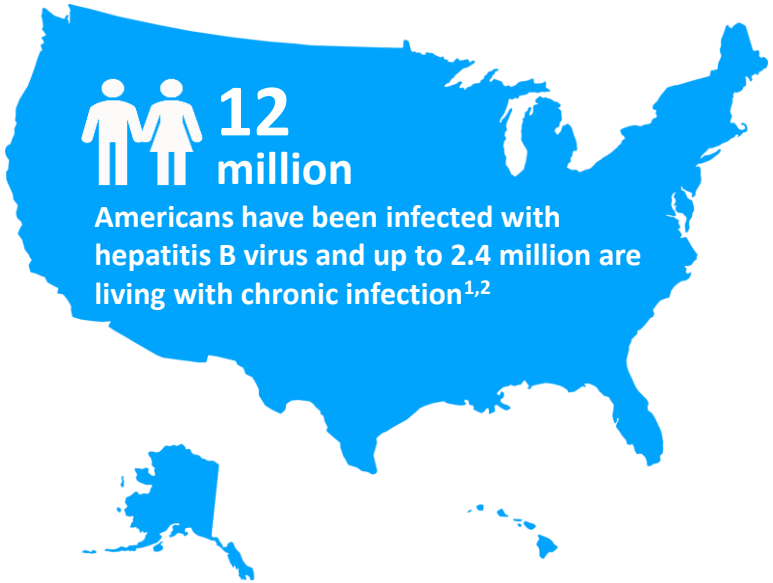
Hepatitis B in the US: Disease Burden, Prevention, and the Goal of Elimination

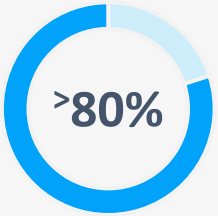
AJ Fernandez, PharmD

Medical Science Liaison

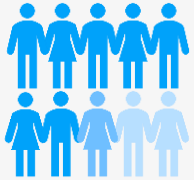
DYNAVAX

Hepatitis B Remains a Significant Clinical and Public Health Burden

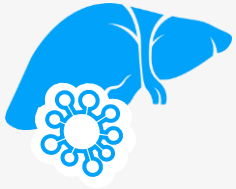




of people **are unaware** they are infected[3]



From 2016-2021, **more than 75%** of acute infections occurred **among people aged 30–59 years**[4]



Chronic infection can progress to advanced liver disease[5] (i.e., cirrhosis, hepatocellular carcinoma, or liver transplant)

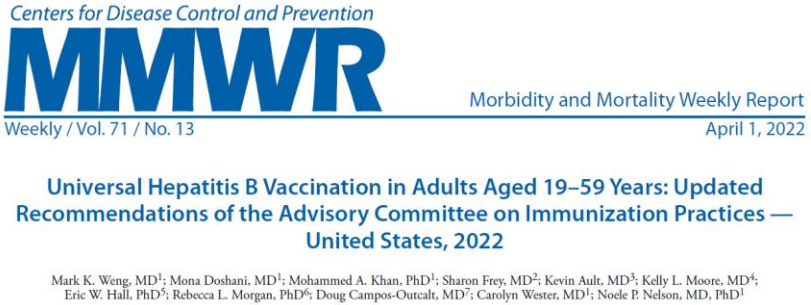
1. Hepatitis B Foundation. Do you know your hepatitis facts from fiction? https://www.hepb.org/blog/do-you-know-your-hepatitis-facts-from-fiction/. Accessed May 27, 2022. **2**. Hepatitis B Foundation. Hepatitis B facts and figures. https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/. Accessed February 28, 2022. **3.** Ogawa E, et al. *JAMA Network Open*. 2020;3:e201844. **4**. CDC. Viral hepatitis surveillance report 2021. https://www.cdc.gov/hepatitis/statistics/2021surveillance/hepatitis-b/figure-2.4.htm. Accessed August 18, 2023. **5**. Doshani M. Evidence to recommendations framework: should all HepB-unvaccinated adults receive hepatitis B vaccination? Presentation to ACIP. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-09-29/03-hepb-Doshani-508.pdf. Accessed April 29, 2022.

