Hepatitis B Vaccination of Adults with Diabetes Mellitus

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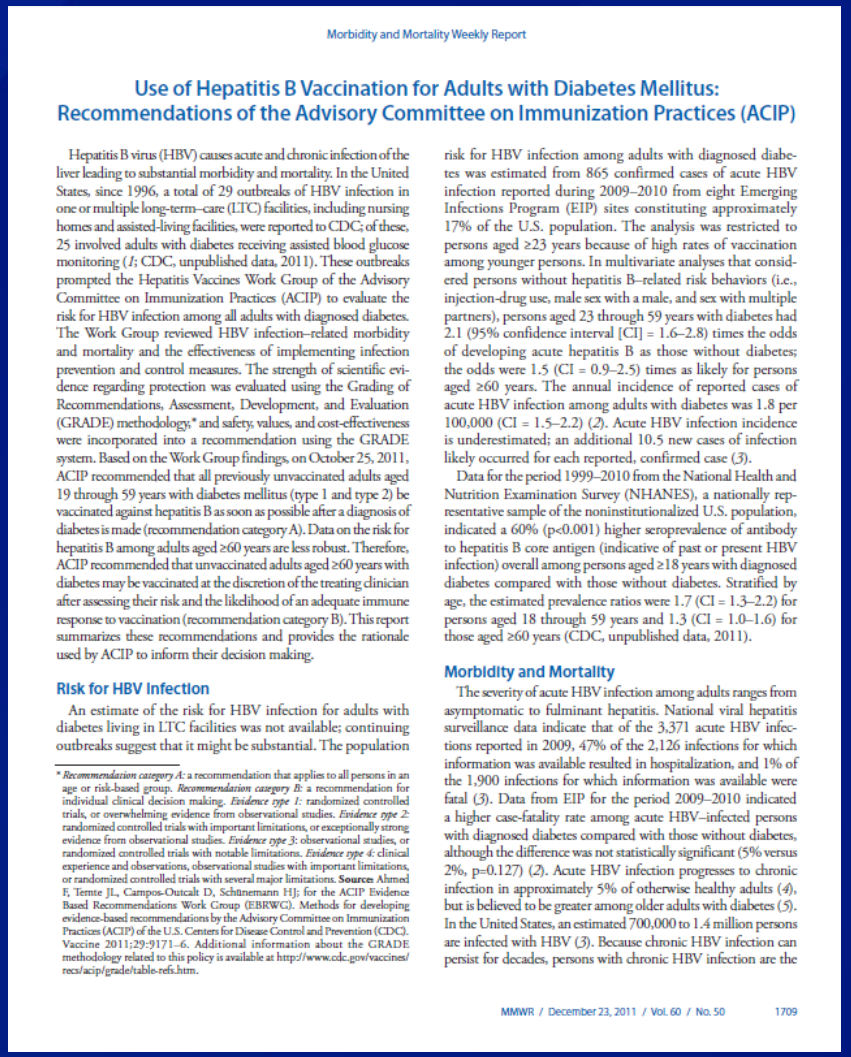
Advisory Committee on Immunization Practices (ACIP) Recommendations

ACIP Recommendation for Hepatitis B Vaccination of Adults with DM

CDC. Use of hepatitis B vaccination for adults with diabetes mellitus: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2011 Dec 23;60(50):1709-11.



Use of Hepatitis B Vaccination for Adults with Diabetes Mellitus: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Hepatitis B virus (HBV) causes acute and chronic infection of the liver leading to substantial morbidity and mortality. In the United States, since 1996, a total of 29 outbreaks of HBV infection in one or multiple long-term–care (LTC) facilities, including nursing homes and assisted-living facilities, were reported to CDC; of these, 25 involved adults with diabetes receiving assisted blood glucose monitoring (*1*; CDC, unpublished data, 2011). These outbreaks prompted the Hepatitis Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) to evaluate the risk for HBV infection among all adults with diagnosed diabetes. The Work Group reviewed HBV infection–related morbidity and mortality and the effectiveness of implementing infection prevention and control measures. The strength of scientific evidence regarding protection was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology;* and safety, values, and cost-effectiveness were incorporated into a recommendation using the GRADE system. Based on the Work Group findings, on October 25, 2011, ACIP recommended that all previously unvaccinated adults aged 19 through 59 years with diabetes mellitus (type 1 and type 2) be vaccinated against hepatitis B as soon as possible after a diagnosis of diabetes is made (recommendation category A). Data on the risk for hepatitis B among adults aged ≥60 years are less robust. Therefore, ACIP recommended that unvaccinated adults aged ≥60 years with diabetes may be vaccinated at the discretion of the treating clinician after assessing their risk and the likelihood of an adequate immune response to vaccination (recommendation category B). This report summarizes these recommendations and provides the rationale used by ACIP to inform their decision making.

