HCV Testing Overview

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Conflict of Interest Disclosure: Consultant to and own Quest Diagnostics stock

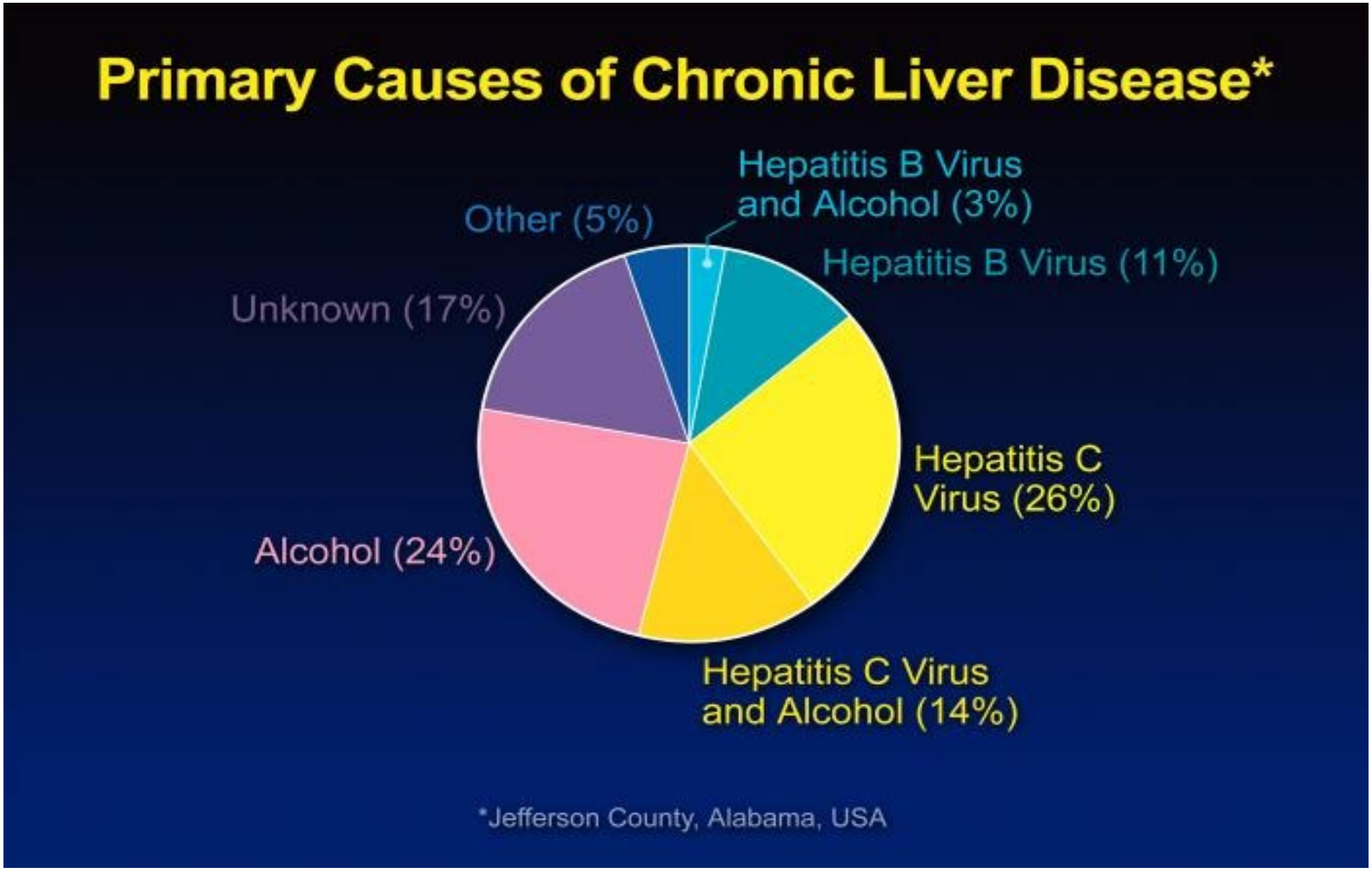
Learning Objectives

1. Brief Review of HCV Disease Progression and Epidemiology
2. Types of HCV Laboratory Tests
3. Why, Whom, and How to Test for HCV Infection
4. HCV Antibody and HCV RNA Test Result Interpretations
5. Challenges with HCV Diagnostic Testing Algorithm
6. Application of HCV RNA Testing to HCV Care Cascade

