Closing the gaps in the hepatitis C care cascade

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The May 2021 Global Progress Report on HIV, viral hepatitis and sexually transmitted diseases, issued by the World Health Organization (WHO), reveals initial signs of a decline in annual mortality for hepatitis C (HCV) and its overall burden worldwide, owing in part to the 9.4 million people who have received HCV treatment—a nine-fold increase from the 1 million people treated in 2015. Worldwide, 58 million people are living with HCV, with an estimated 1.5 million new infections in 2019. An estimated 21% of all those infected with HCV have been diagnosed, and an estimated 62% of those diagnosed have received treatment.

With millions of people infected with HCV still unaware of their status, screening, diagnosis, and linkage to care remain vitally important measures in the battle against the disease. Yet as countries seek to achieve WHO targets for eliminating HCV as a major public health threat by 2030, linkage to care is sometimes overlooked or neglected. What happens when a person receives an initial diagnosis of HCV? Without strong linkage to care, many patients fall off the care cascade and are not treated, lost either in the interval between antibody and confirmatory testing or in the interval between confirmatory testing and treatment.

“Closing the gaps in the hepatitis C care cascade,” organized by the Coalition for Global Hepatitis Elimination (CGHE) and supported by Roche, mapped out key challenges and opportunities related to the case cascade for HCV testing and treatment. Distinguished panelists explored ways to strengthen the care cascade, so that everyone living with HCV can be cured. What is the current status of care linkage, and what research is helping public health experts improve their programs? The webinar offered an overview of recent technical and behavioral interventions that hold promise for engaging or re-engaging patients who have fallen out of the care continuum. In light of World Hepatitis Day and a renewed global commitment to hepatitis elimination, this webinar aimed to explore common barriers faced by HCV programs and introduce new solutions for reducing the operational and programmatic gaps in which patients are too often lost.

Common challenges in the HCV care cascade:

- Lack of individual awareness of HCV infection
- Competing medical priorities by the patient
- Difficulty accessing diagnosis and treatment options in certain regions, including rural areas
- Inadequate or inconsistent access to qualified health services especially among vulnerable populations, such as persons who inject drugs (PWID) and homeless persons
- Overly complicated testing processes can lose patients between antibody diagnosis and confirmatory testing
• Overly centralized care requiring specialists can lose patients between confirmatory testing and treatment

**Opportunities to strengthen the HCV care cascade:**

• Simplify and decentralize: support countries and programs in introducing streamlined, decentralized test-and-treat care pathways, integrated into primary care and harm reduction services.

• Task-share and task-shift: train nurses and other non-specialists to offer HCV testing and care, supporting decentralization and offering expanded access for patients.

• Offer a diverse combination of HCV testing options: this could include combination testing for multiple diseases, dried blood spot testing, self-testing, and “reflex” or “one-step” testing that conducts antibody and viral load analyses using a single specimen.

• Take the HCV care to the patient, rather than bringing the patient to the HCV care. Mobile units, community awareness campaigns, one-time “Test and Treat” options, and the use of rapid diagnostic tests are all tools in the effort to identify infected but undiagnosed persons—and diagnosed but untreated persons—in the community and bring them into the care system.

• Move beyond siloes: the COVID-19 pandemic response demonstrates why testing siloes must be discarded—and why program siloes need to be better integrated as well. Consider ways to integrate the HCV care cascade into HIV care, primary care, drug treatment residential care, homeless and institutionalized population care, veterans healthcare, and rural health outreaches.
Presentation Highlights

Streamlining the HCV care cascade
Dr. Philippa Easterbrook | World Health Organization

New WHO products available for countries working to eliminate HCV:

- Interim Guidance for Country Validation of Viral Hepatitis Elimination (June 2021)
- New WHO Global Progress Report (HCV and HBV), part of the Global progress report on HIV, viral hepatitis and sexually transmitted infections (May 2021)

Existing WHO guidance on promoting testing and treatment uptake and linkage to care:

- 2017 guidelines on testing for hepatitis B and C infection
- 2018 updated guidelines on prevention, care and treatment of hepatitis C

Key takeaways from existing guidance and new evidence:

- Existing recommendations for promoting linkage (2017 testing guidance)
  - Use of DBS specimens for virology ± serology
  - On-site or immediate RDT testing with same day results
  - Trained peer and lay health workers
  - Clinician reminders to prompt provider initiated, facility-based testing
  - Testing as part of integrated services at a single facility
  - HCV dried blood spot testing (both serology and virology)
• Existing good practice principles for simplified HCV service delivery (2018 HCV guidelines)
  ◦ Simplified and standardized algorithms across continuum of care
  ◦ Strategies to strengthen Linkage from testing to care, treatment and prevention
  ◦ Decentralisation of testing and treatment to primary care/harm reduction sites to promote access
  ◦ Task-sharing: Training and mentorship of non-specialists and nurses
  ◦ Integrated testing, care and treatment with other services (eg. HIV and harm reduction services)
  ◦ Engagement with community

