AETC AIDS Education & Training Center Program Southeast

All Hands on Deck: Taking on Hepatitis C in Tennessee

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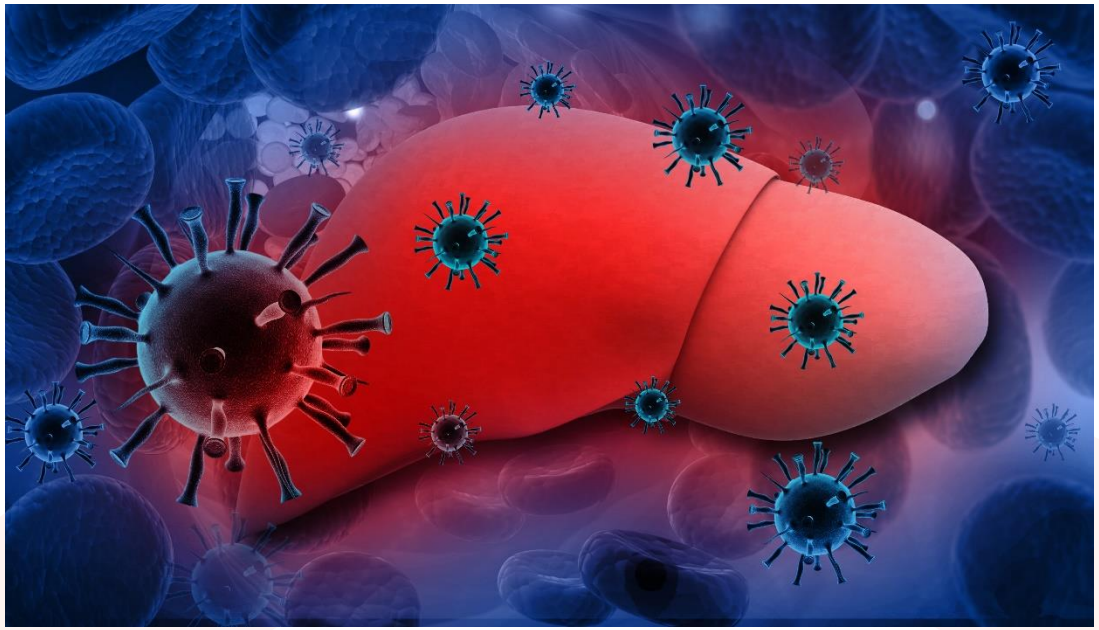
Disclosures

- Research supported by Gilead Sciences Inc.:
  - Site investigator for HIV/HCV SWITCH Registry Study
  - Key faculty personnel for Gilead FOCUS HCV Screening Program through Vanderbilt University Medical Center Emergency Department

Objectives

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

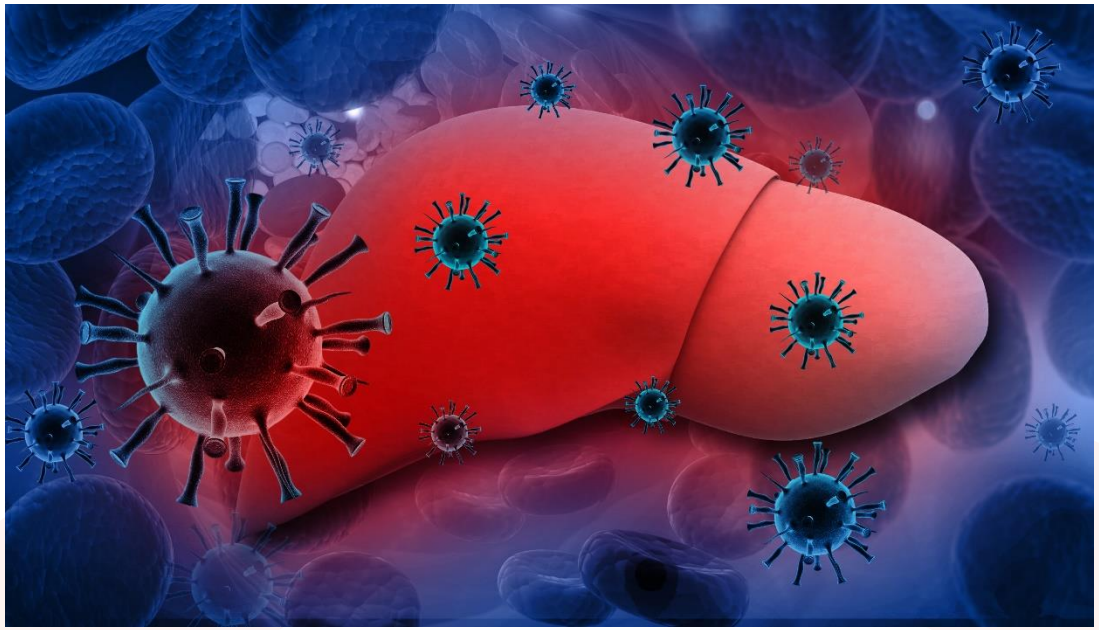
- Review trends in epidemiology of hepatitis C virus (HCV)
- Understand the indications for screening for HCV
- Identify the clinical manifestations of HCV
- Discuss the principles of and indications for treatment of HCV



My "Real" Objectives

At the end of this lecture, the learner will:

- Recognize HCV as an issue in his/her practice
- Agree that this is a major public health and individual health concern
- Identify appropriate screening approaches for his/her practice
- Consider options for engaging patients in HCV evaluation and treatment



Outline

- Epidemiology
- Screening and Diagnosis
- Natural History
- Advances in Treatment

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- Is this a problem for me in my practice?
- Should I care?
- What can be done about it?
- What should I do about it?

Outline

- **Is this a problem for me in my practice?**
- Should I care?
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Audience Response #1: Word Cloud

- What word(s) do you associated with HCV?

Two Cases

Bree

- 25 y/o young woman presents to establish primary care after recent delivery
- PMH: Gestational DM
- Social History: IV Opioid Abuse
- Labs: ALT 255, AST 105
- HCV Ab+, RNA+

Calvin

- 62 y/o engineer presents to establish care after moving to region
- PMH: Hypertension
- Social History: No substance use
- Labs: ALT 40, AST 28
- HCV Ab+, RNA+

