



Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the United States:

Debrief of meeting convened by the Association of Public Health Laboratories (APHL)

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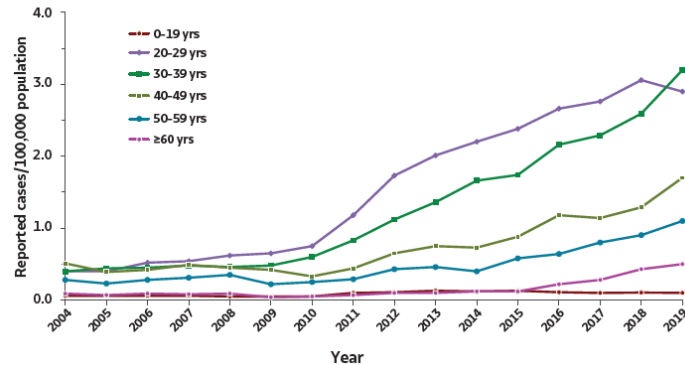
2022 Advancing HIV, STI, and Viral Hepatitis Testing Conference, March 29, 2022

Hepatitis C is a Public Health Crisis in the United States

Acute Infections

- Rate of reported acute hepatitis C cases **increased 333%** during 2010–2019
- Rates are highest among 20–39 year-olds

Figure 3.4. Rates of reported acute hepatitis C virus infection, by age group — United States, 2004–2019

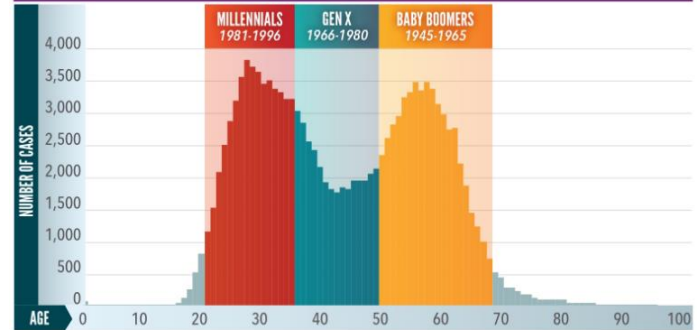


Source: [Hepatitis C Surveillance in the United States for 2019 | CDC](#)

Chronic Infections

- Estimated **2.4 million** people living with hepatitis C
- About 40% of people with hepatitis C are unaware of their infection

New Reports of Chronic Hepatitis C High in Multiple Generations

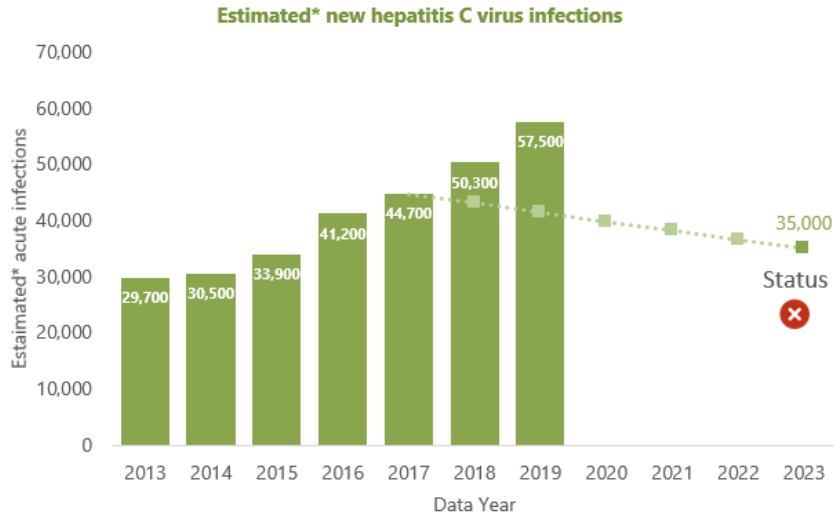


SOURCE: National Notifiable Diseases Surveillance System, 2018

Sources: Hofmeister et al, Hepatology, 2018; Patel et al, CID, 2019; Ryerson et al, MMWR, 2020.

