Pipeline Report » 2020

HCV Diagnostics

HCV Diagnostics Pipeline 2020[1]

By Bryn Gay

Even before the COVID-19 pandemic there were 400,000 annual deaths from liver disease and cancer related to the hepatitis C virus (HCV), and deaths from drug-related overdoses were increasing—worldwide, 585,000 people died as a result of drug use in 2017. COVID-19 could worsen these death tolls as people living with HCV and people who use drugs may be more isolated, miss medical appointments, and lack access to essential support systems. Despite the expanded roll out of generic, curative treatments with pangenotypic direct-acting antivirals (DAAs), political apathy, less than 10% of the necessary funding, and diagnostics barriers have been sabotaging efforts to meet global HCV elimination targets. Enormous amounts of public funding and health resources have been reallocated to respond to COVID-19 around the world, compounding the complications of providing essential services, let alone scaling up the hepatitis C response.

People who recover from COVID-19 have been shown to have elevated liver enzymes; people living with viral hepatitis, liver scarring, liver disease, or other hepatic conditions will need to monitor their liver function following their recovery. The pandemic has also interrupted screening campaigns and routine health visits that confirm HCV diagnoses and identify new cases, as part of efforts to reduce people's risk of exposure to the SARS-CoV-2 virus. During this time, countries with histories of harm reduction services have included needle and syringe programs and opioid substitution therapy (OST) as essential services. Innovative approaches in harm reduction settings, such as wider community distribution of naloxone and take-home and delivered DAA and OST treatment, combined with telemedicine, monitoring, and social support could be made permanent in the post-pandemic period.

Countries should reinforce efforts to curb overlapping HCV, overdose, and COVID-19 epidemics: the mobilization of COVID-19 investments could be used to strengthen lab and diagnostic capacity, invest in multi-disease platforms, diversify and improve supply chains, develop the healthcare workforce, and expand community outreach and awareness raising on available infectious disease services. In fact, COVID-19 tests have been developed for many HCV diagnostics platforms, such as COBAS TaqMan (Roche), GeneXpert (Cepheid), Genedrive, Real*Time* (Abbott), and ARCHITECT (Abbott). Countries could leverage global funding and procurement to include HCV diagnostics and assays in volume-based deals. This approach aligns with HCV elimination strategies to simplify, decentralize, and integrate diagnostics into existing healthcare infrastructure, such as HIV, sexual health, and harm reduction clinics.

One large-scale trial with over 11,000 participants—primarily people who use drugs—across 12 sites in India demonstrated significant impacts and increased treatment uptake when integrating free HCV antibody testing in HIV and harm reduction services. Notable for integration in HIV programs, dried blood spot (DBS) samples, which are widely used in

HIV, have also been shown to be a rapid, effective method for HCV enzyme immunoassay (EIA) and viral load testing in rural, remote, and resource-limited settings. DBS tests require minimal training for collecting, storing, and transporting samples. DBS tests can be sent to labs by mail or courier and has lower costs compared to other methods (plasma, whole blood).

Innovative methods to expand testing emerged before COVID-19, and health departments can explore options while many non-emergency services have been paused or altered. For example, with adequate supplies and healthcare workers, opt-out HCV serology and reflex testing in emergency rooms, screening in pharmacies or at drive-through testing sites alongside COVID-19 testing could ensure some continuity. HCV (antibody and RNA) self-tests are also becoming more available in some high-income countries; with telemedicine support and monitoring, they could connect highly stigmatized communities to healthcare services. Studies are underway, such as the SELFIE and ICECREAM studies, to evaluate the impact and feasibility of HCV RNA self-testing among men who have sex with men (MSM) on reducing the time to diagnose, start treatment for reinfections, and prevent onward transmission. However, the applicability and implementation of self-tests in low- to middle-income countries (LMIC) with limited telemedicine infrastructure is under investigation.

