

11/19/2025

HEPATITIS C REINFECTION

Heather Wingate, MPH (HepTAC | TN)

Paula Shoup, MS (TN)

Kyle Nowotny, MPH (FL)



AGENDA

01.

Introduction

02.

Clearance
Cascade

03.

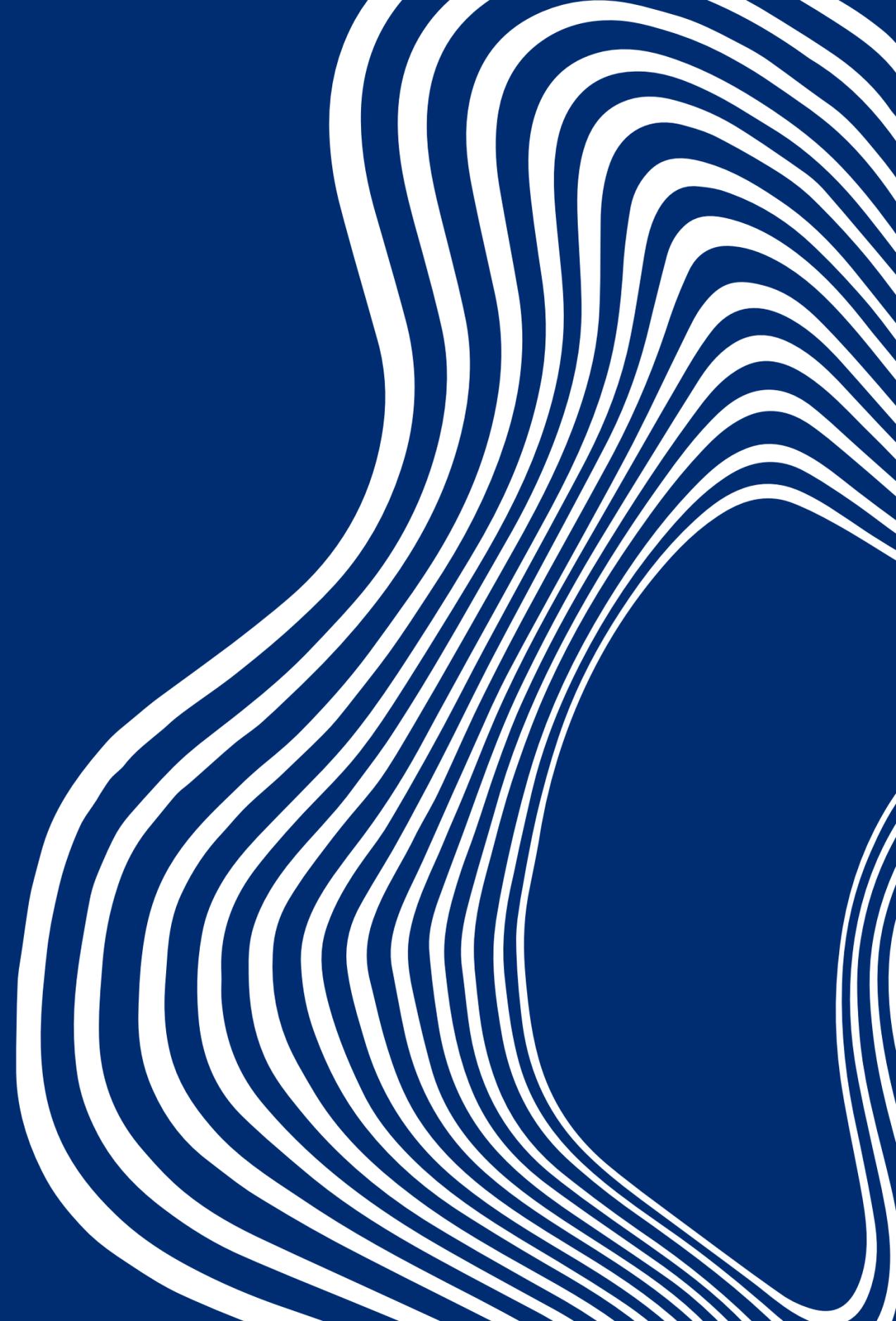
Reinfection
Surveillance

04.

Reinfection
Navigation

05.

Conclusion





01.

INTRODUCTION



HCV REINFECTION

Hepatitis C virus (HCV) reinfection refers to becoming infected with HCV again after having previously cleared the virus, either through successful treatment (such as direct-acting antivirals, DAAs) or through spontaneous clearance by the immune system.

KEY POINTS



Different from treatment failure:

- Treatment failure means the original infection was never fully cleared and returns shortly after treatment.
- Reinfection means the person was cured, then exposed again and acquired a new HCV infection.

Who is at higher risk?

Reinfection is most common among people who continue to have exposure risks, such as:

- People who inject drugs and share equipment
- People in settings with high HCV prevalence (e.g., some correctional facilities)

KEY POINTS



Reinfection rates vary:

- Lower among people who stop high-risk behaviors
- Higher (up to 5–10 infections per 100 person-years) among those with ongoing injection drug use

Can you be treated again?

