



# Hepatitis C Update: *What's New in 2017*

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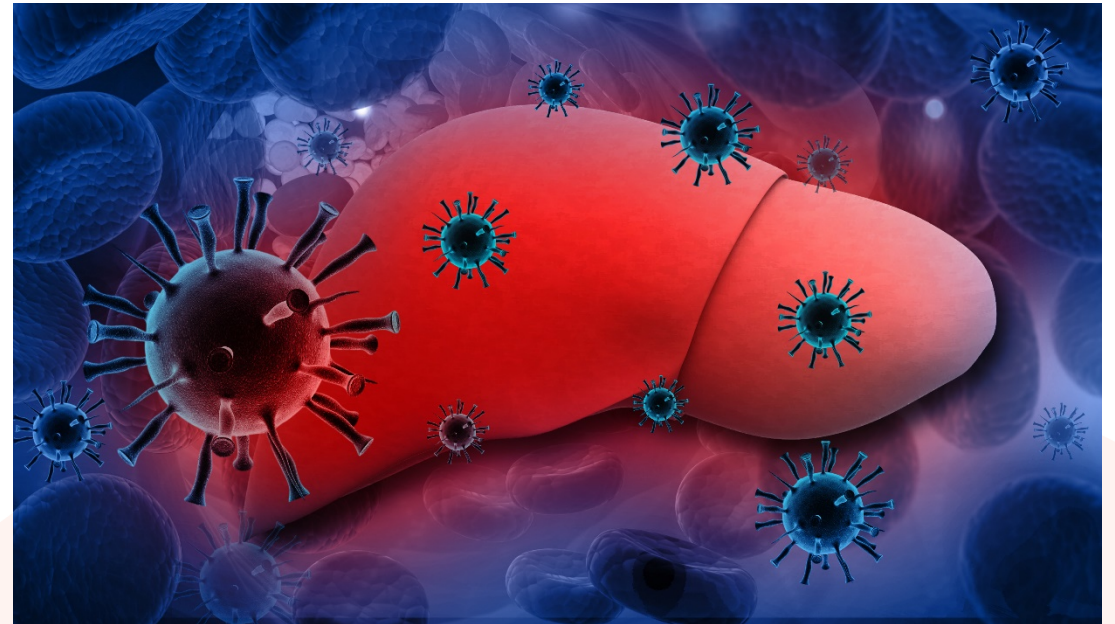
# Disclosures

- 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:

- Understand the evolution of hepatitis C virus (HCV) epidemiology
- Identify newly approved therapies and their role in treating HCV
- Discuss the current and future challenges in addressing the HCV epidemic

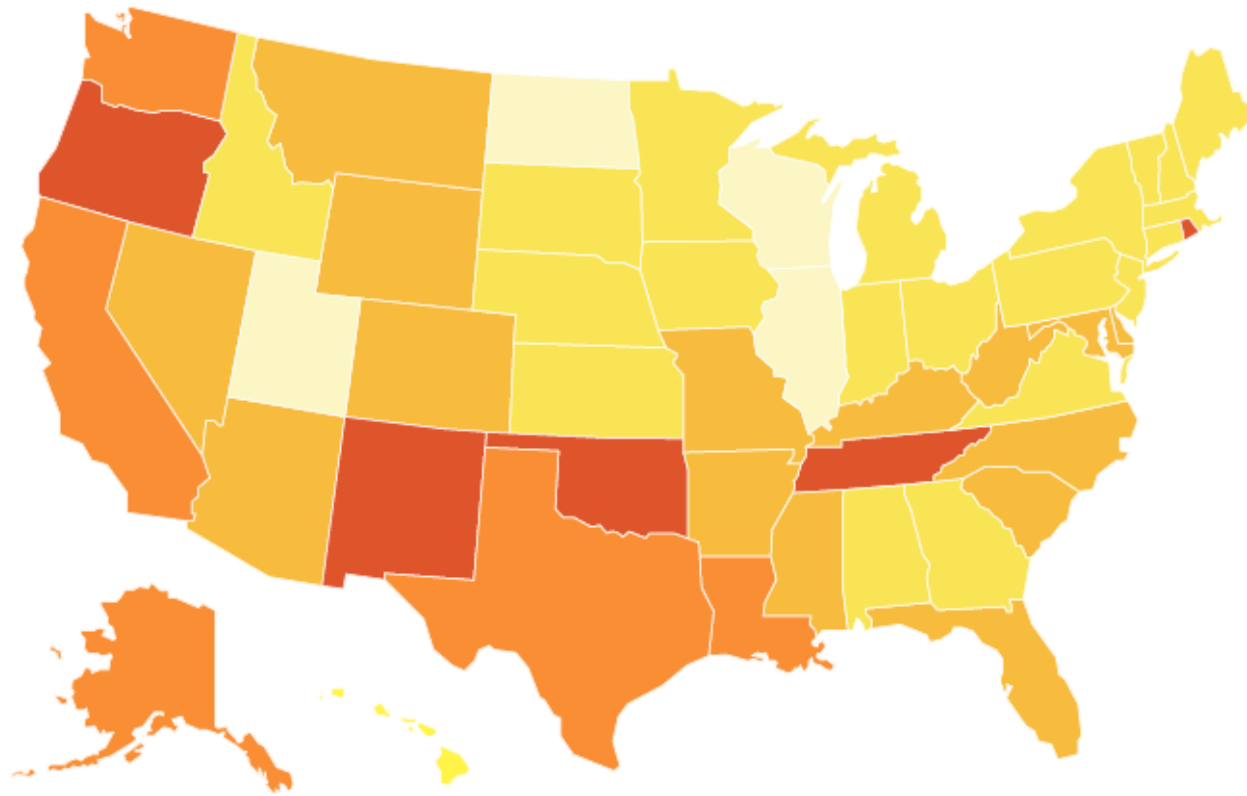


# Outline

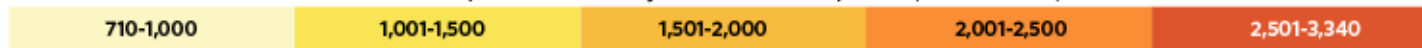
- Epidemiology
- New Therapies
- Current and Future Challenges

