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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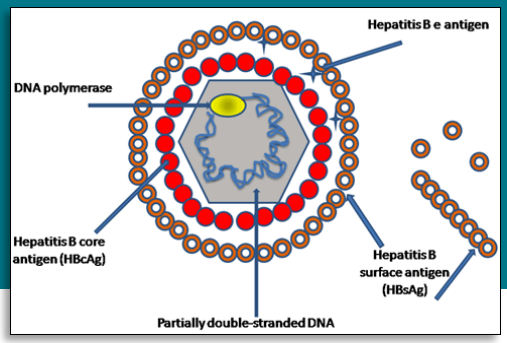
Hepatitis B in the US

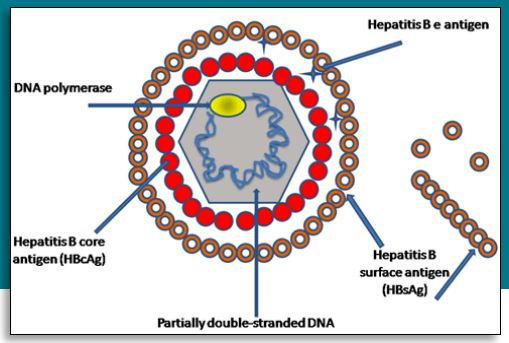


- **20,700 estimated acute HBV infections each year** (95% CI: 11,800–50,800)[1]

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

1) https://www.cdc.gov/hepatitis/statistics/2019surveillance/HepB.htm; 2) Corte et al. J Gastroenterol Hepatol. 2014.

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 infection[3]**

1) Wong et al. Am J Med. 2021 3) https://www.cdc.gov/std/treatment-guidelines/hbv.htm

Simplify a complex adult HepB vaccination schedule

Persons recommended to receive hepatitis B vaccination

Existing Recommendations

Schillie et al, 2018

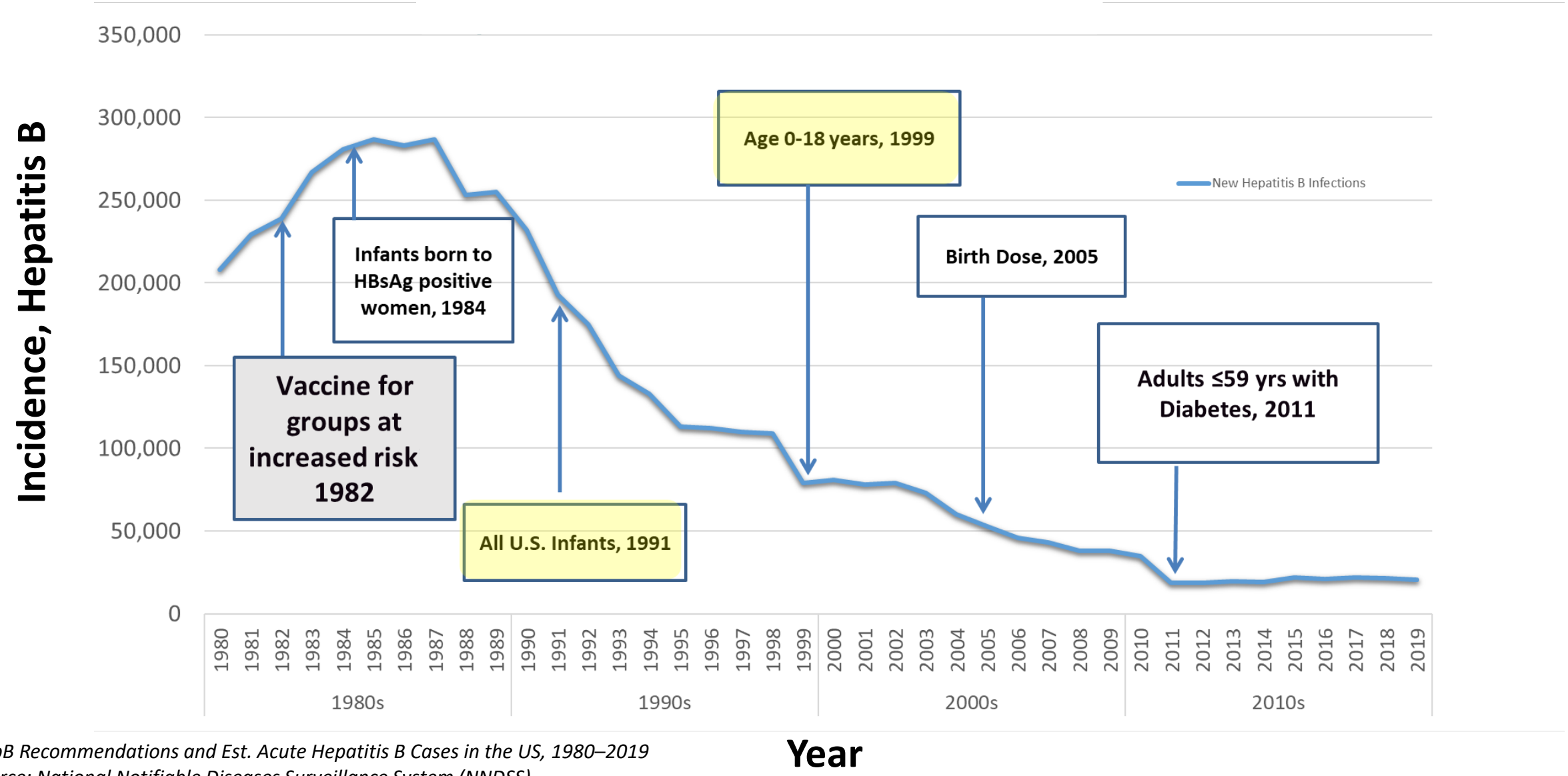
- All infants
- Unvaccinated children aged <19 years
- **Persons at risk for infection by sexual exposure**
  - Sex partners of hepatitis B surface antigen (HBsAg)–positive persons
  - Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one 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
- **All other persons seeking protection from HBV infection**