Risk for HBV Infection

An estimate of the risk for HBV infection for adults with diabetes living in LTC facilities was not available; continuing outbreaks suggest that it might be substantial. The population risk for HBV infection among adults with diagnosed diabetes was estimated from 865 confirmed cases of acute HBV infection reported during 2009–2010 from eight Emerging Infections Program (EIP) sites constituting approximately 17% of the U.S. population. The analysis was restricted to persons aged ≥23 years because of high rates of vaccination among younger persons. In multivariate analyses that considered persons without hepatitis B–related risk behaviors (i.e., injection-drug use, male sex with a male, and sex with multiple partners), persons aged 23 through 59 years with diabetes had 2.1 (95% confidence interval [CI] = 1.6–2.8) times the odds of developing acute hepatitis B as those without diabetes; the odds were 1.5 (CI = 0.9–2.5) times as likely for persons aged ≥60 years. The annual incidence of reported cases of acute HBV infection among adults with diabetes was 1.8 per 100,000 (CI = 1.5–2.2) (*2*). Acute HBV infection incidence is underestimated; an additional 10.5 new cases of infection likely occurred for each reported, confirmed case (*3*).

Data for the period 1999–2010 from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the noninstitutionalized U.S. population, indicated a 60% (p<0.001) higher seroprevalence of antibody to hepatitis B core antigen (indicative of past or present HBV infection) overall among persons aged ≥18 years with diagnosed diabetes compared with those without diabetes. Stratified by age, the estimated prevalence ratios were 1.7 (CI = 1.3–2.2) for persons aged 18 through 59 years and 1.3 (CI = 1.0–1.6) for those aged ≥60 years (CDC, unpublished data, 2011).

Morbidity and Mortality

The severity of acute HBV infection among adults ranges from asymptomatic to fulminant hepatitis. National viral hepatitis surveillance data indicate that of the 3,371 acute HBV infections reported in 2009, 47% of the 2,126 infections for which information was available resulted in hospitalization, and 1% of the 1,900 infections for which information was available were fatal (*3*). Data from EIP for the period 2009–2010 indicated a higher case-fatality rate among acute HBV–infected persons with diagnosed diabetes compared with those without diabetes, although the difference was not statistically significant (5% versus 2%, p=0.127) (*2*). Acute HBV infection progresses to chronic infection in approximately 5% of otherwise healthy adults (*4*), but is believed to be greater among older adults with diabetes (*5*). In the United States, an estimated 700,000 to 1.4 million persons are infected with HBV (*3*). Because chronic HBV infection can persist for decades, persons with chronic HBV infection are the

* *Recommendation category A:* a recommendation that applies to all persons in an age or risk-based group. *Recommendation category B:* a recommendation for individual clinical decision making. *Evidence type 1:* randomized controlled trials, or overwhelming evidence from observational studies. *Evidence type 2:* randomized controlled trials with important limitations, or exceptionally strong evidence from observational studies. *Evidence type 3:* observational studies, or randomized controlled trials with notable limitations. *Evidence type 4:* clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations. **Source:** Ahmed F, Temte JL, Campos-Outcalt D, Schünemann HJ; for the ACIP Evidence Based Recommendations Work Group (EBRWG). Methods for developing evidence-based recommendations by the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (CDC). Vaccine 2011;29:9171–6. Additional information about the GRADE methodology related to this policy is available at http://www.cdc.gov/vaccines/recs/acip/grade/table-refs.htm.

