



ACTIVIST STRATEGIES

**for Increasing Access to
HCV Treatment in
Low- and Middle-Income
Countries**

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TAG
Treatment Action Group

Activist Strategies for Increasing Access to HCV Treatment in Low- and Middle-Income Countries

We hope this guide, which owes a great debt to the many committed activists whose work it describes, is useful to people who are developing HCV treatment access campaigns and programs in low- and middle-income countries.

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ABOUT TAG'S HEPATITIS/HIV PROJECT

TAG's Hepatitis/HIV Project draws from the core values and history of HIV activism, while incorporating hepatitis C-specific information into strategies targeting different constituencies, regions, and countries. The Hepatitis/HIV Project focuses on optimizing quality of, and broadening access to, HCV care and treatment for communities and individuals by continuing its domestic and international work with other activists, regulatory agencies, pharmaceutical companies, clinicians, and the patient community.

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Treatment Action Group

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INTRODUCTION

Liver disease from hepatitis C virus (HCV) is one of the leading causes of death around the world. At least 185 million people have been infected and almost 500,000 people die from it each year. The hope for eradicating HCV has recently gained new momentum: effective treatments reaching a 100 percent cure rate in clinical trials are now available. But unaffordable drug prices and expensive diagnostic tools are keeping HCV cures from the majority of people who need them—those living in low- and middle- income countries (LMICs).

There are many significant barriers to HCV eradication: the lack of accurate epidemiological data, which are necessary for development of policies, programs, and resource allocation; the criminalization of people who inject drugs and the banning of harm reduction programs, which perpetuate ongoing HCV infection; and the absence of global and national political will (with few exceptions) to address the epidemic.

But AIDS activists have developed and implemented successful strategies to overcome similar challenges in addressing the HIV epidemic. From Johannesburg to New York, Río de Janeiro to Bangkok, activist-driven policies have helped more than 10 million people gain access to HIV treatment. Antiretroviral therapy (ART) has saved 4.2 million lives in LMICs—despite the belief among policy makers and world leaders that doing so would be impossible.

While HCV and HIV differ in significant ways (for example, HCV can be cured with short-course treatment, while HIV treatment is lifelong), lessons learned from three decades of AIDS activism are useful for the growing HCV activist movement.

Activist Strategies for Increasing Access to HCV Treatment in Low- and Middle-Income Countries

presents a number of key strategies through real-world case studies and shows how strategies used to combat the AIDS epidemic can be—and have been—adapted to increase HCV treatment access.

These strategies are introduced in three sections:

Section One: Laying the Groundwork through Community Organizing

- Strategy 1: Framing HCV Treatment and Prevention as Basic Human Rights, Particularly for Injection Drug Users
- Strategy 2: Organizing People Living with HCV for Community Education and Mobilization
- Strategy 3: Forming Alliances with Local, Regional, and Global Organizations to Influence Policy
- Strategy 4: Demanding Global HCV Policies and Funding Streams

Section Two: Overcoming the Cost Barriers to HCV Treatment Access

- Strategy 5: Negotiating Lower Prices with Drug Companies
- Strategy 6: Challenging Intellectual Property Barriers through Patent Oppositions
- Strategy 7: Overriding Patent Barriers through Compulsory Licenses and Parallel Importation

Section Three: Collaborating with Researchers to Build Your Case for HCV Treatment Access

- Strategy 8: Using Mathematical Modeling to Predict Cost-Effectiveness and Public Health Benefits of HCV Treatment
- Strategy 9: Advocating for Policies and Programs Based on Evidence Provided by Operational Research

SECTION ONE: LAYING THE GROUNDWORK THROUGH COMMUNITY ORGANIZING

Campaigns to overcome barriers to affordable HCV treatment need support from a strong grassroots foundation. This section will discuss four major components of this foundation: establishing a human rights framework for advocacy; educating the community to build grassroots demand for treatment; convincing national policy makers of the need to prevent and treat HCV; and seeking funding from global donors to support national governments to implement programs.

STRATEGY 1: Framing HCV Treatment and Prevention as Basic Human Rights, Particularly for Injection Drug Users

Repressive drug policies are ineffective, violate basic human rights, generate violence, and expose individuals and communities to unnecessary risks. Hepatitis C is one of these harms—yet it is both preventable and curable when public health is the focus of the drug response. Now is the time to reform.

—Global Commission on Drug Policy (2013)

Injection drug users are one of the most marginalized groups in society. The political response to drug use is to punish and incarcerate rather than to treat. In most countries, harm reduction services such as needle and syringe programs (NSPs) and opioid substitution therapy (OST) are banned.

Criminalization drives drug users underground, keeping them away from essential health care and harm reduction services. People are much less likely to get tested for HIV and HCV, or seek drug treatment or health care, when they risk arrest and imprisonment. When essential harm reduction interventions are not funded, or are illegal, people can't protect themselves from preventable infections such as HIV, hepatitis B, and hepatitis C.

Under these circumstances, it is not surprising that 90 percent of new HCV infections are in injection drug users. Outside sub-Saharan Africa, one in three new HIV infections is injection drug use-related.

Criminalization of drug use causes negative health consequences to millions of people. This is a clear violation of human rights. Article 25 of the United Nation's Universal Declaration of Human Rights states, in part:

Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services.

Member states of the United Nations (UN) are legally bound by signing its human rights treaties to respect, protect, and fulfill human rights obligations for all, in particular the most vulnerable groups.

People who use drugs have long been at the forefront of national, regional, and international efforts to ensure that their human rights are recognized. Meaningful participation is recognized by the World Health Organization (WHO) as essential to a human rights–based approach to health:

In relation to health, a rights-based approach means integrating human rights norms and principles in the design, implementation, monitoring, and evaluation of health-related policies and programmes. These include human dignity, attention to the needs and rights of vulnerable groups, and an emphasis on ensuring that health systems are made accessible to all... Integrating human rights into development also means empowering poor people, ensuring their participation in decision-making processes, which concern them and incorporating accountability mechanisms, which they can access.

—WHO, Human Rights-Based Approach to Health

Around the world, drug user activists and their allies have successfully used this strategy.

Key human rights–based arguments are:

- Thirty-two countries use the death penalty to punish drug offenses. Extrajudicial executions (or state-sanctioned killings) have also been reported, and arrests without cause are common. These policies violate drug users’ rights to freedom from arbitrary arrest, detention, torture, and other cruel, inhumane, and degrading treatment and punishments, under the UN International Covenant on Civil and Political Rights.
- When harm reduction services—namely NSPs and OST are prohibited, people who need them are put at high risk for acquiring HIV and HCV. Criminalization of drug use and possession creates a climate of fear and stigma, putting drug users at higher risk of dying from acute and chronic diseases. Even when they do seek health care, HIV and HCV treatment are often withheld from drug users due to discrimination. These policies violate drug users’ rights to health, well-being, and equal access to services under the International Covenant on Economic, Social and Cultural Rights.

CASE STUDY:

Activists have monitored human rights abuses in their communities, and use their documentation of violations to garner support from powerful regional or global allies to advocate for better programs, policies, and laws.



The Thai Drug Users’ Network (TDN) is an activist group founded by injection drug users and people living with HIV. TDN was established on International Human Rights Day (December 10) 2002 in Bangkok as a grassroots response to a government drug eradication campaign in 2003, when at least 2,800 people suspected of drug offenses were murdered and tens of thousands of others were forced into drug detention camps. They also protested against the Thai government’s inaction in addressing the country’s severe AIDS crisis among drug users.

Human rights violations commonly experienced by drug users in Thailand at the time included:

- police harassment, abuse, and detention without due process;
- extrajudicial executions; and
- denial of health care and harm reduction services.

TDN members started by learning about basic human rights and the Thai government's legal obligations to uphold them. TDN members became empowered with this information. They developed campaigns to demand justice for the drug-related killings, access to clean injection equipment and OST, and access to HIV treatment. Strategies included:

- educating allied nongovernmental organizations on harm reduction and the human rights of people who use drugs;
- meeting with health and justice ministries and the Thai parliament;
- appealing to the UN to conduct health impact assessments of the Thai drug war; and
- holding street protests to end the government crackdown on drugs.

Given the repressive legal and policy situation and the Thai government's inaction, TDN chose to bypass the traditional government-led process for applying to the Global Fund to Fight AIDS, TB and Malaria (GFATM). Instead, they submitted a groundbreaking proposal directly to the GFATM. Four community-based organizations (TDN, Thai AIDS Treatment Action Group [TTAG], the Raks Thai Foundation, and Alden House) were granted US\$1.3 million over three years to develop and scale up community-based NSPs and HIV services (counseling, testing, and referrals to treatment) in central, northern, and southern Thailand.

As the result of TDN's human rights-based campaigns, the Thai government instituted a national harm reduction policy. Now, it covers OST under its national health care program, and tacitly supports peer-run NSPs.

