

Ending an Epidemic

OVERCOMING THE BARRIERS TO AN HCV-FREE FUTURE



Yale Global Health Justice
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Yale Global Health Justice Partnership

The Yale Global Health Justice Partnership (GHJP) is a joint initiative between Yale Law School (YLS) and Yale School of Public Health (YSPH) that trains the next generation of scholars and practitioners to tackle the complex interdisciplinary challenges of global health. The GHJP works with international partners at the interface of law and governance, public health, and medicine to theorize, build analytical frameworks, create knowledge, and mobilize research to help drive the social change necessary for improving the health and wellness of people around the world.

The GHJP offers a practicum course each year that engages students in real-world projects with scholars, activists, lawyers, and other practitioners on issues of health justice. Working papers are produced as a part of these projects, with students as lead authors. Final papers reflect input and revisions by GHJP faculty, partners, staff, and other readers.

Executive Summary

Hepatitis C (HCV) afflicts more than five times as many people as HIV—approximately 185 million people worldwide.¹ The epidemic extends to both rich and poor countries, but the burden is greatest in middle-income countries (MICs).² Nearly a half a million people die every year from HCV-related causes, including cirrhosis and liver cancer.³

Despite the size of the epidemic, HCV has received comparatively little attention in the global health community until recently. Diagnosis and staging for treatment is costly and complicated, and pegylated-interferon- α (peg-IFN) based treatment regimens—until recently, the standard of care—involved a host of potentially dangerous and intolerable side effects, and were often associated with a high risk of treatment discontinuation or treatment failure. However, new oral drugs called direct acting antivirals (DAAs) are now coming to market, offering an unprecedented opportunity to eradicate HCV. These drugs feature high cure rates, short treatment duration, ease of administration, minimal side effects, and excellent safety profiles.

As curing HCV becomes increasingly feasible, it is time for the global health community to take action to ensure that HCV treatment is affordable and accessible to all individuals infected with HCV, particularly disproportionately affected populations such as people who inject drugs (PWID). Towards this end, this paper identifies the following key steps that national and international actors must take in order for DAAs to deliver on their promise:

- National governments, major donors, and HCV activists must come together as they have done for human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), tuberculosis, and malaria, and create dedicated funding streams to combat HCV. Without a sustained international commitment to pay for treatments, diagnostics, and monitoring, it is unlikely that people in low- and middle-income countries (LMICs) will be able to afford the new drugs coming on the market, even at lower prices.
- Drug manufacturers must lower DAA prices to more closely reflect production costs. In addition, to promote access to generic versions and foster price competition, governments should deny patent applications that do not meet a country's novelty, obviousness and efficacy criteria. Should patents be granted, governments should override barriers posed by patents by issuing compulsory licenses to allow for generic production of these essential medications when necessary, particularly when there is an emergency.
- With support from the World Health Organization (WHO), non-governmental organizations, and other donors, LMICs should promote new public health-based treatment paradigms for HCV that bypass the historical requirement that physician-specialists be involved in every step of the HCV diagnosis and treatment process. In addition, efforts should be made to integrate HCV treatment into substance abuse treatment and rehabilitation programs to reach the most difficult-to-treat populations.

HCV treatment activists are playing a critical role in building the political will of governments to prioritize HCV, including treatment. For the first time drugs that could make a real impact on the global pandemic are available, but HCV advocates—including people living with HCV, clinicians, and activists working on other health and human rights issues—must break down entrenched apathy among policymakers. With a path ahead for HCV treatment access that is fraught with obstacles, dedicated activists must continue to play a leading role in moving forward the global HCV agenda. It is vital that governments and the international community marshal an equivalent level of resources and enthusiasm as they did in order to fight HIV.

Eradication of HCV is no longer a dream. With recent therapeutic advances, it is achievable. Determined action to overcome the barriers to treatment and prevention can make global eradication a reality.

Acronyms

ARV	Antiretroviral therapy
CHAI	Clinton Health Access Initiative
DAA	Direct acting antiviral
GFATM	Global Fund to Fight AIDS, Tuberculosis, and Malaria
HBV	Hepatitis B
HCV	Hepatitis C
HIV/AIDS	Human immunodeficiency virus infection / acquired immunodeficiency syndrome
I - MAK	Initiative for Medicines, Access & Knowledge
ICESCR	International Covenant on Economic, Social, and Cultural Rights
LIC	Low-income country
LMIC	Low- and middle-income country
MdM	Médecins du Monde
MIC	Middle-income country
MSF	Médecins Sans Frontières
PCR	Polymerase chain reaction
peg-IFN	Pegylated-interferon- α
PEPFAR	United States President's Emergency Plan for AIDS Relief
PWID	People who inject drugs
RBV	Ribavirin
RNA	Ribonucleic acid
SOF	Sofosbuvir
SMV	Simeprevir
SVR	Sustained viral response
TRIPS	Agreement on Trade Related Aspects of Intellectual Property Rights
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCESCR	United Nations Committee on Economic, Social, and Cultural Rights
UNICEF	United Nations Children's Fund
USD	United States Dollar
WHA	World Health Assembly
WHO	World Health Organization
WHO - PQP	WHO Prequalification Programme
WTO	World Trade Organization

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I. Introduction

Approximately 185 million people worldwide are infected with Hepatitis C (HCV)—more than five times as many people as are infected with HIV.⁴ About 500,000 people die from HCV-related causes, including cirrhosis and liver cancer, every year.⁵ Few people with HCV receive treatment;⁶ in fact, many of those living with HCV do not even know that they are infected.⁷ While HCV has been called a “silent epidemic” because it can show no symptoms for years or decades,⁸ the lack of attention HCV has received from the global health community makes the term equally appropriate.⁹

As new drugs called direct acting antivirals (DAAs) are coming to market, offering an unprecedented opportunity to combat HCV, the silence around the HCV epidemic is finally lifting. With new hope on the horizon and growing recognition of the scope of the problem, civil society groups and people living with HCV in countries like Georgia, Thailand, and Ukraine are successfully pushing their national governments to take action.¹⁰ The World Health Organization (WHO) has taken notice as well. In 2010, the World Health Assembly (WHA), the WHO’s decision-making body, adopted a resolution to recognize the importance of addressing viral hepatitis, with a special focus on hepatitis B (HBV) and HCV, designating July 28th as World Hepatitis Day.¹¹ Recognizing that this was not enough, in June 2014, the WHA approved a second resolution on viral hepatitis that made more targeted recommendations to national governments—as well as the United Nations (UN), the WHO Director General, and others—regarding prevention, diagnosis, and treatment of viral hepatitis.¹² It also issued long-awaited HCV treatment guidelines that incorporated the new DAA treatment regimens in April 2014.¹³

Despite these positive developments, much remains to be done to follow through on the WHO’s recommendations and to ensure more broadly that the new drugs are affordable and accessible to all people with HCV, particularly the most marginalized, such as people in prison, people who inject drugs (PWID), and

people living with HIV/AIDS. Of particular concern are continued inaction by many national and international actors, the high prices of the new drugs and inadequate health care delivery and prevention systems. This paper provides an overview of the current landscape and the potential for new drugs to revolutionize treatment and care. It then discusses the steps stakeholders in the global health community must take to ensure that treatment reaches the patients who need it: increasing global financial and political commitments to combatting HCV; lowering drug prices through various legal options including adoption of more stringent patent standards, patent challenges, and compulsory licensing; and promoting the adoption of new public health-based treatment paradigms.

Throughout, this paper also offers personal stories from people who have lived with HCV infection. Too often, a statistic like “185 million people infected” can be glossed over. Each one of those lives faces their own individual struggle and it is our hope that these stories can bring to life the human dimension of the struggle against HCV and end the silence. It is time for the global community to listen to the voices of those with HCV and respond to their needs.

II. Setting the Stage for Action

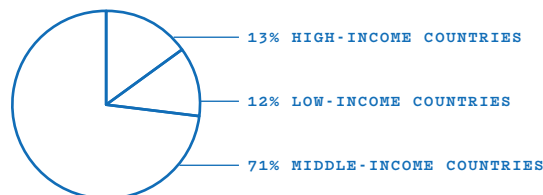
To adequately address HCV worldwide, it is important to understand the extent of the burden and the available tools to combat HCV. This section describes the extent of the HCV epidemic, the lack of adequate and reliable surveillance, and the potential and limits of both old and new medications.

HEPATITIS C'S GLOBAL FOOTPRINT

HCV is a worldwide epidemic. While data are limited, researchers estimate that approximately 185 million people are infected with HCV worldwide,¹⁴ and that an additional 3 to 4 million people acquire HCV each year.¹⁵ The HCV epidemic extends to both rich and poor countries. All regions of the world have a prevalence of HCV over 1%, and over 2% of people are infected in all regions except the Americas and Australia and Oceania.¹⁶

The burden of HCV is greatest in middle income countries (MICs).¹⁷ Four out of the five countries with the greatest prevalence of HCV—Egypt (14%), Cameroon (13.8%), Mongolia (10.7%), and São Tomé and Príncipe (10%)—are classified as lower-middle-income countries (LMICs) by the World Bank.¹⁸ In terms of sheer volume, fifteen of the twenty countries with the greatest number of people living with HCV are MICs, led by China (29.79 million), India (18.22 million), Egypt (11.83 million), Indonesia (9.44 million), and Pakistan (9.42 million).¹⁹

Figure 1. Distribution of people living with HCV in low-income countries, middle-income countries and high income countries



SOURCE: PAULINE LONDEIX, "NEW TREATMENTS FOR HEPATITIS C VIRUS: STRATEGIES FOR ACHIEVING UNIVERSAL ACCESS," *MEDECINS DU MONDE* (2014): 8, AVAILABLE AT [HTTP://HEPCOALITION.ORG/IMG/PDF/DAAS_STRATEGIES_FOR_ACHIEVING_UNIVERSAL_ACCESS_EN.PDF](http://hepcoalition.org/img/pdf/daas_strategies_for_achieving_universal_access_en.pdf) (ACCESSED APRIL 21, 2014).

HCV is a blood-borne pathogen that is transmitted through contact with HCV infected blood. The most common routes of transmission are through sharing of contaminated equipment, and from transfusion of unscreened, contaminated blood. Additionally, contaminated medical and dental equipment and other unsafe injection practices account for many HCV infections in LMICs. Less frequent routes of transmission include occupational exposure among healthcare workers (e.g., HCV contaminated needle-sticks), engagement in high-risk sexual behavior (e.g., unprotected sex with HIV+ partners, particularly among men who have sex with men), and vertical transmission from women who pass HCV to their children.²⁰

Within a given country, prevalence can vary widely.²¹ For example, research in China and India has found infection rates to vary across different areas of each country and among different population groups.²² Yet, certain vulnerable populations are consistently found to have high rates of infection. In particular, PWID are disproportionately affected by HCV infection, with nearly two-thirds of PWID worldwide—10 million individuals—estimated to be infected with HCV.²³ While PWID account for only 5-6% of infections, they disproportionately influence disease incidence, accounting for most new infections globally. High infection rates among PWID are seen in upper- and middle- income countries alike: India, Russia, and Thailand are estimated to have 90% or higher rates of HCV infection, while Germany and the United States have rates of 85% and 80% respectively.²⁴ The total numbers of PWID who are infected with HCV are particularly high in East and Southeast Asia, Eastern Europe, and the United States.²⁵

Other populations at increased risk of contracting HCV include hemodialysis or blood transfusion patients in countries lacking adequate screening procedures (which was common until the 1980s); prisoners; transgender people; and, historically, health care professionals and hemophiliacs.²⁶ People living with

HIV also have markedly higher rates of HCV than the general population. UNAIDS recently reported that prevalence among the 34 million people infected with HIV globally could be as high as 16%, totaling 5.5 million people co-infected with HIV and HCV.²⁷

CAVEAT ON SURVEILLANCE DATA

There is a lack of reliable population-based HCV surveillance data in most LMICs. Obtaining reliable surveillance data is crucial to facilitating evidence-based policy decision-making and effective resource allocation. Additionally, improved epidemiological data will help increase the number of people who are diagnosed with HCV and increase awareness of the epidemic in different settings. According to a 2013 WHO-sponsored report on prevention and control of viral hepatitis, among 139 LMICs only 19% of member states reported having a national surveillance program in place for monitoring acute and chronic HCV infections.

The current lack of reliable surveillance data can be attributed to the limited public health resources that are available for HCV surveillance, the asymptomatic nature of HCV chronic infection in more than 80% of those affected, the sheer number of cases, and the lack of political will to address HCV. The implementation of population-based national HCV surveillance programs, with guidance and technical assistance from WHO, will allow for more accurate estimates of the true burden of HCV infection among the general population and high risk groups. It will also help with providing testing, treatment, and care to people who are in need of services.

Recommendation:

WHO should provide technical assistance for the development and implementation of effective national population-based surveillance programs.

SOURCES: HEISEY-GROVE, D. M., D. R. CHURCH, G. A. HANEY, AND A. DEMARIA. "ENHANCING SURVEILLANCE FOR HEPATITIS C THROUGH PUBLIC HEALTH INFORMATICS." *PUBLIC HEALTH REPORTS* 126, NO. 1 (JAN-FEB 2011): 13-18; LAZARUS, JEFF. "GLOBAL POLICY REPORT ON THE PREVENTION OF HEPATITIS C IN WHO MEMBER STATES." WORLD HEALTH ORGANIZATION, 2014.

EXISTING MEDICAL BARRIERS TO EFFECTIVELY TREATING HCV

HCV has traditionally been both expensive and complex to diagnose and treat, and these characteristics of clinical management are even more problematic in resource-limited settings. As we discuss in this section, the current diagnostic and peg-IFN-based treatment-monitoring cascade is costly and requires multiple interactions with health care specialists and well-equipped laboratory settings. While this section explains the difficulties associated with the current diagnosis and treatment paradigm in LMICs, the introduction of DAAs and new diagnostic testing could change this in the near future. *Section V. Improving HCV Treatment Delivery and Prevention* of this report explains the changes that will be coming to this process in the near future.

