Universal Adult Hepatitis B Vaccination: Work Group Considerations

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Hepatitis Vaccines Work Group, Advisory Committee on Immunization Practices
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Hepatitis B in the US

- 20,700 estimated acute HBV infections each year (95% CI: 11,800–50,800)\(^1\)

- > $1 billion spent on hepatitis B-related hospitalizations each year (not including indirect costs)\(^2\)

Hepatitis B in the US

- 1.89 million persons living with chronic HBV (modeled estimate; range, 1.49–2.40 million)²

- 15-25% risk of premature death from cirrhosis or liver cancer among people living with chronic HBV infection³

Simplify a complex adult HepB vaccination schedule

Persons recommended to receive hepatitis B vaccination

Existing Recommendations

- All infants
- Unvaccinated children aged <19 years
- Persons at risk for infection by sexual exposure
  - Sex partners of hepatitis B surface antigen (HBsAg)–positive persons
  - Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months)
  - Persons seeking evaluation or treatment for a sexually transmitted infection
  - Men who have sex with men
- Persons at risk for infection by percutaneous or mucosal exposure to blood
  - Current or recent injection-drug users
  - Household contacts of HBsAg-positive persons
  - Residents and staff of facilities for developmentally disabled persons
  - Health care and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
  - Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
  - Persons with diabetes aged 19–59 years; persons with diabetes aged ≥60 years at the discretion of the treating clinician
- Others
  - International travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence of ≥2%)
  - Persons with hepatitis C virus infection
  - Persons with chronic liver disease (including, but not limited to, persons with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal)
  - Persons with HIV infection
  - Incarcerated persons

New Recommendations (Proposed)

- All infants [No change]
- Unvaccinated children aged <19 years [No change]

All adults previously unvaccinated for hepatitis B should receive hepatitis B vaccination

Schillie et al, 2018
HepB Immunization Strategy Evolves

HepB Recommendations and Est. Acute Hepatitis B Cases in the US, 1980–2019
Source: National Notifiable Diseases Surveillance System (NNDSS)
Risk-based hepatitis B immunization among adults: a partial success

- Initial decreases in new hep B infections plateaued 10 years ago
- Rates are now highest among adults
- Rates have *increased* among adults >40 years of age

*Rates of reported acute hepatitis B virus infection, by age group — United States, 2004–2019*

2019 CDC Hepatitis Surveillance Report\(^1\)
Hepatitis B vaccine coverage (≥3 doses) among adults aged ≥19 years*

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>30.0</td>
</tr>
<tr>
<td>Travelers</td>
<td>38.9</td>
</tr>
<tr>
<td>Chronic liver conditions</td>
<td>33</td>
</tr>
<tr>
<td>Health care personnel**</td>
<td>67.2</td>
</tr>
<tr>
<td>Diabetes (19-59 years)</td>
<td>33</td>
</tr>
<tr>
<td>Diabetes (&gt;60 years)</td>
<td>15.3</td>
</tr>
</tbody>
</table>

* for adults with diabetes categories: 19-59 years and 60+ years
**Refers to health care personnel (HCP) overall; 75.3% vaccination rate among HCP with direct patient care; 50.9% among HCP without direct patient care

National Health Interview Survey (NHIS) – US, 2018
HepB vaccination coverage decreased in older-aged adults with ≥1 risk factor*

*Risk Factors: Diabetic, has chronic liver disease, OR traveled to HBV endemic country


*95% CI (53.7-60.4) 48.3 (45.3-51.3) 38.2 (35.2-41.2) 30.1 (27.6-32.8) 19.5 (18.0-21.1)
Limitations of risk-based approach

Availability of information regarding risk behaviors or exposures associated with reported cases of acute hepatitis B virus infection — US, 2019


2/3 of reported cases were either missing risk data or reported no identified risk
Health equity: Disparities could be reduced with a universal adult HepB recommendation

- Rates of HBV infection for children and adolescents of all races/ethnicities converged to a lower rate when a universal vaccination strategy was implemented for children ≤18y. \(^1,^2\)

- Current rates among Black American adults are now up to 3x those of Asian/Pacific Islander and Hispanic groups.\(^1\)

- Racial/ethnic disparities remain in hepatitis B virus infections

rates of reported acute hepatitis B virus infections, by race/ethnicity — United States, 2004–2019

2. Wasley et al. MMWR. 2008
3. Harris et al. MMWR. 2016
Health equity: Disparities could be reduced with a universal adult HepB recommendation

Risk-based recommendations favor individuals with:

- Consistent access to preventive health services
- Trust to disclose potentially stigmatizing risk factor(s)
- Awareness of risk (e.g., infected household contact or sex partner)
- Health literacy
1. Can universal recommendations increase vaccine uptake among people with risk factors?

2. Is a universal HepB vaccination recommendation an effective use of resources?

3. Should the proposed HepB recommendation include adults of all ages?
   • Compare with adding an upper age limit at ≤59 years and resuming the existing risk-based recommendation for persons >59 years
1. Can universal recommendations increase vaccine uptake among people with risk factors?