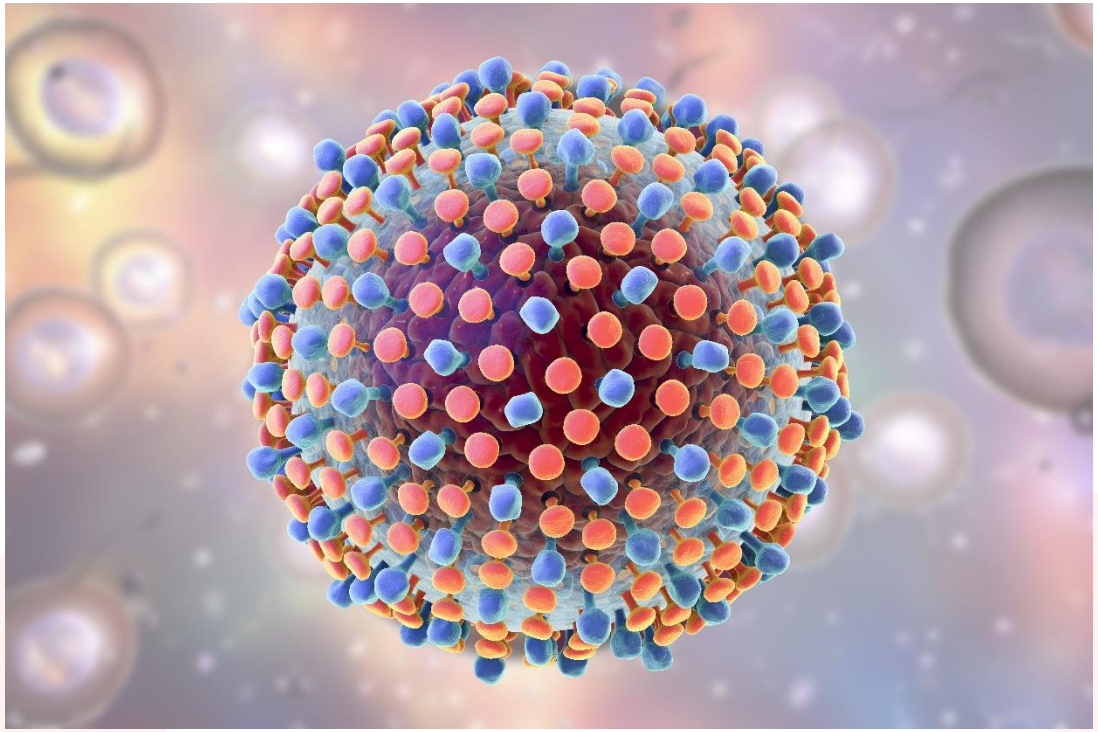
Hepatitis

- Hepatitis = inflammation of the liver

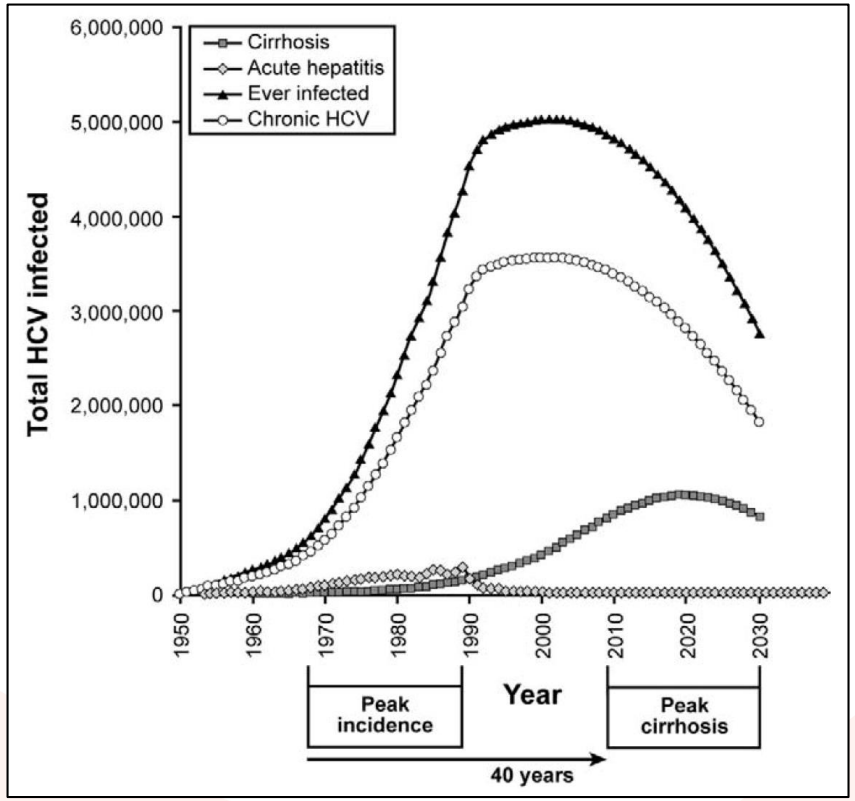
- Differential Diagnosis:
  - Hepatitis viruses
    - Hepatitis A (HAV)
    - Hepatitis B (HBV)
    - **Hepatitis C (HCV)**
  - HIV
  - Cytomegalovirus (CMV)
  - Alcohol
  - Drug and/or supplement toxicity
  - Obesity [leading to non-alcoholic fatty liver disease (NAFLD)]
  - Genetic disorders

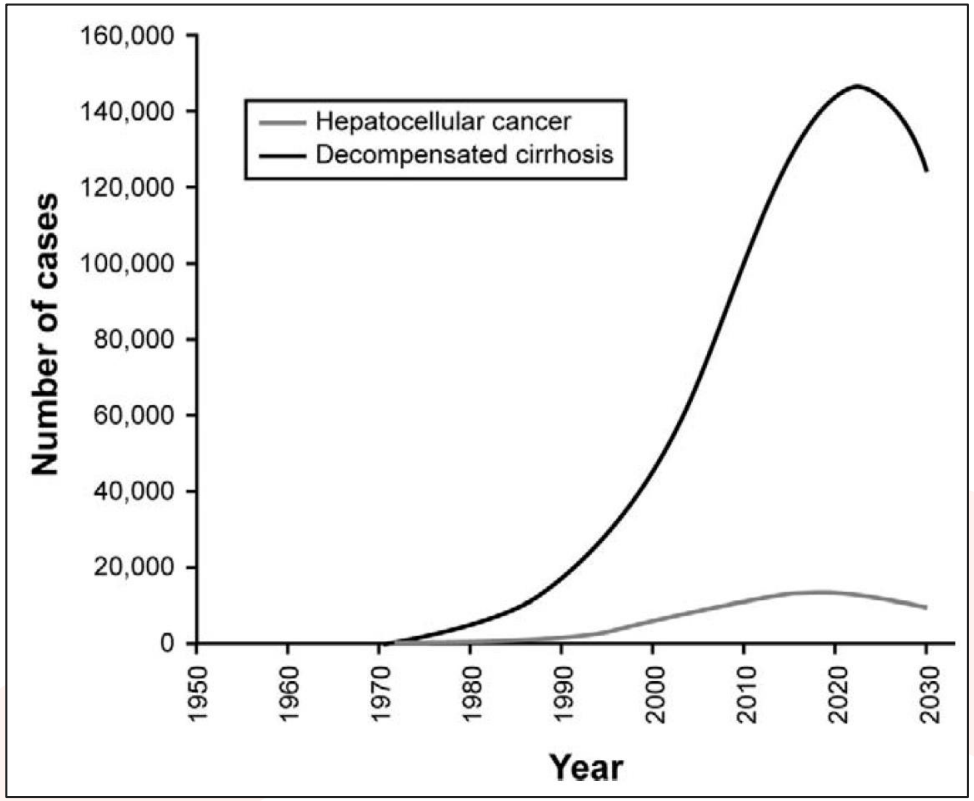
Hepatitis C Virus (HCV)

- Single-strand, positive sense RNA flavivirus
- Spread through blood and body fluids
- Predominantly infects liver cells
- No latent reservoir
  - I.e. no integration with host DNA as with HIV
  - I.e. no covalently closed DNA within host cells
  - I.e. can be eradicated/cured



HCV in the US





2.3-6 million Americans have chronic HCV infection

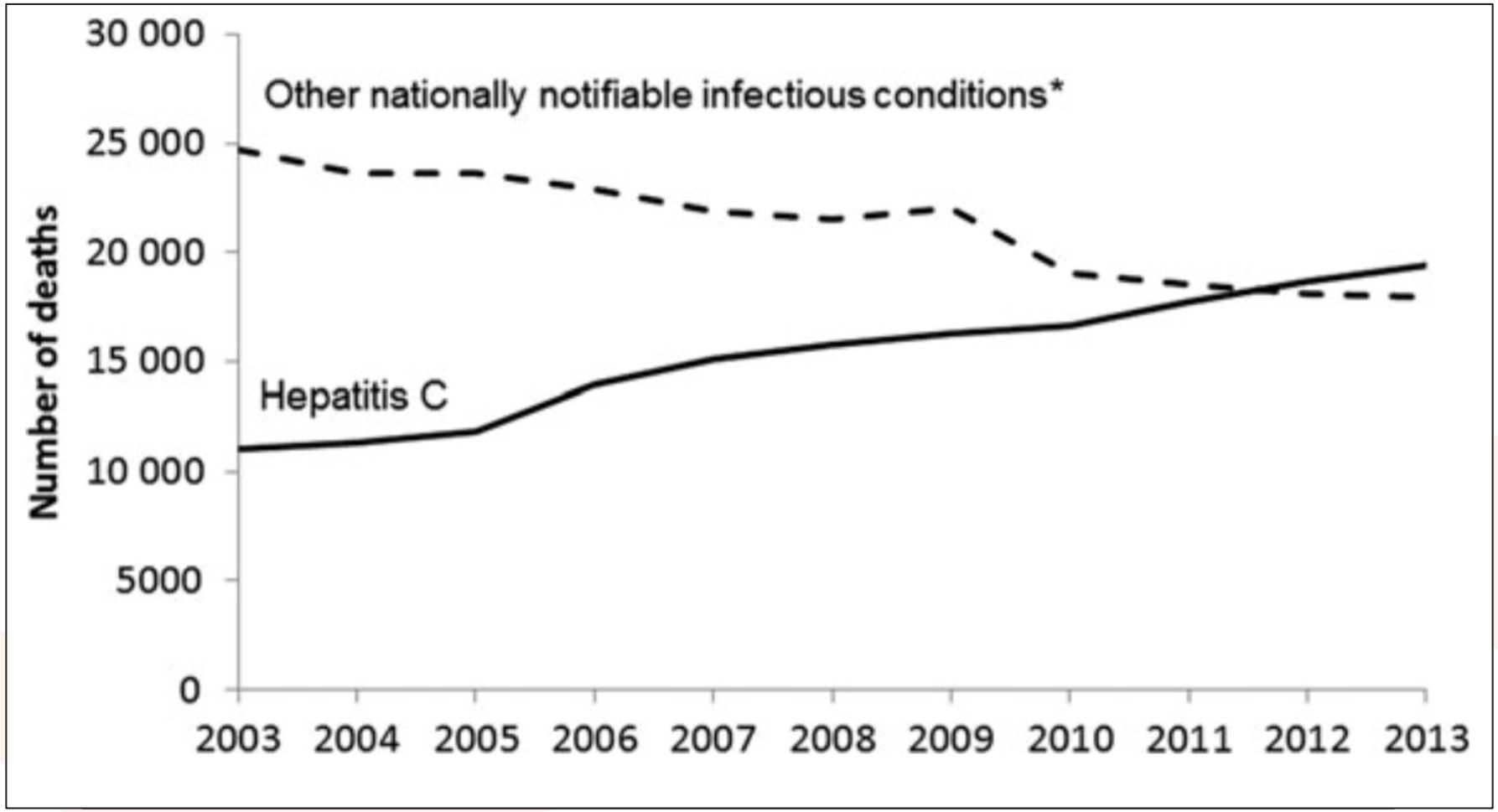
Davis GL et al. *Gastroenterology* 2010. // Ditah I et al J Hepatol 2014. // Edlin BR et al Hepatology 2015.

