Background

Should all unvaccinated adults receive hepatitis B vaccination?

ACIP
Wednesday, February 24, 2021

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CDC Lead, ACIP Hepatitis Work Group
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\(^5\)

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\(^5\) HHS, Viral Hepatitis National Strategic Plan: A Roadmap to Elimination 2021-2025
Estimated Acute Hepatitis B Cases United States — 1980–2018

Infants born to HBsAg positive women, 1984
All U.S. Infants, 1991
Vaccine for groups at increased risk*, 1982
Age 0-18 years, 1999
Birth Dose, 2005
Adults ≤59 yrs with Diabetes, 2011

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

Source: CDC, National Notifiable Diseases Surveillance System
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
### Table 2.3. Reported risk behaviors/exposures† among reported cases of acute hepatitis B — United States, 2018

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

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

Percentage

Overall: 25.8%
Travelers: 32.8%
Chronic liver conditions: 36.7%
Healthcare personnel: 60.5%
Diabetes (19-59yrs): 25.1%
Diabetes (60+yrs): 12.6%

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

<table>
<thead>
<tr>
<th>AGE</th>
<th>25-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=11,884</td>
<td>N=7,942</td>
<td>N=7,725</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>30.4 (29.3-31.7)</td>
<td>20.5 (19.1-21.8)</td>
<td>11.2 (10.1-12.3)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NATIVITY</th>
<th>US born</th>
<th>Non-US born</th>
<th>Non-US born</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.6 (31.2-34.1)</td>
<td>21.0 (19.5-22.5)</td>
<td>11.0 (9.8-12.2)</td>
<td></td>
</tr>
<tr>
<td>23.1 (21.1-25.2)*</td>
<td>17.9 (15.2-20.9)</td>
<td>12.5 (10.1-15.4)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HEALTH INSURANCE</th>
<th>Insured</th>
<th>Uninsured</th>
<th>Uninsured</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.4 (31.1-33.7)</td>
<td>21.1 (19.8-22.6)</td>
<td>11.2 (10.1-12.3)</td>
<td></td>
</tr>
<tr>
<td>20.2 (17.9-22.6)†</td>
<td>13.2 (10.0-17.2)‡</td>
<td>--‡</td>
<td></td>
</tr>
</tbody>
</table>

* $P < .05$ 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

<table>
<thead>
<tr>
<th>Age</th>
<th>19-59 years</th>
<th>≥60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=19,423</td>
<td>N=10,303</td>
</tr>
<tr>
<td>With diabetes</td>
<td>24.4 (21.1-28.0)</td>
<td>12.6 (10.8-14.7)</td>
</tr>
<tr>
<td>Without diabetes</td>
<td>29.5 (28.5-30.6)*</td>
<td>13.0 (11.9-14.1)</td>
</tr>
</tbody>
</table>

* P < .05 comparing with diabetes versus without diabetes.
### Limits of using only presence of a risk factor to initiate HBV testing

<table>
<thead>
<tr>
<th>Population</th>
<th>Germany¹</th>
<th>United States²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>51 primary care clinics 21k patients</td>
<td>9 academic and 9 community oncology centers &gt;3000 cancer patients</td>
</tr>
<tr>
<td>Observation</td>
<td>Missed 33% (31/93) HBsAg+ adults</td>
<td>- No identifiable risk factors in &gt;20% of patients with cancer and HBV - Among chronic HBV patients, 40% were newly-diagnosed</td>
</tr>
</tbody>
</table>

¹Wolffram, J Hepatol, 2015. ²Ramsey, 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

\(^2\text{Collier, MG et al. Vaccine 2015}\)
\(^3\text{Topp, L et al. Drug Alcohol Rev 2009}\)
\(^4\text{Taylor J, et al. BMC Infect Dis. 2019}\)
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

- Rare side effects/adverse reactions

- Immunity lasts at least 3 decades

1Assad et al. Vaccine. 1999  
2Venters et al. Expert Rev Vaccines. 2004  
5Bruce 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
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?
References (1)

1. André FE. Summary of safety and efficacy data on a yeast-derived hepatitis B vaccine. The American journal of medicine. 1989;87(3a):14s-20s.
References (2)