- Yes—HCV reinfection can still be cured with antiviral treatment, but public health efforts increasingly focus on prevention, including harm reduction, education, and linkage to care.

Why it matters in public health:

- As HCV treatment expands, reinfection is a major consideration when planning elimination strategies—especially in high-risk populations.
 - S.1941 - Cure Hepatitis C Act of 2025

Development of a Standardized, Laboratory Result–Based Hepatitis C Virus Clearance Cascade for Public Health Jurisdictions

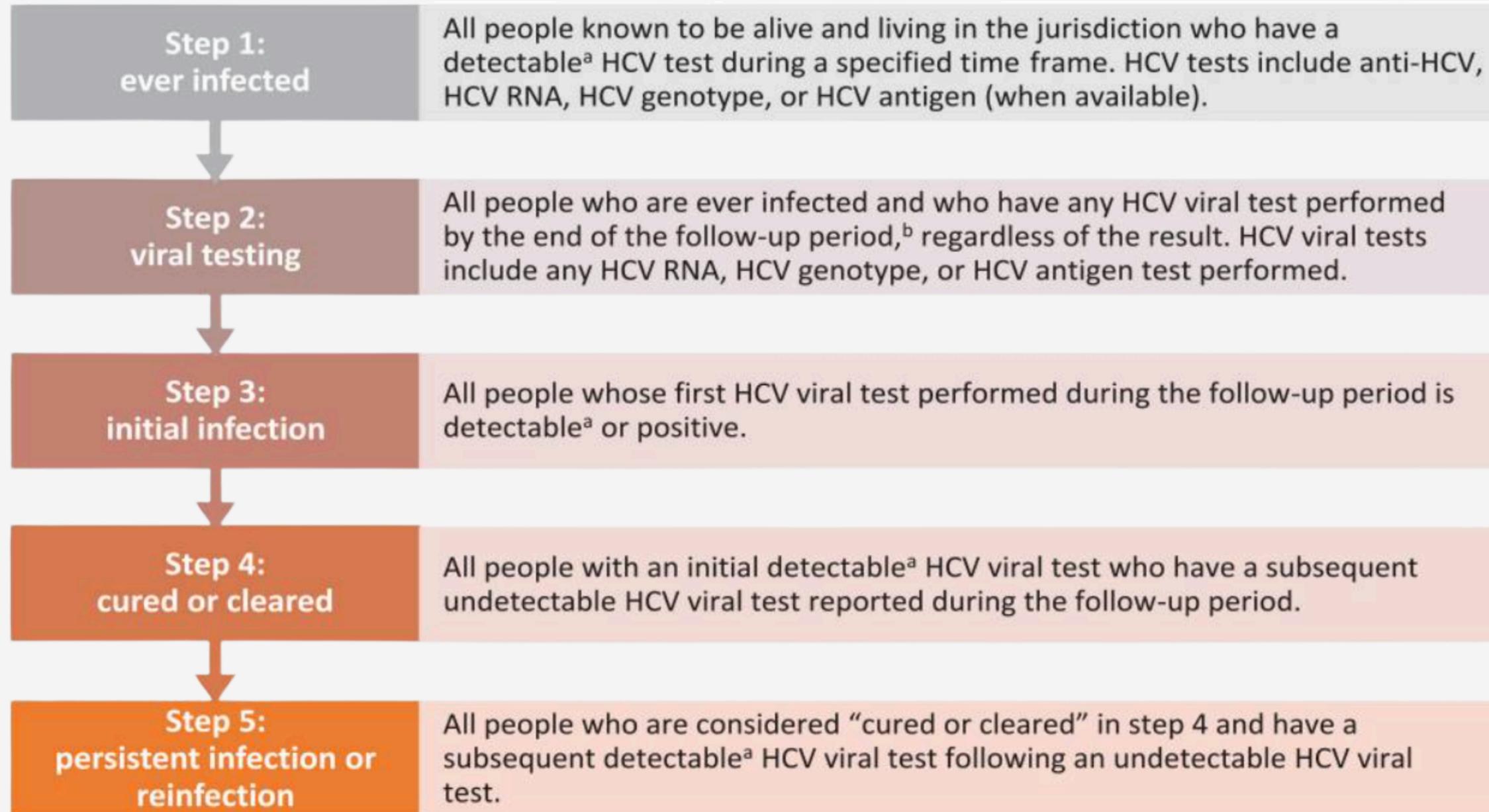
Martha P. Montgomery, MD, MHS¹ ; Lindsey Sizemore, MPH² ; Heather Wingate, MPH² ; William W. Thompson, PhD¹; Eyasu Teshale, MD¹; Ade Osinubi, MS¹; Mona Doshani, MD¹; Noele Nelson, MD, PhD, MPH¹; Neil Gupta, MD, MPH¹; and Carolyn Wester, MD, MPH¹

