prices charged for first generation oral HCV protease inhibitors in developed countries, at around $80,000 per treatment course, with no indication yet of what prices will be in developing countries or where these drugs will be registered. As they are new, the drugs are also likely to be patented in many countries – including India, a country with critically-important generic manufacturing capacity. Early intervention on the part of civil society and governments will be essential to overcoming patent barriers and avoiding treatment being priced out of reach for most people in developing countries who need them.

(c) Rico Gustav

PATENT BARRIERS COULD BLOCK ACCESS TO NEW DRUGS

Patents already granted – or pending – on HCV drugs are posed to hinder the production of more affordable generic versions. Removing patent barriers will therefore be an important strategy to ensure more affordable versions can be produced. Various steps need to be taken in this regard by making use of all public health flexibilities in international trade rules, enshrined in the World Trade Organization's TRIPS Agreement. Opposing patents before or after they are granted could be a viable option in some countries where patent laws enable this.

In other countries where patents are granted, another option to increase access could be issuing compulsory licences to allow manufacturers other than the patent holders to produce more affordable versions. Even as governments prioritise the robust use of TRIPS safeguards to improve access, originator and generic companies can also sign transparent voluntary licence agreements that include favourable terms and conditions to incentivise generic competition where patent barriers exist.

"We need to see, talk and hear more about hepatitis C in the community. It's simple, just the way we did in HIV in the early days. That's how to get things moving."

Loon Gangte, Delhi Network of Positive People, India

CONCLUSION: THE TIME TO ACT IS NOW

The legacy of neglect of hepatitis C must come to an end. With unprecedented opportunities to fundamentally change diagnosis, treatment and care for HCV, now is the time to move and rapidly address this hidden and ignored epidemic. The benefits of new tools and data will not be realised without key market interventions as well as prioritisation of this disease at the WHO and country level. If the choice is made to invest now in the tools needed to fight HCV in low- and middle-income countries, the potential benefits are vast.

HCV is a public health priority, and donors, public health institutions and treatment providers need to ramp up its detection and treatment. Critically, the entry of promising new tools should be urgently prioritised as this will significantly impact scale up. It is therefore urgent that the price of diagnostics and therapies be affordable to all.

For PEG-IFN and ribavirin, the price should be no higher than that negotiated by Egypt of $40 per vial ($2,000 for 48-week treatment course). Efforts to scale up access to HIV treatment over the past decade suggest that for access to an all-oral treatment course to be widely secured, it should cost no more than $500. Ultimately though, affordability of oral HCV treatments will be dependent on entry of generic competition, which will need to be facilitated by existing TRIPS flexibilities.

Support to enable treatment in resource-limited settings could easily be stimulated through traditional funding mechanisms, with support from innovative financing (including from UNITAID, the Global Fund, the US government's PEPFAR programme, and the European Union). However, critical to this will be the need for strong HCV guidelines; here WHO should show leadership in order to set the stage to rapidly implement new oral DAA-based therapy. Civil society, patient and vulnerable groups will need to play a critical role in mobilising and demanding access to testing and treatment as well policies to scale-up optimal treatment.

ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

MSF Access Campaign
Médecins Sans Frontières, Rue de Lausanne 78, CP 116, CH-1211 Geneva 21, Switzerland
Tel: + 41 (0) 22 849 89 02 Fax: +41 (0) 22 849 8902 Email: access@msf.org
www.msfaccess.org facebook.com/MSFaccess twitter.com/MSF_access