

## **CDC Recommendation for Hepatitis B Vaccination among Adults with Diabetes:**

### **Grading of Scientific Evidence in Support of Key Recommendations**

GRADE Tables: Hepatitis B Vaccination Among Persons with Diabetes Referenced in MMWR Dec 23, 2011 / Vol 60(50);1709-11

#### **Methods for Grading of Recommendations Assessment, Development, and Evaluation (GRADE) According to ACIP Guidelines**

Evidence of benefits, harms, values and preferences, and cost effectiveness were reviewed in accordance with GRADE methods to determine the recommendation category (Ahmed F, Temte JL, Campos-Outcalt D, Schönemann 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* 29(49):9171-6, 2011). Pooled data from 6 placebo-controlled randomized trials (5798 subjects) indicated a relative risk for hepatitis B infection events of 0.37 (95% CI 0.29, 0.48) among vaccinated subjects, although evidence type was downgraded for indirectness as trials did not focus on subjects with diabetes. Pooled data from 5 observational studies (285 subjects with diabetes) indicated 91.6% of subjects with diabetes achieved seroprotection, although evidence type was downgraded for imprecision due to small numbers. No serious vaccine-related adverse events were reported in any study. The Institute of Medicine found evidence supporting a causal relationship between hepatitis B vaccination and anaphylaxis in yeast-sensitive individuals; the risk of anaphylaxis following hepatitis B vaccine is estimated at 1.1 per million doses. [IOM (Institute of Medicine). 2011. *Adverse Effects of Vaccines: Evidence and Causality*. Washington, DC: The National Academies Press; Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, Mullooly JP, Thompson RS; Vaccine Safety Datalink Team. Risk of anaphylaxis after vaccination of children and adolescents, *Pediatrics* 2003;112:815-20].



June 13, 2014

**Table 1: Benefits and Harms of Hepatitis B Vaccination Among Persons with Diabetes<sup>a</sup>**

Outcome	No. of subjects (# studies)	Incidence in controls	Incidence in vaccinated	Relative risk (95% CI) of hepatitis B infection events among vaccinated	Seroprotection proportion among subjects with diabetes (95% CI)	Risk difference per 1000 (95% CI), vaccinated versus not vaccinated	Number needed to vaccinate (NNV)
<b>BENEFITS</b>							
Hepatitis B infection events	5798 (6 RCTs)	10.7% <sup>b</sup>	4.1% <sup>b</sup>	0.37 (0.29, 0.48) <sup>b</sup>	--	-67 (-76, -56) <sup>c</sup>	261 <sup>d</sup>
Seroprotection	285 (5 Obs)	--	--	--	91.6% (87.6%, 94.4%)	--	--
<b>HARMS</b>							
Serious adverse events	6251 (6 RCTs and 3 Obs)	0.0% <sup>e</sup>	0.0% <sup>e</sup>	--	--	--	--
Anaphylaxis	6251 (6 RCTs and 3 Obs)	0.0% <sup>e</sup>	0.0% <sup>e</sup>	--	--	--	--

<sup>a</sup> Some studies include persons with and without diabetes

<sup>b</sup> Follow-up ranged from 12-29 months; figures do not account for person-time of follow-up for all studies; relative risk and 95% CI calculated from RevMan software version 5.1

<sup>c</sup> Calculated from GRADE profiler software version 3.6 assuming fixed effects

<sup>d</sup> Number needed to treat (number needed to vaccinate) calculated from modeling analysis of adults with diabetes ages ≥20 years (lifetime perspective)

<sup>e</sup> No serious events reported. Study sizes not sufficient to detect rare serious adverse events

**Table 2: Type of Evidence for Hepatitis B Vaccination Benefits and Harms among Persons with Diabetes<sup>a</sup>**

Outcome	Design (# studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Evidence type
<b>Benefits</b>							
Hepatitis B infection events	RCT (6)	No serious	No serious	Yes (-1) <sup>b</sup>	No serious	No serious	2
Seroprotection	Obs (5)	No serious	No serious	No serious	Yes (-1) <sup>c</sup>	No serious	4
<b>Harms</b>							
Serious adverse events	RCT (6)	No serious	No serious	Yes (-1) <sup>b</sup>	No serious	No serious	2 <sup>d</sup>
	Obs (3)						
Anaphylaxis	RCT (6)	No serious	No serious	Yes (-1) <sup>b</sup>	No serious	No serious	2 <sup>d</sup>
	Obs (3)						

<sup>a</sup> Some studies include persons with and without diabetes

<sup>b</sup> Subjects with diabetes not focus of RCT studies; one RCT used 3 mcg dose on 0,1,2 month schedule; one study used 5 mcg dose on 0,1,2 month schedule with subcutaneous administration

<sup>c</sup> Total number of events <300, 95% CI 0.88, 0.94

<sup>d</sup> Study sizes not sufficient to detect rare adverse events: rate of anaphylaxis estimated 1.1 per million doses (95% CI 0.1, 3.9 per million doses); (Bohlke K. et al. *Pediatrics* 2003;112:815-20). Widespread vaccine use for 30 years has not revealed other serious adverse events (IOM (Institute of Medicine). 2011. *Adverse Effects of Vaccines: Evidence and Causality*. Washington, DC: The National Academies Press)

**Table 3: Summary of Evidence for Benefits and Harms of Hepatitis B Vaccination among Adults with Diabetes<sup>a</sup>**

Comparison	Outcome	Study design (# studies)	Findings	Evidence type	Overall evidence type
Hepatitis B vaccination vs. no vaccination	Hepatitis B infection events	RCT (6)	Decreased risk among vaccinated	2	2
	Seroprotection	Obs (5)	Seroprotection among subjects with diabetes similar to that among subjects without diabetes	4	
	Serious adverse events	RCT (6) Obs (3)	No serious vaccine-related adverse events	2 <sup>b</sup>	
	Anaphylaxis	RCT (6) Obs (3)	No serious vaccine-related adverse events	2 <sup>b</sup>	

<sup>a</sup> Some studies include persons with and without diabetes

<sup>b</sup> Study sizes not sufficient to detect rare adverse events

**Table 4. Considerations for Formulating Recommendations: Hepatitis B Vaccine for Adults with Diabetes**

Key factors	Comments
Balance between benefits and harms	Benefits are greater than potential harms
Evidence type for benefits and harms	Benefits: Evidence type 2 Harms: Approximately 30 year hepatitis B vaccine history indicates serious adverse events and anaphylaxis extremely rare
Values	High values on preventable outcomes <sup>a</sup> for persons <60 years and moderate to high values for persons ≥60 years assigned by ACIP Hepatitis Work Group
Cost-effectiveness	Vaccination is most cost effective for adults with diabetes for ages <60 years

<sup>a</sup>Preventable outcomes consist of acute hepatitis, fulminant hepatitis, chronic hepatitis, cirrhosis, hepatocellular carcinoma, liver transplantation, death

Summary: Benefits are greater than potential harms; overall evidence is type 2. High values were placed on prevention of the morbidity and mortality of hepatitis B virus infection among adults with diabetes.

## Study References

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