Background

Should all unvaccinated adults receive hepatitis B vaccination?

ACIP

Wednesday, February 24, 2021

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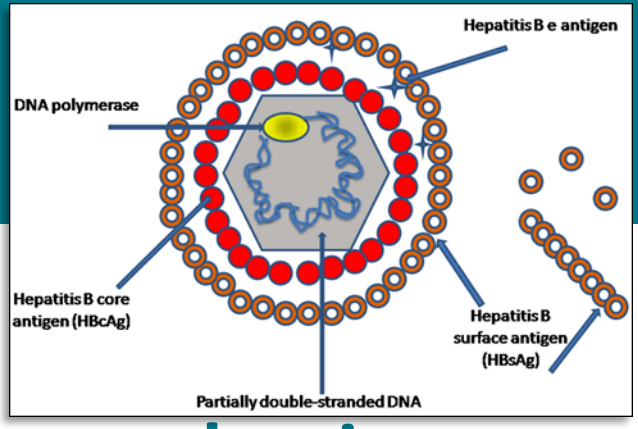
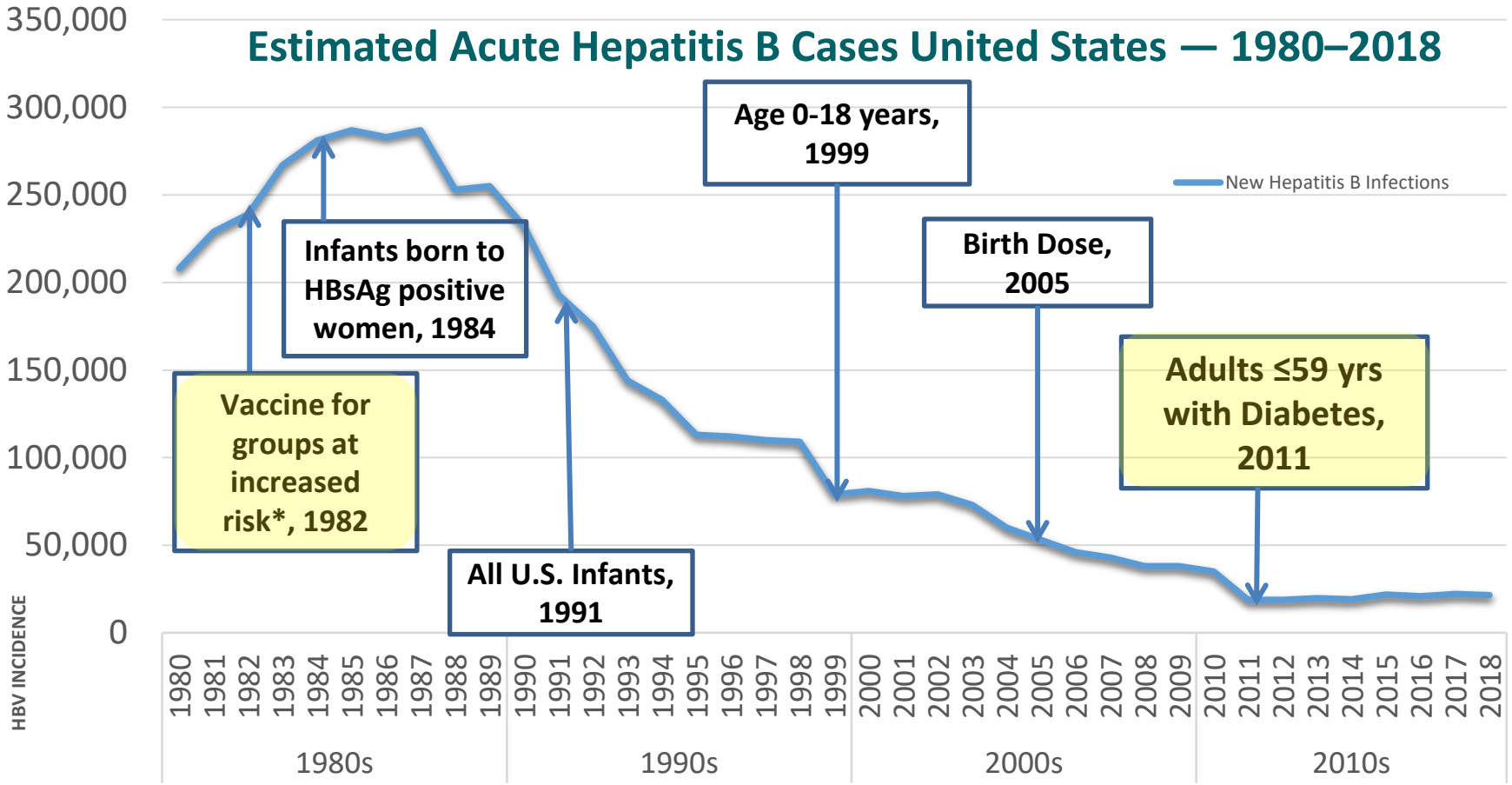
Hepatitis B Virus (HBV)