# Outline

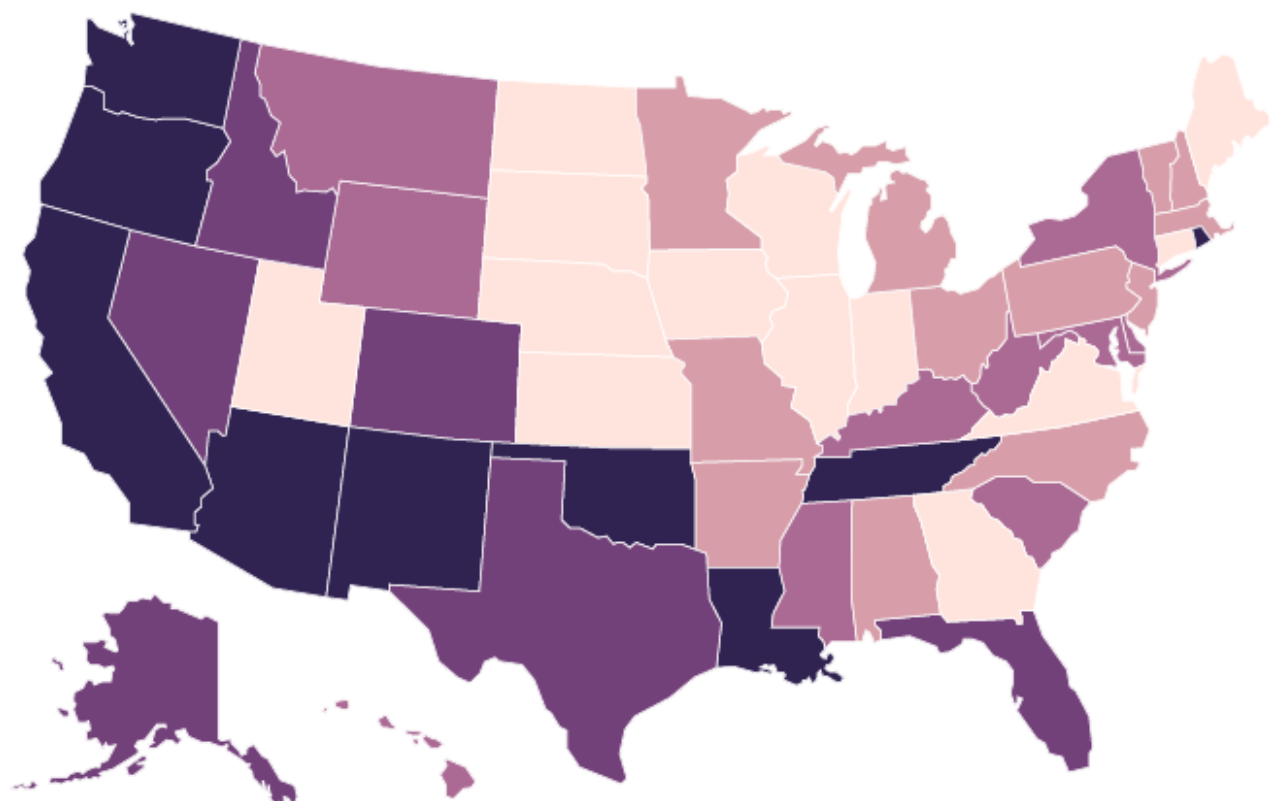
- **Epidemiology**
- **New Therapies**
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Estimated Hepatitis C Antibody Prevalence Rate per 100,000 Persons, 2010



\* Data are not shown to protect privacy. See Data Methods. | \*\* DATA NOT RELEASED TO HEPVU  | \* DATA NOT SHOWN



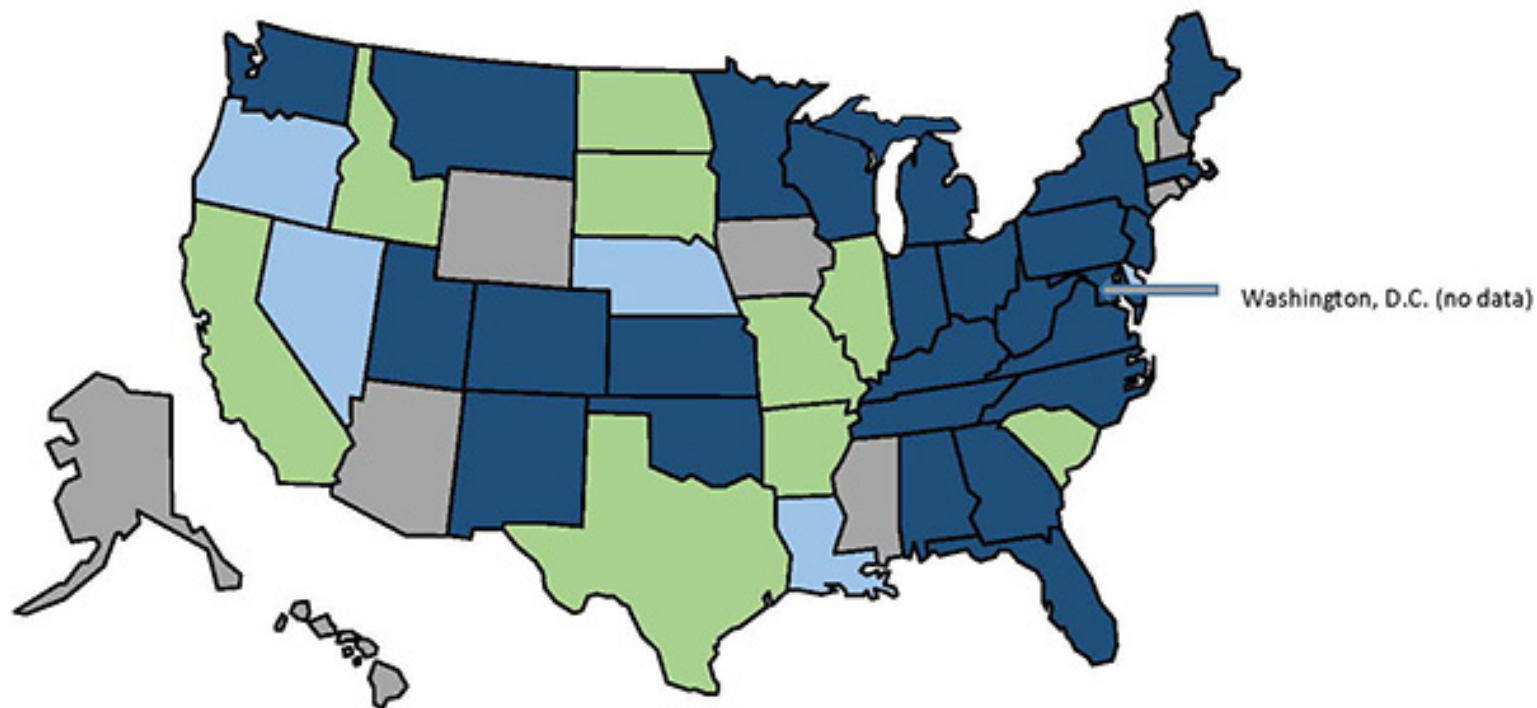
Rate of deaths related to Hepatitis C per 100,000 persons, 2014