Types of Laboratory Tests for Hepatitis C*

- **Screening:** Serologic test for HCV antibody
- **Confirmatory:** HCV current infection requires presence of HCV RNA
- **Genotype:** If HCV RNA is present the specific genotype can be determined
- **Drug Resistance:** Mutations of certain HCV proteins allow for viral replication in the presence of some direct-acting antivirals

* Adapted from https://www.hepatitis.va.gov/hcv/screening-diagnosis/laboratory-tests.asp

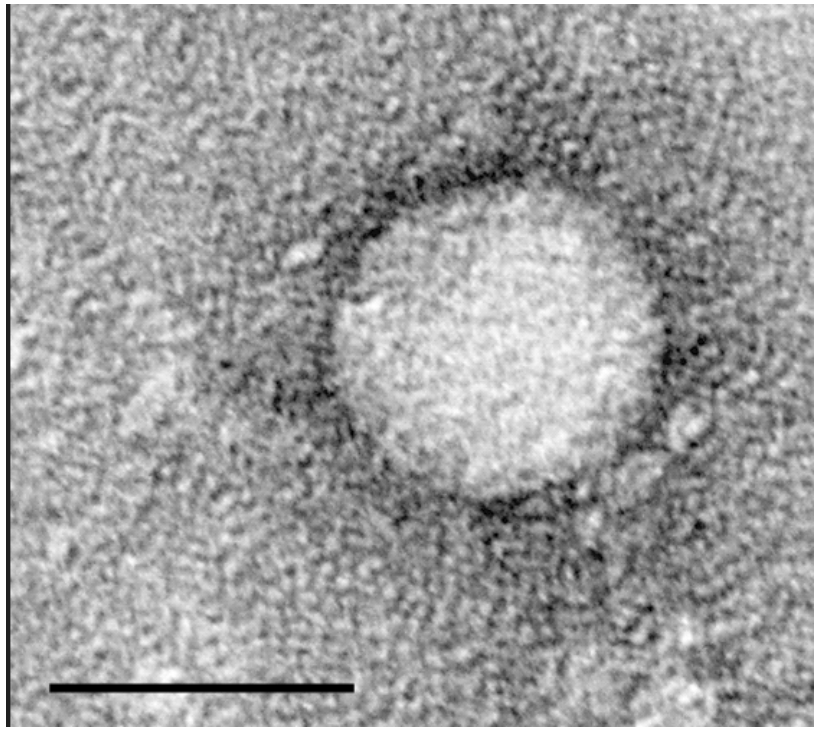


Primary Causes of Chronic Liver Disease. Centers for Disease Control and Prevention. 1997. Accessed 3/6/2023. https://phil.cdc.gov/Details.aspx?pid=83