• New WHO evidence from systematic review of 142 studies
  ◦ Decentralize testing and treatment: Evidence shows that full decentralization of testing and treatment increased uptake of testing, linkage and treatment, and achieved a comparable virologic cure (SVR12). Move treatment out of specialty clinics.
  ◦ Task-shift treatment to trained non-specialists, including nurses. Evidence shows this strategy achieves a similar SVR12 compared to specialist care.
  ◦ Integrate HCV testing, care, and treatment with harm reduction sites, care at prisons, and HIV/TB clinics. Integrated care can also take place at the lab level with integrated combination serology (HIV/HBV/HCV) and at the testing site.

• New WHO guidance on HCV self-testing
  ◦ Offer HCV self-testing.

• Other messages
  ◦ Advocate for “one-stop shop” hepatitis care. Within this one-stop shop, offer on-site point-of-care (POC) viral load or confirmatory testing: patients are more likely to use treatment services, and turnaround time is reduced.
  ◦ Consider mobile testing/treatment units for rural and hard to reach populations.

**Looking ahead:**

• Updated guidance on HCV diagnostics and treatment later this year will address recommendations on simplified service delivery, use of HCV point-of-care viral load and treatment in children and adolescents.

• A new 2022-2030 global strategy for viral hepatitis will launch next year. It will include two overarching strategic directions: (1) leveraging systems and (2) integrating services.

• Key principles will include equity, quality, innovation, and people-centered, community-driven approaches. Just as “Hep can’t wait,” so also “Linkage can’t wait!”
Significant Improvement in Diagnosis of Hepatitis C Virus Infection by a One-Step Strategy in a Central Laboratory: an Optimal Tool for Hepatitis C Elimination

Dr. Francisco Rodriquez-Frias | University Hospital Vall d’Hebron, Barcelona

The need:

- In 2015, only 60% of seropositive HCV cases in primary care and less than 20% of seropositive HCV cases in the drug treatment centers newly associated with University Hospital Valle d’Hebron were being tested for HCV viral load. These patients were being lost in the care cascade.

The response:

- The hospital system introduced one-step testing, also called reflex viral load testing, which unifies the two stages of analytical studies into one: a single phlebotomy is performed to collect two vials of blood, and if the first vial is positive for HCV antibodies, viral RNA is determined from the second sample originally used to measure the red blood cell count. Results of both tests are sent simultaneously to the requesting physician just 2 days after the phlebotomy. (Note: in other settings, reflex testing refers to using one specimen for both HCV antibody and viral load testing).

The results:

- After the application of the one-step diagnostic algorithm, only 5-8% of relevant patients had not received a viral load test, and more than 90% of serologically positive cases were completely diagnosed.
- Today, reflex HCV RNA testing is applied throughout the Spanish states. In 2019, 89% of Spanish laboratories used it. More needs to be done, however, to reach hard-to-reach populations, including PWID.
- Since launching the one-step strategy in drug treatment centers, the Valle d’Hebron team has diagnosed 319 HCV cases. By the old method, just 64 would have been diagnosed.

Key takeaways:

- One-step diagnosis prevents many patients from not completing the diagnostic process, but the quality of the sample used for HCV RNA testing must be guaranteed.
- Using the one-step process in dried blood samples can help with key populations, including immigrants and PWID. The use of rapid diagnostic tests (RDT) for serology and decentralized viral load tests can also help.
- A “test and treat” strategy with point-of-care RDT and viral load testing may be an optimal solution for hardest-to-link patients, including homeless persons, so that all steps can be taken in one time and place.
DECENTRALIZED ALTERNATIVE DIAGNOSTIC ALGORITHMS: STARTING WITH “RAPID DETECTION TESTS “ (RDTS)

A- Diagnosis based on rapid antibody detection tests (RDTs) followed by HCV-RNA conventional study:

In the same place where patient is located, based in “one step strategy”.
- Conventional venopunction if available (1)
- Capillary finger blood if venopunction not available (2)

- Rapid diagnostic tests using serum, plasma, fingerstick whole blood or crevicular fluid (saliva) as matrices can be used instead of classical EIAs as point-of-care tests to facilitate anti-HCV antibody screening and improve access to care (A1).