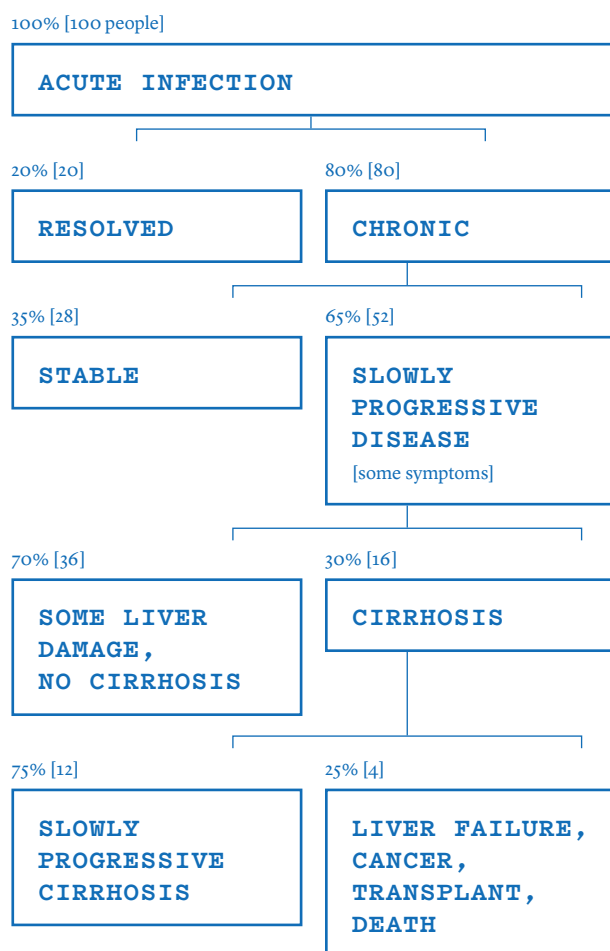
A. DIAGNOSTIC AND MONITORING PROCEDURE AND THEIR BARRIERS

The complex nature of HCV diagnosis and treatment is one of the many barriers to receiving optimal HCV treatment and care. The current screening process to confirm an HCV infection and the complex peg-IFN-based treatment-monitoring paradigm is costly, relying on highly specialized equipment and healthcare specialists. In addition to the resources that are required to conduct these tests, the physical separation between the patient, clinic, and laboratory, and the time required to obtain diagnostic results are additional barriers to treatment in resource-limited settings.²⁸ The lengthy and costly diagnostic paradigm has proven to be especially difficult to manage in LMICs.

HCV is diagnosed by the detection of anti-HCV antibodies in the patient's serum using immunoassay-screening tests and the detection of HCV Ribonucleic acid (RNA), using a nucleic acid test, confirms an HCV infection.^{29,30} HCV infections are often asymptomatic in the initial acute phase—only 20-30% of patients will present clinical symptoms—meaning the majority of acute HCV infections go undetected.³¹ An estimated 80% of patients with acute HCV infections will progress to chronic infection, while the rest will spontaneously clear the virus (Figure 1). Chronic HCV infection is marked by the continued presence of HCV RNA in the patient's blood six months or more after the onset of acute infection.³²

Once HCV infection has been confirmed, a measurement of the patient's viral load and a genotype

Figure 2. HCV disease progression over 10-15 years (mono-infection)



REPRODUCED FROM: NSF ACCESS CAMPAIGN. "DIAGNOSIS AND TREATMENT OF HEPATITIS C: A TECHNICAL LANDSCAPE." GENEVA: MÉDECINS SANS FRONTIÈRES, 2014.

assay are required prior to the initiation of HCV treatment.³³ The genotype assay determines the strain or strains of HCV the patient is infected with and informs the treatment type, duration, and likelihood of success.³⁴ Assuming treatment is initiated promptly following the genotype assay, a baseline measurement of the patient's viral load is needed for monitoring the patient's treatment progress. The quantitative measurement of HCV RNA is also done using nucleic acid testing.³⁵

In addition to the aforementioned tests, because of the serious side effects associated with the peg-IFN-based treatment regimen, a liver biopsy or a non-invasive procedure is often performed on patients who are chronically infected with HCV to help determine

the extent of liver damage. The current available non-invasive methods that are appropriate in LMICs include ultrasound and measurement of serum biomarkers of liver fibrosis.³⁶ Information on the extent of liver damage is especially important for patients who are infected with HCV genotypes 1 and 4 due to their suboptimal response to peg-IFN-based treatment regimens. Additionally, use of peg-IFN treatment is contraindicated in patients with highly advanced liver damage.³⁷

After the initiation of peg-IFN-based treatment, up to four viral load tests are required for monitoring treatment progress. The viral loads are collected during the course of treatment at weeks 12, 24, and 48, and post treatment. For genotypes 2 and 3, viral loads are collected on weeks 12 and 24, and after the completion of treatment. The post treatment viral load test is generally done three or six months after the completion of treatment to confirm viral clearance. Total clearance of the virus at three months post-treatment is referred to as sustained viral response (SVR) and can be considered equivalent to a designation as cured.³⁸

The high cost of the current tests and procedures makes the process discussed above challenging to implement in LMICs. The estimated cost for the diagnostic and pre-treatment assessment tests—HCV antibody test, confirmatory polymerase chain reaction (PCR), genotyping, six viral load tests, and liver function test—even in the absence of a liver biopsy, ranges from 300-1,380 USD (700-2,680 USD including liver biopsy).³⁹ However, with the recent development of DAAs, there is hope that invasive liver staging tests and genotyping may be eliminated, and less monitoring during and after treatment will be needed. Based on the cost of HIV point-of-care tests, the future cost of HCV diagnosis is expected to range from 30-120 USD.⁴⁰

In addition to the cost concerns associated with the initiation of HCV treatment, the time required for obtaining diagnostic results, and the need for well-equipped infrastructure are additional barriers to HCV treatment and care in LMICs. In settings where the clinic and laboratory are located in the same space, patients are still required to visit the clinic at least twice in order to be screened and to receive their results. This is especially problematic in settings where patients are required to travel long distances to reach a health care facility that provides appropriate testing. In addition,

TABLE 1 Current Cost of HCV Diagnostic Tests

Stage of diagnosis	Type of diagnostic	Number required	Price per test (USD)	Total price (USD)
Confirmation of HCV	Immunoassay	1	~20-50	~20-50
	Qualitative assay	1	~40-50	~40-50
Treatment duration decision	Genotype test	1	~20-500	~20-500
Baseline (1), monitoring (3-4) and post-treatment (1)	Qualitative assay (viral load)	5-6	~20-80	~100-480
Treatment decision	Liver function test	1	~100-300 (Biopsy: 500-1600)	~100-300 (Biopsy: ~500-1600)
			Total price	~300-1,380 ~700-2,680 (with biopsy)

TABLE 2 Potential Cost of Future HCV Diagnostic Tests

Stage of diagnosis	Type of diagnostic	Number required	Price (USD)
Confirmation of HCV	POC qualitative RNA assay	1	~10-40
Treatment monitoring	POC qualitative RNA assay	1	~10-40
Post treatment	POC qualitative RNA assay	1	~10-40
		Total price	~30-120

REPRODUCED FROM: UNITAID. "HEPATITIS C MEDICINES AND DIAGNOSTICS IN THE CONTEXT OF HIV/HCV CO-INFECTION: A SCOPING REPORT." 56. GENEVA: WORLD HEALTH ORGANIZATION, 2013.

the HCV RNA tests used to diagnose HCV and monitor HCV treatment outcome require well-equipped laboratories with expensive equipment, chemical supplies and specialists that can perform the necessary tests. With per capita government health expenditures in LMICs frequently falling below 500 USD (often far below), few countries may be willing or able to provide comprehensive diagnostic services without outside financial assistance.⁴¹

B. PROBLEMS WITH PEG-IFN-BASED REGIMENS

Before the introduction of HCV DAAs, the standard of care for HCV consisted of 24 to 48 weekly injections of peg-IFN combined with twice-daily oral ribavirin (RBV) tablets or capsules.⁴² Peg-IFN-based treatment regimens activate the host immune response and inhibit viral replication.⁴³ The treatment duration and efficacy varies depending on the genotype of HCV infection and other host and viral factors. Generally, HCV genotypes 2 and 3 require 24 weeks of treatment and have the highest treatment efficacy rate, with close to 80% of genotype 2 and 65% of genotype 3 achieving

SVR with peg-IFN-based treatment.⁴⁴ Those infected with genotype 1, 4, 5, or 6 require a longer treatment period of up to 48 weeks with treatment efficacy varying significantly by genotype.⁴⁵ The following table provides an overview of peg-IFN and RBV treatment regimen outcomes based on the duration of treatment and genotype of HCV infection.

TABLE 3
Probability of sustained virologic response of peg-IFN and RBV treatment regimen

Genotype	Selectivity	Duration (Weeks)	SVR%
Genotype 1		48 weeks	~44%
Genotype 2		24 weeks	80%
Genotype 3		24 weeks	65%
Genotype 4		48 weeks	40–70%
Genotype 5		48 weeks	49–60%
Genotype 6		48 weeks	60–90%

In addition to their limited efficacy and long duration, a substantial number of patients cannot tolerate peg-IFN-based regimens due to severe side effects. The most common side effects caused by this treatment regimen are fatigue, flu-like symptoms, anxiety, insomnia, irritability, skin rash, itching, depression, and gastrointestinal symptoms.⁴⁶ In addition, more severe side effects, including drops in blood cell counts, sometimes require reducing the dosage of peg-IFN, RBV or both.⁴⁷ Suicidal ideation and suicide, although rare, have also been reported. A reported 10–14% of patients participating in peg-IFN-based treatment trials have had to prematurely withdraw from treatment due to side effects and general intolerance to peg-IFN.⁴⁸ Thus, monitoring and management of side effects caused by the peg-IFN-based treatment regimen are essential to the completion of therapy. Weekly clinic visits are required for safety monitoring and management of side effects.⁴²

The active management required by medical specialists (i.e., need for frequent medical visits, management of side effects, etc.) can be difficult in

resource-limited settings. As with multi-visit diagnosis procedures, this can be especially challenging—and ultimately result in depressed treatment completion and compliance rates—in settings where patients are required to travel long distances to reach a clinic for their weekly injections.⁴⁹ However, many LMICs have effectively overcome the challenges of active treatment management associated with lifelong antiretroviral (ARV) therapy for HIV and therefore can adopt similar strategies for effectively managing peg-IFN-based treatment regimens in LMICs. All of the aforementioned diagnostic and treatment barriers demonstrate the need for a simpler diagnostic and treatment paradigm more suitable and feasible for resource-limited settings.

DMYTRO, 38-YEAR-OLD ENTREPRENEUR, KIEV, UKRAINE

When Dmytro first got a positive test result for HCV in 2008, he thought there had to be a mistake. He was a successful doctor who had left practice to begin a career as an entrepreneur selling medical supplies. He didn’t have any risk factors he could identify. In disbelief, he immediately went to a different lab to be retested. When the second test came back positive, Dmytro was devastated. As a doctor, he knew the implications of his diagnosis.

Dmytro racked his brain, trying to figure out how he might have been infected. All he could come up with was a time in 2001, when he had a needle stick while working as a doctor. The virus must have been silently living inside him, damaging his liver for years before it was finally detected.

Dmytro learned about peg-IFN treatment through internet research. Despite being a doctor with resources, and living in a country with one of the highest HCV prevalences in the world, Dmytro was unable to find a specialist to help him pursue treatment. Dmytro explains, “While today there are 70–80 specialists familiar with HCV treatment in Ukraine, at the time there were probably no more than a half dozen in Kiev, and I had no way of finding out about them.”

Dmytro contacted the Ukrainian distributor of peg-IFN himself to order his supply. He tried to negotiate free treatment, given his status as a doctor, but was unsuccessful. He found himself paying more than 20,000 USD out of pocket to get the treatment and start it on his own.

After three months of treatment, Dmytro was experiencing terrible side effects. He had drops in his white and red blood cell counts, he felt weak, he was losing weight, and he had pain throughout his body to the point he needed a cane to walk. Dmytro was finally connected with the top infectious disease doctor in the Ukraine, who he went to see about his treatment regimen. The top specialist confirmed that the regimen Dmytro chose for himself was correct and that he should continue. Dmytro jokes about the incident now, explaining, “That’s how I became a hepatologist!”

A study was published around that time, showing that 72 weeks of peg-IFN treatment would reduce the risk of the virus returning after treatment for his genotype, but after 60 weeks of treatment, Dmytro could take no more. He had lost 28 kg (61 lbs) and his body was devastated. He lost the medical supply company he had worked hard to build, as he was too weak to work to keep it alive. He had to stop treatment.



Luckily for Dmytro, as of 2014, the virus has not returned and he considers himself cured. His experience struggling to diagnose and treat his own HCV, even as a doctor, inspired Dmytro. He worked to start an organization called Stop Hepatitis, dedicated to getting HCV treatment access to the people of Ukraine.

Working with a growing community of passionate activists in Ukraine, Dmytro and his group successfully

lobbied the Ukrainian government to create a national treatment program in 2011. This burgeoning coalition of Ukrainian activists pushed to get people the testing necessary to show they were eligible for treatment under the national treatment protocol, having successfully identifying 66,000 Ukrainians ready for treatment as of 2014. Today, 2,300 are being treated, but there is still a long way to go. It is estimated that Ukraine may have as many as 4 million people living with HCV.

While at one point, in the midst of his peg-IFN treatment, it seemed Dmytro had lost everything to HCV, today, he is on the front lines making sure others get access to the same life saving treatment he received. He works full time as an HCV activist, fighting to get his people access not just to peg-IFN treatment, but hopefully one day DAA treatment as well.

