



## Background

# Should all unvaccinated adults receive hepatitis B vaccination?

ACIP

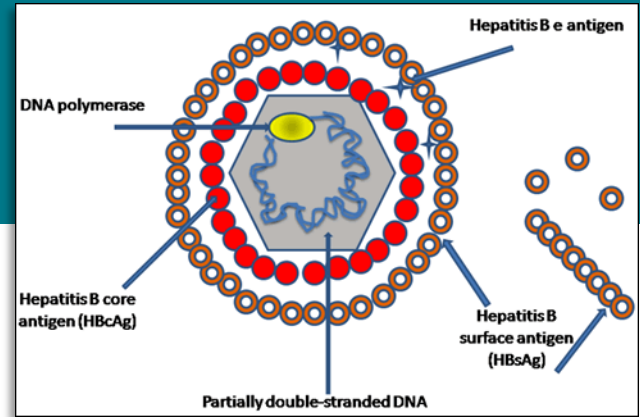
Wednesday, February 24, 2021

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# Hepatitis B Virus (HBV)

- DNA virus
- Causes disease, including cancer, that is vaccine-preventable
  - Premature mortality from chronic liver disease: 15-25%<sup>1</sup>
  - HBV-related complications: 15-40%<sup>2-4</sup>
  - Acute case-fatality rate: 0.5%-1%
- HBV Elimination Goals 2030<sup>5</sup>



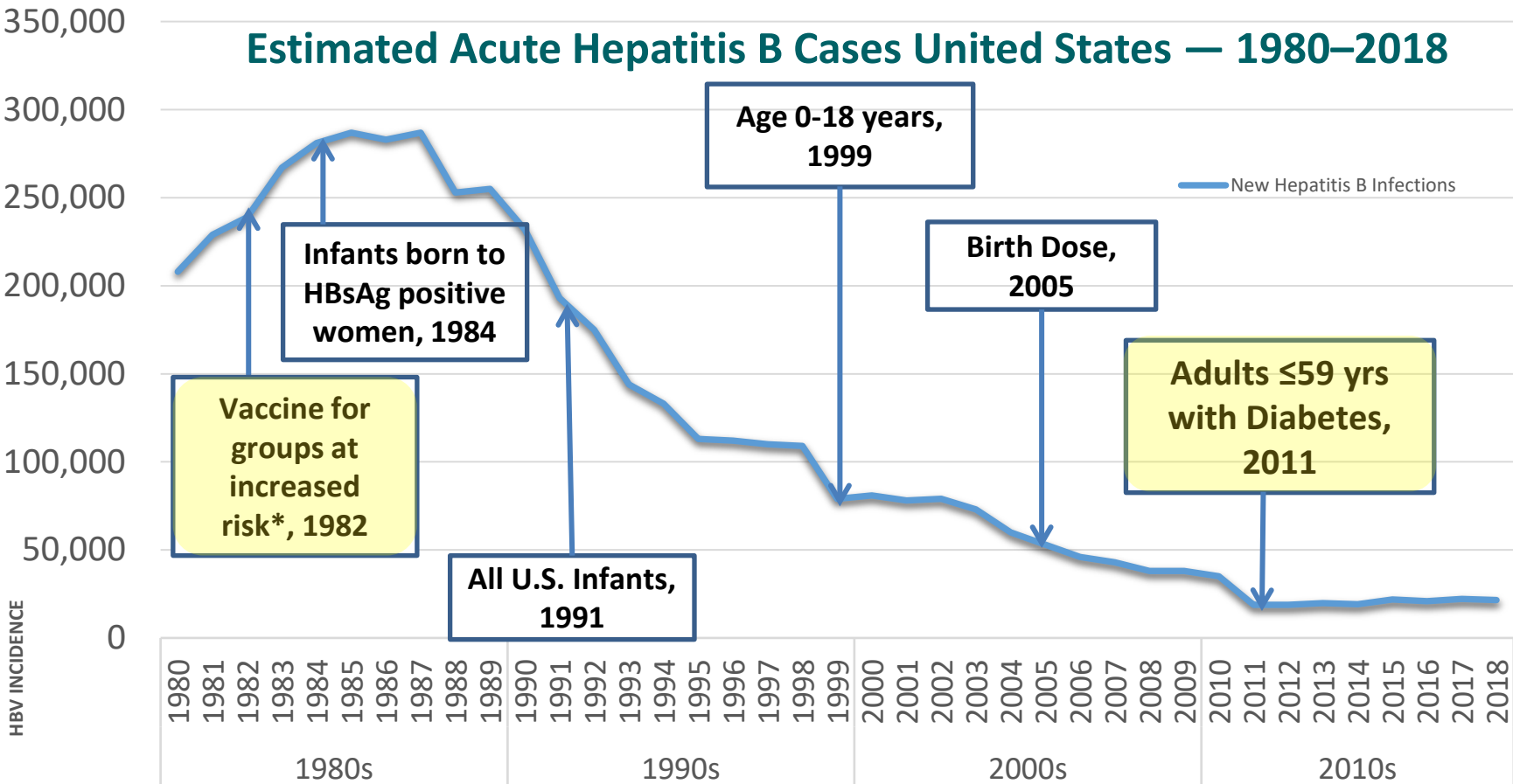
<sup>1</sup>Margolis, H.S., et al., JAMA, 1995. 274(15): p. 1201-8.