U.S. 2025 Goals: Hepatitis C Incidence and Mortality

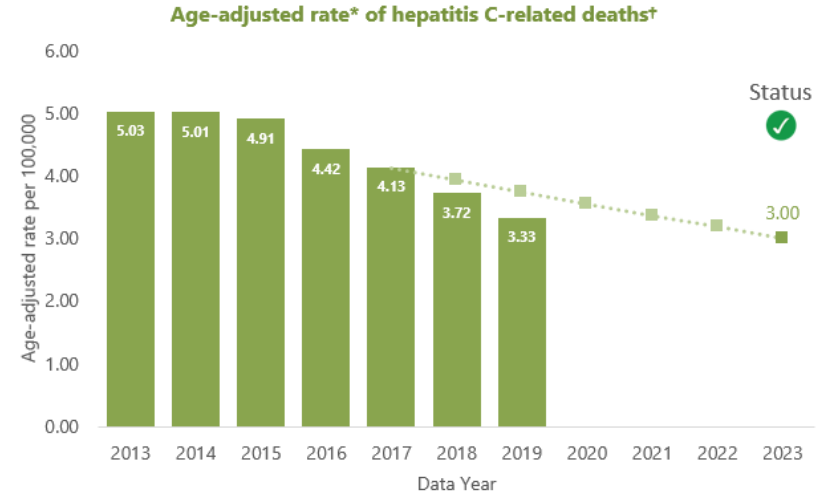
Reduce new infections by $\geq 20\%$



Source: CDC, National Notifiable Diseases Surveillance System

*The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases by a factor that adjusted for under-ascertainment and under-reporting (1-2).

Reduce related deaths by $\geq 25\%$



Source: CDC, National Vital Statistics System (1)

*Rates are per 100,000 and age adjusted to the 2000 U.S. standard population.

†Cause of death is defined as the underlying cause of death or one of the multiple causes of death and is based on the International Classification of Disease, 10th Revision (ICD-10) codes B17.1 or B18.2 (2).

Opportunities to Increase Hepatitis C Virus (HCV) Testing

- CDC's updated HCV screening recommendations (April 2020)



Source: Schillie et al, MMWR, 2020

- **FDA re-classification of HCV Diagnostics from Class III to II**
 - Incentive to bring new technology to the U.S. market
 - Tests affected
 - Qualitative tests for HCV antibody
 - Qualitative and quantitative nucleic acid-based HCV tests (diagnostic and viral load)
 - Nucleic acid-based HCV genotyping tests

Challenges to Increasing HCV Testing in the United States

- Populations affected by recommendations vary widely

Population	Estimated Population Size	Estimated HCV Positivity
Adults (\geq 18 years old)	255,000,000 ¹ (2019)	1.7% ⁴
Pregnant Persons	3,790,000 births ² (2018)	3.8 per 1,000 live births ⁵
People Who Inject Drugs	6,612,488 ³ (2011)	54.2% ⁴

Sources: 1. Census.gov; 2. <https://www.cdc.gov/nchs/fastats/births.htm>; 3. Lansky et al, *PLoS One*, 2014; 4. Schillie et al, *MMWR*, 2020; 5. Schillie et al, *Am J Prev Med*, 2018.