Hepatitis C Virus

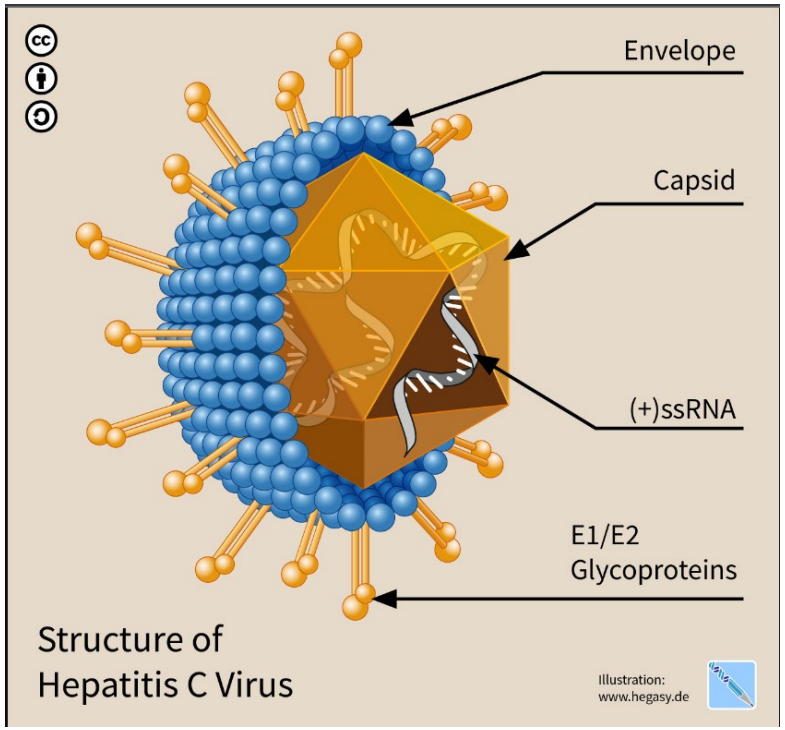
Family: *Flaviviridae* 55 nm in size

Host Range: humans and chimps



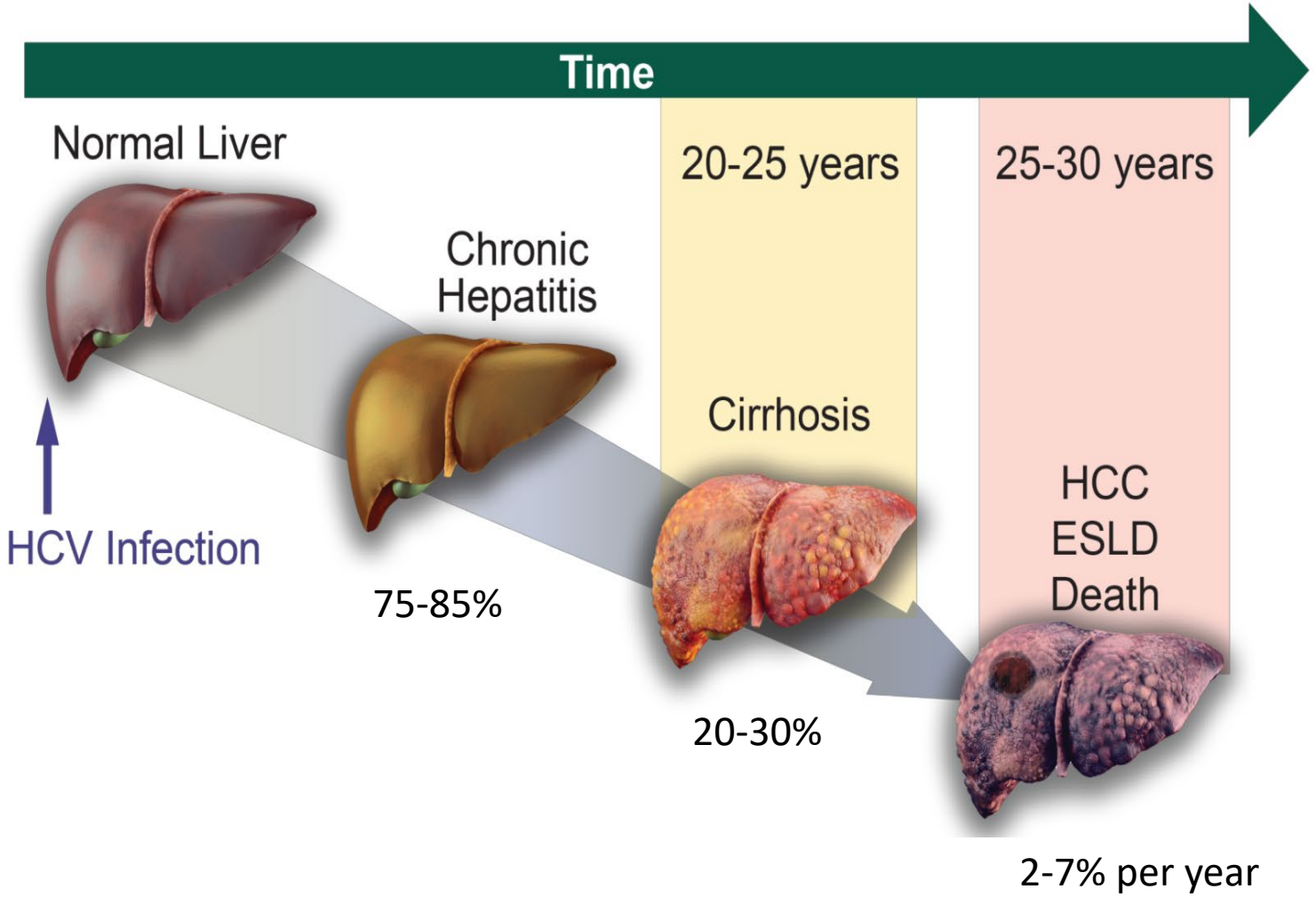
Catanese MT, et al. Electron Micrograph of hepatitis C Virus. (Scale bar = 50 nanometers). Wikimedia Commons; 2010. Accessed 3/6/2023., https://commons.wikimedia.org/w/index.php?curid=10903740