\* Data are not shown to protect privacy. See Data Methods. | \*\* DATA NOT RELEASED TO HEPVU | \* DATA NOT SHOWN

### Map 4.1. 2015 State Acute Hepatitis C Incidence Compared to Healthy People 2020 National Goal\*

- At or below national goal
- Above national goal
- More than twice national goal
- Data unavailable

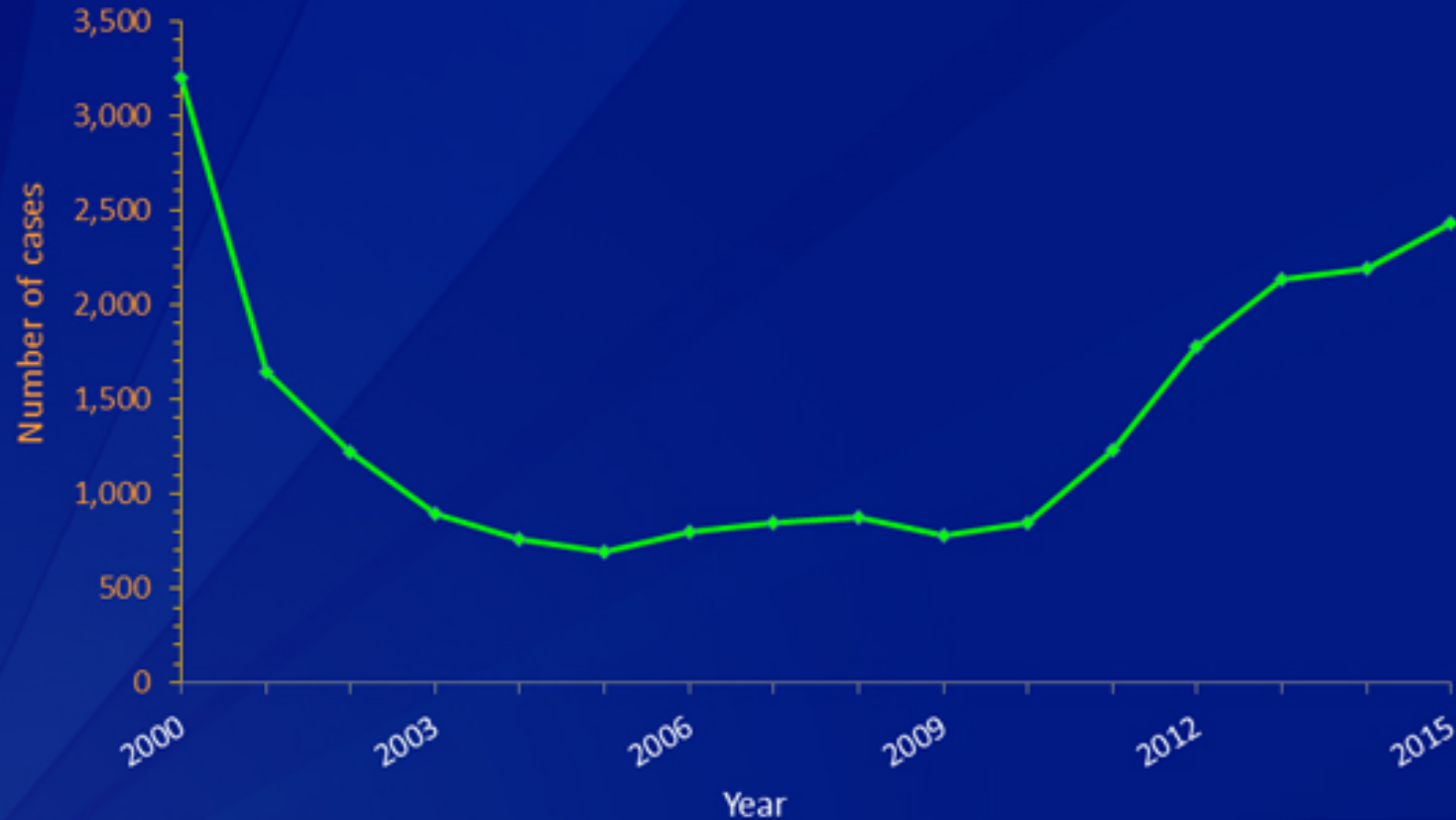


Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)

\*National goal: 0.25 cases/100,000 population



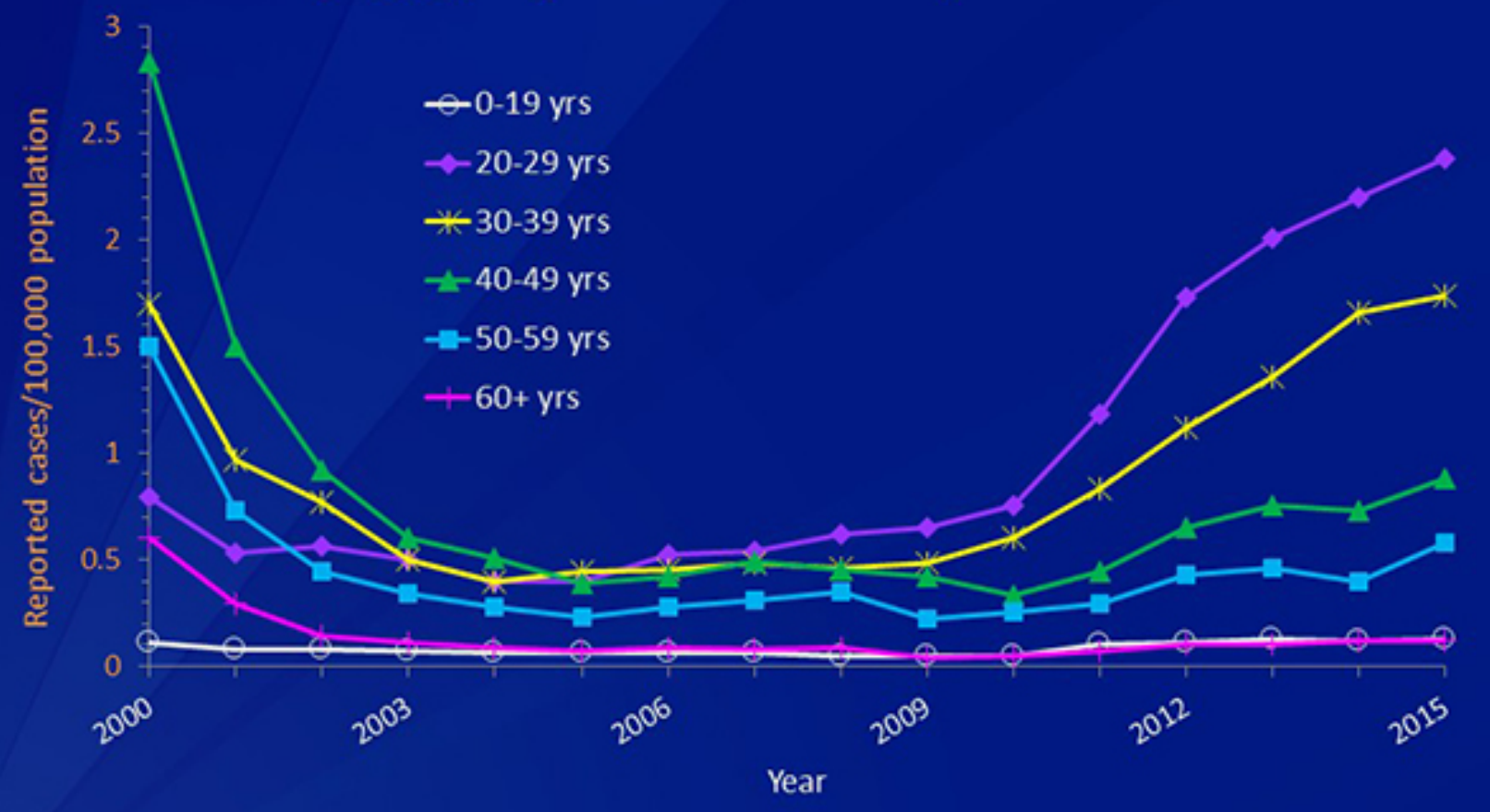
**Figure 4.1. Reported number of acute hepatitis C cases — United States, 2000–2015**



Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)



**Figure 4.2. Incidence of acute hepatitis C, by age group — United States, 2000–2015**



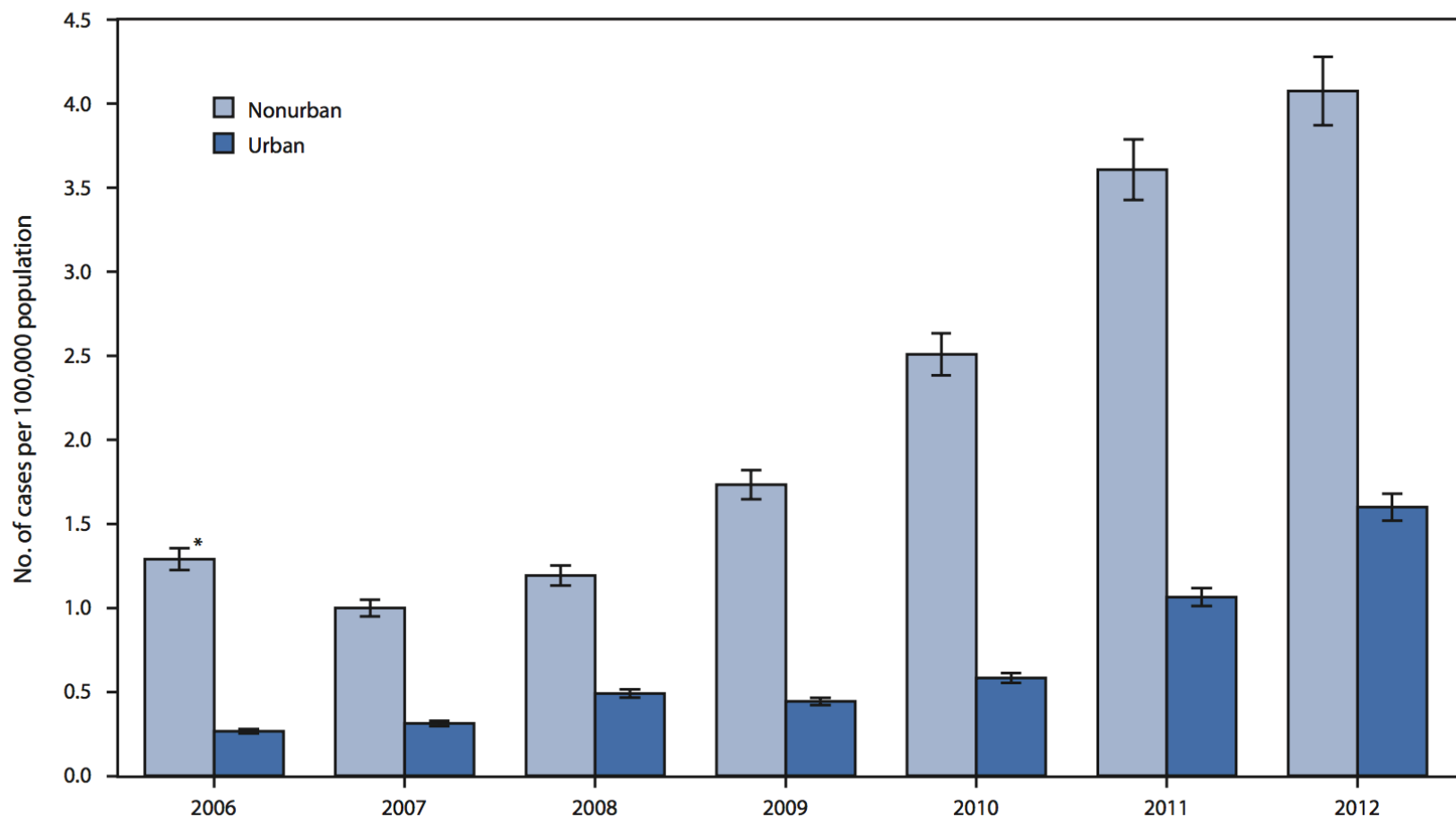
Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)