Recommendations

- **Hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A)**
- **Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥60 years (recommendation category B)**

Category A: Applies to all persons in an age- or risk-based group
Category B: For individual clinical decision making

MMWR 2011 Dec 23;60(50):1709-11.

Hepatitis B Vaccination for Adults with Diabetes

- Vaccination should be completed as soon as feasible after diabetes is diagnosed
- No serologic testing or additional hepatitis B vaccination is recommended for adults who received a complete series of hepatitis B vaccinations at any time in the past
- Available data do not confirm an advantage to any specific vaccine, dosage, or approved schedule for adults with diabetes

MMWR 2011 Dec 23;60(50):1709-11.

Vaccinating Adults with Diabetes Aged ≥60 Years

- **Decisions should incorporate:**
  - Likelihood of acquiring HBV infection, including the risk posed by assisted blood-glucose monitoring in long-term care facilities
  - Likelihood of experiencing chronic sequelae if infected with HBV
  - The declining immunologic responses to vaccines that are associated with frailty

MMWR 2011 Dec 23;60(50):1709-11.

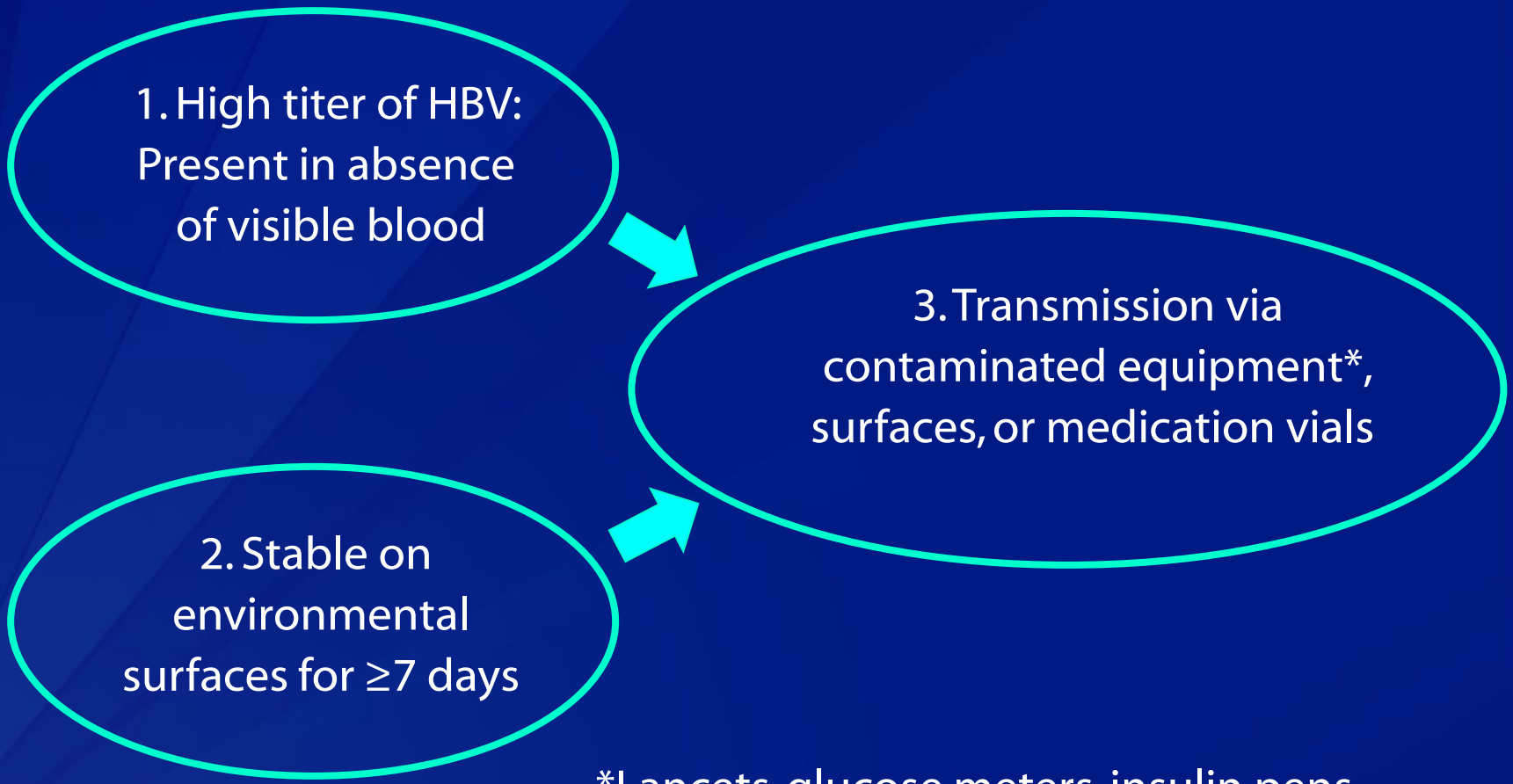
Considerations for Recommendation of Hepatitis B Vaccine for Adults with Diabetes