<sup>2</sup>Lok, A.S., N Engl J Med, 2002. 346(22).

<sup>3</sup>Lavanchy, D., J Viral Hepat, 2004. 11(2): p. 97-107.

<sup>4</sup>Zou, H., et al., J Viral Hepat, 2012. 19(2): p. e18-25.

# Estimated Acute Hepatitis B Cases United States — 1980–2018



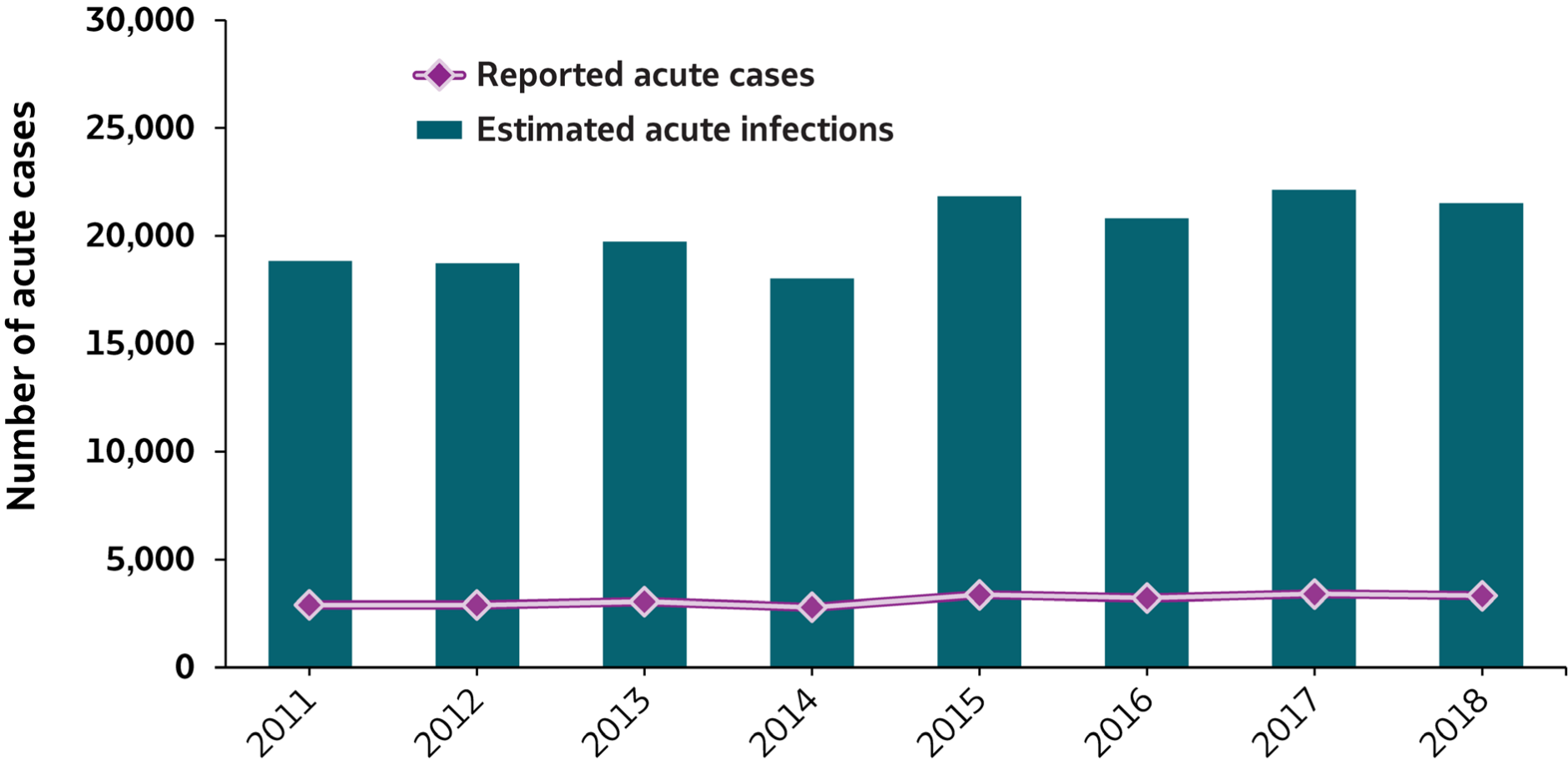
Source: National Notifiable Diseases Surveillance System (NNDSS) Health care providers, MSM, IDU, hemodialysis patients, household & sexual partners of persons with chronic HBV, persons in certain institutional settings, e.g., inmates of long-term correctional facilities.