Audience Response #2: Multiple Choice

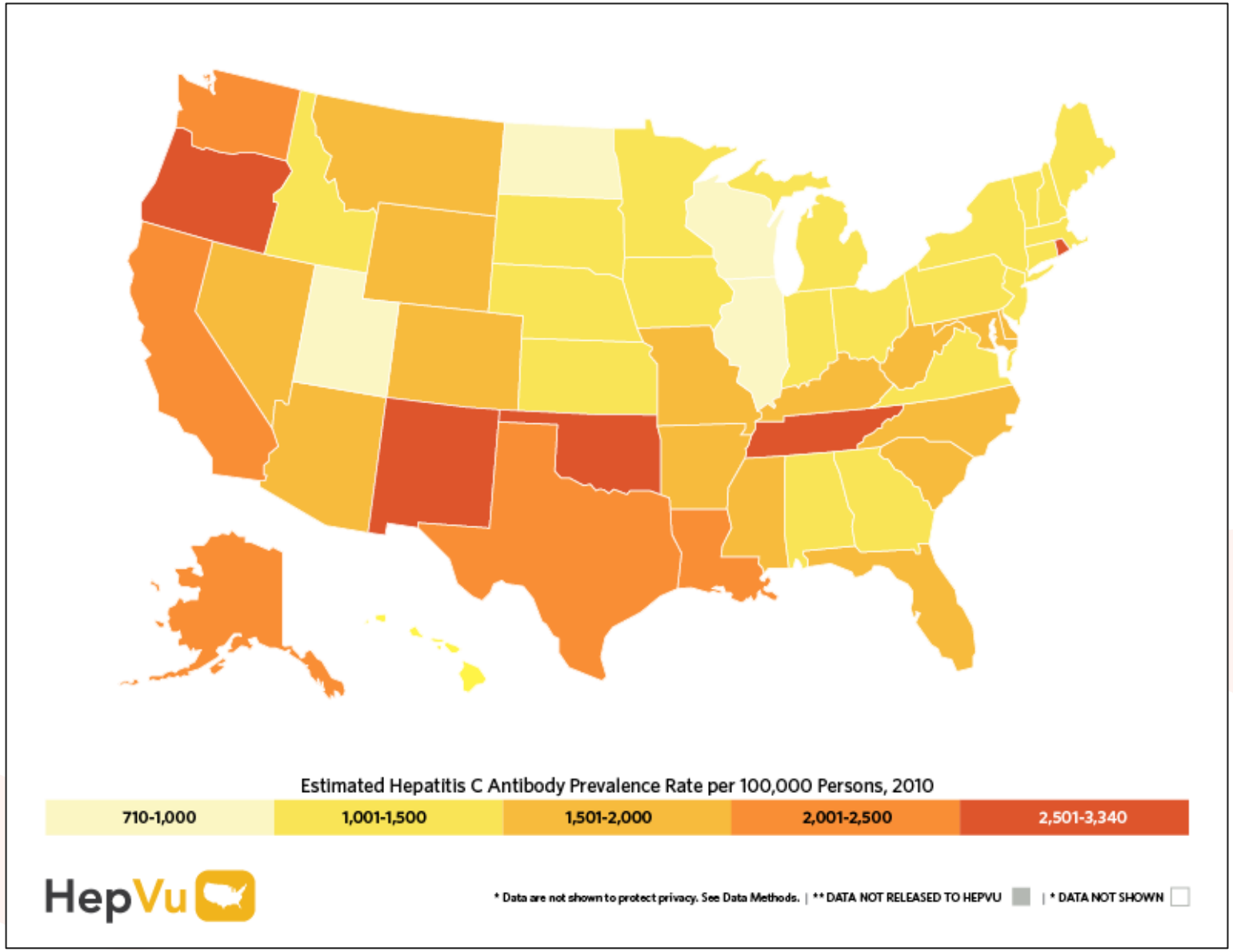
- What infectious disease(s) results in he most deaths each year in the United States?

A. Hepatitis B
B. Hepatitis C
C. HIV/AIDS
D. Tuberculosis
E. A, C, and D combined

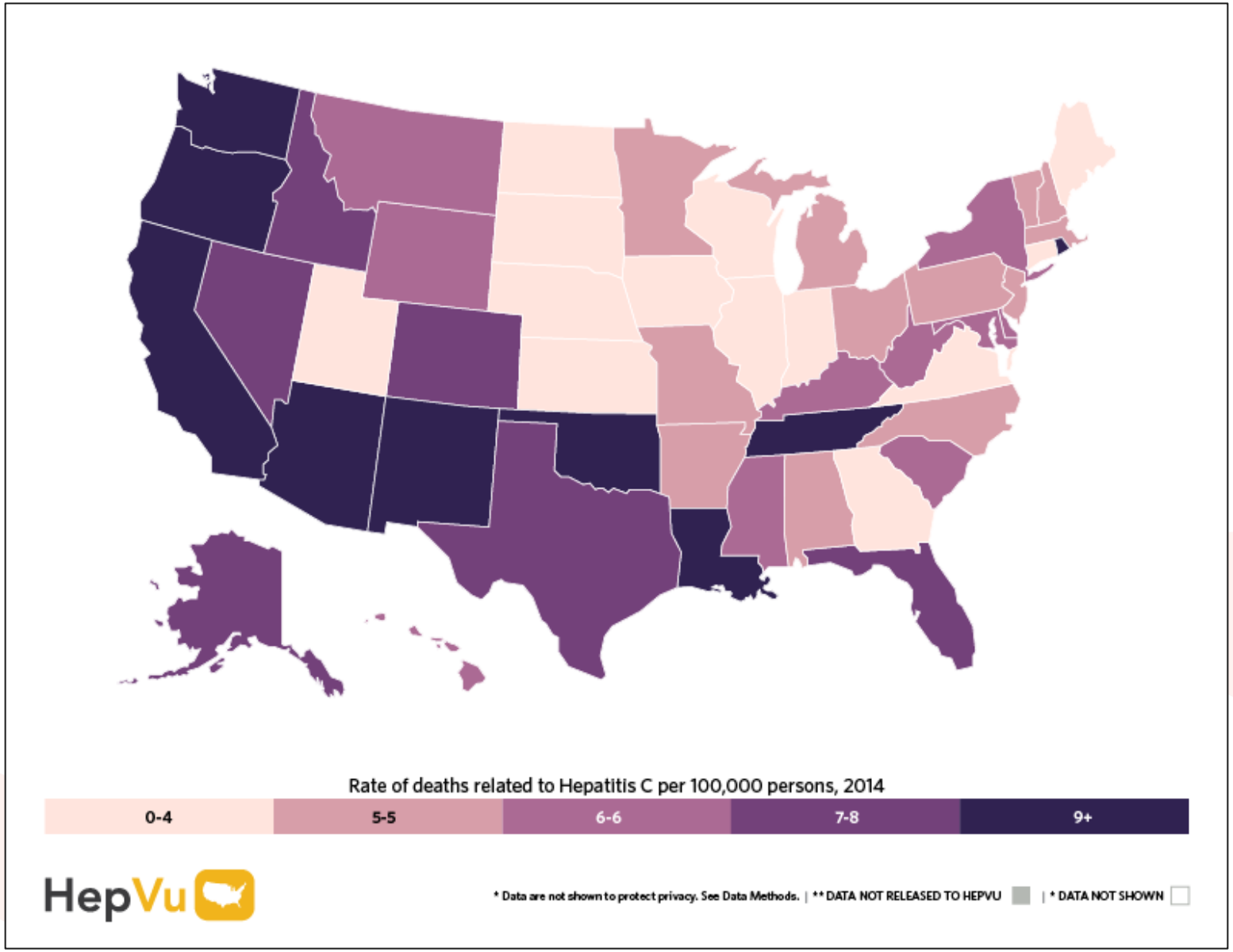
HCV and Mortality in the US



Ly KN et al. *Ann Int Med* 2012. // Ly KN et al. *Clin Infect Dis* 2016.



