

Hepatitis C in 2019:

A Case-based Discussion of Screening,
Evaluation, and Treatment

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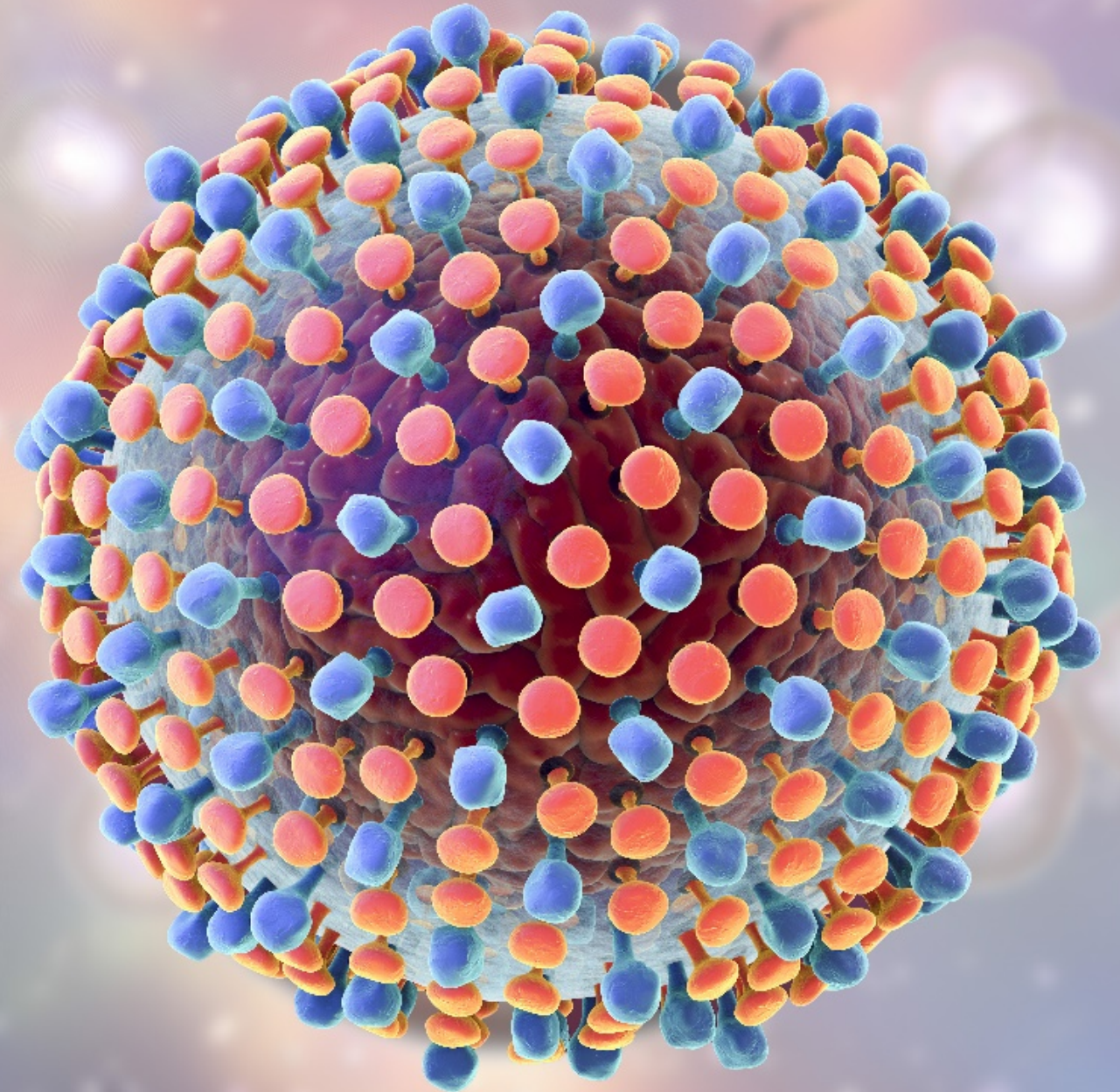
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Disclosures

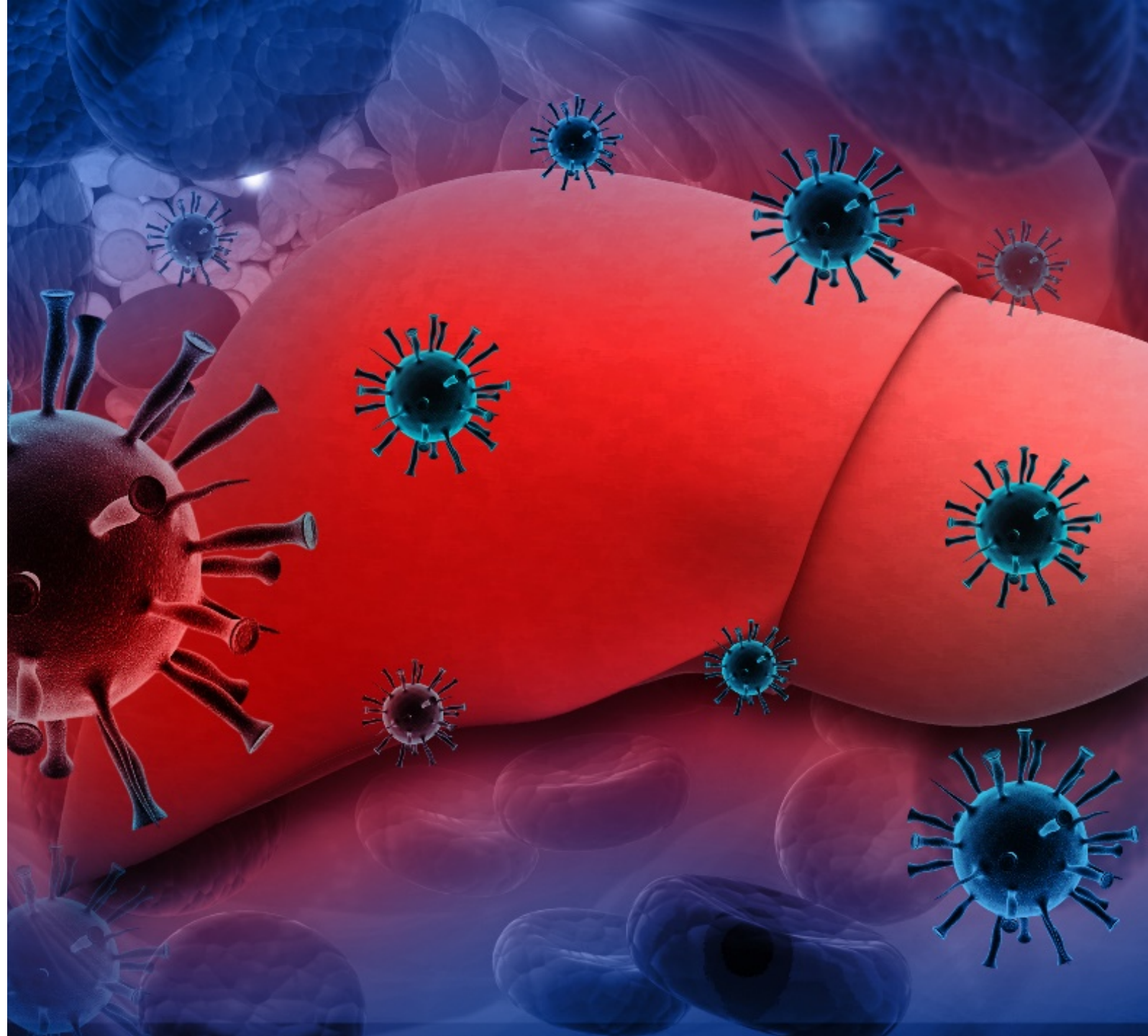
- Dr. Chastain has previously received grant/research support paid to his institution from Gilead Sciences, Inc.:
 - Key faculty personnel for Gilead FOCUS Hepatitis C Virus (HCV) Screening Program through Vanderbilt University Medical Center Emergency Department
 - Site investigator for HIV/HCV SWITCH Registry Study