Enveloped, single-stranded, positive-sense RNA virus with 7 major genotypes



Structure of Hepatitis C Virus. Wikimedia Commons; 2020. Accessed 3/6/2023. https://commons.wikimedia.org/wiki/File:Hegasy_Hep_C_Virus_EN-01.jpg

HCV Disease Progression

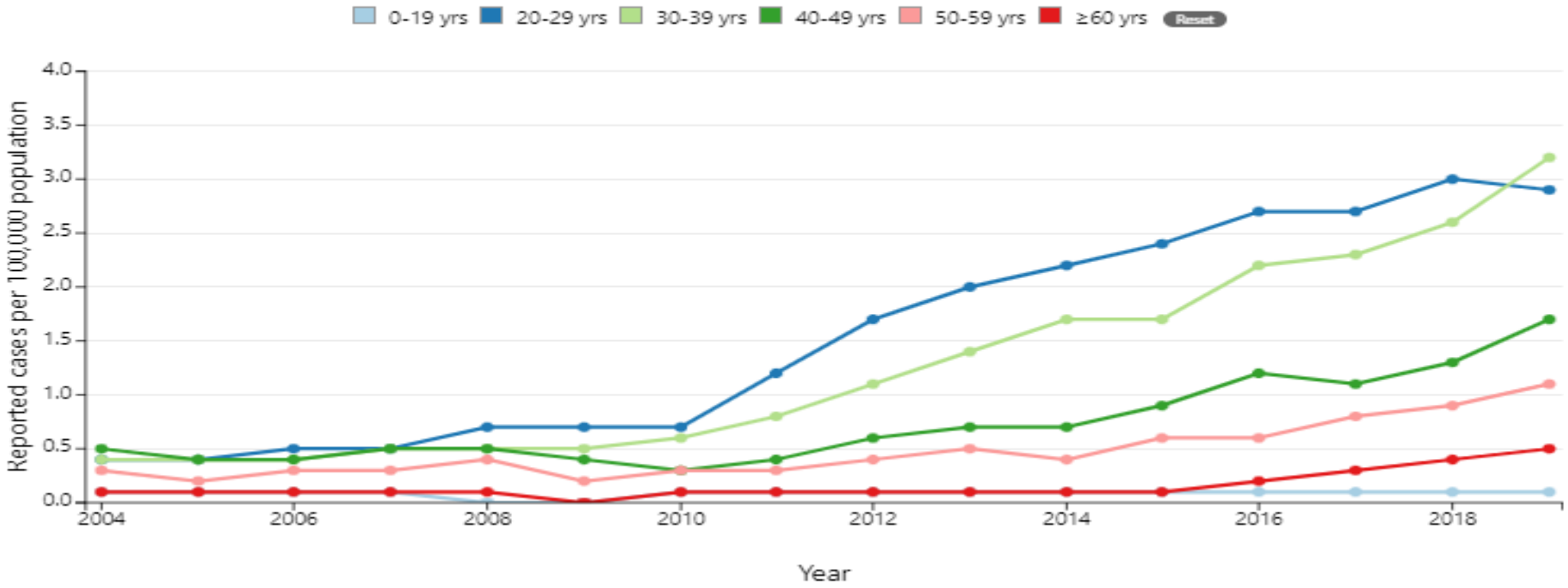


Slide courtesy of Berry Bennet, MPH, Technical Consultant to the Florida Bureau of Public Health Laboratories

Prevalence and Incidence of HCV in USA

HCV Prevalence: 2013 to 2016 estimate = 2.4 million people living with HCV[1]

HCV Incidence: 2019 estimate = 57,500 new cases[2]



1. Hofmeister MG, et al. Estimating prevalence of hepatitis C Virus Infection in the United States, 2013-2016. Hepatology 2019;69:1020–31
2. https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1

Why HCV Diagnostic Testing?