Research and development (R&D) in diagnostics and validation studies, such as for HCV self-tests, experienced delays as companies rushed to approve and market diagnostics for the SARS-CoV-2 virus. Nonetheless, since July 2019, the HCV diagnostics options expanded and several tests were approved for WHO prequalification (PQ) (for diagnosis only, not SVR because lower limit of detection (LLoD) has not yet been determined): Standard-Q antibody test (SD Biosensor); Monolisa antigen/antibody combo test (Bio-Rad); a portable HCV RNA test (Genedrive); Alinity-m quantitative PCR test (Abbott); Real*Time* HCV viral load test (Abbott); and ARCHITECT core antigen test (Abbott). Furthermore, an additional portable HCV PCR, TrueNAT (Molbio), was approved in India and currently being considered for WHO PQ.

Additional evidence showed the costs of test-and-treat programs and cost effectiveness when using a simplified diagnostics pathway. The lowest market prices for all the components to test and treat patients, using Global Fund's pooled procurement mechanism, were US$79 per patient per 12-week course for fixed-dose combination of sofosbuvir/daclatasvir and US$94 per patient per 12-week course for individual sofosbuvir + daclatasvir. Based on Rwanda's pricing, and aligned with the WHO simplified testing guidelines, the test-and-treat program included one rapid diagnostic test, one confirmatory viral load test, one treatment course, and one SVR12 test to confirm cure. The program also assumes that prior to treatment, liver staging tests, assessment of any pregnancy, comorbidities, and drug-drug interactions, and genotype testing for adolescents are conducted. In a separate study in Cambodia, simplifying the diagnostics pathway shows cost-effectiveness, with a reduced cost of US$376 (Interquartile Range US$344–422). This Cambodian test-and-treat program includes similar steps as in Rwanda and follows the WHO simplified testing guidelines. It also includes associated costs for two education/informational sessions, a FibroScan exam to check liver staging, assessment of any pregnancy, comorbidities, and drug-drug interactions, two consultations

with physicians and one with a pharmacist, and related staff time/salaries. The simplified model of care can save money and result in better treatment outcomes compared to long-term costs associated with undiagnosed and untreated patients.

Governments and procurement agencies could also streamline registration of WHO PQ'd generic DAAs and diagnostics and save bureaucratic costs through the WHO Collaborative Registration Procedure (CRP). The CRP for diagnostics—starting with an HIV viral load platform, m-PIMA Analyser (Abbott)—piloted in Cameroon, Côte d'Ivoire, Ethiopia, Nigeria, and Tanzania at the end of 2019. If used for HCV, this process could help save time and improve access to generic DAAs and diagnostics by simplifying national registration steps, analyzing the regulatory bottlenecks, and ensuring product sameness with WHO PQ'd products.

Advocacy points for different stakeholders to accelerate affordable access to simpler HCV testing and the developments in diagnostics products are highlighted below. See *Pipeline Report 2019* for developments before July 2019.

Advocacy points

For companies:

- Reduce the price of tests regardless of volumes so that they are more in line with the cost of goods, and have savings reflected by iterative decreases in list prices (e.g., savings from royalty expiration, increased manufacturing efficiencies, increased volumes).
- Divulge transparent and disaggregated pricing in the *ex works* price on the total costs of diagnostics. Pricing should be transparent along the value chain.
- Minimize and ensure transparency of service/maintenance costs for instrument-based platforms to better inform procurement and health program costs in LMIC.
- Offer different types of procurement contracts (e.g., reagent rental or price per test, with bundled pricing across disease areas), which may be better suited for countries. Pooled procurement should be facilitated either globally or regionally to improve negotiations and to take advantage of higher volumes.
- Prioritize and register professional use antibody tests with less invasive sampling procedures (oral, capillary blood) for self-testing.
- Develop and validate DBS protocols and submit them for in vitro diagnostics (IVD) stringent regulatory authority approval so that DBS is a manufacturer-recommended sample type.
- Prioritize the development of POC ribonucleic acid (RNA) test and POC HCV core antigen (cAg) with acceptable diagnostic accuracy (sensitivity/specificity), and promote operational research of these technologies as soon as possible to understand their advantages/disadvantages when used in routine settings and in resource-limited countries.