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

[1]Margolis, H.S., et al., JAMA, 1995. 274(15): p. 1201-8.
[2]Lok, A.S., N Engl J Med, 2002. 346(22).
[3]Lavanchy, D., J Viral Hepat, 2004. 11(2): p. 97-107.
[4]Zou, H., et al., J Viral Hepat, 2012. 19(2): p. e18-25.
5. HHS, Viral Hepatitis National Strategic Plan: A Roadmap to Elimination 2021-2025

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.

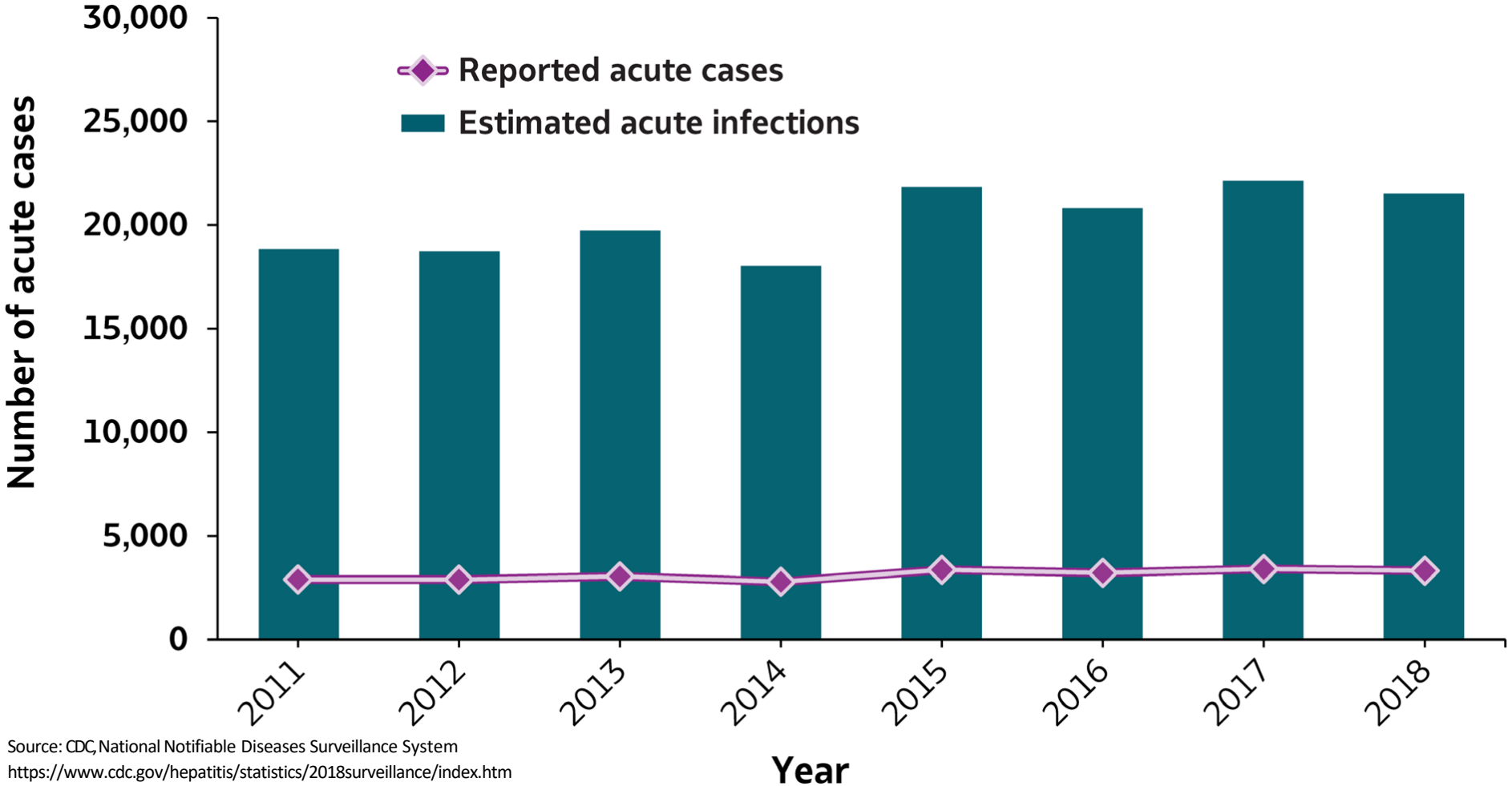
Current HepB Recommendation

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