Objectives

At the end of this lecture, the learner will be able to:

- Recommend appropriate, guideline-based screening for HCV
- Discuss the key components of clinical and laboratory evaluation of HCV
- Identify the primary factors to selecting HCV treatment



Menti Word Cloud

What words come to mind when you think about HCV?



Think-Pair-Share

- Think about a patient you have cared for with hepatitis C.
- Pair up with a colleague.
- Share your thoughts and experiences.
- Spend no more than 1-2 minutes.

- GO!

- Anyone willing to share?



Walter White Presents To Your Clinic



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- 50 y/o man presents to establish primary care.
- Past Medical History:
 - Hypertension
 - Recent cough and fatigue
- Past Surgical History:
 - Tonsillectomy as a child
- Past Family History:
 - CAD, DM, prostate cancer
- Past Social History:
 - Chemistry teacher
 - Denies tobacco
 - Occasional social alcohol use
 - Tattoo placed in high school “with friends”
 - Experimental intranasal drug use in distant past

Walter's Physical Exam & Laboratory Studies

Physical:

- General, HEENT, CV, lung, and skin examination are unremarkable
- Abdominal exam reveals mild hepatomegaly three finger breadths beneath the R rib cage without splenomegaly or ascites

Labs:

- CBC notable for white blood cell count of 3.7 and platelet count of 115
- CMP notable for AST of 87 and ALT of 65 with a normal bilirubin and a normal albumin

Menti Question

What is THIS patient's indication for HCV screening as per the USPSTF?

- A. Age
- B. Substance use history
- C. Laboratory findings
- D. Tattoo



Risk Factors for HCV That Warrant Screening:

FIND OUT IF YOU HAVE HEPATITIS C
IT COULD SAVE YOUR LIFE

BORN FROM 1945-1965?

SOME PEOPLE DON'T KNOW HOW OR WHEN THEY WERE INFECTED

People born from 1945-1965 are **5X MORE LIKELY TO BE INFECTED WITH HEPATITIS C**

3 OUT OF EVERY 4 people with Hepatitis C were born between these years

Up to **75%** of people living with Hepatitis C **DO NOT KNOW THEY ARE INFECTED**

Many people can live with **HEPATITIS C** for **DECADES** with **NO SYMPTOMS**

CDC recommends anyone born from 1945-1965 GET TESTED

TESTED	NOT TESTED
KNOWING YOU HAVE HEPATITIS C can help you make important decisions about your health	LEFT UNTREATED, HEPATITIS C can cause liver damage and LIVER FAILURE
Many people can get LIFESAVING CARE AND TREATMENT	HEPATITIS C is the #1 CAUSE OF LIVER TRANSPLANTS
Successful treatments can ELIMINATE THE VIRUS from the body	HEPATITIS C is a leading cause of LIVER CANCER

Don't go down the wrong path, talk to your doctor about getting tested. It could save your life.

CDC U.S. Department of Health and Human Services
KNOW MORE HEPATITIS

- Current or prior injection or inhaled drug use
- Unregulated tattoo and/or piercing
- Blood/clotting protein transfusion prior to 1992
- Birth to from HCV+ mother
- Hemodialysis patients
- People with HIV
- Occupational exposures
- Born between 1945-1965 (“baby boomer” generation)