THE POTENTIAL OF THE NEW DRUGS

The introduction of DAAs provides hope for overcoming many of the existing testing and treatment barriers. As clinical practice moves away from peg-IFN-based regimens to pan-genotypic DAA treatments, fewer tests and less time will be required to treat HCV. Fewer tests that require well-resourced laboratories and specialized procedures performed by trained professionals will hopefully allow for treatment scale up in LMICs. And, most importantly, the safety, tolerability, and efficacy of the new regimens are far better than peg-IFN-based treatment.

The first generation DAAs, HCV protease inhibitors—telaprevir and boceprevir—revolutionized HCV treatment by drastically improving the SVR rates of patients infected with HCV genotype 1 when added to peg-IFN and RBV. However, this initial set of drugs made management far more complex for the patients and their providers. Triple therapy (boceprevir or telaprevir in combination with peg-IFN and RBV) cured 65-80% of treatment-naïve patients, but caused their own side effects—some potentially life-threatening—and exacerbated those associated with peg-IFN and RBV alone.⁵⁰ In addition, 50-60% of those who had previously not responded to peg-IFN/RBV also did not respond to the triple therapy regimen.⁵¹ Therefore, despite the improved SVR rates in HCV genotype 1 patients achieved by HCV protease inhibitors, the additional challenges in managing and monitoring has

TABLE 4 Probability of sustained virologic response of approved DAA regimens

Drug regimen	Genotype selectivity	Duration, weeks	SVR, %
Telaprevir or boceprevir with peg-IFN-alpha and ribavirin	1	24–48 weeks	65–80%
Sofosbuvir with peg-IFN and ribavirin	1, 4, 5, and 6	12 weeks	Genotype 1 89% Genotype 4 96% Genotype 5 100% Genotype 6 100%
Sofosbuvir with ribavirin	1, 3, 4	24 weeks	Genotype 1 78% Genotype 3 87–94% Genotype 4 100%
Sofosbuvir with ribavirin	2, 4	12 weeks	Genotype 2 86–97% Genotype 4 79%
Sofosbuvir and simeprevir	1	12 weeks	~95%

made the use of these first-generation protease inhibitor DAAs difficult for LMICs.

Both patients and clinicians have looked forward to the approval of HCV treatments based on oral, peg-IFN-free, DAA regimens. These new DAAs are more effective, easier to administer, require shorter duration of treatment, and have fewer side effects. The first of the new DAAs—Sofosbuvir (SOF; Sovaldi) and Simeprevir (SMV; Olysio)—were approved in the US in late 2013. SOF is part of the first all-oral HCV drug regimen, approved for use in combination with RBV, for patients infected with HCV genotype 2 or 3. It also requires only 12 weeks of treatment, when combined with peg-IFN and RBV treatment for patients with HCV genotype 1 or 4; or 24 weeks with RBV alone for HCV genotype 1, 3 and 4.⁵² Additionally, SMV has been approved for use with peg-IFN and RBV in HCV genotype 1.⁵³ However, because this regimen requires peg-IFN and RBV and more frequent HCV RNA testing during treatment, this regimen is less likely to be used in resource-limited settings anywhere after October 2014 when all-oral drugs are approved. In addition to these already approved DAAs, several other regimens are nearing approval or are in late-stage clinical trials. There are

currently 22 compounds in phase II and 11 compounds in phase III clinical development. At least two all-oral regimens are likely to secure FDA approval in the USA by the end of 2014.⁵⁴ Although SOF and SMV have been used with peg-IFN and/or RBV, peg-IFN-free regimens are now on the horizon. SMV combined with SOF and RBV, and daclatasvir and ledipasvir have shown cure rates over 90%. There is now hope for peg-IFN-free HCV treatment for all HCV genotypes. Pan-genotypic regimens will simplify treatment by obviating the need for genotypic assays.

DAAs will remove many of the old barriers to HCV treatment. Peg-IFN-based treatment has significant side effects and comparatively low chances of a cure, while requiring a battery of expensive and complicated tests not needed with the new DAAs. HCV treatment is now simpler, more potent, of shorter duration, and with fewer side effects than ever before.

**PAMELA, 67-YEAR-OLD RETIRED
SCHOOLTEACHER, FLORIDA, USA**

Starting in the late 90s, Pamela recalled feeling like “something was wrong with her internally.” She always felt exhausted, lacked stamina, and noted that her energy levels were low: “I wasn’t sure what it was. I wasn’t in any pain but I didn’t feel that things were right. I went to the doctor and he kind of ignored that.” Ten years later, in July of 2008, Pamela was finally diagnosed with HCV infection and extensive liver damage during a routine checkup. She believes that she became infected during surgery in 1979 as a result of a blood transfusion. (There was not a test for HCV until 1989 and the United States did not begin widespread screening of blood donations for HCV until 1992.)



Pamela started a treatment regimen of peg-IFN and RBV in October 2008, but she quickly started experiencing side effects, including difficulty breathing. She was forced to miss a significant amount of work due to the severity of the side effects and soon was admitted to the hospital with interstitial pneumonia and pneumonitis. In addition, as the result of the weekly peg-IFN injections, her skin was completely “burned” at the injection site. Although the peg-IFN injections and RBV were effective at significantly lowering her viral load, she was forced to discontinue her treatment regimen after a mere 10 weeks because of the severe side effects.

For the next six years, Pamela would visit an infectious disease doctor every six months and get annual ultrasounds to monitor the progression of her HCV and the development of liver cancer. Given her bad reaction to peg-IFN, though, she was unable to return to the traditional treatment, and was denied a chance to get on two drug trials.

FDA approval of SOF offered Pamela a second chance at treatment, but it didn’t come without a fight. Her insurance company denied her request to cover SOF four times before she finally was able to get an order for coverage through mediation with the help of her doctor. “They initially approved the ribavirin,” which is much less expensive than new treatments, “but they wouldn’t approve the [sofosbuvir].” They first said it was not on the formulary and then not medically indicated, but according to Pamela, “I’m sure that it was because of the cost. At its release, a [sofosbuvir] treatment course cost 84,000 USD.” Thankfully, a non-profit dedicated to helping individuals with chronic or life-threatening illness access treatment offered to help cover her share of costs, so she was able to pursue treatment without having to pay any out-of-pocket costs.

Pamela began treatment with peg-IFN-free SOF and RBV in February of 2014. Her viral load was down to barely detectable levels just one week into treatment, and has been completely undetectable since March. This time, her side effects are limited to anemia, a dull headache, and nausea “that’s not bad enough to get a prescription.” This is a remarkable change from her previous treatment regime. Pamela has been told that she will need to take her regimen for six months, rather than the normal three months required when peg-IFN is included in the regimen for her genotype. The longer treatment course doesn’t trouble Pamela: while she is now retired, she reports that she could easily be going to work every day on the new regimen.

III. Global Prioritization: Committing to HCV Treatment

The global HCV epidemic has yet to receive the attention that is warranted given the number of people infected and the morbidity and mortality associated with HCV infection. Despite the 2010 WHO resolution urging governments to take action,⁵⁵ a UNITAID 2013 report notes that “many national governments have so far not identified HCV and HIV/HCV as a strategic priority.”⁵⁶ With only a few exceptions—including Egypt, Georgia, and Thailand⁵⁷—national policies are nonexistent or remain unfinished, treatment targets have not been established, and country- and local-level data on prevalence is often unavailable or out-of-date.⁵⁸ While the high cost of the new drugs presents a very real challenge, most countries, wealthy and poor alike, have signed on to the International Covenant on Economic, Social, and Cultural Rights (ICESCR), a legally binding human rights treaty that establishes a right to the highest attainable standard of health. Additionally, many countries have also adopted a right to health in their national constitutions.⁵⁹ Even when resources are limited, states are obligated to take steps towards “achieving progressively the full realization of the rights.”⁶⁰

Over the past few decades, inaction at the national level has been matched by a lack of adequate attention to HCV at the international level. Governments have received little technical or financial support to tackle HCV, in contrast to other major diseases, like HIV/AIDS and malaria. Major global health donors and procurement agencies, such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), the Bill and Melinda Gates Foundation, and UNITAID, have yet to address HCV in a comprehensive manner, generally limiting their efforts to HCV/HIV co-infection.⁶¹

However, the tide may be starting to turn. In April 2014, WHO released new treatment guidelines with recommendations for both health care providers and government officials regarding screening, treatment, and general care for people infected with HCV.⁶² A month later, the 67th WHA approved a second resolution on the prevention, diagnosis, and treatment

of viral hepatitis.⁶³ Notably, this resolution includes a number of targeted recommendations, including calling on countries to engage civil society in national strategies on HCV; use flexibility under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to promote access to drugs and diagnostics; and implement comprehensive prevention, diagnosis, and treatment programs for people who inject drugs.⁶⁴ Moreover, the resolution calls on the UN, the WHO Director-General, and other stakeholders to incorporate viral hepatitis into their health programs and provide technical support and guidance to help countries fulfill the resolution’s tasks.⁶⁵

Four steps should be taken to build on this momentum and to institutionalize a global commitment combatting HCV:

- Create dedicated funding streams to combat HCV;
- Place DAAs on the WHO Model Essential Medicines List;
- Prequalify generic HCV treatments to support price competition and assure access to high quality treatments; and
- Engage civil society to drive action.

CREATE DEDICATED FUNDING STREAMS TO COMBAT HCV

A lack of financing for HCV diagnostics and treatment is often cited by governments as the primary reason for not providing treatment. National governments and major donors must come together, as they have done for HIV/AIDS, tuberculosis, and malaria, to create dedicated funding streams to combat HCV, a curable disease affecting nearly 200 million people worldwide. Without a sustained international commitment to pay for treatments, diagnostics, and monitoring, it is unlikely that most people in LMICs will be able to afford the new DAAs.

Few LMICs currently subsidize the costs of HCV diagnosis and treatment. In 2012, just over one-third (37%) of LMICs surveyed by WHO reported that they

offer HCV testing free of charge (the remainder either did not respond or reported that they did not offer free testing).⁶⁶ Among those countries responding in the affirmative, many noted that free testing is limited to certain groups, such as blood donors, pregnant women, people living with HIV, and health care workers. Only three countries explicitly included PWID in the list of groups eligible for free testing.⁶⁷ Moreover, even in some countries with free antibody testing, it—along with other HCV monitoring and diagnostic tools—may only be available in limited locations and under narrow circumstances.

Just over a quarter (26.6%) of LMICs reported that they provide publicly funded treatment for HCV. The majority of these countries are classified as upper-middle-income by the World Bank; only four of the 37 are classified as low-income and 10 were lower-middle income.⁶⁸ As with testing, however, this data was not confirmed by third parties and most countries answering with publicly funded HCV treatment reported that such care was limited to certain, distinct populations.⁶⁹ For example, some countries only provide funding for government employees or patients seeking care at certain locations. Some countries also reported that free treatment was limited to acute care only.⁷⁰

Given the high price of the new DAAs, which is discussed in more detail in the subsequent section, it is unlikely that many LMICs will be able to expand public funding for HCV treatment without support of external donors. Even in the best-case scenario, where LMICs and procurement agencies are able to secure significant price reductions from DAA manufacturers, the cost of providing broad access to treatment will far exceed what national governments will be available to afford. For example, according to Médecins du Monde (MdM), providing SOF alone at 2000 USD for a 12-week treatment to half of the people currently infected with HCV in Indonesia would have exceeded the country's total public health expenditures in 2011.⁷¹ While MdM's report acknowledges that not everyone presently infected will need immediate treatment, the work demonstrates that current prices far exceed what individual countries can realistically afford.

Such high costs necessitate coordinated action at the international level. This would not be unprecedented: In the early 2000s, the international community came

together to “establish a ‘war chest’ of funds to fight three of the deadliest infectious diseases the world has ever known”: HIV/AIDS, tuberculosis, and malaria.⁷² With support from the UN General Assembly and the Group of Eight (G8), GFATM was created in 2002.⁷³ By the end of 2011, GFATM had approved 22.6 billion USD in grants.⁷⁴ Ninety-five percent of funds came from governments,⁷⁵ led by more than 13 billion USD in pledges from the United States between 2001 and 2016.⁷⁶ The remainder has come from a mix of private sector sources, such as 1.6 billion USD from the Bill & Melinda Gates Foundation and smaller amounts from aid organizations, churches, private corporations, and others.⁷⁷

Previous efforts have also shown that donations need not be the only source of funding to combat HCV. More than half of UNITAID's recent funds have come from an “air ticket levy” implemented in nine countries: Cameroon, Chile, Congo, France, Madagascar, Mali, Mauritius, Niger, and the Republic of Korea.⁷⁸ The levy can range from 1 USD to approximately 40 USD depending on the country and type of ticket, and is notable for promoting “South-South cooperation by allowing new actors from Africa and Latin America to participate in financing international development.”⁷⁹ Norway also contributes portion of its tax on carbon dioxide emissions to UNITAID.

Critically, international coordination can also play a big role in reducing the total financial resources needed to respond to epidemics. The Clinton Foundation HIV/AIDS Initiative (CHAI) has successfully negotiated price ceilings to make ARVs more affordable for members of the CHAI procurement consortium. One analysis comparing the prices paid for generic ARVs by CHAI and non-CHAI member countries found CHAI prices to be between 6% and 36% less than non-CHAI prices.⁸⁰ Similarly, analyses have shown that the United States President's Emergency Plan for AIDS Relief (PEPFAR) has been able to save hundreds of millions of dollars in just a few years by significantly increasing procurement of generic drugs.⁸¹

Recommendations:

- *National and international stakeholders should establish dedicated funding streams to combat HCV. In particular, MICs should adopt airplane tax levies or similar creative measures to finance HCV prevention, diagnosis, and treatment,*
- *International efforts should foster price reductions through bulk purchasing initiatives and support generic competition for brand-name drugs.*

CLASSIFY DAAs AS ESSENTIAL MEDICINES

The global health community should work together to ensure that new HCV DAAs are added to WHO's Model List of Essential Medicines when it is next updated in 2015. Placement of DAAs on the WHO Essential Medicines List will signal to countries and donors that they should prioritize the provision of these drugs. In countries that have recognized a right to health, classification as an essential medicine may create a legal obligation on the government to make DAAs available and affordable.