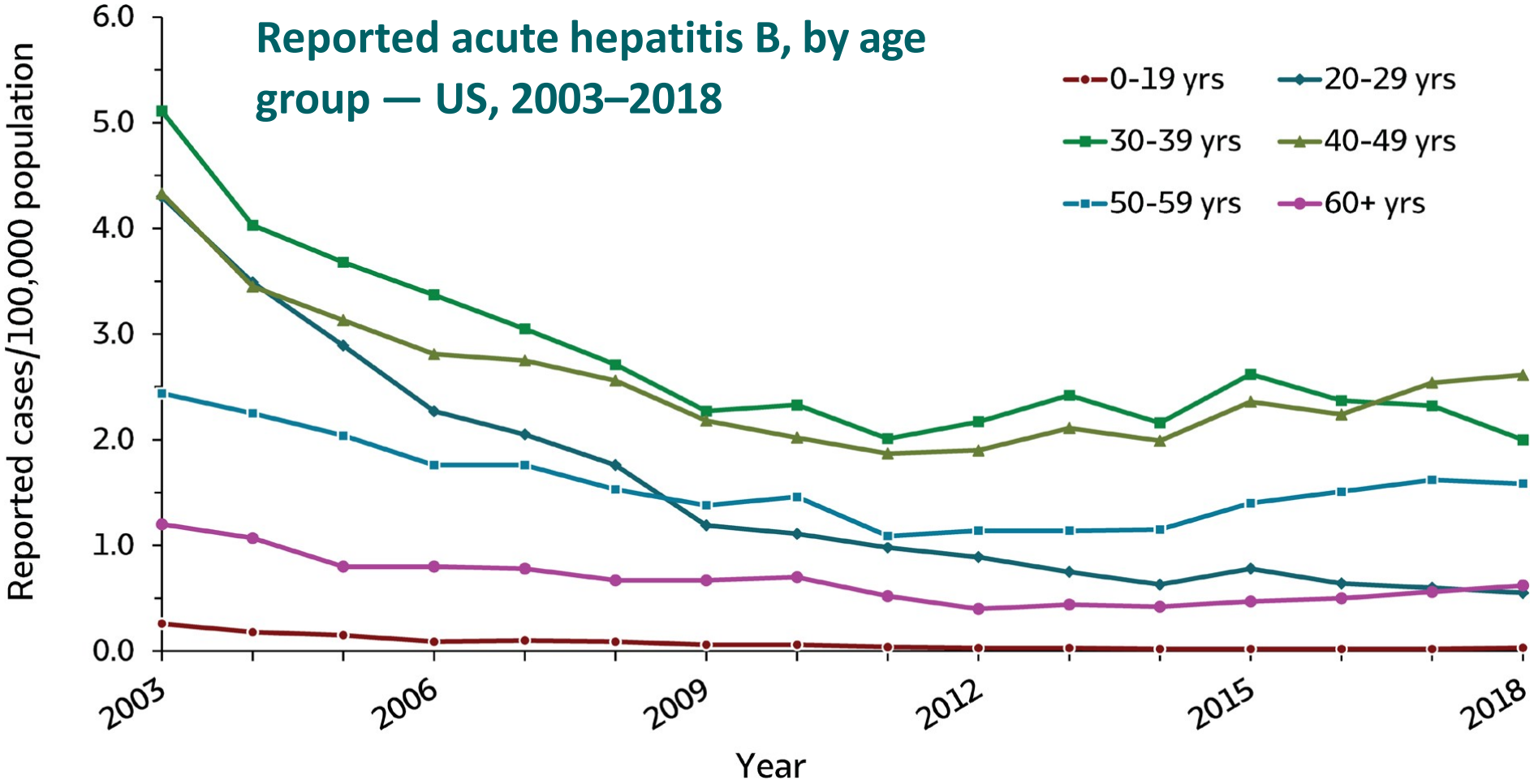
Schillie et al. 2018

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



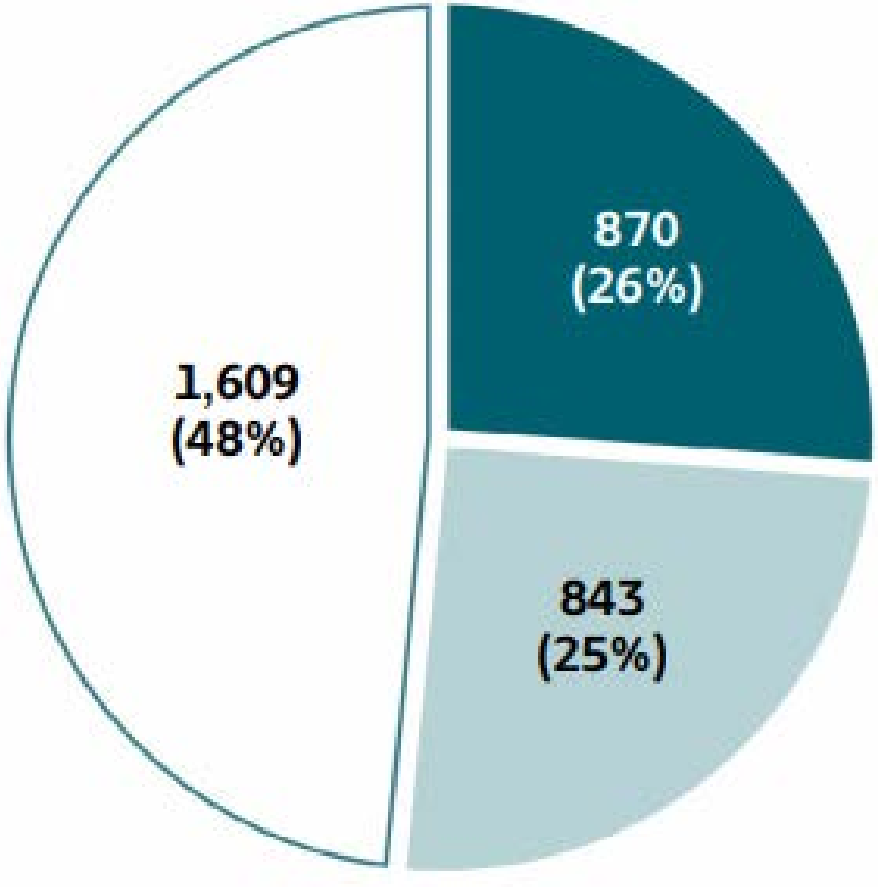
Source: CDC, National Notifiable Diseases Surveillance System
https://www.cdc.gov/hepatitis/statistics/2018surveillance/index.htm

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



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

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



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

Table 2.3. Reported risk behaviors/exposures† 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 §	49	353	1,648
Sexual contact ¶	42	603	2,677
Needlestick	71	959	2,292
Household contact (non-sexual) §	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.

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

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

¶ 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 ≥ 18 years

Intervention: Universal vaccination strategy (2- and 3-dose schedules)