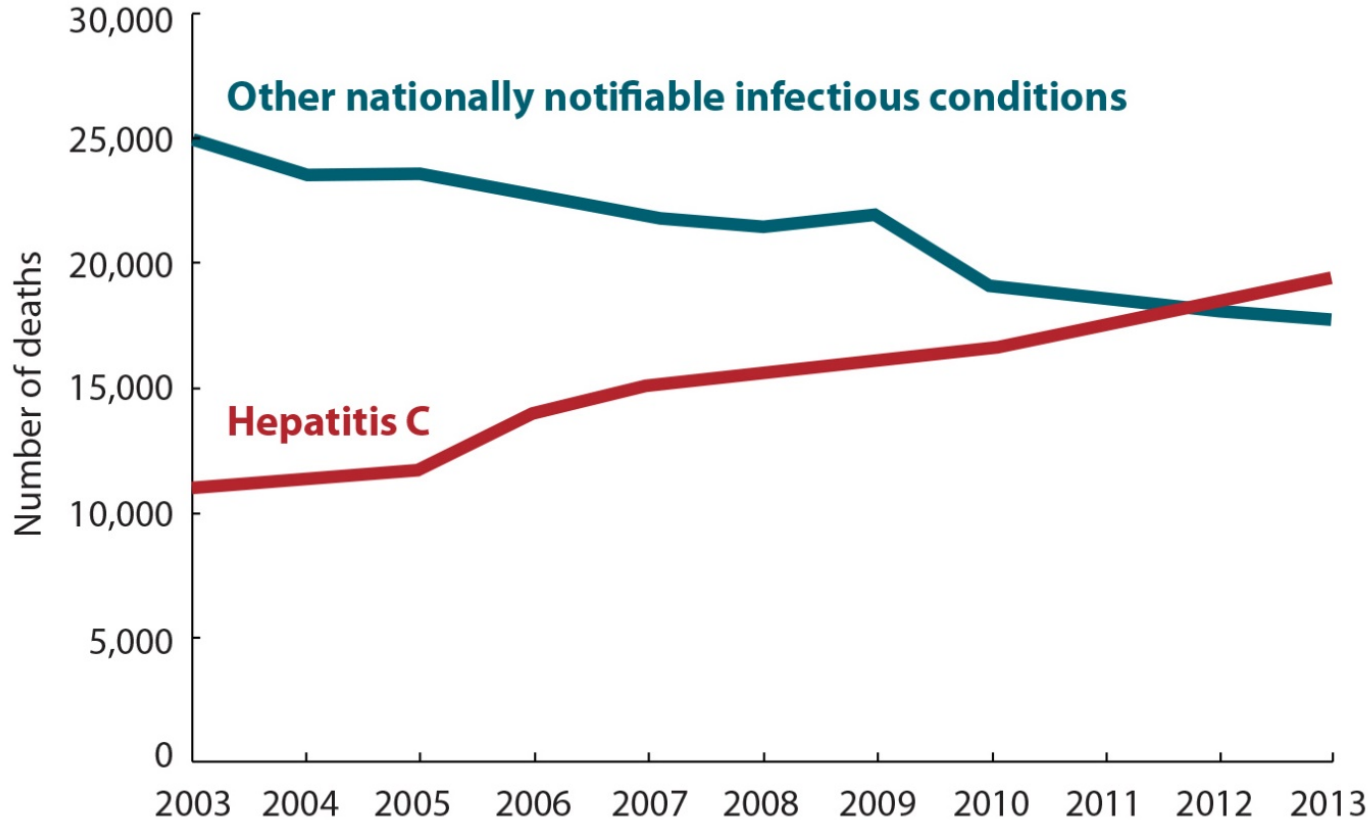
Draft Recommendation Statement

Hepatitis C Virus Infection in Adolescents and Adults: Screening

This opportunity for public comment expires on September 23, 2019 at 8:00 PM EST

Population	Recommendation	Grade (What's This?)
Adults ages 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults ages 18 to 79 years.	B

Annual number of hepatitis C-related deaths vs. other nationally notifiable infectious conditions in the US, 2003-2013



HCV and Mortality in the USA

Ly KN et al. *Clin Infect Dis* 2016.