Diabetes Mellitus (DM) and Hepatitis B Virus (HBV) Infection

- **Increased risk of HBV infection among persons with DM**
  - Persons with DM may acquire HBV infection from lapses in infection control during blood glucose monitoring

Klonoff DC. Improving the safety of blood glucose monitoring. J Diabetes Sci Technol. 2011 Nov 1;5(6):1307-11.

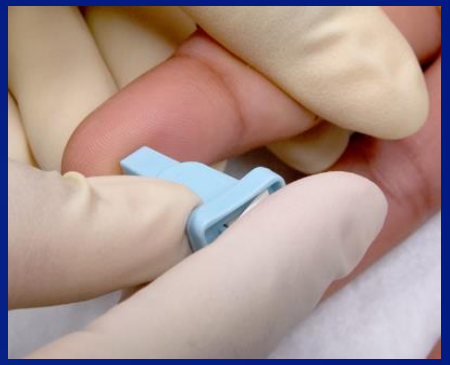
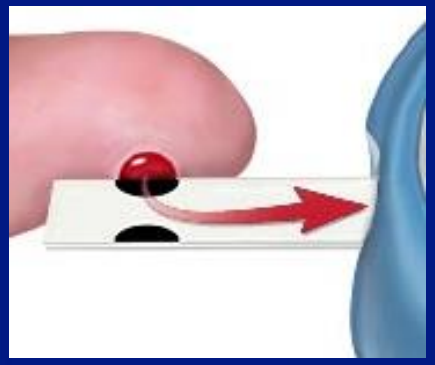
Transmission of HBV during Healthcare Delivery