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

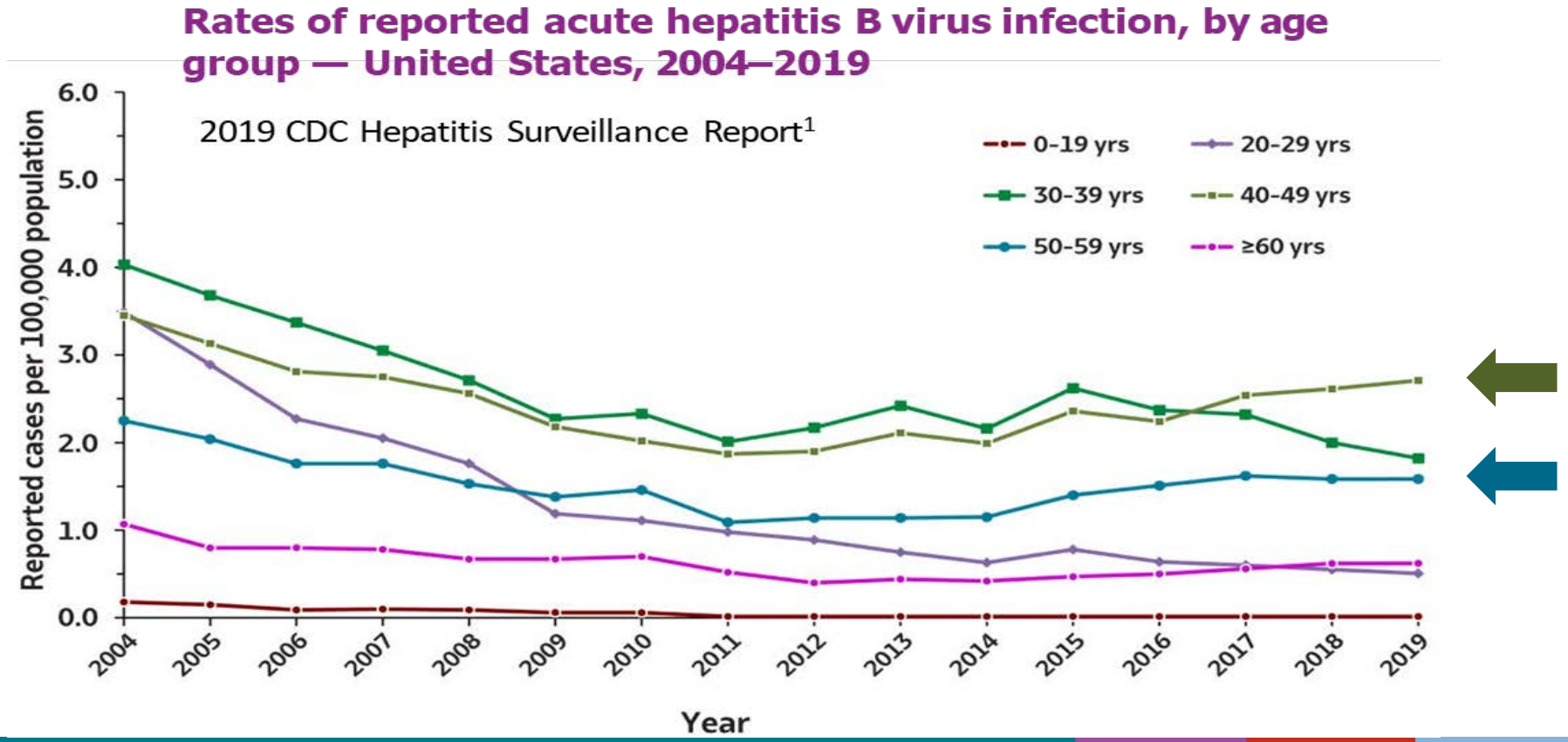
HepB Immunization Strategy Evolves



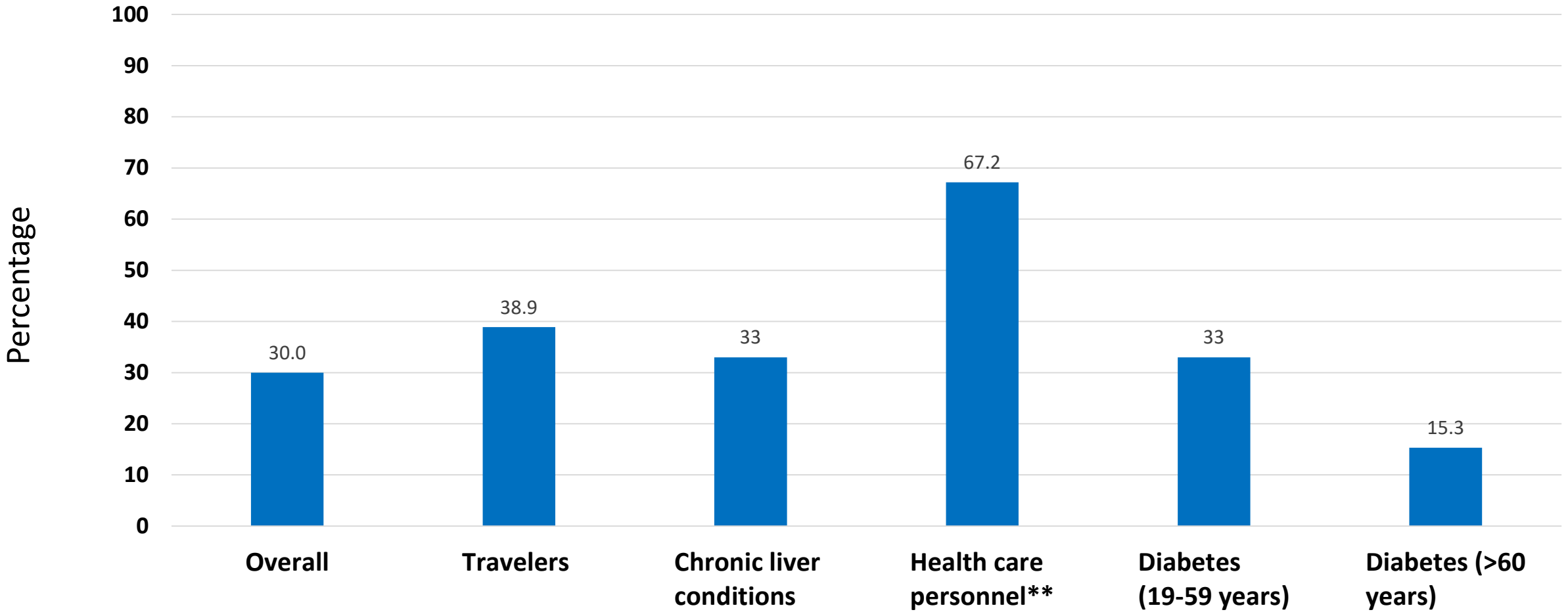
HepB Recommendations and Est. Acute Hepatitis B Cases in the US, 1980–2019
Source: National Notifiable Diseases Surveillance System (NNDSS)