Source: Slide 19, Presentation from Dr. Rodriguez-Frias
Making Laboratory Diagnostics Accessible: Performance of HCV Assays from Dried Blood Spots and Plasma Separation Card
Dr. Elena Ivanova, Foundation for Innovative New Diagnostics (FIND)

The problem:

- Confirmatory or viral load testing traditionally requires a centralized lab facility, specialized equipment, and substantial time/travel, posing challenges especially for low-and-middle-income countries (LMICs).

The alternative:

- Dried blood spot testing (DBS) represents an appealing and practical alternative to plasma testing.
- Advantages: it allows decentralization of sample collection; finger-prick and venous blood can both be used; cold chain is not required; costs are reduced; and it can be used for antibody screening, RNA testing and genotyping if needed.
- DBS can also provide accurate results, at 98% pooled specificity for DBS HCV RNA and for DBS HCV EIA (enzyme immunoassay).

Testing the dried blood spot approach:

- FIND’s Prospective Diagnostics Accuracy Study aimed to evaluate the diagnostic performance of dried blood spot testing compared to plasma testing of the same assay, using different tests (Abbott Real Time HCV VL; Roche 4800 HCV VL; Roche 6800 HCV VL), across multiple study sites and three different population groups.
- Real-life settings were recreated (transportation required, no refrigeration, etc).
- Results:
  - Overall, laboratory assays from DBS and plasma separation cards (PSC) both performed well, indicating that these sample types can be used for the screening and diagnosis of HCV.
  - For individuals already treated for HCV, the RNA assays from both PSC and DBS specimens showed lower sensitivity, probably because the sustained virologic response (SVR) was already lowered by the patients’ medications. More studies are needed.

Key takeaway:

- The demonstrated accuracy of DBS for laboratory assays enables a true one-step sampling strategy. steps can be taken in one time and place.
DEMONSTRATED ACCURACY OF DBS FOR LABORATORY ASSAYS ENABLES ONE STEP SAMPLING STRATEGY

Source: Presentation from Dr. Elena Ivanova
iThemba Life: Empowering HCV patients to engage in care and treatment
Dr. Samanta Lalla-Edward | University of the Witwatersrand, Johannesburg, South Africa

The iThemba Life mHealth solution: What it is

- A digital solution to empower patients to engage in care
- A health management solution designed to support the goals of disease elimination programs in LMICs
- iThemba Life leverages clinical outcomes, patient behavior, and bi-directional feedback to provide aggregated data insights supporting program level decision making.
- The initial focus was HIV, but iThemba is now expanding to TB, HPV, HCV, and HBV to support multi-disease testing to achieve efficiencies and improve outcomes.

iThemba Life components
Supporting multiple stakeholders in the value chain

iThemba for patients:

- A mobile app with an information hub to provide appointment reminders, timely delivery of test results, healthcare education, longitudinal follow-up, medication reminders and medication compliance support, and more.
- Designed for older, less expensive smartphones to ensure broader access
- Private and secure for patients
- The app can support multiple users in a family (for example, parent and child).
iThemba for labs and for disease program leaders:

- Aggregated dashboards provide individual patient details
- Comprehensive reports can be generated focused on actionable populations.
- Program dashboards offer insights into population health and help guide interventions and decisions regarding resource allocation and more.
- Can be adapted for specific contexts, including digital solutions for HCV elimination

Key takeaways:

- Lessons learned from its initial use in HIV mean that iThemba is already tested in the field of infectious disease elimination/monitoring.
- HCV programs would need to adapt for specific issues they want to address
- The app has the potential to integrate test results from point-of-care (PoC) and central labs, a key challenge currently under discussion across HCV programs.
Reengaging Patients in HCV care: Real-World Experience from the US Department of Veterans Affairs
Rachel Gonzalez, MPH, and Angela Park, PharmD | US Department of Veterans Affairs

The Hepatitis C Innovation Team (HIT) Collaborative: What it is
• Launched by US Department of Veterans Affairs (VA) in 2014, HIT is a learning community of multidisciplinary teams committed to process improvement across the HCV care cascade.
• The HIT Collaborative takes HCV care to the veterans where they are.
• It is achieving micro-elimination of HCV within the VA system: over 100,000 veterans have been treated and cured of HCV to date. Within the at-risk birth cohort of persons born between 1945–1965, over 85% of veterans have been tested. Within the entire veteran population, more than ¾ have been screened, and more than 90% of those who tested positive have been treated.