Purpose

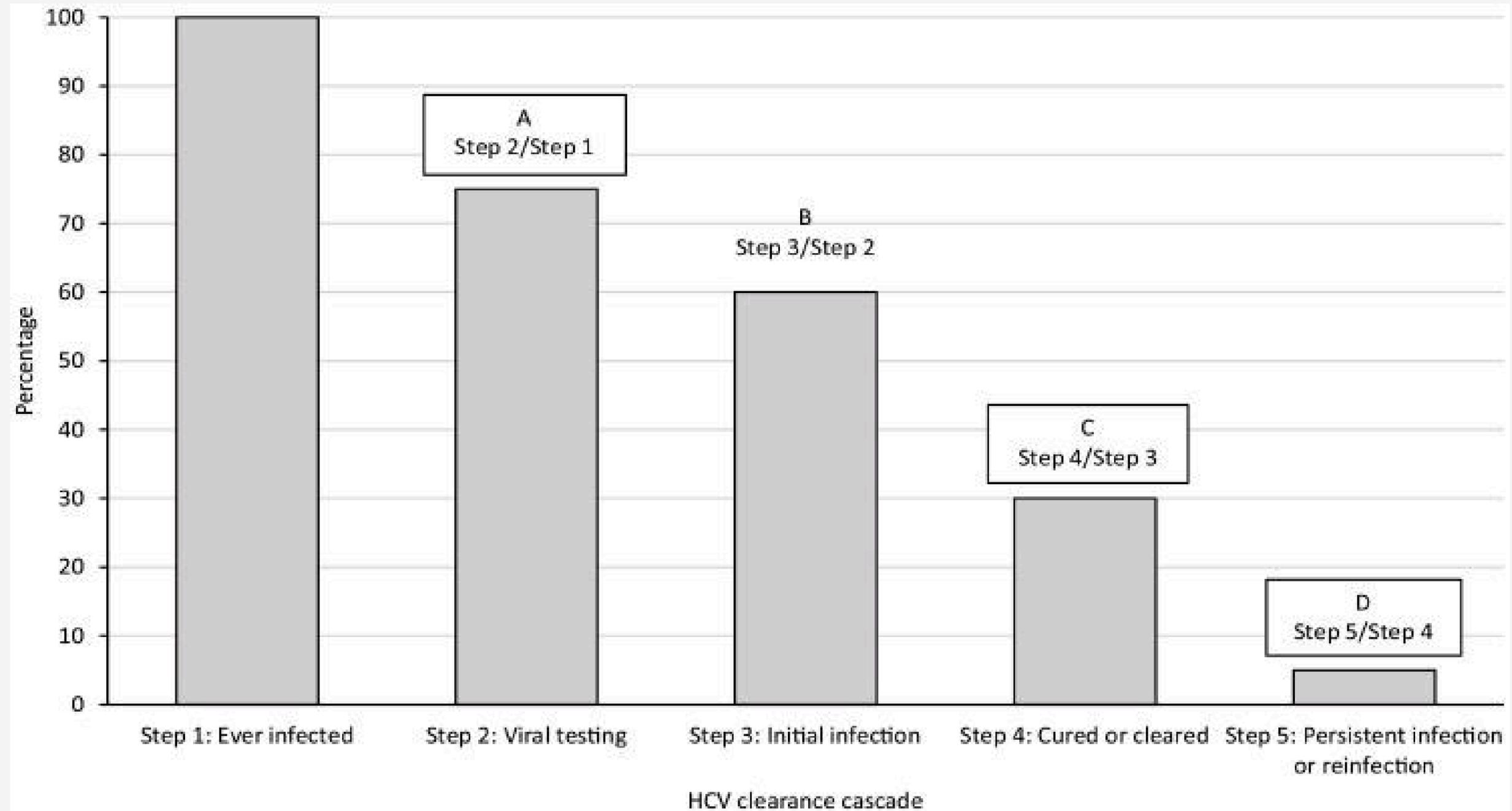
The authors set out to develop a standardized, laboratory result–based “clearance cascade” for HCV that public-health jurisdictions can use. The goal is to help track progress toward HCV elimination, identify disparities in testing/treatment, and monitor outcomes like clearance and reinfection.



CASCADE



CASCADE



IMPLEMENTATION REQUIREMENTS & CONSIDERATIONS

- Receive person-level longitudinal laboratory data from multiple sources (public health labs, commercial labs, clinical systems) so people can be tracked across systems
- Deduplicate and link lab reports so that duplicate results from the same person are not counted as separate individuals
- Have reportable lab results including reactive HCV antibody, detectable/undetectable HCV RNA (and if available HCV core antigen)
 - CDC-RFA-PS21-2103
- Optionally, include data elements that allow identification of disparities (e.g., by race/ethnicity, geography, setting) so inequities in testing or treatment access can be addressed

VALUE & USE OF THE CASCADE

- This standardized cascade enables benchmarking: jurisdictions can compare how many people progress through each step and identify bottlenecks
- Helps monitor for reinfection or persistent infection after clearance
- Supports data-to-care efforts: for example, if someone has a positive viral test but no clearance test after an expected period, public health can intervene
- Allows tracking of progress toward the U.S. goal of HCV elimination

LIMITATIONS & CHALLENGES

- Many jurisdictions may not have complete lab linkage across systems, which limits the ability to build full cascades.
- Treatment information may not be available or fully captured in surveillance systems. The cascade uses lab data rather than detailed treatment data.
- The method relies on frequent, accurate reporting of lab results; jurisdictions might miss people who are tested, but results are not reported or linked.
- Cannot differentiate between persistent infection and reinfection
- Requires routine hepatitis C testing
- Misses subsequent RNA-positives if first RNA is negative