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

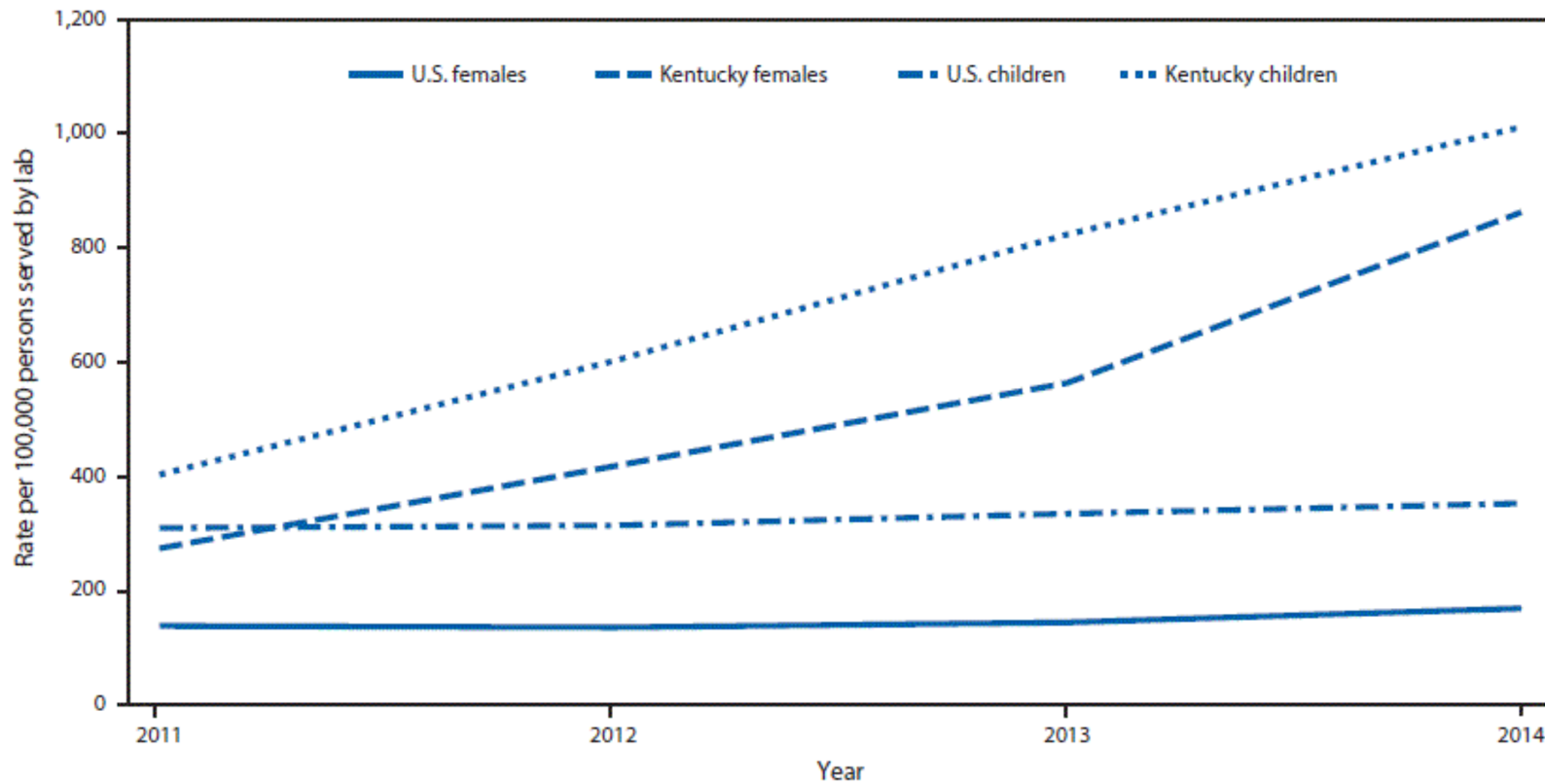
Jon E. Zibbell, PhD<sup>1</sup>, Kashif Iqbal, MPH<sup>1</sup>, Rajiv C. Patel, MPH<sup>1</sup>, Anil Suryaprasad, MD<sup>1</sup>, Kathy J. Sanders, MSN<sup>2</sup>, Loretta Moore-Moravian<sup>3</sup>, Jamie Serrecchia, MPA<sup>4</sup>, Steven Blankenship, MS<sup>5</sup>, John W. Ward, MD<sup>1</sup>,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

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

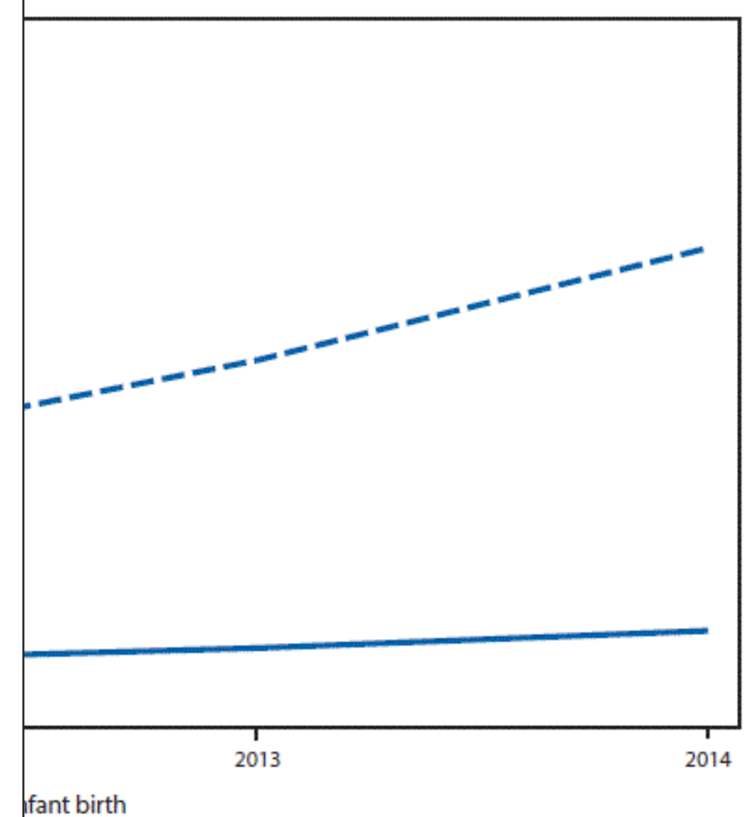


# Pregnant Women and HCV

FIGURE 1. Hepatitis C virus (HCV) detection rate among females aged 15–44 years and HCV testing rate among children aged =2 years –United States and Kentucky, 2011–2014\*