HCV infection is curable in >95% of patients treated with Direct Acting Antiviral combination therapies*

*Falade-Nwulia O, et al. Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection: A Systematic Review. *Ann Intern Med*. 2017 ;166(9):637-648. doi: 10.7326/M16-2575. Epub 2017 Mar 21. PMID: 28319996; PMCID: PMC5486987

Whom to Test for HCV Infection?*

1. HCV testing at least once in a lifetime **for all adults ≥ 18 years of age** (except where prevalence of infection is less than 0.1%) (unclear how healthcare provider can determine local prevalence)

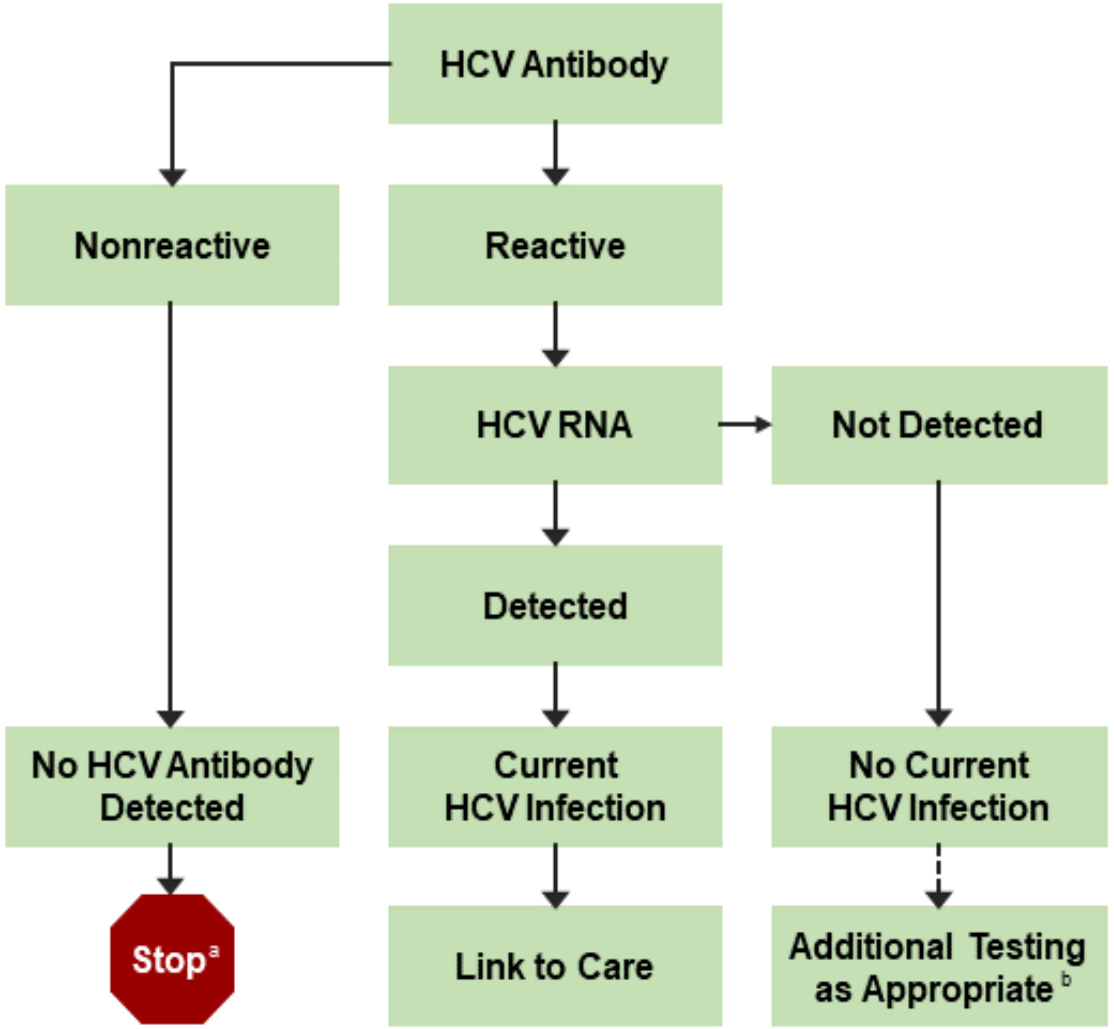
2. HCV testing **for all pregnant women during each pregnancy** (except where prevalence of infection is less than 0.1%) (unclear how healthcare provider can determine local prevalence)

3. HCV testing on a periodic basis **for people with ongoing risk factors**

4. HCV testing **for any person who requests hepatitis C testing**

* https://cdc.gov/hepatitis /hcv/guidelines.htm

How to Test for HCV Infection?