Source: Centers for Disease Control and Prevention

Estimated Rate of People Living with Hepatitis C, 2013-2016

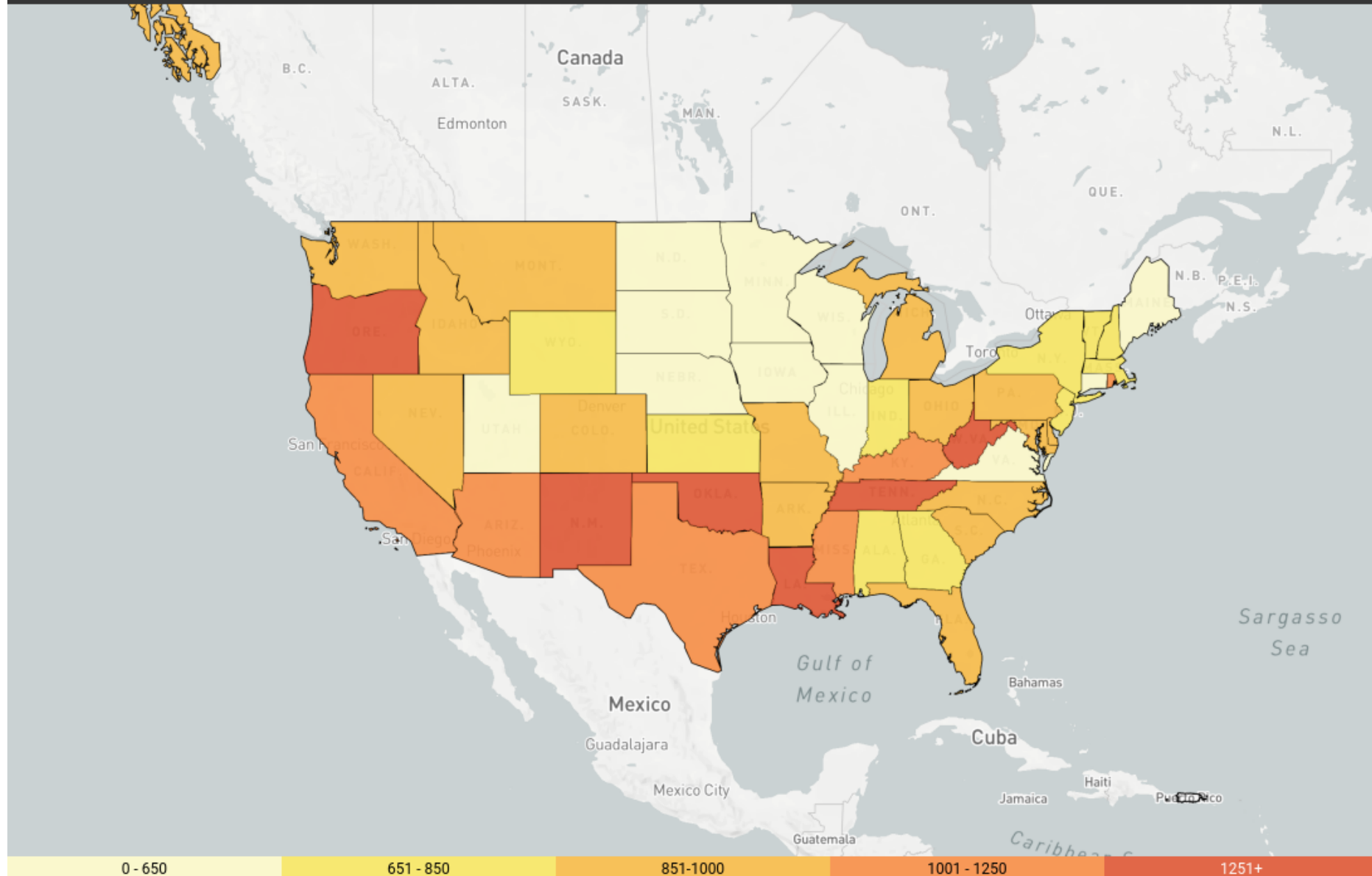
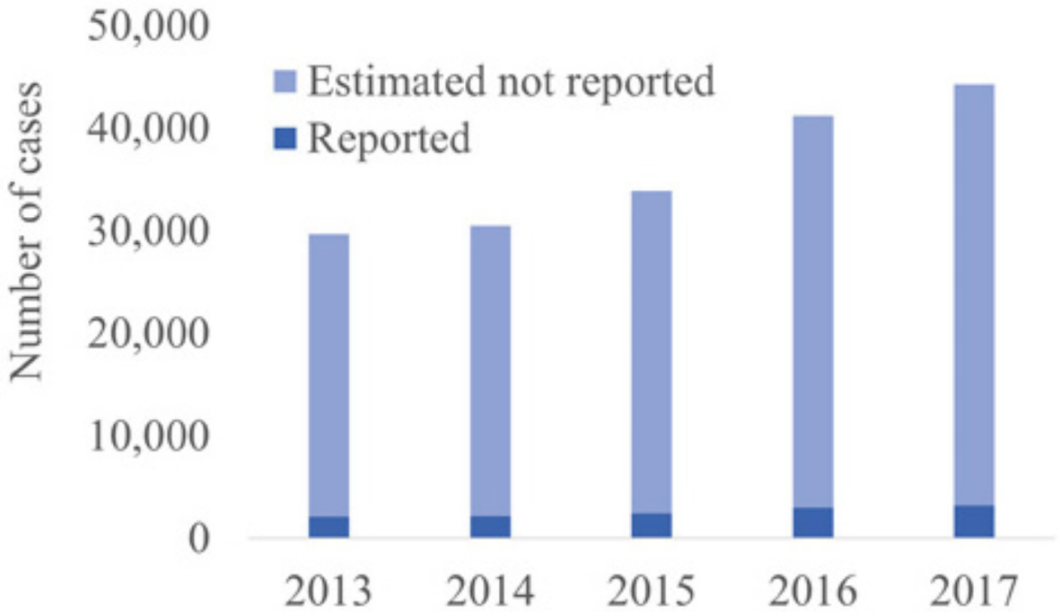
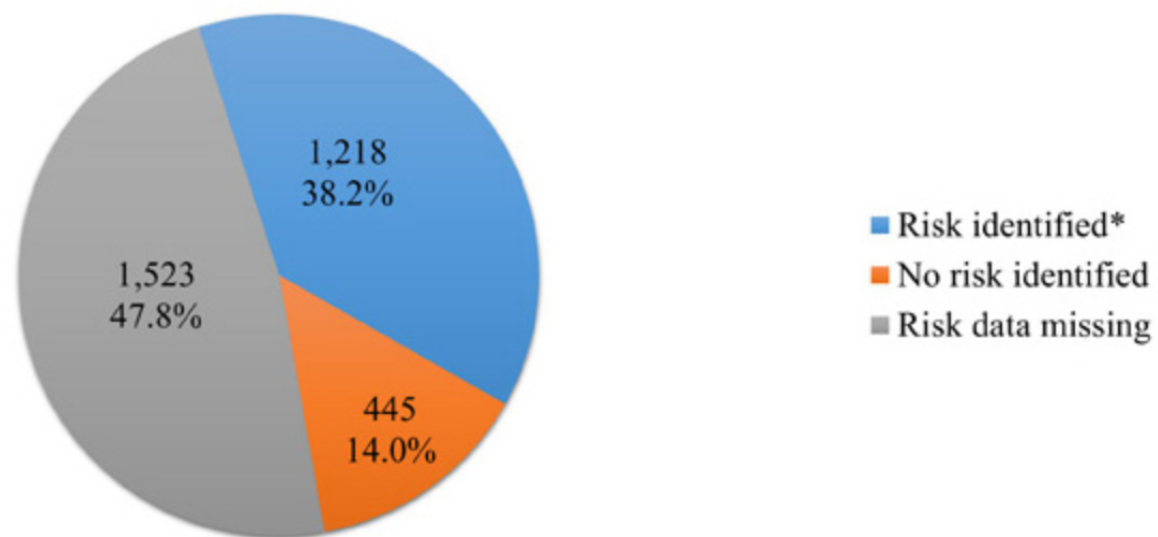


Figure 4.1. Actual number of acute hepatitis C cases submitted to CDC by states and estimated* number of acute hepatitis C cases — United States, 2013–2017.



Source: CDC, National Notifiable Diseases Surveillance System.

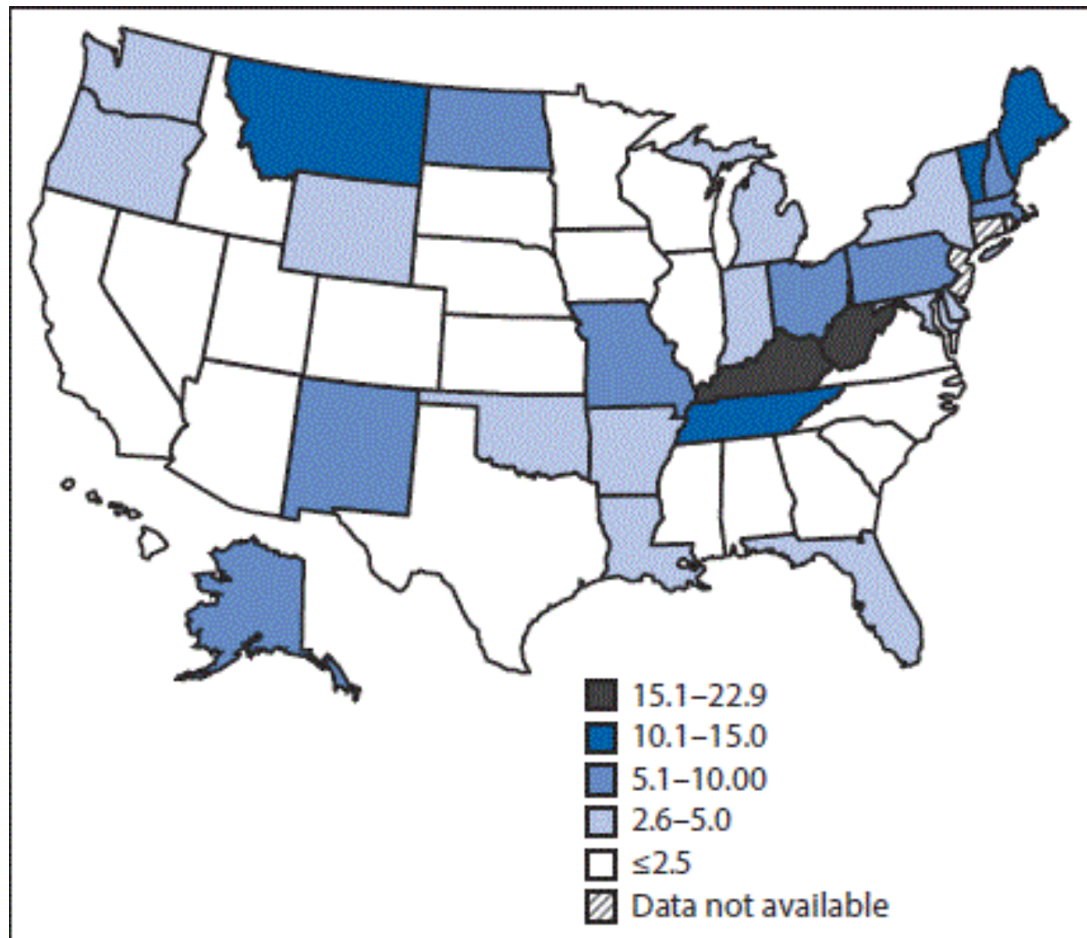
Figure 4.6. Availability of information on risk behaviors/exposures* associated with reported cases of acute hepatitis C — United States, 2017.