RESOURCES:

Asia Catalyst. *Know It, Prove It, Change It: A Rights Curriculum for Grassroots Groups*. Available at: http://asiacatalyst.org/nonprofit_survival_skills/.

Count the Costs. *The War on Drugs: Undermining Human Rights*. Available at: http://www.countthecosts.org/sites/default/files/Human_rights_briefing.pdf.

Global Commission on Drug Policy. *The Negative Impact of the War on Drugs on Public Health: The Hidden Hepatitis C Epidemic*. Available at: <http://www.globalcommissionondrugs.org>.

Médecins du Monde and International Network of People Who Use Drugs. *Nobody Left Behind*. Available at: <http://www.hepcoalition.org/IMG/pdf/201406-mdm-policy-vhc-en-web.pdf>.

United Nations. *Universal Declaration of Human Rights*. Available at: <http://www.un.org/en/documents/udhr/>.

World Health Organization. *2014 Viral Hepatitis Resolution*. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R6-en.pdf?ua=1.

STRATEGY 2: Organizing People Living with HCV for Community Education and Mobilization

As an activist, I never thought of HIV in relation to health. That is what inspired me and other colleagues to form the Treatment Action Campaign. We realized that unless you know about your illness, how to treat it, the dangers of your treatment, and the political and economic context in which you need treatment, you are not going to survive the epidemic.

—Zackie Achmat, South African AIDS activist

The lack of awareness about HCV prevention, transmission, diagnosis, and treatment is a major barrier for activists who want to address the epidemic in their communities. HCV is sometimes called a “silent killer” because people with HCV can live healthy lives for decades without symptoms. During this time, liver disease develops and can worsen. But hepatitis C can be treated—and now, with new drugs, usually cured.

Most people with hepatitis C have not been diagnosed. Tests that are used to tell whether someone has ever been infected with hepatitis C (called screening) and to confirm that a person has the actual hepatitis C virus in her or his bloodstream (called diagnostics) are often unavailable or—in the case of diagnostic tests—prohibitively expensive, especially in LMICs.

Since most people are unaware that they have hepatitis C, and access to treatment is so limited, less than five percent of the estimated 185 million people with hepatitis C receive treatment.

HIV and HCV are both transmitted through contaminated injection equipment. Most HIV-positive injection drug users also have HCV. Communities of people living with HIV began to become aware of hepatitis C after they fought for access to treatment and regained their health. They started to see friends and family members get sick and die from liver disease caused by HCV. The lack of information and services spurred activists to organize themselves, starting by asking the some basic questions: What is HCV? Why is it important to know about? and What can we do about it in our communities?

CASE STUDY: Lessons from a community-driven HIV movement

In the 1990s, people with HIV in Thailand launched a campaign for universal access to health care with one slogan: “Why are medications so expensive?” Within a decade, Thailand was a widely praised success story in the global response to AIDS. Today nearly half of all people who need treatment receive it for free under a national health care program.

In Thailand, the role of people with HIV was central to effective HIV treatment scale-up. Their self-empowerment and advocacy movement was a response to the lack of information on a disease that people in their communities are dying from. When people realized that the information would not be forthcoming from the government, they found the information themselves and educated their own communities.

The Thai Network of People Living with HIV/AIDS created an HIV 101 curriculum of basic HIV/AIDS information developed and implemented by and for peers. Today, tens of thousands of people have been through these peer-driven trainings. This community education strategy has provided an important foundation for activists to galvanize demand for treatment and to mobilize their communities to engage their governments. HIV treatment-access activists have used similar strategies effectively across the globe.

Where to find the information you need

Contact local hospitals to see if they have hepatitis C information or materials, and if local hepatitis, infectious disease, or gastrointestinal doctors or nurses are available to provide additional information and support. Hepatitis C materials are often not provided in a community-friendly or advocacy-oriented way. If there is no HCV information available in local languages or in the format you need, look to national, regional, or global networks for resources. Frequently, you can get help from the people who produced the information and collaborate with them to adapt it to your community's needs. When planning educational workshops, find local health care providers who are knowledgeable about HCV to help develop or co-conduct the medical parts of your meeting.

How to move from information to action

Engaging in a process of learning about an issue relevant to one's community often leads to action. Communities often find that simply acquiring information about an issue like HIV or HCV is not sufficient. Once people begin to discuss these issues, questions emerge about why certain information, tools, tests, and treatments are not available. Typically, gaining access to information feeds a hunger for more knowledge and leads to discovering and ultimately overcoming access barriers.

For example, when learning about HCV screening and diagnostics, find out what tests are available in the community, and at what price. Ask workshop participants if they know of people who have been tested, and if they haven't been tested, why this might be. Bringing information close to home and discussing its real-life relevance is a basic strategy for mobilizing communities.

CASE STUDY: International collaboration to increase access to HCV information and education



Even where there is information about HCV, it may be overly medical, or written at a literacy level that is too high for a particular community. It may leave out key considerations critical for a particular group of people, such as drug users. That is why many communities choose to produce their own educational materials. The process of creating this information for a community can raise awareness that “knowledge” is often produced and not neutral. Taking control of information—what is important to know and how to communicate it—can become a key component of community empowerment.

Thai AIDS Treatment Action Group (TTAG) in Bangkok works with many people living with HIV and people who inject drugs. Some started finding out that they were coinfecting with HCV, and realized the information they needed was not in their language, or available from where they accessed services, such as harm reduction programs. TTAG reached out to Treatment Action Group (TAG), a New York-based research and policy think-tank with an activist-oriented hepatitis/HIV project, to co-develop a community-driven hepatitis C education and advocacy curriculum, focused on the needs of injection drug users and people living with HIV in Thailand.

Key steps of the TTAG/TAG collaboration:

- Conduct community consultations about HCV and HIV/HCV information, to find out what people already know, and what they want to learn.
- Develop a draft curriculum based on what Thai communities wanted to learn, including an advocacy discussion section at the end of each chapter to stimulate action at the community level.
- Invite a committee of community members to review the draft curriculum content and add their feedback.
- Hold a pilot “Training of Trainers” workshop with Thai people with HIV, people who inject drugs, and people with hepatitis C, to test the draft curriculum; adapt and revise in response to community feedback.
- Finalize the curriculum and translate into Thai; have another community review and finalize the Thai version.
- Develop a work plan and fundraising strategy (TTAG) to enable the rollout of the curriculum.
- Revise a policy brief on HCV and HIV/HCV coinfection for national-level advocacy.

Key outcomes of the collaboration:

- Thousands of people with HIV, people with HCV, and people who inject drugs were trained in a broad range of basic HCV and HIV/HCV coinfection issues. Many have become effective trainers at the local, district, or provincial level.
- Informed community members started to advocate to have HCV treatment added to the national essential medicines list, and provided at no charge. They worked to remove discriminatory policies that excluded them from receiving treatment.
- Lessons from the Thai HCV treatment education and access movement have been presented at international conferences and meetings.

RESOURCE:

Kaplan K, Swan T. *Training Manual for Treatment Advocates: Hepatitis C Virus and Coinfection with HIV*. Available at:

<http://www.treatmentactiongroup.org/hcv/publications/training-manual-hcv-hiv>.

STRATEGY 3: Forming Alliances with Local and Regional Organizations to Influence Policy

An ally can be a doctor or researcher, a lawyer in a human rights organization, a staff member in a UN agency, or a regional network of people living with HIV/HCV. Allies can help make an otherwise impossible advocacy goal possible. Seeing this in action can be extremely heartening to advocates who often face constant rejection and pushback while working on difficult challenges.

Generally, allies can help you:

- improve your strategy by explaining how a particular system works and how it can be changed;
- offer solidarity and increased protection through numbers and visibility, especially with controversial or politically dangerous issues;
- help reach and persuade your advocacy target (someone with an ability to end the problem); and
- provide additional human, financial, and other resources.

It is important to understand what a specific ally can offer before asking for help. This way you will not waste their time and both parties can be clear about the purpose of the collaboration.

Local, regional, or international activist networks: In March 2014, four global networks issued a collective press release in solidarity with participants of the first HCV World Community Advisory Board (CAB) meeting, which was held to strategize and fight for increased access to HCV treatment. The press release described the outcome of its meeting with six pharmaceutical companies. The Global Network of People Living with HIV/AIDS (GNP+), the International Network of People Who Use Drugs (INPUD), the International Treatment Preparedness Coalition (ITPC), and the Global Forum on MSM and HIV (MSMGF) were able to shine a spotlight on HCV treatment access to tens of thousands of their members working on similar issues. Their collaboration started a dialogue about the ways people can address HCV treatment access in their own communities.