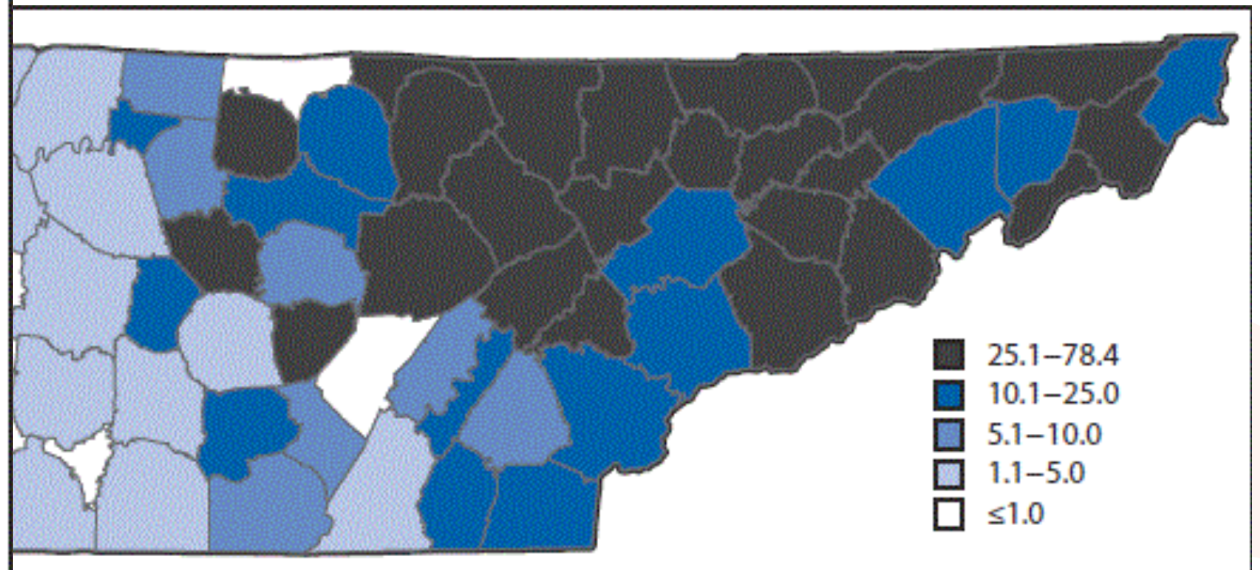
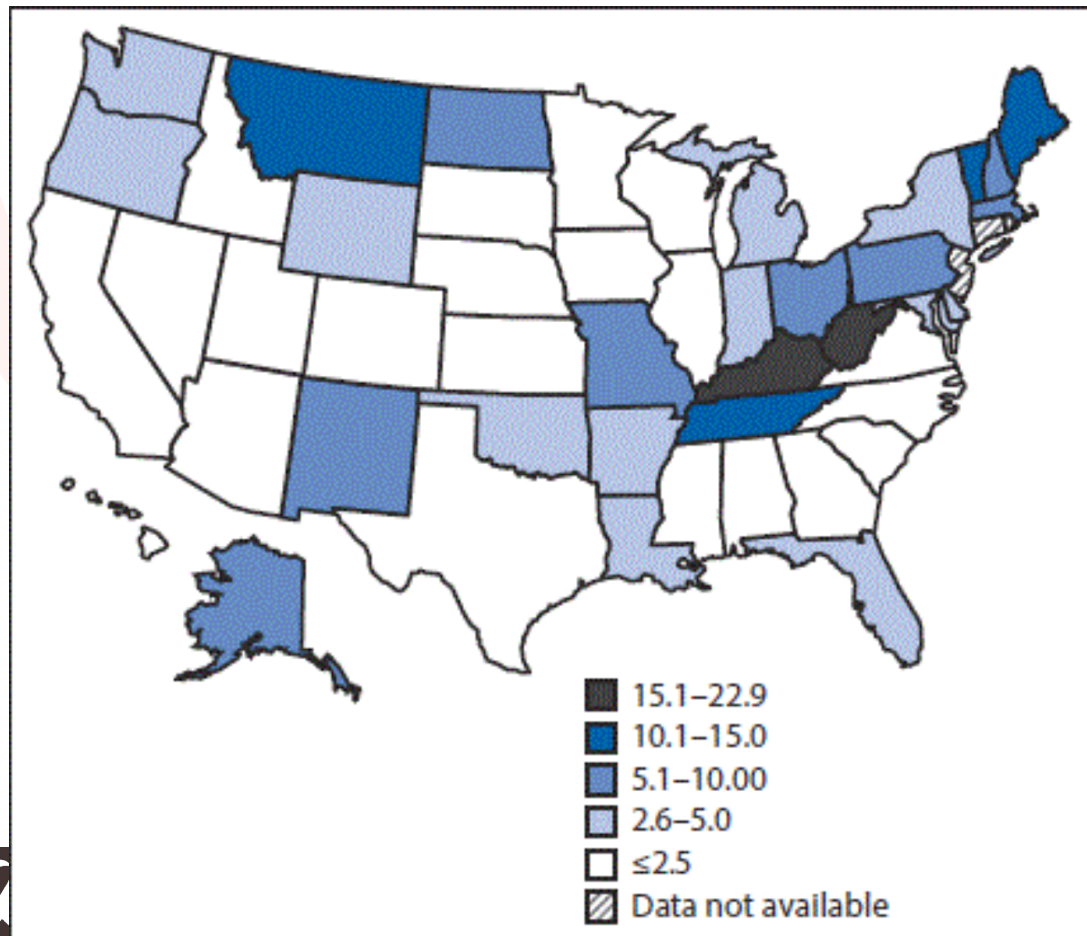
HCV)-infected women† – United States and Kentucky,





# Pregnant Women and HCV Cont.

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



# Outline

- Epidemiology
- **New Therapies**
- Current and Future Challenges

# HCV Approved Agents

## FDA Approved Therapies Through 2010

Interferon (1986)

Ribavirin (1998)

Pegylated Interferon (2001)

## Since Then

Telaprevir (2011)

Boceprevir (2011)

Simeprevir (2013)

Sofosbuvir (2013)

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)**

# HCV Therapies: The Past, Present, and Future

<u>Pre-2011</u>	<u>July 2011</u>	<u>Nov-Dec 2013</u>	<u>Oct-Dec 2014</u>	<u>July 2015</u>	<u>Jan-Jun 2016</u>	<u>July-Aug 2017</u>
IFN	IFN	IFN	IFN	IFN	IFN	IFN
PEG-IFN	PEG-IFN	PEG-IFN	PEG-IFN	PEG-IFN	PEG-IFN	PEG-IFN
RBV	RBV	RBV	RBV	RBV	RBV	RBV
	<b>Telaprevir</b>	Telaprevir	<b>Telaprevir</b>	Telaprevir	Telaprevir	Telaprevir
	<b>Boceprevir</b>	Boceprevir	Boceprevir	<b>Boceprevir</b>	Boceprevir	Boceprevir
		<b>Simeprevir</b>	Simeprevir	Simeprevir	Simeprevir	Simeprevir
		<b>Sofosbuvir</b>	Sofosbuvir	Sofosbuvir	Sofosbuvir	Sofosbuvir
			<b>Ledipasvir</b>	Ledipasvir	Ledipasvir	Ledipasvir
			<b>Paritaprevir</b>	Paritaprevir	Paritaprevir	Paritaprevir
			<b>Ombitasvir</b>	Ombitasvir	Ombitasvir	Ombitasvir
			<b>Dasabuvir</b>	Dasabuvir	Dasabuvir	Dasabuvir
				<b>Daclatasvir</b>	Daclatasvir	Daclatasvir
					<b>Elbasvir</b>	Elbasvir
					<b>Grazoprevir</b>	Grazoprevir
					<b>Velpatasvir</b>	Velpatasvir
						<b>Voxilaprevir</b>
						<b>Glecaprevir</b>
						<b>Pibrentasvir</b>