MMWR Morb Mortal Wkly Rep. 2013;62(18):362-365.

Laboratory Markers of HCV Infection

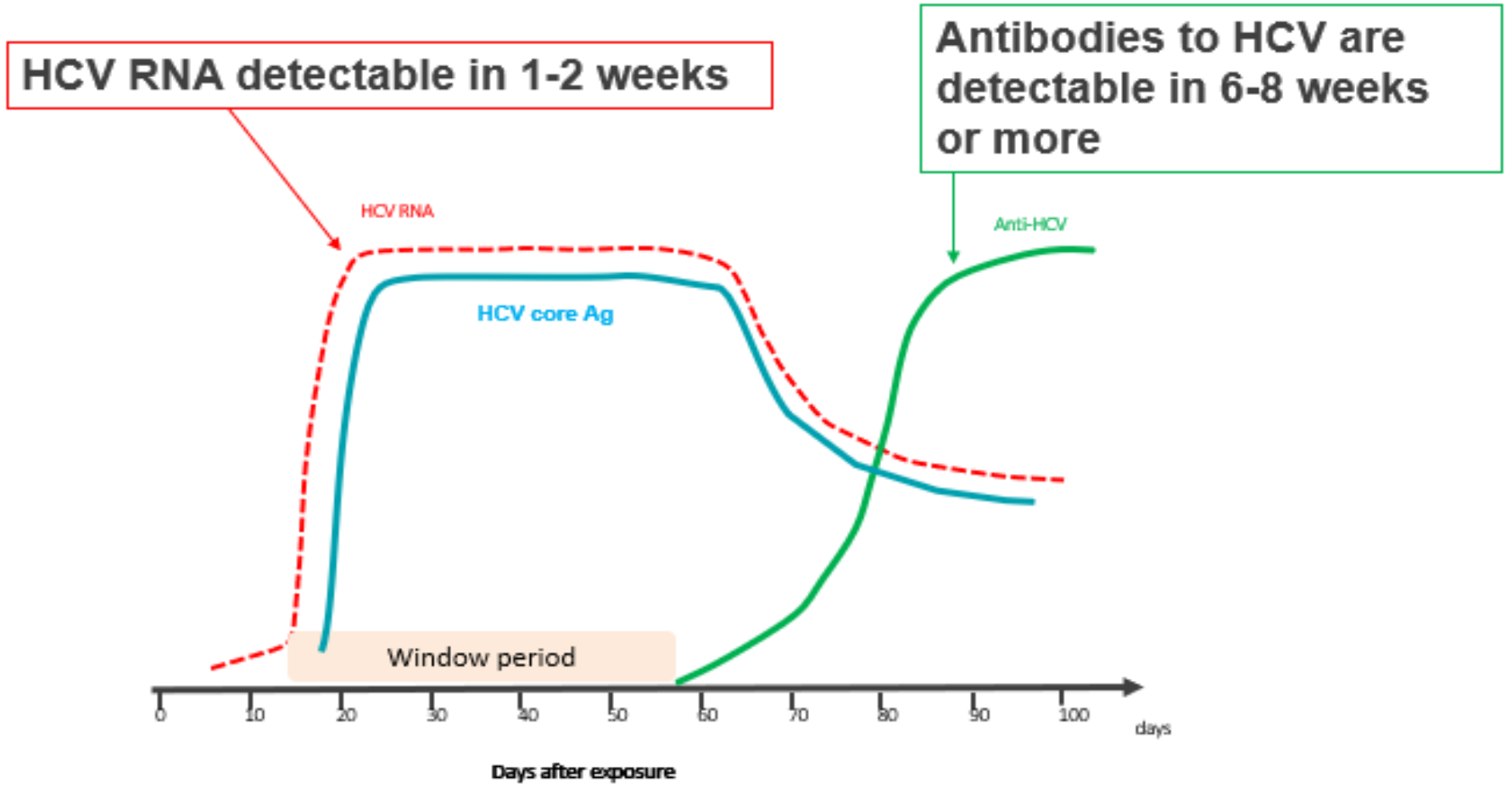


Figure provided by S. Kamili, DVH, CDC

HCV Antibody and HCV RNA Result Interpretations *

Test Outcome	Interpretation	Further Action
HCV Ab negative	Never exposed to HCV.	• If the antibody result is negative (nonreactive), no further action is required. • If acute HCV is suspected, test for HCV RNA, as the HCV Ab result may not be positive yet.

* Adapted from https://www.hepatitis.va.gov/hcv/screening-diagnosis/laboratory-tests.asp

HCV Antibody and HCV RNA Result Interpretations *

Test Outcome	Interpretation	Further Action
HCV Ab positive	Indicates exposure to HCV. Test for HCV RNA to determine chronic or resolved infection.	• HCV Ab is positive in either active HCV infection or past HCV infection that has resolved. It is also possible to have a false-positive antibody result. The next step is to test for HCV RNA to determine if there is active infection. • Once the HCV Ab result is positive, the test does not need to be repeated in the future. The result will remain positive. • The antibody result also will remain positive after successful HCV treatment (achievement of an SVR).

* Adapted from https://www.hepatitis.va.gov/hcv/screening-diagnosis/laboratory-tests.asp

HCV Antibody and HCV RNA Result Interpretations *

Test Outcome	Interpretation	Further Action
HCV Ab positive, HCV RNA detected	Active HCV infection. If infection occurred >6 months ago, this is chronic HCV infection.	• Provide the patient who was tested with appropriate counseling and link that person to medical care, including treatment.