Progressive government officials: Some of your best allies may be midlevel civil servants, ministers, or other officials in your local or national government. They may be willing to help take the lead on pushing for policy changes or funding proposals. They may be in a position to get hard-to-find health statistics, monitor policy implementation, or cut through red tape from within the system. Sometimes they can set up meetings with key officials or help increase visibility by cosponsoring a forum on your issue.

Researchers, doctors, and nurses: Researchers can provide important data about the local epidemic or how well new diagnostic tools and treatments work.

Doctors and nurses may be just as frustrated by the lack of access to lifesaving drugs as activists, because they cannot treat people without them. Doctors can share information at community education forums and provide technical advice to ensure that medical information activists provide is current and accurate. They can establish treatment guidelines that ensure people get the best possible care—and work with activists to get enough funding to provide it. Working with doctors and nurses adds legitimacy to activist demands and can help open doors to government officials.

CASE STUDY: Ukraine: mobilization of communities to create treatment demand



Ukrainian activists have galvanized a national movement to increase access to HCV treatment. In Ukraine, an estimated 1.3 million people—or three percent of the population—has hepatitis C, but access to treatment is scarce. Activists realized that a national plan was needed to address Ukraine’s hepatitis C epidemic. They worked with their government to develop a national plan that greatly improved access to testing and treatment.

1. The International HIV/AIDS Alliance (Alliance Ukraine) established the **All-Ukrainian Network of NGOs** (the Network), bringing together community representatives, experts, advocates, and patient groups from across the country to focus on HCV. Many of these groups had worked for 15 years on harm reduction activities across the country.
2. The Alliance Ukraine conducted targeted trainings on hepatitis C for medical professionals, patients, and activists and started to integrate HCV prevention services into harm reduction programming.
3. They increased awareness about hepatitis C by holding regular public events that included HCV screening in all Ukrainian regions. They did outreach to local and national media, which covered these testing events. Once people were tested, they were motivated to seek care, and they began to demand access to HCV treatment at local and national government health care facilities.

After this successful HCV awareness and testing campaign, the Ukrainian government responded by creating a national hepatitis plan. The Network pushed for more funding so that the national program would cover as many people as possible.

- Activists met with representatives from companies that make HCV diagnostics and drugs to provide a realistic picture of the HCV epidemic in Ukraine. They argued for lower prices, given the number of Ukrainians living with hepatitis C.
- Activists and patient groups pushed the government to offer a tender to treatment and diagnostics companies for them to submit their best-price bids to sell their products in Ukraine. The tender created price competitions and in the process lowered prices: the Ukrainian government got Merck to reduce the price of one of its hepatitis C medicines, pegylated interferon (PEG-IFN). Before these negotiations, a 48-week treatment course cost US\$16,000; the Ukrainian government lowered it to US\$5,000.
- They advocated for inclusion of drug users and people living with HIV on local decision-making commissions to ensure that people from these groups had access to HCV treatment programs and a say in how they were designed.
- The Alliance Ukraine and partners are working with local and national authorities to develop treatment guidelines and models of care for providing HCV treatment to people on opioid substitution therapy, showing that treatment for this key population is effective.

RESOURCE:

In 2012, a new global HCV activist movement—**HepCoalition**—came together. It is a global coalition of individuals and organizations working for universal access to affordable HCV testing and treatment. The group has representation from nearly every continent. Members communicate via an e-mail listserv to share information on drug development, debate advocacy strategies, and support each other’s local work through technical assistance and connections to needed expertise. Members organize meetings and launch campaigns to lower drug prices and demand HCV leadership from the WHO. New working groups often form when members want to focus on a specific issue, such as patent oppositions as a means to overcome access barriers. To get involved, visit <http://www.hepcoalition.org>.

STRATEGY 4: Demanding Global HCV Policies and Funding

At least 185 million people have been infected with hepatitis C, and nearly 500,000 die from it each year. Yet the global response to HCV has been feeble. One of the major barriers—the difficulty of treating hepatitis C—is gone: new safe, effective oral drugs can cure HCV, usually in 12 weeks. But several obstacles to HCV eradication remain: surveillance is inadequate; many countries do not have national plans or evidence-based testing, care, and treatment guidelines; and there is a lack of funding. International political leadership is needed to overcome these barriers.

Act globally

Though the UN system can seem remote, impenetrable, and less relevant than national governments for grassroots activists, it is a crucial advocacy target. The World Health Assembly (WHA) at the UN is the decision-making body that dictates policy for the WHO. Activists have successfully advocated for policies through the WHA that are sometimes more favorable to people with HCV than are the policies in their own countries.

Activists may interact with the UN on HCV issues in a number of ways, including:

- monitoring the WHO’s viral hepatitis policies and guidelines;
- participating in the UN meetings that are open to civil society members, including activists;
- holding agencies accountable to their promises and plans; and
- making sure that community participation is inclusive of a broad range of activists, and that marginalized groups—such as injection drug users, sex workers, migrants, people living with HIV, and other affected groups are represented.

CASE STUDY: Demanding global leadership



In 2010, a viral hepatitis resolution was passed at the UN WHA. The resolution mandated leadership from the WHO. But the WHO’s Director-General, Margaret Chan, did not lead the agency to adequately respond to the HCV pandemic. Activists from the **HepCoalition** launched the “Missing” campaign to hold Dr. Chan accountable and demand leadership.

Armed with demands and posters, activists launched the campaign at the 2013 International Harm Reduction Conference in Vilnius, Lithuania, to generate support from organizations around the world. The campaign circulated an online sign-on petition to Dr. Chan, gathering nearly 2,000 signatures. Posters and postcards in eight languages were available on the coalition website for activists to use in their own local campaigns. On World Hepatitis Day, 2013, coalition members delivered the petition to the WHO office in New York City; afterward, they protested outside of the office to generate press attention for the campaign.

As a result of the “Missing” campaign, the WHO:

- established and convened a permanent Strategic and Technical Advisory Committee on Viral Hepatitis, which includes activists from HepCoalition, to advise Dr. Chan;
- held a broad civil-society consultation on viral hepatitis and issued the *Call to Action to Scale Up Global Hepatitis Response*;

- established a permanent Civil Society Reference Group on viral hepatitis; and
- released its *Guidelines for the Screening, Care and Treatment of Persons with Hepatitis C Infection*.

Activists kept up the pressure in 2014 with a “Still Missing” campaign during high-level WHO meetings where an updated WHA resolution on viral hepatitis was being developed. They successfully lobbied to get more government cosponsors for the new resolution—especially in countries where the HCV burden is high. They pushed for the inclusion of harm reduction services and access to generic drugs for LMICs in the resolution.

When it came to a vote, a much-improved viral hepatitis resolution passed unanimously. As a result, the WHO, member governments, and other stakeholders are now expected to increase their commitment to address viral hepatitis. The new resolution is an important tool that activists can use to expand HCV treatment access in their countries.

RESOURCES:

HepCoalition. *Defuse Hepatitis C, the Viral Time Bomb: Test and Treat Hepatitis C*. Position Paper for the 67th World Health Assembly, May 19–24, 2014. Available at: <http://hepcoalition.org/advocate/advocacy-tools/article/defuse-hepatitis-c-the-viral-time>.

HepCoalition. *Missing Campaign*. Available at: <http://hepcoalition.org/advocate/campaigns/missing/article/missing>.

Sixty-Seventh World Health Assembly. *The 2014 WHA67.6 Hepatitis Resolution*. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R6-en.pdf.

CASE STUDY: Removing barriers to global HCV donor support

The World Health Organization Essential Medicines List (EML) is a list of medicines the WHO considers essential to a basic health care system. Many governments refer to the WHO recommendations to inform decisions on health care spending. When a drug is included on the WHO EML, it is more likely to appear on a country’s national EML and be given priority for coverage.

Adding HCV treatment to the WHO’s EML sends an important signal to global donors. **Médecins Sans Frontières/Doctors Without Borders (MSF)**, a global health advocacy group with significant clout and visibility, decided to push the WHO to include pegylated interferon (PEG-IFN) as part of the standard of care for hepatitis C virus on its EML. MSF did not proceed alone because it understood that support from allies added significant value and helped amplify its demand. In solidarity, Treatment Action Group (TAG) developed a guide for activists to explain why adding PEG-IFN to the WHO’s EML could influence global donors and thereby empower LMIC governments to start treatment programs. TAG disseminated the guide and appealed for letters of support via HCV and HIV activist networks. Ultimately, hundreds of signatures and letters were collected from people with HCV and from high-profile allies including the executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATAM), the UN special rapporteur on the right to health, and leaders of regional UNAIDS agencies.

WHO technically considers only medical evidence when determining whether to place a drug on its EML. But the campaign forcefully demonstrated that HCV is of major concern to a broad range of people across dozens of countries, and that they are looking to the WHO

for leadership on this critical issue. In the end, PEG-IFN made it onto WHO's complementary EML instead of the main list, given concerns about its cost. It is a partial victory, but there were other positive results: MSF developed new allies, and activists around the world connected with powerful leaders in the emerging global HCV advocacy movement.