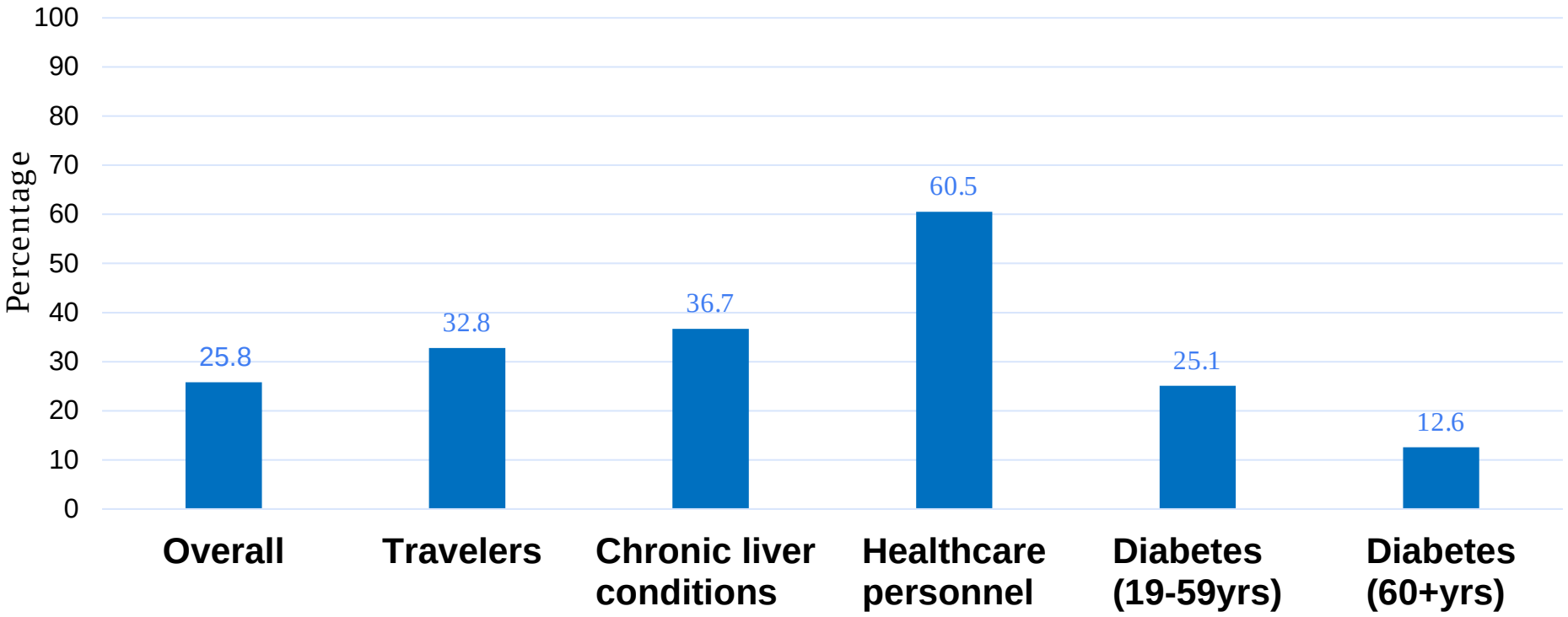
Comparison: Current risk-based vaccination strategy (2- and 3-dose schedules)

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 (≥3 doses) among adults aged ≥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 (≥3 doses) by age, nativity, and health insurance - NHIS 2015

	AGE		
	25-49 years N=11,884	50-64 years N=7,942	≥65 years N=7,725
	% (95% CI)	% (95% CI)	% (95% CI)
TOTAL	30.4 (29.3-31.7)	20.5 (19.1-21.8)	11.2 (10.1-12.3)
NATIVITY			
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)
HEALTH INSURANCE			
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)†	13.2 (10.0-17.2)†	--‡

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

† *P* <.05 comparing insured and uninsured.

‡ Estimate may not be reliable due to relative standard error >30%.

courtesy Walter Williams et al, CDC

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

	Age	
	19-59 years	≥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.

courtesy Walter Williams et al, CDC

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

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

[1]Wolffram, J Hepatol, 2015. [2]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[4]
  - In the ongoing opioid crisis, stigma associated with drug use may keep people from reporting risk factors to their clinicians[1]
  - 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[1,2,3]

- The proposed policy recommendation could reduce stigma among "hidden" people at increased risk and immigrants with concerns about stigma associated with HBV-related care

[1]Figgatt M, et al. Public Health Rep. 2020
[2]Collier, MG et al. Vaccine 2015
[3]Topp, L et al. Drug Alcohol Rev 2009
[4]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 ≥ 18 years

5. **Heplisav-B (monovalent, 1018 adjuvant)**
   Approved for use in adults ≥ 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[1-3]
- Rare side effects/adverse reactions[1,4]
- Immunity lasts at least 3 decades[5]

[1]Assad et al. Vaccine. 1999
[2]Venters et al. Expert Rev Vaccines. 2004
[3]Andre et al. Am J Med. 1989
[4]Lewis et al. Pediatr Infect Dis J. 2001
[5]Bruce et al. J Infect Dis 2016

Status Update on 2-dose vaccine

- **Heplisav-B vaccine trials showed statistically insignificant increase in cardiovascular events[1]**

- **Postmarketing surveillance study is anticipated in 2021**

[1]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**

Work Group Discussion Points

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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