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



Hepatitis B vaccine coverage (≥3 doses) among adults aged ≥19 years*



National Health Interview Survey (NHIS) – US, 2018
Lu et al. Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2018. 2021 May 14;70(3):1-26. Surveillance of Vaccination Coverage Among Adult Populations -United States, 2018 - PubMed (nih.gov)

* 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

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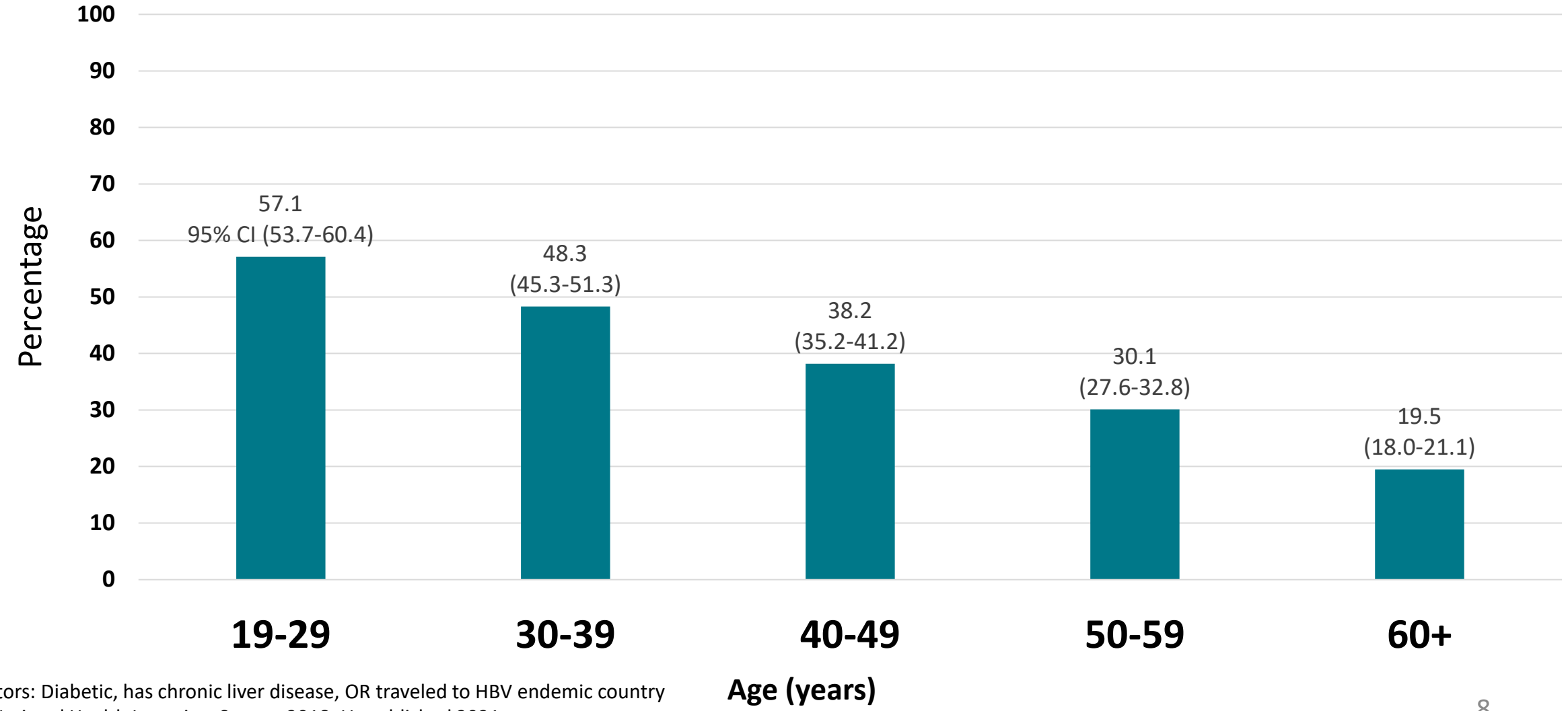
HepB vaccination coverage decreased in older-aged adults with ≥1 risk factor*



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

Lu et al. National Health Interview Survey, 2018. Unpublished 2021.