According to WHO, "[e]ssential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness."⁸² Medicines may be included on either the "core" or "complementary" lists. The core list:

"presents a list of minimum medicine needs for a basic health care system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment."⁸³

The complementary list "presents essential medicines for priority diseases which are efficacious, safe and cost-effective but not necessarily affordable, or for which specialized health care facilities or services may be needed."⁸⁴

In 2013, after an extensive Médecins Sans Frontières (MSF)-led campaign with significant support from HCV activists around the world, WHO added peg-IFN to the complementary list in light of "the high level of expertise and specialized facilities needed for safe

and effective use of interferons, as well as its high cost."⁸⁵ DAAs, particularly peg-IFN-free regimens, may be made available in less specialized settings than combinations that include peg-IFN. However, they may face a similar hurdle to making the core list without reductions in price, as they may not satisfy the cost-effectiveness standard in the WHO policy. When the dossier is reviewed by WHO, prices paid in LMICs, not upper-income countries should be considered in cost-effectiveness analyses.

There are many benefits that come from being listed as an essential medicine. First, the WHO list serves as a model for national-level essential medicine lists in all LICs and most MICs.⁸⁶ These, in turn, guide the training and supervision of health care workers, the procurement of medicines in the public sector, reimbursement schemes, and local production efforts.⁸⁷ International organizations that help procure or fund medicines in LMICs prioritize drugs on the WHO list.⁸⁸

If a medicine is on the WHO list or a national list but is not routinely available in a given location, its listing can also serve as a point of leverage for policy or legal advocacy.⁸⁹ Importantly, the right to health as embodied in the ICESCR includes provisions related to access to essential medicines as defined by the WHO.⁹⁰ While not all national courts have found that social, cultural, and economic rights are enforceable, "[b]eing a State party to a human rights treaty that is internationally binding creates certain State obligations to its people" and can support the creation of similar constitutional provisions at the national level.⁹¹ However, a WHO-funded study assessing outcomes in right to health cases in LMICs found that the majority of cases were decided in the affirmative, in favor of the right to health.⁹² In some of these cases, the court awarded access to medicines that went beyond the national essential medicines list, occasionally including medicines not even approved for reimbursement, but the study authors recommend that "constitutional guarantees on access to health care services should be well defined, for example through reference to a national list of essential medicines, to prevent abuse."⁹³ Progress towards providing access to "affordable essential drugs in developing countries" is also included as a target of the Millennium Development Goals.⁹⁴

To add DAAs to the WHO Essential Medicines

List, a WHO representative or an outside institution, such as MSF, which submitted the dossier for peg-IFN in 2013,⁹⁵ must prepare and submit application materials for consideration. If the submission comes from an outside institution, a WHO representative must offer their support for an application.⁹⁶ Patient advocacy organizations and health care industry representatives may provide comments on applications and draft recommendations.⁹⁷ In the peg-IFN case, a global network of HCV advocates led by Treatment Action Group (TAG) mobilized letters of support for MSF's application to WHO from more than 3,000 organizations and individuals, including Mark Dybul, the head of the GFATM.

Given the WHA's recent proclamations regarding HCV, WHO representatives should proactively submit application materials for DAAs to be considered for the WHO Essential Medicines List rather than waiting for outside institutions to act. In addition, because national essential drug lists may diverge from the WHO list to reflect local needs and resources,⁹⁸ stakeholders should also advocate for the addition of DAAs to national essential medicines lists in countries with high HCV burdens.

Recommendations:

- *The WHO and national governments should classify DAAs as essential medicines.*
- *Patient advocacy organizations should use this status to demand access to affordable DAAs at the global and national level.*

PRE-QUALIFY DAAS

Generic drug production can significantly lower drug prices by increasing competition. However, acceptance of generics can be hindered by fears of poor quality. To avoid such problems, manufacturers of generic DAAs and biosimilar peg-IFN should seek product approval from the WHO Prequalification Programme (WHO-PQP), which LMICs countries, major global health donors, and procurement agencies often use as an indication that a generic drug is safe and effective.

LMICs often do not have adequate drug regulatory systems in place to ensure the quality, safety, and efficacy of medicines. Indeed, a 2004 assessment by the WHO found that only “20 percent of member states, largely in developed countries, had the capacity

to effectively regulate medicinal products.”⁹⁹ WHO-PQP was created to fill this gap and provide a stringent review process for medicines for marketing and use in the developing world, including medicines for HIV/AIDS, tuberculosis, malaria, reproductive health, pandemic influenza, and acute diarrhea.¹⁰⁰

Increasingly, donors and procurement organizations are restricting their procurement to drugs that have been prequalified or authorized by a stringent drug regulatory authority, like the U.S. Food and Drug Administration or the European Medicines Agency. Up to 90% of the market of ARVs, anti-malarials, and anti-tuberculosis medicines for the GFATM, United Nations Children's Fund (UNICEF), and UNITAID have been prequalified.¹⁰¹ Individual countries also use prequalification to expedite their drug registration processes.¹⁰² Prequalification of generic versions of DAAs would “give confidence to donors, patients, and implementing organizations and would allow developing countries to fast-track registration” of globally sourced, generic versions of these drugs.¹⁰³

In order to begin the prequalification process, the WHO-PQP, the Joint United Nations Programme on HIV/AIDS (UNAIDS), UNICEF, and UNITAID must issue an Invitation for Expression of Interest for products treating HCV.¹⁰⁴ An Expression of Interest will only be issued for products that are included on either the WHO Model List of Essential Medicines or the WHO treatment guidelines.¹⁰⁵ In addition, because funding for the program has primarily been limited to donations from two organizations, UNITAID and the Bill and Melinda Gates Foundation, the scope of products has been constrained to drugs for diseases matching these organizations' priorities.¹⁰⁶ While UNITAID has expressed interest in addressing HCV to the extent it presents as a co-infection with HIV, it has indicated that it is unlikely to prioritize interventions that focus solely on HCV.¹⁰⁷

In light of recent developments, these hurdles should not present as great a barrier now as in the past. As noted above, WHO released treatment guidelines for HCV in April 2014, which highlight the disease as a priority for the agency. In addition, last year, WHO announced that it would begin charging fees from companies applying for pre-qualification.^{108 109} Greater financial independence for WHO from donor priorities may offer more flexibility to expand the WHO-

PQP to new areas, including HCV.

As peg-IFN will continue to be used in the treatment of HCV for the near future, stakeholders should also continue to push for a similar quality approval process for biosimilar products, which currently are excluded from the prequalification process.¹¹⁰ Peg-IFN is a biologic compound, meaning that its generic production would require the creation of a biosimilar, rather than a “generic” small molecule copy (as would be the case for SOF and other traditional non-biologic, chemical pharmaceuticals). If the WHO offered a prequalification process to biosimilar products, prequalification for generic manufacture of peg-IFN would become a possibility. Like with DAAs, prequalification of biosimilar peg-IFN-based treatments would give more countries confidence in their quality, encourage procurement, and put further downward pressure on prices.¹¹¹

WHO also prequalifies certain diagnostic equipment for high burden diseases.¹¹² Due to perceptions about small size of the potential market, WHO has not prequalified any HCV rapid tests.¹¹³ However, as the new DAAs come on the market and efforts to expand screening increase, the need for rapid diagnostic tests for resource-limited settings will become critical. Accordingly, stakeholders should be sure to jointly push for the prequalification of DAAs, peg-IFN, and HCV rapid diagnostic tests as quickly as possible.

Recommendations:

- *UNITAID and the Bill & Melinda Gates Foundation should identify combatting HCV as a priority and support efforts to prequalify generic DAAs, biosimilar interferon formulations, and HCV rapid tests.*
- *WHO-PQP, UNAIDS, UNICEF, and UNITAID should issue an Invitation for Expression of Interest for products treating HCV, including diagnostics, and establish a similar pathway for biosimilar peg-IFN formulations.*
- *Generic manufacturers should respond to this invitation and get their products prequalified.*
- *Once HCV-related products are prequalified, procurement agencies, donors, and national drug regulators should act swiftly to bring affordable, quality generic HCV drugs and diagnostics to markets in LMICs.*

ENGAGE CIVIL SOCIETY TO DRIVE ACTION

HCV treatment activism must continue to play a critical role in overcoming barriers to treatment. In many places, activism on HCV has grown out of the efforts on HIV/AIDS and the rights of PWID. However, HCV activism needs to be expanded and strengthened in order to effectively pressure governments, corporations, and international organizations to take the actions necessary to make HCV treatment accessible for all. To enable this development, funders must not only provide money for treatment and prevention, but also support the growth of a strong activist community focused on HCV. Funders cannot simply support technical responses to the epidemic; they must support the grassroots efforts that put pressure on policy makers to effect change.

Dedicated activists—passionate about saving the lives of those living with HCV and the injustices that perpetuate it—play an important role in moving forward the global HCV agenda. People infected with HIV/AIDS have overcome many of the same barriers to treatment faced by those infected with HCV. Activists played a pivotal role in bringing ARV treatment to more than 10 million people across the globe in both high- and low-income countries. HIV/AIDS activists helped secure substantial dedicated funding streams, provided by PEPFAR and GFATM, to treat people in resource-limited settings.

The story of HIV/AIDS activism provides a story of how, in country after country, small groups of people with HIV and their allies were able to move from local action to national achievements, and eventually an internationally coordinated campaign for access to AIDS treatment for all. The world of early AIDS activism is different than the world is today. Global health is a far more important international priority than it was all those years ago and the internet connects people across the planet with new opportunities for organizing. HCV activists in some senses have a head start on their work. However, the world today also comes with new challenges. In late 1990s and 2000s, the world was in the midst of an economic boom with funding for global health on the rise. Now the world has experienced a severe economic crisis with the future of global health funding in jeopardy and the World Trade Organization (WTO) playing an active role under the TRIPS agreement to prevent the generic manufacture of life-saving

medications in LMICs.

Civil society groups engaged in activism to advocate for HCV treatment access have already been hard at work in LMICs, with many successes to show for their efforts. In Thailand, grassroots activism arising out of HIV/AIDS activist and harm reduction networks, have framed the issue of HCV treatment around the needs of those co-infected with HIV/AIDS and people who inject drugs. The Thai AIDS Treatment Action Group (TTAG), the Thai Network of People Living with HIV/AIDS (TNP+), and other grassroots groups pushed the Thai government through community organizing, education, and lobbying to put peg-IFN onto the Thai National Essential Medicines List. In August 2012, their efforts culminated in success with the medication being added to the list, which led to coverage under the Universal Healthcare Scheme.¹¹⁴

Groups working on HIV/AIDS in Ukraine have also taken up the cause of HCV treatment. In 2011, Ukrainians launched the “Do You See the C?” campaign to highlight the one million Ukrainians living silently with HCV. In 2012, the “Deputy-Altruist” campaign tracked spending on health and spa treatments for Ukrainian government officials in contrast to the lack of spending on HCV, taking pledges from officials to forego their wellness budget to contribute towards HCV treatment. In April 2013, Ukrainian activists calling themselves “the Condemned,” protested in the government halls with cloth hoods covering their faces, demanding funding for HCV treatment. Within weeks, the government announced it was creating a national plan for HCV treatment.¹¹⁵ By September 2013, the government announced that they would work with the International HIV/AIDS Alliance Ukraine to provide 4.2 million USD for peg-IFN-based HCV treatment. As of 2014, 2,300 Ukrainians are receiving treatment through the program.¹¹⁶

In other LMICs, groups with ties to PWID have led the charge. In India, Sankalp Rehabilitation Trust, a local non-governmental organization that works with PWID, was able to successfully file a challenge to the Roche Pegasys (peg-IFN-alfa-2a) patent. In 2012, the Indian authorities deemed Roche’s peg-IFN unworthy of a patent, opening the door for manufacture of biosimilar peg-IFN. These grassroots activists played a key role in this decision, opening up the possibility for the emergence of less expensive generic equivalents,

which could improve HCV treatment access.¹¹⁷ In Georgia, PWID advocates have also played a leading role. The Georgian Harm Reduction Network (GHRN) has been lobbying the government to create a fully funded HCV treatment program. In 2013, they secured a commitment to treat 300 prisoners with HCV, expanding the program to 500 in the following year.¹¹⁸

HCV activism is growing. HIV/AIDS activists and other organizations representing HCV patients are growing in power and sophistication with global organizing around access issues in LMICs proceeding apace. In February 2014, the first meeting of the HCV World Community Advisory Board (CAB) brought together 38 activists from 22 countries, to begin to build the kind of global activist network that has made such an impact in the HIV/AIDS epidemic. These activists met with representatives from six pharmaceutical companies that currently hold patents on HCV treatments (AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Merck, and Roche) to demand a comprehensive plan for expanding HCV treatment access, requiring plans for registration, licensing, and pricing strategies.¹¹⁹

In 1982, a group of people living with HIV developed the Denver Principles, promoting self-empowerment of those with HIV and fighting the stigmatization of the disease. A coalition of activist organizations at the 2012 International AIDS Conference in Washington, DC developed a similar set of principles as a blueprint for HCV activism going forward. This set of principles known as the “Washington Call for Access to HCV Diagnostics, Treatment and Care for All!” laid out a plan for engaging pharmaceutical companies, international organizations, funders, political leaders, and researchers in the quest for access to HCV treatment.¹²⁰

The HCV activist movement is poised to become a truly international, collaborative effort to break down the barriers to HCV treatment access. Many lessons can be learned from the AIDS activism of US groups like ACT UP and Health GAP, South Africa’s Treatment Action Campaign (TAC), the Thai Network of People Living with HIV/AIDS, and many others across the global who have continued to fight for universal HIV treatment access in LMICs since the 1990s and 2000s. Funding for building this network of HCV activists will be critical to moving the agenda forward on HCV

treatment access. With a strong global network of HCV activists, governments, corporations, and international organizations will no longer be able to ignore the HCV epidemic, and their advocacy, like the advocacy of AIDS activists before them, will help to make HCV treatment access a reality.