RESOURCES:

Treatment Action Group. *Support Inclusion of Pegylated Interferon in the World Health Organization's Essential Medicines List*. Available at:

<http://www.treatmentactiongroup.org/hcv/pegifn-who-eml-support-letter>.

World Health Organization. *WHO Model Lists of Essential Medicines*. Available at:

<http://www.who.int/medicines/publications/essentialmedicines/en/>.

Demanding global HCV funding

The creation of global funding pools was critical for HIV treatment scale-up in low-income countries. Unlike with AIDS, there is currently no dedicated global funding mechanism to pay for HCV prevention, diagnostics, or treatment. Activists have been calling on two international funding organizations to start addressing HCV.

- **The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM)** is the largest funder for HIV globally, providing billions of dollars to governments and civil-society organizations to address local and regional epidemics. The GFATM currently supports a small number of HCV treatment slots in several countries and supports access to HCV information and testing via harm reduction programs. Currently, the GFATM board of directors is considering whether to continue funding HCV treatment.
- **Unitaid (UTD)** is an organization financed by airline taxes. It helps reduce prices by shaping the market for treatments and diagnostics for HIV/AIDS, malaria, and tuberculosis in low-income countries. UTD has included HCV in its 2013–2016 strategic objectives, and in May 2014 committed up to US\$20 million to advance access to HCV treatment for people coinfecting with HIV and to facilitate negotiating prices for HCV diagnostics. Ultimately, this investment will benefit all people with HCV.

SECTION TWO: OVERCOMING THE COST BARRIERS TO HCV TREATMENT ACCESS

Access to essential medications is a human right that governments must uphold. Governments have a vested interest in securing the lowest price for a medication so that they can treat the greatest number of people. This section discusses several strategies activists have used to lower drug prices: using public pressure to force originator drug producers to lower their price; challenging intellectual property barriers to generic drugs through patent opposition; and working with governments to issue compulsory licenses. Often, these strategies will need to be deployed together to increase HCV treatment access.

STRATEGY 5: Negotiating with Drug Companies to Lower Drug Prices

Price negotiations between companies and governments usually happen behind closed doors. One way activists can influence pricing is by establishing community advisory boards (CABs) that meet directly with representatives from pharmaceutical companies. By meeting with activists, companies can gain insight about local social and economic factors that can influence pricing decisions.

Activists are also instrumental in creating community demand for testing and treatment programs from governments and international health agencies, creating funding streams and drug markets that otherwise would not exist.

CAB meetings are also opportunities for activists to obtain information from companies, share local treatment access strategies, and formulate united regional or global price reduction demands. Drug companies are sensitive to negative public images. Activists have successfully used publicity pressure to force price reductions for some countries.

Learning about originator-company pricing tactics that inhibit treatment access is key to formulating effective strategies and arguments to lower drug prices. These tactics include:

- delayed registration,
- tiered pricing, and
- restrictive voluntary licensing.

How originator companies price their drugs

Originator drug companies are secretive about how they set drug prices. Activists have challenged the companies to be more transparent and disclose how they make their pricing decisions, but they have consistently refused to do so. One common explanation given by the companies for high drug prices is their need to recoup research and development (R&D) costs—though many experts believe companies actually spend more money on advertising and marketing. Public funding also subsidizes treatment R&D in the form of drug discovery conducted by university-based and government research institutions.

“Opportunity costs”—meaning what companies could have invested in the development of other, more profitable products instead—add to drug pricing.

Drug prices and actual production costs

Andrew Hill from the University of Liverpool and colleagues compared the production cost of new HCV direct-acting antivirals (DAAs) with those of similar HIV drugs. They found that actual production costs of the new DAAs—if increased to millions—would be no more than a few hundred U.S. dollars per treatment course.

Table 1. Predicted costs of key drug combinations

Combination treatment	Daily dose, mg	Duration, weeks	Predicted cost, US\$
MK-8742 + MK-5172	50+100	12	\$118
Daclatasvir + sofosbuvir	60+400	12	\$121
		24	\$242
Sofosbuvir + ledipasvir	400+90	8	\$129
		12	\$193
Sofosbuvir + ribavirin	400+1200	12	\$149
		24	\$298

Source: Hill A, van de Ven N, Simmons B, et al. Minimum target prices for production of treatment and associated diagnostics for Hepatitis C in developing countries (Abstract LBPE12). Poster presented at: 20th International AIDS Conference; 2014 July 20–25; Melbourne, Australia.

Blocking generic drug competition

The availability of generic HIV drugs has been—and continues to be—critical to bringing down drug prices. Generic competition helped reduce the price of first-line HIV drugs by 99 percent within a decade, from US\$10,000 to under US\$100 per person per year. Where generic drugs are available, originator companies are forced to lower their prices in order to compete. To prevent this from happening, originators use many anticompetitive tactics to block the entry of generic drugs.

Industry tactic: Delaying registration

Before drugs can be marketed in a country, they must be registered—approved for use by that country’s regulatory authorities. Registration policies and processes differ by country, but data on quality, safety, efficacy, and other characteristics of pharmaceutical products usually must be provided. Some regulatory authorities accept data from trials conducted in other countries, but others require originator and generic drug producers to conduct local studies.

For generic drugs, a full clinical development program is not necessary, but the drugs must demonstrate bioequivalence—meaning that they must contain the same active pharmaceutical ingredients, route of administration (e.g., oral), formulation (e.g., capsule or tablet), dosing (e.g., once-daily), and rate of absorption—as the originator products.

Originator companies may delay or fail to register their drug in a country. Where a drug is not registered, countries will not be able to import the drug legally or produce a generic version domestically. Failure to register effectively blocks access to the drug.

Activist demand: Originator companies should register their drugs in all countries where there are people living with the relevant disease

Industry tactic: Tiered pricing of originator drugs

An originator's initial drug price is set in a high-income country, where the drug is developed—and the primary market where a company can make most of its profit. Companies then use the initial drug price as the standard to set up pricing tiers (also called differential pricing or marketing segmentation) for LMICs. These tiers are based on each country's gross national income (GNI, an economic development indicator set by the World Bank) and other factors—which companies do not disclose—rather than what is affordable for governments.

Multinational pharmaceutical companies consider middle-income countries (MICs) as emerging markets. Yet MICs have the greatest income inequality. According to the World Bank, nearly 75 percent of the world's poorest people (earning less than US\$1.25 a day) live in MICs. Tiered prices in MICs are usually too high, leaving governments unable to address large epidemics such as HCV. When MIC governments cannot provide medicines, people must pay for the drugs themselves. Most people cannot afford them.

Activist demand: Global donors should demand that originators' tiered pricing formulas be transparent and be based on the actual income level of people who need HCV treatment, not the GNI

Industry tactic: Voluntary licensing of generic drugs

Originators hold patents on drugs they develop. They can grant voluntary licenses (VLs) that allow another drug company to manufacture a generic version of their drug. The patent holder sets conditions and may receive a fee or royalty. VLs allow originators to control the market by limiting the countries licensed to produce and sell generics. Countries that are not included in licensing agreements must buy more expensive drugs from the originator companies. VLs can include additional restrictions, such as the number of people who can be treated, what drugs can be co-formulated, and which suppliers must be used for the active pharmaceutical ingredients (APIs) needed to make drugs.

Activist demand: Generic drug producers and governments should reject restrictive voluntary licenses

CASE STUDY: Gilead's VL for HCV DAAs

In the United States, Gilead charges US\$84,000 for a three-month course of sofosbuvir—about US\$1,000 a pill. Sofosbuvir is needed most in MICs, where HCV and poverty are rampant. MICs are home to 130 million people with hepatitis C.

As of 2014, Gilead had registered and licensed sofosbuvir (Sovaldi) in only one middle-income country: Egypt. Gilead sells Sovaldi to the Egyptian government for US\$900 for a three-month treatment course. But the private-market price—for people who do not have insurance—is expected to be much higher, at US\$9,000. This will be unaffordable for uninsured Egyptians, where the average annual income is US\$3,314. Sofosbuvir can be made for far less; the analysis of production costs from Andrew Hill and colleagues found that three months of sofosbuvir could be mass-produced at a profit, and sold for as little as US\$101.

Gilead announced voluntary licensing agreements for generic sofosbuvir in 91 LMICs in September 2014. The company did not offer licenses for generic sofosbuvir to five of the 20 countries with the largest number of hepatitis C cases (China, Brazil, the Philippines, Ukraine, and Turkey): approximately 38 million people. Instead, Gilead chose to include several sparsely populated countries with smaller epidemics, such as Antigua and Barbuda, Dominica, Nauru, Seychelles, and Tuvalu—where less than 2,000 people have hepatitis C. This is a common industry tactic: beefing up the scope of the license for public relations purposes, while keeping what they see as more lucrative markets to themselves.