- Develop probes to identify people with difficult-to-treat genotype subtypes that can help with adjusting treatment regimens.
- Evaluate the performance of RDTs and EIAs in adolescents and children (for testing after 18 months old, once maternal antibodies may have cleared).
- Validate non-invasive tests for assessing liver disease in children.
- Cepheid should disclose the public investments that were made to develop GeneXpert; this significant public contribution should be reflected in the prices of their platforms and cartridges. Other companies, including Abbott, Biocentric, bioMérieux, Hologic, and Qiagen, should offer diagnostics access initiatives and pricing regardless of volume for both standard purchase and reagent rentals.
- Include community and civil society organizations in the design, research, and implementation of diagnostics, which could address affordability, simplicity, and community-friendly testing settings.

For World Health Organization:

- Facilitate the prequalification process for open platforms, which already have other quality certifications (such as from the US Food and Drug Administration, CE-IVD marking, ISO 13485:2003 standard, etc.).

For governments and implementing partners:

- Use pangenotypic DAAs to simplify the diagnostics algorithm and increase patients' linkage and retention in care.
- Promote the integration of HCV assays on polyvalent, open platforms, which enables cost-sharing of operational costs across programs and facilitates price negotiations with the manufacturer by bundling items that aid in bulk purchasing and ease distribution. The Global Fund to Fight AIDS, TB and Malaria (GFATM) provides the option for countries to purchase open platforms, reagents for HIV, TB and malaria, and consumables through the procurement platform, WAMBO. Countries should purchase polyvalent, open diagnostics platforms.
- Streamline registration of WHO PQ'd generic DAAs and diagnostics through WHO CRP.
- Facilitate the integration of diagnostic services and move away from vertical disease specific management models.
- Standardize and harmonize regulatory requirements for the in-country registration process for in vitro diagnostics (IVDs), and establish fast-track procedures for quality-assured (i.e., stringent-regulatory approved, WHO PQ) diagnostics products from the WHO Essential Diagnostics List.
- Establish national external quality assurance schemes for facilities and services performing HCV screening and/or confirmatory testing (through external collaboration or internal development).

- Demand companies divulge transparent and disaggregated pricing on the total costs of diagnostics, and/or demand all-inclusive pricing in the *ex works* price.
- Increase the number of patients screened and tested and ensure bundled procurement, competition, and diverse distributor options to bring down diagnostics prices in countries.
- Minimize the layers of distribution, ensure transparency and accountability along the global and domestic supply chains to reduce costs, and exclude taxes on public goods.
- Utilize diagnostics to support surveillance studies to understand countries' local epidemics, monitor impact, and adapt testing strategies. When feasible, prioritize surveys across infectious diseases for efficient use of resources.
- Consider renewing antibody screening campaigns if previously conducted using older, less specific, non-PQ/non-CE-IVD marked tests.

For donors:

- Invest in and prioritize development of POC ribonucleic acid (RNA) test and POC HCV core antigen (cAg) with acceptable diagnostic accuracy (sensitivity/specificity), and promote operational research of these technologies as soon as possible to understand their advantages/disadvantages when used in routine settings and in resource-limited countries.
- Include hepatitis C test instruments, reagents, and commodities, along with ongoing reagent, commodity, service and maintenance, and training costs in diagnostics procurement budgets.
- Facilitate the integration of disease-specific programs by promoting the sharing of multiplexed platforms across different programs and offering cross-disease instead of vertical funding.
- Central procurement platforms, such as Global Fund's WAMBO and the Global Drug Facility, should cover diseases beyond HIV, TB, and malaria, at minimum for HIV coinfection, to enable countries to procure reagents at the same price points as in these programs, or at least have transparent price information available via these platforms to improve domestic procurement negotiations.
- Utilize good practices for procurement, which include centralized or pooled procurement (i.e., globally or regionally via pooled procurement mechanisms); use competitive tender processes, which deliver the total package required to perform testing in countries; allow split tenders to increase the number of suppliers and to incentivize suppliers to improve services; and put long-term agreements in place that can guarantee a stable price but flexible test quantities according to changing forecasts and needs across diseases.