*Lancets, glucose meters, insulin pens

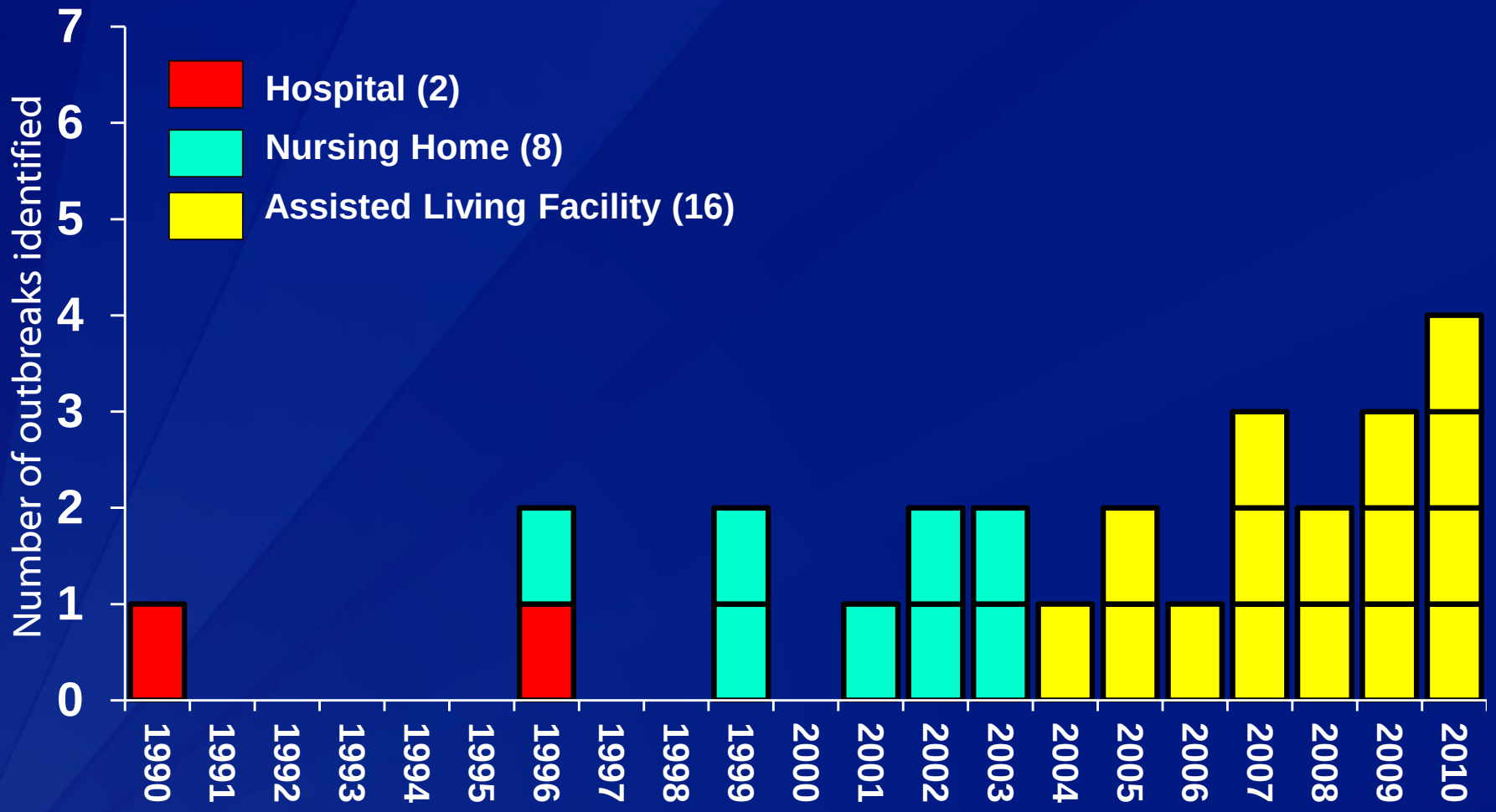
Blood Glucose Monitoring

- **Essential component of diabetes management**
  - ~86% check blood glucose at least monthly*, including persons treated with insulin, oral medications, and nutritional therapy
- **Procedure**
  - Test strip inserted into meter
  - Blood drawn with fingerstick device
  - Blood applied to test strip

CDC. Diabetes Data and Trends: National Diabetes Surveillance System, www.cdc.gov/diabetes/statistics; Behavioral Risk Factor Surveillance System

Outbreaks of Hepatitis B Virus (HBV) Infection associated with Blood Glucose Monitoring — United States, 1990-2010



Thompson ND, Perz JF. Eliminating the blood: ongoing outbreaks of hepatitis B virus infection and the need for innovative glucose monitoring technologies. J Diabetes Sci Technol. 2009 Mar 1;3(2):283-8.

Mis-use of Diabetes Equipment: Recent Patient Notifications

Year, setting	Equipment misused	Length of misuse	Persons at risk
2008, Hospital	Insulin pen	7 months	908
2009, Hospital	Insulin pen	7 months	2114
2009, Community Health Center	Multi-lancet finger stick device	6 months	283
2010, Health fair	Multi-lancet finger stick device	1 day	64
2011, HMO, certified diabetes educator	Multi-lancet finger stick device, insulin pen	5+ years	2345

Guh. Patient Notifications for Bloodborne Pathogen Testing Due to Unsafe Injection Practices in U.S. Healthcare Settings, 1999–2009. [Abstract 633]. Presented at: International Conference on Healthcare Associated infections 2010. Atlanta. GA. 2011: media release

Settings Where Persons Receive Assistance with Blood Glucose Monitoring

- Hospitals
- Nursing homes
- Assisted living facilities
- Prisons
- Home health care
- Medical practitioners' offices or clinics
- Diabetes research laboratories
- Health fairs
- Schools
- Children's camps
- Shelters

Klonoff DC. Improving the safety of blood glucose monitoring. J Diabetes Sci Technol. 2011 Nov 1;5(6):1307-11.