- Service delivery settings vary widely

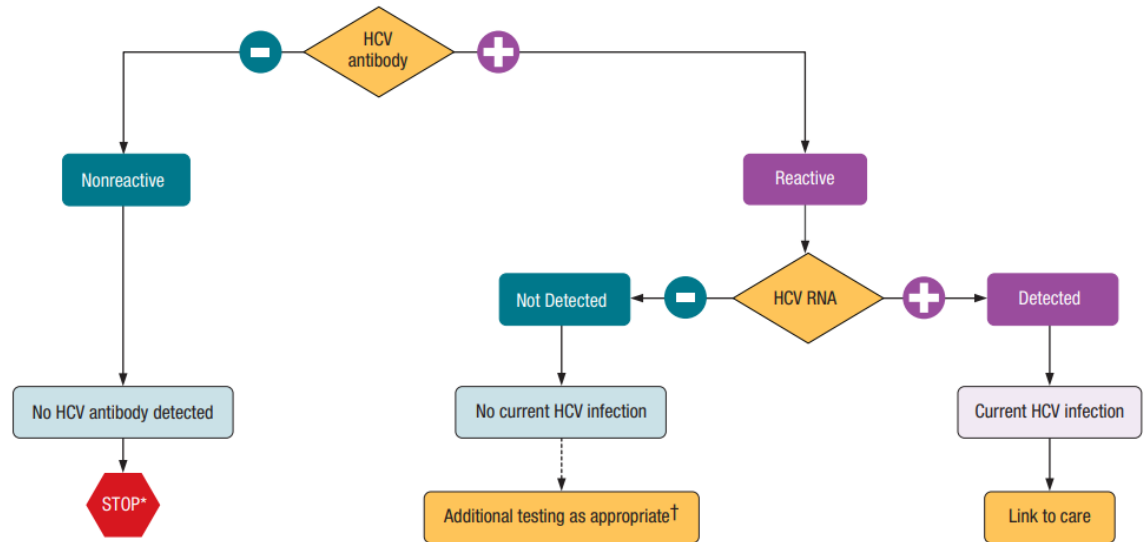
- Primary care settings
 - Type of care, client volume, engagement in care, insurance coverage
- Settings serving PWID
 - SSPs, SUD treatment providers, justice-involved settings, emergency departments

Challenges to Increasing HCV Testing in the United States (2)

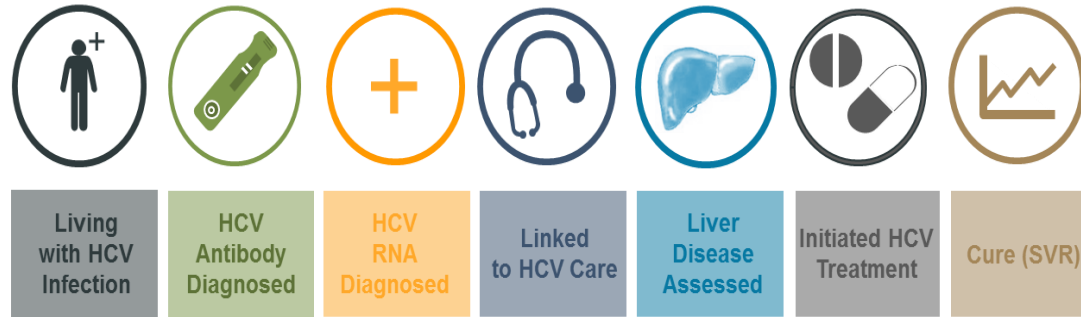
- FDA-approved tests for the diagnosis of HCV infection