Source: CDC, National Notifiable Diseases Surveillance System.

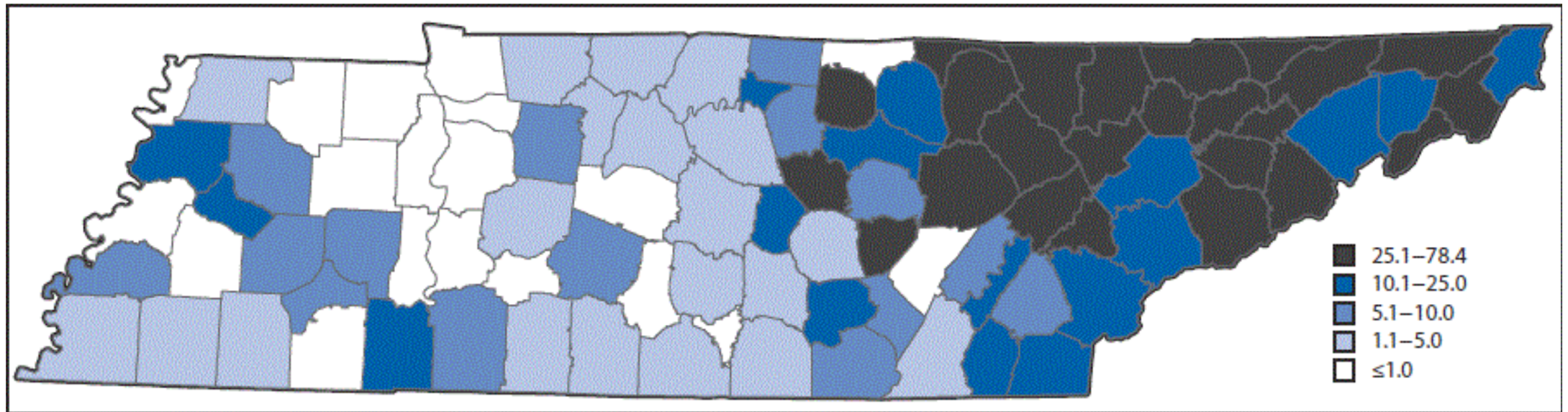
Pregnant Women and HCV Cont.

Rate of HCV Among Pregnant Women Per 1000 Live Births in US and TN



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Diagnostics Review

HCV Antibody

- Tests for ***exposure***
- Near 100% sensitivity once >6 months after infection