* Adapted from https://www.hepatitis.va.gov/hcv/screening-diagnosis/laboratory-tests.asp

HCV Antibody and HCV RNA Result Interpretations *

Test Outcome	Interpretation	Further Action
HCV Ab positive, HCV RNA not detected	No active HCV infection. Patient spontaneously cleared HCV and did not become chronically infected, or was successfully treated and achieved SVR.	• No further action required in most cases • If there is concern about a false-positive antibody screen, consider a repeat HCV Ab test using a different assay.

* Adapted from https://www.hepatitis.va.gov/hcv/screening-diagnosis/laboratory-tests.asp

Challenges with HCV Diagnostic Algorithm

False Negative/Positive HCV Antibody Test Results

False Negative HCV Ab

- When Ab testing is performed during the "Window" period or in immunocompromised
- Solution: Also perform separate HCV RNA testing

False Positive HCV Ab

- May occur because of cross-reactivity with other viral antigens or the presence of immunologic disorders (eg, lupus, rheumatoid arthritis)
- Solution: automatic reflexing of all Positive HCV Antibody specimens to HCV RNA testing

Challenges of Implementing the HCV Antibody/HCV Reflex Algorithm (1 of 2)

1) Get Medical Administration “Buy In”

2) Get Compliance/Legal “Buy in”

3) Determine Costs to Implement Different HCV Antibody/RNA Reflex Options

4) Determine Impact of Change on Client’s Use of the Laboratory Service

5) Perform Technical Validation of HCV Antibody/HCV Reflex Testing

6) Identify Implementation Team and Assign Project Manager

Challenges of Implementing the HCV Antibody/HCV Reflex Algorithm (2 of 2)

