



# Activist Guide to Hepatitis C Virus Diagnostics

October 2019

## About Treatment Action Group

**Treatment Action Group (TAG) is an independent, activist, and community-based research and policy think tank fighting for better treatment, prevention, a vaccine, and a cure for HIV, tuberculosis, and hepatitis C virus (HCV).**

TAG works to ensure that all people with HIV, tuberculosis (TB), or HCV receive life-saving treatment, care, and information. TAG is an organization of science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end HIV, TB, and HCV.

## About TAG's hepatitis C virus project

**TAG's HCV Project works to improve affordable treatment and diagnostics access, research, policy, and programs for HCV at the local, state, national, and global levels.**

The *Activist Guide to Hepatitis C Virus (HCV) Diagnostics* was conceptualized and produced with support from the Foundation for Innovative New Diagnostics (FIND). FIND also helped facilitate workshops at which critical ideas that form the basis of this guide were developed, and also provided technical input, supported the writing, and enabled its publication.

Thanks to our contributors, to TAG's board and staff, and to TAG's generous donors, who have made this work possible. TAG thanks Chloe Forette, Constance Lau, and Priyanka Patel for providing research support. Peer review from Emmanuel Fajardo, Annette Gaudino, Maka Gogia, Elena Ivanova, Erica Lessem, Ed Low, Sonjelle Shilton, and Navneet Tewatia is greatly appreciated.

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# Foreword

**Diagnosis refers to detecting a disease or condition. Access to affordable, quality healthcare, including diagnostic services, is a human right. Everyone has the right to know their health status and receive quality treatment and care, including for infectious diseases like hepatitis C.**

The purpose of this guide is to provide information for you and your community. It builds on TAG's [Training Manual for Treatment Advocates: Hepatitis C Virus and Coinfection with HIV](#), which you can refer to for more detailed information about the prevention, latest treatments, and care for hepatitis C and HIV coinfection. This Activist Guide to Hepatitis C Virus (HCV) Diagnostics aims to provide a deeper focus on diagnosis with updated information about the steps and different technologies involved in diagnosing a person with hepatitis C. It outlines major barriers to accessing testing technologies and services, similar to affordable access to the cure.

The information here is written by and for people who are not medical specialists—namely for patients, community members from affected communities, researchers, educators, and treatment activists.



**TAG is comprised of treatment activists who learned about hepatitis C because it was a problem for people in our communities.**

TAG designed the Activist Guide to help you discuss the barriers and use the advocacy exercises to strategize campaigns and action steps to overcome them.

## Objectives of the Guide

- Translate the scientific research about HCV diagnostics to increase treatment activists' and community members' technical knowledge and the capacity that they need to mobilize communities and demand access to diagnostics;
- Strengthen activists' ability to participate in planning and policy processes related to national HCV elimination;
- Serve as a resource when activists engage in community monitoring and surveillance related to the quality, affordability, and accessibility of HCV testing and care services;
- Provide advocacy exercises to help activists' explore ways to overcome diagnostics barriers.

## Development of the Guide

TAG conducted a literature review to expand on HCV diagnostics basics, types of tests and technological platforms, changes in global testing guidelines, and common barriers to accessing testing and care services. In 2019, TAG, in partnership with FIND, developed a

[training curriculum \(available here\)](#)

and conducted in-country diagnostics advocacy trainings with partner organizations in Malaysia (Positive Malaysian Treatment Access and Advocacy Group) and Georgia (Georgian Harm Reduction Network).

These organizations listened to perspectives from community members from key populations on a number of topics, including:

- The most relevant concepts and features about HCV diagnostics;
- How to tailor awareness and screening campaigns to connect to specific key affected communities;
- Concerns about patients lost to follow up and along the care cascade;
- Recommendations for making HCV testing more accessible in their communities.

The questions and feedback received from the trainings helped to adapt the training curriculum and capture the most important, community-friendly information in this Activist Guide.

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## How to Use the Guide

This guide encourages participatory learning with interactive discussions. It is organized into six sections. Each section can be presented and shared by a community health educator or other educators with lived experience with a small group of people in two-hour sessions. At the end of each section, there are advocacy exercises. Advocacy exercises include discussion points and action steps. The discussion points are intended to start conversations about the key issues raised in each section. The action steps are intended to start conversations about how to translate the key issues into advocacy in the community and to allow participants to find solutions together.



# Introduction

## Addressing the ‘Diagnostic Burnout’

Breakthrough all-oral direct-acting antivirals (DAAs) effectively cure all genotypes of the hepatitis C virus (HCV) in 2–3 months. Yet monopolies, licensing, registration, and pricing barriers remain for some low- and middle-income countries (LMICs), where two-thirds of people living with hepatitis C and people who use drugs live.

Globally, an estimated 71 million people are living with chronic HCV, yet since the launch of sofosbuvir in December 2013, less than 5 million people have been treated.<sup>1</sup> Annually, there are an estimated 400,000 deaths worldwide related to HCV.<sup>2</sup>

### New infections continue to outpace annual cures.

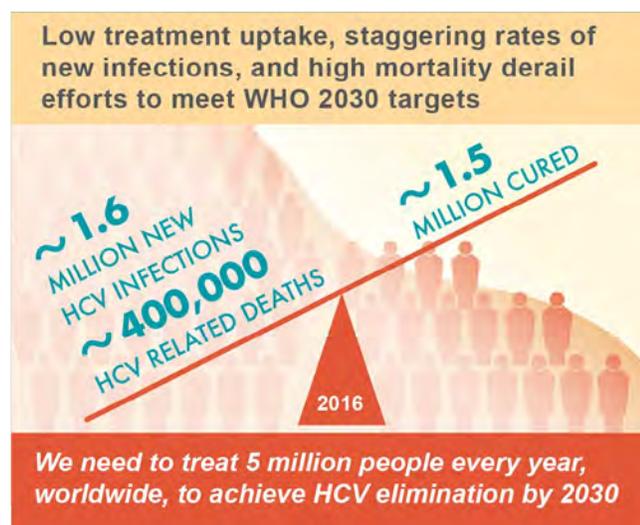


Figure 1. HCV infections, HCV-related deaths, and cures.

Estimates in 2016 illustrate that we are off course to achieving WHO HCV Elimination Targets by 2030 (see Figure 1). Diagnosis of new infections is crucial for early detection and treatment and to prevent onward transmission of the virus.

The World Health Organization (WHO) set global targets to eliminate viral hepatitis as a public health threat by 2030. Achieving elimination requires:

- **90 percent reduction in incidence;**
- **65 percent reduction in mortality;**
- **90 percent of people infected with hepatitis C to be diagnosed; and**
- **80 percent of people diagnosed to be treated.<sup>3</sup>**

Expanded generic availability and competition has reduced DAA prices in some countries. However, even in countries with access to affordable generic treatment, complicated, expensive diagnostics have presented obstacles to people knowing their HCV status. Worldwide, less than 20 percent of people living with HCV have been diagnosed; of those, less than 5 percent are people living in LMICs.<sup>4</sup> Countries with high treatment uptake among people known to have HCV will experience ‘diagnostic burnout’, or the phenomenon in which countries have failed to diagnose new infections and run out of diagnosed patients to treat. This may occur because the people who have been treated were mainly diagnosed at the hospital when they are very sick with chronic HCV infection or advanced liver disease. To identify more people who have no symptoms and who live in semi-urban or rural areas, countries will need to decentralize testing and treatment services. If this approach is not shifted, HCV infections will continue to proliferate—we will fail to treat new infections and to prevent advanced liver disease and liver-related deaths associated with HCV.

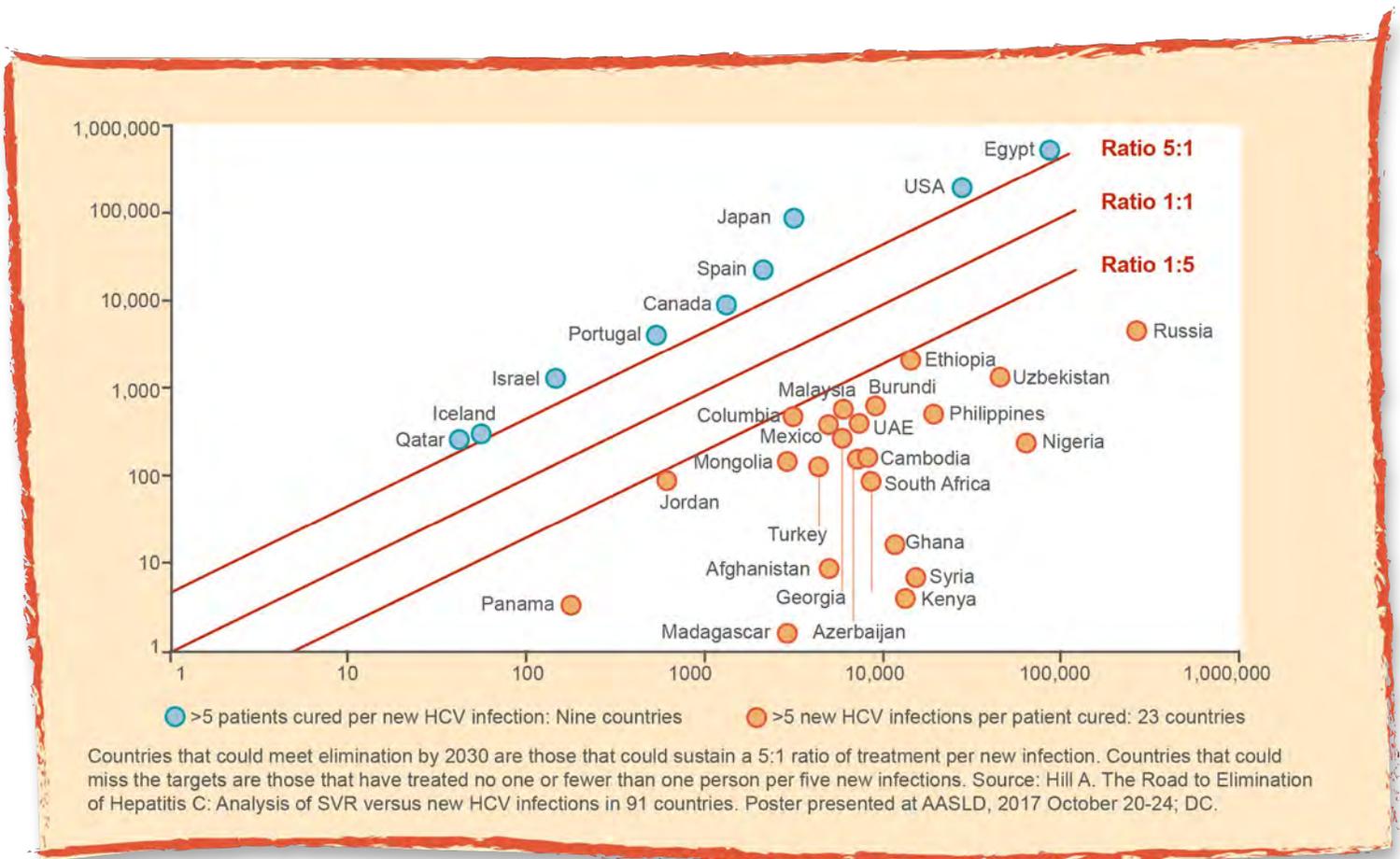


Figure 2. The road to elimination.

Hill A et al.<sup>5</sup> modeled countries' trends toward HCV elimination with ratios of patients cured to new infections. Countries with higher cure rates to new infections (5:1 or more) were projected to achieve elimination by 2030 or sooner (see Figure 2).

For example, in Table 1, modeling forecasts that Brazil, Spain, and Portugal could soon reach the stage where there are no more diagnosed patients available to treat. The modeling demonstrates that annual cures must exceed annual new infections in order to bend the curve towards elimination. However, this sample of countries will reach 'diagnostic burnout' before 2030, derailing national elimination efforts.

**Modeling suggests the countries on track to achieving elimination by 2030 are those that treat more than five patients for every new infection.<sup>7</sup>**

The Activist Guide to Hepatitis C Virus (HCV) Diagnostics pulls together basic information about HCV diagnostics to help activists become more familiar with the issue and to think through the diagnostic burnout problem.

Table 1. "Diagnostic burnout": Potential outcomes, based on 2016 data<sup>6</sup>

| Country  | HCV epidemic | Diagnosed before 2016 <sup>8</sup> | New HCV diagnoses <sup>9</sup> | Cumulative Cures in 2016 | Outcome            |
|----------|--------------|------------------------------------|--------------------------------|--------------------------|--------------------|
| Brazil   | 1.8 million  | 235,000 (13%)                      | 10,000 (0.6%)                  | 43,000 (2.4%)            | Dx burnout in 2025 |
| Spain    | 328,000      | 140,000 (43%)                      | 5500 (1.7%)                    | 25,000 (8%)              | Dx burnout in 2022 |
| Portugal | 96,000       | 37,000 (39%)                       | 1300 (1.3%)                    | 4400 (4.6%)              | Dx burnout in 2026 |

The WHO HCV guidelines and Essential Diagnostics List are briefly examined for advocates to understand whether their countries align with global guidelines. Then different screening strategies and considerations for key affected communities are outlined for activists to brainstorm ways to improve the inclusion of affected communities in national plans and to reach the millions of people globally who have not been diagnosed.

There are several models for reducing the number of steps to confirm diagnosis and to start people on treatment as early as possible, which include integrating HCV care into existing health programs and services. Significant barriers exist for people, particularly in LMICs, to access HCV testing, and activists are tasked with identifying the most problematic obstacles in their contexts. The final section considers key recommendations and lessons for activists.

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<sup>1</sup> hepCoalition. Sofosbuvir turns 5 years old: The vast majority of people with chronic hepatitis C still have not been treated. 2018 December (cited 2019 September 10). Available from: [https://hepcoalition.org/IMG/pdf/factsheet\\_sofosbuvir\\_5\\_anniversary-2.pdf](https://hepcoalition.org/IMG/pdf/factsheet_sofosbuvir_5_anniversary-2.pdf).

<sup>2</sup> World Health Organization. Hepatitis C Fact Sheet. Geneva: WHO; 2019 July 9 (cited 2019 September 10). Available from: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>.

<sup>3</sup> World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018 July (cited 2019 June 10). Available from: <https://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1>.

<sup>4</sup> World Health Organization. Global report on access to hepatitis C treatment. Focus on overcoming barriers. Geneva: WHO; 2016 October (cited 2019 September 10). Available from: <https://apps.who.int/iris/bitstream/handle/10665/250625/WHO-HIV-2016.20-eng.pdf?sequence=1>.

<sup>5</sup> Hill A, Nath S, Simmons B. The road to elimination of hepatitis C: analysis of cures versus new infections in 91 countries. *J Virus Eradication*. 2017;3:117–23. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518239/pdf/jve-3-117.pdf>.

<sup>6</sup> Hill A, Khan A, Nath S, and B Simmons. The road to elimination of hepatitis C: analysis of SVR versus new HCV infections in 91 countries. Poster presented at AASLD, 2017 October 20-24; DC.

<sup>7</sup> Hill A. Prices versus costs of medicines in the WHO Essential Medicines List. Presentation at: WHO, Geneva. 2018 February 26 (cited 2018 November 29). Available from: <https://www.who.int/phi/1-AndrewHill.pdf>

<sup>8</sup> Cumulative diagnoses up until the year 2016. Polaris database. Polaris Observatory [Internet]. Available from: [cdafound.org/Polaris-hepc-dashboard](https://cdafound.org/Polaris-hepc-dashboard)

<sup>9</sup> New diagnoses in the year 2016. Polaris database. Polaris Observatory [Internet]. Available from: [cdafound.org/Polaris-hepc-dashboard](https://cdafound.org/Polaris-hepc-dashboard)

# Section 1

## Diagnostics Basics

The first step in finding out if you have HCV is to get laboratory tests from a medical provider. You may be asked to take laboratory tests that can tell:

- if you have been infected with HCV;
- if you are still infected with HCV;
- the amount of HCV in the bloodstream;
- the subtype of the virus (genotype) you have;
- if your liver has been damaged;
- if you have been infected with other viruses (such as HIV or hepatitis B virus);
- if you are infected with HCV and have underlying conditions (such as pregnancy, diabetes, kidney disorders, etc.).

**Diagnosing hepatitis C is a two-step process: screening and virological (also known as confirmatory) testing.**

### What is screening?

Screening looks to see whether someone who is apparently healthy and without any symptoms might have an infection or a disease. For HCV, screening means looking for antibodies that the body makes in reaction to the virus, instead of looking for the virus itself. HCV triggers an immune response—the immune system makes HCV-targeting **antibodies**.

### What are antibodies?

Antibodies are Y-shaped proteins made by a person's immune system. They are part of the immune system's response to viruses, bacteria, and other harmful substances (called **antigens**).

Antibodies attach themselves to antigens or infected cells and tag them so that other immune cells can find and attack them. It takes six to 24 weeks for a person to make antibodies to HCV (often called the **window period**). Antibodies stay in a person's body long after the antigen that triggered them disappears (this is called **immunological memory**). If the same antigen enters a person's body again, even years later, the immune system will remember it—and send antibodies to target it for destruction.

When HCV enters a person's bloodstream, it triggers an immune response. The immune system makes HCV-targeting antibodies. Sometimes, the immune system gets rid of HCV by itself (this is called **spontaneous viral clearance**). The WHO estimates around 30 percent (between 15 and 45 percent)<sup>10</sup> of people with hepatitis C will spontaneously clear the virus.

**Generally, one in four people will spontaneously clear the virus within six months of becoming infected.<sup>11</sup>**

This is more likely in young people (especially women), people who do not have HIV, and people who are born with gene variations that may strengthen their immune system.

**Even when a person has cleared HCV or has been cured by treatment, HCV antibodies remain in a person's blood for years, possibly for the rest of the person's life.**

That means they will always test positive for HCV antibodies, even if they don't have virus in their bloodstream and are not at risk for getting sick.

## Antibody screening

Antibody screening involves either a **rapid diagnostic test (RDT)** that uses oral fluid (saliva) or blood from your veins or from a fingerstick or an **enzyme immunoassay (EIA)** that uses blood or plasma samples. When antibody screening uses blood, it is also known as serological screening. RDTs are designed for **point-of-care (PoC)** settings, which are conducted at the time and place of the patient seeking care, such as community clinics, harm reduction sites, prisons, etc. RDT results can take between 5 and 20 minutes. EIAs are conducted in laboratory settings, and results become available usually in a few days. EIAs are conducted in batches of 96 tests and labs must wait until there are a sufficient number of samples to run the tests.

Although RDTs that use capillary blood or oral fluid have the potential to be used for self-testing, in which patients can conduct and interpret the test for themselves, they are not yet available on the market and have not been certified for this purpose yet. Current fingerstick and oral fluid tests have been validated only for professional use (such as for trained healthcare workers) to date.

There are several multiplex RDTs, which are RDTs that use the same sample and simultaneously detect antibodies to different diseases like HIV, hepatitis B virus (HBV), HCV, and, syphilis, available in the market. However, these tests have not been properly certified (or achieved stringent regulatory authority [SRA] status) and remain for ‘research use only’. Therefore, there needs to be more independent research to determine their quality, their usefulness, and the right combination of tests, depending on the disease burden, in real-world settings.