TABLE 1. HCV Diagnostics Pipeline: Products with New Published Data or Regulatory Updates Since July 2019

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
ANTIBODY ASSAYS—SCREENING				
HCV Self-Test[2]	Oral fluid, capillary blood POC; sexual health clinics and harm reduction settings; at home	OraSure (US)	TK	Target: <US$4 per test
■ An HCV self-test would not be helpful if treatment and care is not accessible, or if there is no counseling component. For highly stigmatized communities, HCV self-tests may provide the confidentiality and telehealth support needed to encourage people to get tested ■ FIND conducted a series of studies in different countries to assess the usability and acceptability of HCV self-testing, using tests donated by OraSure. Awaiting WHO guidelines review and regulatory status in 2020.				
STANDARD Q HCV Ab Test	Serum, plasma, or whole blood POC	SD Biosensor (Korea)	CE-IVD; WHO PQ (March 2020)	TK
■ Showed final (n=163) sensitivity 100% (95% CI: 97.8–100%) and (n=320) specificity 100% (95% CI: 98.9–100%). ■ Two steps in total; one step required for precision pipetting (for serum/plasma/whole blood). ■ Store at 2–40°C; 2-year shelf life. ■ Time to results: 10–15 minutes (endpoint stability at 15 minutes).				
Monolisa HCV Ag-Ab ULTRA V2	Serum, plasma Lab	Bio-Rad (US)	CE-IVD; WHO PQ (Jan 2020)	TK
■ (N=483) initial sensitivity of 100% (95% CI: 97.1–99.9%) and (n=483) initial specificity of 100% (95% CI: 98.5–100%). ■ Store at 2–8°C; one-year shelf life. ■ Four reaction steps in total. ■ Estimated time to results when following good laboratory practices: 2.5–3 hours. ■ To obtain WHO PQ status through an abridged process the Bio-Rad company must revise and submit instructions for use, which include results of analytical specificity and a statement on intended use for HCV screening and diagnosis, by October 31, 2023. The company also will be required to submit technical specifications in the detection of HCV antibody and/or antigen by January 24, 2023.				
Well anti-HCV RDT; Self-Test	Oral POC	Jiangsu Well Biotech Co., Ltd. (China)	TK	TK
■ (N=1179) of whom 486 patients were living with chronic HCV infection, 108 patients had other liver diseases, and 585 individuals considered healthy; 199 participants also self-tested. ■ Sensitivity of 91.88% (95% CI: 88.97–94.09%) and specificity of 98% (95% CI: 96.58–98.86%). ■ The Well RDT showed high consistency of 98.50% (197/200) with OraQuick and consistency of 97.02% (1138/1179) with InTec; self-administered tests were consistent with researcher-administered tests. ■ Time to results: 15–20 minutes; a reddish line appears when the result is positive. If no line appears, the test is invalid, which may be due to insufficient sample fluid. ■ False negative rates for the three research sites were 2.68% (Center 1), 11.65% (Center 2), and 9.06% (Center 3); 39 cases were false negatives and with further analysis most were found to have no detectable virus in the serum tests. ■ Evaluated as potential HCV self-test with proper training and instructions; possible for use in universal screening campaigns (such as places with limited medical personnel and resources), primary care, and at-home settings.				

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
RNA ASSAYS—CONFIRMATORY AND TEST OF CURE				
Genedrive® HCV RNA	30 µL plasma POC	Genedrive (UK)	CE-IVD; WHO PQ (May 2020)	US$5000 per device; US$25–35 per test; List price: US$30–40 per test in India; List price: US$14–18 per test for African region[3]

- Genedrive showed (n=81) sensitivity of 98.8% (95% CI: 93.3–99.97%) and (n=46) specificity of 100% (95% CI: 92.6–100%) therefore slightly less sensitive with an indeterminate rate of 3.1% (four samples).
- Four of six genotypes were consistently detected, with genotypes 1a and 5a required to repeat the detection.
- One study in Singapore[4] showed high sensitivity (100%) and high specificity (100%) for genotype 3 (n=240) and genotype 6 (n=16), prevalent in Asia. In this study, the LoD = 3203 IU/mL for samples with low viral loads.
- Similarly, a validation study in India demonstrated high sensitivity (100%) and high specificity (100%) for genotype 1 (n=35) and genotype 3 (n=68), which remained above LoD = 2362 IU/mL. The lowest LoD Genedrive could detect was 103 IU/mL.
- Store at 2–30°C; one-year shelf life.
- Requires 13 steps total, 5 precise pipetting steps (still requires a specialist, or nurse with training, to do pipetting).
- Time to results: 90-minutes, possible to use for task-shifting.
- New Genedrive model has Bluetooth capability and system for managing patient data with confidentiality. The user downloads app, which allows confidential data to be shared between healthcare providers and patients; decisions about care can be made locally with care team.
- Decentralized POC diagnosis, such as in “test-and-treat” scenarios, can help minimize patients lost to follow up.
- In published studies, the LoD for viral load = 2000 IU/mL.
- Genedrive may be less sensitive but governments could weigh sensitivity with faster return of results and fewer patients lost to follow up in their national testing strategies.
- Genedrive registered in additional African countries in 2019: Rwanda, Uganda, Kenya; evaluation study in prisons on pause due to COVID-19.