In response, the HepCoalition produced an activist tool to help educate health ministers and policies makers in LMICs about the problems with VLs. They created a list of myths and facts to counter Gilead's claim that they are helping to expand HCV treatment access through VLs.

RESOURCES:

HepCoalition. *Gilead's License on Hepatitis C Drugs, Sofosbuvir and Ledipasvir: A Fool's Bargain—Myths and Facts*. Available at:

<http://www.hepcoalition.org/news/article/gilead-s-license-on-hepatitis-c>.

Hill A, Khoo S, Fortunak J, Simmons B, Ford N. *Minimum Costs for Producing Hepatitis C Direct-Acting Antivirals for Use in Large-Scale Treatment Access Programs in Developing Countries*. *Clinical Infectious Diseases*. Apr 2014;58(7):928–936. Available at:

<http://cid.oxfordjournals.org/content/58/7/928.long>.

Kaplan K, Swan T. *The Road to Treatment Access*. *TAGline*, vol. 21, no. 2, October 2014. Available at: <http://www.treatmentactiongroup.org/tagline/2014/fall/road-treatment-access>. The preceding case study was adapted from this article.

Médecins Sans Frontières. *Untangling the Web of Antiretroviral Price Reductions*.

Available at: <http://www.msfaccess.org/content/untangling-web-antiretroviral-price-reductions-17th-edition---july-2014>. This pricing guide published by MSF lists the

prices of various HIV drugs worldwide. The lack of clear information on drug prices is a significant barrier to improving access in developing countries. While no equivalent guide to the price of HCV drugs yet exists, activists have used their networks and the international HCV coalition listserv to obtain HCV drug prices to inform their treatment access strategies.

CASE STUDY: Promoting access to biosimilar PEG-IFN

PEG-IFN is a synthetic, or man-made, version of the interferon protein made in the body to fight infections. It is a biologic, rather than a chemical drug, and must be produced in living cells. For this reason, biosimilars—cheaper, generic versions of a biologic—are harder to make than generic drugs. Proving their safety and efficacy to regulatory authorities requires expensive clinical trials, and the guidelines for doing so are unclear.

Access to PEG-IFN is still important for millions of people in LMICs who have advancing liver damage from hepatitis C that need to be treated now. They cannot wait for affordable HCV DAAs. But brand name PEG-IFNs, made by Roche and Merck, can cost up to US\$30,000 per treatment course. Biosimilars of PEG-IFN are available (produced in Egypt and India) and under development (in Brazil and Cuba), but the difficulties in determining their quality, safety, and efficacy—and proving they do the same job as the originals—create critical access barriers in many countries.

Activists have been calling on the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the WHO to help create a clear and simple path to approval so that more biosimilar PEG-IFNs can enter the market and create the price competition needed to increase access.

The WHO can also facilitate prequalification of biosimilars according to standards they set, including ensuring biologic manufacturers' compliance with Good Manufacturing Practices. This is particularly important because biologics like PEG-IFN have complex structures, which may vary from batch to batch. Impurities from the manufacturing process—or in the product itself—can trigger an immune response (called *immunogenicity*) that may cause acute or delayed hypersensitivity reactions or injection-site reactions, and may reduce treatment efficacy.

Without clear regulations about manufacturing and approval, it is difficult to find information about the development and regulatory status of biosimilar PEG-IFNs. But the existence of a biosimilar has already brought the price of PEG-IFN down in Egypt, where Roche and Merck were forced to compete with the price of the Egyptian-made biosimilar PEG-IFN (Reiferon Retard, made by Minapharm). The competition led to lowered prices for the Roche and Merck products—around US\$2,000 per treatment course.

While Thailand, Georgia, and Ukraine have also successfully negotiated PEG-IFN price reductions with Roche or Merck, the reduced prices are not low enough to enable those governments to treat all who need the drug. Without biosimilar competition, further price reductions—such as those obtained by the Egyptian government—will be difficult to secure.

RESOURCES:

Couzin O, Kaplan K. *Pills Cost Pennies, Greed Costs Lives—1st HCV World CAB Report*. Available at: <http://www.treatmentactiongroup.org/hcv/publications/wcab-report-2014>. The preceding strategy was adapted from this report.

Swan T. *Access to Hepatitis C Treatment: A Global Movement Gains Momentum*. TAGline, vol. 17, no. 3, October 2010. Available at: <http://www.treatmentactiongroup.org/tagline/2010/fall/access-hepatitis-c-treatment-global-movement-gains-momentum>. The preceding case study was adapted from this article.

STRATEGY 6: Challenging Intellectual Property Barriers through Patent Oppositions

Patent protection on new drugs is a major barrier to lifesaving treatments for people in LMICs because it eliminates generic competition, allowing brand name–drug companies (originators) to sell their drugs at astoundingly high prices. Activists have filed patent oppositions to overcome this hurdle. While this strategy requires a significant time and resource commitment, they can and have been successfully implemented.

Understanding Patent Laws

In most countries, originators can apply for patent protection for the drugs they develop. A patent grants the originator the exclusive right to sell the drug in a country, prohibiting a third party (such as a generic drug manufacturer) from producing, distributing, selling, or importing the drug for a certain length of time. The patent is applicable only in the country in which it was granted.

Internationally, the World Trade Organization’s (WTO) 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) drastically strengthened the power of the pharmaceutical industry, subjecting treatment access to market pressures and corporate greed. Under the agreement, WTO member countries must allow patent protection with a minimum term of 20 years in order to conduct international trade.

Patent oppositions involve reviewing the merits of a pharmaceutical patent application in your country and determining whether the patent should be granted (pre-grant opposition) or revoked (post-grant opposition). Each country sets its own criteria for patentability.

A pre-grant patent opposition is when a third party, such as an activist group, is granted the right to submit evidence on patentability. For example, U.S.-based Initiative for Medicines, Access & Knowledge (I-MAK) with the Delhi Network of Positive People (DNP+) was allowed to contest the patentability of sofosbuvir in India. In January 2015, the controller of the Delhi Patent Office ruled in IMAK/DNP+’s favor.

A post-grant patent opposition allows for the invalidation of a patent that has already been granted. For example, in 2013, China revoked Gilead’s patent on tenofovir on the grounds that it lacked novelty. Generic companies in China can now produce tenofovir domestically, decreasing its price.

Finding information regarding drug patents can be difficult; often patent offices and pharmaceutical companies do not publicize patent information, or they release information that is not easily accessible or useful. Few country patent databases are digitized.

I-MAK’s *Patent Landscape Report for Pegylated Interferon Alfa 2a and 2b* provides information and increases transparency on PEG-IFN patents worldwide. Available at: <http://essentialdrugpatents.com/hepcdatabase.php>.

Table 2: Status of patents that block biosimilar PEG-IFN access in the countries with the highest HCV prevalence

Product	Patent Type	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
Pegasys	A	✓	✓	✓	✓	X	?	✓	?	✓
	B	X	?	X	X	✓	~	✓	~	X
	C	?	?	?	?	?	?	?	?	?
	D	X	?	X	X	✓	~	✓	~	X
PegIntron	A	X	?	X	X	X	~	X	?	X
	B	X	?	X	X	✓	~	X	~	X
	C	X	?	X	X	✓	?	X	?	X

✓ = Patent granted X = No patent found ~ = Patent pending ? = Information not available

I-MAK is currently researching the patent landscape for new HCV DAAs. Originators will often apply for patents that protect their DAA in every possible way, making it harder for generic drug manufacturers to challenge these barriers. They include patents that protect the:

- active pharmaceutical ingredients (APIs);
- intermediate compounds needed to make the API;
- different formulations and dosages (even though only one might be used);
- processes for manufacture; and
- different drug combinations (i.e., drug cocktails); and
- different methods of use (e.g., treatment of HIV or HCV).

CASE STUDY: PEG-IFN patent oppositions in India

Before 2005, patents on drug products were not allowed in India, but patents for drug processes could be granted. The minimum patent duration was only seven years. As a result of this unique situation, India emerged in the early 2000s as one of the world's leading exporters of generic drugs. Between 2006 and 2010, 80 percent of generic HIV drugs were supplied by India. India's generic drug industry makes it an important country for HCV as well, since it has the potential to produce and export generic HCV medications.

In 2005, India reformed its patent laws to conform to the TRIPS Agreement. Following the change, the first patent protection granted by India was to Hoffmann-La Roche (Roche) for its version of the HCV treatment PEG-IFN (Pegasys). Having gained a monopoly, Roche began to sell Pegasys at US\$8,752 for six months of treatment, more than 10 times the average annual income in India (US\$830).