## What does a negative HCV antibody test result mean?

A negative antibody test result usually means that the person has not been infected with HCV—unless they were infected very recently, they have a weakened immune system, or there was a testing error.

The body needs at six to 24 weeks (and sometimes up to nine months) to make antibodies. People with weakened immune systems (from an illness or certain medications) are not always able to produce antibodies. This might happen in people with autoimmune disorders (when a person’s immune system attacks their own organs or tissues), people living with HIV with a CD4 cell count below <200 cells/mm<sup>3</sup>, and people taking immunosuppressants.

| Step 1. HCV Antibody Test   |  |
|---|--|
| Positive Result   | Negative Result  |
| <p>There are three potential meanings:</p> <ol style="list-style-type: none"> <li>1 The person was recently infected with HCV; or</li> <li>2 The person may have chronic HCV; or</li> <li>3 The person was infected in the past, but has cleared HCV and is no longer infected.</li> </ol> <p><b><i>This person needs a viral load test to confirm.</i></b></p> | <p>There are three potential meanings:</p> <ol style="list-style-type: none"> <li>1 The person has never been infected with HCV.<br/><b><i>This person does not need a viral load test to confirm.</i></b></li> <li>2 The person may have been recently exposed to HCV within the last 2 weeks; or</li> <li>3 If the person is HIV positive, with a CD4 count &lt;200 cells/mm<sup>3</sup>, or has a weakened immune system. The person may have chronic HCV.<br/><b><i>This person needs a viral load test to confirm.</i></b></li> </ol> |

Testing errors (or false negative results) can occur when a diagnostic test of questionable quality is used or when the person administering the test makes a mistake in the testing procedure.

### What does a positive HCV antibody test result mean?

A positive antibody test result means that a person has been infected with hepatitis C. It does not mean that the person still has active hepatitis C infection. A different test, to look for the actual HCV, is needed to make a diagnosis.

### What is virological (also known as confirmatory) testing?

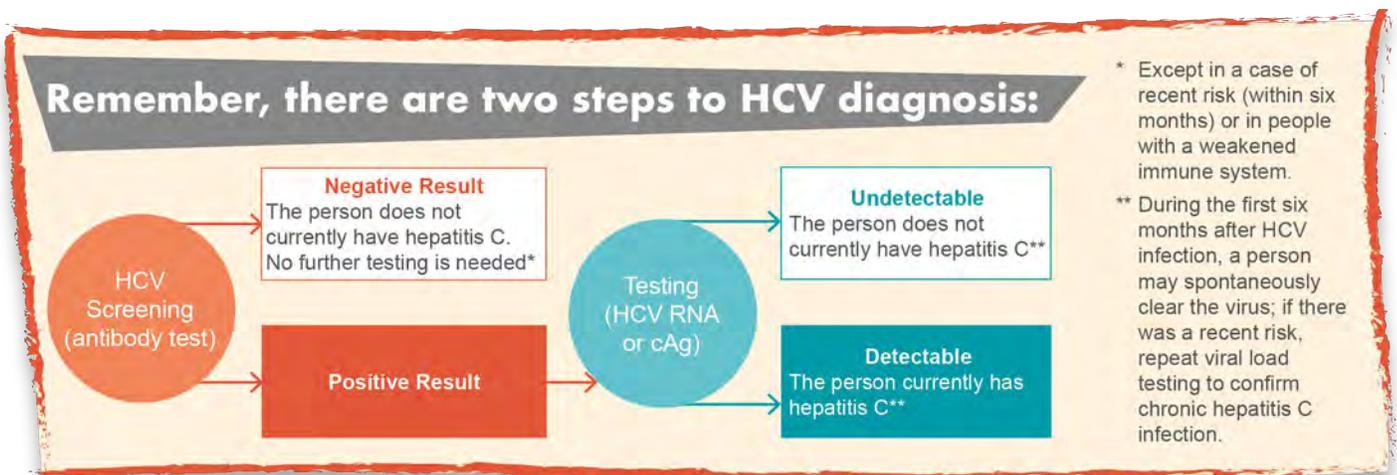
Virological testing will confirm—or rule out—whether someone has hepatitis C disease.

Virological testing, as you might have guessed from the name, looks directly for the virus (or pieces of it).

### How is a person diagnosed for hepatitis C?

There are two tests to diagnose someone with HCV. A **viral load** test (called HCV RNA or NAT—nucleic acid testing) is used to check for HCV in the bloodstream. An HCV **core antigen** test detects the viral protein of hepatitis C—which can be found in the bloodstream within two weeks. HCV core antigen (cAg) testing is only available in large laboratory settings, such as a central hospital.

| Step 2. Confirm Diagnosis   |   |
|---|---|
| Detectable Result   | Undetectable Result   |
| <p>There are two potential meanings:</p> <ol style="list-style-type: none"> <li>1 The person may be recently infected with HCV; or</li> <li>2 The person may have chronic HCV.</li> </ol> <p><b>This person should be assessed for HCV treatment.</b></p> | <p>There are two potential meanings:</p> <ol style="list-style-type: none"> <li>1 The person has never been infected; or</li> <li>2 The person was once infected in the past, but has now cleared HCV.</li> </ol> <p><b>This person should be assessed for follow up testing.</b></p> |



If a person has an undetectable result and engaged in behaviors that may put them at risk of infection, they should be assessed for follow-up testing.

## Viral load tests

These tests are also known as RNA tests, molecular tests, or nucleic acid tests. A person should get tested regularly if they are at risk. If a viral load test result is also undetectable, it means that HCV has been cleared. In order to diagnose cases of reinfection, RNA testing is recommended for people with ongoing risk behaviors or abnormal liver function tests. HCV viral loads are usually much, much higher than HIV viral loads, but a high viral load does not mean that HCV is more serious or that liver damage will happen faster.

At this time, viral load tests are more likely to be used than core antigen tests. There are two types of viral load tests:

- **Qualitative testing** checks whether there is HCV in the bloodstream. The test result is either positive (virus is detectable) or negative (virus is undetectable).
- **Quantitative testing** measures the amount of HCV in the bloodstream. These tests, while not available in every country, are used during HCV treatment to see if it is working.

New research provides guidance to the manufacturers of point-of-care HCV diagnostics on the **optimal limit of viremic detection as close to 1300 IU/mL**.<sup>13</sup> This threshold would detect 97 percent of active HCV infections and minimize false negatives.

## HCV core antigen tests

HCV core antigen (HCV cAg) can be detected in the bloodstream earlier than viral antibody tests—two weeks after infection. HCV core antigen testing—which is based on enzyme immunoassay technology—is simpler and should be less expensive than viral load testing. However, it is less sensitive, meaning it might miss some infections.

The most common lab-based, HCV core antigen diagnostic platform, Abbott ARCHITECT i2000, is used mainly in high-income countries and less marketed in LMICs. However, we need price transparency for core antigen tests so that countries can compare and negotiate more aggressively.

**Point-of-care core antigen tests are still under development and will not be available in resource-limited settings for several years.**

|                                       |  |   |   |
|---------------------------------------|--|---|---|
| <p><b>What the result SAYS</b> →</p>  | <p>Undetectable, the lower limit of detection (LLOD) varies; it can be as low as &lt;5 IU/mL*</p>  | <p>Detectable, below the lower limit of quantification (LLOQ); the lowest amount of hepatitis C virus that the test can measure</p> | <p>Detectable</p>   |
| <p><b>What the result MEANS</b> →</p> | <p>No hepatitis C Virus was found in the bloodstream (this means that a person either spontaneously cleared HCV or that they were cured)</p> | <p>Hepatitis C was found</p>  | <p>Hepatitis C was found in the bloodstream; the amount of virus is reported in international units per milliliter (IU/mL). A person with a positive antibody test result and detectable HCV RNA has chronic hepatitis C (unless they were recently infected)</p> |

\*Unit of measurement (international units per milliliter)

Core antigen testing has the following characteristics:

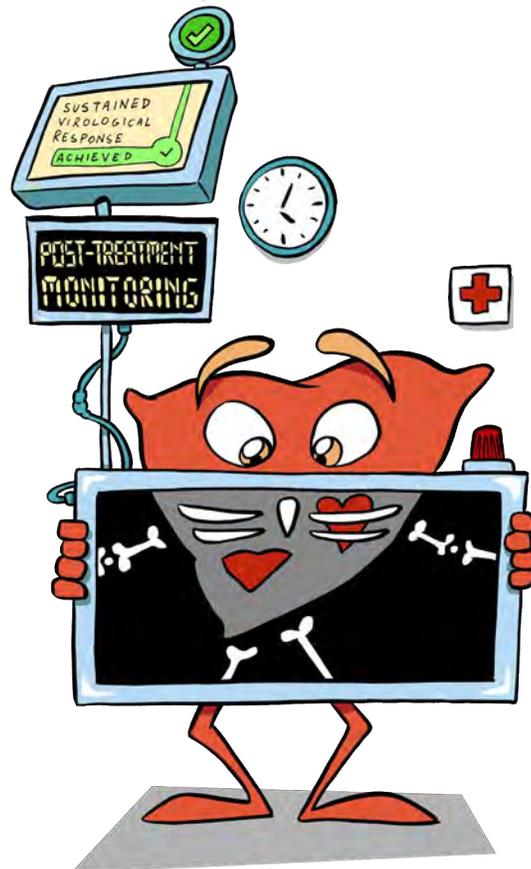
- Can be used with HCV antibody testing to detect acute HCV
- Confirms chronic HCV infection—which is an infection that can last for weeks, months, or a lifetime and causes more damage to the affected tissue or organs
- Less sensitive—does not detect low levels of HCV (threshold: 3000 IU/mL depending on the genotype).

It may be possible to use core antigen to confirm cure at week 12 (or achieving sustained virological response at week 12 [SVR12]), but there are currently not enough data to know.

## HCV genotype tests

**There are six known hepatitis C genotypes**; there are also subtypes. People can be infected with more than one HCV genotype (called **mixed infection**). People who already have HCV can get infected again (**reinfected**) with the same or a different genotype.

Now that there are DAAs that treat all genotypes (called **pangenotypic**), **HCV genotyping is becoming unnecessary**. In fact, the WHO 2018 Guidelines recommend eliminating genotype tests if pangenotypic DAAs are used.



## Liver disease staging

Liver disease staging is an important part of learning about an HCV diagnosis and in preparation for starting treatment. The type and length of HCV treatment depends on liver damage.

### Treating HCV early is critical before the liver becomes more damaged.

DAAs can cure HCV infection in over 95 percent of people without cirrhosis; however, HCV with cirrhosis can be more difficult to cure.

People with cirrhosis might need to take ribavirin or may need to be treated for a longer period. If people with an HCV infection and cirrhosis go untreated, their cirrhosis may become **decompensated**, meaning their liver is beginning to fail. Furthermore, people with genotype 3 and cirrhosis are more likely to have **steatosis** (fat in the liver). Pangenotypic treatments are effective for these conditions, and HCV genotype tests are no longer necessary when pangenotypic DAAs are used.

There are two types of liver disease **staging** to assess the extent of liver damage before starting treatment:

- **Invasive** (biopsy: takes blood or tissue sample with needle)—these tests should no longer be used; and
- **Noninvasive** (ultrasound imaging or blood biomarkers)—safer, less expensive, easier to perform.

Cirrhosis can be assessed without a liver biopsy. Examples of noninvasive, ultrasound imaging tests that are operated by liver specialists are **FibroScan** or **FibroTest/ActiTest**, which look at liver stiffness using sound waves.

FibroScan can determine the level of liver damage and the degeneration of liver cells. Results from FibroTest/ActiTest may need additional time because they require results to be shipped to the BioPredictive company for analysis

by its own software. FibroScan is recommended in the WHO Guidelines,<sup>14</sup> but FibroTest is not.

FibroScan and FibroTest are more expensive and are not widely available in most countries, particularly in resource-limited settings. However, in Georgian harm reduction clinics, portable FibroScan devices, with appropriate training and under the supervision of medical professionals, were used to assess liver disease of people who inject drugs.<sup>15</sup> The examinations were conducted within 5 minutes and patients received results immediately.

FibroScan has been used as a prevention and noninvasive assessment tool to engage people who are often excluded from the healthcare system. The device has been used in harm reduction and other community settings, such as mobile clinics, to educate people about their liver health and risk factors, monitor liver disease progression, and link people to other testing, treatment, care, and social services.

In resource-limited settings, the WHO recommends liver function tests called **FIB-4** or **APRI**, which are less expensive, for assessing liver health. However, these blood tests add wait time for the results, which delays treatment. More tests amount to more costs in the overall diagnosis, treatment, and care of a person with HCV.

## Liver Function Tests (LFTs)

You may be asked to take liver function tests to check enzyme levels in the liver. People taking HIV antiretrovirals (ARVs) or tuberculosis (TB) treatments (whether or not coinfecting with HBV or HCV) should have liver enzymes checked regularly as these medications might be hard for the liver to break down.

There are several types of enzymes:

- **Alanine aminotransferase** (**ALT**, also called **serum glutamic-pyruvic transaminase** [**SGPT**]) is made in the liver.

If ALT keeps increasing over time, it may be a sign of hepatitis C progression. The results cannot predict or tell someone how much liver disease they have.

- **Aspartate aminotransferase (AST; also called serum glutamic-oxaloacetic transaminase [SGOT])** is made in the heart, intestines, and muscles and is used to measure liver health.
- **Alkaline phosphatase (ALP)**, gamma glutamyl transferase (GGT), bilirubin, albumin, and prothrombin (PT) are other important liver enzymes used to measure liver health.

One liver function test is an **APRI** or aspartate aminotransferase to platelet ratio index, which is a formula used to determine level of cirrhosis.

The **FIB-4** is another test that is inexpensive and noninvasive. FIB-4 is a calculation to determine the amount of liver scarring by using patient's age, platelet count, AST, and ALT.

$$\text{APRI} = \frac{\text{AST LEVEL (AST UPPER LIMIT OF NORMAL)}}{\text{PLATELET COUNT (10}^9\text{/L)}} \times 100$$

$$\text{FIB-4} = \frac{\text{AGE (YEARS)} \times \text{AST (U/L)}}{\text{PLATELET COUNT (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

Table 2. Comparison of FibroScan and FibroTest.<sup>16</sup>

| Features                      | Fibroscan   | Fibrotest  |
|-------------------------------|---|--|
| <b>Pricing</b>                | Platform price: <b>US\$300,000</b><br>Mini platform price: <b>US\$70,000</b><br>Minimum <b>US\$50</b> , generally <b>US\$60–80</b> per test   | <b>US\$59 to over US\$100</b> per test, depending on the country, to analyze results with BioPredictive's technology   |
| <b>Setting</b>                | Generally for clinics or PoC settings. For large numbers of patients, multiple devices would be needed<br><br>To consider for rural patients<br><br>Can be used in community settings and to engage patients and peers, and link patients to services | Hospital laboratory settings   |
| <b>Obtaining results</b>      | Provides detailed imaging   | Not an imaging platform; works with blood tests results to be shipped to BioPredictive company for interpretation<br><br>Seen as better than FIB-4 or APRI for accuracy/reading the results, especially for people with cirrhosis or advanced liver disease<br><br>Requires reliable shipping/transport infrastructure |
| <b>Patient care</b>           | Patients need referral or follow up in hospital, especially for HCC diagnosis   | Patients need referral or follow up in hospital  |
| <b>Inputs and maintenance</b> | No reagents required, but plan for maintenance every 6 months   | Company has monopoly on reagents   |

## Other important parts of the laboratory process

There are several key terms in the laboratory process that are important to know because they may affect decisions when selecting diagnostic platforms. Costs for platforms that require frequent maintenance or expensive replacement parts need to be included in national testing budgets. Some machines can save time by running several different tests using the same sample at the same time (known as **multiplexing**), and bulk purchasing these tests together can be a way for governments to negotiate better pricing and save costs.

- HCV tests require **reagents**, or chemical ingredients that react to a patient's sample, which require refrigeration.
- A container with prefilled reagents to be loaded inside a diagnostics device is a **reagent cartridge**. Each cartridge is one test.
- Many laboratories conduct multi-disease testing (**polyvalency**), meaning they use a machine that tests for more than one infection but use different samples and not always at the same time, such as TB, HIV, HBV, and HCV.

be more readily offered at PoC settings where communities most affected by HCV receive their services, such as at harm reduction sites or sexual health clinics. In some contexts, and with the appropriate training, staff, and resources, it might be possible to offer antibody and confirmatory testing at pharmacies, in which someone could pick up their DAA prescription once they are diagnosed and counseled.

The 'ideal' HCV test<sup>17</sup>:

- uses either HCV ribonucleic acid (RNA) or HCV cAg—performed using a fingerstick or dried blood spot (DBS);
- is accurate, with high sensitivity and specificity (both are closer to 100 percent);
- confirms diagnosis in 20 minutes;
- costs less than US\$5 per test (including the reagent cost);
- is instrument free (does not require equipment maintenance); and
- enables a person to initiate a pangenotypic DAA immediately (that is, after conducting the liver disease staging and checking for any other complications), then return for test of cure at 12 or 24 weeks (SVR12 or SVR24) after completion of treatment.

Unfortunately, the ideal test is still several years away, and we lack simple, quality-assured, affordable tests in LMICs. Until then, the different types of existing tests and predominant diagnostic platforms on the market have advantages and limitations that need to be considered.

## Challenges and gaps in diagnostics: How far are we from the ideal test?

Now that HCV treatment is simpler, safer, and more effective, we need to find a simpler, PoC, inexpensive, RDT. Scaling up diagnosis requires moving at least partially away from centralized laboratory facilities; rather, HCV testing should

## Screening tests

### Screening tests: rapid diagnostic antibody tests<sup>18</sup>

#### Advantages

- Easy to use (minimal training which allows task-shifting)
- Oral fluid (saliva), whole blood, serum or plasma (fingerprick and oral fluid allow decentralization of testing)
- Equipment free (can be used at PoC settings with limited lab infrastructure/electricity)
- Good sensitivity and specificity
- Qualitative (yes/no) results
- Fast delivery of results (less than 20 minutes)
- 1–2 years of shelf life (if stored correctly at room temperature)

#### Limitations

- Low throughput (rate/performance for processing results; amount of tests that can be processed at a given time)
- Subjective interpretation (operator dependent), inadequate for people with a low amount of antibodies or compromised immune system (such as PLHIV)
- Possible higher cost (compared with lab-based tests) depending on volume
- Difficult for quality-control activities

### Screening tests: enzyme immunoassay antibody tests<sup>19</sup>

#### Advantages

- High sensitivity
- High specificity (~100%)
- High sample throughput (good for processing large volumes of samples)
- Possible lower cost based on high volumes
- Data-processing filing of results
- Cost-effective in large numbers of samples
- Allows easier oversight of quality-control activities
- The same equipment can be used for serological screening of other diseases e.g. HIV, HBV, etc.