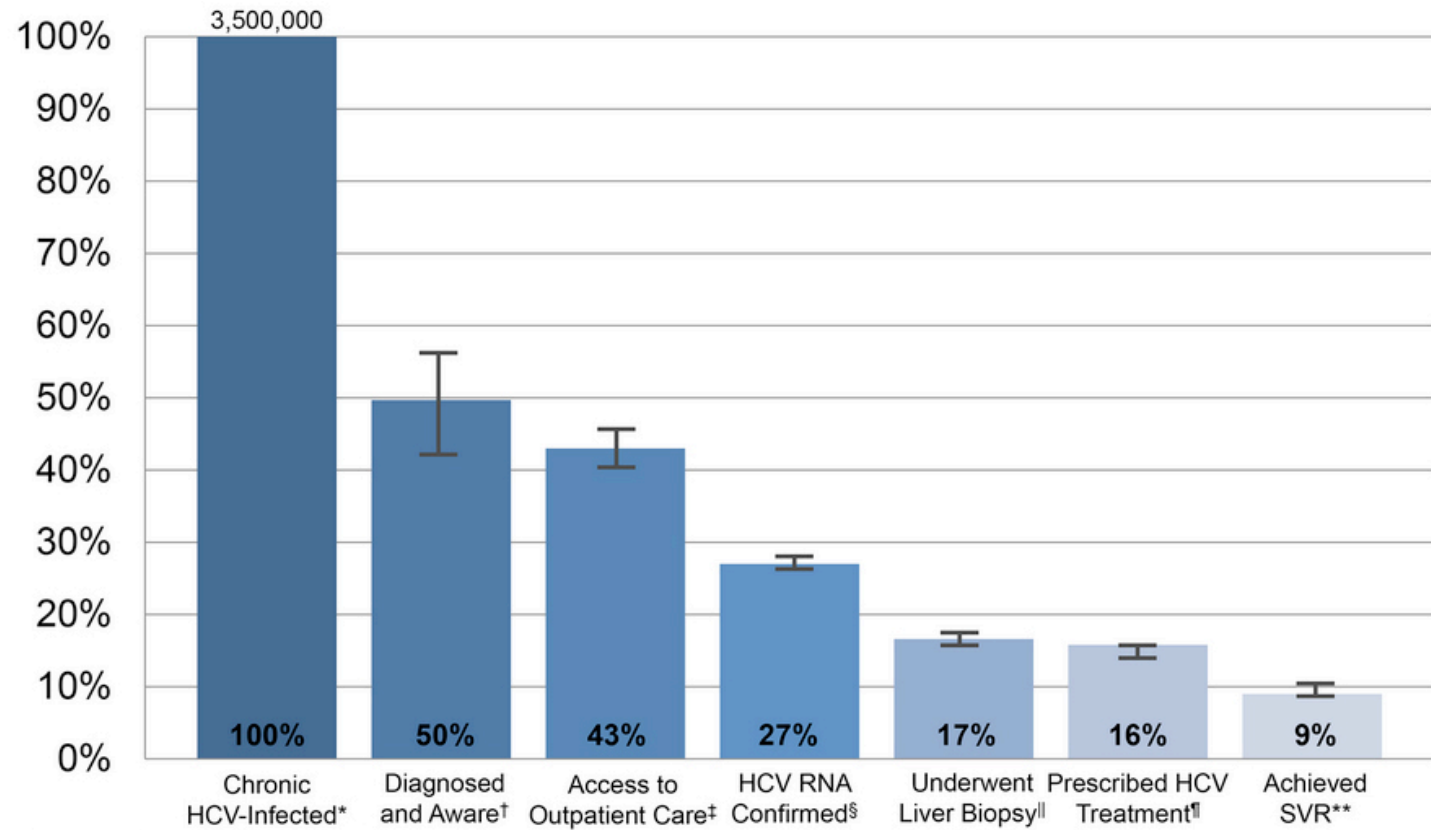
HCV RNA

- Tests for ***active infection***
- ~20% of patients spontaneously clear HCV

HCV Genotype

- Defines genetic subtype for prognostic information and treatment guidance

Yehia BR et al. *PLoS One* 2014.



* Chronic HCV-Infected; N=3,500,000.

† Calculated as estimated number chronic HCV-infected (3,500,000) x estimated percentage diagnosed and aware of their infection (49.8%); n=1,743,000.

‡ Calculated as estimated number diagnosed and aware (1,743,000) x estimated percentage with access to outpatient care (86.9%); n=1,514,667.

§ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage HCV RNA confirmed (62.9%); n=952,726.

|| Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage who underwent liver biopsy (38.4%); n=581,632.

¶ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage prescribed HCV treatment (36.7%); n=555,883.

** Calculated as estimated number prescribed HCV treatment (555,883) x estimated percentage who achieved SVR (58.8%); n=326,859.

Note: Only non-VA studies are included in the above HCV treatment cascade.

Walter: The Diagnosis

Walter's HCV antibody is positive.

HCV RNA PCR is ordered and found to be 600,000 copies/mL.

You inform the patient of his laboratory testing.

Upon his return, the patient asks how this will impact his lifespan (in order to make vocational and financial plans...)



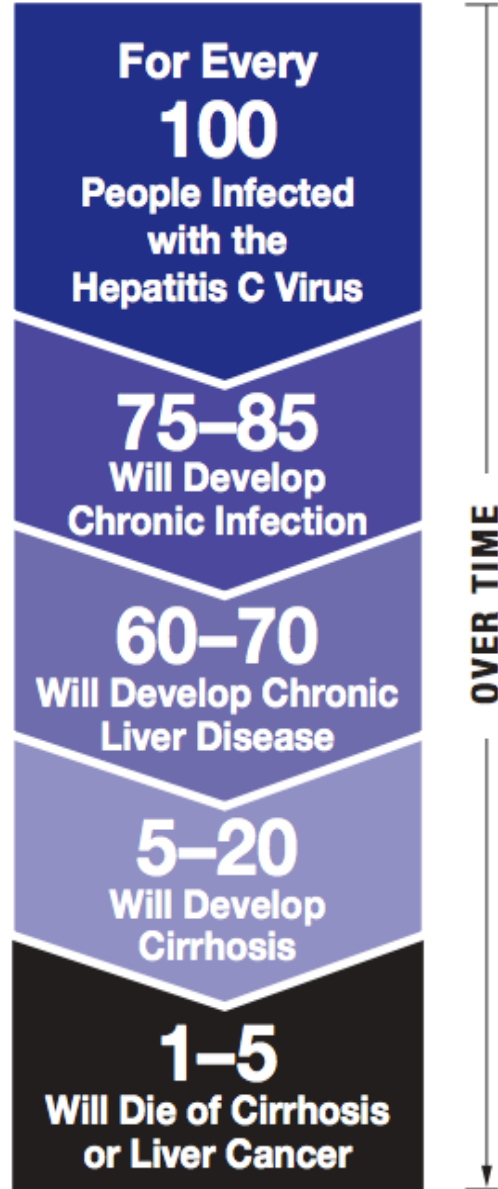
Menti Question

What proportion of people infected with HCV die of liver failure or hepatocellular carcinoma?