Past HBV Infection: National Health and Nutrition Examination Survey, 1999-2010

- **Nationally representative survey of non-institutionalized adults; tested for antibody to hepatitis B core antigen (anti-HBc)**

- **Unadjusted prevalence ratios of anti-HBc among adults with diabetes (vs. without diabetes)**
  - Ages 18-59 years: 1.7 (1.3-2.2)
  - Ages ≥60 years: 1.3 (1.0-1.6)

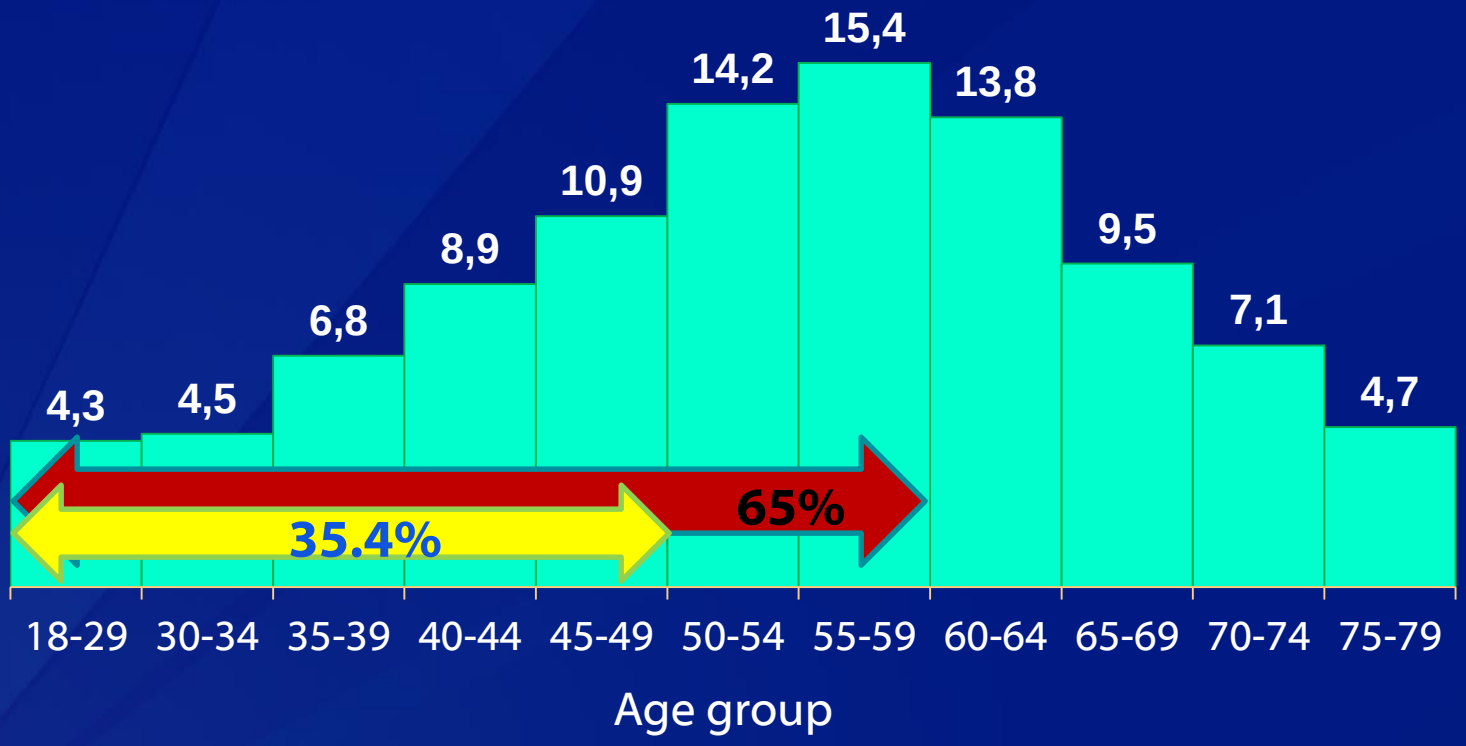
Schillie SF, Xing J, Murphy TV, Hu DJ. Prevalence of hepatitis B virus infection among persons with diagnosed diabetes mellitus in the United States, 1999-2010. J Viral Hepat. 2012 Sep;19(9):674-6.