Recommendations:

- *Funders must provide financial support to further develop a strong global community of HCV treatment activists who can effectively push corporations, governments, and international organizations to act to expand access to HCV treatment.*
- *UN agencies, in particular WHO, must actively engage a diverse representation of people with HCV, including people living with HIV, PWID, and their allies, in their international- and national-level policy and other work*

UMESH, 49-YEAR-OLD HUSBAND, FATHER, AND ACTIVIST, MANIPUR, INDIA

Over nine months of painful HCV treatment, including peg-IFN injections and RBV, Umesh lost over 20 pounds, suffered damage to his pancreas, and saw his CD4 count, critical to immune system health, drop dangerously low. He had to quit his job due to pain and fatigue and was very depressed. Worse yet: it was all for naught. His HCV relapsed within six months.

“When I realized the virus was back I was very sad,” Umesh recounted. The pain and side effects from treatment had taken a serious toll, both mentally and physically. It’s been more than five years and his CD4 count still hasn’t recovered. He knows he can’t try again, at least not if he has to take peg-IFN. So he’s helping to wage a campaign to bring the new DAAs to India at an affordable price by increasing awareness about HCV among high-risk populations.

Umesh originally contracted HCV through unsafe practices injecting drugs. For Umesh, injecting heroin was a social event, and sharing needles and syringes among friends was common. Unaware of the risks he was exposing himself to, Umesh recalled that “during my shooting days I did not insist on shooting first, I would always be last. I do have close friends with whom I would inject regularly and my nature allows me to wait for my turn.”

Umesh did not get tested for HCV until 1995 when he was abroad, long after he had quit injecting drugs and

five years after he had tested positive for HIV. According to Umesh, the Indian government only began testing for HCV in the early 2000s, as an increasing number of people began dying of liver cancer. Even now “people need to pay for it themselves [and] it is difficult to get to a proper place to get your testing. For example, in my home town in Manipur, people need to send blood samples to Delhi or Mumbai to get tested, and it takes two weeks to get results.”

But Umesh is working to change things. In particular,



he is trying to increase knowledge about HCV among the approximately 180,000 people in India who inject drugs. According to Umesh, “Knowing about hepatitis C is big challenge for high risk populations . . . One of the main advocacy efforts we are doing is going to remote places and gathering people and talking about hepatitis C so they know what it is and how to get tested. If they get tested, they will ask for treatment which will help us show demand and push the government for access to treatment.”

IV. Lowering Drug Prices and Promoting Generic Competition

Although new DAAs, such as SOF and SMV, have arrived on the market, high drug prices continue to make treatment unavailable to many people in both high and low-income countries (LICs). In the U.S., Gilead charges 84,000 USD for SOF and Janssen's SMV costs 66,000 USD for 12 weeks of treatment (though some genotypes require a longer treatment course).¹²¹

There are several ways to bring down the high price of these drugs. One way relies on the pharmaceutical companies voluntarily offering discounts to LMICs through tiered or differential pricing. Unfortunately, while pharmaceutical companies may offer discounts to the poorest nations, they are unlikely to offer similar price reductions to MICs, where 73% of people with HCV—and where they see lucrative markets,¹²² despite great income inequality.¹²³ The prices set under tiered pricing are often higher than governments in MICs are willing and/or able to pay, leaving patients to bear the cost. This section examines additional non-industry-dictated strategies that could more sustainably expand access to HCV treatment. It recommends:

- Adopting stringent standards for evaluating patents and enabling pre- and post-patent award challenges; and
- Using compulsory licenses when patents have been granted.

CURRENT DRUG PRICES

Current prices for new DAAs on the market cost up to 84,000 USD for a 12-week regimen, as in the case of SOF (~1,000 USD per pill) in high-income countries like the United States (and this does not include the cost of other medications, diagnostic tests). It is still unclear what the companies will charge for the DAA treatments in LMICs. Current negotiations between Egypt and Gilead indicate that Gilead will offer SOF to Egypt for use in public programs for 900 USD for 12 weeks of treatment. Unfortunately, even a 900 USD price tag will be far out of reach for most people with HCV in LMICs.¹²⁴ In Egypt, treatment at 900 USD is limited to only those who are part of the government health plan and the discounted price may prove unaffordable for the government over the long-term as the per capita GDP is only 3,314 USD.¹²⁵ Private sector prices will be as much as ten times higher for those that do not qualify for the government price.¹²⁶

The actual production costs for these new drugs do not justify the high prices. It is estimated that large-scale manufacturing of two or three HCV DAA combinations could be done for approximately 171-450 USD each for a 12-week regimen.¹²⁷ MSF has advocated for a complete HCV diagnostic, monitoring and treatment package for less than 500 USD.¹²⁸

Table 5: Predicted Minimum Costs of Hepatitis C Virus Direct-Acting Antivirals

Agent	Daily dose, mg	Overall dose per 12, wk, g	Estimated cost per gram, USD	Predicted cost, USD
Ribavirin	1,000–1,200	101	0.34 ^a	\$50
Daclatasvir	60	5	4	\$20
Sofosbuvir	400	34	3	\$102
Ledipasvir	90	8	11.6	\$93
MK-8742	50	4	11.0	\$44

^a CURRENT MIDPOINT OF ACTIVE PHARMACEUTICAL INGREDIENTS COST PER GRAM FROM 3 CHINESE SUPPLIERS.

SOURCE: HILL A ET AL. MINIMUM TARGET PRICES FOR PRODUCTION OF DIRECT ACTING ANTIVIRALS AND ASSOCIATED DIAGNOSTICS TO COMBAT HEPATITIS C IN DEVELOPING COUNTRIES (PRESENTATION, WORLD AIDS CONFERENCE, JUNE 20, 2014), AVAILABLE [HTTP://ONLINELIBRARY.WILEY.COM/DOI/10.1002/HEP.27460/FULL](http://onlinelibrary.wiley.com/doi/10.1002/HEP.27460/FULL)

Table 6. Duration and Cost of HCV Treatment, by Drug Regimen

Regimen	Duration, wk	Predicted cost, USD
Daclatasvir + sofosbuvir	12	\$78–166
Daclatasvir + sofosbuvir + ribavirin	12	\$112–214
Sofosbuvir + ribavirin	12	\$102–184
Sofosbuvir + simeprevir	12	\$198–406
Sofosbuvir + simeprevir + ribavirin	12	\$232–454

SOURCE: HILL A, ET AL. MINIMUM COSTS FOR PRODUCING HEPATITIS C DIRECT-ACTING ANTIVIRALS FOR USE IN LARGE-SCALE TREATMENT ACCESS PROGRAMS IN DEVELOPING COUNTRIES. CLIN INFECT DIS. 2014 APR;58(7):928–36.

PATENT CHALLENGES

Patents provide drug companies with time-limited marketing exclusivity, allowing them to seek legal action against any other party making, using, selling, or importing their patented product. An argument frequently cited in favor of product patents is that they incentivize innovation by providing a temporary monopoly, which allows companies to charge high prices to recoup the investment they made in the research and development of the drug. However, while there has been an increase in the protection of intellectual property rights globally since the World Trade Organization (WTO) promulgated the TRIPS in 1995, the WHO Commission on Intellectual Property Rights, Innovation and Public Health concluded that “there are no documented cases of positive impact on innovation in the medical field as yet.”¹²⁹ This is in significant part because markets for pharmaceuticals are predominantly located in developed countries, which already have expansive patent laws. Adding more patents in jurisdictions with smaller markets does little to increase incentives for innovation but can significantly hinder access to medications. In addition, there are also significant concerns across all jurisdictions today about patent quality.¹³⁰ Many pharmaceutical patents today are a result of “evergreening,” where companies patent new forms of existing medicine, extending their exclusivity beyond the 20-year period for a single patent, by stacking multiple patents on top of one another.¹³¹ Unjustified patents, granted for products that are only trivially inventive, act as a barrier to research and restrict the

public’s access to medicines.

Unjustified patents can be challenged depending on the laws of a country. TRIPS, an international agreement that requires member countries of the WTO to put in place forms of intellectual property regulations, requires that all middle-income and least-developed countries comply fully with its intellectual property provisions around pharmaceuticals by 2005 and 2021, respectively. There are no international patents. Countries generally review patent applications at the national level to ensure they meet local legal standards (though in a few cases patent examination is done regionally). Under the guidance of TRIPS, patent laws generally require applicants to meet three key requirements: they must show “novelty,” an “inventive step,” and that the invention is “capable of industrial application.”¹³² However TRIPS does not define these criteria, leaving it is up to each WTO member state to determine what would meet these criteria.¹³³

India is a good example of a MIC where progressive patent laws have been useful in expanding access to medicines, while maintaining compliance with TRIPS. India’s laws set a high standard for patentability and make it difficult to obtain a patent for a product that is not truly inventive. Section 3(d) of the Indian Patent Act is of particular importance, and provides that patents cannot be granted for:

“the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a

known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.”¹³⁴

Citing these provisions, India has denied many patents that were granted in other countries, including patents sought by multinational pharmaceutical companies such as Roche, GlaxoSmithKline, Pfizer, and Merck.¹³⁵ In 2007, the Indian Patent Office relied on Section 3(d) to reject a patent on a Novartis cancer drug.¹³⁶ In a landmark ruling, the Indian Supreme Court in 2013 upheld that decision, and clarified India’s patent laws require enhanced therapeutic efficacy before a patent on a new form of a known substance will be permitted.¹³⁷

India also has a higher standard of what constitutes “inventive step.” The Patent Act defines inventive step as an “invention that involves technical advance as compared to the existing knowledge, or having economic significance or both and that makes the invention not obvious to a person skilled in the art.”¹³⁸ Thus while something might be inventive as the term is generally understood, it would not qualify as inventive under the Indian Patent Act. India has rejected patents including Novartis under this criteria, sometimes without Section 3d being cited.¹³⁹ Under Article 1.1 of the TRIPS, countries are free to define strict standards for what constitutes novelty, inventive step, and industrial applicability.¹⁴⁰ Therefore developing countries that might not be able to emulate India’s Section 3(d) provisions for economic or political reasons can still set higher criteria for what constitutes inventive step.

In conjunction with progressive patent laws, India has strong procedural provisions that allow third parties to challenge a patent application both before and after its grant.¹⁴¹ Pre-grant patent oppositions are particularly important given the difficulty of challenging a patent once it has been granted. According to UNDP, UNAIDS and WHO, allowing pre-grant oppositions can help avoid the patenting of products and processes that are not truly innovative.¹⁴² Like pre-grant patents, post-grant patent oppositions can also prevent the patenting of products that are not truly innovative.¹⁴³ However, even those countries that allow for post-grant patent challenges sometimes restrict the ability to file a post-grant challenge to “interested persons”—defined specifically as commercial entities—thereby excluding

civil society groups from making such challenges. Civil society groups committed to improving access to medicine are often likely parties to file post-grant patent challenges. Permitting any person to bring post-grant challenges, including civil society groups, can help prevent non-meritorious patents from being granted.

CURRENT PATENT CHALLENGES AGAINST SOFOSBUVIR

The Initiative for Medicines, Access & Knowledge (I-MAK) and the Delhi Network of Positive People are two civil society groups that are challenging patents for SOF in India based on the lack of novelty and inventiveness. Two pre-grant oppositions were filed against two key patents relating to SOF:

1. An opposition against the base compound patent, which would be the main blocking patent (6087/DELNP/2005). The grounds of the opposition are that the base compound that is used for SOF lacks novelty and inventive step and is a new form of a known substance that does not show enhanced efficacy (s3d).
2. An opposition against the pro-drug form that is marketed as SOF (3658/KOLNP/2009). The patent challenge is based on lack of novelty and inventive step, is a new form of a new substance, and is also a new use of a known substance (s3d).

In January 2015, India’s patent office rejected Gilead’s request for a patent for SOF based on Section 3d of the India patent Act which does not recognize new uses of an existing drug as an innovation unless there is increased efficacy. The patent office held that although SOF meets the novelty and inventive step requirement, it lacks “significantly enhanced therapeutic efficacy,” compared to its “closest prior art.”

This is a major victory for public health. It allows generic companies to start producing affordable versions of SOF, which will result in increased access to the drug for millions of people who urgently need it. It also underscores that patent law should not allow companies to receive patents for old science.