#### Limitations

- Requires an effective specimen transport system
- Cold chain, in which temperature is controlled generally between 2 °C and 8 °C (36 °F to 46°F), is needed for reagents (not always possible in some LMIC settings)
- Requires additional equipment (high precision pipettes, centrifuges, etc.)
- Longer time for results
- May have interference from sample matrices: whole blood, plasma, capillary samples
- Requires skilled technical staff
- Requires equipment service and maintenance
- EIAs usually run tests in batches of 96 samples, which can delay turnaround time for results. Companies should offer different test configurations for different volumes, such as running 12 or 24 tests at a time

## Core antigen (confirmatory) test platforms: Abbott ARCHITECT i2000<sup>20 21</sup>

### Advantages

- Conducts core antigen tests: good for high-volume settings (100 tests per hour)
- Also screens HIV and other diseases; activists need to confirm whether the HIV platform is licensed for HCV in their country
- cAg is detected in the bloodstream earlier than with viral antibody tests—two weeks after infection
- Possible lower cost based on high volumes
- Allows easier oversight of quality-control activities

### Limitations

- Cannot use an effective specimen transport system
- Is not validated/certified for use with dried blood spot samples
- Cannot confirm cure<sup>22</sup>
- Less sensitive—it might miss some infections
- Requires central labs that can handle large volumes
- Longer time for results
- HCV: US\$8–23 (€7–20) per test
- Requires skilled technical staff
- Requires equipment service and maintenance

## RNA (confirmatory) test platforms: Abbott Realtime<sup>23</sup>

### Advantages

- Conducts RNA tests: good for high-volume settings (93 tests per batch)
  - Possible lower cost based on high volumes
  - Screening multiple diseases using different samples (HIV, HCV, genotyping, but activists need to confirm whether the HIV platform is licensed for HCV in their country)
  - Allows easier oversight of quality control activities
- Requires an effective specimen transport system
  - Is not validated/certified for use with dried blood spot samples
  - Longer time for results
  - US\$11–23 per test (Global Fund price, which varies depending on volume and term commitment)
  - Requires skilled technical staff
  - Requires equipment service and maintenance (unless a reagent rental agreement was negotiated)

### Limitations

## RNA (confirmatory) test platforms: Cepheid GeneXpert<sup>24</sup>

### Advantages

- Xpert Viral Load (VL) has an RNA quantification assay (using plasma samples) and fingerstick (using whole blood samples)
- RNA quantification assay has Conformité Européenne (CE) and WHO pre-qualified (PQ) quality certifications
- Xpert VL Fingerstick is CE-marked and WHO PQ
- Xpert VL Fingerstick is appropriate for people who may not have easy vein access (such as some people who inject drugs)
- Xpert VL Fingerstick cartridge allows for simplification in sample collection
- Xpert VL: very accurate, simple to operate and good for shifting tasks to auxiliary healthcare professionals to facilitate decentralized testing
- Xpert VL: same-day results in 108-110 minutes; Xpert VL FS: in 60 minutes
- The GeneXpert instrument has an extensive test menu, which means there is opportunity to integrate testing across other disease programs (e.g., TB, HIV, HPV, HBV, etc.)
- Cepheid offers preferential pricing in 145 LMICs

### Limitations

- Xpert VL and fingerstick tests: Not available in many countries (not approved in the United States)
- Xpert VL: high cartridge costs if countries must pay in advance and in US dollars
- Xpert VL and Fingerstick: requires incinerator for biowaste, which may not be available in some decentralized settings
- While Xpert VL and Fingerstick tests are simplified, the GeneXpert instrument (including Edge) still requires lab infrastructure (e.g., constant electricity, air conditioning) to store reagents and function correctly
- Xpert VL: when using plasma, requires a centrifuge and transport costs for centralized testing
- Xpert VL: US\$17,000 per device plus US\$14.90 per test plus distributor mark-ups<sup>25</sup>; additional service and maintenance costs
- No volume-based pricing: price per test is fixed regardless of volumes

## RNA (confirmatory) test platforms: Roche Cobas® Taqman<sup>26 27</sup>

### Advantages

- Conducts qualitative and quantitative RNA tests: good for high-volume settings (93 tests per batch)
- Qualitative tests are cheaper than quantitative tests
- Possible lower cost based on high volumes
- HCV is part of Global Access Program, whereby reduced test pricing is offered to 85 LMICs
- Highly automated system
- Screening multiple diseases (TB, HIV, HCV, genotyping, etc.), but activists need to confirm whether the HIV platform is licensed for HCV in their country
- Allows easier oversight of quality-control activities

### Limitations

- The Taqman platform is being phase out for the Cobas® 4800 and 6800 systems
- Requires an effective specimen transport system
- Is not validated/certified for use with dried blood spot samples
- Longer time for results
- Requires large lab infrastructure to house equipment
- Requires skilled technical staff despite being fully automated
- Requires equipment service and maintenance (unless a reagent rental agreement was negotiated)
- Lack of transparency in pricing (information on preferential pricing is not publicly available)

## RNA (confirmatory) test platforms: Genedrive HCV<sup>28</sup>

### Advantages

- Point of care: small, portable (weighs 1 kilogram) system
- Results are qualitative (positive or detected/negative or undetected)
- Detection in less than 90 minutes, allowing for same-day diagnosis
- For settings with low numbers of patients (few number of patients/day)
- Reagents can be stored at room temperature (no refrigeration is required)

### Limitations

- High costs per patient
- Pricing US\$5000 per device; US\$25–35 per test
- Less sensitive than lab-based methods: lower limit of detection is above the recommended 1000 IU/mL for PoC testing (i.e., 2362 IU/mL)
- Low throughput per device: 90 min/test
- Requires 30 µL plasma, which could be challenging to obtain in PoC settings (requires phlebotomists to draw blood to obtain plasma and to use a centrifuge)
- Requires precise steps, using micropipetting instruments, for sample/reagent preparation (not fully automated)
- Requires uninterrupted power supply, which may not be reliable in some LMIC settings. WiFi connectivity is optional
- The device is not appropriate for multi-disease testing (only an HCV test is available)

## Antibody screening and RNA (confirmatory) tests: dried blood spot samples<sup>29</sup>

### Advantages

- DBS is an alternative to plasma samples: small volume samples collected by fingerstick
- DBS can be used instead of RDTs, such as in harm reduction or prison settings
- Can be used to detect HBV/HCV antibodies<sup>30</sup>, for HBV/HCV RNA testing, for genotyping, and for treatment resistance testing
- Useful for early diagnosis of pregnant parent-to-infant HCV transmission and for detection in children
- Inexpensive
- Can be used in large-scale testing campaigns
- Facilitates decentralized collection of samples on filter paper, which can be put in the mail or delivered by courier because it is nonhazardous material
- Stable for transport at room temperature
- Requires low level of training and could be done by auxiliary health professionals, community health workers, peer educators

### Limitations

- DBS requires a strong transport system to get the samples to central labs. For example, in South Africa and Tanzania, motorbike couriers are used to pick up diagnostics samples and deliver test results
- DBS has reduced analytical sensitivity for RNA compared to plasma and serum samples (due to small sample volume)
- Results are not immediately provided to the patient
- Need to develop quality standards for DBS
- DBS is currently limited to research use: companies have not yet sought stringent regulatory authority (SRA) status
- Requires additional studies and validation to scale up DBS testing in LMICs, which will take time

Diagnostic technologies that are currently being researched and developed in the quest for the ideal test are summarized in TAG's annual Pipeline Report.<sup>31 32</sup>

<http://www.treatmentactiongroup.org/pipeline-report>

## Advocacy Exercise



### Discussion questions:

- What tests would be most appropriate for testing people in my community?
- Would an HCV self-test improve diagnosis in my community?
- How would an HIV/HCV combined test improve diagnosis in my community?

### Action steps:

- How can we integrate HCV testing into existing laboratory infrastructure for multi-disease platforms?



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# Section 2

## Brief Introduction to WHO Guidelines for People Diagnosed with Chronic HCV

**Everyone has the right to know their health status and to be diagnosed with accurate, high-quality diagnostics.**

It is important for you to understand what is included in national hepatitis guidelines and what types of tests are available in your country.

The WHO offers guidance to help countries plan HCV elimination strategies, including adapting their national testing and treatment guidelines. In July 2018, WHO updated guidelines to help low- and middle-income countries plan for the screening, testing, treatment, and care of people diagnosed with chronic HCV.<sup>33</sup>

The WHO recommends diagnosing hepatitis C in **two steps**. First, to identify people who might be infected with HCV, medical providers should take a blood sample and use either a **rapid diagnostic test** (RDT) or a lab-based test that can detect antibodies, antigens, or a combination of both, called **enzyme immunoassays**.

If a person has a positive antibody test or is thought to have been exposed to the virus, the second step is to take a **viral load** or **core antigen test** to confirm active HCV infection.

**Key recommendations and updates are<sup>34</sup>:**

### Screening

- **All individuals** who have ever been **part of a population with high rates of HCV infection** should be screened with an antibody test. This includes people who inject drugs (PWID), people living with HIV (PLHIV), sex workers, and men who have sex with men (MSM), among others.
- RDTs are recommended for limited resource settings and can be used as initial steps to link people to treatment and care.
- RDTs should be offered at point of care in community settings.
- In the general population and settings where hepatitis C **antibody prevalence is greater than or equal to two percent or five percent, all adults** should have access to and be offered the antibody test. The threshold used will depend on other country considerations and epidemiological context.

## Confirmatory testing

- Any person with a **positive antibody test should have a hepatitis C viral load test** (also known as an HCV RNA or nucleic acid [NAT] test) to confirm active HCV infection.
- **Qualitative tests** are less expensive and just as sensitive as quantitative RNA. They can be a more cost-effective option for scaling up diagnosis.
- **Core antigen tests** are alternative confirmation tests to RNA/NAT but are less sensitive and might miss some infections. Core antigen tests are simpler to run and should be less expensive than molecular methods but are currently only available in large, central lab settings. Point-of-care core antigen tests will not be available in limited-resource settings for several years.
- **Genotype testing** of the HCV is **not needed** before starting treatment with a pangenotypic DAA regimen. Use of this test depends on the availability of pangenotypic regimens in your country.
- Move away from on-treatment viral load tests, which are primarily used to check treatment adherence, especially when using pangenotypic DAAs.
- A viral load confirmation test is still recommended to **check sustained virological response (SVR) at week 12** after the end of treatment, but medical providers should skip viral load adherence checks at weeks 4 and 8.

## Care and liver assessment

- Monitor patients with cirrhosis for hepatocellular cancer (liver cancer) every 6 months with an ultrasound or alpha fetoprotein (AFP) blood tests.
- To ensure there is no cirrhosis before starting treatment, **noninvasive liver assessment tests** that calculate liver enzyme levels, platelets, and patient's age, such as aspartate aminotransferase to platelet ratio index (APRI) or FIB-4, are recommended in limited resource settings **instead of liver biopsies**.
- Liver damage can also be assessed by other noninvasive methods, such as ActiTest or FibroTest, or ultrasound imaging with FibroScan, but these are usually found in high-income settings.
- Additional conditions such as **comorbidity, pregnancy, or drug-drug interactions** should also be evaluated.
- Information on how to prevent hepatitis B and C infection and offering vaccination against HBV, including to PWID, can avoid the risk of people having two liver infections at the same time.
- For people diagnosed with active HCV infection, providers should **ask about alcohol use** and counsel patients with moderate or high levels of alcohol use on steps to reduce alcohol consumption, prevent further liver damage, and care for their overall liver health.

The WHO also released the Model List of Essential In-Vitro Diagnostics,<sup>35</sup> which complements the Essential Medicines List. It is not prescriptive, but serves to guide countries in making decisions on the selection and implementation of diagnostic technologies needed to address their specific public health burdens (see Table 3).

Just like with medicines, we need to ensure the tests we use are accurate, simple to use, and high quality. We do not want to miss an active infection or give someone a false positive diagnosis. For HCV antibody RDTs, there are over 72 tests on the market with varying degrees of quality, accuracy, and pricing. Of the 72 tests, 23 had manufacturers provide pricing information, indicating a range of US\$0.18–1.50 per test.

There are several ways that countries can assure the quality of diagnostic products. In choosing an optimal test, looking at a test's **sensitivity**

and **specificity** are important characteristics for determining the quality. Sensitivity is the true positive rate, or the test's ability to correctly identify people with HCV.<sup>36</sup>

**High sensitivity, which is closer to 100 percent, avoids missing an HCV infection** (that is, saying someone is not infected when they are).

**Specificity** is the true negative rate, or the test's ability to correctly identify people without HCV.

**High specificity, which is close to 100 percent, helps to determine the quality of a test to avoid misinforming a person about being infected when they are not.**

**Table 3. Types of Hepatitis C Tests in the WHO Model List of Essential In-Vitro Diagnostics**

|                                       | Diagnostic test   | Test purpose  | Assay format                      | Specimen type                         |
|---------------------------------------|---|---|-----------------------------------|---------------------------------------|
| <b>Hepatitis C</b>                    | Antibodies to HCV (anti-HCV)  | Screening for HCV infection: Infants over 18 months of age, children, adolescents, adults                 | RDT                               | Venous whole blood<br>Plasma<br>Serum |
|                                       |   |   | EIA (microplate)<br>Manual method | Serum<br>Plasma                       |
|                                       |   |   | CLIA/ECL (automated instrument)   | Serum<br>Plasma                       |
|                                       | Antibodies to HCV (anti-HCV) and HCV core antigen (HCV cAg)   | Screening for HCV past of present infection: infants over 18 months of age, children, adolescents, adults | EIA (microplate)<br>Manual method | Serum<br>Plasma                       |
|                                       |   |   | CLIA/ECL (automated instrument)   | Serum<br>Plasma                       |
|                                       | HCV core antigen (HCV cAg)  |   | NAT                               | Serum<br>Plasma                       |
| HCV RNA (qualitative or quantitative) | For the diagnosis of viraemic HCV infection and monitoring of response to treatment as a test of cure | NAT   | Serum<br>Plasma                   |                                       |

One regulatory standard is the WHO prequalification (PQ) process. WHO PQ assesses the quality, safety, and efficacy of medicines, active pharmaceutical ingredients, medical products, and quality in vitro diagnostics particularly suitable for use in low- and middle-income countries. It is not a prescriptive list, but it can be used as a standard to help large international procurement agencies (e.g., the Global Fund on AIDS, Malaria and Tuberculosis, UNICEF, UNITAID, etc.) and countries, especially in resource-limited settings and with limited domestic regulatory frameworks and capacity to consider medicines and medical devices that meet high quality standards to procure for national programs and to avoid duplicative regulatory approval procedures. The WHO PQ process involves a manufacturer submitting an application for prequalification; a dossier review to determine the safety, performance, design, and manufacturing of a product; a manufacturing site inspection to evaluate compliance with international quality management standards; a laboratory evaluation of the product; and post-marketing surveillance.<sup>35</sup>

PQ assessment fees can cost US\$5000–12,000 per product plus an annual fee of US\$4000 to keep products listed on the WHO PQ list.<sup>36</sup> Smaller firms or those with smaller markets may not be incentivized to submit to this process. While the process ideally takes less than one year to review,<sup>37</sup> there may be lengthy periods of communication to clarify and gather additional information from the manufacturer, which may add months to the process. Manufacturers that wait through the WHO PQ process may lose sales and see reduced cash flow, which may cause them to withdraw from the process or enter the market later than planned.<sup>38</sup> Additional staffing and funding, and streamlining for reviewing products suitable for LMICs, are recommendations to speed up the WHO PQ process.<sup>39</sup>

The US Food and Drug Administration (FDA) and Conformité Européenne (marked as CE or CE-IVD) also serve as regulatory standards for in vitro diagnostics. However, there are few PQ and CE-marked products; countries procuring diagnostics through the Global Fund are limited to these. There is only one PQ and CE-marked viral load test and one for core antigen tests (see Table 4).

Table 4. WHO Prequalified and CE-Marked HCV Tests: Challenges Remain <sup>40 41 42 43</sup>

| Test                      | Sample        | Result time | Multi-plexing             | Price (ex works or free carrier)<br><sup>46 47</sup> | Regulatory Status                 | Under WHO PQ Review | Suitable for LMICs; Needs Advocacy                                   |
|---------------------------|---------------|-------------|---------------------------|--|-----------------------------------|---------------------|--|
| <b>Enzyme Immunoassay</b> |               |             |                           |  |                                   |                     |  |
| <b>INNOTEST HCV Ab IV</b> | Serum, plasma | 179 min     | Yes (HIV & other markers) | ND   | <b>WHO PQ</b>                     |                     | Suitable for central labs  |
| <b>INNO-LIA HCV Score</b> | Serum, plasma | 1 day       | No                        | ND   | <b>WHO PQ</b><br><b>CE-marked</b> |                     | Strip-based method but requires cold chain and other small equipment |

Table 4. WHO Prequalified and CE-Marked HCV Tests: Challenges Remain <sup>40 41 42 43</sup>

| Test                          | Sample                            | Result time | Multi-plexing                     | Price (ex works or free carrier)   | Regulatory Status               | Under WHO PQ Review | Suitable for LMICs; Needs Advocacy    |
|-------------------------------|-----------------------------------|-------------|-----------------------------------|------------------------------------|---------------------------------|---------------------|---------------------------------------|
| <b>Enzyme Immunoassay</b>     |                                   |             |                                   |                                    |                                 |                     |                                       |
| Bioelisa HCV 4.0              | Serum, plasma                     | 150 min     | Yes (HIV, HBV, HEV, among others) | ND                                 | WHO PQ, CE-marked               |                     | Suitable for central labs             |
| Murex Anti-HCV 4.0            | Serum, plasma                     | 120 min     | Yes (HIV, HBV, HEV, among others) | ND                                 | WHO PQ, CE-marked               |                     | Suitable for central labs             |
| Enzygnost Anti-HCV 4.0        | Serum, plasma                     | 120 min     | Yes (HBV, HAV)                    | ND                                 | Did not receive WHO PQ approval |                     | Suitable for central labs             |
| <b>Rapid Diagnostic Tests</b> |                                   |             |                                   |                                    |                                 |                     |                                       |
| OraQuick HCV RDT              | Oral, fingerstick, venous blood   | 20 min      | No                                | US\$8 (MSF price); US\$12 per test | WHO PQ, CE-marked, FDA approved |                     | Price remains too expensive for LMICs |
| SD Bioline                    | 10 µL whole blood, serum, plasma  | 5-20 min    | HIV                               | US\$1-2.40 per test                | WHO PQ                          |                     |                                       |
| Intec Rapid anti-HCV          | 10 µL, whole blood, serum, plasma | 15-20 min   | No                                | <US\$1-2.40 per test               | WHO PQ, CE-marked               |                     |                                       |
| Standard Q HCV Ab Test        | Whole blood, serum, plasma        | 5 min       | No                                | ND                                 |                                 | WHO PQ under review |                                       |