Hoping to spur generic and biosimilar competition by removing this patent barrier, **Sankalp Rehabilitation Trust**, a Mumbai-based NGO providing HIV/AIDS and HCV care and education to injection drug users, submitted a post-grant opposition. Represented by the **Lawyers Collective's HIV/AIDS Unit** (a human rights group), Sankalp argued that the process used to make Pegasys was neither "novel" nor involved an "inventive step." After an initial setback, Sankalp appealed to India's Intellectual Property Appellate Board (IPAB), which ruled in favor of Sankalp in 2012, thereby revoking Roche's patent protection. Roche has since filed an appeal with the Indian High Court. The case is ongoing.

While its patent opposition case has not yet resulted in a biosimilar version of Roche's Pegasys in India, Sankalp and the Lawyers Collective's efforts were vital in setting an important legal precedent. In India, anyone can submit a pre-grant opposition, but persons submitting post-grant oppositions must have a commercial interest in the product. Sankalp argued that they represented Roche's patient population and therefore had a commercial interest, and the IPAB agreed by expanding the criteria to include patient and activist groups.

In a hopeful parallel development, a biosimilar PEG-IFN (based on Merck's PegIntron) made by the generic company Virchow has entered the Indian market. Virchow is fighting a patent infringement lawsuit filed by Merck, using the same legal argument as the one established by Sankalp vs. Roche. This case is also pending.

Before pursuing a patent opposition, it is important to first educate yourself and prepare. Activists should assess whether or not your strategy has legal grounding, or if action should be taken to advocate for a change in national intellectual property laws. Activists should find a local lawyer who specializes in intellectual property, right to health, HIV, or HCV issues. Ideally, the lawyer should have the experience and technical capacity (or at least the interest and willingness) to help with the patent opposition. Activists should also be aware of—and fight—any free trade agreements currently being negotiated, which may include higher standards of patent protections. Such standards could make patent oppositions illegal or harder to win.

Activists should share their experience with opposition procedures, whether successful or not. Where an opposition seems particularly promising, people in relevant countries can coordinate and collaborate to file oppositions at or near the same time (a recent example of this would be the pre-grant oppositions to Gilead's sofosbuvir in various countries submitted around the same time).

RESOURCES:

Initiative for Medicines, Access & Knowledge. *I-MAK Patent Landscapes*. Available at: <http://essentialdrugpatents.com/hepcdatabase.php>.

Initiatives for Medicines, Access & Knowledge. *Legal Documents for Opposition to Sofosbuvir (India)*. Available at: <http://www.i-mak.org/sofosbuvir>.

PatentOppositions.org. *Guide on How to Build Your Own Patent Opposition*. Available at: http://patentoppositions.org/how_to_build_an_opposition.

World Health Organization. *How to Conduct Patent Searches for Medicines*. Available at: <http://apps.who.int/medicinedocs/documents/s17398e/s17398e.pdf>.

World Health Organization. Analysis of the patent situation of new hepatitis DAAs. Available at: http://www.who.int/phi/implementation/ip_trade/ip_patent_landscapes/en/.

World Intellectual Property Organization. Directory of Intellectual Property Offices. Available at: <http://www.wipo.int/directory/en/urls.jsp>.

World Intellectual Property Organization. WIPO Lex. Available at: <http://www.wipo.int/wipolex/en/index.jsp?tab=3>. WIPO Lex is a database of information regarding national legislation on intellectual property laws.

World Trade Organization. *TRIPS and Pharmaceutical Patents Fact Sheet*. Available at: http://www.wto.org/english/tratop_e/trips_e/tripsfactsheet_pharma_2006_e.pdf.

STRATEGY 7: Overriding Patent Barriers through Compulsory Licenses and Parallel Importation

Another strategy to overcome patent barriers is the use of compulsory licenses (CLs). Governments can issue a CL to allow a third party to produce a patented product or process, without the consent of the patent owner—subject to an obligation of adequate payment (remuneration). The patent owner does not lose its patent under a CL; it merely shares its patent rights with a third-party manufacturer.

Article 31 of the TRIPS Agreement makes clear that CLs be used for any public interest reason, with expedited procedures and special rules applying for “public, non-commercial use,” “emergencies or matters of extreme urgency,” or to “correct anti-competitive practices” by patent holders.

If a country’s state-owned or private pharmaceutical companies lack manufacturing capacity, the government can import a drug from another country in which there is no patent or import relatively small quantities (e.g., enough to supply a clinic or for government use only) of a generic drug produced under another country’s CL. This is called parallel importation.

Article 6 of the TRIPS Agreement prohibits World Trade Organization (WTO) members from bringing claims against other members relating to parallel importation, allowing countries to comparison shop for innovator medicines that have been sold more cheaply in another country.

CASE STUDY: Fighting a legal challenge in South Africa



In 1997, South Africa passed the South Africa Medicines Act, allowing the importation of generic drugs under TRIPS. In protest, the U.S. government and multiple pharmaceutical companies and trade associations filed a lawsuit against the South African government in 1998. There was fierce public outcry.

Treatment Action Campaign (TAC), a grassroots HIV/AIDS advocacy organization in South Africa, mobilized nationally and helped create a global coalition that fought against the lawsuit. It worked with AIDS Law Project to pioneer a legal defense against the suit, submitting a request to the court to demand that originator companies release closely guarded data on their research investment.

Campaigns against the lawsuit emerged globally. MSF launched a global petition (with 300,000 signatures from individuals from 130 countries) against the 39 pharmaceutical companies, demanding that they withdraw the lawsuit. The European Union also came out in opposition to the suit. Activists in the United States, led by Health GAP (Global Access Project), launched a campaign against then–Vice President Al Gore, the co-chairman of the United States-South Africa Binational Commission. The activist group AIDS Coalition to Unleash Power (ACT UP) used the slogan “Gore’s Greed Kills” and held public actions to garner greater public awareness about the issue.

Bowing to pressure, the drug companies eventually dropped their lawsuit against South Africa. Soon after, in 2001, the WTO issued the Doha Declaration on the TRIPS Agreement and Public Health. The Declaration clarified that TRIPS “can and should be interpreted and implemented in a manner supportive of WHO Members’ right to protect public health.”

After Doha, countries began to issue CLs to combat the exploding AIDS pandemic. The majority of CLs issued in the past decade have been for HIV drugs. These have all resulted in significant price reductions and dramatic increases in the number of patients getting treatment.

CASE STUDY: CLs for HIV treatment in Indonesia



Responding to the AIDS crisis in their country, the Working Group on HIV/AIDS of the University of Indonesia's Faculty of Medicine, known as **Pokdisus**, tried various approaches to expand HIV treatment access. They directly negotiated with originator and generic companies for lower drug prices and worked with the government to provide subsidies for patients. Despite these approaches, which enabled some treatment expansion, the prices of HIV drugs were still unaffordable for most Indonesians living with HIV.

After refusals from originator companies to further reduce drug prices, Pokdisus launched the **National Movement for Improved Access to HIV/AIDS Treatment**. This broad-based coalition, including people living with HIV, health care providers, NGOs, and journalists, worked with the government to set national treatment targets, and worked with two state-owned drug companies to produce generic HIV drugs locally. After careful analysis of patent laws in Indonesia, as well as close work with the regulatory and health agencies responsible, the coalition successfully persuaded the Indonesian government to issue a compulsory CL for three HIV drugs under the "government use" option of TRIPS, via a presidential decree.

Under TRIPS Article 10, originator companies have up to three months to file legal objection, but it would not stop the CL's implementation. There were also no criteria provided on how to calculate the amount of remuneration.

The presidential decree in 2004 opened the door for state-owned drug producers to import raw ingredients from India and for generic drug producers to determine how much to pay to the originator patent holder (in this case, 0.5% of the net selling value). The originator companies failed to make legal objections, and locally produced generic HIV drugs were produced and distributed through government health centers. By 2007, the cost of a fixed-dose HIV regimen dropped from US\$800–\$1,000 a month to US\$38 a month. In 2012, Indonesia issued more CLs for second-line HIV drugs, and by 2013, more than 30,000 Indonesians were able to get HIV treatment, a fourfold increase from 2008.

CASE STUDY: Fighting back against U.S. trade sanctions in Thailand



Most countries that have exercised their right to issue a CL have experienced political backlash. Repercussions have come from multinational drug companies, the U.S. government, or both, even though technically it is illegal for the United States to interfere in countries' ability to respond to their domestic public health crises (see Doha Declaration, above). LMICs may be reluctant to issue compulsory licenses out of fear of the economic and political consequences from trade sanctions. But there are many successful examples of CLs, usually with strong grassroots activist campaigns and international NGO support.