# 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)

# Goals for HCV Therapy

- Interferon-free
- Ribavirin-free
- Improved efficacy overall
- Improved efficacy for subgroups (i.e. black, HIV/HCV)
- Decreased side effects
- Minimal drug-drug interactions
- Increased genotype options (including pangenotypic)
- Renal impairment
- Retreatment options
- Lower prices

# Goals for HCV Therapy

- ~~Interferon-free~~
- ~~Ribavirin-free~~
- ~~Improved efficacy overall~~
- ~~Improved efficacy for subgroups (i.e. black, HIV/HCV)~~
- ~~Decreased side effects~~
- ~~Minimal drug-drug interactions~~
- ~~Increased genotype options (including pangenotypic)~~
- Renal impairment
- Retreatment options
- Lower prices

# Sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX; Vosevi™)

- FDA Approval
  - July 2017
- Class
  - NS5B RNA polymerase inhibitor
  - NS5A inhibitor
  - NS3/4A protease inhibitor
- FDA Indication
  - GT 1-6 previously treated with NS5A inhibitor
  - GT 1 or 3 previously treated with SOF without NS5A inhibitor
- Notes
  - Not recommended with severe renal impairment (GFR <30 ml/min/1.73m<sup>2</sup>)
  - Not recommended in moderate/severe liver impairment
  - Contraindicated with amiodarone

# POLARIS-1 and POLARIS-4

- POLARIS-1
  - GT1 who had previously failed NS5A-based regimen
  - Compared SOF/VEL/VOX with placebo
  - SVR 96% with SOF/VEL/VOX
- POLARIS-4
  - GT1-3 who had previously failed non-NS5A DAA regimen
  - Compared SOF/VEL/VOX with SOF/VEL
  - SVR 98% with SOF/VEL/VOX compared to 90% with SOF/VEL

# Glecaprevir/Pibrentasvir (GLE/PIB; Mavyret™)

- FDA Approval
  - August 2017
- Class
  - Glecaprevir
    - NS3/4A protease inhibitor
  - Pibrentasvir
    - NS5A replication complex inhibitor
- FDA Indication
  - GT 1-6 who are treatment without cirrhosis x 8 weeks
  - GT 1-6 who are cirrhotic x 12 weeks
  - Non-NS3/4a DAA retreatment for certain genotypes with varying length of therapy
- Notes
  - No dose adjustment for renal impairment
  - Not recommended in moderate/severe hepatic impairment
  - MSRP reportedly ~\$13,200 per month of therapy (prior to discounts)

# Two GLE/PIB Clinical Trials...

- Phase 3 Trial for HCV GT 1, 2, 4, 5, or 6 with Compensated Cirrhosis (EXPEDITION-1)
  - 146 patient with HCV and compensated cirrhosis
  - Treated with GLE/PIB x 12 weeks
  - 99% SVR12 rate (145/146)
- Phase 3 Trial for HCV in Severe Renal Impairment
  - 104 patients with HCV and CKD Stage IV or V
  - Treated with GLE/PIB x 12 weeks
  - 98% SVR rate (102/104)

# HBV Reactivation and DAA Therapy

- Descriptive case series published 6/2017
- 29 cases of HBV reactivation noted via US FDA Adverse Event Reporting System
- 2 deaths and 1 liver transplant
- Many had detectable sAg at baseline (n=13), though some did not (n=4)
- Most had no baseline data available
- Black box warning added to DAA therapies