HepVu (www.hepvu.org). Emory University, Rollins School of Public Health.



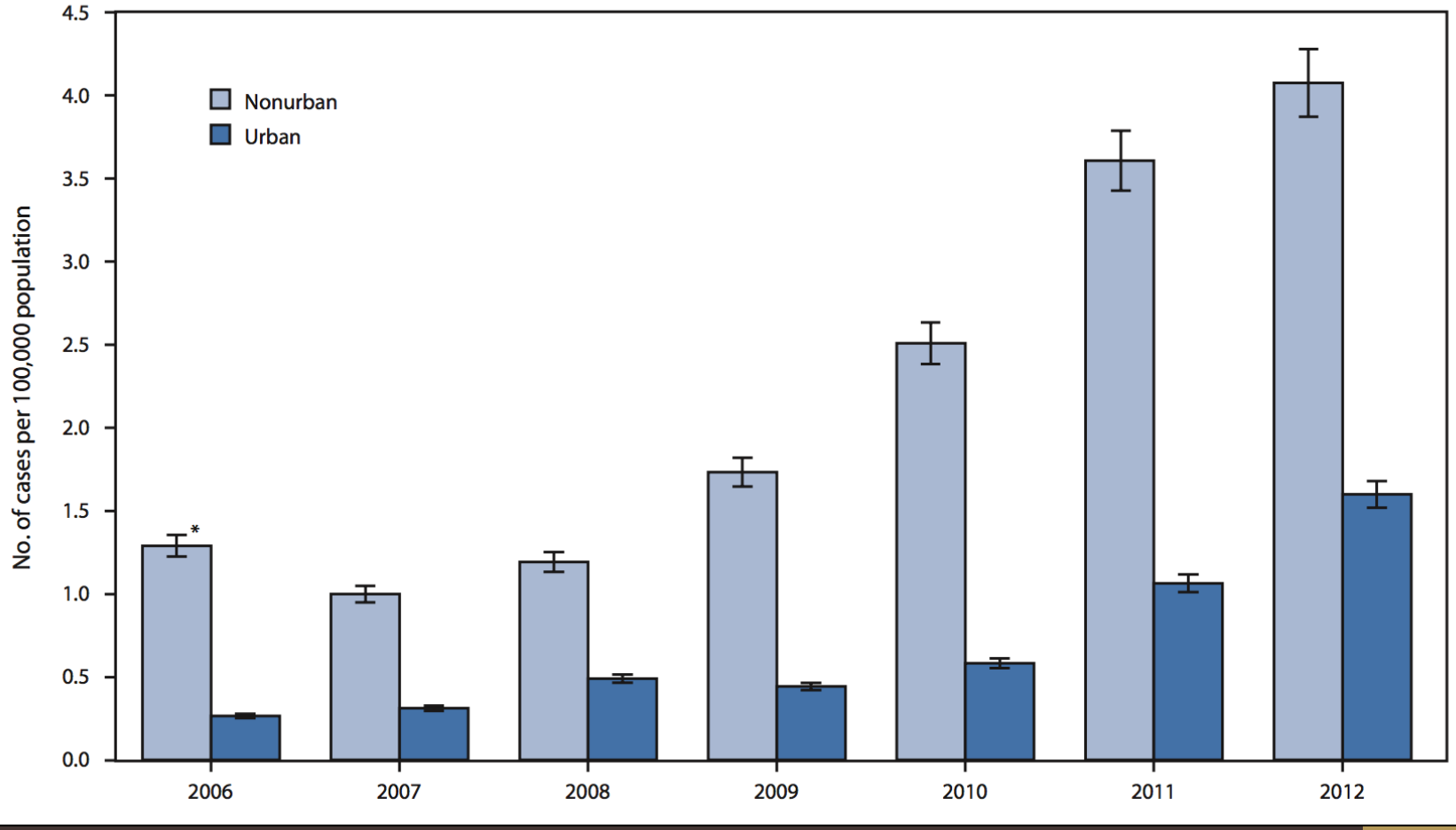
HepVu (www.hepvu.org). Emory University, Rollins School of Public Health.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 64 / No. 17
May 8, 2015

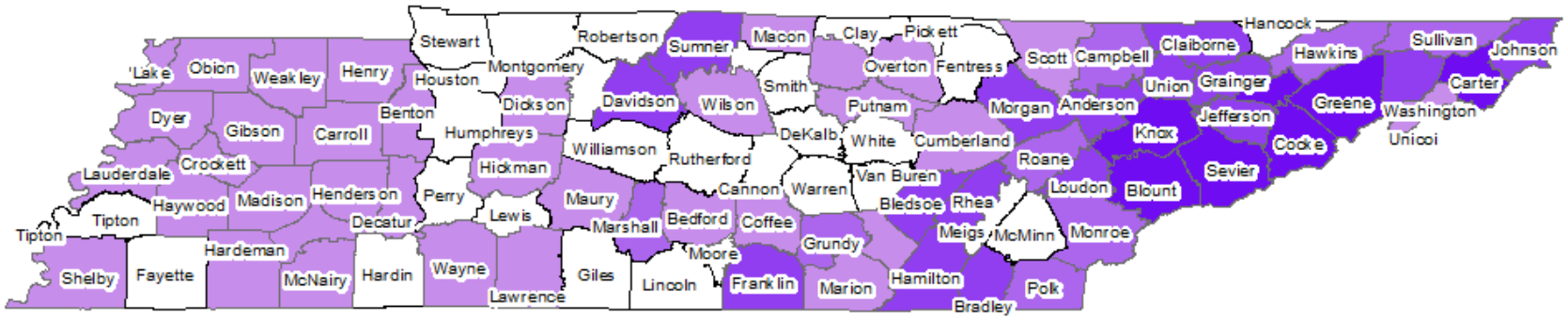
Increases in Hepatitis C Virus Infection Related to Injection Drug Use Among Persons Aged ≤30 Years — Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012

Jon E. Zibbell, PhD[1], Kashif Iqbal, MPH[1], Rajiv C. Patel, MPH[1], Anil Suryaprasad, MD[1], Kathy J. Sanders, MSN[2], Loretta Moore-Moravian[3], Jamie Serrecchia, MPA[4], Steven Blankenship, MS[5], John W. Ward, MD[1], Deborah Holtzman, PhD[1] (Author affiliations at end of text)

FIGURE 1. Incidence of acute hepatitis C among persons aged ≤30 years, by urbanicity and year — Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012



Acute Cases of Hepatitis C in Tennessee by Case Count 2011-2015



Case Count
n=630

- 0.0
- Less than 5
- 5.1 - 10.0
- 10.1 - 25.0
- 25.1 - 54.0

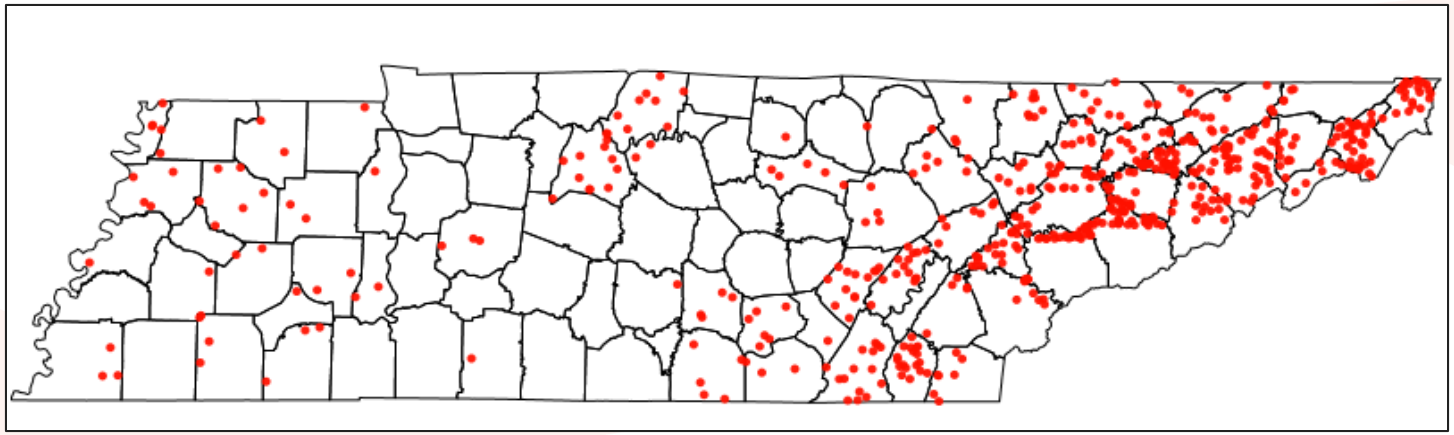
TN Department of Health

Map Created by Viral Hepatitis Surveillance
Data Source: NBS, accessed April 2016
Method: Manual, 5 Classes
Map Created April 25, 2016

Courtesy of Michael Rickles and Lindsey Sizemore, Tennessee Department of Health.