CSTE REINFECTION



Reinfection is suggested when:

- A person with previously confirmed chronic HCV has two sequential negative viral detection tests (indicating treatment and sustained virologic response), followed later by a new positive viral detection test.
- These two negative tests should be at least 3 months apart, though this interval may change as treatment guidelines evolve.
- Reinfection can also be supported by:
 - A new genotype detected after the person previously cleared a different genotype.
- Step 3 of the cascade only include first RNA collected

Assessing SVR at 4 Weeks After Hep C Treatment Proves as Predictive as SVR12

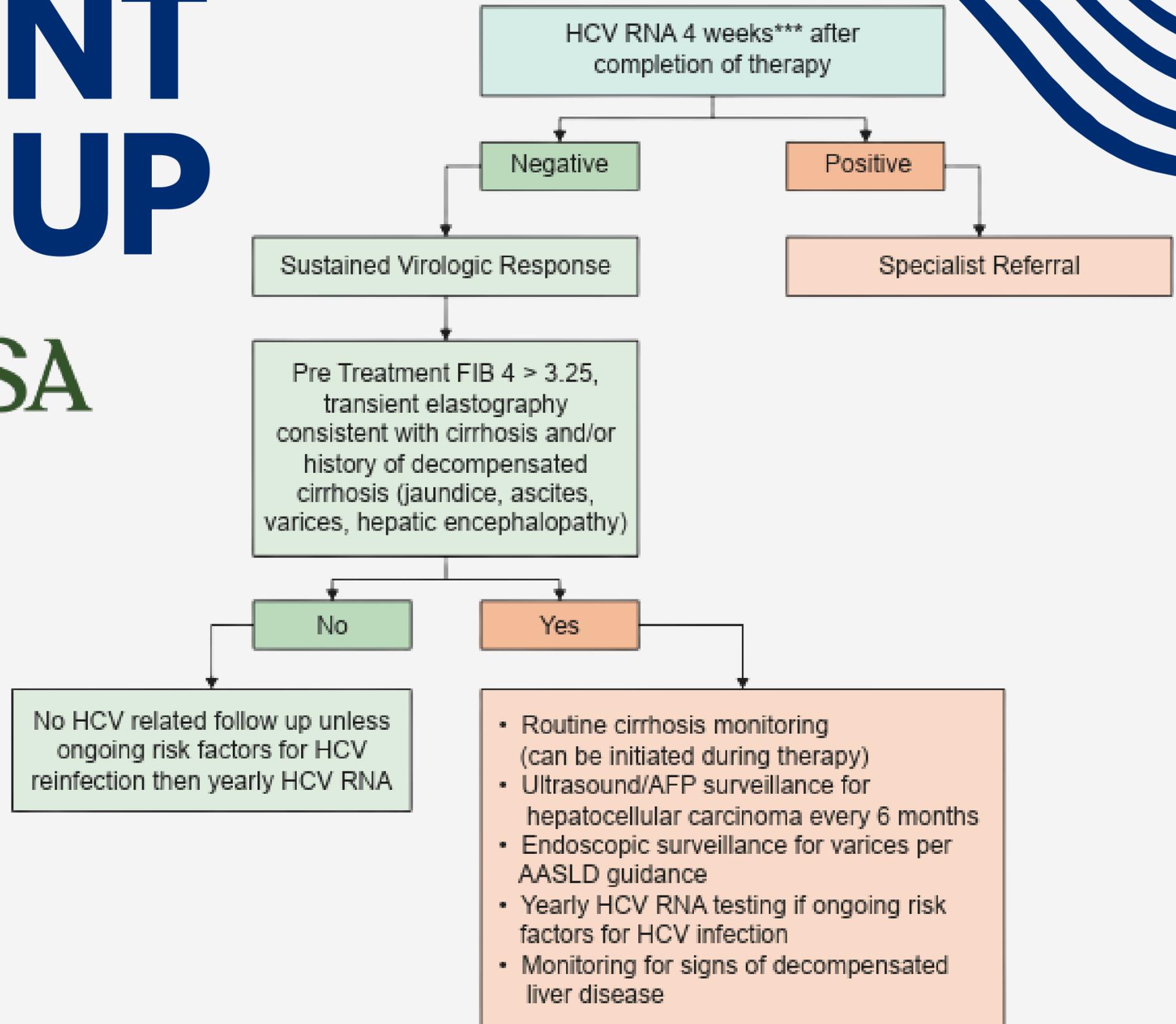
— The faster cure assessment can help clinicians determine who needs re-treatment sooner

by [Terrence Rudd](#), Staff Writer, MedPage Today

November 9, 2025 · 3 min read

- SVR measured **4 weeks after HCV treatment (SVR4)** is as predictive of cure as the standard **12-week measure (SVR12)**.
- In the POLARIS trials, **99.2%** of patients who achieved SVR4 also achieved SVR12 (1,001 of 1,009).
- SVR4 had a **100% negative predictive value** — no one who failed SVR4 achieved SVR12.
- SVR4 showed **100% sensitivity** and **74.2% specificity** for predicting SVR12.
- Only **26%** of patients who relapsed had achieved SVR4; most relapses occurred in:
 - Men (74%)
 - Genotype 1 infection (61%)
 - People with prior HCV treatment (52%)
- Predictive accuracy of SVR4 held for both 8-week and 12-week treatment regimens.
- Using SVR4 may **reduce loss to follow-up**, especially in high-risk or hard-to-reach populations.
- Experts recommend continued surveillance to catch relapse or reinfection early.
- AASLD/IDSA's 2025 HCV Point-of-Care Test and Treat Algorithm accepts SVR4 as a cure marker for people without cirrhosis and without prior DAA therapy.