# Current HepB Recommendation

**HepB vaccination is recommended for all unvaccinated adults at risk for HBV infection and for all adults requesting protection from HBV infection**

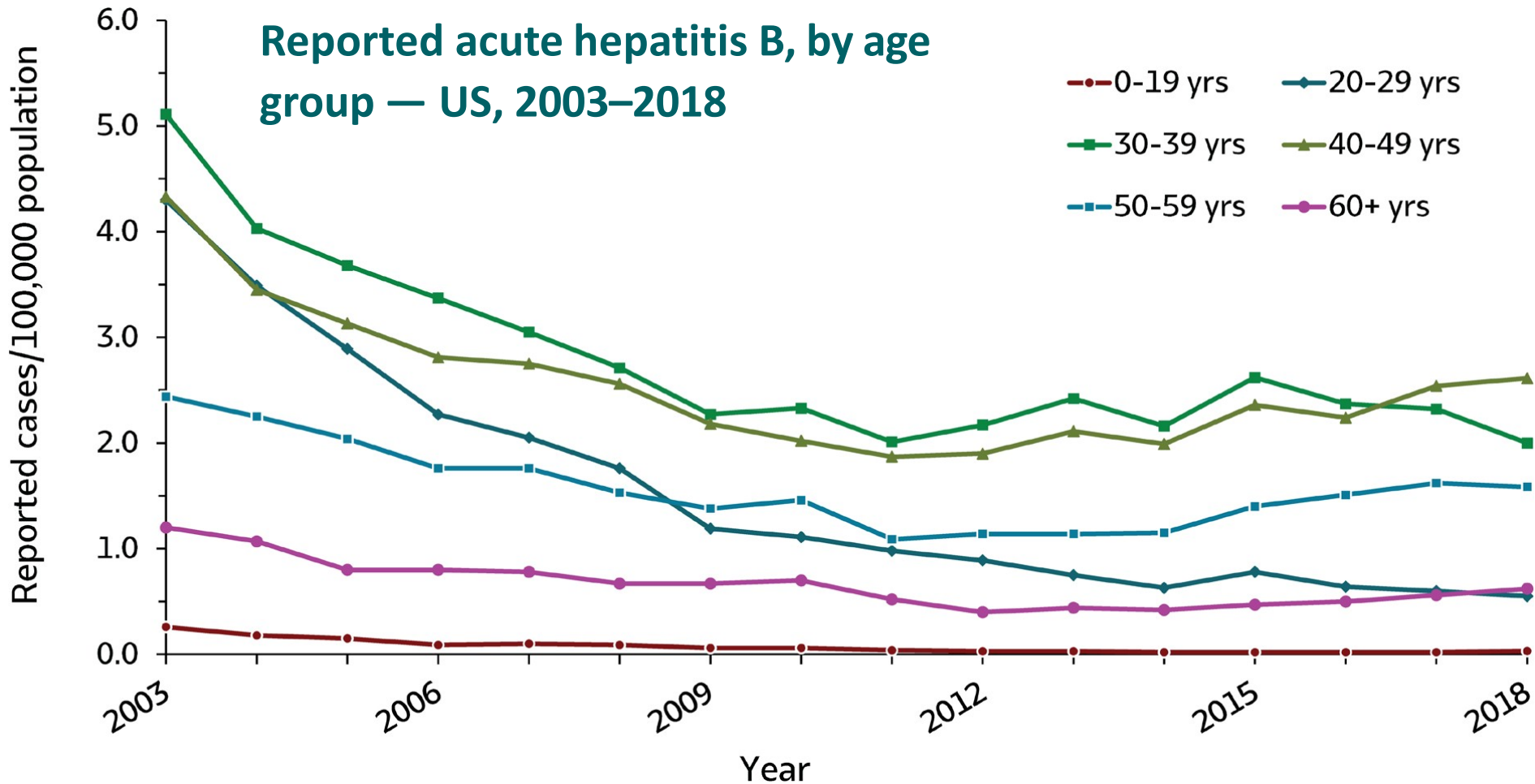
- Sex partners of HBV-infected persons
- Sexually active persons with multiple partners, men who have sex with men
- Persons seeking evaluation or treatment for STI
- Current or recent injection-drug users
- Household contacts of HBV-infected persons
- Residents and staff of facilities for developmentally disabled persons
- Healthcare and public safety workers
- Persons with end-stage renal disease
- Persons with diabetes
- International travelers to regions with high/intermediate HBV infection
- Persons with chronic liver disease (updated and clarified in 2018 recommendations)
- Persons with HIV infection
- All other persons seeking protection from HBV infection