| Test   | Sample  | Result time                     | Multi-plexing | Price (ex works or free carrier)   | Regulatory Status  | Under WHO PQ Review  | Suitable for LMICs; Needs Advocacy   |
|--|---|---------------------------------|---------------|--|--|--|--|
| <b>(Rapid Diagnostic Tests cont'd)</b>                           |   |                                 |               |  |  |  |  |
| <b>Premier Medical Corporation First Response® HCV Card Test</b> | Whole blood, serum, plasma  | ND                              | No            | US\$0.60-1 per test  | <b>CE-marked</b>   | <b>WHO PQ</b> under review (Expert Review Panel for Diagnostics) |  |
| <b>ABON HCV Rapid Test Device</b>                                | Whole blood, serum, plasma  | ND                              | No            | ND   |  | <b>WHO PQ</b> under review                                       |  |
| <b>Viral Load (RNA/NAT)</b>                                      |   |                                 |               |  |  |  |  |
| <b>Cepheid Xpert VL Assay (use with Cepheid GeneXpert)</b>       | Plasma samples, can be PoC  | Same-day results in 108-110 min | HIV, TB       | US\$17,000 per instrument; US\$14.90 per test (for all virological tests in LMICs) | <b>WHO PQ, CE-marked</b> , not approved in United States |  | Can be used for all genotypes; need WHO recommendations for use in all genotypes   |
| <b>Cepheid Xpert VL Fingerstick</b>                              | 100 µL, capillary blood, Fingerstick Tertiary PoC: harm reduction settings, may be easier to give for some PWID with poor vein access | Within 60 min                   | HIV           | ND   |  |  | Modified version of the VL assay; <b>CE-marked</b> , not approved in United States |
| <b>Genedrive HCV RNA</b>   | 30 µL plasma, serum   | 90 min                          | No            | US\$5000 per device; US\$25-35 per test  |  | <b>CE-marked, WHO PQ</b> under review                            |  |

| Test                                    | Sample                           | Result time | Multi-plexing | Price (ex works or free carrier)   | Regulatory Status | Under WHO PQ Review  | Suitable for LMICs; Needs Advocacy |
|---|----------------------------------|-------------|---------------|--|-------------------|--|------------------------------------|
| <b>(Viral Load (RNA/NAT) cont'd)</b>    |                                  |             |               |  |                   |  |                                    |
| <b>RealTime HCV Viral Load</b>          | 0.5 mL plasma, 0.2 mL serum, DBS | ND          | HIV           | US\$11–23 per test; Global Fund price varies according to test volume/term commitment  |                   | <b>CE-marked</b> for HIV DBS and HCV RNA plasma and serum only, <b>WHO PQ</b> under review |                                    |
| <b>Abbott Alinity m HCV assay RNA</b>   | Plasma, serum                    | ND          | No            | US\$50 per test  |                   | <b>CE-marked, WHO PQ</b> under review  |                                    |
| <b>Hologic Aptima HCV Quant</b>         | Serum, plasma<br>Lab-based       | ND          | HIV           | US\$10–15 per test; US\$12 all-inclusive price for HCV VL                              |                   |  | <b>CE-marked, FDA-approved</b>     |
| <b>Biocentric Generic HCV PCR assay</b> | Serum, plasma                    | ND          | HIV           | US\$23 per test<br>US\$13.50–17 (€12–15) per test (updated price expected by end-2019) |                   |  | <b>CE-marked</b>                   |

| Test   | Sample                                   | Result time  | Multi-plexing                     | Price (ex works or free carrier)  | Regulatory Status                | Under WHO PQ Review        | Suitable for LMICs; Needs Advocacy |
|--|--|--|-----------------------------------|---|----------------------------------|----------------------------|------------------------------------|
| <b>(Viral Load (RNA/NAT) cont'd)</b>           |  |  |                                   |   |                                  |                            |                                    |
| <b>Roche Cobas 6800/8800 systems (HCV RNA)</b> | Lab-based, high-volume clinical settings | First 96 results <3.5 hours, every 90 min for 96 more results (Cobas 6800 System); first 96 results <3.5 hours, every 30 min for 96 more results (Cobas 8800 System) | HIV                               | US\$35–45 per test;<br><br>US\$340,000- US\$475,000 per instrument (depending on instrument and volume) |                                  |                            | <b>CE-marked</b> , FDA-approved    |
| <b>Core Antigen</b>                            |  |  |                                   |   |                                  |                            |                                    |
| <b>Abbott ARCHITECT HCV Ag</b>                 | Serum, plasma                            | ND   | Yes (HIV, HBV, HAV, among others) | US\$8-23 (€7–20) per test; US\$100,000 per instrument   | <b>CE-marked</b> , <b>WHO PQ</b> |                            | Suitable for central labs          |
| <b>Monolisa HCV Ag-Ab ULTRA V2</b>             | Serum, plasma                            | ND   | Yes (HIV, HBV, HAV, among others) | ND  | <b>CE-marked</b>                 | <b>WHO PQ</b> under review | Suitable for central labs          |

Rigorous regulatory approval processes can delay market entry of diagnostics and creates artificial monopolies in countries waiting to approve alternative platforms and tests.

Diagnostics advocacy is vital for ensuring people have access to high-quality, simple, affordable diagnostics in their countries. Part of this advocacy needs to ensure that there is competition in the diagnostics market.

## Advocacy Exercise

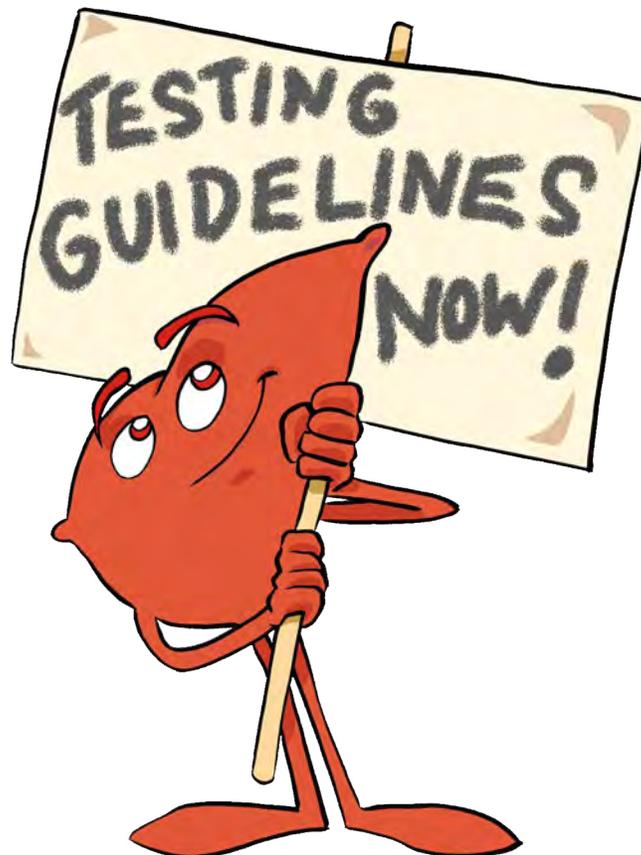


### Discussion questions:

- What is included in our national testing guidelines?
- How does this differ from WHO Testing Guidelines?
- What tests are available in our healthcare system?
- How does this differ from the WHO Essential Diagnostics List?

### Action steps:

- How can we effectively change and improve testing guidelines in my country?
- Have there been any campaigns to widen access to HCV diagnostics for key affected communities in my country or region?
- What are some ways that we can demand simpler, non-invasive, more affordable tests in my country?



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<sup>33</sup> World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018 July (cited 2019 June 10). Available from: <https://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1>.

<sup>34</sup> See also TREAT Asia/amFAR. Fact sheet: WHO guidelines for the screening, care, and treatment of persons with hepatitis C infection. Bangkok: TREAT Asia/amFAR; 2019 January 9 (cited 2019 September 10). <https://www.amfar.org/who-factsheet2019/>.

<sup>35</sup> World Health Organization. Model list of essential in-vitro diagnostics, 2nd edition. Geneva: WHO; 2019 (cited 2019 July 10). Available from: [https://www.who.int/medical\\_devices/publications/Standalone\\_document\\_v8.pdf?ua=1](https://www.who.int/medical_devices/publications/Standalone_document_v8.pdf?ua=1).

<sup>36</sup> Fajardo E. Hepatitis diagnostics: Landscape, pipeline, priorities and market. Presentation at: Global Health Diagnostics; 2018 June 13; McGill University, Montreal, Canada.

<sup>37</sup> WHO. Overview of prequalification of in vitro diagnostics. Geneva: WHO; 2018 (cited 2019 September 10). Available from: <https://www.who.int/medicines/regulation/prequalification/prequal-in-vitro-diagnostics/ivd-prequal-process/en/>.

<sup>38</sup> Ibid.

<sup>39</sup> Ibid.

<sup>40</sup> Morin S, Bazarova N, Jacon P, Vella S. The manufacturers' perspective on World Health Organization Prequalification of in vitro diagnostics. *Clin Inf Dis*. 2018 January 15;66(2):301–5. doi: 10.1093/cid/cix719.

<sup>41</sup> Ibid.

<sup>42</sup> Fajardo E. Hepatitis diagnostics: Landscape, pipeline, priorities and market. Presentation at: Global Health Diagnostics; 2018 June 13; McGill University, Montreal, Canada.

<sup>43</sup> World HCV Community Advisory Board. Forging a path to HCV elimination: Simpler tests and affordable generics. Report of the World Community Advisory Board on HCV Generics and Diagnostics. Bangkok, Thailand; 2017 July 18–20 (cited 2019 September 10). Available from: [https://www.hepcoalition.org/IMG/pdf/hcv\\_world\\_cab\\_report\\_2017.pdf](https://www.hepcoalition.org/IMG/pdf/hcv_world_cab_report_2017.pdf).

<sup>44</sup> Treatment Action Group. HCV Diagnostics: Pipeline Report 2018. New York: Treatment Action Group. Available from: <http://www.treatmentactiongroup.org/pipeline-report>.

<sup>45</sup> Treatment Action Group. HCV Diagnostics: Pipeline Report 2019. New York: Treatment Action Group. Available from: <http://www.treatmentactiongroup.org/pipeline-report>.

<sup>46</sup> Prices vary and depend on the licensing agreements and volume in which they are procured. The pricing information in Table 4 derives from the HCV Community Advisory Board meetings with diagnostics companies and gives a general benchmark. The prices reflect ex works price, or when the supplier must cover the transportation costs, or the free carrier price, in which the company handles the customs and transportation costs. It is important for companies to be transparent about their pricing and for purchasers and advocates to ask companies what is included in the price.

<sup>47</sup> Shilton S. Diagnostics for hepatitis C: where do we stand and what lies ahead? Presentation at: INHSU; 2019 September 12; Montreal, Canada.

# Section 3

## Determining Whom to Test

A number of factors determine who is tested and treated and how national plans incorporate WHO screening and testing strategies, including epidemiology, funding and resources, and the health priorities in the country. Before the arrival of DAAs, people diagnosed with HCV either were treated with less tolerable, less effective pegylated interferon regimens or were not linked to treatment. As DAAs become more widely available in countries, people already diagnosed are prioritized for treatment.

Yet diagnosing new active infections has not kept up with numbers of initiated treatments.

**Diagnostic burnout and finding the tens of millions of people with new active infections is one of the greatest challenges that countries now face.**

### Screening strategies: who to test for HCV?



To scale up diagnosis, the WHO Guidelines focus on three testing strategies to assist countries with identifying new active infections<sup>48</sup>:

| Testing Strategy  | Settings / Populations  | Recommendations   |
|---|---|---|
| <p>Targeted testing in the most affected populations (key populations). These communities are considered most affected due to the significant stigma, discrimination, criminalization, marginalization, vulnerability, high HIV and HCV incidence and prevalence, and tremendous barriers they face in access in healthcare services.</p> | <p>People who inject drugs, men who have sex with men, incarcerated people, sex workers, indigenous people, people coinfecting with HIV/HCV</p> | <ol style="list-style-type: none"> <li>1 Antibody tests should be offered, and adults and adolescents, either from communities with high HCV seroprevalence, who have had a history of exposure to infectious diseases, and/or who engage in higher-risk behaviors, should be linked to prevention, harm reduction, treatment, and care services.</li> <li>2 Adults, adolescents, and children who are suspected to have chronic viral hepatitis, such as through symptoms, laboratory markers, or other signs, should be offered testing.</li> <li>3 People who show ongoing risks of acquiring HCV or who have been reinfecting should be considered for periodically retested for HCV with viral load tests.</li> <li>4 In FIND studies, one-step screening and antibody rapid diagnostic tests are shown to reduce patients who may be lost to follow-up visits.</li> <li>5 In FIND studies, when patients take rapid diagnostic tests, the results are given on the same visit. If a patient tests antibody positive, then two samples are taken: one for RNA and one for liver staging. Patients who return can be given their RNA and liver staging results on the same visit, then assessed for treatment.</li> </ol> |

| Testing Strategy           | Settings / Populations  | Recommendations  |
|----------------------------|---|--|
| General population testing | Settings with greater or equal to 2% or 5% HCV antibody prevalence (depending on the overall epidemiological context)   | <ol style="list-style-type: none"> <li>1 All adults in this setting should have access to and be offered HCV antibody testing with linkage to prevention, harm reduction, treatment, and care services.</li> <li>2 Countries can make use of existing community or lab-based testing, such as at HIV/sexual health or TB clinics, drug treatment facilities, or antenatal clinics.</li> <li>3 In FIND studies, one-step screening and antibody rapid diagnostic tests are shown to reduce patients who may be lost to follow-up visits.</li> <li>4 In FIND studies, when patients take rapid diagnostic tests, the results are given on the same visit. If a patient tests antibody positive, then two samples are taken: one for RNA and one for liver staging. Patients who return can be given their RNA and liver staging results on the same visit, then assessed for treatment.</li> </ol> |
| Birth cohort testing       | Specific identified birth cohorts at higher risk of infection and death relative to the general population, such as older adult exposure to unscreened blood products or unsterile vaccination injections | <ol style="list-style-type: none"> <li>1 Antibody tests should be offered to all adults in this birth cohort.</li> <li>2 In FIND studies, one-step screening and antibody rapid diagnostic tests are shown to reduce patients who may be lost to follow-up visits.</li> <li>3 In FIND studies, when patients take rapid diagnostic tests, the results are given on the same visit. If a patient tests antibody positive, then two samples are taken: one for RNA and one for liver staging. Patients who return can be given their RNA and liver staging results on the same visit, then assessed for treatment.</li> </ol>  |

Broad, diverse, and inclusive partnerships among government agencies, the private sector, civil society, and grassroots organizations, including the meaningful and active participation by community members, play a strong role in awareness-building, screening, and confirmatory testing strategies. Diagnostics and liver

assessment tools can connect community members, who may otherwise be underserved or distrusting of the health system, to a range of healthcare and social services, including harm reduction, mental health, housing, and legal services.



## Diagnosing HCV in key affected populations

People who belong to groups who are disproportionately affected by HCV should be prioritized in national testing strategies. Screening and testing these groups wherever they are receiving services could also link them to other essential prevention, sexual health, and harm reduction services:

- People who receive hemodialysis
- People who have had a blood transfusion or received blood products that may not have been screened by national blood banks
- Health professionals exposed to blood products
- People living with HIV
- Men who have sex with men
- Transgender or gender non-conforming people
- People who inject or use drugs (and their sexual partners)
- Women of reproductive age (due to lack of preventative vaccine and prophylaxis to prevent parent-to-child transmission of HCV)
- Incarcerated persons
- Sex workers

The criminalization of drug use, sex work, homosexuality, and transgender and gender-nonconforming identities in the majority of countries make targeted, risk-based testing among vulnerable, affected populations extremely challenging. In this context, health authorities may opt for general population screenings, such as for people seeking driving licenses or visas or enrolling in university or the military. However, this approach misses infections and overlooks communities most affected by hepatitis C.

Different populations will require different strategies and outreach to conduct HCV screening. A combination of targeted screening among key affected populations and universal screening in settings with high prevalence, such as prisons, harm reduction sites, overdose

prevention centers, and migrant or detention centers, could reduce transmission and work toward elimination. We need to explore different approaches that work in different key affected populations because they may be getting their related care in different settings.

Opioid substitution therapy (OST)/medication-assisted treatment (MAT) and needle syringe exchange programs (NSEPs) provide critical, life-saving services for people who use drugs. Harm reduction services in the response to HIV can be scaled up for HCV, yet these services need to be expanded and adapted according to changing drug use patterns in your country. People who use stimulants, which may include men who have sex with men, recreational users, participants in the ‘chemsex’ scene, and sex workers, may be accessing care through sexual health clinics. People conducting screening and counseling need to consider the range of higher-risk behaviors and that people who use drugs and their sexual partners should be offered comprehensive health services, including testing.

Organizations working with non-heterosexual or gender non-conforming people, including transgender people, are important for raising awareness on HCV and linking peers to testing services.

**Peer-led, informal, safe, community-friendly discussions about HCV and referral to services could be more appropriate, especially in current stigmatized, criminalized contexts.**

Community leaders, such as mentors or “house mothers or fathers” for LGBTQ+ youth, should be part of outreach and screening strategies. They can disseminate accurate HCV-related information in communities often overlooked.

Prison health budgets are limited for the full range of HCV care. In this setting, ‘opt-out’ HCV screening can be offered to everyone; this gives

incarcerated individuals the choice not to take the antibody test. 'Opt-out' HCV screening can link people to confirmatory testing, treatment, and care following their release from prison.

Treatment advocates need to be engaged in planning processes to inform national or local screening strategies. Until wider, affordable access to DAAs and PoC diagnostics is secured, health authorities could prioritize screening in health facilities, such as antenatal clinics and hospitalized patients. Then strategies could shift to scaling up screening among key higher-risk populations, before universal screening for all adults is considered.

## We need to find the 'Missing Millions'



To raise awareness on the need to increase testing and treatment, the World Hepatitis Alliance, a global patient advocacy organization, launched the global 'Missing Millions' campaign.<sup>49</sup> HCV advocates across the civil society spectrum can take part in the campaign on World Hepatitis Day (every 28th of July) or any hepatitis C-related events in your country.

## Find The Missing Millions.

The campaign objectives are as follows:

1. To raise awareness of the importance of increasing diagnosis and linkage to care.
2. To encourage people to get tested.
3. To underscore the need for national testing policies, in line with WHO Guidelines.
4. To educate and inform wider audiences about viral hepatitis, with a specific focus on prevention, treatment, and testing.

# Advocacy Exercise

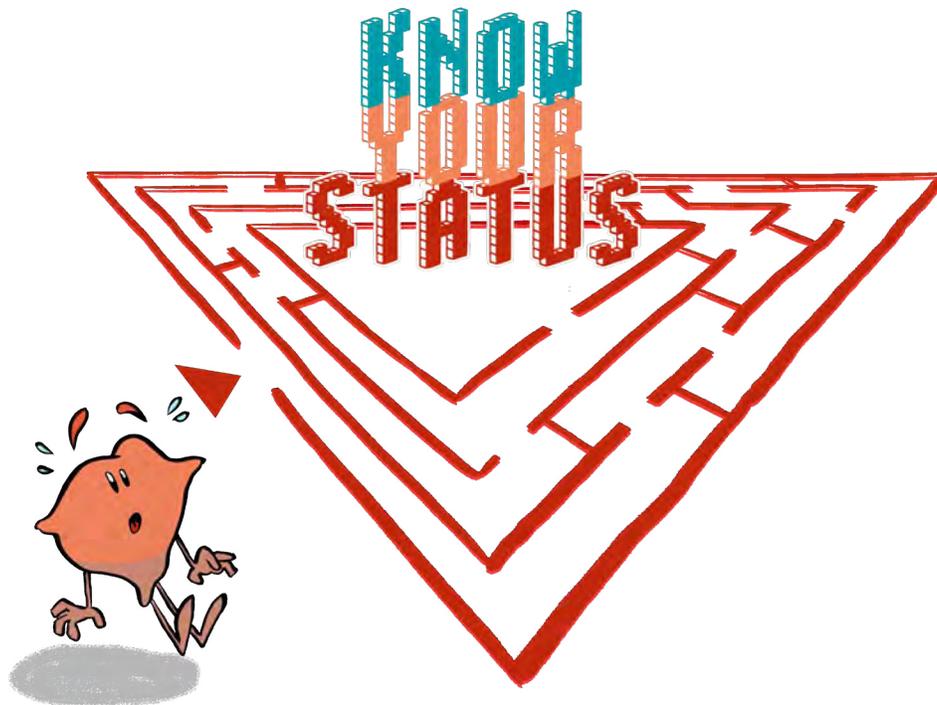


## Discussion questions:

- Do you know where people can get tested for HCV in your community?
- What questions should people ask their doctors to know their HCV status?
- Does the doctor take time to explain the different tests?
- Are there free testing sites? If not, how much do the tests cost?