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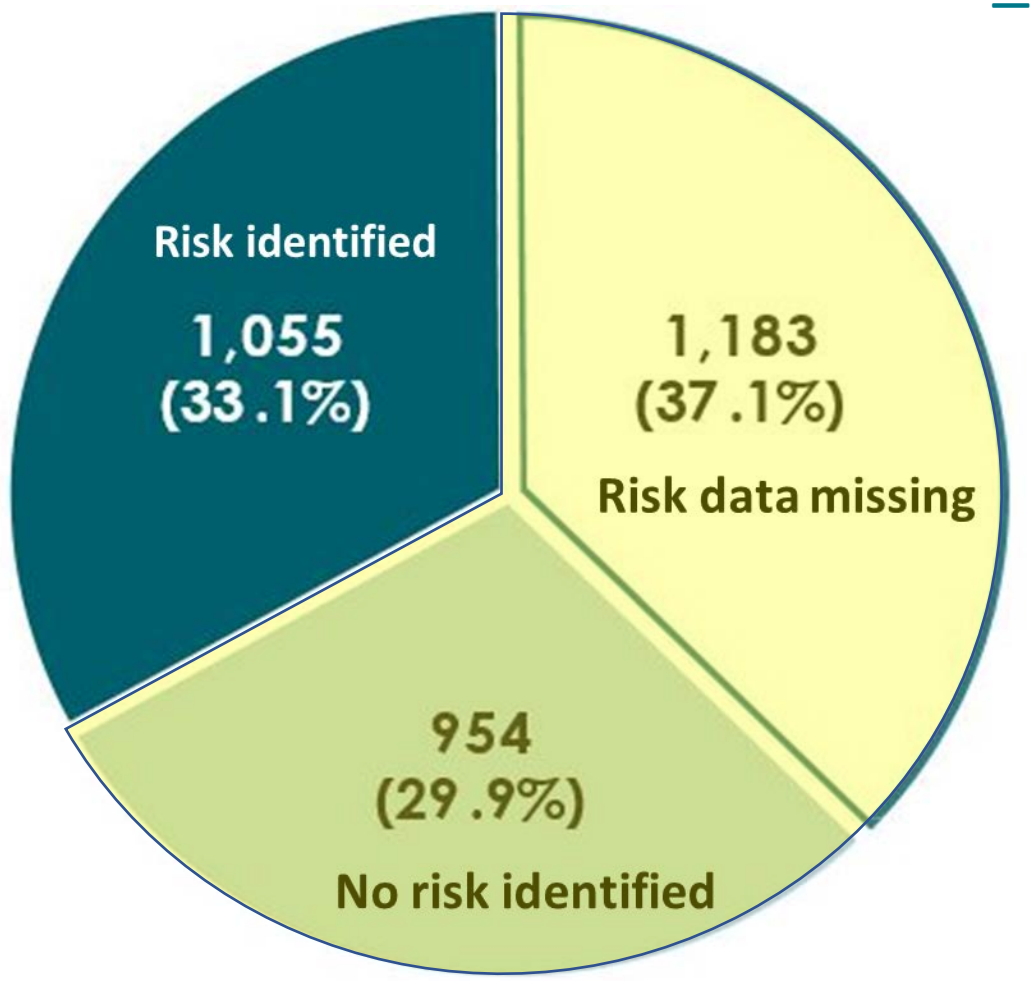
Limitations of risk-based approach