Reported Cases of Acute HCV in Tennessee

		2011	2012	2013	2014	2015
US	case rate	0.4	0.6	0.7	0.7	0.8
	cases	1,229	1,778	2,138	2,194	2,436
TN	case rate	1.3	2.0	1.5	1.9	2.6
	cases	83	129	98	123	173
	rank	**4th**	**4th**	**6th**	**5th**	**4th**



http://www.cdc.gov/hepatitis/statistics/2015surveillance/pdfs/2015hepsurveillancerpt.pdf

* per 100,000 population

Courtesy of Michael Rickles and Lindsey Sizemore, Tennessee Department of Health.

TN Primary Care Panel Estimates

Low Estimate

- 1,000 patient panel
- 1.5% prevalence
  - 1,500/100,000 patients
  - National estimate
- ***15 patients are HCV Ab positive***

High Estimate

- 2,500 patient panel
- 3.0% prevalence
  - 3,000/100,000 estimate
  - High estimate for TN
- ***75 patients are HCV Ab positive***

Takeaway Message #1

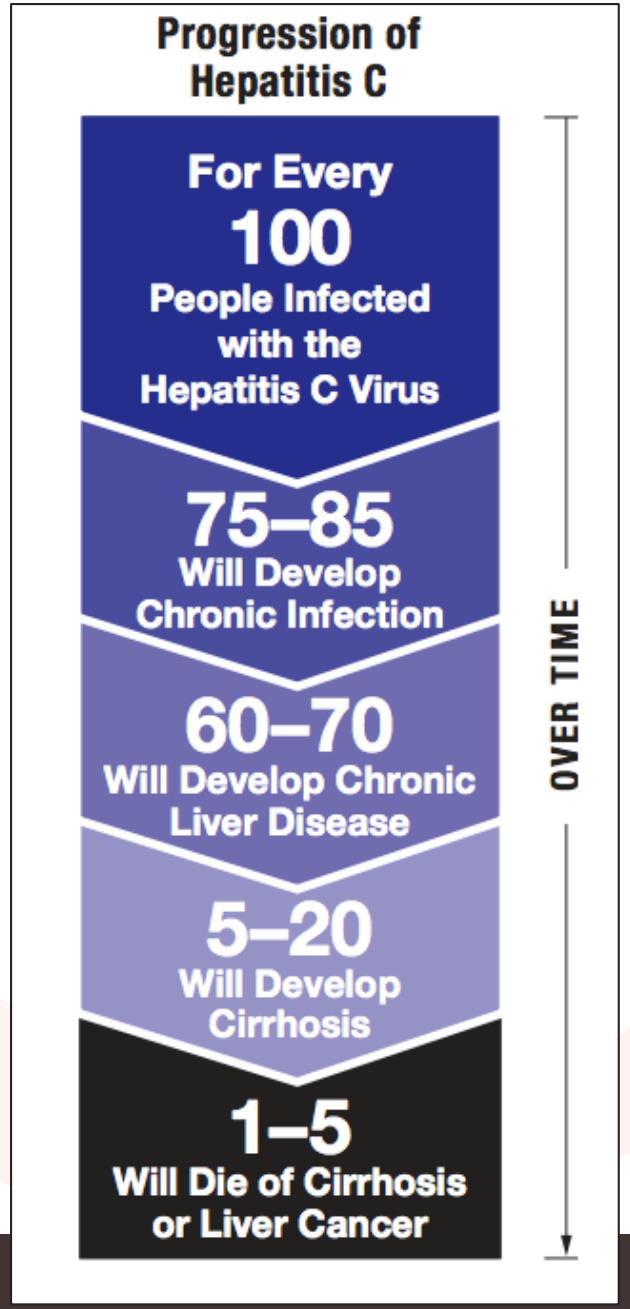
HCV is a major public health issue in the US, in Tennessee, and likely within your own practice of medicine.

Outline

- Is this a problem for me in my practice?
- **Should I care?**
- What can be done about it?
- What should I do about it?

Manifestations of HCV

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



Natural History of HCV

- Cirrhosis usually takes years to develop in the absence of comorbidities
- Timeline may be accelerated by comorbidities, including
  - Alcohol use
  - HBV and/or HIV co-infection
  - Immunosuppression
  - Obesity
  - Insulin resistance

Immune-related extrahepatic manifestations

- Mixed cryoglobulinemia
- Cryoglobulinemic vasculitis
- B-cell NHL
- Sicca syndrome
- Arthralgia/myalgia
- Autoantibody production (i.e. cryoglobulins, rheumatoid factor, and antinuclear, anticardiolipin, antithyroid and anti-smooth muscle antibodies)
- Polyarteritis nodosa
- Monoclonal gammopathies
- Immune thrombocytopenia

Inflammatory-related extrahepatic manifestations

- Type 2 diabetes mellitus type 2
- Insulin resistance
- Glomerulonephritis
- Renal insufficiency
- Fatigue
- Cognitive impairment
- Depression
- Impaired quality of life
- Polyarthritis/fibromyalgia
- Cardiovascular disorders (i.e. stroke, ischemic heart disease)

Cacoub P et al. *Ther Adv Infect Dis* 2016.

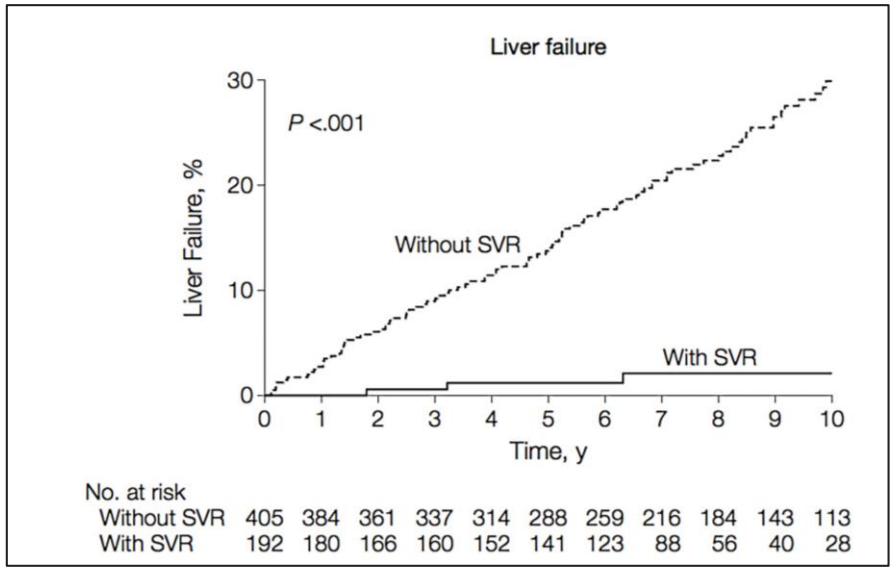
Takeaway Message #2

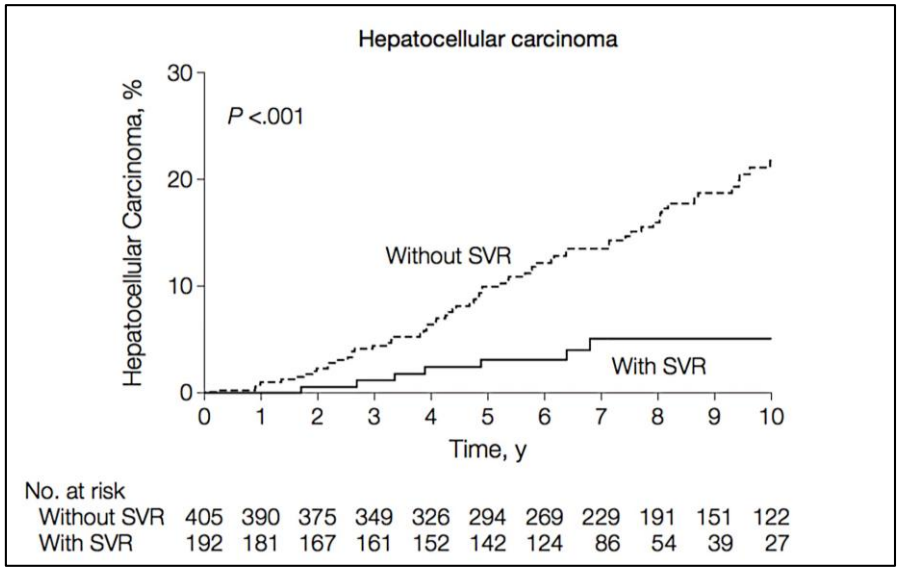
HCV-related morbidity and mortality due to both hepatic and extrahepatic disease processes are significant and numerous.