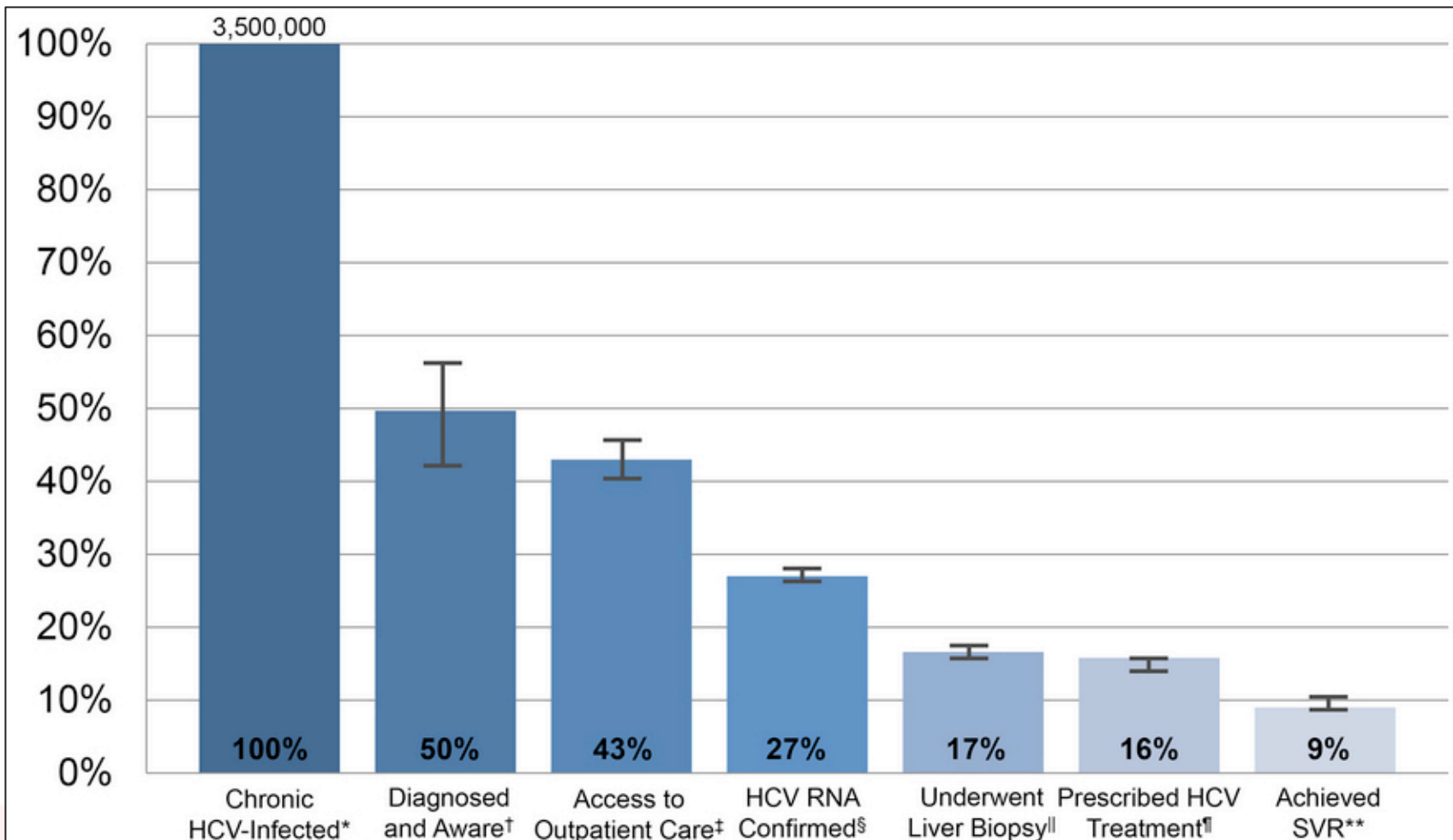


# Recommendations for HBV Management in Patients Treated with DAAs

- Check HBV sAg, cAb, and sAb at baseline
- Immunize if not previously exposed
- If sAg positive, determine whether appropriate for treatment based on AASLD recommendations:
  - If so, treat
  - If not, monitor closely
- If cAb positive but sAg negative, most appropriate approach is uncertain

# Outline

- Epidemiology
- New Therapies
- **Current and Future Challenges**



\* 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.

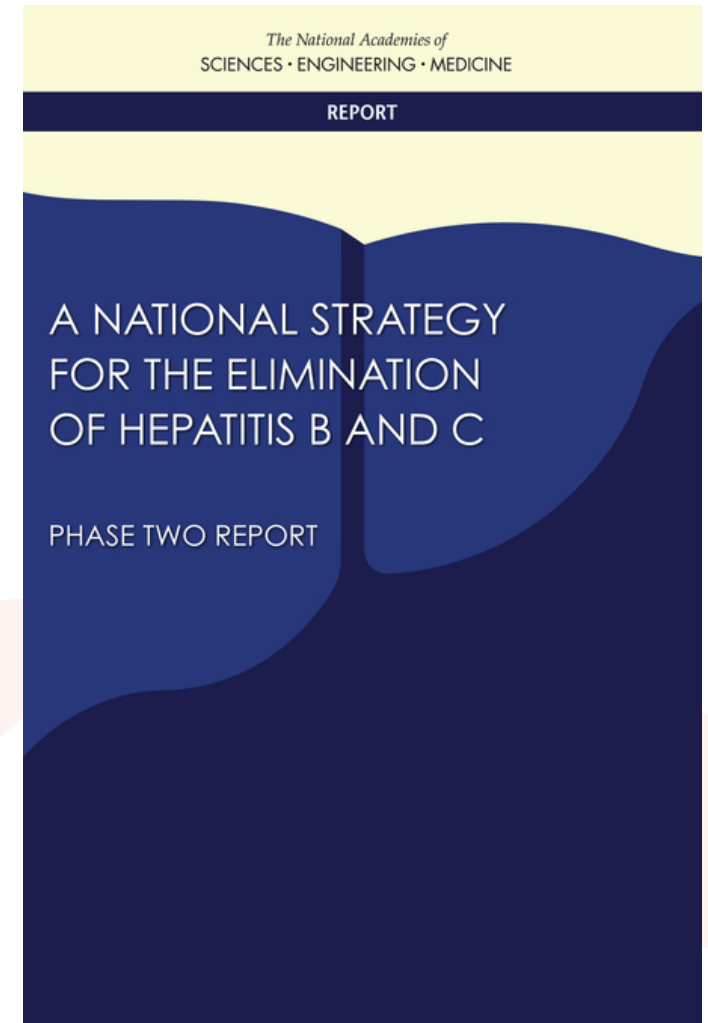
Note: Only non-VA studies are included in the above HCV treatment cascade.

# The Cochrane Review Controversy

- Cochrane Database of Systematic Reviews published review on 6/6/17:
  - “Overall, DAAs on the market or under development do not seem to have any effects on risk of serious adverse events...we could neither confirm nor reject that DAAs had any clinical effects. DAAs seemed to reduce the risk of no sustained virological response. The clinical relevance of the effects of DAAs on no sustained virological response is questionable, as it is a non-validated surrogate outcome.”
- Significant controversy with direct opposing statements from AASLD, IDSA, and co-chairs of AASLD/IDSA HCV Guidance Writing Group.
- Review conclusions revised 9/18/17:
  - “The evidence for our main outcomes of interest come from short-term trials, and we are unable to determine the effect of long-term treatment with DAAs. The rates of hepatitis C morbidity and mortality observed in the trials are relatively low and we are uncertain as to how DAAs affect this outcome. Overall, there is very low quality evidence that DAAs on the market or under development do not influence serious adverse events. There is insufficient evidence to judge if DAAs have beneficial or harmful effects on other clinical outcomes for chronic HCV.”

# “The Committee's Conclusions Regarding Targets for Hepatitis C Elimination”

- “A 90 percent reduction in incidence of hepatitis C (relative to the 2015 incidence carried forward) is possible in the United States by 2030. Meeting this goal will require treatment without restrictions on severity of disease and a consistent ability to diagnose new cases, even as prevalence decreases.”
- “The same levels of diagnosis and treatment would reduce mortality from hepatitis C in 2030 to 65 percent relative to 2015, and avert 28,800 deaths by 2030.”
- “Meeting these targets depends on diagnosing at least 110,000 cases a year until 2020, almost 89,000 a year between 2020 and 2024, and over 70,000 each year between 2025 and 2030.”



# The Path to Elimination: An ID Physician's View

- Enhanced public health surveillance
- Expansion of access to prevention services
- Expansion of screening
- Removal of barriers to treatment
- National coordination of surveillance, research, and capacity

# Challenges and Opportunities

- Ongoing and evolving epidemic
  - *Strategic surveillance*
- Effective screening
  - *New diagnostic tools*
- Linkage to care
  - *Novel access and treatment programs*
- Cost of therapies
  - *Evolving pricing and distribution*

Thank You!

Questions?

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