

Eradicating HCV: A Global Initiative

Guideline Updates and Health Economic Drivers

Expanded HCV Serology Testing

With the advent of advanced, highly effective therapies, hepatitis C virus (HCV) infection is now largely curable.

Viral hepatitis elimination programs that include HCV are achieving progress,¹ with key reduction targets identified for 2030 (Table 1).¹⁻⁴ Data show mortality from hepatitis C has declined since 2019, associated with increased HCV treatment rates.¹

Challenging these efforts are the estimated 78.6% of chronic HCV infections that remain unidentified.¹ Chronic HCV is typically asymptomatic, so testing for evidence of infection is essential for treatment and elimination.² Left untreated, about one out of four people with HCV will progress to liver cirrhosis, with sequelae that may include liver failure, cancer, or death (Figure 1).³

The Coalition for Global Hepatitis Elimination (CGHE), a program of the Task Force for Global Health, includes multiple partners worldwide dedicated to the elimination of viral hepatitis. More information can be found at <https://www.globalhep.org/>

The U.S.^{4,5} and the WHO⁶ are among countries and organizations that have published plans and targets toward the global elimination of HCV (Table 1). Both identify increased testing as an essential element in eradication efforts.

Table 1. Global HCV elimination efforts

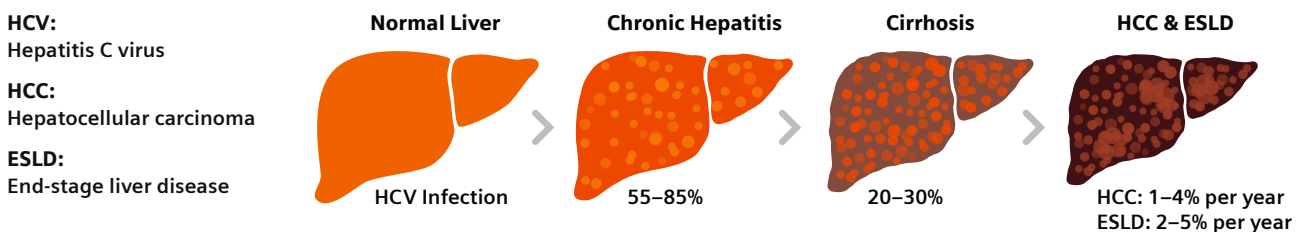
Viral Hepatitis National Strategic Plan (U.S.)^{4,5}

TARGET:
 ≥80% viral clearance in persons with chronic HCV by 2030

World Health Organization (WHO)⁶

TARGET:
 Treatment for 80% of those with chronic HCV, 90% reduction in incidence, 65% reduction in liver-related mortality by 2030

Figure 1. Disease progression in chronic viral hepatitis C



Economic drivers: Reducing healthcare spending on HCV-related liver disease



A significant financial benefit from broader HCV detection and treatment is anticipated.⁷⁻¹¹ The Congressional Budget Office (CBO), a nonpartisan agency in the U.S., estimates that increased testing and linkage to care could save Medicaid billions of dollars over 10 years.⁹

The cost of increased testing and treatment is projected to be offset by savings achieved by averting healthcare costs associated with chronic HCV liver disease.^{8,11} Similar data has been estimated for the WHO HCV elimination targets, with a predicted net economic benefit of \$22.7 billion by 2030.⁷ Indirect economic benefits projected include prevention of premature deaths and increased workforce participation among people who are successfully treated.⁷

Updated Testing Guidance: The Essential Role of Serology

Elimination efforts are expected to increase test demand, especially for HCV serology. The WHO, CDC, and U.S. Preventive Services Task Force (USPSTF) now recommend HCV serology testing for all adults, regardless of risk, with repeat testing suggested for those at elevated risk.¹⁰⁻¹² Universal testing for HCV during each pregnancy is also advocated.^{11,13,14} A two-step testing sequence for an HCV diagnosis is typically used to confirm infection in individuals with reactive serology for treatment referral (Figure 2).^{12,15-17}

Serology for HCV antibody is used as the first-line diagnostic test

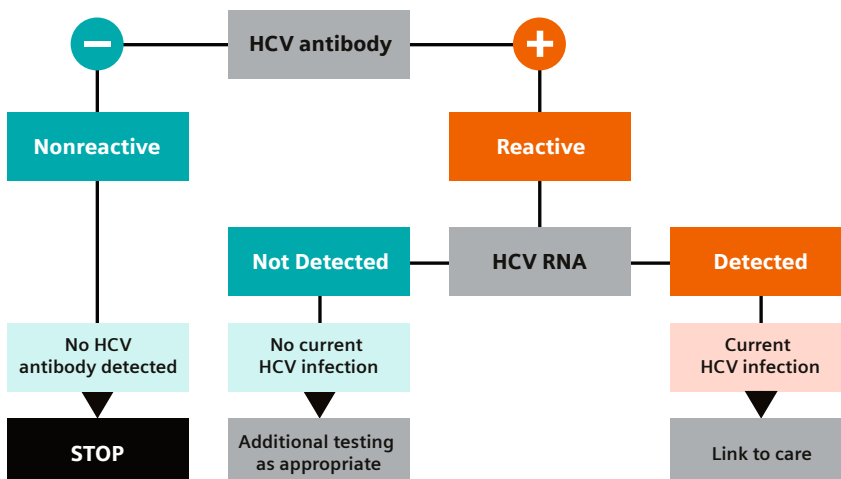
Antibodies form and persist in most people following HCV infection. Detection of HCV antibodies using sensitive and widely available lab-based automated serology assays is a common method of testing, although point-of-care assays may be useful in some settings.¹⁹ Importantly, the presence of HCV antibody alone cannot confirm current infection and the need to treat, as many individuals will successfully clear the virus (~30%, though estimates vary).^{11,17,20}