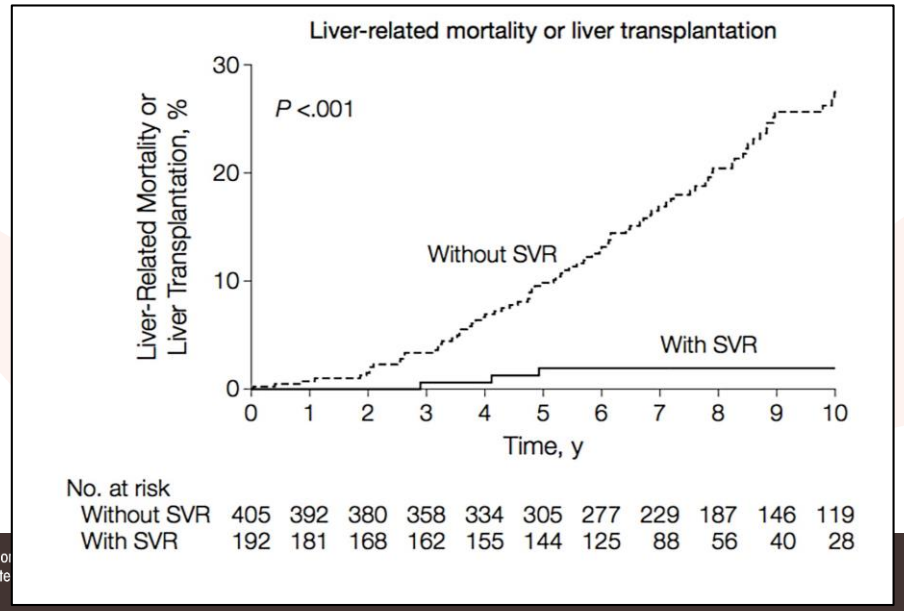
Outline

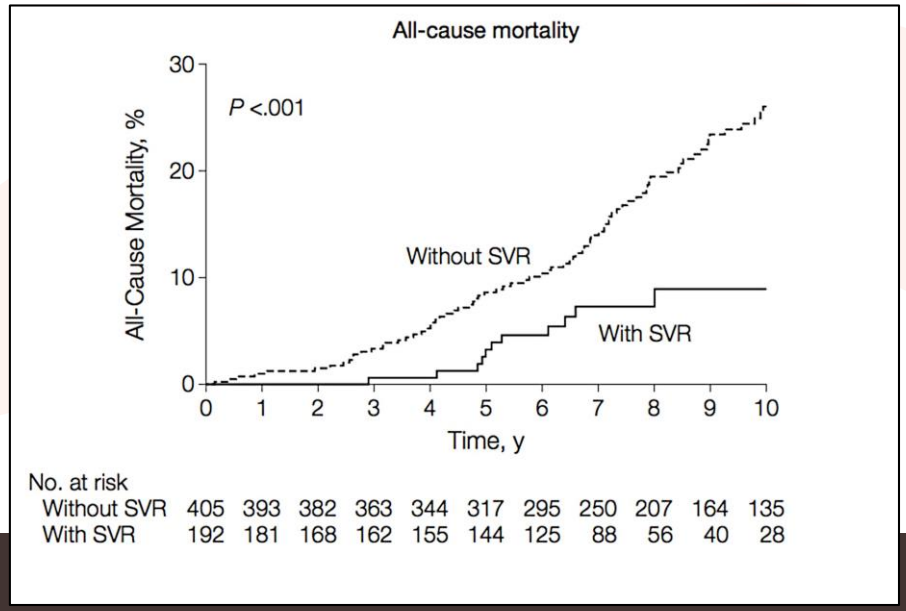
- Is this a problem for me in my practice?
- Should I care?
- **What can be done about it?**
- What should I do about it?

How Does Treatment Impact HCV Outcomes?



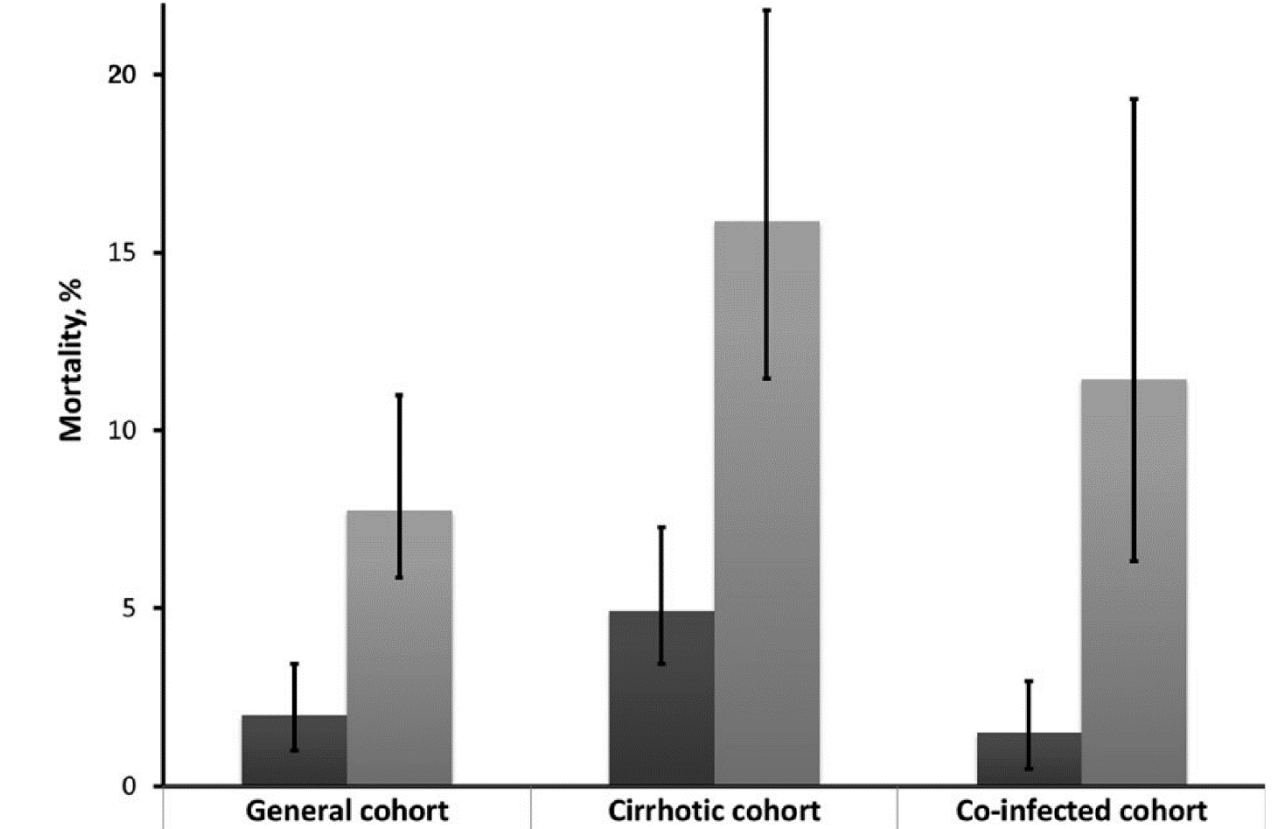






Van der Meer AJ et al. *JAMA* 2012.

How Does Treatment Impact HCV Outcomes? Cont.



	General cohort	Cirrhotic cohort	Co-infected cohort
SVR	1.98 (1.00, 3.45)	4.90 (3.45, 7.28)	1.49 (0.50, 2.96)
non-SVR	7.75 (5.86, 10.98)	15.88 (11.44, 21.80)	11.44 (6.33, 19.31)

Figure 1. Five-year mortality rates (95% confidence interval) for sustained virologic response (SVR) vs non-SVR groups for each cohort.

Simmons B et al. *Clin Infect Dis* 2015.

How Does HCV Treatment Impact Other Disease Outcomes?