TREATMENT FOLLOW UP





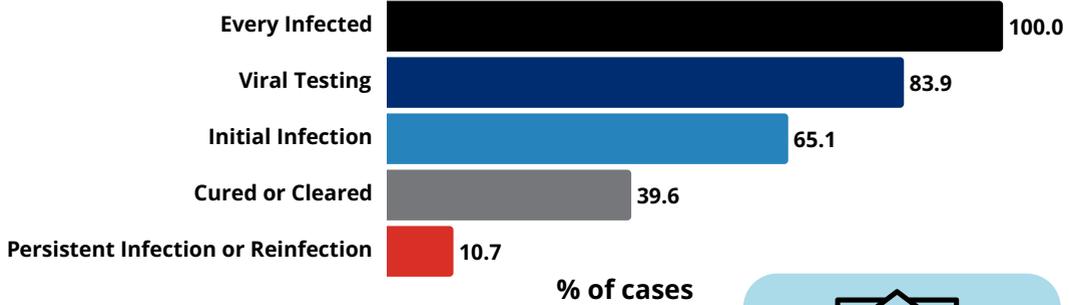
02.

CLEARANCE CASCADE

Hepatitis C Clearance Cascade

Surveillance

Hepatitis C Clearance Cascade, Tennessee, 2020-2024



From 2020 to 2024, 83.9% of exposed individuals were virally tested. Upon testing, 65.1% of exposed individuals had an initial infection but 39.6% had cured or cleared the infection after initial infection. Of those individuals, 10.7% had persistent infection or were reinfected.

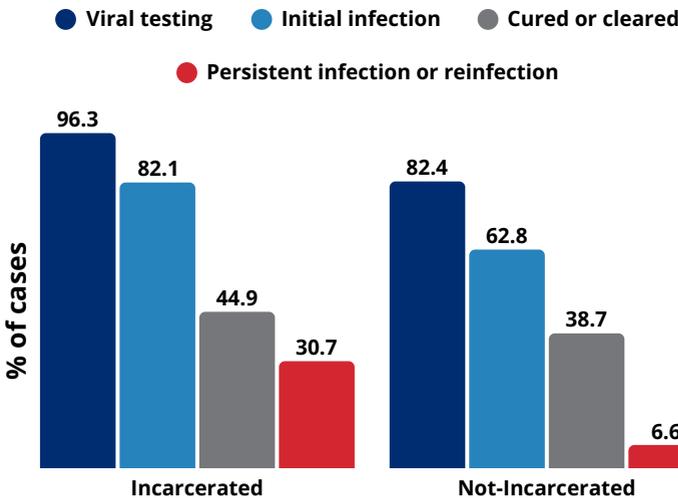


Incarcerated individuals were 4.7x more likely to have a persistent infection or reinfection of Hepatitis C

When compared to non-incarcerated individuals, those incarcerated had higher percentages of initial infection and reinfection. However, the percentage of cured or cleared infection was higher in those incarcerated than in the non-incarcerated population.

Incarceration

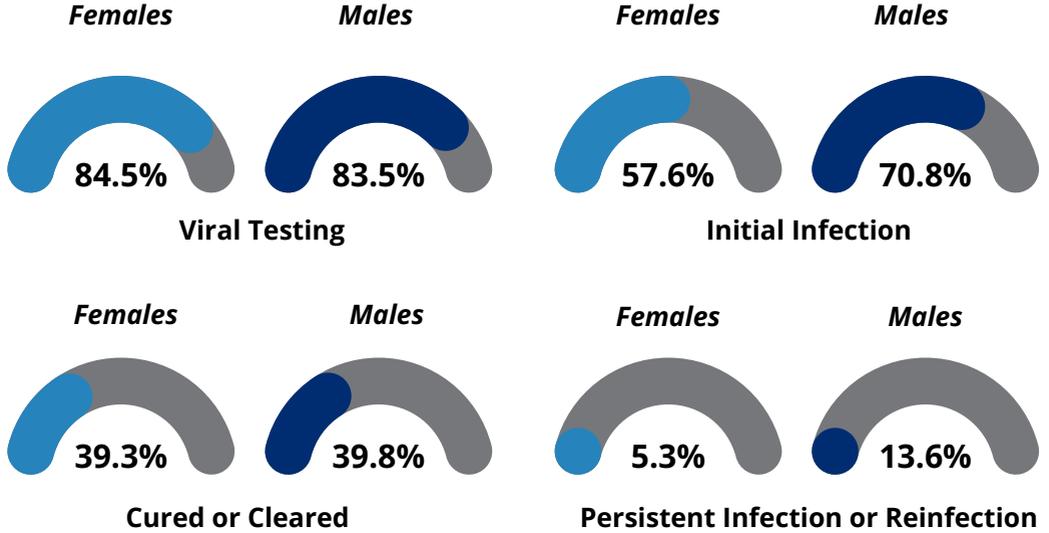
Hepatitis C Clearance Cascade, Incarcerated vs Non-Incarcerated, Tennessee, 2020-2024