- A. 5%
- B. 15%
- C. 25%
- D. 33%
- E. 50%

Natural
History of
HCV

Progression of
Hepatitis C



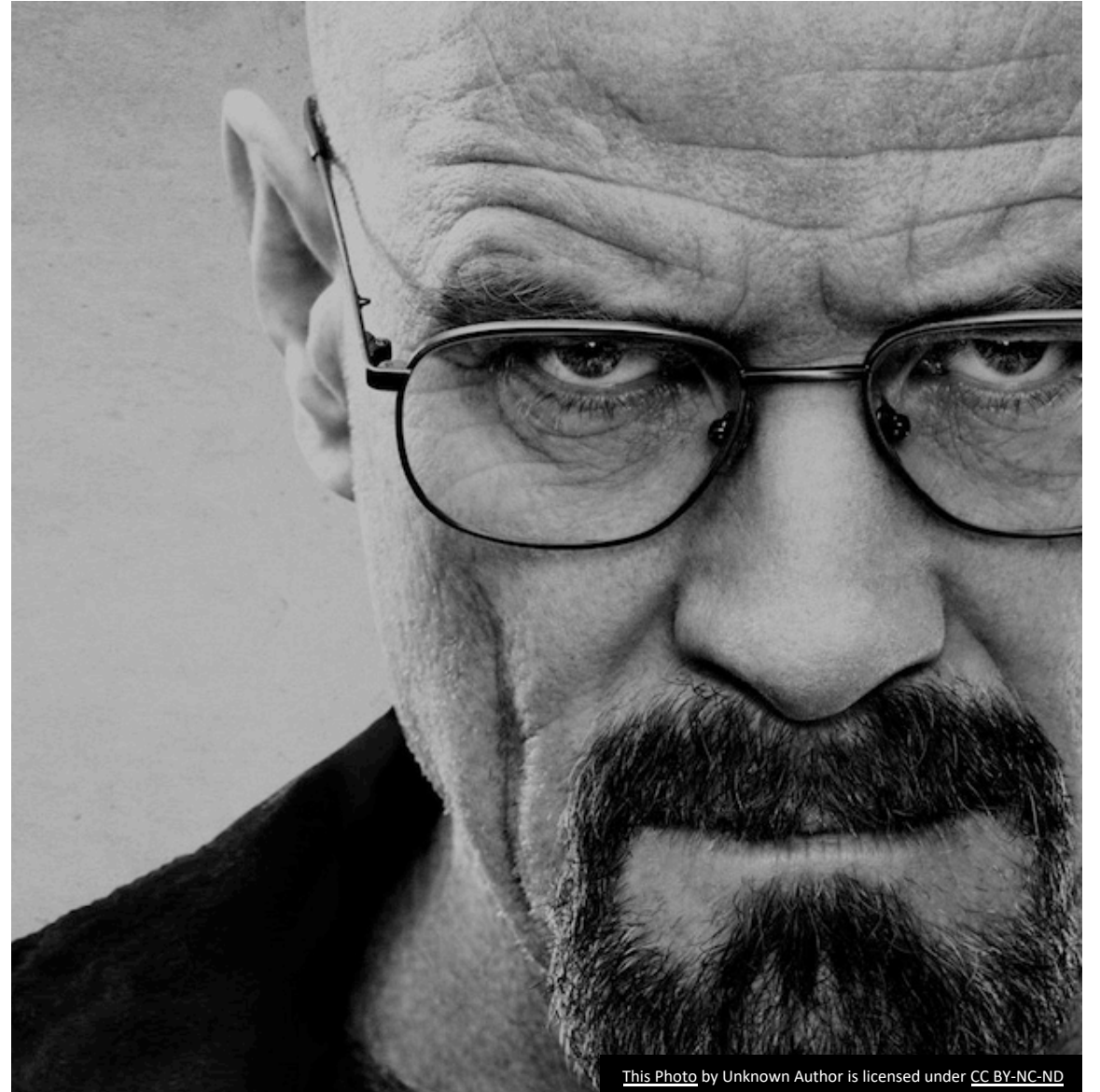
Factors Associated with HCV Accelerated Fibrosis Progression (www.hcvguidelines.org)

Host	Viral
Nonmodifiable	HCV genotype 3
Fibrosis stage	Coinfection with hepatitis B virus or HIV
Inflammation grade	
Older age at time of infection	
Male sex	
Organ transplant	
Modifiable	
Alcohol consumption	
Nonalcoholic fatty liver disease	
Obesity	
Insulin resistance	

Updated February 24, 2016.

Walter: The Evaluation

- You reassure Walter that he is unlikely to imminently die of liver failure.
- The patient would like to be assessed for treatment, as he is not convinced of your estimates.
- You recommend additional evaluation to assess his disease, liver function, and comorbid conditions...



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Clinical Manifestations of HCV

- Acute HCV (~20%)
 - Fever
 - Fatigue and anorexia
 - Nausea and vomiting
 - Abdominal pain
 - Jaundice, dark urine, and clay-colored stools
 - Arthralgias
- Chronic HCV (~80%)
 - Often asymptomatic
 - May cause fatigue, insomnia, depression, and mental status changes
 - May cause extrahepatic manifestations including vasculitis and renal disease
 - Long-term outcomes include cirrhosis, liver failure, and hepatocellular carcinoma

HCV Patient History

Disease History

- When? How? Why?
- Prior Staging
- Prior Treatment

Symptoms of chronic HCV infection:

- Fatigue
- Arthralgias
- Chronic abdominal pain
- Insomnia
- *Many patients are asymptomatic!*

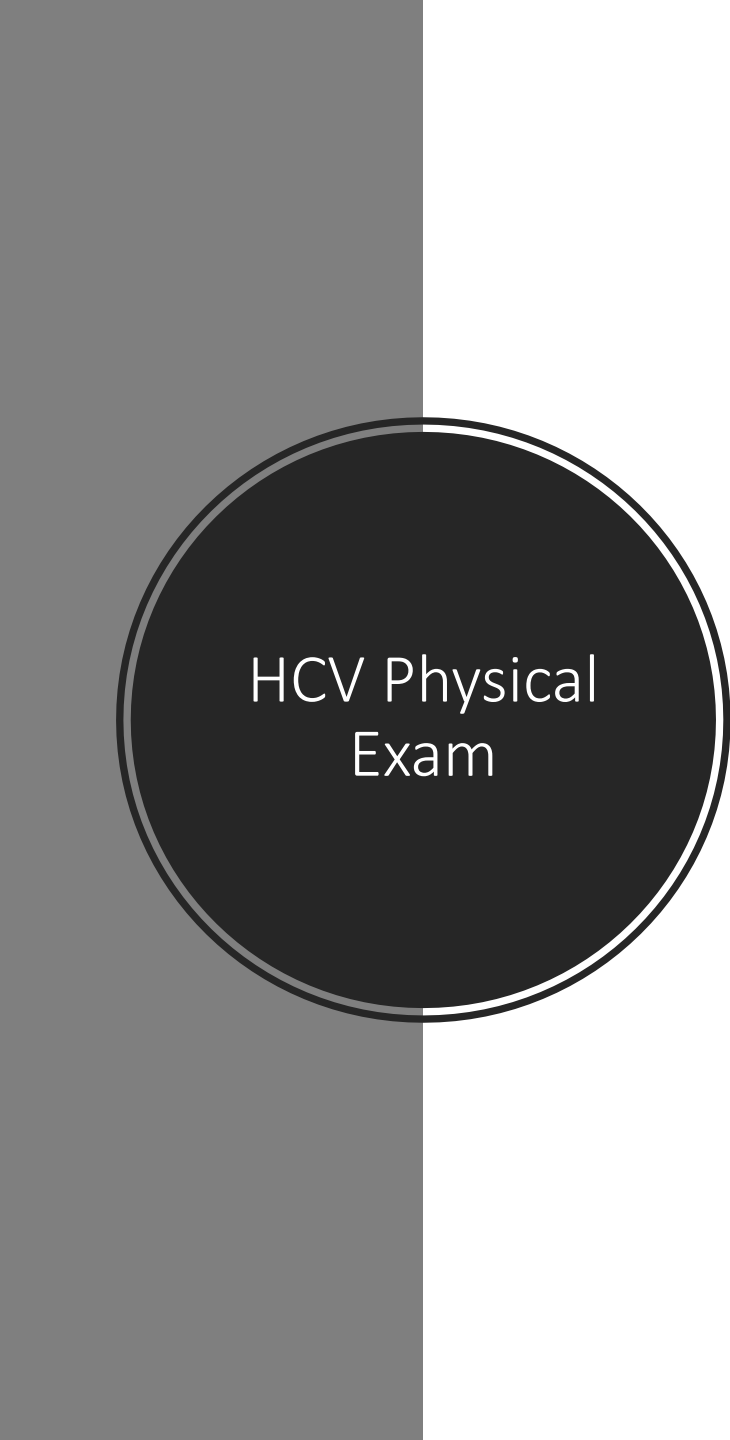
Symptoms of advanced liver disease:

- Upper GI bleeding
- Ascites
- Hepatic encephalopathy
- Liver failure

Medication History

Alcohol Use History

Substance Use History



HCV Physical
Exam

Palmar erythema

Spider nevi

Gynecomastia

Jaundice

Ascites

Asterixis

Encephalopathy

HCV Laboratory Assessment

Complete blood count

Comprehensive metabolic profile

HAV and HBV screening

HIV screening

HCV Genotype (?)

Staging Liver Disease

Importance of Staging

- Identify patients with greatest need for therapy
- Identify patients for cirrhosis-specific care
- Triage resources

Types of Staging

- Liver biopsy
- Biomarkers
- Elastography

Education and Counseling



Transmission



Natural history



Alcohol and substance use abstinence



HAV and HBV
immunization

Walter: The Treatment

- His laboratory studies and staging are most consistent with HCV genotype cirrhosis.
- He undergoes imaging, which does not reveal hepatocellular carcinoma.
- Walter would like to pursue treatment

AMERICAN ASSOCIATION FOR
THE STUDY OF LIVER DISEASES



**Recommendations for Testing, Managing,
and Treating Hepatitis C**

www.hcvguidelines.org

Recommendations for When and in Whom to Initiate Treatment

- **Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.**

Rating: Class I, Level A

Primary Factors when Selecting HCV Treatment



Genotype



**Degree of fibrosis
(non-cirrhotic vs. cirrhotic)**



**Treatment history
(naïve vs. experienced)**

FDA Approved HCV Therapies

Nonspecific Antivirals

Interferon (IFN)

Ribavirin (RBV)

Pegylated Interferon (PEG-IFN)

NS3/4 Protease Inhibitors

Telaprevir (TPV)

Boceprevir (BOC)

Simeprevir (SMV)

Paritaprevir (PTV)

Grazoprevir (GZP)

Voxilaprevir (VOX)

Glecaprevir (GLE)

NS5A Inhibitors

Ledipasvir (LDV)

Ombitasvir (OBV)

Daclatasvir (DCV)

Elbasvir (EBR)

Velpatasvir (VEL)

Pibrentasvir (PIB)

NS5B Polymerase Inhibitors

Sofosbuvir (SOF)

Dasabuvir (DBV)

Menti Question

What is the MOST appropriate treatment regimen for this patient?

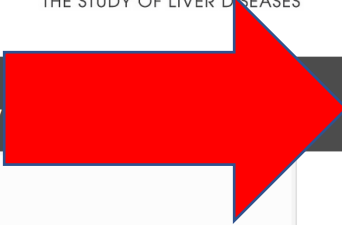
- A. Glecaprevir/pibrentasvir
- B. Ledipasvir/sofosbuvir
- C. Sofosbuvir/velpatasvir
- D. Surely you can't be serious.
- E. I am serious. And don't call me Shirley.





HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C



- Home
- Test, 
- Treatment-Naive
- Treatment-Experienced
- Unique & Key Populations
- About



New and updated:

'HCV in Pregnancy' Updated

With the current increases in HCV among young adults, including women of childbearing age, there is now discussion about universal screening of pregnant women.

Search the Guidance

Start Here: Choose a patient profile from the menu above. ↑

Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a guidance section below, or use the search box to begin.

- + Contents and Introduction - *Select a Page*
- + Testing, Evaluation, and Monitoring of Hepatitis C - *Browse Topics*
- + Initial Treatment of HCV Infection - *Choose Patient Genotype*

Home

Test, Evaluate, Monitor

Treatment-Naive

Treatment-Experienced

Unique & Key Populations

About



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Enter your keywords

Search

Genotype 1

Genotype 2

Genotype 3

Genotype 4

Genotype 5 or 6

patient profile from the menu above. ↑

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Genotype 1

GT1a: No Cirrhosis

GT1a: Compensated

Genotype 3

GT1b: No Cirrhosis

Genotype 4

GT1b: Compensated

Genotype 5 or 6

click on a guidance section below, or use the search box to begin.

[+ Contents and Introduction - *Select a Page*](#)

[+ Testing, Evaluation, and Monitoring of Hepatitis C - *Browse Topics*](#)

[+ Initial Treatment of HCV Infection - *Choose Patient Genotype*](#)

menu above. ↑




rg


have created an updated web experience to facilitate

to this important resource. Please select a patient profile from the menu above,

www.hcvguidelines.org

Recommended and alternative regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis^a 

RECOMMENDED	DURATION	RATING 
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs ^b for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^c	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

Most Common HCV Treatment Naive Regimens In My (and Most) HCV Practices

Glecaprevir/pibrentasvir (Mavyret®)

- 3 tablets by mouth daily
- GT 1-6
- 8-12 weeks

Ledipasvir/sofosbuvir (Harvoni®)

- 1 tablet by mouth daily
- GT 1, 4, 5, 6
- 8-12 weeks

Sofosbuvir/velpatasvir (Epclusa®)

- 1 tablet by mouth daily
- GT 1-6
- 12 weeks



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Congratulations

- You cured Walter White of HCV, preventing him from breaking bad...

Key Points



HCV screening should be obtained in people born between 1945-1965 and those with risk factors... for now.



Clinical evaluation includes history physical, laboratory studies, and assessment of liver fibrosis.



HCV treatment may be selected based on genotype, fibrosis stage, and treatment experience status.



HCV treatment is relatively straightforward and highly effective!



Thank You!

Questions?

Cody.a.chastain@vumc.org