- Anti-HCV
- HCV RNA

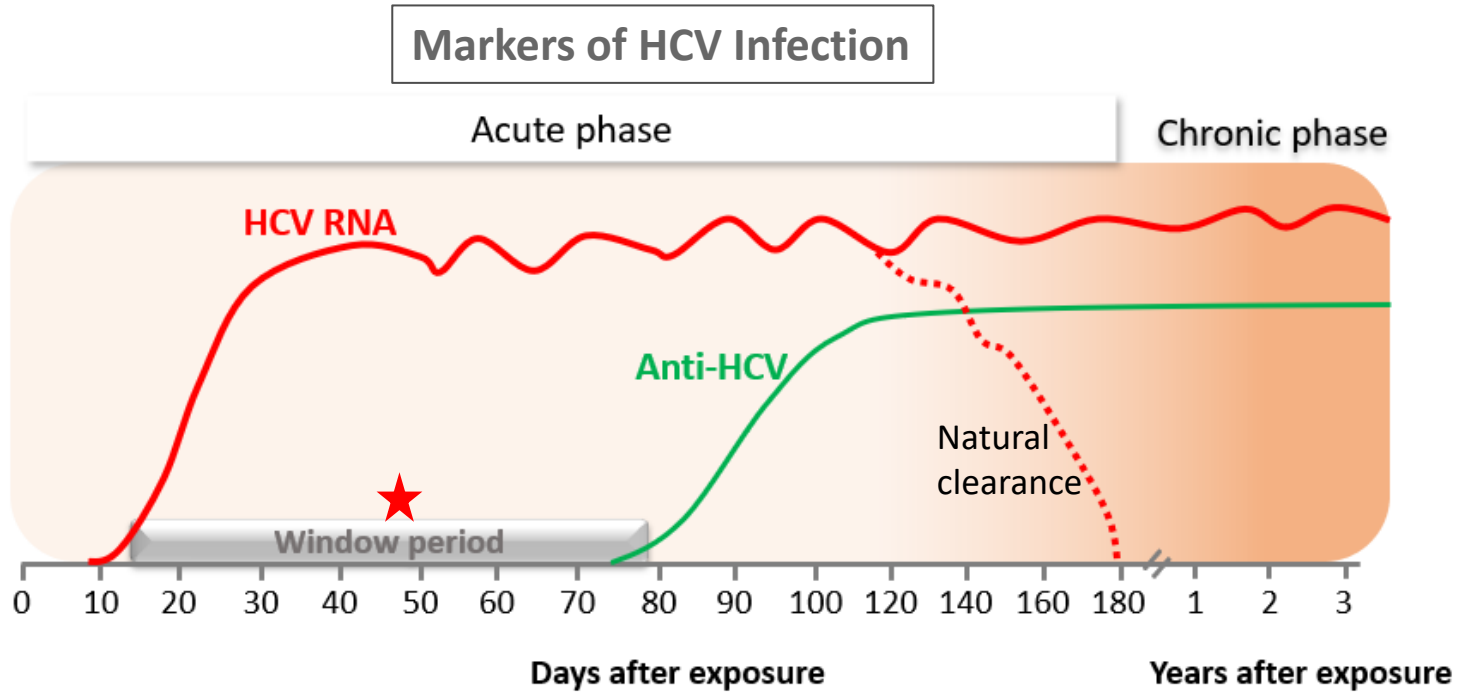
- Two-step HCV testing algorithm



Two-Step Diagnostic Process: Bottleneck in HCV Cure Cascade



Two-Step Diagnostic Process: Missed Opportunities to Diagnose Early HCV Infection



HCV Core Antigen

- Detectable within 1–2 weeks after exposure to HCV
- Sample types
 - Serum, plasma, dried blood spots
- May become undetectable when HCV RNA <2000 IU/ml

Hepatitis C Virus Diagnostic Algorithms

Strategies	Visit #1		Visit #2		Visit #3
	Point of Care	Laboratory	Point of Care	Laboratory	Point of Care
Currently available <u>inside and outside</u> the United States	Venipuncture	→ Ab	Venipuncture	RNA	Results
	Venipuncture or DBS (HC)	→ Ab (+ reflex to RNA)	Results		
	RDT (Ab) + Venipuncture or DBS (HC)	→ RNA	Results		
Currently available <u>outside</u> the United States	RDT (Ab) + Venipuncture or DBS	→ cAg	Results		
	RDT (Ab) + RDT (RNA) + Results				
	RDT (RNA) + Results				
Not currently available	RDT (cAg) + Results				

Sources: Adapted from Bajis, *J Infect*, 2020; and FIND presentation at EASL, 2019.