Hepatitis C Clearance Cascade

Sex

Hepatitis C Clearance Cascade by Sex, Tennessee, 2020-2024



From 2020 to 2024, females were more likely to receive a viral test than males. However, males had higher percentages of initial infections and persistent infections or reinfections. Additionally, the rate of being cured or cleared of infection was equal between males and females.



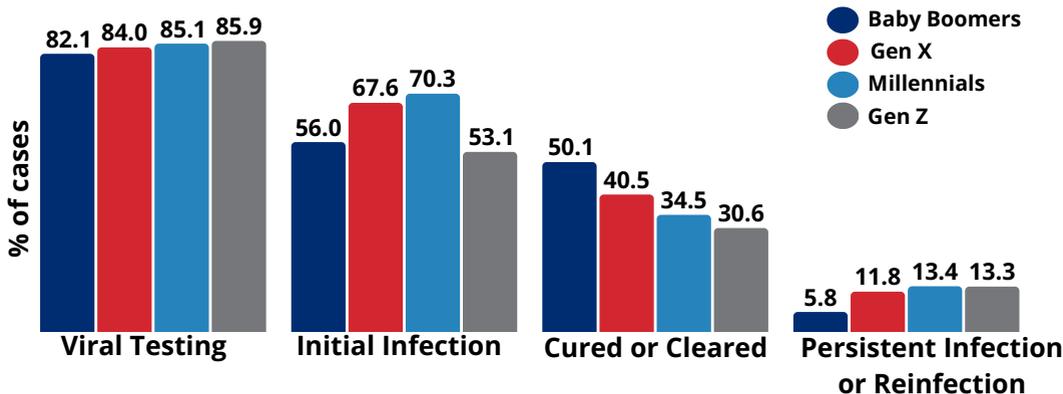
Compared to females, males were 2.6x more likely to have a persistent infection or reinfection of HCV.



Hepatitis C Clearance Cascade

Age

Hepatitis C Clearance Cascade by Generation, Tennessee, 2020-2024



From 2020 to 2024, the Baby Boomer generation had a higher percentage of being cleared or cured and a lower percentage of having a persistent infection or reinfection compared to younger generations.

Hepatitis C Clearance Cascade by Reproductive Age, Tennessee, 2020-2024



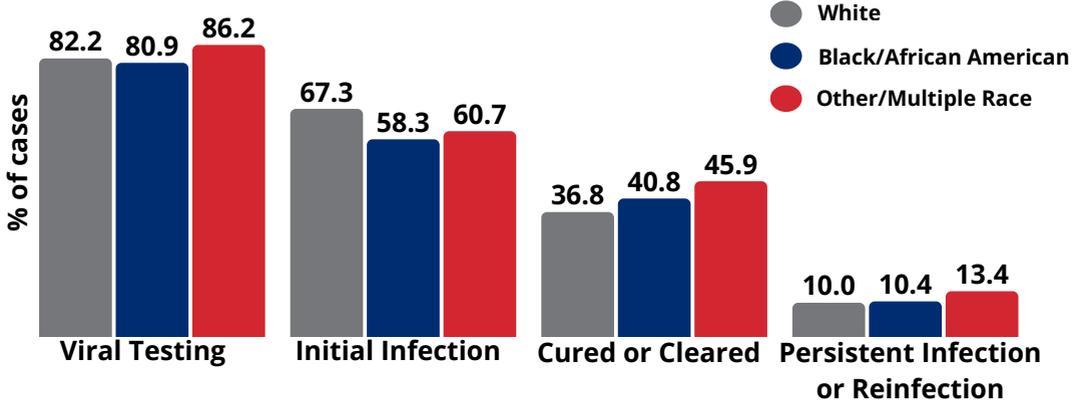
Those of reproductive age were 1.3x less likely to be cured or cleared of their HCV infection.

	Yes	No
Viral Testing	84.9%	82.4%
Initial Infection	69.2%	59.1%
Cured or Cleared	35.5%	46.7%
Persistent Infection or Reinfection	13.2%	7.5%

Hepatitis C Clearance Cascade

Race

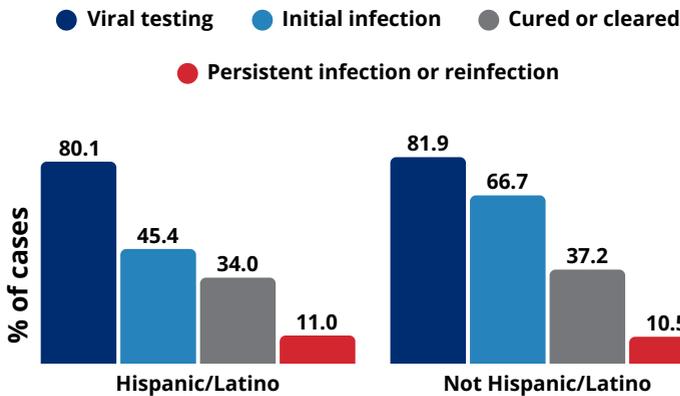
Hepatitis C Clearance Cascade by Race, Tennessee, 2020-2024



From 2020 to 2024, Other/multiple races had the highest percentage of viral testing, followed by Whites, then Black/African Americans. However, Whites had the lowest percentage of having cured or cleared their HCV infection when compared to other races.