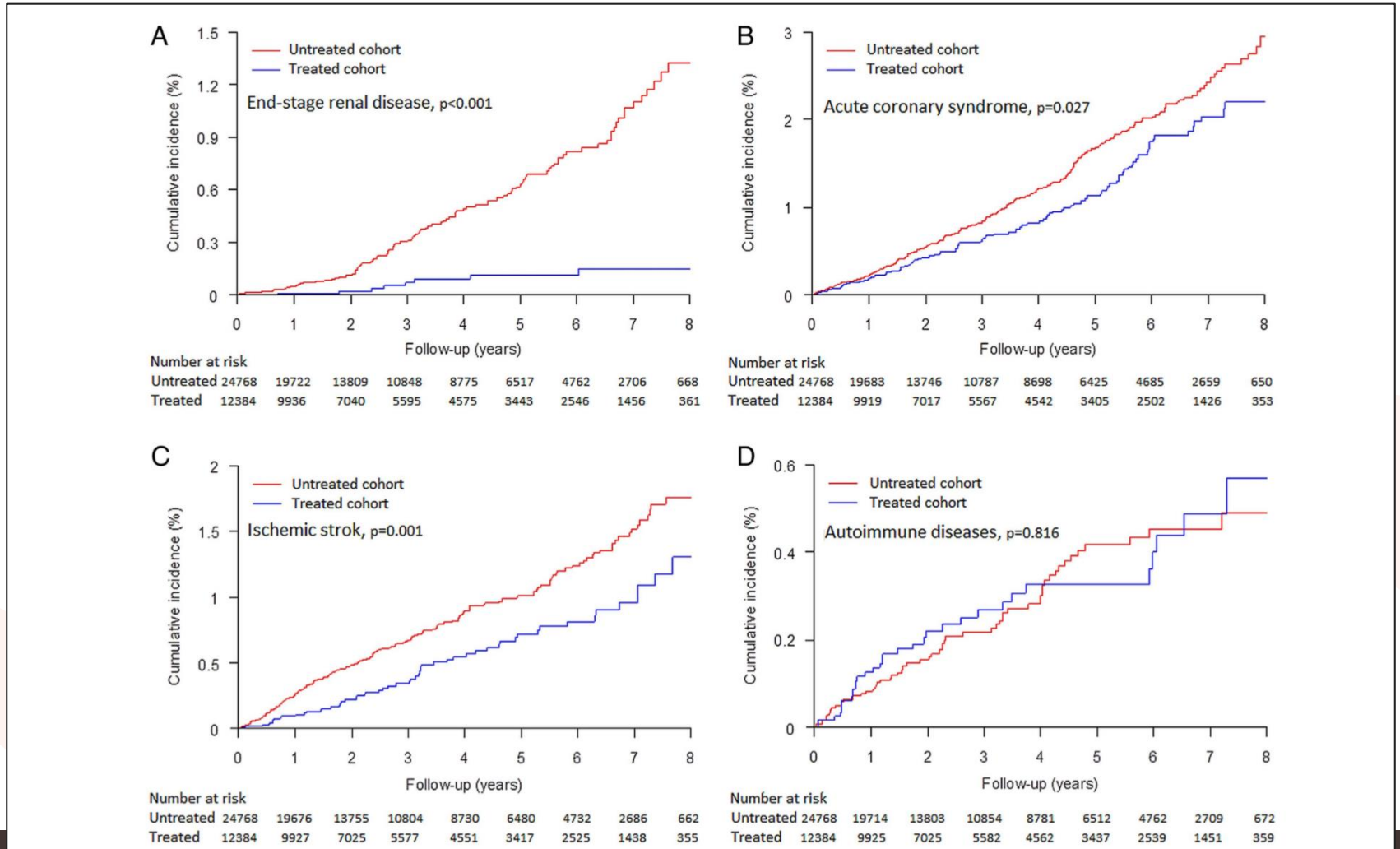


Figure 3 Cumulative incidence of extrahepatic outcomes between the treated and untreated cohorts: end-stage renal disease (A), acute coronary syndrome (B), ischaemic stroke (C), and autoimmune diseases (D); death was managed as a competing cause of risk.

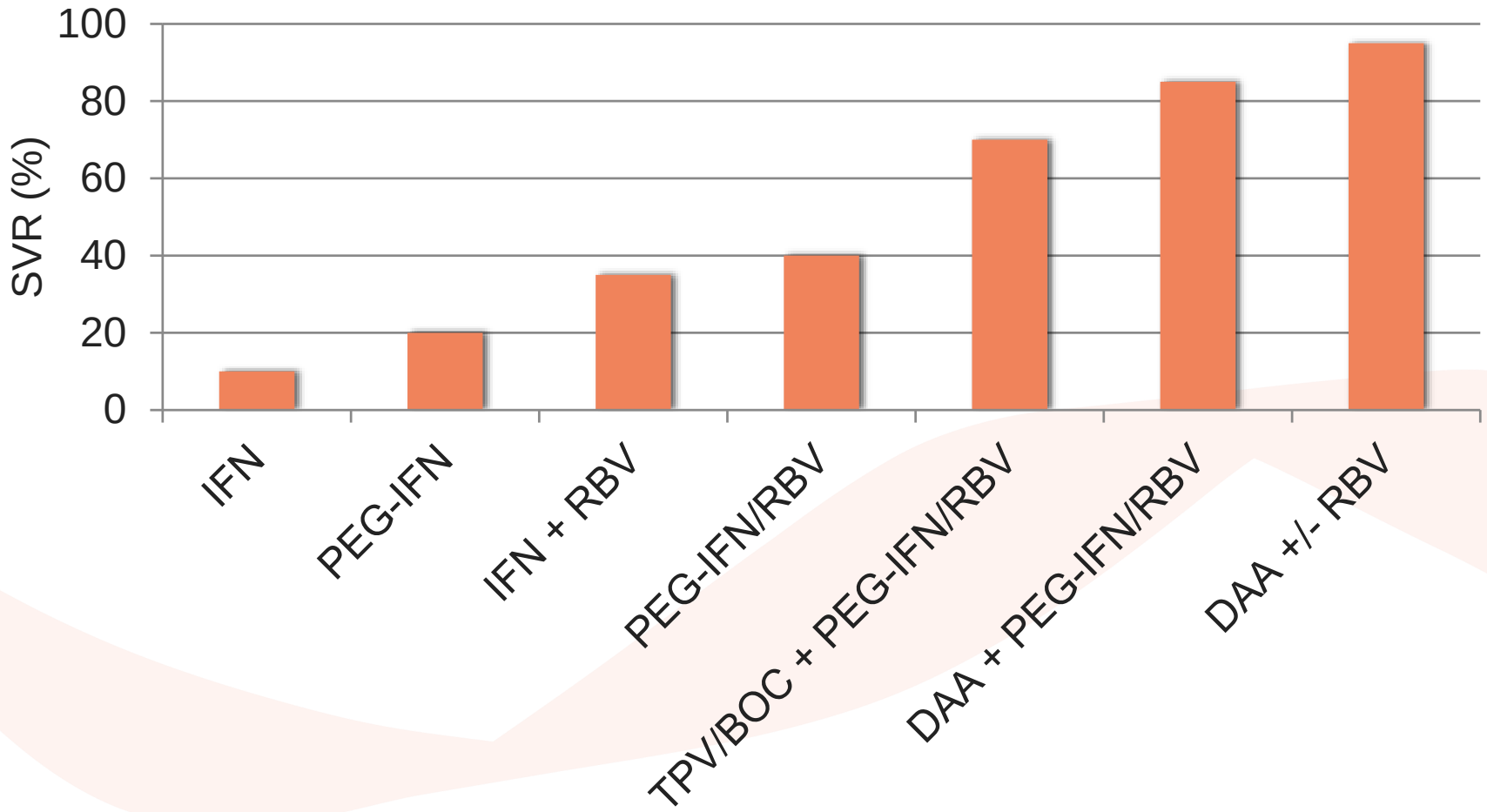
Hsu Y-C et al. *Gut* 2015.

In Sum: Why Should We Treat HCV?

- Improved quality of life
- Improved work productivity
- Improved outcomes of non-hepatic conditions
- Lower liver-related and all-cause mortality
- Treatment is recommended for **ALL** patients with chronic HCV (except those with short life expectancies due to unrelated causes)

Smith-Palmer J et al. *BMC Inf Dis* 2015. // Nahon P et al. *Gastroenterology* 2017. // www.hcvguidelines.org.

Treatment Response in Direct Acting Antiviral (DAA) Era



Slide courtesy of and adapted from Dr. Susanna Naggie

Audience Response #3

- How many HCV medications have been approved by the Food and Drug Administration (FDA) since the introduction of new direct acting antivirals (DAAs)?