## Action steps:

- What can we do to make HCV testing easier to access?
- What can we do to increase access to expensive tests?
- What are some good examples of where people can be tested outside a laboratory or central hospital?



<sup>48</sup> Adapted from World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018 July (cited 2019 June 10). Available from: <https://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1>.

<sup>49</sup> Campaign tools, graphics and messaging can be found at: <http://www.worldhepatitisalliance.org/missing-millions/>.

# Section 4

## Minimizing Steps to Diagnosis



**With pangenotypic DAAs, the aim should be to confirm diagnosis and start treatment on the same day.**

That means:

1. Every positive antibody (screening) tested goes on to RNA (confirmatory) testing automatically. This is known as reflex testing;
2. A liver staging test, such as APRI, FIB-4, FibroScan, or other test, is done to determine the level of cirrhosis; and
3. The appropriate DAA regime is provided.



### Simplifying the diagnostics pathway

In many settings, especially those without access to pangenotypic DAAs, the numerous steps to diagnosis, treatment initiation, and test-of-cure at week 12 or 24, after treatment, are complicated for the patient and result in losing patients to follow-up visits. Often, many patients from marginalized populations who receive an HCV antibody test do not return for confirmatory testing.<sup>50</sup> Centralized testing, in which clinics and small labs send samples and rely on infrastructure at central laboratories, certainly has role in scaling up the number of people who are diagnosed with HCV and linking people to care. When antibody and confirmatory testing is only available at central labs, this presents costly barriers that require patients to take a lot of time and to sometimes travel great distances.

**Decentralized testing brings testing to points of care**, such as at NSEPs or wherever people are receiving their services, and can retain people in care.<sup>51</sup>

Taking samples at decentralized points of care and sending them to centralized labs has also been shown to be effective in scaling up diagnoses and linking people to care.

DAAs are safe, effective, and easy for nonspecialist providers to administer, and the WHO no longer recommends viral load monitoring and adherence checks at weeks 4 and 8 during a treatment course. National guidelines can be updated to shift DAA prescriber status from liver and infectious diseases specialists to general practitioners. When simpler diagnostics become more available in countries, the HIV, sexual health, and harm reduction infrastructure can be leveraged for HCV testing. This creates opportunities to shift and expand diagnostics tasks, such as conducting blood tests, from physicians and nurses to other health professionals, including community health workers and peer educators, with the appropriate training.

Relying only on centralized testing and treatment creates a bottleneck and puts a huge strain on resources, staffing, and the overall healthcare system. **Adding steps to diagnosis adds costs.**

### Minimum steps to diagnosis<sup>53 54</sup>

The steps to diagnosis could be reduced by taking a sufficient quantity of a patient's sample so that when a patient has a positive antibody test, the sample, if correctly stored, is automatically ordered for confirmatory (RNA or cAg HCV) testing (also known as **reflex testing**). The same sample could be used for liver disease staging, too.

While a patient waits for the confirmatory test results, a liver disease staging test, such as FIB-4 or APRI in resource-limited settings, could be conducted to assess the extent of liver damage. Patients below or above a FIB-4 score of 3.25 would start treatment. Someone with a FIB-4 score higher than 3.25 should be assessed for cirrhosis and other liver complications.

The extent of liver damage determines the length of DAA treatment.<sup>55</sup> In resource-limited settings, the generic pangenotypic combination of sofosbuvir and daclatasvir is a cost-saving, effective regimen. With a pangenotypic regimen, genotype testing would not be necessary.<sup>56</sup>

Confirmation can be done by qualitative (“positive”/“negative”) RNA tests, which may have reduced sensitivity but a shorter time to result.<sup>57</sup>

RNA tests to confirm that a patient achieved sustained virological response should be conducted at week 12 (or week 24 for patients with cirrhosis). Patients who did not achieve SVR would be considered as failing treatment and would be assessed and counseled for other treatment regimens, or other medical interventions in cases of liver failure.

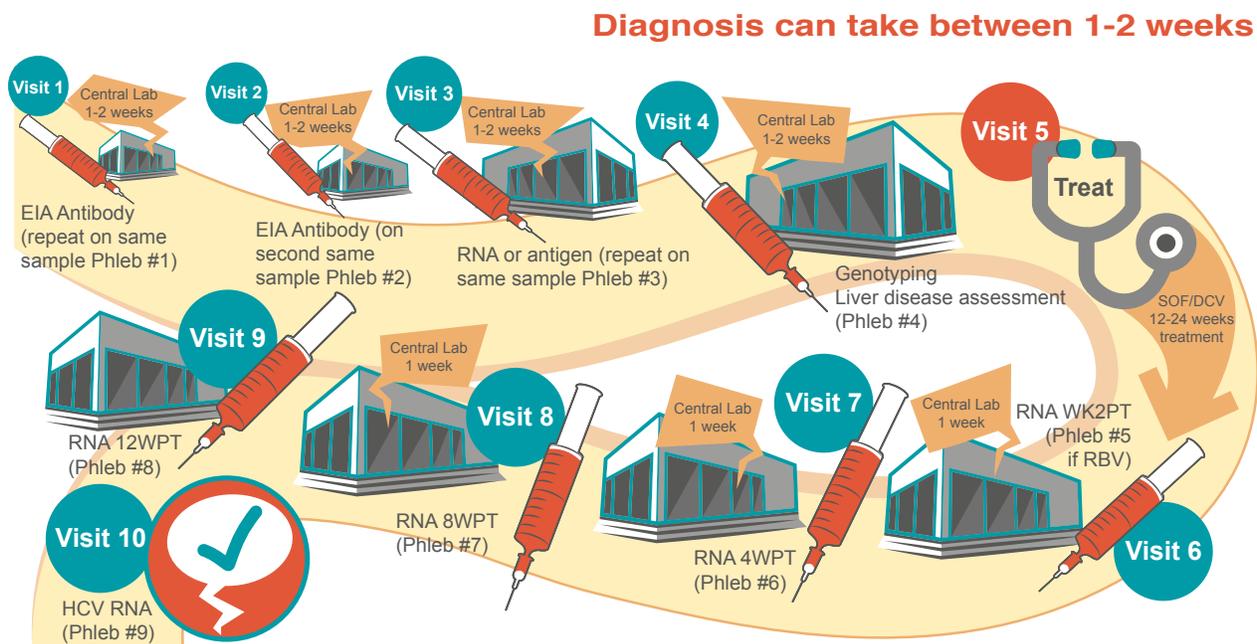
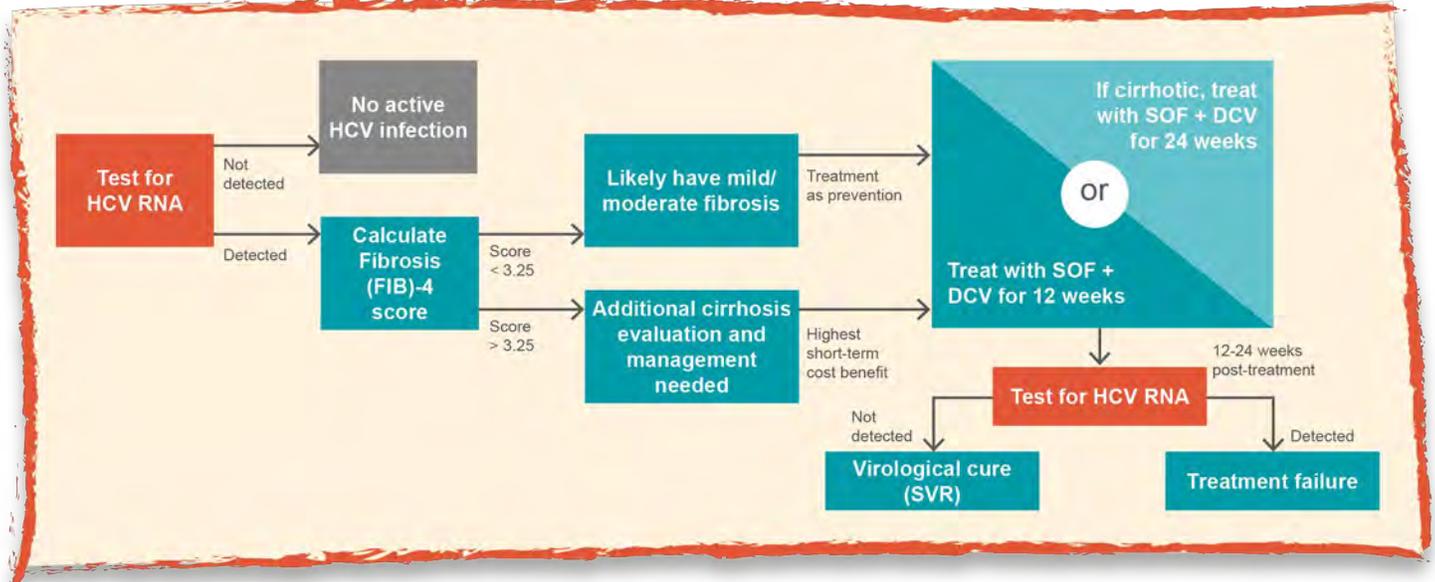


Figure 3. Example of previous, complicated diagnostics pathway.<sup>52</sup>



In communities or settings with high HCV prevalence, such as among people who inject drugs or in prisons, it might be advisable to skip antibody screening and start with confirmatory testing, in order to prevent loss to follow up and to increase treatment starts.<sup>58</sup>

In LMICs, where patients may have to take off a day's work, arrange for childcare, and travel long distances, the number of patient visits can be reduced and other services can be integrated to retain patients in care.

For example:

**Visit 1:** HCV antibody and PoC RNA tests can be conducted along with liver disease assessment, such as APRI, FIB-4 or FibroScan.

**Visit 2:** Patient receives test results, check-in and counseling with physician/healthcare professional, and prescription for generic pangenotypic DAA.

**Visit 3:** SVR12 test depending on whether patient completed treatment.

**Follow-up visits:** For people who may be at risk of reinfection or who have advanced liver disease, re-testing and monitoring for liver cancer would need to be performed.

Other services, such as HAV/HBV testing and vaccination, HIV testing and counseling, pregnancy testing and family planning, prevention, mental health and harm reduction services, and other consultations for referral services, could be offered so that clinics become 'one-stop shops' where patients can receive comprehensive services in one visit.

In some real-world studies, such as in Cambodia,<sup>59</sup> simplifying the diagnostics pathway has been shown to increase the number of patients who were screened, confirmed as HCV positive, and started treatment. In Cambodia, the simplified pathway and model of care retained nearly all patients in care until they tested for the confirmation of cure at week 12.

## Decentralization



After defining the national epidemic and determining whom to test in the national testing strategy, health authorities should plan for the decentralization of HCV diagnostics according to affordability, availability, quality, and lab/health systems infrastructure. Decentralization brings testing closer to people, wherever they may be receiving services, and provides opportunities to link and retain patients in care.

A number of models of care are being explored to expand decentralization. In urban areas, one-stop shops are poly-clinics that offer all HCV test-and-treat services or multiple healthcare services in one clinic. HCV care is being integrated into HIV, sexual health, and family planning clinics, and integration can be considered for expanding HCV care to rural and remote areas. In countries with existing harm reduction programs, HCV is being integrated at harm reduction centers and in mobile clinics that serve people who inject drugs. Other diagnostic implementation research highlights the roles of primary healthcare, community health clinics, needle syringe exchange programs, substance use disorder centers, overdose prevention sites, prisons, homeless shelters, youth centers, pharmacies, and mobile units in offering community-based testing and linking people to treatment and care.

Telemedicine and the Extension for Community Health Outcomes (ECHO) model are other ways that can reshape healthcare delivery, beyond viral hepatitis, in resource-limited settings, including for geographically isolated and underserved populations. The ECHO model involves training physicians, physician assistants, nurses, pharmacists, and educators in HCV, using web-based software. Clinical knowledge is brought to the patient and physicians who are treating patients with HCV are responsible for managing patients' health outcomes through 'teleECHO' clinics to provide case-based guided practice. Data, health outcomes, and the cost-effectiveness of the programs are collected centrally, such as a main city with access to specialists and resources. This differs from traditional telemedicine, in which specialists manage patients remotely. The ECHO model is one way to build capacity of general practitioners and auxiliary health professionals, complement the decentralization of diagnostics, and help improve HCV treatment uptake.<sup>60</sup>

## Task-shifting



Decentralization of HCV diagnostics involves massive training and capacity building of a wide range of healthcare workers. Continued medical education and community health education need to be included in national HCV programs. Testing and treatment guidelines need to be simplified so that service delivery can be shifted to other health professionals (**task-shifting**) and made more efficient.<sup>61</sup>

Task-shifting should be tailored according to countries' needs and should occur alongside strategies to increase the numbers of skilled healthcare workers through expanded educational and training programs. People living with HIV/HCV or most affected by these diseases should be consulted and included in the design, leadership, and decision-making in the HCV response. Policy and regulatory changes, such as shifting RDT testing to community health workers through training and simplified reporting systems, lifting restrictions on prescriber status for DAAs, and standardized medical certifications required for administering HCV care by other healthcare workers, should be fast-tracked. Clinical mentoring and supportive supervision to healthcare workers should be regularly provided, and opportunities to evaluate competency and performance should be planned.<sup>62</sup>

**People with lived experience, such as peer educators, play a critical role in scaling up diagnostics and increasing the number of people cured.**

They bring invaluable expertise, knowledge, and ways of connecting and bringing members of their community, who may be distrusting of the healthcare system, to seek services in a more welcoming, community-friendly environment.

Shifting testing tasks to more community health workers and peer educators, with the appropriate training and fair remuneration, can be an efficient and cost-saving way to help with patient follow-up and retention in care.<sup>63</sup>

Scaling up diagnosis and implementing a simpler diagnostics pathway involves other factors, such as the resources allocated to increase the outreach and engagement of communities disproportionately affected by HCV.

Diagnostics availability and access in countries and the simplification of treatment protocols so that nonspecialists can prescribe pangenotypic DAAs are also part of the equation to determine a successful HCV response.



## Advocacy Exercise

### Discussion questions:

- What steps can be minimized to simplify the diagnostic pathway in your country?
- What are the guidelines toward viral load adherence?
- What are the guidelines toward genotype testing?

### Action steps:

- What ways can community members contribute to reducing the number of patients lost to follow-up?

- 
- <sup>50</sup> Feld JJ. Hepatitis C virus diagnostics: the road to simplification. *Clin Liver Dis*. 2018;12:125–9. doi:10.1002/cld.760.
- <sup>51</sup> Applegate TL, Fajardo E, Sacks JA. Hepatitis C virus diagnosis and the holy grail. *Inf Dis Clin NA*; 2018;32(2):425–45. doi:10.1016/j.idc.2018.02.010.
- <sup>52</sup> Adapted from Applegate T, Asian Pacific Conference for the Study of the Liver 2018 in Gaudino A. The cost of diagnostics. Presentation at: INHSU; 2018 September 20; Cascais, Portugal.
- <sup>53</sup> Adapted from Graham CS and Swan T. A path to eradication of hepatitis C in low- and middle-income countries. *Antiviral Res*. 2015 Jul;119:89–96. doi: 10.1016/j.antiviral.2015.01.004. Epub 2015 Jan 20.
- <sup>54</sup> Dr Saeed Hamid's real-world protocol in Pakistan in Luhman N. The rocky road to viral hepatitis elimination: Approaches for simplified HCV diagnostics and screening algorithms: Thoughts about a public health approach for LMICs. Presentation at: 4th International HIV/Viral Hepatitis Co-infection Meeting. Paris, France; 2017 July 22-23 (cited 2019 September 10). Available from: [http://www.iasociety.org/Web/WebContent/File/3\\_D\\_1150-1215\\_Niklas\\_Luhmann.pdf](http://www.iasociety.org/Web/WebContent/File/3_D_1150-1215_Niklas_Luhmann.pdf).
- <sup>55</sup> For more detailed information about available hepatitis C treatment regimens: Treatment Action Group. HCV Fact Sheets. New York: Treatment Action Group. Available from: <http://www.treatmentactiongroup.org/hcv/factsheets>.
- <sup>56</sup> World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018 July (cited 2019 June 10). Available from: <https://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1>.
- <sup>57</sup> Feld JJ. Hepatitis C virus diagnostics: the road to simplification. *Clin Liver Dis*. 2018;12:125–9. doi:10.1002/cld.760.
- <sup>58</sup> Scott N, Sacks-Davis R, Pedrana A, Doyle J, Thompson A, and M Hellard. Eliminating hepatitis C: The importance of frequent testing of people who inject drugs in high-prevalence settings. *J Viral Hepatol*. 2018 Dec;25(12):1472–80. doi: 10.1111/jvh.12975.
- <sup>59</sup> Iwamoto M, Dousset J-P, Kimchamroeun S, et al. Identifying the optimal model of care for HCV in Cambodia. Presentation at World Hepatitis Summit; Sao Paulo, Brazil; 2017 November 1–3 (cited 2019 September 10). Available from: [http://www.worldhepatitissummit.org/docs/default-source/presentations/strategic-direction-5/identifying-the-optimal-care-model-for-hcv-care-in-cambodia-\(momoko-iwamoto\).pdf?sfvrsn=2](http://www.worldhepatitissummit.org/docs/default-source/presentations/strategic-direction-5/identifying-the-optimal-care-model-for-hcv-care-in-cambodia-(momoko-iwamoto).pdf?sfvrsn=2).
- <sup>60</sup> Tan SS. Project ECHO model: one example of scaling up treatment. Presentation at: Hepatitis C virus diagnostics advocacy workshop; 2019 March 2; Penang, Malaysia.
- <sup>61</sup> Coalition PLUS. Mind the gap: HCV policies versus community experiences. Paris: Coalition PLUS; 2018 August (cited 2019 September 10). Available from: <http://www.coalitionplus.org/wordpress/wp-content/uploads/2019/03/FULL-REPORT-MTG.pdf>.
- <sup>62</sup> WHO. Task Shifting: Global recommendations and guidelines. Geneva: WHO; 2008 (cited 2019 September 10). Available from: <https://www.who.int/healthsystems/TTR-TaskShifting.pdf?ua=1>.
- <sup>63</sup> Ibid.

# Section 5

## Diagnostics Access and Barriers

**Barriers to diagnostics differ in each country, and activists can identify and discuss strategies to overcome the biggest hurdles according to the available resources and local contexts.**



**Social determinants of health: ending stigma, marginalization, and criminalization**

Health is a human right. Treatment and diagnostics should be affordable and accessible to everyone. Health inequities stem from societal conditions, known as the social determinants of health. Economic status, education, housing conditions, employment and decent work, the environment and access to clean natural resources, fair legal system, and whether people are treated with respect and dignity are all part of determining inclusive, equitable, and healthy communities and the health of a person.