# Acute hepatitis B cases and estimated infections — US, 2011–2018

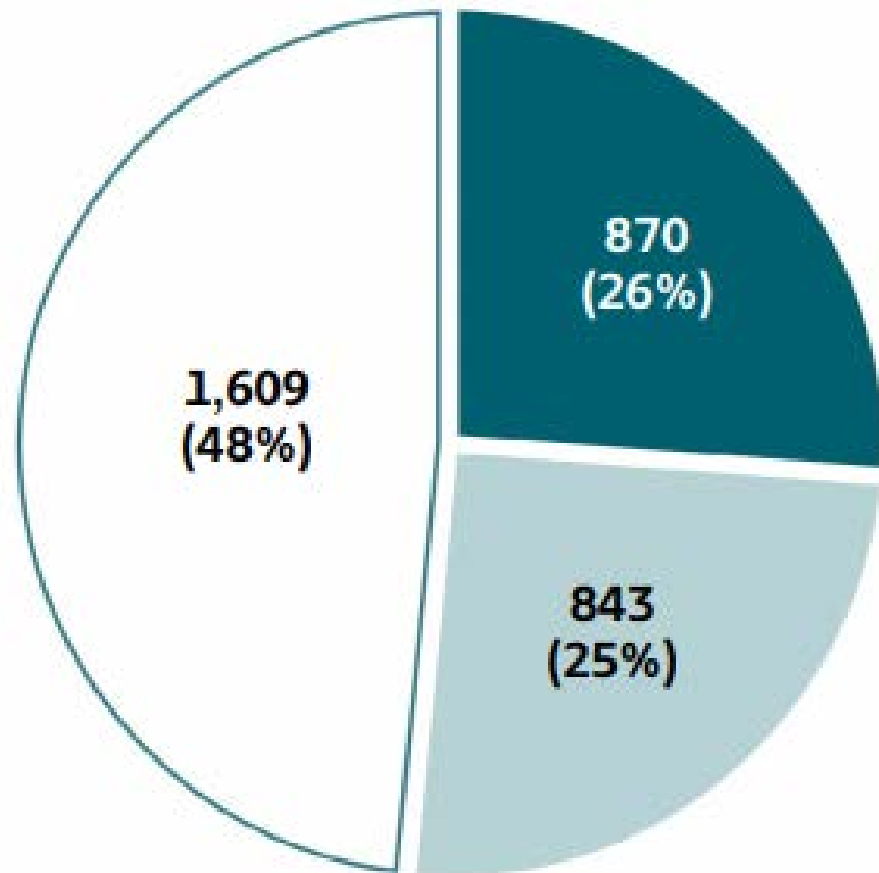


Source: CDC, National Notifiable Diseases Surveillance System  
<https://www.cdc.gov/hepatitis/statistics/2018surveillance/index.htm>