7) Identify and Implement Information Technology (IT) Changes

8) Identify and Implement Billing Department Changes

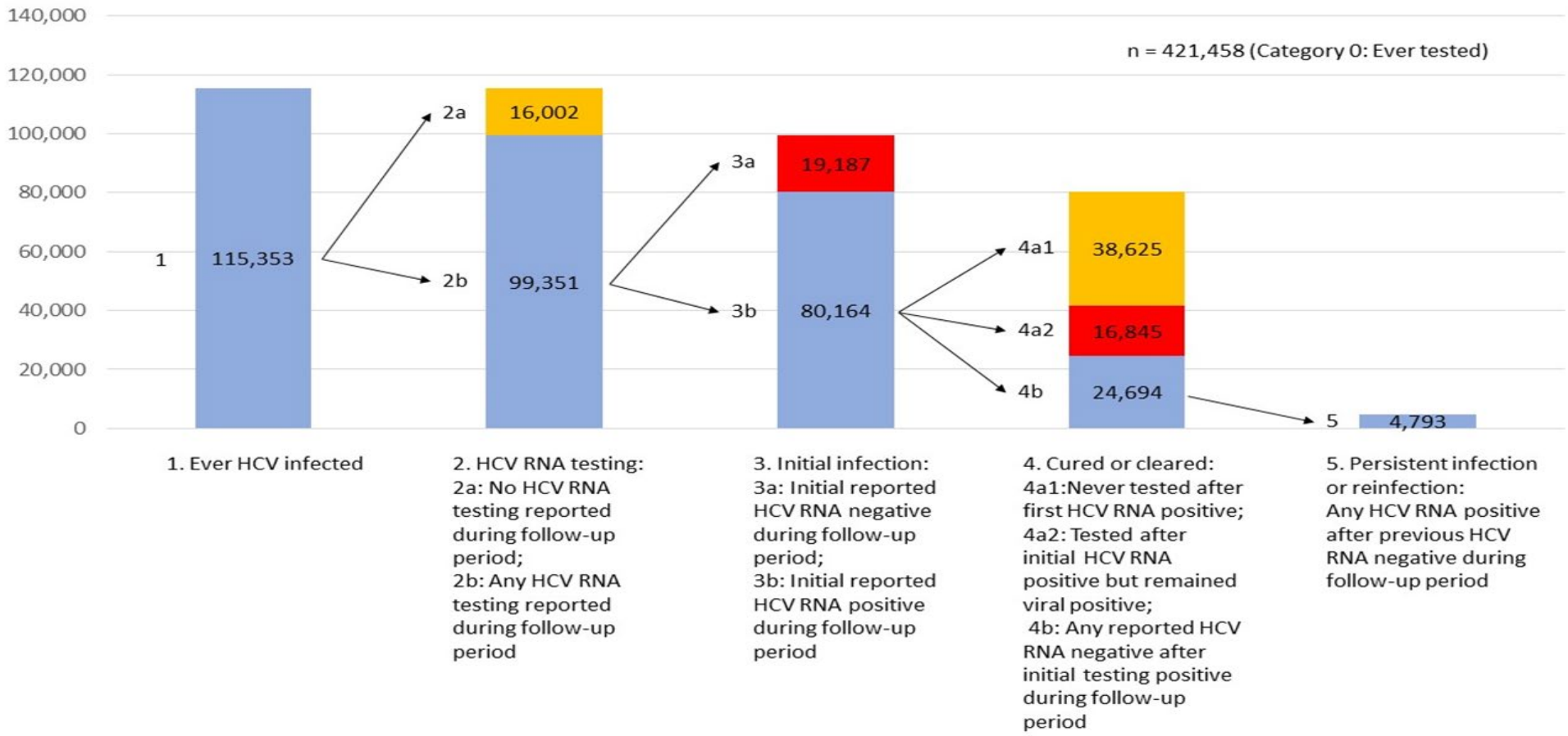
9) Train Non-Molecular Staff on Pre-Analytical Specimen Handling Changes

10) Medical Director Review of New HCV Reflex Algorithm Laboratory Result Reports

11) Provide Clients with Advanced Notice of HCV “Reflex Only” Testing Option Start

12) Monitor Post Implementation Monitoring Process for Client Impact

Application of HCV RNA Testing to HCV Care Cascade



Kaufman, HW., Meyer III, WA, Huang, X. (2023) Hepatitis C Care Cascade among Incarcerated or Detained Persons and General Population in California, 2011-2021. Ann Gastroenterol Dig Dis, 6(1): 06-16.

Summary

1. HCV infection is the leading cause of infectious chronic liver disease.
2. Implementation of the CDC 2013 HCV Diagnostic Algorithm will allow for better linkage to care for those who are actively infected.
3. HCV screening should be a regular part of adult healthcare services.
4. Cure rates of HCV infection are high with DAA use.
5. Implementation of a “HCV Antibody to HCV RNA Reflex” only test offering requires careful planning and implementation