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
TrueNAT HCV PCR	250 µL whole blood, 500 µL plasma POC, primary healthcare	Molbio (India)	CDSCO-India approval in 2019; WHO PQ and CE-IVD (Estimated in 2020)	US$10,000 (small); US$14,000–18,000 (large)[5] US$18 per test, depending on volume[6] *Ex works* pricing, including service, maintenance, warranty
■ The polyvalent, two-step, portable RNA confirmatory platform weighs: small 5–6kg (10–12 tests per hour); large 10kg (24–48 tests per hour during an 8-hour period). ■ Battery-operated with 8-hour battery life, overnight battery recharging (≈ 4 hours). ■ Sample preparation takes ≈ 20 minutes with two or four slots in the PCR module. A maximum of six tests can be run per hour with the small device and 12 tests per hour with the larger device, excluding the ≈ 20 minutes preparation time per test. ■ Time to results per test: ≈ 40 minutes. ■ Sensitivity: 100%; specificity: 100%. ■ LoD: 235 IU/mL; manufacturer needs to evaluate assay for determining SVR, but LLoD for SVR 12 has not yet been determined. ■ One–two days training required provided by Molbio. ■ Automatic results on touchscreen; Bluetooth wireless connectivity. ■ Price includes one-year pre-warranty, which would replace the device and provide servicing during that time; then continuous contract.				
Alinity m HCV assay	Plasma, serum Lab, clinical	Abbott (US)	CE-IVD; FDA-approved in March 2020; WHO PQ (March 2020)	US$50 per test
■ A real-time quantitative PCR assay that uses three steps for one sample; diagnoses all six genotypes. ■ Three-step process; simplified monitoring viral load/adherence method using specific hybridization probes, to be combined with simple RNA extraction. ■ (n=97) sensitivity: 100%; (n=97) specificity: 100%. ■ LoD: 11 IU/mL (95% CI: 6.8–25.3 IU/mL); verified Abbott's claim of 12 IU/mL. ■ Time to results ≈ 2.25 hours. ■ Need to ensure correct storage to achieve sensitivity. ■ Requires 2–2.5 days of training, adequate lab equipment, and sufficient space.				

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
COBAS® Plasma Separation Card	Whole blood, plasma, dried plasma spots Lab	Roche (Switzerland)	CE-IVD (for HIV only, in development for HCV in 2020/2021); Not FDA-approved	TK, but PSC cards for HIV are priced much more comparatively than DBS cards COBAS PCR and reagents included in Global Access Program, with HIV, HBV, HCV and other molecular diagnostics GPRO (global procurement fund) range: US$10-15 per test Egypt (high-volume): ≈ US$7 per test