# Reported acute hepatitis B, by age group — US, 2003–2018



## Figure 2.7. Availability of information on risk behaviors/ exposures\* associated with reported cases of acute hepatitis B — United States, 2018



**Table 2.3. Reported risk behaviors/exposures<sup>†</sup> among reported cases of acute hepatitis B — United States, 2018**

Risk behaviors/exposures	Risk identified*	No risk identified	Risk data missing
Injection drug use	549	969	1,804
Multiple sex partners	199	671	2,452
Surgery	117	962	2,243
Men who have sex with men <sup>§</sup>	49	353	1,648
Sexual contact <sup>†</sup>	42	603	2,677
Needlestick	71	959	2,292
Household contact (non-sexual) <sup>§</sup>	12	633	2,677
Occupational	4	1,369	1,949
Dialysis patient	13	1,022	2,287
Transfusion	1	1,103	2,218

Source: CDC, Nationally Notifiable Diseases Surveillance System.

\* Case reports with at least one of the following risk behaviors/ exposures reported 6 weeks to 6 months prior to symptom onset: 1) injection drug use; 2) multiple sex partners; 3) underwent surgery; 4) men who have sex with men; 5) sexual contact with suspected/confirmed hepatitis B case; 6) sustained a percutaneous injury; 7) household contact with suspected/confirmed hepatitis B case; 8) occupational exposure to blood; 9) dialysis; and 10) transfusion.

<sup>†</sup> Reported cases may include more than one risk behavior/exposure.

<sup>§</sup> A total of 2,050 acute hepatitis B cases were reported among males in 2018.

<sup>†</sup> Cases with more than one type of contact reported were categorized according to a hierarchy: (1) sexual contact; (2) household contact (non-sexual).



## Proposed Policy Question

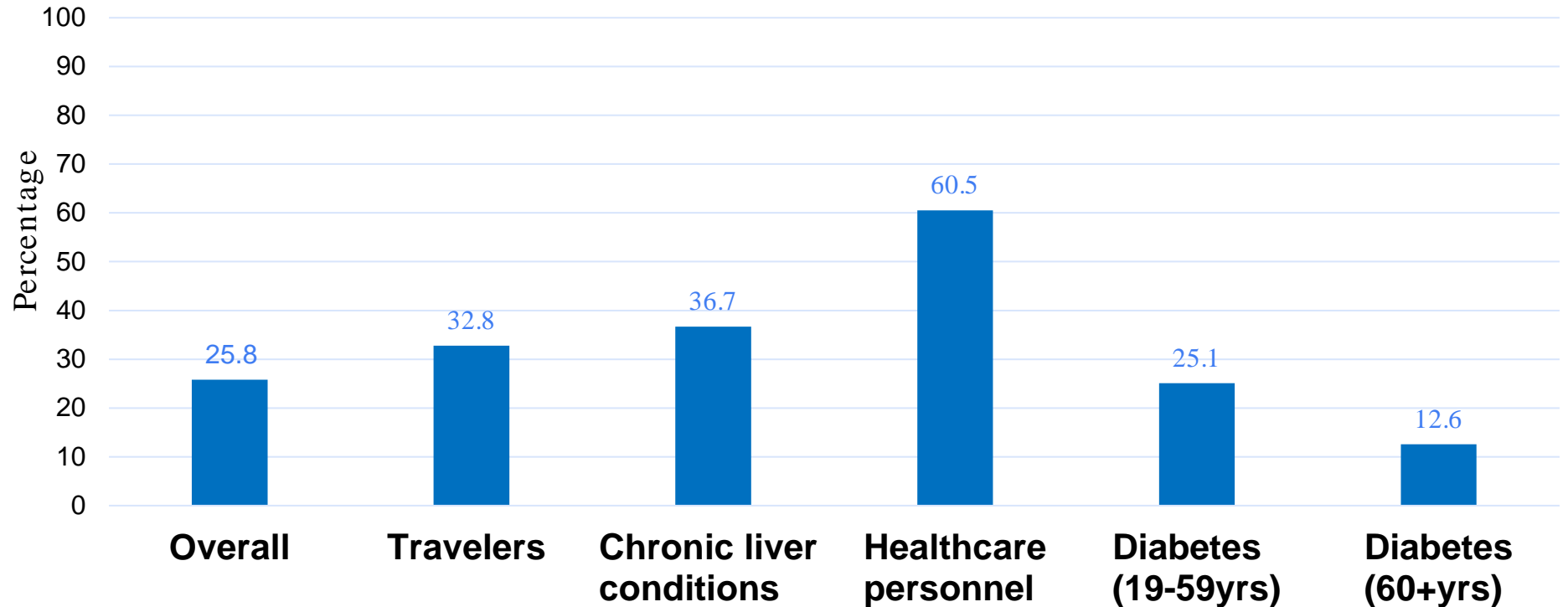
**Should all unvaccinated adults  
receive hepatitis B vaccination?**