Stigma, discrimination, marginalization, and the criminalization of community members remain one of the most significant barriers for people affected by HCV and create distrust of the healthcare system. Seventy-one countries have criminalized homosexuality, which can result in the death penalty in 13 of these countries.<sup>64</sup> This risk **makes it nearly impossible for gay, MSM, and gender-nonconforming people to access preventative and treatment services for HIV, HCV, and other STIs.**

The criminalization of sex work is pervasive in the majority of countries, and even condoms can be used as evidence in prosecutions. This also stigmatizes sex workers and prevents them from access the essential healthcare, legal, and other services they need.<sup>65</sup>

Drug use is widely criminalized. Injecting drug use is still present in 179 of 206 countries worldwide.<sup>66</sup> **Criminalization of drugs does not deter use and is not an effective public health strategy for curbing the global HCV epidemic.**

The HCV prevalence is an estimated 52.3 percent among the 15.6 million people who inject drugs; however, less than half (86) of countries have NSEPs and OST programs of varying levels.<sup>67</sup>

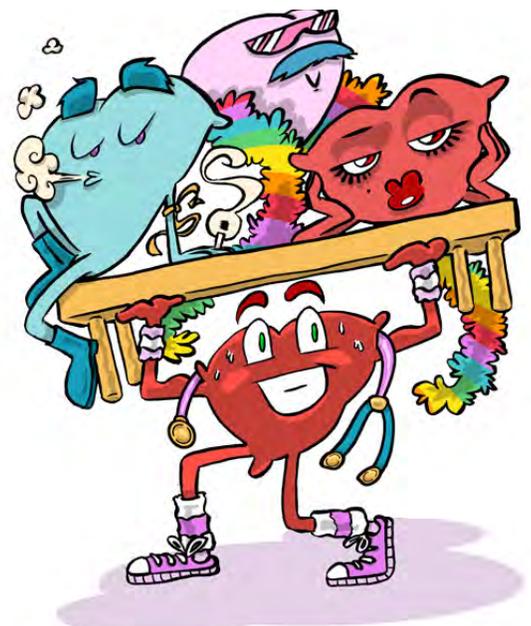
In Georgia, the first country to commit to national HCV elimination and with a history of robust harm reduction programs, diagnostics advocacy workshop participants cited several barriers to testing and treatment. Barriers include the myths and stereotypes about hepatitis and key affected communities; co-payment of diagnostics and sustainable financing by the national health program; deterrence of community members to seek services; internalized stigma by patients; stigma by medical personnel towards patients from key affected communities; and lack of confidentiality by medical providers. Human rights workshops to build awareness among community members on legal protections against discrimination are some ways to fight these systemic barriers in Georgia.<sup>68</sup> In Malaysia, the Ministry of Health has partnered with civil society organizations to develop learning modules on stigma and discrimination and integrated this as part of medical and community health education activities related to the expanding and decentralization HCV services.<sup>69</sup>

Improving the social determinants of health requires decriminalizing communities most affected by HCV and reducing stigma and discrimination. This can be accomplished by implementing and enforcing anti-discrimination and other laws that protect human rights; developing systems and procedures to track and confront stigma and discrimination; ensuring that healthcare workers are trained, sensitized, and penalized if discriminating and denying services; supporting advocacy to reform the criminal justice system; and establishing community-friendly, peer-led healthcare services.<sup>70</sup>

Strong political commitment is needed to put HCV on national and global health agendas. National policies and guidelines must be adopted that lift treatment restrictions and expand prescriber status to general practitioners as part of strategies to increase and decentralized testing.

Stronger surveillance, monitoring, and reporting systems should also be part of efforts to strengthen health systems for the HCV response. The quality of data on HCV prevalence, access to prevention tools, the availability and pricing of diagnostics and DAAs, and what is included in national HCV plans dramatically differs across countries. Community monitoring of the HCV care cascade, including testing and treatment uptake, is an essential part of tracking progress toward national elimination targets: [https://www.hepcoalition.org/IMG/pdf/factsheetmenu.v2\\_english.pdf](https://www.hepcoalition.org/IMG/pdf/factsheetmenu.v2_english.pdf) (see Figure 4, over the page).

Online dashboards that document national health indicators offer opportunities for affected communities to discuss and provide feedback about the results and hold health systems and public officials accountable. Dashboards have become useful, transparent tools for civil society to monitor HIV and HCV responses.



## Health system challenges

Stronger health systems require:

- a deeper understanding about viral hepatitis among the general public as well as medical providers;
- additional trainings and cultural competency by medical providers about affected communities;
- easily accessible testing;
- streamlined procurement;
- more affordable tests for public and private laboratories;
- insurance coverage for diagnostics to remove patient out-of-pocket costs; and
- social support for patients to meet their follow-up visits. This includes prevention and harm reduction counseling, employment, housing, legal, transportation assistance, child care, and other social services.

## Who counts in our national hepatitis plans?

Activists and community members need meaningful ways to talk with policy-makers about how to improve national hepatitis targets. Remember to ask your Ministry of Health when monitoring results along the hepatitis C care cascade:



What does our epidemic look like in our country? How do you take into the account our issues and the concerns of key populations? What reliable data and sources are being used?



What opportunities exist for strengthening the political education of patients, people at risk, and community members to meaningfully participate in the national hepatitis/elimination process?



How are people accessing accurate health information on the hepatitis C virus? How is national progress on hepatitis C disseminated to key populations? What mechanisms are in place for community members to provide feedback on the results?



Who can access and who is covered for using affordable needle syringe programs, opioid substitution therapy, and overdose prevention services?



Who can access affordable hepatitis C testing? How much do people need to pay out-of-pocket?



In active hepatitis C antibody screening campaigns, what is the percentage of people who have received confirmatory testing? What is the percentage of people who have been diagnosed?



Where is hepatitis C testing available? What measures have been taken to shift testing from hospitals to alternative, point-of-care settings?



How are people diagnosed with hepatitis C counseled and linked to affordable treatment? Are high quality, generic, direct-acting antivirals available? How much do people need to pay out-of-pocket?



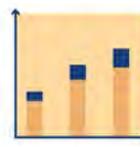
How many people have been treated with direct-acting antivirals? How many people have been effectively cured by achieving a sustained virological response?



How many people are engaged in hepatitis prevention programs after they completed treatment?



How many people are monitored post-treatment for liver damage and liver cancer?



How many reinfections have been diagnosed and treated?



How are we funding the viral hepatitis response? What is the national budget for viral hepatitis? What is included in the viral hepatitis budget?



What policy reforms, trainings, awareness-building, and other measures have taken place to create an enabling environment for stigmatized and marginalized communities to seek essential healthcare and other services?



Figure 4. Who counts in our national hepatitis plans?

Online dashboards that document national health indicators offer opportunities for affected communities to discuss and provide feedback about the results and hold health systems and public officials accountable. Dashboards have become useful, transparent tools for civil society to monitor HIV and HCV responses.

Another online crowdsourcing platform, mapCrowd, is designed to gather and publicize the most up-to-date country-level information on HCV.

Providing free access to national, regional, and international data, [mapCrowd](#)<sup>71</sup> allows users to draw visual comparisons between countries, using interactive graphs, tables, and maps. In-country contributors who collect the data must build relationships and interact with health authorities; the process of asking the specific, pointed questions on diagnostics and treatment availability and pricing are an advocacy tactic in itself, in that they provoke a public response.

## Advocacy Exercise



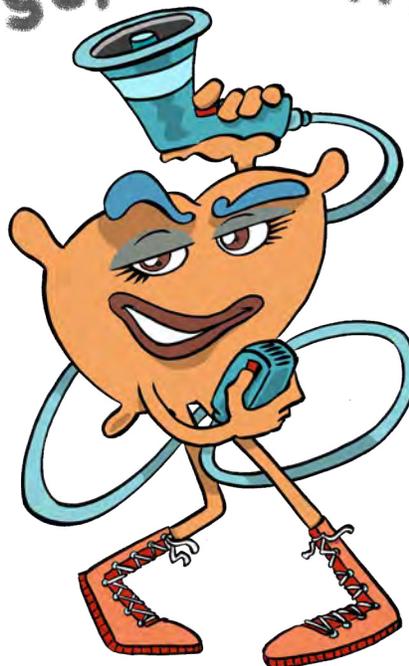
### Discussion questions:

- What are the top three barriers to achieving diagnosis in your community?
- Do members of your community access diagnostics without discrimination?
- How do medical providers treat members of your community when administering HCV tests?

### Action steps:

- What steps are needed to lift treatment restrictions in your country?
- How can we guarantee social supports and assistance for people seeking HCV testing?
- What are some approaches that can reduce the number of patients who drop out between screening and confirmatory testing visits?

NO MORE  
DISCRIMINATION!!!





## Monopolies and licensing barriers

There are only a few diagnostics companies with NAT platforms that can confirm HCV diagnosis. Abbott, Roche, and Cepheid are the primary companies with PoC viral load or lab-based core antigen devices, and having only one or two companies in a country creates a monopoly condition that allows them to set high prices on the sale of their platforms as well as the testing kits/consumables required. They may also add high fees for equipment maintenance, repairs, and the specific reagents and cartridges required. Their own cartridges may fit only with their platforms, locking countries into paying their prices.

Some platforms may be available to diagnose only specific diseases, such as HIV or TB, depending on how they are procured and funded by donors. Abbott, Cepheid, and Roche have multiplex platforms, but exclusive licenses might permit countries to run only HIV, HCV, or TB tests. Instead, countries could renegotiate their agreements to open up the platforms for HBV or HCV viral load testing.

**Procuring tests at higher volumes can help negotiate lower prices.**

In addition, countries could consider open licensing agreements. The BLINK company has developed an open-license, polyvalent diagnostics platform (in early prototype stage). It has been developing a PoC HCV RNA assay that can return results in less than 20 minutes.<sup>72</sup> Any developer can develop its own assay for any molecular diagnostics and then use (or 'rent') the BLINK technology to perform the chemical reactions needed to diagnose the disease. This aligns with a more integrated service delivery approach and could bring down diagnostics costs if multiple tests could be bundled together during procurement. BLINK has also minimized costs in the design stage by decreasing the complexity and number of component parts and disposable materials used and increasing the recyclability of plastic consumables.<sup>73</sup>

These cost savings can be transferred to the end product and reduce prices.

The development of both diagnostics and medicines relies on public and philanthropic funding to invest in the earlier, riskier stages. Yet once the technologies are proven as viable candidates, they may be acquired by larger companies and the benefits privatized under patents or exclusive licensing. This is the case for FibroScan and FibroTest/ActiTest, which were developed by French public research institutions and universities. The companies set extortionate pricing, making these technologies unaffordable for many LMICs.<sup>74</sup> As these devices are not widely available in LMICs, countries can use FIB-4 and APRI liver function tests to assess liver damage, but they require labs and can add additional steps and time before a patient is diagnosed and started on treatment.

Activists can challenge monopolies and licensing barriers by demanding that the medicines and diagnostics, which receive public funding for the research and development, to remain affordable and accessible to everyone who needs them. Public institutions can prepare licensing agreements that require royalty payments for the use of technologies that they financed; this revenue can help sustain these institutions. Student advocacy through Universities Allied for Essential Medicines adopted a Global Access Licensing Framework at universities in Canada.<sup>75</sup> The Framework works towards transparency and equitable licensing on medicines in order to increase access in LMICs, and similar approaches can be applied to open up licensing on diagnostic technologies.

Activists can also benefit from understanding which diagnostics have been approved by national regulatory authorities and put on essential diagnostics lists. By demanding simpler, affordable, PoC diagnostics, activists can help break the monopolies in their country.

## Advocacy Exercise

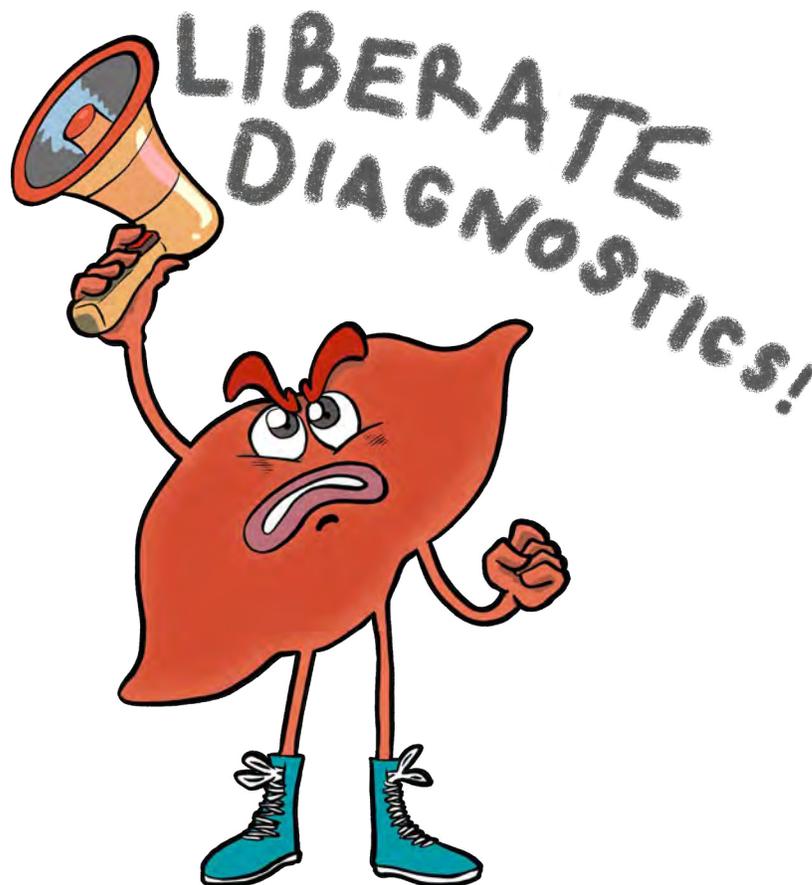


### Discussion questions:

- What are the licencing agreements for the diagnostics available in your country?
- What alternative agreements or flexibilities are available that will expand access to diagnostic technologies?

### Action steps:

- What steps are needed to prevent monopolies on diagnostic technologies in your country?
- What partners and campaigns can inform our efforts for open licence platforms?





## Pricing barriers

A diagnostics platform can cost tens of thousands of US dollars, which can be priced out of reach for LMICs. Machines procured through international donors still require costly cartridges, reagents, and maintenance, and only the disease areas that fit within the scope of the donor-funded project may be covered.

Distributor markups, value-added taxes, and customs fees present additional barriers. Local distributors may apply additional markups, resulting in increases to the final price of the tests.

By waiving value-added taxes and customs fees for essential diagnostics aimed at combatting infectious diseases and setting caps on distributor markups could put a price control and reduce end prices on the tests.<sup>76</sup> This could help health budgets to fully cover more diagnostics costs.

One survey<sup>77</sup> among community health workers in India, Indonesia, Malaysia, Morocco, and Thailand highlighted the immense barriers to care resulting from out-of-pocket costs in both the private and public health sectors.

Limited trained staff for HCV testing and long waiting lists for testing or treatment means added time for patients.<sup>78</sup> Patients often take off work for each step in the diagnostics pathway, which results in lost time and income and should be analyzed as part of overall costs.

Transparency on diagnostics prices and the volume-based discounts companies offer to different countries is needed to inform government negotiations and procurement decisions. Based on data from in-country advocates, HCV tests can be priced at US\$15–30 per test (in the public sector) to US\$60–200 per test (in the private sector), depending on the product and country.<sup>79</sup>

Figure 5 gives a range on the total prices of tests, depending on the diagnostics pathway and the available tests in a country.

| Test  | Prices                         |
|---|--------------------------------|
| <b>Rapid diagnostic test</b>  | = US\$1                        |
| <b>Test to confirm active infection</b><br>Nucleic acid testing (NAT)   | US\$15 to<br>= US\$200         |
| <b>Test to assess level of fibrosis</b><br>APRI or FIB-4                | US\$0.83 to<br>= US\$3.70      |
| Fibroscan   | US\$0 to<br>= US\$200          |
| FibroTest   | = US\$50                       |
| <b>Test to evaluate efficacy of cure</b><br>Nucleic acid testing (NAT)  | US\$15 to<br>= US\$200         |
| <b>Genotyping</b>   | US\$10 to<br>= US\$350         |
| <b>Total average for tests needed to confirm HCV diagnosis and cure</b> | <b>US\$44 to<br/>= US\$951</b> |

Figure 5. Price range of HCV diagnostics in standard use.<sup>80</sup>

**Pressure from advocates is needed to convince governments to finance HCV diagnostics and to provide free and simplified testing for all.**



## Advocacy Exercise



### Discussion questions:

- What are the out-of-pocket costs in your country for diagnostics?
- What tests are covered by national insurance schemes?

### Action steps:

- How can we use diagnostics pricing information from similar countries to add pressure on our government during procurement negotiations?
- What are some approaches that can reduce drop off of patients between screening and confirmatory testing visits?

<sup>64</sup> International Treatment Preparedness Coalition-Global. Activist toolkit on PrEP. Johannesburg: ITPC Global; 2018 February (cited 2019 September 10). Available from: <http://itpcglobal.org/wp-content/uploads/2018/02/ITPC-PrEP-Toolkit-English.pdf>.

<sup>65</sup> Ibid.

<sup>66</sup> Harm Reduction International. Global state of harm reduction 2018. London: HRI; 2018 December (cited 2019 September 10). Available from: <https://www.hri.global/files/2019/02/05/global-state-harm-reduction-2018.pdf>.

<sup>67</sup> Degenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Global Health*. 2017;5(12):1192–207.

<sup>68</sup> hepCoalition. Hepatitis C treatment and diagnostics advocacy in Georgia. Workshop summary report. Tbilisi, Georgia; 2019 May 13–15 (cited 2019 September 10). Available from: [https://hepcoalition.org/IMG/pdf/georgia\\_summary\\_report\\_hepatitis\\_c\\_treatment\\_and\\_diagnostics\\_advocacy\\_final.pdf](https://hepcoalition.org/IMG/pdf/georgia_summary_report_hepatitis_c_treatment_and_diagnostics_advocacy_final.pdf).

<sup>69</sup> hepCoalition. Hepatitis C virus diagnostics advocacy workshop. Summary report. Penang, Malaysia; 2019 March 1–3 (cited 2019 September 10). Available from: [https://hepcoalition.org/IMG/pdf/malaysia\\_summary\\_report\\_hcv\\_diagnostics\\_advocacy\\_workshop.pdf](https://hepcoalition.org/IMG/pdf/malaysia_summary_report_hcv_diagnostics_advocacy_workshop.pdf).

<sup>70</sup> International Treatment Preparedness Coalition-Global. Activist toolkit on PrEP. Johannesburg: ITPC Global; 2018 February (cited 2019 September 10). Available from: <http://itpcglobal.org/wp-content/uploads/2018/02/ITPC-PrEP-Toolkit-English.pdf>.

<sup>71</sup> Developed by Treatment Action Group (TAG) and Médecins du Monde (MdM), [www.mapCrowd.org](http://www.mapCrowd.org).