SOURCES:
INITIATIVE FOR MEDICINES ACCESS KNOWLEDGE, “BRIEFING NOTE: SOFOSBUVIR PATENT OPPOSITION IN INDIA,” NOVEMBER 24, 2013, 1DELHI NETWORK OF POSITIVE PEOPLE (DNP+) AND THE INITIATIVE FOR MEDICINES, ACCESS & KNOWLEDGE, INC (I-MAK) V INDIAN APP NO. 6087/DELNP/2005 BY

GILEADPHARMASSET LLC INITIATIVE FOR MEDICINES, ACCESS & KNOWLEDGE, INC (I-MAK) V INDIAN APP NO. 3658/ KOLNP/2009 BY GILEAD PHARMASSET LLC NATCO TRIES TO BLOCK HEPATITIS C PATENT IN INDIA, MAY 23, 2014, GENERICS AND BIO SIMILARS INITIATIVE, [HTTP://26 WWW.GABIONLINE.NET/GENERICS/GENERAL/NATCO-TRIES-TOBLOCK-HEPATITIS-C-PATENT-IN-INDIA](http://26 WWW.GABIONLINE.NET/GENERICS/GENERAL/NATCO-TRIES-TOBLOCK-HEPATITIS-C-PATENT-IN-INDIA) K. M. GOPAKUMAR, INDIAN PUBLIC OPPOSITION TO HEPATITIS C MEDICINE PATENT CLAIM, THIRD WORLD NETWORK, MARCH 25, 2014, [HTTP://WWW.TWNSIDE.ORG.SG/TITLE2/HEALTH.INFO/2014/HI140303.HTM](http://WWW.TWNSIDE.ORG.SG/TITLE2/HEALTH.INFO/2014/HI140303.HTM) WILLIAM NEW, "KEY HEPATITIS C PATENT REJECTED IN INDIA," INTELLECTUAL PROPERTY WATCH, (JANUARY 14, 2015), [HTTP://WWW.IP-WATCH.ORG/2015/01/14/KEY-HEPATITIS-C-PATENT-REJECTED-IN-INDIA-FOR-LACK-OF-NOVELTY-INVENTIVE-STEP/](http://WWW.IP-WATCH.ORG/2015/01/14/KEY-HEPATITIS-C-PATENT-REJECTED-IN-INDIA-FOR-LACK-OF-NOVELTY-INVENTIVE-STEP/)

Other countries are following India's example. In a landmark decision, the Supreme Court of Thailand rejected a "new use patent" and held that it is not patentable.¹⁴⁴ Philippines has put in place measures similar to Section 3(d) through the Universally Accessible Cheaper and Quality Medicines Act of 2008 and does not allow the patenting of newly discovered uses of known drugs which do not result in enhanced efficacy.¹⁴⁵ China rejected Gilead patents for its HIV and HBV drug, tenofovir disoproxil fumarate (Viread), because the drug lacked novelty.¹⁴⁶ Brazil rejected a patent on the same drug in 2008.¹⁴⁷ Brazil is currently in the process of attempting to reform its patent laws to reject patents on new forms of known substances or substances that do not meet efficacy or inventive step requirements, as well as to include a more rigorous pre-grant patent opposition mechanism.¹⁴⁸ In 2012, Argentina's patent office and health department released guidelines instructing patent examiners to reject what are merely new uses or forms of existing drugs.¹⁴⁹ Peru, Bolivia, Columbia, and Ecuador do not allow new use patents.¹⁵⁰ South Africa is currently considering reforming its patent laws to impose stricter standards for patents, implement a patent examination system, adopt opposition procedures, and broaden the grounds for issuance of compulsory licenses.¹⁵¹

Historically, unfettered generic competition has proved to be one of the most effective means of driving down the cost of drugs. When HIV/AIDS drugs were expensive, competition (in the absence of a product patent regime in India) from generic drug producers drove ARV prices down from 10,000 USD to 100 USD per patient per year.¹⁵² After India passed a law providing patent protection to drug products, patent challenges served as a critical strategy to promote competition. People are able to access ARVs today because activists challenged key patents

and highlighted their detrimental effects on public health.¹⁵³ A similar approach should be adopted for HCV drugs.

Recommendations:

- *Countries should put in place a robust patent review system that sets clear patent criteria and incorporate TRIPS flexibilities into national law.*
- *Countries should adopt laws similar to India's 3(d) law or Argentina's resolution to ensure patents are only issued for drugs that meet the TRIPS criteria, i.e. agents that are novel, inventive and "capable of industrial application."*
- *Countries should allow invalidation proceedings for unjustified patents.*
- *Countries should allow pre-grant patent oppositions any time prior to the grant of a patent. Although some countries allow for pre-grant opposition, the window for opposition after the publication of the patent application is often short, limiting the ability of public interest groups to challenge patents, by not providing enough time to review information on a patent.*
- *Countries should allow post-grant patent oppositions and allow any person to submit them including civil society.*
- *Countries should broadly construe the flexibilities provided by TRIPS, such as the ability to define novelty strictly.*¹⁵⁴
- *Countries, particularly least-developed countries, should utilize the TRIPS waiver that permits them to avoid adhering to TRIPS until 2021 and should not offer patent protection for pharmaceuticals until the expiration of the waiver.*

COMPULSORY LICENSING

To increase access to essential medications even when drugs are patented, governments can issue compulsory licenses—a process that overrides a patent in exchange for a royalty.¹⁵⁵ Article 31 of TRIPS allows countries to issue compulsory licenses when they see fit, as long as they follow certain procedures.¹⁵⁶ It is especially simple if there is a national emergency or other situations of extreme urgency or where public non-commercial use is involved. In these cases, countries do not need to follow certain procedural requirements, such as prior negotiation with the rights holder.¹⁵⁷

In other cases, compulsory licenses can be issued

after failed negotiations with the patent holder. In general, compulsory licenses may be used only for supply of the domestic market. However, the WTO General Council on August 30, 2003, agreed to allow exporters to override patents to supply member states that do not have manufacturing capacity.¹⁵⁸ To date, Rwanda is the only country to use the export mechanism, signaling that the existing mechanism is unduly cumbersome.¹⁵⁹

Compulsory licenses can also be issued as a remedy for patent abuse and anti-competitive pricing. Article 8.2 of TRIPS allows countries to take “appropriate measures” against activities that “reasonably restrain trade or adversely affect the international transfer of technology.”¹⁶⁰ Unlike a compulsory license under Article 31(b), with a compulsory license issued under Article 8.2, there would be no obligation to conduct prior negotiations with the patent holder or to notify the patent holder. The export restrictions that ordinarily govern compulsory licenses would also be waived. For serious instances of anti-competitive conduct, the country would not be obligated to pay remuneration to the patent holder. Here too, TRIPS does not define terms such as anti-competitive, and important examples exist that give the concept expansive implications. For example, the 2002 Egyptian Intellectual Property Rights law permits steep pricing to qualify as anti-competitive conduct.¹⁶¹ In 2002, South Africa’s Competition Commission recommended the issuing of a compulsory license and punitive measures against GlaxoSmithKline and Boehringer Ingelheim for excessively pricing patented ARVs (zidovudine, lamivudine, and nevirapine) and denying generic producers manufacturing licenses.¹⁶²

Compulsory licenses not only enable the production of essential medications, they can also be used to convince patent holders to reduce their prices. In 2001, Brazil used the threat of compulsory licensing to negotiate lower prices on key HIV drugs. In the same year, Brazil publicly announced its intention to issue a compulsory license for peg-IFN, to compel the patent holders to reduce the price of this HCV medication.¹⁶³ In South Africa, GlaxoSmithKline and Boehringer Ingelheim agreed to voluntarily license their ARV drugs to generic companies at a royalty not to exceed 5% in order to avoid the issuance of compulsory licenses. In 2010, the Ecuadorian Intellectual Patent Office

granted a compulsory license on the ARV combination lopinavir/ritonavir, to Eskegroup, a local distributor for the Indian generic pharmaceutical Cipla.¹⁶⁴ This significantly reduced the price the Ecuadorian government subsequently paid for ARVs.¹⁶⁵

However, in some instances, it will be difficult for countries to issue compulsory licenses. They can only be issued after the grant of a patent. Furthermore, countries that have issued them, like Thailand, have faced considerable political backlash.¹⁶⁶ A lawsuit was brought against South Africa when it attempted to issue compulsory licenses.¹⁶⁷ Political pressure by both pharmaceutical companies and countries, such as the United States, and member states of the European Union, has dissuaded some countries from implementing compulsory licenses. Thus, first focusing on rejecting patents may be the more strategic option for countries to consider.

Nonetheless, as more stringent patentability standards are implemented, and options for patent challenges, are exhausted, compulsory licenses provide an additional key strategy towards increasing access to essential medicines.

Recommendations:

- *Countries should enact laws—if they do not currently exist—that allow the government to exercise their rights under TRIPS to issue compulsory licenses. They should initiate compulsory licensing whenever necessary to promote the public health, including in cases when patent holders engage in anti-competitive conduct.*
- *Countries should set in place a framework to govern the issuance of compulsory licenses. This should include: defining reasonable terms for a license, timelines during which voluntary licenses can be negotiated, and a default rule that when negotiations fail, compulsory licenses should be issued with a reasonable royalty.*
- *Countries should allow expedited approval of compulsory licenses in case of national emergencies.*
- *Countries should cooperate regionally to develop policies that will enable them to fully utilize TRIPS flexibilities.*

STRATEGIES COMPANIES USE TO AVOID PATENT CHALLENGES OR COMPULSORY LICENSES

Most pharmaceutical companies adopt different marketing strategies in different settings, often demanding exorbitant prices in high-income countries, offering tiered pricing in MICs, and establishing lower prices or voluntary licensing in LICs. Although these strategies seem to promote accessibility, they are problematic in practice. They leave control in the hands of companies, who typically impose restrictions on discounts that support their profits, but can harm patients.

A. TIERED PRICING

Pharmaceutical companies routinely negotiate different, non-transparent pricing agreements with MICs. Although this system might seem fair, it does not do enough to increase access to drugs for several reasons. Determinations of what constitutes a MIC are based on World Bank classifications, which are an assessment of the general economic development of a country. These classifications reflect neither the state of the health systems nor the inequities present in access to health services in these nations.¹⁶⁸ In addition, the arbitrary threshold for distinguishing LICs from MICs means that countries that have similar economic profiles may be offered very different prices on drugs from multinational pharmaceutical companies.¹⁶⁹

Although larger MICs may be able to negotiate better prices with pharmaceutical companies, smaller MICs that lack production capacity will get less favorable prices. For example, although Honduras and Brazil had similar HIV prevalence rates, in 2006 Hondurans were paying six times more than their Brazilian counterparts for HIV/AIDS medication, despite the fact that Honduras' per capita gross national income was one-fourth of Brazil's at that time.¹⁷⁰ This price differential was a direct result of Brazil's ability to leverage its larger market and threaten the use of compulsory licensing to force drug companies to accept a lower price.¹⁷¹

Finally, tiered pricing ignores the fact that many MICs have high levels of income inequality. Over 70% of the world's poor now live in MICs.¹⁷² Although wealthier individuals in MICs may be able to afford tiered pricing, the price levels set in MICs often put drugs out of the reach of the poor. Most developing countries lack insurance markets or government

coverage for pharmaceutical products and the poor have to pay out of pocket for their treatment costs.¹⁷³ Tiered pricing does not address these inequities and will not sufficiently improve the accessibility of life saving HCV medications.¹⁷⁴

B. VOLUNTARY LICENSING

Companies that hold patents can give permission to generic manufacturers to make, sell, or import the drug in a particular country, and thus bring prices down and expand manufacturing capabilities. Such "voluntary licenses" have become more common, but also have serious limitations. For example, such licenses often only allow generic manufacture in LICs, excluding MICs entirely. Restrictions may also be imposed on suppliers of raw materials, interfering with economies of scale needed to reduce price to their lowest level.¹⁷⁵ These licenses are also sometimes offered to deter countries from taking advantage of TRIPS flexibilities. By offering voluntary licenses, a company can ensure a country will not issue or at least threaten to issue compulsory licenses. Furthermore, even when patents have been rejected, a company can issue a voluntary license. For example, after Egypt rejected a patent for SOF, Gilead issued a voluntary license, with license terms that restricted competition; thereby ensuring generic competition is not maximized.¹⁷⁶ Like tiered pricing, voluntary licenses are "second-best" tools for expanding equitable access to medicines.

Gilead has set up voluntary licenses with a number of countries for its HCV DAAs, SOF and ledipasvir. At the first HCV World Community Advisory Board (CAB) in Bangkok, Thailand in February 2014, Gilead detailed the scope of the SOF voluntary licenses, which, in their original form, would exclude 48 million people in MICs.¹⁷⁷ Gilead initially planned to restrict the licenses to 60 countries—far fewer than the voluntary licenses Gilead issued for HIV/AIDS medication.¹⁷⁸ The countries covered were predominantly LICs in Africa and South East Asia, many of which have low rates of HCV prevalence.¹⁷⁹ Although Gilead has increased the scope of the license to 80-90 countries, the license issued largely excludes MICs—the countries most affected by the HCV epidemic.¹⁸⁰ Countries left out include China, which has the largest HCV burden in the world at approximately 30 million, Brazil (2.6 million), the Philippines (1.9 million), Turkey (1.5 millions),

Thailand (1.4 million), and Mexico (1.1 million).¹⁸¹ Thus, even with these voluntary licenses, less than half of the people with HCV worldwide will benefit from these prices.

Gilead has recently signed voluntary licenses with a few countries originally excluded from the initial license, such as Egypt.¹⁸² As discussed above, in Egypt, the terms of these licenses establish two prices for the drug within the country. Drugs procured by the Egyptian Ministry of Health will be 300 USD per box per month, and therefore 900 USD for a 12-week treatment.¹⁸³ According to some sources, it is estimated that drugs procured for the private market will cost ten times the government price.¹⁸⁴ Although the price Egypt negotiated for the government programs is currently the lowest price for SOF, it is still substantially higher than the projected generic prices discussed above. Furthermore, SOF will still be unaffordable for the many HCV patients who do not qualify for government coverage.¹⁸⁵ The total price paid for treatment overall will also be higher since SOF must be used alongside other drugs for maximum effectiveness.¹⁸⁶

In India, which has pending patent oppositions to SOF, Gilead has signed agreements with generic companies to offer the drug for 2,000 USD for a 12-week regimen.¹⁸⁷ Gilead and the Indian generic companies are signing the agreements before the Indian patent office has determined whether patents on the drug should be granted.¹⁸⁸ The company claims that under the terms of voluntary licenses, generic companies could choose to sell the drug for a lower price, but will be bound by the terms of these licenses even if Gilead's patents are invalidated in Indian courts. These terms could deter generic companies from filing patent challenges since the companies might prefer to maintain their relationship with Gilead so as to become a preferred commercial partner for a future license.¹⁸⁹ They also place restrictions on the manufacturing and sale of the drug and limit the market making it difficult for generic producers to achieve economies of scale. This puts generic Indian manufacturers in the difficult position of agreeing to a license now on Gilead's terms, when they may be able to produce the drug anyway if the patent on SOF is invalidated.