Hepatitis B Vaccination Recommendations for US Adults

Universal Hepatitis B Vaccination Recommended in Adults*

Updated policy simplifies hepatitis B vaccine recommendations in adults[1,2*]

- All adults aged 19–59 years should receive hepatitis B vaccination
- Adults aged ≥60 years with risk factors for hepatitis B should receive hepatitis B vaccination
- Adults aged ≥60 years without known risk factors for hepatitis B may receive hepatitis B vaccination



Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 71 / No. 13

April 1, 2022

Universal Hepatitis B Vaccination in Adults Aged 19–59 Years: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

Mark K. Weng, MD[1]; Mona Doshani, MD[1]; Mohammed A. Khan, PhD[1]; Sharon Frey, MD[2]; Kevin Ault, MD[3]; Kelly L. Moore, MD[4]; Eric W. Hall, PhD[5]; Rebecca L. Morgan, PhD[6]; Doug Campos-Outcalt, MD[7]; Carolyn Wester, MD[1]; Noele P. Nelson, MD, PhD[1]

"Removing the risk factor assessment previously recommended to determine vaccine eligibility in this adult age group could increase vaccination coverage and decrease hepatitis B cases."[2]

*Recommendations are for individuals who have not already received a complete vaccine series.

1. Weng M. CDC ACIP presentation. November 2021. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/02-HepWG-weng-508.pdf. Accessed February 8, 2022. **2.** Weng MK, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(13):477-483.

HepB-CpG

HepB-CpG Vaccine for Hepatitis B

Indication

- HepB-CpG is indicated for prevention of infection caused by all known subtypes of hepatitis B virus for adults 18 years of age and older

Important Safety Information

- Do not administer HepB-CpG to individuals with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of HepB-CpG, including yeast.
- Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of HepB-CpG.
- Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to HepB-CpG.
- Hepatitis B has a long incubation period. HepB-CpG may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration.
- The most common patient reported adverse reactions reported within 7 days of vaccination were injection site pain (23%-39%), fatigue (11%-17%) and headache (8%-17%).

HEPLISAV-B [package insert]. Emeryville, CA: Dynavax Technologies Corporation; 2023

HepB-CpG Vaccine for Hepatitis B

Dosing and Administration

- 2 doses administered 1 month apart
- Intramuscular injection

Formulation, How Supplied, and Storage

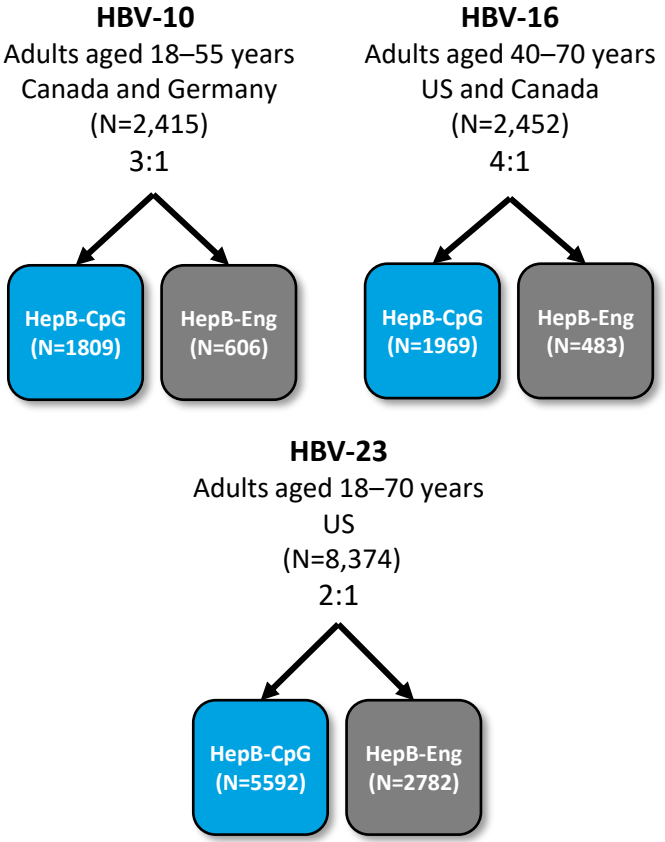
- Each 0.5-mL dose is formulated to contain 20 mcg of HBsAg and 3000 mcg of CpG 1018 adjuvant
- Supplied in prefilled syringes
  - Tip caps and stoppers of the prefilled syringes are not made with natural rubber latex
  - Formulated without preservatives
- Store in a refrigerator at 2°C to 8°C (36°F to 46°F)
  - Do not freeze; discard if the vaccine has been frozen