<sup>72</sup> Treatment Action Group. HCV diagnostics: Pipeline Report 2019. New York: Treatment Action Group. Available from: <http://www.treatmentactiongroup.org/pipeline-report>.

<sup>73</sup> Ivanova, Elena (FIND, Geneva). Personal communication with Bryn Gay and Annette Gaudino (Treatment Action Group, New York, NY). 2019 August 19.

<sup>74</sup> Londeix P. Diagnosis and monitoring of hepatitis C (HCV) in Morocco: Current status and strategies for universal access: Benchmarking HCV diagnostics, fibrosis evaluation, and treatment monitoring. Casablanca and Paris: ALCS and Coalition PLUS; 2018 May (cited 2019 September 10). Available from: <https://www.alcs.ma/wp-content/uploads/2018/05/BenchmarkVA.pdf>.

<sup>75</sup> Universities Allied for Essential Medicines University of McGill chapter. Affordable, life-saving medicines for all: McGill adopts Global Access Licensing Principles for research conducted on campus. Press release; 2019 May 23 (cited 2019 September 10). Available from: <https://uaem.org/cms/assets/uploads/2019/05/Press-Release-McGill-GALF.pdf>.

<sup>76</sup> World HCV Community Advisory Board. Forging a path to HCV elimination: Simpler tests and affordable generics. Report of the World Community Advisory Board on HCV Generics and Diagnostics. Bangkok, Thailand; 2017 July 18–20 (cited 2019 September 10). Available from: [https://www.hepcoalition.org/IMG/pdf/hcv\\_world\\_cab\\_report\\_2017.pdf](https://www.hepcoalition.org/IMG/pdf/hcv_world_cab_report_2017.pdf).

<sup>77</sup> Coalition PLUS. Mind the gap: HCV policies versus community experiences. Paris: Coalition PLUS; 2018 August (cited 2019 September 10). Available from: <http://www.coalitionplus.org/wordpress/wp-content/uploads/2019/03/FULL-REPORT-MTG.pdf>.

<sup>78</sup> Ibid.

<sup>79</sup> hepCoalition. Have a heart, save my liver! Fact sheet; 2019 February 13 (cited 2019 September 10). Available from: <https://www.hepcoalition.org/advocate/campaigns/have-a-heart-save-my-liver/article/have-a-heart-save-my-liver-454>.

<sup>80</sup> Ibid.

# Section 6

## Activist Lessons

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### People living with HCV and community voices need to be centered in HCV elimination efforts

Beyond raising awareness among the general population, diagnostics and treatment literacy for people disproportionately affected by HCV is essential to ensure communities, particularly key affected communities, are represented and meaningfully participate in national elimination planning and policy processes. Community engagement should involve opportunities to strategize ways to overcome diagnostics barriers, regular consultations, and provide feedback on mechanisms to improve the implementation of national HCV plans.

### Determine the national epidemiology and tailor the HCV response to communities who are disproportionately affected

Communities need to be included at the start and in all phases of developing national HCV strategy and response. They can identify opportunities for integrating HCV into existing services and the kinds of trainings and skill-building required for including community health workers and peer educators in the HCV response. Peer-led and peer-designed programs are more effective in linking and retaining often overlooked and underserved communities to treatment and care. Decentralized testing services and peer-led programs would need to use simpler diagnostic tools, such as viral load with fingerstick or dried blood spot samples.<sup>81</sup>

### Decriminalize the communities most affected and destigmatize HIV/HCV

Meeting global and national targets cannot be achieved without massive policy reforms that decriminalize key affected communities, including people who use and inject drugs, MSM, transgender and gender nonconforming people, sex workers, immigrants, and migrants. This includes drug policy reforms so that personal use, possession, and low-level drug-related offenses are not criminalized and do not result in incarceration. Harm reduction services should be expanded for people who use and inject drugs to access sterile injecting and smoking equipment, treatment for substance use disorders, and other services such as mental health and social services. Access to NSPs and OST while taking DAAs can prevent reinfection and onward transmission of HCV.

### Learn from HIV activism and response

We have an effective cure for hepatitis C. We cannot graft the HCV response entirely onto HIV and its already constrained resources. However, there are opportunities to leverage the HIV and harm reduction infrastructure and resources as part of the HCV fight. Many diagnostics platforms, lab resources, medical trainings, and community education/outreach can be utilized for the HCV response. Blood samples obtained in one visit could be analyzed for multiple diseases: HIV, HBV, HCV, and other STIs. Massive awareness raising, screening (“Know Your Status”) campaigns, and prevention messaging can integrate HIV and HCV. Additional community health workers and peer educators would need to be increased and trained, but this approach can be cost-saving and effective in retaining patients in care.

We can learn from HIV activism in deploying numerous access-to-medicines strategies, such as challenging patents and issuing **compulsory licenses** (CL), in order to win access to generic DAAs.



## Just do something!

There is no time to lose! Even if a country is off track of the WHO HCV targets by 2030, it could use the 2020 targets as milestones in its national response. Multiple strategies can be undertaken by Ministries of Health in countries, such as conducting awareness-raising campaigns and providing medical/community trainings, while government agencies work on regulatory and approval processes that open up greater access to diagnostics and DAAs. In addition, health programs must focus on retaining people in care while they wait to start treatment. In settings such as prisons, which may not have access to DAAs, people diagnosed with HCV or who know their status, and then leave prison and reintegrate into the community, must be linked to services to continue treatment and care. Lack of access to DAAs in the public sector or waiting for a windfall in funding is not an excuse to delay planning and implementation of an HCV response. Simply convening local stakeholders can be a powerful first step on the path the HCV elimination.

## “Take back our diagnostics”<sup>82</sup>

Diagnostics developed with public (tax revenue) and philanthropic funding should be kept as public goods so that they are affordable and accessible for every patient and every country. FibroScan and FibroTest/ActiTest were developed by French public research institutions and universities but are patented and exclusively licensed. The patent and licensing barriers set extortionate pricing, making these simpler,

PoC liver disease assessment technologies unaffordable for many LMICs. FIB-4 and APRI can still be conducted in resource-limited settings and are recommended by the WHO, but they require laboratory blood tests and can add additional steps and time to the diagnostics pathway. Rather, open diagnostics platforms for viral load, such as for HIV, HBV, and HCV, can generate competition and lower prices for tests. Countries can bundle tests and procure diagnostics commodities in bulk. This can help with price negotiations and with healthcare cost savings.

## Budget and funding advocacy provokes and kickstarts dialogue with policy makers

Patient groups should not be pitted against each other to compete for funding. There is always money in the budget and it is the activists' role to make noise to prioritize health and access to life-saving diagnostics and treatments, rather than the criminalization of our communities. Budget advocacy involves determining advocacy targets at the Ministries of Finance and Health in countries and directing specific, technical questions about spending and allocation, such as for HIV/HCV and harm reduction, during the budget cycles. Several arguments can be effective, for example: early treatment can save healthcare costs in the long term; increasing and fairly remunerating peer educators can employ knowledgeable and experienced skilled healthcare workers while retaining patients from key affected communities in care, etc. A number of tools to help community activists prepare their budget advocacy are available by organizations like the Eurasian Harm Reduction Association.<sup>83</sup>

Advocacy toward donors needs to be ramped up to secure funding for HCV mono-infection—we are at a defining moment in history that will determine whether we pave a path to elimination or completely fail tens of millions of people with hepatitis C.

Civil society delegates on the boards of multilateral agencies and community representatives to the Country Coordinating Mechanisms of the Global Fund can raise concerns and offer strategies to expand access to diagnostics and treatment.

### Key messages and demands:

- Decriminalize drugs and end the war on drug users!
- Universal antibody screening should be used in high-prevalence settings.
- In high-prevalence populations, such as people who inject drugs or incarcerated people, it could be possible to skip antibody tests and start with confirmatory testing, then start treatment once HCV diagnosis is confirmed.
- Skip genotyping if pangenotypic DAAs are used.
- Remove HCV viral load monitoring until week 12 to confirm SVR. DAAs achieve SVR in over 95 percent of patients and viral load monitoring can be skipped.
- Treat everyone! Reinfections will occur and must be considered in national responses. People should be offered unlimited treatment regardless of whether they have been reinfected.
- ‘One-stop shops’ can offer a range of services: HIV/HBV/HCV screening, testing, and treatment; harm reduction services; and referrals to mental health and other social services.
- Integrate HBV vaccination and sexual health services for MSM and PWID.
- Peer-led and peer-designed programs are an important part of achieving national HCV elimination. They would require continued training and education, task-shifting key aspects of HCV care, and buddy programs that aim to refer peers to services.
- Housing and employment are healthcare.
- Gender-sensitive harm reduction services need to include intimate partner violence, childcare, counseling, and legal aid programs for womxn and gender nonconforming people who use drugs.
- National HCV budgets need to estimate what the costs would be to test and treat the populations disproportionately affected by HCV, such as people who inject drugs, incarcerated people, and MSM.
- National HCV dashboards can be transparent and participatory tools for communities to be involved in the monitoring of the HCV care cascade and the implementation of national elimination plans.



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<sup>81</sup> Applegate T. We can diagnose: what now? Experiences in HCV diagnostic implementation research: an Australian perspective. Presentation at: Global Health Diagnostics; 2018 June 13; McGill University, Montreal, Canada.

<sup>82</sup> Inspired by Universities Allied for Essential Medicines' Take Back Our Meds campaign: <https://uaem.org/our-work/campaigns/tbom/>

<sup>83</sup> Eurasian Harm Reduction Association. Budget advocacy: a guide for community activists. 2018 October 17 (cited 2019 September 10). Available from: <https://harmreductioneurasia.org/budget-advocacy-guide/>.

# Appendices

## Illustrated glossary of HCV diagnostic-related terms

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### AASLD/IDSA

American Association for the Study of Liver Diseases/Infectious Diseases Society of America.

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### Abbott m-Pima™ Analyser



A portable diagnostics platform that uses a fully integrated cartridge to process whole blood and plasma samples. It has a turnaround time of less than 70 minutes and is used at the time and place of patient care, known as point of care. It already has HIV early infant diagnosis and HIV viral load tests; a cartridge that can detect HCV is in development to be used on this platform.

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### Abbott ARCHITECT i2000



A platform that can confirm HCV infection using core antigen, or part of the HCV viral protein. It can be used in high-volume settings, such as 100

tests per hour, and can screen multiple diseases at once. It operates in large, central laboratories, and there is currently no point-of-care core antigen available.

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### Abbott RealTime HCV Viral Load



HCV viral load confirmation test, using plasma or blood samples. Off-label studies show the potential of using dried blood spot samples in resource-limited settings, which could be an alternative method for people who use drugs with poor vein access.

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### ActiTest

A noninvasive test to determine the extent of liver inflammation, damage and scarring; however, it is not widely available outside high-income countries. This test is assessed on FibroTest and must be analyzed using BioPredictive diagnostics services. The test was developed using French public funding, then granted exclusive licensing to FibroTest.

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### Acute Infection

A recently acquired infection, which may have mild or no symptoms; acute HCV infection may result in some inflammation to the liver.

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### ALP

Alkaline phosphatase, an important liver enzyme used in determining your liver health.

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## ALT; SGPT

Alanine aminotransferase or serum glutamic-pyruvic transaminase—liver enzymes used in determining your liver health.

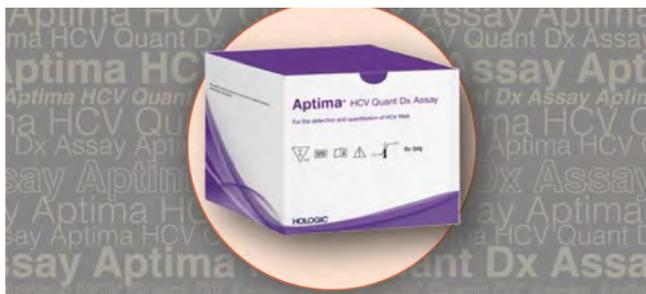
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## Antibody

Part of a person's immune system that responds to viruses, bacteria, and other harmful substances.

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## Aptima HCV Quant Dx Assay



Test licensed for the confirmation of active infection and viral load monitoring for HCV, using blood or plasma samples. This test is run on the Hologic Panther diagnostics platform.

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## APRI

$$\text{APRI} = \frac{\text{AST LEVEL (AST (UPPER LIMIT OF NORMAL))}}{\text{PLATELET COUNT (10}^9\text{/L)}} \times 100$$

Aspartate aminotransferase (AST) to platelet ratio index—a formula used to determine the level of liver disease.

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## ART

Antiretroviral therapy—a combination of antiretroviral drugs to suppress HIV and to stop HIV from progressing

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## ARV

Antiretroviral drugs—in the context of HIV, these medications suppress viral activity by preventing the virus from reproducing

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## Assay

A diagnostic test performed to determine the presence of an infectious disease (qualitative assay) and if present, the amount (quantitative assay).

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## AST; SGOT

Aspartate aminotransferase or serum glutamic oxaloacetic transaminase—a liver enzyme made in the heart, intestines, and muscle used in determining your liver health.

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## Bloelisa HCV 4.0

A WHO prequalified HCV enzyme immunoassay test that uses blood or plasma samples to detect the presence of antibodies.

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## BLINK One



A portable cartridge-based diagnostics platform that can run multiple assays at once, including HCV RNA in less than 20 minutes.

The open licensing business model allows any developer to develop tests for diagnosing a range of infectious diseases.

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### **cAG**

HCV core antigen—the viral protein of HCV, which can be found in the bloodstream within two weeks of infection. This type of confirmation test detects whether a person is currently infected with the virus.

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### **CD4**

Cluster of differentiation 4—a type of protein found in immune cells such as T cells, a type of white blood cells that lead the fight against infections. HIV infects the CD4 cells and then uses them to make copies of the virus. The CD4 count test calculates the total white blood cells and the proportion of cells that are CD4 positive. CD4+ cell count and is used to monitor the health of the immune system and antiretroviral treatment success. If the count drops lower than 200 cells per millionth of a liter, the person is at higher risk of opportunistic infections. Current WHO treatment guidelines indicate a person should start treatment at the time of diagnosis, regardless of CD4+ cell count. This improves the health of the person living with HIV and helps reduce the amount of the virus in the blood (viral load) and other bodily fluids to undetectable levels, which prevents transmission.

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### **CDC**

Centers for Disease Control and Prevention—the U.S. agency that develops and applies disease prevention and control programs, as well as environmental health, health promotion, and health education activities.

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### **CE-marked**

Conformité Européenne—a certification mark that shows the compliance to safety, health, and environmental protections for products within the European Economic Area.

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### **Chemsex**

Also referred to as “party-n-play”—subculture among gay men and MSM in which a combination of street drugs are taken, facilitating sex with multiple partners and with more frequency. This may include condomless sex and can increase the risk of becoming infected with HIV, HCV, or other sexually transmitted infections.

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### **Chronic Infection**

An infection that can last for weeks, months, or a lifetime, causing more damage to the affected tissue or organs.

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### **Cirrhosis**

Serious liver scarring or damage that can lead to liver failure.

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### **CKD**

Chronic kidney disease—a condition where the kidneys’ ability to filter harmful waste and excess fluid from the blood deteriorates over time.

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### **CL**

Compulsory license—a license granted by a governmental administrative or judicial body to a third party to manufacture or use a patented product, such as a medication, without the consent of the patent holder. A CL is an effective strategy to enable generic competition and reduce the price of patented medicines. The patent holder is remunerated, such as through royalty payments.

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### **CLIA**

Clinical Laboratory Improvement Amendments—U.S. federal regulations that establish quality standards for laboratory testing.

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## COBAS® TaqMan®



A nucleic acid amplification diagnostic platform developed by Roche that uses RNA to confirm the presence of HIV-1 (most common type of HIV) and HCV viral loads.

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## Community

A form of self-organization of a group of people with one or several characteristics that unite people living in nearby locations, foster relations between them, and share culture and values within the scope of these relations. A community can be defined by the following: people, location, and relationship.

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## DAA

Direct-acting antivirals—all-oral, highly effective medications for treating hepatitis C in usually 8 or 12 weeks. People with cirrhosis or other conditions may need to be treated longer to achieve sustained virological response, or when the virus is undetectable. DAAs can achieve sustained virological response in over 95% of patients, and the latest regimens treat all genotypes of the virus with similar results.

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## DBS

Dried blood spot—blood sample obtained by pricking the finger or heel that is preserved and dried on filter paper. DBS can be easily shipped from a remote testing site to a lab for analysis.

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## DCV

Daclatasvir (also abbreviated as DAC); a direct-acting antiviral that is taken with sofosbuvir, once daily with or without food for 12 or 24 weeks.

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## Diagnostic Burnout

The phenomenon in which countries are treating mainly patients known to have HCV and are failing to diagnose new infections. In this case, countries will run out of diagnosed patients to treat, HCV transmission will continue to proliferate, and new infections will go undiagnosed, leading to advanced liver disease and liver-related deaths.

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## EASL

European Association for the Study of the Liver.

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## EDL

Essential Diagnostics List—WHO guidance and reference on the tests and medical devices needed to diagnose the most common conditions as well as a number of global priority diseases. The EDL helps countries decide on the type and categories of diagnostics depending on their epidemiology, testing strategies, human resources, and healthcare and laboratory infrastructure.

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## EIA

Enzyme immunoassay—antibody tests used in labs that detect antibodies in blood samples.

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## ESLD

End-Stage Liver Disease—chronic liver failure, often as a result of cirrhosis.

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## FBC

Full blood count—a measure of the number of red blood cells, white blood cells, and platelets in the blood.

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## FDC

Fixed-dose combination—two or more drugs contained in a single dosage form, such as a capsule or tablet.

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## FibroScan



An ultrasound machine for your liver that measures liver stiffness, scarring, and damage as well as the accumulation of fat in the liver.

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## FibroTest

A noninvasive blood test that can measure the degree of liver damage in a person; it requires results to be analyzed by BioPredictive software.

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## FIB-4

$$\text{FIB-4} = \frac{\text{AGE (YEARS)} \times \text{AST (U/L)}}{\text{PLATELET COUNT (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

An inexpensive, noninvasive calculation to determine the amount of liver scarring by using patient's age, platelet count, AST, and ALT.

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## Fingerstick



Also known as fingerprick—a method of collecting a small amount of blood by pricking a finger with a lancet, or a sharp needle-like instrument.

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## g/dL

grams per deciliter—unit of measurement for fluid volume, used in medical tests

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## g/L

Grams per liter—unit of measurement for fluid volume, used in medical tests.

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## Genedrive



A portable, point-of-care confirmatory test, using plasma, for the detection of HCV RNA. It is designed for use in low-resource settings and delivers results in 90 minutes.

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## GeneXpert



A diagnostic platform developed by Cepheid that can run tests for multiple diseases, including HIV, HBV, HCV, and TB, using different cartridges. The Xpert HCV Viral Load confirms diagnosis using RNA.

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## Genotype

Abbreviated as GT—different subtypes of HCV, or a way to put HCV into categories based on similar genes. HCV has six genotypes, labeled 1 through 6. There are also subtypes labeled with letters, for example, genotypes 1a and 1b. Genotypes respond differently to medicines that treat and cure HCV, but pangenotypic (all-genotypes) DAAs have similar SVR rates for all genotypes.