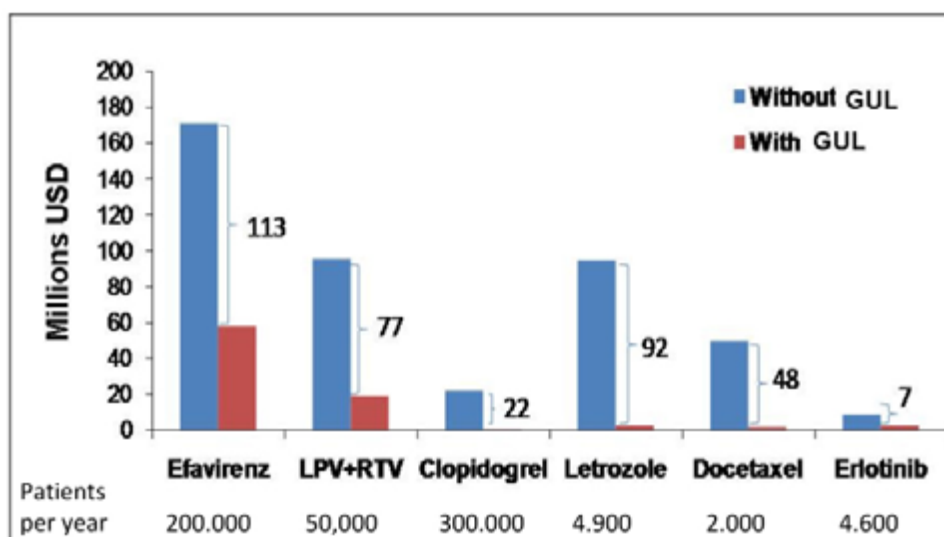
In Thailand, pressure from the **Thai Network of People Living with HIV/AIDS (TNP+)** resulted in the creation of a government price negotiation committee for the Thai universal health care plan, comprising Thailand’s Food and Drug Administration, Patent Office, and Internal Trade Department. The threat of CLs motivated some price reductions from originators, but not enough to meet the number of Thais who needed to be treated. After multiple unsuccessful negotiations with originator companies, the Thai government started issuing CLs for HIV and other diseases in 2006.

Under its CLs, Thailand was able to domestically produce, as well as import in parallel, several generic drugs—in the process greatly reducing drug prices and increasing the number of people treated.

Price Reductions as a Result of Thailand’s Compulsory Licenses

Price Reductions From 2007 - 2012

Source: Thai Ministry of Health



Source: University of Cape Town: Property Law and Policy Research Unit. Use of Compulsory Licenses Selected National Experiences. 2009 July 12. Available from: http://unctad.org/Sections/dite_totip/docs/tot_ip_0018_en.pdf.

Originator companies retaliated by withdrawing drug registrations from the Thai Food and Drug Administration, thereby withholding access to new medications. Both the American pharmaceutical industry and the United States-Association of Southeast Asian Nations (US-ASEAN) Business Council either stopped or reduced business with Thailand. The U.S. trade representative placed Thailand on its international trade watch list. Trade privileges aimed to promote economic growth were revoked for three of Thailand’s export products. Meanwhile, American and other foreign media—most prominently, the Wall Street Journal—attacked Thailand’s actions.

Activist groups fought back: TNP+ and its global allies organized protests at the multinational drug company headquarters in Bangkok and at shareholder conferences. They launched a boycott against one of the companies (Abbott) and organized an online action to temporarily shut down Abbott’s website. International health organizations came onboard to support the Thai government, including MSF, the Clinton Foundation, the European Council, and the WHO. Despite the backlash, the Thai government held firm to its decision to issue the CLs. Thailand continues to be a leading world example of a government taking full responsibility to provide

affordable treatment to all in need. Through the threat of—and eventual issuing of—CLs, the Thai government was able to lower both originator and generic drug prices for HIV, heart disease, and cancer medicines.

RESOURCES:

Public Citizen. *Examples of Compulsory Licensing for Pharmaceuticals Worldwide*. Available at: [http://www.citizen.org/documents/CL chart short version-final.pdf](http://www.citizen.org/documents/CL_chart_short_version-final.pdf).

Thailand Ministry of Public Health and National Health Security Office. *The 10 Burning Questions on the Government Use of Patents on the Four Anti-Cancer Drugs in Thailand*. Available at: http://www.moph.go.th/hot/Second_white_paper_on_the_Thai_CL_%5BEN%5D.pdf.

World Trade Organization. *Compulsory Licensing of Pharmaceuticals and TRIPS*. Available at: http://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm.

SECTION THREE: COLLABORATING WITH RESEARCHERS TO BUILD YOUR CASE FOR HCV TREATMENT ACCESS

Treatment access activists often find themselves in a catch-22 when they meet with reluctant policy makers: a country's lack of HCV testing, surveillance, or treatment programs creates an information vacuum where policy makers don't have the information they need in order to fix the problems. Questions about the scale of the local epidemic, the potential resources needed to address it, and the eventual health outcomes of an intervention are hard to answer, and can then become excuses for inaction.

STRATEGY 8: Using Mathematical Modeling to Predict Cost-Effectiveness and Public Health Benefits of HCV Treatment

Treatment access campaign demands need to be supported by convincing arguments for policy change. Policy makers may also respond better to fiscal rather than human rights arguments, particularly in times of economic uncertainty. One branch of research—mathematical modeling—and the researchers who practice it, can help overcome this barrier.

What is mathematical modeling?

Mathematical modeling uses available research data to make predictions on the public health benefits and budgetary impacts of a specific policy. It can help policy makers understand health problems at the population level and inform the development of national plans and programs.

Mathematical models can be used to:

- understand disease patterns (such as which groups have the highest disease burden and who is most at risk of transmission);
- predict the impact of interventions in different settings;
- evaluate whether an intervention has had an effect;
- estimate how much it would cost to deliver an intervention program; and
- compare the costs and benefits (such as health outcomes) of an intervention, to determine whether it is worthwhile.

Researchers from many different disciplines use and develop mathematical models. Along with people who specifically call themselves “infectious disease modelers,” health economists, epidemiologists, and statisticians also design and use mathematical models.

You and your activist community may be able to help find someone with expertise in modeling who is willing to help your campaign. The good thing about modeling is that it can be done from anywhere. Even if there isn't someone in your country who is doing it, a modeler from elsewhere might be able to work on the problem (provided there are sufficient data to work with).

What are assumptions?

Modeling predictions are only as good as the assumptions on which they are based. If a model looks at the benefit of treatment, assumptions such as how well a treatment works, what the price is, and the number of people who need it will make a big difference on what the model predicts. For a model to be useful, it needs to be credible. Therefore, the best models are realistic. For example, if a model assumes that everyone treated for HCV will be cured, it will not be taken as seriously as one that uses more realistic cure rates. A good model will be clear and up-front about the assumptions.

Some things to look out for are:

Who is included in the model? Is it the whole population of a country or only a particular risk group?

Are the sources of the base data reliable? These might include the number or proportion of people infected with the disease (prevalence), rate of new infections (incidence), and disease progression rates. If no local data are available, can information from another setting with similar epidemics be generalized for your country?

What risk behaviors are included (injecting, sex, etc.)? How were these behaviors measured? If they were self-reported, do they seem realistic?

What treatment response rate is used? Is it from data in a controlled trial or the real world, where outcomes may be worse? What uptake and drop-out rates are used? Are these rates (in the case of PEG-IFN) adjusted for HIV-coinfected individuals?

How are the costs calculated? If it is a treatment program, do the costs include staff time, buildings, transportation, etc.? Do they include other costs aside from drugs, such as doctors, nurses, and laboratory tests? What costs are associated with different disease stages? Are they country-specific?

What time frame does the model examine? Is it sufficient to account for public health and cost benefits, which may not be immediate or short term?

What are sensitivity analyses?

Researchers will re-run the model projections with different assumptions to see how much the main results change. All assumptions have some uncertainty, and it is important to show how different assumptions affect the results. For example, how do the results differ if a 60 percent treatment efficacy is used? What about 70 or 80 percent?

Limitations

Models are most useful for their ability to give general results, or estimate the probability that an outcome may be achieved. But they are theoretical—they are only what we think might happen. No model is 100 percent accurate.

It is important that model predictions are explored fully through sensitivity analyses and that real-world data are eventually generated to verify the model predictions.

CASE STUDY: Modeling HCV treatment as prevention

Currently, programs to prevent HCV transmission among people who inject drugs generally center on needle and syringe exchange programs and OST. Evidence suggests that either intervention can reduce HCV transmission by about 50 percent, but that combining them could reduce HCV risk by 80 percent. However, in many settings with high coverage of these interventions (such as the United Kingdom), the number of people with chronic HCV remains high. It's clear that we need to quickly find a new way of tackling the problem.

Recently, HCV treatment has been proposed as a form of prevention, eliminating forward transmission. Once people are cured, they cannot transmit HCV to others. However, as INPUD and MdM have noted, "biomedical solutions should not be used as an excuse to undermine proven, community-based prevention programs," namely harm reduction services, and should be accompanied by activities to reform punitive drug policy.