Ab = anti-HCV; RNA = HCV RNA; cAg = HCV core antigen; DBS = dried blood spot; HC = collected in health care setting; RDT = rapid diagnostic test.

Priorities for Advancing HCV Diagnostics in the United States

■ Indications

- Determine current infection, response to treatment

■ Characteristics

- Accurate, simple, rapid, affordable, single-step

■ Settings

- Clinical, outreach, home

■ Specimen collection

- Venipuncture, fingerstick, dried blood spot, oral fluid

Meeting Summary: Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the U.S. (Oct 19-20, 2021)

Convened by the Association of Public Health Laboratories (APHL)

Overview

- **Purpose**

- Identify and prioritize diagnostic approaches needed to advance the diagnosis and treatment of **current** HCV infection in the **US** over the next **5 years**

- **Objectives**

- Foster **inclusive and transparent engagement between sectors** engaged in public health efforts to eliminate HCV.
- Identify and prioritize diagnostic tools needed, as well as opportunities and challenges by **key questions**
- Summarize the prioritized needs, opportunities, and challenges in a **meeting report**

- **Participants**

- Federal agencies, public health agencies, laboratorians, academics, clinicians, national & community-based organizations, and diagnostic manufacturers

Opportunities for Input

- **Facilitated discussion for each of 4 Key Questions**
 - 75 minutes per Key Question
 - Presentation & panelist remarks (25 minutes)
 - Invited comments (10 minutes)
 - Discussion (40 minutes)
 - Summary of diagnostic tools needed, opportunities, challenges, recommendations
- **Post meeting**
 - APHL received written comments up to 2 weeks after the meeting
- **Summary Report**
 - Draft report to be posted for public comment
 - Final report issued after public comment

Key Questions

- 1) What HCV diagnostic tools are needed to optimize diagnosis of current HCV infection in moderate to **high volume laboratories** performing **moderate or high complexity** testing?
 - **Focus settings:** Large commercial, hospital, and public health laboratories
 - **Focus diagnostics:** HCV RNA, HCV core antigen, integrated testing
- 2) What HCV Diagnostic Tools are needed to advance diagnosis of current HCV infection in **low volume settings** performing **moderate complexity** laboratory testing or CLIA-waived testing in clinical settings?
 - **Focus settings:** Settings facilitating rapid diagnosis and/or same day HCV test-and-treat
 - **Focus diagnostics:** HCV RNA, HCV core antigen

Key Questions

- 3) What HCV Diagnostic tools are needed to advance diagnosis of current HCV infection in **outreach** settings and **self-testing**?
 - **Focus settings:** Non-clinical sites, self testing in non-clinical sites
 - **Focus diagnostics:** HCV antibody (alone or combined with other pathogens), HCV RNA, HCV core antigen

- 4) What other tools are needed to support **same-day diagnosis and treatment** of current HCV infection?
 - **Focus settings:** Settings facilitating same-day HCV test-and-treat
 - **Focus diagnostics:** HBsAg, liver cirrhosis, hepatocellular carcinoma, other?

Recommendations (Preliminary)

- **Development/ Approval of POC RNA Test is Highest Priority**
 - Diagnosis and therapeutic monitoring
 - Time to result, cost, CLIA waiver are all key considerations
- **Development/ Approval of HCV Core Antigen Test**
 - Detection threshold is a key consideration
 - Diagnosis (stand-alone vs. combination antigen/antibody)
- **Improve existing laboratory-based testing**
 - Ensure auto-reflex testing of all positive anti-HCV specimens to HCV RNA
 - Encourage submission of diagnostic claims for HCV RNA assays
 - Expand menu of specimen types and kit sizes
- **Revise existing HCV diagnostic algorithm to advance detection of current infection**
 - Consider role(s) for stand-alone HCV RNA testing as well as HCV core antigen testing

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■ Meeting Participants

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- Public health agencies
- Laboratorians
- Academics
- Clinicians
- National & community-based organizations
- Diagnostic manufacturers

■ Webster Group

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