Confirming existing infection following a reactive HCV antibody test

Since HCV antibody persists in both resolved and chronic cases, sensitive molecular testing for HCV RNA is typically recommended and used to confirm infection and need to treat.^{16,17} However, in some settings, especially with limited access to molecular testing, HCV antigen may be an alternative to RNA testing to aid confirmation.¹⁶ However, a negative HCV antigen result following a reactive antibody should reflex to the more sensitive HCV RNA assay, as antigen can miss samples with lower viral loads.^{16,21}

Figure 2 shows testing guidance from EASL (European Association for the Study of the Liver)¹⁶ and the U.S. CDC-recommended algorithm^{17,18} to identify HCV infection. Specific testing algorithms can vary by region. Some may include use of a second alternate HCV antibody test prior to confirming for presence of virus.

Figure 2. CDC HCV Testing Guidance



Guidance from the 2020 EASL recommendations on HCV testing include:

- Patients with suspected acute or chronic HCV infection should be tested for anti-HCV antibodies in serum or plasma as first-line diagnostic test.
- HCV RNA should be determined in serum or plasma by a sensitive molecular method.
- If anti-HCV antibodies are detected, the presence of HCV RNA by molecular assay or HCV core antigen should be determined.
- HCV core antigen assays are less sensitive than HCV RNA assays for detection of viremia.

Sample Collection Strategies to Improve Treatment Referral Rates

While confirmatory testing with RNA is recommended, a significant percent of patients with a reactive antibody test can be lost to follow-up, rendering testing incomplete.²² To improve confirmation and linkage to care, the CDC now recommends a single-visit patient sampling operational strategy, facilitating immediate RNA confirmation for antibody-reactive samples.²² Approaches include either a single-tube collection used for both serology and RNA, or collection of two separate tubes at the initial visit for antibody and confirmatory testing.



Selection of a one- vs. two-tube collection procedure may be impacted by the analyzer used for the HCV serology testing. CDC data shows HCV RNA carryover can occur when using an immunoassay platform with washable probes, meaning cross-contamination could cause erroneous results in a negative sample.²³ In contrast, no carryover was observed for analyzers using disposable tips. The authors caution that a single-tube sampling strategy is supported if the lab is using a platform with disposable tips vs. washable probes.²³ Other data substantiates the potential for HCV RNA carryover when using an analyzer employing washable probes for antibody testing.²⁴ A two-tube strategy might be more appropriate when using an analyzer lacking disposable tips.

Data Shows Good Performance of Lab-based Automated HCV Serology Assays

Multiple studies have investigated the comparative clinical performance of commercially available, lab-based automated HCV assays. Published peer-reviewed studies investigating the clinical concordance of Atellica aHCV assay from Siemens Healthineers to HCV antibody assays from Roche, Abbott, and Diasorin indicate good agreement and comparable diagnostic performance, although modest differences have been observed (Tables 2a and 2b).²⁵⁻²⁸

Table 2a. Comparative performance of anti-HCV antibody assays (Keong et al. study).²⁵

HCV Antibody Assay	Reported Sensitivity	Reported PPV
Atellica (aHCV)	97.5%	98.1%
ALINITY (Anti-HCV)	99.4%	98.2%
ELECSYS (Anti-HCV II)	86.5%	89.8%

Table 2b. Comparative performance of anti-HCV antibody assays (Arcot et al. study*[†]).²⁶

HCV Antibody Assay Manufacturer	Reported Sensitivity	Reported Specificity	Reported NPV	Reported PPV
Siemens Healthineers (aHCV)	100%	99.9%	100%	92.9%
Abbott Diagnostics (Anti-HCV)	100%	99.8%	100%	81.2%

Correlation of ADVIA Centaur and Atellica IM aHCV assays

While some published comparison studies used the ADVIA Centaur platform vs. Atellica IM Analyzer, the aHCV assay shares an identical design and reagents on both platforms. Data show highly comparable performance for aHCV,²⁹ indicating findings should be generalizable regardless of which platform was used (Table 3).

Table 3. Sensitivity & specificity correlations

Analyzer (across two lots)	Relative Sensitivity	Relative Specificity
Atellica IM	100%	100%
ADVIA Centaur XP	100%	100%

Conclusion

HCV testing is now broadly recommended for all adults independent of risk, as well as testing at each pregnancy. Availability of high-performing, automated HCV antibody assays are essential to meet expanding demand for HCV serology. Increasing the awareness of ordering clinicians to the updated testing recommendations is vital to expand the testing population and achieve meaningful progress toward elimination.

Talk to your Siemens Healthineers representative to discover how Atellica Solution can support your testing demands. Learn how Atellica Solution can provide optimized process efficiencies while delivering clinical confidence in test results across the ID assay menu.

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*Atellica aHCV assay is not available for blood screening in the U.S.

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Hemogenomics Pvt. Ltd. is a distributor for Siemens Healthineers.

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