A. 5
B. 8
C. 10
D. 12
E. 15

HCV Approved Agents

FDA Approved Therapies 1/2014

Interferon (1986)
Ribavirin (1998)
Pegylated Interferon (2001)
Telaprevir (2011)
Boceprevir (2011)
Simeprevir (2013)
Sofosbuvir (2013)

Since Then

Ledipasvir (2014)
Paritaprevir (2014)
Ombitasvir (2014)
Dasabuvir (2014)
Daclatasvir (2015)
Elbasvir (2016)
Grazoprevir (2016)
Velpatasvir (2016)
Voxilaprevir (July 2017)
Glecaprevir (August 2017)
Pibrentasvir (August 2017)

FDA Approved HCV Therapies (9/2017)

Nonspecific Antivirals

Interferon (IFN)
Ribavirin (RBV)
Pegylated Interferon (PEG-IFN)

NS3/4 Protease Inhibitors

Telaprevir (TPV)
Boceprevir (BPV)
Simeprevir (SMV)
Paritaprevir (PTV)
Grazoprevir (GZP)
Voxilaprevir (VOX)
Glecaprevir (GLE)

NS5A Inhibitors

Ledipasvir (LDV)
Ombitasvir (OBV)
Daclatasvir (DCV)
Elbasvir (EBV)
Velpatasvir (VEL)
Pibrentasvir (PIB)

NS5B Polymerase Inhibitors

Sofosbuvir (SOF)
Dasabuvir (DBV)

Takeaway Message #3

Nearly all patients may be treated with a simple, non-IFN, non-RBV regimen with minimal side effects and >90% cure rate.

Outline

- Is this a problem for me in my practice?
- Should I care?
- What can be done about it?
- **What should I do about it?**

Why Were They Screened for HCV?

Bree

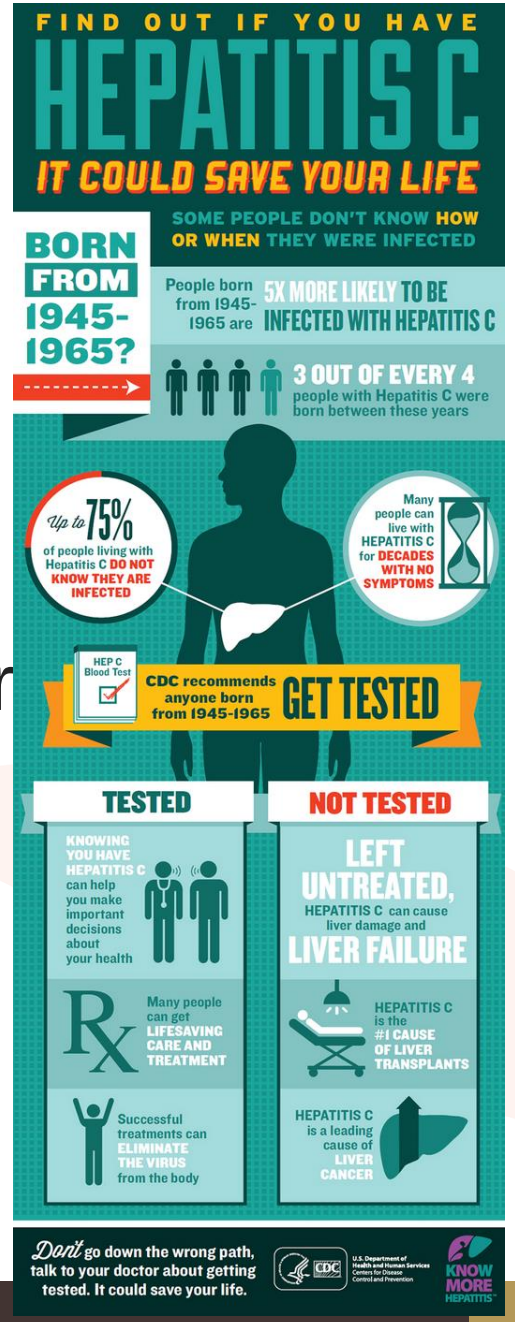
- 25 y/o young woman presents to establish primary care after recent delivery
- PMH: Gestational DM
- Social History: IV Opioid Abuse
- Labs: ALT 255, AST 105

Calvin

- 62 y/o engineer presents to establish care after moving to region
- PMH: Hypertension
- Social History: No substance use
- Labs: ALT 40, AST 28

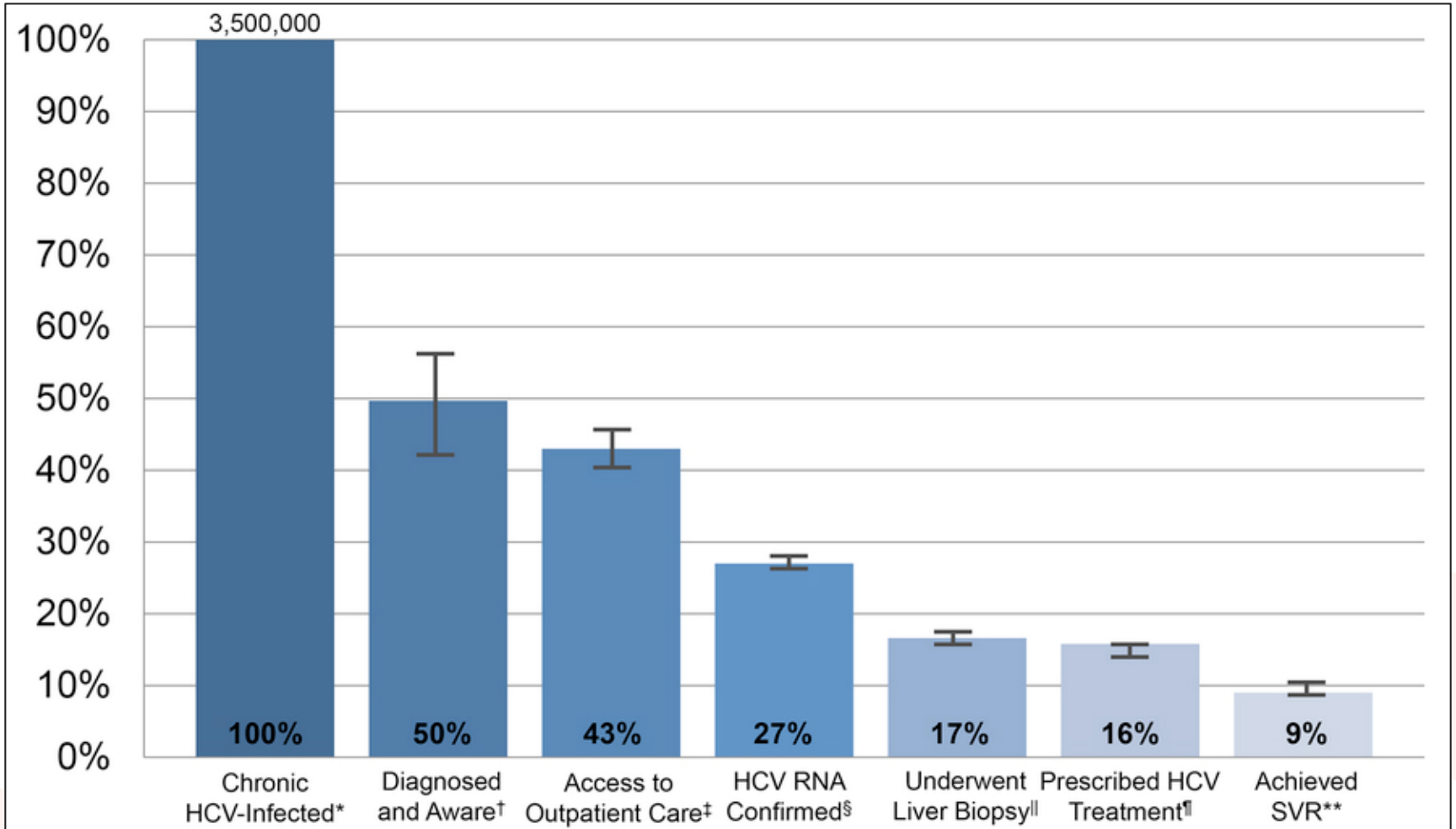
Who is at Risk for HCV?

- IV drug users
- Tattoo/piercing recipients
- Blood/clotting protein recipients prior to 1992
- Mother-to-child transmission from HCV+ mother
- Hemodialysis patients
- People with HIV
- Occupational exposures
- Born between 1945-1965 (“baby boomers”)



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



* 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.

Yehia BR et al. *PLoS One* 2014.

Takeaway Message #4

Effective screening and diagnosis is essential to impacting the HCV epidemic.

Screen patients for HCV based on risk factors and/or the "baby boomer" age cohort (born between 1945 and 1965).

Screen patients with an HCV antibody test. Confirm active/chronic infection with an HCV RNA polymerase chain reaction (PCR) test.

Interested in Treating?

- New diagnostic testing makes it easier to assess HCV than ever before.
- New therapies have streamlined approach to HCV treatment.
- Multiple training resources available for provider education for those interested in treating HCV directly.
- Email me!
  - Cody.A.Chastain@Vanderbilt.edu

Summary

- HCV is a major cause of morbidity and mortality in our country, region, and state.
- Treatment of HCV can improve many patient outcomes.
- New treatments are well tolerated and dramatically effective.
- Screening, diagnosis, and treatment are critical to impacting the HCV epidemic.

Thank You!

Questions?

Cody.A.Chastain@Vanderbilt.edu