# PICO Question

- Population:** Previously unvaccinated adults age  $\geq 18$  years
- Intervention:** Universal vaccination strategy (2- and 3-dose schedules)
- Comparison:** Current risk-based vaccination strategy (2- and 3-dose schedules)
- Outcomes of interest**
1. Vaccine uptake
  2. Incidence of hepatitis B
  3. Morbidity related to hepatitis B
  4. Mortality related to hepatitis B
  5. Serious adverse events associated with the 2-dose vaccine\*

\* This outcome is solely aimed at assessing the 2-dose HEPLISAV-B (approved in 2018), for which a standard postmarketing surveillance study in progress is to be presented prior to any votes on the proposed policy question. The 3-dose HepB vaccines have already been evaluated for their adverse events profiles and recommended by ACIP based on their safety records.

# Hepatitis B vaccine coverage ( $\geq 3$ doses) among adults aged $\geq 19$ years\*, National Health Interview Survey (NHIS) – US, 2017



Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2017.

<https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2017.html#box2>

\* 19-59 years plus adults with diabetes

# Hepatitis B vaccination coverage ( $\geq 3$ doses) by age, nativity, and health insurance - NHIS 2015

	AGE		
	25-49 years N=11,884	50-64 years N=7,942	$\geq 65$ years N=7,725
	% (95% CI)	% (95% CI)	% (95% CI)
<b>TOTAL</b>	<b>30.4 (29.3-31.7)</b>	<b>20.5 (19.1-21.8)</b>	<b>11.2 (10.1-12.3)</b>
<b>NATIVITY</b>			
US born	32.6 (31.2-34.1)	21.0 (19.5-22.5)	11.0 (9.8-12.2)
Non-US born	23.1 (21.1-25.2)*	17.9 (15.2-20.9)	12.5 (10.1-15.4)
<b>HEALTH INSURANCE</b>			
Insured	32.4 (31.1-33.7)	21.1 (19.8-22.6)	11.2 (10.1-12.3)
Uninsured	20.2 (17.9-22.6) <sup>†</sup>	13.2 (10.0-17.2) <sup>†</sup>	-- <sup>‡</sup>

\*  $P < .05$  comparing US born and non-US born.

<sup>†</sup>  $P < .05$  comparing insured and uninsured.

<sup>‡</sup> Estimate may not be reliable due to relative standard error  $> 30\%$ .

# Hepatitis B vaccination coverage ( $\geq 3$ doses) among adults aged $\geq 19$ years with and without diabetes, NHIS 2015

	Age	
	19-59 years	$\geq 60$ years
	N=19,423	N=10,303
	% (95% CI)	% (95% CI)
With diabetes	24.4 (21.1-28.0)	12.6 (10.8-14.7)
Without diabetes	29.5 (28.5-30.6)*	13.0 (11.9-14.1)

\*  $P < .05$  comparing with diabetes versus without diabetes.