- Registered for HIV RNA testing for confirming positive HIV results by measuring baseline levels or to monitor ART, but technology could be developed for other diseases (validation for HCV is in development for 2020/2021).
- Requires minimum sample of 140 µL whole blood.
- The LoD is <1000 IU/mL (below EASL guidelines); Plasma Separation Card LoD: 866 IU/mL (95% CI: 698, 1153 IU/mL) and LoD: 408 IU/mL (95% CI: 336, 544 IU/mL) using an optimized assay specific analysis package protocol.
- Dried plasma spot must dry for four hours before packing for sample transport.
- Can courier/transport the sample up to 28 days at 18–45°C and with up to 85% humidity; after transportation the sample can be stored at room temperature (18–30°C), at 2–8°C or at -10°C for up to 56 days (with and without the layer separations).
- One Amsterdam study, using COBAS Ampliprep/COBAS TaqMan (Roche) among MSM for self-sample collection and which require transportation to the lab by mail or courier; this shows that HCV (and HIV-1) RNA can be self-sampled using DBS reliably, when stably stored at room temperature, for up to 21 days.
    - In labs, HCV RNA LoD varies between 2.2–3.4 log10 IU/mL; DBS LoD can be 0.5-1.7 log10 IU/mL more than in plasma. DBS using self-sample collection is possible for diagnosing HCV because most patients have viral loads higher than 3.0 log10 IU/mL.
    - Both self-sample and lab collected DBS tests showed high sensitivity: 95.7% (95% CI: 78.1–99.9%) for self-sample and 96.4% (95% CI: 81.7–99.9%) for lab-based, but less sensitive than plasma samples. Therefore, some infections may be missed and re-testing may be needed if a person believes they have an acute infection.
    - However, patients would need to self-collect good quality dried blood spots and follow the video and written instructions to ensure HCV infections are detected.

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
Real*Time* HCV Viral Load	0.5 mL plasma, 0.2 mL serum DBS (fingerstick) Lab	Abbott (US)	CE-IVD (for HIV DBS and HCV RNA); WHO PQ (Dec 2019)	US$11–23 per test; Global Fund price varies according to test volume/term commitment
■ Registered for HCV viral load using plasma or serum. Several studies are underway using DBS. ■ Store reagent kits at –10°C or colder; 18-month shelf life. ■ Requires adequate lab equipment and sufficient space. ■ To obtain SRA and WHO PQ status, Abbott must submit a table with the number of specimens per analyte that is tested as part of instructions for use by May 31, 2024. Abbott is using FIND data for submission for SRA and PQ. ■ (n=99) sensitivity: 100% (95% CI: 96.3–100%); (n=98) specificity: 100% (95% CI: 96.2–100%). ■ LoD: 31 IU/mL (95% CI: 11–52 IU/mL); verified Abbott's claim of 30 IU/mL. ■ All six genotypes detected.				
Xpert® HCV VL FS assay	100 µL, capillary blood, fingerstick Tertiary POC, harm reduction settings	Cepheid (US)	CE-IVD; Not FDA-approved	TK
■ The VL fingerstick assay was a modified version of the HCV RNA assay. ■ Xpert® HCV VL fingerstick test for HCV RNA quantification demonstrates high sensitivity: 100.0% (95% CI, 93.9–100%) and specificity: 100.0% (95% CI: 96.6–100%). ■ Time to results <1 hour; this reduces wait times and can prevent patients lost to follow up. ■ Median time to results depends on RNA level; this study among 1426 participants showed faster results for people with detectable HCV RNA (32 minutes) versus people with undetectable HCV RNA (57 minutes). ■ Screening tool that can be used for HCV RNA detection in high-prevalence settings, particularly in hospital emergency departments and services for people who inject drugs and/or people who experience homelessness.				
DBS on various PCR platforms	0.2 mL serum DBS (finger-stick) Lab	Various	Real*Time* HCV Viral Load CE-IVD (for HIV DBS and HCV RNA); WHO PQ (Dec 2019) COBAS® AmpliPrep/ COBAS TaqMan HCV Test CE-IVD (for HIV only) Aptima® HCV Quant Dx Assay TK	TK
■ Supports evidence for decentralized POC testing using DBS in resource-limited settings: ■ Studies conducted by FIND are in the process of recruitment to evaluate manufacturer protocols for DBS on various platforms, including Abbott *m2000*; COBAS® AmpliPrep/COBAS TaqMan HCV Test from DBS; cobas® HCV for use on the cobas® 6800/8800 Systems from PSC and DBS; Aptima® HCV Quant Dx Assay from DBS.				