Furthermore, as the patent holder, Gilead sets the license terms dictating where and under what circumstances the drugs can be sold.¹⁹⁰ The voluntary

license terms for SOF are highly restrictive and will only allow drugs to be manufactured outside the licensed territory if there is "no reasonable possibility of obtaining such a Product Patent within a reasonable period of time (for example, through pending patent applications, the filing of patent applications, or by legal action (including appeals))" in India and "such country outside of the Territory."¹⁹¹ It will also only permit the licensed generic company to produce the drug in countries where there is no product patent owned or controlled by Gilead.¹⁹² The "reasonable possibility" restriction includes patents filed but not granted or amended applications for patents. This process could take years given that as long as there is a pending patent application relating to SOF or Gilead's other DAA, ledipasvir, in India, even if it is rejected and under appeal (the Novartis case took almost ten years¹⁹³), Gilead can prevent generic companies that signed on to the voluntary license from selling the drug to these countries.

While voluntary licenses and tiered pricing might increase access to drugs for some, they are not implemented in accordance with public health aims. Rather, their terms often reflect the companies' desire for profits. They are also designed to undermine countries' willingness to use TRIPS flexibilities to protect their local generic companies and to promote competition that could lower drug prices. Ultimately, they cannot be expected to adequately address the gaps in access to HCV medicines. More fully utilizing TRIPS flexibilities, by pursuing patent challenges and compulsory licensing, offers the promise of enhanced competition in the market, and will lower drug prices, and promote wider access to drugs for the poor, particularly for those living in MICs.

PABLO, 52-YEAR-OLD PUPPETEER AND ACTIVIST, MAR DEL PLATA, ARGENTINA

At 41 years old, Pablo almost died in a hospital in Mar del Plata, Argentina. That was when he found out he was HIV positive. At the time, Pablo had a secure "white collar job" and had been happily married for more than 10 years with a daughter who depended on him. As best he can guess, Pablo contracted HIV when he was 26 or 27. After more than a decade of the virus silently living inside him, Pablo was suddenly near death from complications of his HIV infection at a time when his family needed him most.

Thankfully, Pablo survived his hospital stay and went on ARV treatment to control his HIV infection. In 2003, when his life slowly seemed to be returning to normal again, he got the news from his doctors that he was also infected with HCV. He had a negative HCV test when he had entered the hospital, so he believes he contracted HCV from a blood transfusion he received during his hospitalization. After all he had been through, the news sent Pablo into a spiral of depression.

At the time Pablo was diagnosed in 2004, there was no treatment available for HCV in Argentina. However, he was told there were treatments being researched that soon might be available. He had a biopsy in 2004 that showed he only had a low level of liver fibrosis from the virus at that point, so Pablo hoped that treatments would be developed before his HCV developed into cirrhosis.

In 2007, Pablo was enrolled in a HCV treatment program using peg-IFN and RBV at the public hospital. A second liver biopsy showed that his fibrosis had progressed, but still was not at the level of cirrhosis, making him a good candidate for peg-IFN treatment. He was told there was a 40% chance of treatment success for a person with his genotype, but the fact that he was also infected with HIV lowered his chances.

According to Pablo, “The treatment attacked my spirit.” While Pablo also had side effects of pain, weakness, and anemia, the worst part of it all was his mood swings and irritability. As his treatment progressed, he made a habit of going up into the mountains with a backpack full of ice packs and his peg-IFN vials to administer his treatments in a soothing environment, with the sounds of a river and birds to keep him calm.

After four months of peg-IFN treatment, PCR testing revealed that HCV was still detectable in Pablo’s blood. His peg-IFN was stopped. The treatment had been a failure. “It was like a bucket of cold water. I was in hell,” Pablo recalls. After all his suffering and waiting for a treatment to be developed, he was still left living with the virus. Pablo’s depression deepened and he had to leave his job, unable to work because of his emotional state at the time.

In the course of his HIV and HCV treatment, Pablo joined support groups and he slowly became more involved with his new friends. They convinced him to come to a national meeting of HIV activists. Pablo “listened, participated, and made more friends.” His



new friends got him involved in the fight to make HIV treatment affordable, and soon Pablo found himself taking a leadership roles in the Red Argentina de Personas Viviendo de VIH (Argentina Network of People Living with HIV). For the last three years, Pablo has served as the Secretary of this national network, building a collaboration of similar networks across Latin America. Their most recent focus has been lobbying to make Atripla (a single, daily pill combining three ARVs) affordable for those with HIV.

Pablo is excited about the release of SOF in Argentina. “They say it’s practically a cure, but we’ll have to see at what price,” he explains. When asked if he is interested in trying the new treatments to make a second attempt at curing his HCV, Pablo eagerly answers “Yes! Of course!” but he worries that at the prices that are currently being charged, it will be a long time before peg-IFN-free DAA therapy will be available to the people of Argentina. Pablo is already thinking about how he can mobilize the co-infected members of his HIV activist network to make DAA treatment possible for himself and his people.

v. Improving HCV Treatment Delivery and Prevention

Improvements in health care delivery systems are required to provide universal access HCV treatment. Universal access to HCV treatment for those in LMICs, including for PWID, is essential to cure HCV patients and prevent future infections.

Access to HCV treatment will not only require affordable medication, but also strengthening of health care systems and development of new models of care that can effectively deliver treatment. The development of new DAAs and point-of-care HCV RNA testing provides the opportunity to shift away from traditional reliance on specialists in the diagnosis and treatment of the disease. To effectively deliver HCV treatment and bring the epidemic under control, LMICs should strongly consider:

- Developing public health-based HCV treatment programs drawing on the successful lessons from similar approaches to HIV treatment;
- Integrating HCV prevention, screening, testing and treatment into primary care;
- Integrating HCV prevention, screening, testing and treatment with drug rehabilitation harm reduction programs to reach the most marginalized and vulnerable populations with high HCV prevalence; and
- Prioritizing HCV treatment for vulnerable populations, with high transmission rates, especially PWID, in order to use treatment as an effective prevention measure.

PUBLIC HEALTH-BASED APPROACH TO HCV TREATMENT

The systems for delivering care for HCV in LMICs are inadequate and are a major barrier to expanding access to treatment for the disease. In the USA, HCV treatment traditionally has been provided by gastroenterologists: physician-specialists in liver disease (and other digestive system diseases).¹⁹⁴ However, if HCV treatment is to become widely accessible in LMICs,

this model of treatment must change. There are simply not enough specialists currently practicing in LMICs to make HCV treatment widely available with this model. For example, many African countries do not have a single gastroenterologist in the entire country.¹⁹⁵ One solution to this problem would be to improve human resources for health in LMICs—training the physicians needed to provide specialist care to all those suffering from HCV—but the development of human resources required would be time-consuming and costly. While developing more physician expertise is an important long-term goal, people living with HCV should not have to wait for specialists to access care. The public health-based approach to treatment of HIV in LMICs provides a model for extending access to HCV treatments in resource-limited settings.

WHO recommends a public health approach to HIV treatment in resource-limited settings that relies on standardized treatment regimens and integrated health care teams.¹⁹⁶ While HIV treatment in a high resource setting tends to be highly individualized with frequent monitoring and switching of regimens, the adoption of standardized first-line and second-line regimens allows for the provision of HIV ARV treatment by non-specialists.¹⁹⁷ The public health approach to HIV treatment depends on decentralized integrated health teams that are overseen by physicians, but make extensive use of nurses, community health workers, and community members living with HIV/AIDS to initiate care, ensure continued compliance, and monitor treatment.¹⁹⁸ While treatment regimens are frequently adjusted in high resource settings in response to changes in viral load, HIV viral loads are typically not monitored in the public health approach to HIV treatment. Instead of checking viral loads, a patient's symptoms are monitored as a proxy for treatment efficacy to conserve resources. Treatments are adjusted and additional viral loads are measured only when a patient's clinical condition begins to deteriorate. Though this approach may be modified to include viral

load monitoring in the future, this basic model has been the backbone of treatment scale-up for HIV for close to a decade.¹⁹⁹

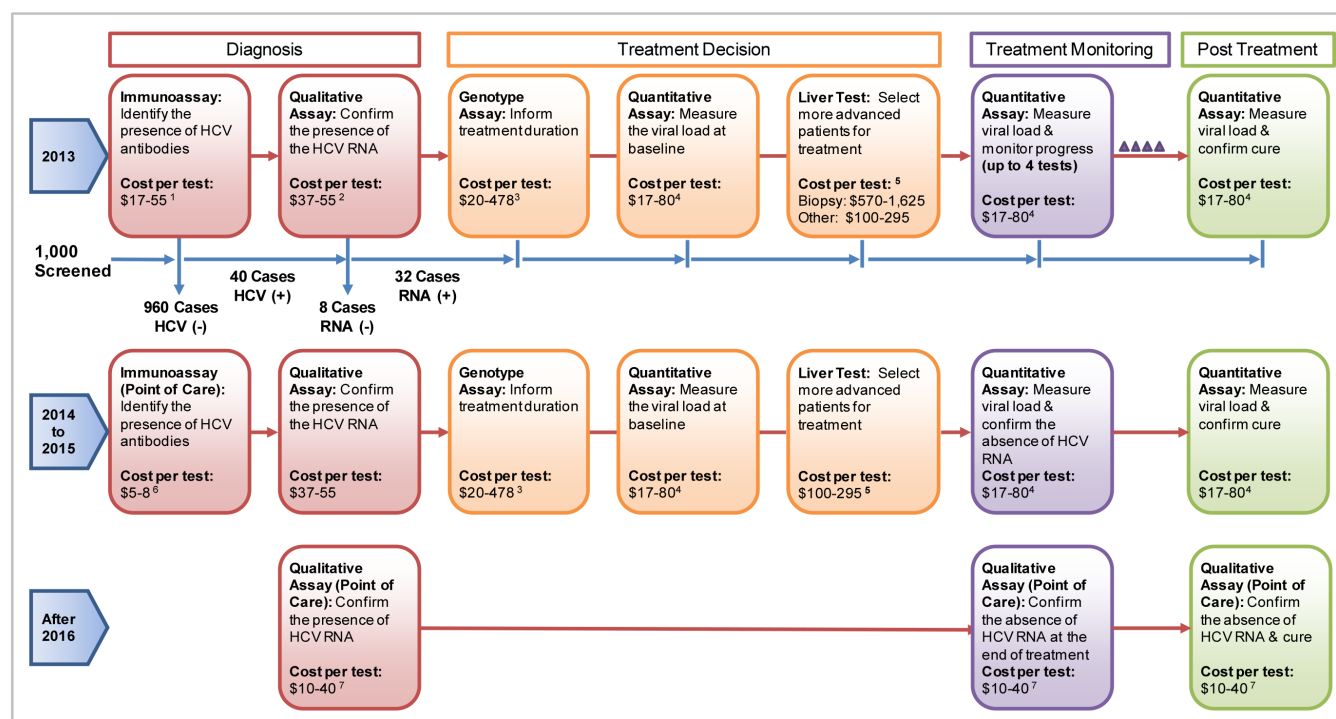
The public health approach to HIV treatment has allowed ARV therapy to be successfully delivered to millions of people worldwide living in resource-limited settings. While the model of care is different and simpler than in resource-rich countries, clinical trials have shown the effectiveness of the public health approach is comparable to what is seen in places with more complex models of care.²⁰⁰

In the past, treatment of HCV required a battery of complicated diagnostic tests and peg-IFN-based treatment caused serious side effects that needed to be constantly monitored. However, DAAs and the new

point-of-care HCV RNA tests provide the opportunity to revolutionize the way HCV is treated, opening the door for a simplified and streamlined public health-based approach to HCV treatment.

As safe, tolerable, pan-genotypic, oral DAA regimens enter the market, anyone with confirmed HCV infection will become medically eligible for these treatments. This will eliminate the need for genotype testing and liver biopsies for staging of cirrhosis to determine treatment eligibility. Furthermore, rather than using the current multi-step laboratory process for diagnosis and treatment monitoring (HCV Ab test, HCV RNA, and HCV viral load testing pre-, post-, and mid-treatment), new point-of-care qualitative HCV RNA and HCV antigen tests are nearing release to the market, allowing

Figure 3. Simplified HCV diagnostic paradigm, today and in the future in a resource-limited settings



The above figure illustrates a simplified evolution of diagnostic technologies in a resource constraint setting. After 2016, the focus of the analysis was to illustrate the preferred technologies in regions where testing at a central laboratory is not feasible or it is more efficient to test patients locally rather than send samples away to a central laboratory.