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



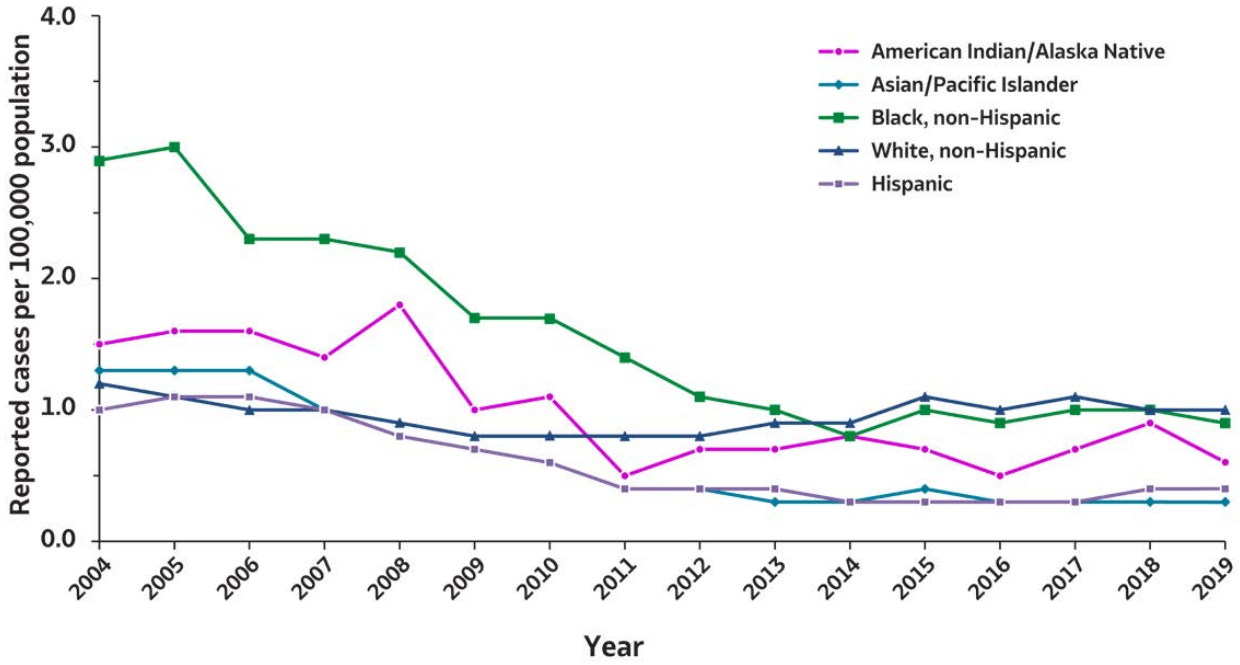
2/3 of reported cases were either missing risk data or reported no identified risk

Source: https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm

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



1. https://www.cdc.gov/hepatitis/statistics/2019surveillance/HepB.htm
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

ACIP Hepatitis Work Group:

Responses to Committee Comments from Prior ACIP Meetings

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?

Vaccine Date of relevant recommendation	Risk-based Cohort	Coverage (95% CI)	"Universal" Cohort	Coverage (95% CI)
Flu **2010**	25–64y +high risk conditions[1] 2009-10 season	**28.6%** (±1.1)	**51.0%** (± 1.4)	18–64 years +high risk conditions[1] 2020-21 season
Pneumococcal **2012**	19–64y at increased risk[2] 2018	**23.3%** (22.0-24.6)	**69.0%** (67.5-70.4)	≥65y[2] 2018
HepB-BD **2005**	Newborns[3] 1/2003 – 6/2005	**50.1%** (±1.1)	**79.6%** (78-81)	birth year 2018[4]

[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.

Limitations

- **Level of future increased vaccine uptake is not known**
  - However, can infer magnitude from public health experience with other vaccines

Advantages

- **Patient: Reduce stigma, barriers**
  - Remove need to disclose risk factors
- **Provider: Simpler recommendation; easier implementation**
- **Practice: Eliminate hepatitis B nationally and globally**
- **Advance health equity goals**

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

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

[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

Limitations

- **Lower incidence among age >59y** (higher ICER for older populations)
- **Improved specificity with age limit**
  - Risk-based recommendation still needed for adults >59y
- **Difficult to pinpoint future vaccine uptake**

Advantages

- **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
- **Simplified implementation is likely to be followed by patients, providers**
- **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**

1. National Academies of Science, Engineering, and Medicine. https://www.nationalacademies.org/our-work/a-national-strategy-for-the-elimination-of-hepatitis-b-and-c

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.