Assay	Sample/ Setting	Company	Regulatory Status	Price (*ex works* or *free carrier*)
CORE ANTIGEN—CONFIRMATORY				
ARCHITECT HCV cAg assay	Serum, DBS Lab	Abbott (US)/Denka Seiken Co., Ltd. (Japan)	CE-IVD; WHO PQ (July 2019)	US$8–23 (€7–20) per test

- To obtain WHO PQ status for diagnosis only, through an abridged process, Abbott is required to submit revised instructions for use with the intended population, the specifics on level of skills of the platform user, and which instruments to use by March 31, 2022.
- A retrospective study demonstrated HCV RNA and cAg results to be in agreement at week 24, suggesting cAg could be measured then and become part of a one-step method to confirm cure. This is in line with 2018 EASL recommendations that cAg is only considered for SVR24. The study measured HCV cAg at baseline, weeks 4, 12, 24 of treatment, and end of treatment. False negatives were associated with low viral load; cAg increases over time for patients with treatment failure; cAg could become positive after treatment ends.
- HCV core antigen testing is less expensive in LMIC, and currently used in some countries, including Georgia and Uzbekistan. Uzbekistan's program had used core antigen as part of its reflex testing to confirm diagnosis in 2-3 days, but shifted to Roche COBAS PCR in 2020 due to Abbott's shipment delays and customer service issues.
- Overall, core antigen testing is less sensitive and could miss infections.
    - One study examined core antigen using DBS samples. Research investigated factors such as temperature stability, whether the sensitivity varied when using different sources of blood (venous compared to fingerstick), and results from samples with one or two DBS.
    - The study showed minimal differences in sensitivity and storage temperature, yet samples with a lower volume (3–10 fmol/L) and temperatures above 37°C could affect sensitivity.
    - Type of sample did not affect sensitivity, which was about (~94%) for diagnosis.
    - Larger studies could improve and standardize protocols for cAg DBS collection.
    - cAg DBS may be a potential method for diagnosing active infection, then sending negative results for RNA testing. Alternatively, it could be used in settings with high HCV-prevalence instead of antibody screening.

Abbreviations

Ab: Antibody
Ag: Antigen
ART: Antiretroviral therapy
cAg: Core antigen
CDSCO: Central Drugs Standard Control Organisation (India)
CE: Conformité Européene/European Conformity
CI: Confidence interval
CRP: Collaborative Registration Procedure
DAA: Direct-acting antivirals
DBS: Dried blood spot
EASL: European Association for the Study of the Liver
EIA: Enzyme immunoassay
FDA: Food and Drug Administration (U.S.)
fmol/L: femtomole(s) per liter
FS: Fingerstick
GFATM: Global Fund to Fight AIDS, TB and Malaria
HBV: Hepatitis B virus
HCV: Hepatitis C virus
IU/mL: International unit per milliliter
IVD: In vitro diagnostics
LLoD: Lower limit of detection
LoD: Limit of detection
LMICs: Low- and middle-income countries
MSM: Men who have sex with men
ND: No data
OST: Opioid substitution therapy
PCR: Polymerase chain reaction
POC: Point-of-care
PQ: Prequalification (For HCV, PQ is approved for diagnosis only, not SVR as LLoD has not yet been determined).
R&D: Research and development
RDT: Rapid diagnostic test
RNA: Ribonucleic acid, or HCV RNA test
SVR: Sustained virological response
TK: To come
uL: unit of liquid volume equal to one millionth of a liter, or 1 mm3
VL: Viral load
WAMBO: Global Fund's procurement platform
WHO: World Health Organization

Endnotes

1. Thank you to Sonjelle Shilton, Emmanuel Fajardo, and Homie Razavi, whose comments and suggestions helped improve and clarify this section.
2. Ivanova E (FIND, Geneva). Personal communication with: Bryn Gay and Annette Gaudino (Treatment Action Group, US). 2019 February 20.
3. Amphlett M (Genedrive, UK). Personal communication with: Bryn Gay (Treatment Action Group, US). 2020 May 20.
4. Tay AYL, Khine HHTW, Tan SJ, et al. Clinical validation of Genedrive point of need device in the Asian population to address decentralized Hepatitis C confirmation. Poster session presented at: 28th Annual Conference of the Asian Pacific Study of the Liver; 2019 February 20–24; Manila, Philippines.
5. Sumit M and Sriram N (Molbio, India). Personal communication with: Bryn Gay (Treatment Action Group, US). 2020 May 20.
6. *Ibid*.