How it works:
• HIT Collaborative teams redesigned care including patient outreach via letter and phone, offering evaluation and treatment for HCV. Additional outreach efforts included mass media, community outreach events/health fairs, social media campaigns, and partnering with community organizations.
• After two years, teams had reached ~68,000 Veterans.
• Despite this success, teams recognized barriers that prevented all patients from pursuing treatment
• Veterans living with HCV could be lost to follow-up between diagnosis and linkage to treatment. Preliminary data from one region estimated that about 20% of patients were delaying treatment and 3% were unreachable. One third were not pursuing treatment even though it had been offered. Barriers included unstable housing, substance abuse, mental health concerns, and more.
• In addition, partnerships were formed with subject matter experts within the VA to address barriers to care, including from the Office of Mental Health & Suicide Prevention, and Peer Support Services. Local teams applied interventions to address barriers to care. One local team partnered with a substance abuse residential treatment program to treat patients with HCV. Within the first year 28 patients were referred for HCV treatment; in the previous year, only 1 patient had been referred.
• Across VA, HIT teams are finding creative partnerships to provide care to meet veterans’ needs
Key takeaways:

- Adopt a genuinely patient-centered approach.
- Take the time to connect to stakeholders with established expertise (on homelessness, transportation, peer support, mental health).
- Engage veterans where they are, not where we wish they were.
- Expand and extend the “front line” of HCV care.

Source: 5, Presentation from Rachel Gonzalez and Angela Park

Taking HCV Care to the Veterans

Anne Bailey, PharmD and team bringing care to the Veterans in Columbia, SC.

Miguel Luna, advanced medical support assistant, approaches an area frequented by homeless Veterans in Fresno, Calif. When the team locates homeless Veterans, they ask if they would like to be Hep C tested and if there is anything else they need.

Source: Slide 9, Presentation from Rachel Gonzalez and Angela Park

Download slides
Watch presentation
A Digital Case-Finding Algorithm for Diagnosed but Untreated HepC: A Tool for Increasing Linkage to Treatment and Cure
Brooke Wyatt, MPH | Icahn School of Medicine at Mount Sinai

The need:

- New York City is making progress toward WHO targets but has a way to go. Only 50% of NYC residents with a positive HCV RNA test in 2015 were treated by 2019.
- Mt. Sinai Hospital has implemented reflex testing since 2016 and operates in a task-shifting and decentralized model. But many diagnosed cases still needed to be treated.

Algorithm project:

- Combines advanced medical informatics and traditional multidisciplinary care methods to engage patients in HCV treatment and reduce HCV infections.
- A case-finding algorithm was developed by identifying key data elements utilizing fields within the electronic medical record that served as indicators of HCV care and treatment.
- Algorithm performance was evaluated by comparing it to a manual chart review.

Findings:

- The algorithm compared very well to the manual chart review, with results showing that it is a highly effective case-finding tool (positive and negative predictive values were 88% and 97%, respectively), greatly reducing the human resources needed to find diagnosed but untreated patients.
- Miscalls by the algorithm were typically associated with unstructured data reported in idiosyncratic syntax, sometimes in the media section.
Follow up:

- After identifying diagnosed but untreated HCV patients, navigators attempted to contact potential treatment candidates by phone. 48% could not be reached.
- Patients who could not be reached by phone were younger, less likely to have fibrosis, and less likely to have private insurance (18% vs 50%).
- Letters were sent to 619 patients, but only one engaged in care after the mailing.
- 31% of the algorithm-defined positive patients did go on to engage in the HCV care and treatment pipeline. Care coordination was beneficial for these patients. Those who enrolled in care coordination had significantly different rates of treatment start (81% vs. 58%), completion (72% vs 54%), and cure (66% vs 46%).
Key takeaways:

- Case-finding algorithms are useful tools in identifying diagnosed but untreated patients.
- Gaps in service delivery must be avoided or minimized while considering new approaches that continue to move away from previous restrictive treatment guidelines.
- The algorithm will be available for free download once the accompanying journal article is published:

Conclusion

HIV and TB have taught us that maintaining patients along a cascade of care is complex. Yet successful treatment, the final step of the cascade, is essential to saving lives and producing positive health outcomes. Eliminating HCV requires coordination at every step of care, from diagnosis to cure and monitoring. In the United States, with new CDC HCV screening guidelines now recommending HCV screening for nearly all adults, not just baby boomers and other high-risk individuals, the challenges posed by care linkage are likely to increase. Innovative and timely solutions are needed to increase access to testing and treatment for all.

Worldwide, the best programs are those that (1) decentralize care, (2) task-shift and task-share so that non-specialists can deliver HCV education and treatment, and (3) embrace new technologies and strategies—both digital and communal—for identifying patients who have HCV but do not know their status or who know their status but have not been treated. Bringing HCV care to patients where they are—including rural areas, prisons, homeless shelters, residential treatment programs, and other key institutions—will save countless lives as countries work to eliminate HCV as a major public health threat by 2030.