1. Rein et al., 2012 estimated a range of \$17-\$55 (92); Medicare/Medicaid 2013 reported \$27-37 per test (93); point-of-care OraSure test was estimated at €14 or \$19 according to MSF report.(5)
2. Medicare/Medicaid 2013 reported \$37 per test (93); MSF reported a range of \$49-\$55 for Roche COBAS test; for future therapies, MSF reported a cost \$20 per test for the reagents for the Wave 80 test.(5)
3. Medicare/Medicaid 2013 reported \$478 per test (93); MSF reported a cost of \$20 for the reagents for the Sacace test which is not approved in the US and a cost of \$50 for the reagents for the reagents for the Wave80 test.(5)
4. Medicare/Medicaid 2013 reported \$80 per test (93); MSF reported a cost of \$42-64 for the reagents for the Roche COBAS tests, \$22 for the reagents for the QIAGEN test, and \$17 per test for the reagents for the Sacace test; it also reported a reagent cost of \$40 per test for Wave80, which is a pipeline product.(5)
5. McGarry et al., 2012 reported an average biopsy cost of \$570 (94); in other studies, liver biopsy cost was estimated at \$974-1,623 per patient and Fibrotest cost was estimated at \$100-295.(95) (96)
6. Point-of-care CD4 tests were used as an analogue for point-of-care immunoassay test for HCV with a cost of \$5-8 per test (97). Test prices for Dakari, MBio, and Zymyx CD4 tests were included in this analysis. The cost per test would be as low as \$2 if flow cytometers were considered. Qualitative RNA test are more complex.
7. HIV tests were used as an analogue for HCV. Cepheid's GeneXpert's price per cartridge is estimated at \$10, bioMérieux's nucliSens HIV Solution average price was estimated at \$24, and Abbott RealTime's price was estimated at \$25-40.(97)

SOURCE: WOUTER DEELDER ET AL., "HEPATITIS C MEDICINES AND DIAGNOSTICS IN THE CONTEXT OF HIV/HCV CO-INFECTION: A SCOPING REPORT," UNITAID (2013): 21.

a relatively cheap (10-40 USD) and quick means of assessing whether a patient is infected with HCV. Future diagnostic protocols could be simplified to a single point-of-care HCV test with oral DAA treatment beginning in the same visit. Monitoring of treatment to assess progress and SVR could be accomplished with just two subsequent qualitative HCV RNA tests or a single post-treatment HCV antigen test. A simple model like this, with only two to three HCV tests and a standardized oral DAA regimen would be easy to implement and would not require specialist physicians or advanced laboratory support. ^{201,202}

One concern raised about the decentralization of HCV treatment without frequent monitoring by physicians could lead to the development of drug resistance. ²⁰³ Indeed, interruption in treatment with antivirals has been shown to lead to development of resistance in some resource-poor settings. ²⁰⁴ However, HCV would present less risk for the development of viral resistance compared to HIV, as the duration of treatment can be as short as 8-12 weeks, compared to a lifetime of ARV therapy for HIV. In addition, when public health approaches to treatment are properly implemented they can ameliorate the interruptions in treatment that lead to the development of resistance. Preventing treatment interruptions requires a stable drug supply chain, as well as involving the community in promoting treatment adherence. In many places, people living with HIV/AIDS have served as counselors to those on treatment and their support has improved patient adherence to these medications in resource-limited settings. ²⁰⁵

Recommendations:

- *Develop a public health-based HCV treatment programs drawing on the successful lessons from similar approaches to HIV treatment.*

A PRIMARY CARE - INTEGRATED HCV TREATMENT APPROACH

The push for expanding access to HIV treatment has often been criticized for its focus on a single disease, rather than on the broader health needs of resource-limited communities, and that it has crowded out many other more cost effective health interventions. ²⁰⁶ Critics of these disease-specific or vertical programs have argued that limited funding might be better

spent on health services more generally, in order to allow prioritization of those interventions that deliver the largest impact on health for the money. Yet, the health sector in many LMICs is weak and waiting for a robust health system before addressing the mortality associated with AIDS would require a delay measured in years or decades before offering treatment for HIV. Moreover, many of these critiques of the vertical nature of HIV treatment programs are based on outdated notions of how these programs work. Integration of HIV treatment into primary care has been a focus of many in the field for a decade or more. ^{207,208}

Health systems need focus and breadth. HCV treatment programs need not wait for the strengthening of health care systems overall before being initiated and mounting a response to the HCV epidemic should not be delayed. However, these programs can be integrated into primary care programs and offer a chance to strengthen health systems at the same time. Expanding access to the HCV treatment though will require a move away from specialist care, which will be easier as the pan-genotypic DAAs and new point-of-care RNA tests become more available.

Recommendations:

- *In LMICs with strong primary care systems, integrate HCV prevention, screening, testing and treatment into primary care.*

A TREATMENT APPROACH TO PEOPLE WHO INJECT DRUGS (PWID)

Developing effective treatment delivery strategies for PWID is especially important in controlling the HCV epidemic. HCV treatment programs for PWID achieve similar SVR rates compared to the general population. ²⁰⁹ Data from HIV treatment programs show us that treatment integration with harm reduction services, such as opioid substitution therapy and needle and syringe programs, can improve treatment adherence and clinical outcomes even further. Adherence rates to HIV treatment among PWID increased by 50% when provided alongside methadone treatment. ²¹⁰ Integration of HCV treatment into community-based harm reduction programs for PWID is critical in engaging this population effectively. Treatment of PWID, in combination with infection prevention efforts, is essential in stemming the spread

of HCV and bringing the epidemic under control. Including PWID in the planning and execution of these programs will be critical to gaining their trust and respect, and to the success of efforts in this community.

Furthermore, providing access to HCV treatment for PWID is a matter of human rights. A 2013 report by the United Nations Special Rapporteur on torture and other cruel, inhuman, or degrading treatment or punishment addresses this issue in the context of HIV/AIDS treatment:

“The common practice of withholding anti-retroviral treatment from HIV-positive people who use drugs, on the assumption that they will not be capable of adhering to treatment, amounts to cruel and inhumane treatment, given the physical and psychological suffering as the disease progresses; it also constitutes abusive treatment based on unjustified discrimination solely related to health status.”²¹¹

Similarly, denying PWID access to treatment for HCV, whether treatment is withheld at a local facility or as a matter of national policy, should be considered an abusive and discriminatory practice prohibited by international law. Indeed, the United Nations Committee on Economic, Social, and Cultural Rights (UNCESCR) has also stated that “health is a fundamental human right indispensable for the exercise of other human rights.”²¹² Specifically, the right to non-discrimination with respect to health means that “health facilities, goods and services must be accessible to all, especially the most vulnerable or marginalized sections of the population, in law and in fact, without discrimination on any of the prohibited grounds.”²¹³ More broadly, UNCESCR has affirmed that “[w]ith respect to the right to health, equality of access to health care and health services has to be emphasized.”²¹⁴ This extends to the allocation of health resources: “[f]or example, investments should not disproportionately favour expensive curative health services which are often accessible only to a small, privileged fraction of the population, rather than primary and preventive health care benefiting a far larger part of the population.”²¹⁵ Discriminatory treatment also may run afoul of national constitutions and official policies that guarantee equal rights to citizens.

Recognizing such concerns, WHO released new Guidance on the Prevention of Viral Hepatitis B and C among People Who Inject Drugs in 2012 “based on a six-part framework of human rights, access to health care, access to justice, the acceptability of services to people who use drugs, health literacy and integrated service provision.”²¹⁶ Specifically, the Guidance calls on policymakers to “establish and enforce antidiscrimination and protective laws, derived from international human rights standards, in order to eliminate stigma, discrimination, and violence faced by PWID and to reduce their vulnerability to infection with viral hepatitis and other bloodborne infections,” while asking health care providers and institutions to “serve PWID based on the principles of medical ethics and the right to health.”²¹⁷

Governments should follow WHO’s lead and specifically prohibit the exclusion of PWID from HCV treatment programs. Governments should also reform existing drug control policies that exacerbate the HCV epidemic, such as the criminalization and incarceration of PWID and prohibitions or restrictions on harm reduction services including needle and syringe programs. Low-threshold harm reduction services are instrumental in engaging PWID, assisting them in ameliorating the harms associated with drug use and serving as an entry point for PWID into other social and health services. Supporting the introduction of harm reduction programs is important for the success of efforts to control HCV because harm reduction services can provide an essential gateway to HCV treatment and an improved quality of life for PWID.

Recommendations:

- *Integrate HCV prevention, screening, testing and treatment with drug rehabilitation and harm reduction programs to reach the most marginalized and vulnerable populations with high HCV prevalence.*
- *Increase use of harm reduction services, including peer-led harm reduction programs, at a scale proportional to the need.*
- *Reform punitive laws that penalize, stigmatize, and alienate PWID in order to facilitate engagement in treatment.*

PREVENTION OF NEW INFECTIONS VIA HCV TREATMENT

Treatment is not only important for curing those with HCV, but also essential for preventing new HCV infections. Globally, PWID bear the burden of the majority of new HCV infections that occur each year. Despite the fact that up to 90% of new HCV infections occur among PWID,²¹⁸ less than 10% of PWID worldwide benefit from harm reduction services, including opioid substitution therapy and needle and syringe programs that might prevent these infections.²¹⁹ An even lower percentage of PWID who are infected with HCV (2-4%) are believed to be currently receiving treatment for their infection.²²⁰ Many policymakers still believe “that ‘active injectors should not be treated’ and should be ‘forced’ to discontinue their illicit drug consumption before being considered for antiviral therapy.”²²¹ In many countries, PWID face mass incarceration, where drugs remain readily available but harm reduction services are commonly denied.²²² Unsurprisingly, rates of HCV infection are particularly high in parts of Eastern Europe and Asia with strict anti-drug policies, like Russia and Thailand.²²³

Recent studies have demonstrated that increasing the number of PWID treated may be an effective primary prevention tool for reducing HCV prevalence rates among this population. Projections of the potential impact of treatment on HCV prevalence among PWID found that annually treating 10 infections per 1000 injecting drug users results in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% in the context of pre-treatment prevalences of 20%, 40%, or 60%, respectively.²²⁴ In another projection, based on the Australia—where only 1% of PWID are currently receiving treatment—if HCV treatment were increased to 10% of PWID, the HCV prevalence among this marginalized population would be reduced by 30% from its current level (assuming 45% prevalence of HCV infection).²²⁵ As these estimates are based on peg-IFN-based treatment regimens, the possible preventative effects of all-oral DAA regimens are likely to be much greater.

Recommendations:

- *Prevention strategies for HCV infection should include harm reduction-based services for PWID, especially*

with PWID participation in program planning.

- *Governments should prioritize PWID for HCV treatment and develop appropriate targeted services and support as this strategy could offer a way to reduce overall prevalence of the disease by preventing many new infections.*

ANCHALEE, 45 YEAR-OLD DOCTOR, PATIENT, AND ACTIVIST, BANGKOK, THAILAND

Anchalee has worked tirelessly to provide desperately needed treatment for HIV and HCV infected patients in Thailand. Based in Bangkok, she raises awareness among patients and policymakers about HCV and HIV. She runs a clinic for drug users, and works with civil society groups to develop national treatment guidelines for HCV.

She has experienced the debilitating effects of HCV first-hand. She contracted HCV from a needle stick injury in 1997 during her time as a medical resident. Initial follow-up tests were negative, but she began to experience symptoms three months later and got re-tested. This time, it was positive. Because she was working at a publicly funded university hospital, she was able to access treatment. Original, non-pegylated interferon had just been released in Thailand and she began receiving injections three times a week. “It was horrible for me because it was the pure interferon. I was training at the infectious disease department at the university and worked 6am to 10pm but I had fever, headache, nausea.” She was treated for 8 months, but her doctor realized it was not working. Her doctor then began treating her with a higher dose of peg-IFN combined with RBV and she was eventually cured.

Anchalee acknowledges that in some ways she was lucky. She was able to access treatment that remains unaffordable for many because she worked for a hospital. Most of her patients do not have that option. In February of 2014, she screened 100 HIV-coinfected patients but many could not benefit from government-funded HCV treatment because they cannot take interferon and DAAs are not currently covered. At the time of her interview, two of her patients were close to death. “I don’t know what to do. It is frustrating. I want to help them but I do not [know] how [to] get them health care.” Even with the new drugs, the pricing is still a barrier. “The negotiating [on drug prices] has focused

on LICs, but how about middle-income countries like Thailand and Indonesia? We have a lot of patients. Focusing on LICs ignores the fact that people in middle-income countries cannot access these drugs. We would very much like to have sofosbuvir. It should not only be focused on the least-developed countries. There is more need for treatment here.”

The lack of political will to take action against HCV frustrates her. This is in part due to the stigma associated with HCV. She points out that there is a perception that HCV infections are only related to drug



use. PWID have a particularly difficult time accessing treatment. “It is hard for a marginalized population like drug users since in Thailand there is still a law against drug use.”

However, she remains optimistic things will change: “We did it for HIV.” She points out that there has been progress since she first contracted the disease but more needs to be done. Governments need to collect epidemiological data, and most importantly drug prices should be lowered.

VII. Conclusion

We stand at a critical juncture in the HCV epidemic. For the first time, effective, safe, tolerable, and easy-to-administer treatments exist for HCV. While more people are infected with HCV today than ever before, there is more hope than ever that HCV can be eradicated. There is light at the end of tunnel, but still a long way to go.

Many barriers to HCV eradication exist, including inadequate epidemiologic data, the high price of drugs and diagnostics, a lack of funding for widespread HCV programs, and inadequate models of care and support. These, and other obstacles, all stand in the way but are not insurmountable. In this report, we have laid out key barriers to universal HCV treatment access and steps to overcome them.

The world has faced a similar juncture before. In the 1990s, HIV/AIDS treatment was not considered an option for LMICs. Today, dedicated funding, lower drug prices, and innovations in healthcare delivery—driven by activists who pushed

governments to make HIV/AIDS a priority—have revolutionized the response to the epidemic. Today, millions of people in LMICs can access HIV/AIDS treatment as a result.

This success can be repeated. We are at a critical turning point for HCV. With a growing global network of activists for HCV treatment, it is only a matter of time before governments and other institutions respond to the call for access. The light at the end of the tunnel is growing brighter every day.

HCV eradication is no longer a dream. With recent therapeutic advances, eradication has become a possibility. If we work to overcome the barriers to treatment, eradication can become a reality in our lifetimes.

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Addendum to *Ending an Epidemic: Overcoming Barriers to an HCV-Free Future*

Below are key updates that have occurred since the report, *Ending an Epidemic: Overcoming Barriers to an HCV-Free Future*, was written.

- On February 9, 2015, researchers published in the journal *Hepatology* new estimates of the predicted minimum costs of diagnostic monitoring and HCV treatment using new direct acting antivirals (DAAs). According to the report, “minimum costs of treatment and diagnostics to cure HCV were estimated at US\$174-354 per person without genotyping and US\$264-444 per person with genotyping.” Nikolien van de Ven et al., “Minimum target prices for drug production of direct-acting antivirals and associated diagnostics to combat hepatitis C virus,” *Hepatology*, 2015, <http://dx.doi.org/10.1002/hep.27641>.
- On January 30, 2015, the Delhi High Court set aside the Indian Patent Office’s order rejecting Gilead’s patent application for Sovaldi due to “procedural irregularities.” The Court remanded the application back to the patent office for reconsideration, including taking into consideration pre-grant oppositions filed by I-MAK and other organizations. Adheesh Nargolkar & Nisha Austine, “Delhi High Court sets aside Patent Office order rejecting Gilead’s patent application for Hepatitis C drug Solvadi on procedural grounds,” *Khaitan & Co.*, Feb. 4, 2015, <http://www.lexology.com/library/detail.aspx?g=dc51e9c5-c801-4644-ba67-6cd8a33cb480>.