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Date of relevant recommendation</th>
<th>Coverage (95% CI)</th>
<th>“Universal” Cohort Coverage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flu</strong></td>
<td>25–64y +high risk conditions(^1) 2009-10 season</td>
<td>28.6% (±1.1)</td>
<td>51.0% (±1.4) 18–64 years +high risk conditions(^1) 2020-21 season</td>
</tr>
<tr>
<td><strong>Pneumococcal</strong></td>
<td>19–64y at increased risk(^2) 2018</td>
<td>23.3% (22.0-24.6)</td>
<td>69.0% (67.5-70.4) ≥65y(^2) 2018</td>
</tr>
<tr>
<td><strong>HepB-BD</strong></td>
<td>Newborns(^3) 1/2003 – 6/2005</td>
<td>50.1% (±1.1)</td>
<td>79.6% (78-81) birth year 2018(^4)</td>
</tr>
</tbody>
</table>

\(^1\)CDC FluVaxView
\(^2\)NHIS 2018. NHIS captures “any” pneumococcal vaccination; risk-based recommendation includes groups with different pneumococcal recommendations.
\(^3\)Allred, NJ et al CDC MMWR 2008. Birth Dose, to 3 days from birth
\(^4\)CDC ChildVaxView, HepB Birth Dose by Age 0-3 Days
1. Can universal recommendations increase vaccine uptake among people with risk factors? Yes.

<table>
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<tr>
<th>Limitations</th>
<th>Advantages</th>
</tr>
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<tbody>
<tr>
<td>▪ Level of future increased vaccine uptake is not known</td>
<td>▪ Patient: Reduce stigma, barriers</td>
</tr>
<tr>
<td>▪ However, can infer magnitude from public health experience with other vaccines</td>
<td>• Remove need to disclose risk factors</td>
</tr>
<tr>
<td></td>
<td>▪ Provider: Simpler recommendation; easier implementation</td>
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<td></td>
<td>▪ Practice: Eliminate hepatitis B nationally and globally</td>
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<td></td>
<td>▪ Advance health equity goals</td>
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</tbody>
</table>
1. Can universal recommendations increase vaccine uptake among people with risk factors?

In a WG straw poll, 100% said “Yes”
2. Is a universal HepB vaccination recommendation an effective use of resources?

- ICER: $153,000 per QALY gained\(^1\)
  - ICER decreases as coverage improves in groups at higher risk*

- Conservative economic model was presented, estimating health improvements from universal adult HepB vaccination
  - Reduce acute HBV infections by 24%
  - Reduce HBV-related deaths by 23%

\(^1\)Hall et al, ACIP Presentation, Feb 2021. Assumptions: 3-dose vaccine; base case summary input of ~30% coverage (based on 35.8% protected, with varying age-group specific coverages among people with risk factors; 50% vaccination coverage in general population)

*With 20% additional coverage in high-risk groups, the $/QALY was $135,000, illustrating the benefits of increased access
2. Is a universal HepB vaccination recommendation an effective use of resources?

In a WG straw poll,
70% said “Yes”
30% said “Probably Yes”
3. Should the proposed recommendation include adults of all ages? vs. including an upper age limit at ≤59 years

<table>
<thead>
<tr>
<th></th>
<th>Subanalysis(^1) (≤59y)</th>
<th>Base Case(^2) (all adults)</th>
</tr>
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<tbody>
<tr>
<td>ICER per QALY gained</td>
<td>$117,000</td>
<td>$153,000</td>
</tr>
<tr>
<td>Total incremental cost (2019 USD)</td>
<td>~$22 billion</td>
<td>~$32 billion</td>
</tr>
<tr>
<td>NNV to avert an acute infection</td>
<td>271</td>
<td>372</td>
</tr>
<tr>
<td>Doses given</td>
<td>298 million</td>
<td>352 million</td>
</tr>
<tr>
<td>Increase persons protected by</td>
<td>61%</td>
<td>89%</td>
</tr>
<tr>
<td>Reduce acute HBV infections by</td>
<td>23%</td>
<td>24%</td>
</tr>
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</table>

\(^1\) Hall et al 2021. Single model run applied to age ≤59y  
\(^2\) Assumptions: 3-dose vaccine, base case: 50% vaccination coverage in general population; ~30% coverage (summary input based on 35.8% protected, with varying age-group specific coverages) among people with risk factors.
3. Should the proposed recommendation include adults of all ages?
vs. including an upper age limit at ≤59 years

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| - Lower incidence among age >59y (higher ICER for older populations) | - HBV can still cause significant disease in adults >59y
  - Many adults will acquire risk factors as they age (diabetes, renal disease)
  - Immunize before acquiring comorbidities that reduce response |
| - Improved specificity with age limit
  - Risk-based recommendation still needed for adults >59y | - Simplified implementation is likely to be followed by patients, providers |
| - Difficult to pinpoint future vaccine uptake | - Improve health equity across all ages |
3. Should the proposed recommendation include all ages? vs. including an upper age limit at ≤59 years

In a WG straw poll, 56% felt an age cut-off should NOT be applied

- One-time HepB completion gives lifetime protection
- Mitigate dynamic risk
- Decreasing immune response at upper extremes of age
WG Summary
Preferred Adult HepB Recommendation

Current risk-based 0%  Universal 100%
WG Summary:
HHS and NASEM\(^1\) have called for viral hepatitis elimination

- Evidence supports where universal recommendations are preferred over risk-based vaccination approaches

- More vaccine tools available than when risk-based policy was first recommended
  - Two 3-dose monovalent vaccines are available; safe, effective with long-term immunogenicity (>35 y)
  - One 2-dose vaccine is available; safe and effective
  - One vaccine in the pipeline

- Universal hepatitis B vaccination recommendation among adults would provide best chance of achieving HBV elimination goals

Proposed Recommendation

All adults previously unvaccinated for hepatitis B should receive hepatitis B vaccination.
Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.