Ethnicity

Hepatitis C Clearance Cascade, Hispanic/Latino vs Non-Hispanic/Latino, Tennessee, 2020-2024



Hispanic/Latinos were 1.5x less likely to have an initial infection after viral testing.

Not Hispanic/Latinos experienced higher percentages of initial infection, and being cured or cleared of infection compared to Hispanic/Latinos. Percentages for viral testing and persistent infection or reinfection were similar between the two groups.



03.

REINFECTION SURVEILLANCE

TRACKING

Reinfection Local Definition:



- Local condition created in 2021
- Track quarterly

Reinfection Demographics:

- 2021–2025: 750 Cases
- Male: 79%
- Race: 81% White, 8% Black, 11% Other
- Average age: 44
- Average time to reinfection: 8 months
- Incarcerated at time of reinfection: 54%
- 44% last RNA result was negative



04.

REINFECTION NAVIGATION

NAVIGATION

- Reinfections initially assigned to a Viral Hepatitis Case Navigator for navigation
- Investigation included risk factors, previous treatment regimen, treatment completion, and referral to services
- 141 Cases navigated

Where we went wrong:

Asked the navigator to classify reinfection **OR** treatment failure

Suspected Condition

[Collapse Subsections](#)

Evaluation

Provide rationale for selection in General Comments section of Case Info tab.

Select suspected reinfection or treatment failure based on **Suspected Reinfection**
assessment and medical records.

Treatment Information

[Back to top](#)

[Collapse Subsections](#)

Treatment Information

Please document number of contact attempts in the General Comments section within the Case Info tab.

Request medical records from provider of most recent RNA negative result:

HCV Treatment Regimen (if applicable):

Was treatment completed?:

Suspected Condition

[Back to top](#)

[Collapse Subsections](#)

Evaluation

Provide rationale for selection in General Comments section of Case Info tab.

Select suspected reinfection or treatment failure based on assessment and medical records.:

Contact With A Case

[Back to top](#)

[Collapse Subsections](#)

Contact with a Case

The time period of interest differs for Acute Hepatitis B and C. For Hepatitis B, the time period is 6 weeks - 6 months prior to onset of symptoms. For Hepatitis C, the time period is 2 weeks - 6 months prior to onset of symptoms.

During the 2-6 weeks prior to onset, was patient a contact of a case?:

Types of Contact

Sexual And Drug Exposures

[Back to top](#)

[Collapse Subsections](#)

Sexual Exposures in Prior 6 Months

What is the sexual preference of the patient:

Note: If 0 is selected on the form, enter 0; if 1 is selected on the form, enter 1; if 2-5 is selected on the form, enter 2; if >5 is selected on the form, enter 6.

During the time period prior to onset, did the patient:

In the 2-6 weeks prior to onset, how many male sex partners did the patient have:

In the 2-6 weeks prior to onset, how many female sex partners did the patient have:

Was the subject ever treated for a sexually transmitted disease?:

Needle Sharing Exposures in Prior 6 Months

Number of needle sharing partners:

Example reinfection investigation questionnaire





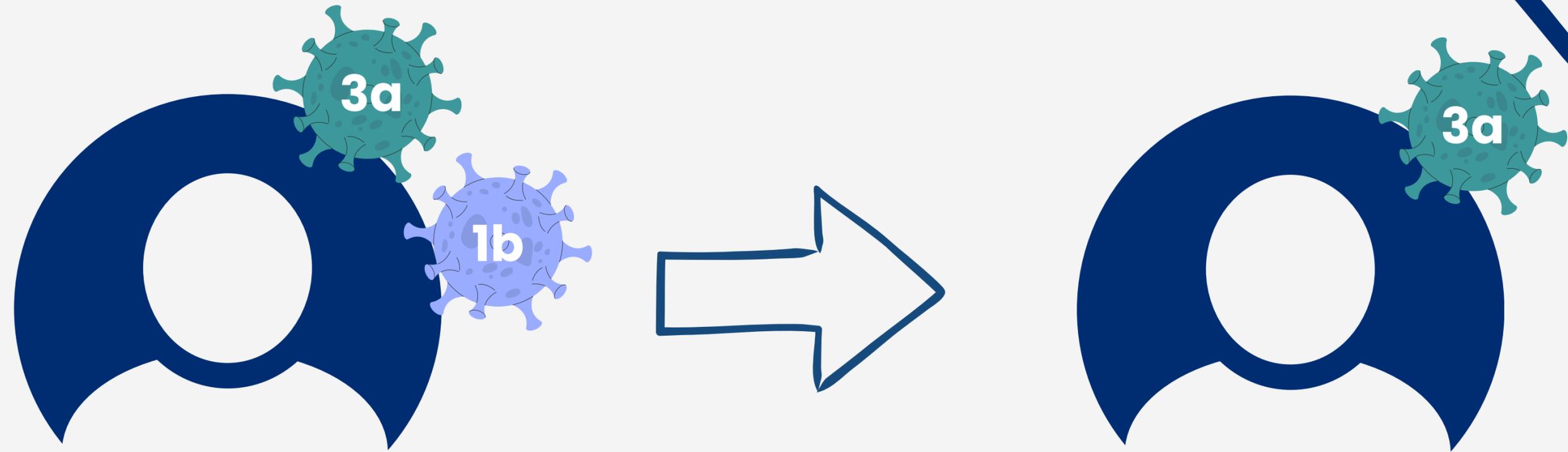
TREATMENT FAILURE VS REINFECTION

Clues in making the distinction:

- Direction of trending viral load
- Change in genotype
- Antacids taken during treatment
- Ongoing risk factors

Does the distinction matter for surveillance?

A Note on Genotypes



- As of October 2024, 8 known genotypes and 93 known subtypes of HCV
- Having multiple genotypes is transitory and usually lasts less than 6 months, as one genotype or subtype will outcompete the other
- Indicator of recent infection

EXAMPLE CASES



Case 1

SCDs	1/23/19	10/8/20	6/3/21	10/19/22
Labs	genotype 3 285,795 IU/mL	RNA Negative	RNA Negative	genotype 2 1,366,334 IU/mL

Case 2

SCDs	4/24/18	11/19/21	5/24/22	11/9/22
Labs	19,000,000 IU/mL	RNA Negative	RNA Negative	33 IU/mL

EXAMPLE CASES

Case 3

SCDs	8/14/17	1/3/18	9/3/21	11/3/22	3/6/23
Labs	320,000 IU/mL	<15 RNA not detected	<15 IU/mL	30 IU/mL	RNA not detected

Case 4

SCDs	10/12/20	5/6/21	7/7/21	3/8/22	9/22/22	4/18/23	11/29/23
Labs	genotype 1a	56 IU/mL	<12 IU/mL RNA negative	<12 IU/mL RNA negative	15 IU/mL	131,000 IU/mL	genotype 3a

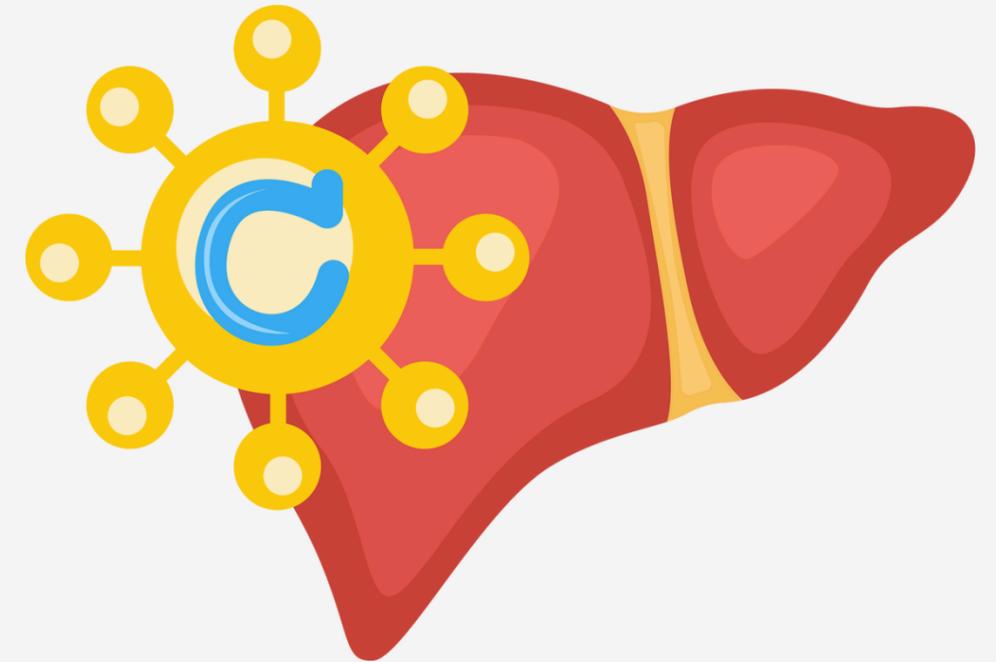


05.

CONCLUSION

CONCLUSION

- Reinfection is more common in high-risk settings and can be difficult to distinguish from treatment failure.
- The Clearance Cascade provides actionable insight into testing, treatment, and outcomes.
- Strong surveillance + navigation improves early detection and linkage to care.
- Reinfection data support HCV elimination efforts in Tennessee and beyond.



Thank You

Contact Us:

Heather.Wingate@tn.gov

Paula.Shoup@tn.gov

Kyle.Nowotny@flhealth.gov