# Limits of using only presence of a risk factor to initiate HBV testing

	Germany <sup>1</sup>	United States <sup>2</sup>
Population	<b>51 primary care clinics 21k patients</b>	<b>9 academic and 9 community oncology centers &gt;3000 cancer patients</b>
Observation	<b>Missed 33% (31/93) HBsAg+ adults</b>	<b>- No identifiable risk factors in &gt;20% of patients with cancer and HBV - Among chronic HBV patients, 40% were newly-diagnosed</b>

<sup>1</sup>Wolffram, J Hepatol, 2015. <sup>2</sup>Ramsey, JAMA Oncology, 2019

# Role of HBV Testing

- Certain populations may benefit from HBV testing
- HepWG recognizes its mandate to address the role of vaccination policy (not testing)
- HBV testing guidelines are concurrently being assessed by a parallel advisory group

# Stigma as a Barrier to Risk-based HepB Vaccination

- Risk factors assessed include socio-structural factors that may criminalize and stigmatize<sup>4</sup>
  - In the ongoing opioid crisis, stigma associated with drug use may keep people from reporting risk factors to their clinicians<sup>1</sup>
  - Currently, health care providers may rely on self-reported vaccine history to determine need for vaccination, but self-reported vaccination history does not predict immunity well<sup>1,2,3</sup>
- The proposed policy recommendation could reduce stigma among “hidden” people at increased risk and immigrants with concerns about stigma associated with HBV-related care

<sup>1</sup>Figgatt M, et al. Public Health Rep. 2020

<sup>2</sup>Collier, MG et al. Vaccine 2015

<sup>3</sup>Topp, L et al. Drug Alcohol Rev 2009

<sup>4</sup>Taylor J, et al. BMC Infect Dis. 2019



# Available HepB Vaccines

- 1. Recombivax-HB (monovalent, aluminum adjuvant)**  
Approved for use at any age
- 2. Engerix-B (monovalent, aluminum adjuvant)**  
Approved for use at any age
- 3. Pediarix (combination DTaP-IPV-HepB)**  
Approved for doses administered at 6 weeks to 6 years of age
- 4. Twinrix (combination HepA-HepB)**  
Approved for use in adults  $\geq 18$  years
- 5. Heplisav-B (monovalent, 1018 adjuvant)**  
Approved for use in adults  $\geq 18$  years, 2-dose series over 1 month

# Safety, immunogenicity, and efficacy of HepB Vaccines: Recombivax-HB, Engerix-B, Twinrix

- **>90% protection among healthy adults who complete the 3-dose series<sup>1-3</sup>**
- **Rare side effects/adverse reactions<sup>1,4</sup>**
- **Immunity lasts at least 3 decades<sup>5</sup>**

<sup>1</sup>Assad et al. Vaccine. 1999

<sup>2</sup>Venters et al. Expert Rev Vaccines. 2004

<sup>3</sup>Andre et al. Am J Med. 1989

<sup>4</sup>Lewis et al. Pediatr Infect Dis J. 2001

<sup>5</sup>Bruce et al. J Infect Dis 2016

# Status Update on 2-dose vaccine

- **Heplisav-B vaccine trials showed statistically insignificant increase in cardiovascular events<sup>1</sup>**
- **Postmarketing surveillance study is anticipated in 2021**

<sup>1</sup>Schillie et al. MMWR. 2018

Among subjects receiving HEPLISAV-B, 45.6%, 5.4%, and 0.27% experienced a mild adverse event, serious adverse event, or cardiovascular event, respectively. Among subjects receiving ENGERIX-B, 45.7%, 6.3%, and 0.14% experienced a mild adverse event, serious adverse event, or cardiovascular event, respectively.

# Conclusions

- **Major achievements with incremental HepB vaccine policy over the past 4 decades, but recent trends in HBV incidence demonstrate limits of current risk-based HepB recommendations**
  - Recent surveillance shows risk factor identified in merely 25% of acute HBV cases
  - Evidence of inefficiency in performing HBV risk-factor assessment in clinical settings
- **Policy tool revision could overcome inherent challenges in ascertaining important risk factors and reducing stigma in clinical settings (health equity)**
- **Universal adult vaccination policy could increase adult HepB vaccine coverage and thus could advance towards hepatitis B elimination in the US by 2030**

# Work Group Discussion Points

Discussed adding the following age caveat to the proposed policy question:

- Adults aged 59 years and under

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Discussed adding the following age caveat to the proposed policy question:

- Adults aged 59 years and under

Should all unvaccinated adults **age 59 years and under** receive hepatitis B vaccination?

# Questions to ACIP

- 1. Should HepB vaccination be recommended for all unvaccinated adults?**
- 2. Furthermore, should such a recommendation be limited to adults age 59 years and under?**
- 3. What other types of evidence are important to the Committee that would help with the above questions?**

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