Acute Hepatitis B: Emerging Infections Program (EIP), 2009-2010

- 865 cases from 8 EIP surveillance sites
- To determine the odds of acute hepatitis B among adults with diabetes, controlling for potential confounders
- Adjusted OR (Models controlled for sex, age, and race/ethnicity and excluded persons with other HBV risk behaviors):
  - Ages 23-59 years: 2.1 (1.6-2.8)
  - Ages ≥60 years: 1.5 (0.9-2.5)

Reilly ML, Schillie SF, Smith E, Poissant T, Vonderwahl CW, Gerard K, Baumgartner J, Mercedes L, Sweet K, Muleta D, Zaccaro DJ, Klevens RM, Murphy TV. Increased risk of acute hepatitis B among adults with diagnosed diabetes mellitus. J Diabetes Sci Technol. 2012 Jul 1;6(4):858-66.

Distribution (%) of Age at Diagnosis of Diabetes, 2011



CDC. Diabetes Data and Trends: National Diabetes Surveillance System
www.cdc.gov/diabetes/statistics. Data from the National Health Interview Survey.

Burden of HBV Prevented with 10% Vaccine Uptake (Lifetime Perspective): Modeling Analysis

Age (years)	Infected	Hospital-izations	Chronic cases	Cirrhosis	HCC	Trans-plants	Deaths
20-59	4,271	467	256	202	33	13	130
≥60	723	79	43	22	3	1	11

HCC=hepatocellular carcinoma

Hoerger TJ, Schillie S, Wittenborn JS, Bradley CL, Zhou F, Byrd K, Murphy TV. Cost-effectiveness of hepatitis B vaccination in adults with diagnosed diabetes. Diabetes Care. 2013 Jan;36(1):63-9.

Number Needed to Vaccinate

- **Number of persons with diabetes needed to vaccinate to prevent one HBV infection (modeling analysis)**
  - Age 20-59 years: 124
  - Age ≥60 years: 1,071