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## GGT

Gamma glutamyl transferase—an important liver enzyme used in determining your liver health.

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## G/P

Glecaprevir and pibrentasvir—DAA taken once daily, as three pills, with food, that treats all genotypes of HCV in 8 weeks for people with no cirrhosis, or 12 or 16 weeks for people with compensated cirrhosis or other complications. It has been approved by the FDA for children and adolescents aged 12 and older who weigh at least 99 pounds (44 kilograms).

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## HAV

Hepatitis A virus—a highly contagious virus that infects the liver through fecal matter getting into the mouth from contaminated food or water, poor sanitation, or unprotected mouth-to-anal sex. HAV can be prevented through vaccination.

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## HBIG

Hepatitis B immune globulin—an injection used to protect against hepatitis B within 24 hours of exposure.

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## HBV

Hepatitis B virus—a highly contagious virus that infects the liver transmitted through blood, semen, and vaginal fluid. You can protect yourself against hepatitis B by getting vaccinated or having an injection of HBIG within 24 hours of exposure.

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## HCC

Hepatocellular carcinoma—liver cancer, occurring most often in people with chronic liver diseases.

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## HCV

Hepatitis C virus—a virus transmitted through blood, although small amounts have been found in semen and vaginal fluid, that causes hepatitis C, a liver infection that causes inflammation and tissue damage. There is no preventative vaccine, but all-oral DAAs can now effectively cure HCV. Untreated HCV can lead to severe liver damage and liver cancer.

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## HIV Self Test



A simple blood test that a person can use on themselves to test for HCV; expected to become available in 2020.

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## HDV

Hepatitis D virus—a virus that causes hepatitis D, a liver infection that can only occur in people already infected with HBV. HDV is usually transmitted from parent to child during birth through bodily fluids.

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## HEV

Hepatitis E virus—a virus that causes hepatitis E, a liver disease caused by consuming contaminated water or food or by ingesting undercooked animal meat that has been infected with HEV.

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## HGV

Hepatitis G virus—often called GB virus C (GBV-C), does not make people sick or cause liver damage. HGV is transmitted through blood. Contaminated blood or blood products, unsterile drug use, injection or tattoo equipment can transmit the virus.

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## HICs

High-income countries.

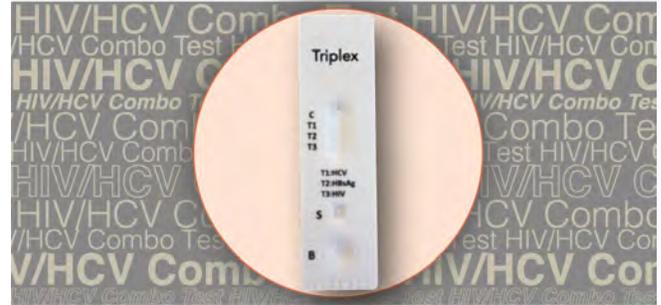
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## HIV

Human immunodeficiency virus—a virus that weakens the immune system, ultimately leading to acquired immunodeficiency syndrome (AIDS).

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## HIV/HCV Combo Test



Rapid diagnostic blood test that allows for simultaneous testing of HCV and HIV.

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## IL28B CC genotype

The IL28B gene is involved in the immune response to certain viruses, including HCV. There are three IL28B subtypes (genotypes): CC, CT, and TT. People with the CC genotype have a stronger immune response to HCV infection than people with the CT or TT genotypes. In the pegylated interferon treatment era, IL28B genotype determined the type—and possibly length—of HCV treatment.

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## INHSU

International Symposium on Hepatitis Care in Substance Users.

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## INNO-LIA® HCV Score



A WHO prequalified immunoassay developed by Fujirebio, using blood and plasma, for detecting HCV antibodies in less than 30 minutes.

## INNOTEST® HCV Ab IV



A WHO prequalified enzyme immunoassay (the fourth-generation test) developed by Fujirebio, using blood or plasma, to detect HCV antibodies for HCV genotypes 1a, 1b, 2, and 3a.

## Invasive Test

Any type of medical test that requires use of instrumentation to physically enter the body, such as a liver biopsy

## IP

Intellectual property—refers to the concept of ownership over an idea or design, in which the person or entity that developed that idea or design is given exclusive right over it for a period of time, usually 20 years under international agreements. No one can copy or reuse the idea or design without the owner's permission.

Common forms of intellectual property include patents, copyrights, trademarks, industrial design rights, geographical indications, and trade secrets. In international law, legal mechanisms, such as compulsory licenses and patent oppositions, exist to gain access and manufacturer technological advancements, such as medicines, in order to create less expensive, generic versions.

## IU/mL

International units per milliliter.

## L

Liter.

## LGBTQ+

Lesbian, gay, bisexual, transgender, queer/questioning, and others—an umbrella acronym that encompasses a spectrum of gender and sexual identities but is not comprehensive as the terminology is evolving and changing.

## LED

Ledipasvir—a direct-acting antiviral that is taken with sofosbuvir as two drugs in one pill, taken daily, with or without food, for 8 to 24 weeks. It is used to people with genotypes 1, 4, 5, and 6 who are over 12 years old.

## LFT

Liver function test—a group of blood tests used to detect, evaluate, and monitor liver disease or damage.

## LMIC

Low-and middle-income countries.

## LoD

Limit of detection—in chemistry, smallest amount of a microorganism or genetic material from a virus in a sample that can be reliably detected in optimal conditions. LoD is a step in determining the sensitivity of a test.

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## MAT

Medication-assisted treatment, which uses medications such as buprenorphine, methadone, and naltrexone, often combined with counseling and behavioral therapy to treat opioid use disorders, also referred to as OST.

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## mg

Milligram—unit of measurement for weight, such as amount of an ingredient in a medication tablet.

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## mg/dL

Milligram per deciliter—unit of measurement for density, such as the amount of blood sugar in the blood.

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## MIC

Middle-income country.

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## Mixed Infection

People who are infected with more than one HCV genotype. This is most likely to happen to people who received blood products or blood transfusions many years ago or in a place where the blood supply was not checked for HCV, people on kidney dialysis, or people who inject drugs with shared, unsterilized equipment.

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## mm<sup>3</sup>

Millimeters cubed—unit of measurement for volume, used in medical tests.

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## μmol/L

Micromoles per liter—unit of measurement for fluid volume, used in medical tests.

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## Molbio TrueNAT™ HCV test



Portable viral load test that confirms HCV diagnosis in an estimated 35 minutes.

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## MSM

Gay, bisexual, and other men who have sex with men.

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## Multiplexing

Testing for more than one infection at the same time on one device, such as HIV, HBV, and HCV.

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## Murex anti-HCV 4.0

A WHO prequalified test (fourth generation) developed by DiaSorin, using blood or plasma, to detect HCV antibodies.

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## NAT

Nucleic acid amplification test—a highly sensitive laboratory process used to detect genetic material, such as RNA of HCV. The NAT uses repeated chemical reactions (polymerase chain reaction) to make multiple copies of the HCV RNA that is trying to be detected. In this way, it is easier to detect tens of thousands of copies of a gene than only a few copies.

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## ND

No data.

## NHANES

National Health and Nutrition Examination Survey—a survey conducted by the CDC assessing the health and nutritional status, including the hepatitis epidemiology of adults and children in the United States. There are limitations because it did not include homeless people, incarcerated people, nursing home residents, people living on Native American reservations, or active military personnel, and it did not show wide geographic representation. Information on members of additional racial and ethnic groups was classified as “other”.

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## Noninvasive Test

Medical test that does not require a medical instrument to physically enter in the body, such as using ultrasound.

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## NSEP

Needle syringe exchange programs.

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## OraQuick® HCV Test



A WHO prequalified test used for detecting HCV antibodies, using blood samples collecting from fingerstick or the veins.

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## OST

Opioid substitution therapy, which uses medications such as buprenorphine, methadone, and naltrexone, is often combined with counseling and behavioral therapy to treat opioid use disorders, also referred to as MAT.

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## Pangenotypic

DAA treatments that can effectively cure all HCV genotypes at nearly the same rates.

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## PCR

Polymerase chain reaction—process during a nucleic acid amplification test to detect genetic material, such as HCV RNA, by making multiple copies of the HCV RNA that is trying to be detected. The PCR HCV RNA test determines how much of the virus (or viral load) is in the bloodstream.

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## PEG-IFN

Pegylated interferon—an older treatment regimen requiring regular injections, combined with oral doses of ribavirin, between 12 to 48 weeks; no longer recommended by WHO, AASLD/IDSA, or EASL. Countries without access to direct-acting antivirals or prisons may still be using pegylated interferon.

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## PLHIV

People living with HIV—preferred to use the people-centered term instead of the abbreviation.

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## PoC



Point-of-care test—diagnostic testing conducted at the time and place of patient care, such as community clinics, harm reduction sites, and prisons.

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## Polyvalency

One machine can do different tests, but using a different sample and not always at the same time.

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## PT

Prothrombin time—measurement for how long it takes for blood to clot.

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## PWID

People who inject drugs—preferred to use the people-centered term instead of the abbreviation.

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## Qualitative RNA

Viral load test that checks whether there is RNA genetic material, such as from HCV, in the bloodstream. The test result is either positive (virus is detectable) or negative (no virus can be detected).

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## Quantitative RNA

Viral load test that measures the amount of RNA genetic material, such as from HCV, in the bloodstream. These tests, while not available in every country, are also used to monitor HCV treatment to see if it is working.

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## R&D

Research and development.

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## RBV

Ribavirin—oral treatment for hepatitis C, given as pills or capsules, twice a day. The dose depends on a person's weight. Ribavirin can increase cure rates in people with cirrhosis and is sometimes added to DAAs, although it causes side effects, such as anemia, insomnia, fatigue, irritability, and depression. Ribavirin is not recommended for men and women who are planning a pregnancy because it causes birth defects. Male partners of women who become pregnant or are nursing should use condoms for six months after completing HCV treatment.

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## RDT

Rapid diagnostic test—antibody tests designed for use at the point of care.

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## Reagent



Chemical ingredients that are added to test a patient's sample to see if a reaction occurs. A change in color, intensity in light, or other difference may occur. The change is measured against a known change, or control, and then calculated for a test result.

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## Reagent cartridge



A container with prefilled reagents to be loaded inside a diagnostics device.

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## Reflex testing

When additional tests are automatically ordered after a specific test result. For HCV, if a patient has a positive antibody test, confirmatory tests (HCV RNA or core antigen) would be automatically ordered.

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## Reinfection

When a person who has been successfully treated, such as for HCV, becomes infected again. HCV RNA testing is recommended for people with ongoing behaviors that may put them at risk of HCV infection. Access to sterile injection equipment, OST, and comprehensive prevention and harm reduction services is necessary to prevent reinfection.

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## RVD

Ravidasvir (also abbreviated as RAV)—taken with sofosbuvir as a generic regimen that under study in clinical trials, which may be used to treat all genotypes. It is taken once daily for 12 weeks, or 24 weeks for people with compensated cirrhosis.

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## SAMBA II



NAT-based PoC rapid HCV viral load test, using blood samples, developed by Diagnostics for the Real World.

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## SD BIOLINE HCV



A WHO prequalified antibody test, using blood or plasma, to detect HCV antibodies.

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## Sensitivity

True positive rate—a test's ability to correctly identify people with an infection, such as HCV. High sensitivity—closer to 100%—helps avoid missing an HCV infection and determines the quality of a test.

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## Serological tests

Also known as screening or antibody tests—generally used as the first step in a testing strategy due to the relatively lower cost. These tests detect antibodies or a viral antigen, and which people may have an active infection. They can be conducted with rapid diagnostic tests or laboratory-based enzyme immunoassays.

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## Serum

Clear and watery part of the blood that separates when the blood clots or is centrifuged (spun at high speeds).

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## SI

International system of units.

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## SOF

Sofosbuvir—an HCV-fighting DAA that must be used with other drugs. In combination with other DAAs, it can treat all genotypes in patients 18 years old and older; sofosbuvir with or without ribavirin can be used to treat genotype 2 and 3 in patients 12–17 years old (2018 WHO Guidelines). Sofosbuvir is taken once daily, with or without food, for 12 to 24 weeks, depending on a person’s liver damage, other health conditions, and treatment experience.

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## Specificity

True negative rate—the test’s ability to correctly identify people without HCV. High specificity—closer to 100%—helps avoid misinforming a person about being infected when they are not and determines the quality of a test.

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## SRA

Stringent Regulatory Authority—a quality assurance policy to ensure certain requirements are met at a manufacturing facility for medicines or medical devices. This includes a list of countries with a national drug regulatory authority that are members, observers, or associates of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The SRA aligns with the Global Fund Quality Assurance Policy for Pharmaceutical Products which took effect on July 1, 2009.

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## Steatosis

Accumulation of fat in the liver; sometimes referred to as fatty liver.

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## STI

Sexually transmitted infection.

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## SVR

Sustained virological response—a person has no detectable HCV after treatment has been completed.

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## TAG

Treatment Action Group.

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## TB

Tuberculosis.

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## Throughput

Rate of production, or amount, of tests that can be run through a diagnostics system at a time.

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## VEL

Velpatasvir—combined with sofosbuvir as fixed-dose combination that treats all HCV genotypes, taken once daily, with or without food, for 12 weeks. People who have advanced (or decompensated) cirrhosis will need to add ribavirin twice daily.

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## Virological testing

Also known as confirmatory testing—uses NAT laboratory processes to detect genetic material (DNA or RNA) of a virus and determine if the infection is active and to decide whether to start a patient on treatment. It is also used to confirm sustained virological response (for HCV) or effective suppression of the virus (for HBV).

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## VL

Voluntary license—a patent holder allows another pharmaceutical company to manufacture a generic version of their medication. The patent holder sets conditions and may receive a fee or royalty. In effect, voluntary licenses permit patent holders/originator companies to control the market by limiting the countries that are licensed to produce and sell generics. Countries that are not included in licensing agreements must buy more expensive drugs from the originator companies. Voluntary licenses can also include other restrictions, such as the number of people who can be treated, whether drugs can be co-formulated, and which suppliers must be used for the active pharmaceutical ingredients needed to make the medication.

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## WHO

World Health Organization.

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## WHO PQ

World Health Organization Prequalification—a process conducted by the WHO using unified standards to assess the quality, safety, and efficacy of medicines, active pharmaceutical ingredients, medical products, and quality control laboratories. It is not a prescriptive list; rather, this standard can help countries consider medicines and medical devices that meet high quality standards to procure for their national programs.

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# Sample HCV Advocacy Workshop Learning Evaluation Form

**Instructions: Please circle the correct answers.**

**1. There are \_\_\_\_\_ types of viral hepatitis.**

- A. Only one
- B. Four
- C. Five
- D. Six

*Answer: D*

**2. You can catch hepatitis C through:**

- A. Unsterilized tattoo or piercing equipment.
- B. Sharing eating utensils or glasses with someone who has hepatitis C.
- C. Sharing unsterilized needles with someone who injects drugs.
- D. Receiving blood donation or blood products that have not been screened.
- E. Having condomless anal sex without lube with someone who has hepatitis C.

*Answer: All except B.*

**3. Circle the things that can cause faster liver damage from hepatitis C.**

- A. Living with HIV.
- B. Being coinfecting with hepatitis B and C.
- C. Drinking excessive amounts of alcohol.
- D. Having excess fat in your liver.
- E. The amount of time you have had hepatitis C.

*Answer: All*

**4. Which of the following statements is correct?**

- A. The majority of HCV-infected persons will not have a persistent infection.
- B. People with acute HCV infection often do not show any symptoms.
- C. Once HCV is cleared from the body, the antibodies to HCV usually disappear and will no longer show up positive on a screening test.
- D. People who are coinfecting with HIV/ HCV have a slower progression of liver disease.

*Answer: B*

**5. Circle the false statement about direct-acting antivirals (DAAs).**

- A. DAAs are oral medications, taken either once or twice a day.
- B. DAAs have high cure rates, sometimes reaching over 95% sustained virological response.
- C. DAAs can effectively cure people with HCV in 8–12 weeks.
- D. DAAs are effective against many or all HCV genotypes.
- E. DAAs have many intolerable side effects.

*Answer: E*

**6. Which one of the following is NOT a hepatitis C treatment that treats all genotypes of the virus?**

- A. Sofosbuvir and ledipasvir
- B. Sofosbuvir and daclatasvir
- C. Sofosbuvir and velpatasvir
- D. Glecaprevir and pibrentasvir

*Answer: A*

**7. You cannot be retreated for hepatitis C if you have become reinfected.**

- A. True
- B. False

*Answer: False*

**8. People who actively use drugs do not achieve the same cure rates as people who do not use drugs.**

- A. True
- B. False

*Answer: False*

**9. What does a positive HCV antibody test mean? Circle the true statement.**

- A. A person may have been exposed recently.
- B. A person may have chronic hepatitis C.
- C. A person may have had hepatitis C in the past but has cleared the virus.
- D. A person needs a viral load confirmation test.

*Answer: All*

10. Circle all the steps needed to diagnose hepatitis C and start treatment.

- A. Antibody screening test
- B. Viral load confirmation test
- C. Liver biopsy
- D. Liver damage assessment
- E. Liver function tests

*Answer: All, except C*

# Suggested Resources for Planning and Facilitating HCV Advocacy Workshops

Anti-Oppression Resource and Training Alliance. Facilitation for democratic process: Making meetings awesome for everyone. 2017 June. <http://aorta.coop/wp-content/uploads/2017/06/AO-Facilitation-Resource-Sheet.pdf>

Eurasian Harm Reduction Association. Budget advocacy: a guide for community activists. 2018 October 17. <https://harmreductioneurasia.org/budget-advocacy-guide/>

International HIV/AIDS Alliance. A facilitators' guide to participatory workshops with NGOs/CBOs responding to HIV/AIDS. 2001. [http://www.lupinworks.com/roche/workshops/Participatory\\_Workshops.pdf](http://www.lupinworks.com/roche/workshops/Participatory_Workshops.pdf)[http://www.lupinworks.com/roche/workshops/Participatory\\_Workshops.pdf](http://www.lupinworks.com/roche/workshops/Participatory_Workshops.pdf)

Kaner S, Lind L, Toldi C, Fisk S, and D Berger. Facilitator's guide to participatory decision-making, 3rd edition. San Francisco, CA: John Wiley & Sons, Inc; 2014.

TREAT Asia/amFAR. Fact sheet: WHO guidelines for the screening, care, and treatment of persons with hepatitis C infection. Bangkok: TREAT Asia/amFAR; 2019 January 9. <https://www.amfar.org/Articles/Around-The-World/TreatAsia/2019/Fact-Sheet--WHO-Guidelines-for-the-Screening,-Care,-and-Treatment-of-Persons-with-Hepatitis-C-Infection/>

Treatment Action Group. Updated training manual for treatment advocates: Hepatitis C virus & coinfection with HIV. New York: Treatment Action Group; 2018 February 1. [http://www.treatmentactiongroup.org/sites/default/files/HCV\\_curriculum\\_FINAL\\_ENG\\_0.pdf](http://www.treatmentactiongroup.org/sites/default/files/HCV_curriculum_FINAL_ENG_0.pdf)

Treatment Action Group. HCV Fact Sheets. New York: Treatment Action Group. <http://www.treatmentactiongroup.org/hcv/factsheets>