Modeling HCV treatment as prevention

Researchers have used mathematical modeling to try to determine the population impact, cost-effectiveness, and affordability of HCV treatment as prevention strategy. The models are dynamic, in that a person's risk of acquiring HCV is related to the prevalence in a particular setting. Where the prevalence is very high, a person's risk of infection or reinfection is high. If few people are infected, then the risk of infection is low.

One model done by Natasha Martin and colleagues showed that scaling up HCV treatment using PEG-IFN and ribavirin for people who inject drugs (PWID) could reduce transmission in the population. Using a 60 percent cure rate (based on clinical research data), this model showed that modest, achievable levels of treatment (5–20 of 1,000 PWID treated each year) could dramatically reduce the proportion of people infected in a range of settings (20, 40, or 60 percent chronic prevalence of HCV among PWID). Less impact is seen if lower cure rates are used (which may be the case in settings with large numbers of PWID coinfecting with HIV and HCV), but substantial reductions in prevalence could still be achieved. This work is supported by another modelling study done by Nicolas Durier and colleagues that predicted substantial prevention benefit of HCV treatment for PWID in Vietnam.

These models counter the argument that reinfection is a reason for delaying or denying treatment to injection drug users and provide activists with a science-based rationale for HCV treatment scale-up for prevention.

Recently, modeling has been used to explore the potential impact and affordability of future interferon-free DAA treatments. Natasha Martin and colleagues modelled HCV epidemics among people who inject drugs in three settings: Edinburgh, Scotland; Melbourne, Australia; and Vancouver, British Columbia. Their analysis showed that HCV prevalence among PWID could be halved within 15 years with achievable levels of treatment in each setting. A 90 percent cure rate was assumed from 2015 onward, and slightly less impact was seen if an 80 percent cure rate was assumed. Another sensitivity analysis showed that it didn't matter whether treatment was given only to those who are "low risk," because PWID often circulate between high and low risk stages (such as when they are on or off opiate substitution therapy). However, it was estimated that halving prevalence could require drug-only treatment costs of US\$3.2 million a year in Edinburgh, and over US\$50 million a year in Melbourne and Vancouver.

These models demonstrate that new HCV DAAs could be even more effective at preventing transmission, but affordability will be a key issue. These analyses can be used to help convince LMIC governments of the necessity of HCV drug price negotiations.

Modeling analyses have highlighted the importance of scaling up traditional harm reduction interventions (such as OST and high-coverage NSPs) alongside HCV treatment. The study by Natasha Martin and colleagues showed that scaling up harm reduction reduces HCV prevalence among injection drug users and can also reduce the number of HCV treatments needed in a setting.

As many LMICs have low coverage of traditional harm reduction interventions, activists can use these analyses to argue for a combination strategy of increased harm reduction and HCV treatment.

We still need real-world evidence on the impact of treatment on HCV transmission, and whether expanding access to treatment will be affordable for low- and middle-income countries. And we need more data to demonstrate that providing treatment to injection drug users is effective in tackling the HCV epidemic in the long run.

RESOURCES:

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STRATEGY 9: Advocating for Policies and Programs Based on Evidence Provided by Operational Research

Just a decade ago, when AIDS activists pushed for expanding access to HIV treatment in LMICs, some policy makers and global donors questioned the feasibility of scaling up treatment in settings without well-developed health care infrastructures. Similar excuses are now surfacing with regard to HCV. While practical considerations about the availability of diagnostic tools, drug distribution and storage, and clinic staffing are important, the feasibility and effectiveness of treatment in resource-limited settings can be demonstrated through well-designed pilot programs and documented through operational research.

Operational research conducted by MSF provided the evidence that HIV treatment programs are feasible in LMICs and that the possibility of HIV treatment access is a powerful incentive for individuals to get tested. Subsequent operational research has also demonstrated that drug users can adhere to treatment and that a decentralized, simplified model of treatment delivery by nurses was feasible in rural South Africa and other settings.

These research results were used to convince governments and global funders to support and implement HIV treatment programs. Operational research can—and will—play an important role in activists' efforts to expand HCV treatment access.

What is operational research?

Operational research collects and analyzes information on the quality and effectiveness of a specific intervention in a real-world setting. It is designed to answer questions that have direct, practical relevance to guiding policy and improving health care delivery.

CASE STUDY: Using cross-sectional surveys to gather epidemiological data

Specific details about the size of a local HCV epidemic, population affected, particular strains of HCV (genotypes), and urgency of treatment needs are important for the development of effective HCV control and treatment programs. These data are usually generated by time-consuming and costly populationwide surveillance. Cross-sectional surveys can reduce the time and expense by sampling a representative subset of the population.

Médecins du Monde (MdM, Doctors of the World) has conducted a cross-sectional study to document the HCV treatment needs and genotype distribution among PWID in Tbilisi, Georgia. MdM collaborated with New Vector, a support group of drug users providing harm reduction services, and Hepa+, a patient organization of people living with hepatitis C in Tbilisi, to design a study in a representative sample of PWID in Tbilisi. The survey of 216 PWID showed a high rate of infection: 82 percent had chronic HCV; most had HCV genotype 3 (66.9%) although mixed-genotype infections were relatively common. Severe liver fibrosis was found in 24.2% of the group.

Based on this information, MdM was able to estimate that about 5,000 of the PWID in Georgia have severe liver disease and need HCV treatment. The study was published in a peer-reviewed medical journal, providing a credible evidence base for activists to demonstrate the urgent need for HCV treatment programs and, reinforced ongoing advocacy for scaling up syringe exchange and opiate substitution therapy programs to prevent further HCV transmissions in Georgia.

MdM is conducting follow-up studies to evaluate the feasibility and effectiveness of providing strong peer-supported HCV treatment program for injection drug users using a biosimilar PEG-IFN.

Other barriers to HCV treatment access may be overcome with evidence provided by operational research. These include studying the feasibility and effectiveness of:

- generic HCV DAAs and biosimilar PEG-IFNs;
- cheaper and more user-friendly point-of-care HCV viral-load and genotype tests;
- heat-stable formulations and simplified drug dosing;
- treatment side effects management;
- peer-supported treatment adherence programs; and
- harm reduction approaches to prevent HCV reinfection.

Collaborating with researchers is a powerful way to document the need for HCV treatment in your country. Using operational research on pilot HCV treatment programs from other countries can help guide the creation of programs, based on evidence of feasibility and effectiveness, for your country.

CASE STUDY: Pilot program in Southeast Asia to treat HCV in people coinfecting with HIV

An estimated 49–64 million people in Asia have been infected with HCV. **TREAT Asia**, a regional HIV research program of amfAR, the Foundation for AIDS Research, has launched the first multisite clinical study to address barriers to treating HCV in people living with HIV. The trial will evaluate the effectiveness and tolerability of PEG-IFN plus ribavirin in 200 HIV/HCV-coinfecting people in four sites: Jakarta, Indonesia; Bangkok, Thailand; Hanoi, Vietnam; and Kuala Lumpur, Malaysia. Treat Asia negotiated donations of the study drugs and diagnostics from the originator companies.

Q&A with Dr. Nicolas Durier of TREAT Asia

What do you wish to achieve through this study?

TREAT Asia's objectives are to develop a model of care that can be used for replication and scale-up and to demonstrate that HCV treatment in HIV-positive people in resource-limited settings is feasible—with good outcomes. We hope to increase awareness about hepatitis C and its current treatment in the region and to increase demand for treatment. Last but not least, we want to offer treatment to 200 people who need it.

What change in the pharmaceutical industry do you hope to bring about?

As the industry often downplays cost barriers to point to the challenges of treatment implementation, we hope that by implementing a model of care and demonstrating the feasibility of treatment, advocates will have additional evidence to support their work on price reductions.

Do you have any advice for others setting up similar studies?

Before setting up similar studies or implementing HCV treatment projects, I would advise others to have solid patient education and support systems in place, have good care provider training and education on the management of HCV treatment, and have staff who can dedicate enough time to supervise the project. It is also important to consider the refrigeration requirements (in health facilities but also in patients' homes if they are self-injecting PEG-IFN) for the proper storage of PEG-IFN, and also to remember that contraception is required for patients (and their partners) because ribavirin can cause birth defects.

What have been the challenges so far? What others do you anticipate encountering?

Most of the challenges we have faced in preparation for this project were related to the requirements for conducting it as a clinical research study (writing a full study protocol, developing patient informed consents, obtaining approval from ethical committees, designing data collection forms, etc.). Designing patient education and treatment preparedness materials in all relevant local languages was a huge undertaking as well. Staff training was not a big issue. Coordinating preparation and progress across four study sites was also a challenge.

As the study has now started, we expect that the main challenges we will face will relate to the management of side effects. We expect that some patients will have serious adverse events, and some cases might be difficult to handle (in part because of the limited resources available).

RESOURCES:

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