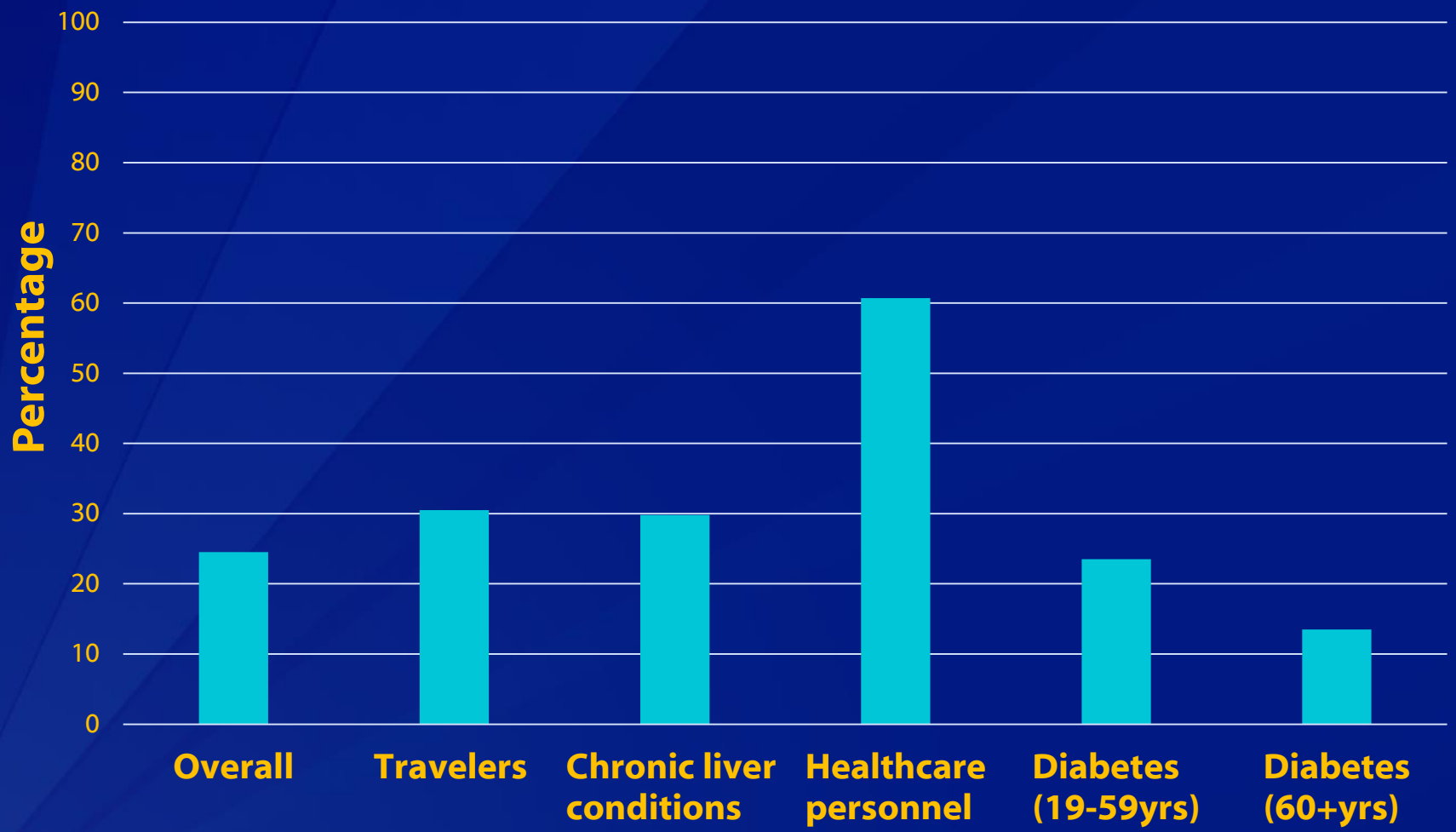
Hoerger TJ, Schillie S, Wittenborn JS, Bradley CL, Zhou F, Byrd K, Murphy TV. Cost-effectiveness of hepatitis B vaccination in adults with diagnosed diabetes. Diabetes Care. 2013 Jan;36(1):63-9.

Hepatitis B Vaccine Seroprotection (anti-HBs ≥10 mIU/mL) among Persons with Diabetes

Author, year	Total N	Mean age*	Dose (mcg)	Route	Schedule (mos)	Diabetes (%, 95% CI)	Non-Diabetes (%, 95% CI)
Arslanoglu, 2002	150	11	10	IM	0,1,6	94 (88-98)	98 (88-100)
Bouter, 1992	64	34	20	IM	0,1,6	75 (56-88)	97 (82-100)
Douvin, 1997	71	52/46	20	IM	0,1,2,12‡	92 (82-97)	--
Li Volti, 1998	42	9	3-20	IM, ID	0,1,6§	89 (64-98)	100 (83-100)
Marseglia, 1996	239	17	10¶	IM	0,1,6	95 (86-99)	98 (95-100)

*Among subjects with diabetes, ‡30 subjects received a booster dose at month 4, §2, 4, 6, 8 weeks for ID route; ¶One 4.5 year-old subject received 5 mcg

Hepatitis B Vaccine Coverage (≥3 doses) among Adults Aged ≥19 Years, National Health Interview Survey (NHIS) – U.S., 2014



Williams WW,, et. al. Surveillance of Vaccination Coverage Among Adult Populations - United States, 2014. MMWR Surveill Summ. 2016 Feb 5;65(1):1-36.

Conclusions

- **Adults with diabetes at elevated risk for HBV infection**
  - Infection control lapses with blood glucose monitoring
- **Hepatitis B vaccination recommended for adults with diabetes in United States since 2011**
  - Aged 19-59 years: All persons
  - Aged 60 years and older: Based on risk
- **Vaccine coverage among adults with diabetes remains low**

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Questions?

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