HBsAg, hepatitis B surface antigen; mcg, micrograms

HEPLISAV-B [package insert]. Emeryville, CA: Dynavax Technologies Corporation; 2023

Pivotal Study Design

- 3 randomized, active-controlled, observer blinded, multi-center Phase 3 clinical trials (HBV-10[1], HBV-16[2], and HBV-23[3])
- Evaluate the non-inferiority of 2 doses HepB-CpG (dosed at 0, 1 month) compared to 3 doses HepB-Eng (dosed at at 0, 1, and 6 months) measured by seroprotection rates
  - HepB-CpG group received placebo at month 6
- Evaluate safety of HepB-CpG
- Exclusions include[1, 2, 3]
  - Current or previous hepatitis B infection or hepatitis B vaccine
  - HIV infection, immunosuppression, or history of autoimmune disease
  - Pregnancy or breastfeeding



HIV, human immunodeficiency virus

1. Halperin S, et al. *Vaccine.* 2012;30:2556-2563. **2.** Heyward WL, et al. *Vaccine.* 2013;31:5300-5305. **3.** Jackson S, et al. *Vaccine.* 2018;36(5):668-674.

How Do We Define Seroprotection Following HepB Vaccination?

Vaccine-Induced Seroprotection: a surrogate of clinical protection[1]

- Persons who have vaccine-induced anti-HBs levels of ≥10 mIU/mL after completing a HepB series are considered seroprotected
- Immunocompetent persons initially responding to a full HepB vaccine series who are later found to have anti-HBs <10 mIU/mL are thought to remain protected
  - Current data suggest protection from disease lasts at least 35 years in persons who achieved seroprotection after vaccination[3]

Vaccine	Test	Correlate of Protection
Hepatitis B	ELISA	10 mIU/mL

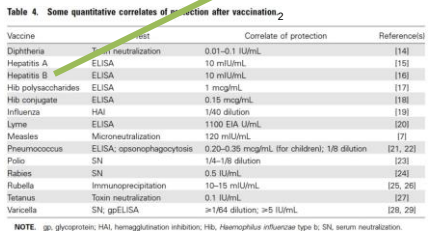


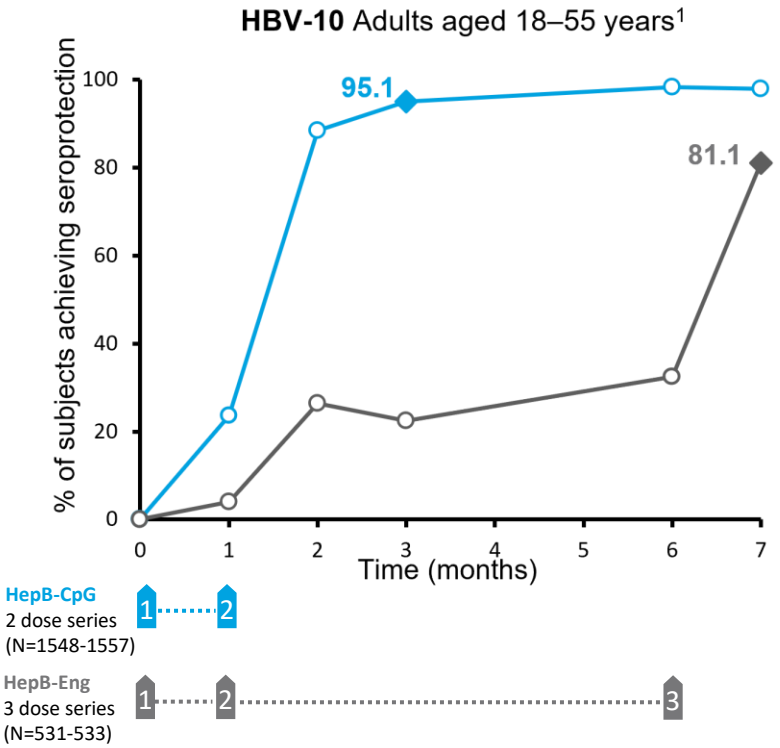
Table 4. Some quantitative correlates of protection after vaccination[2]

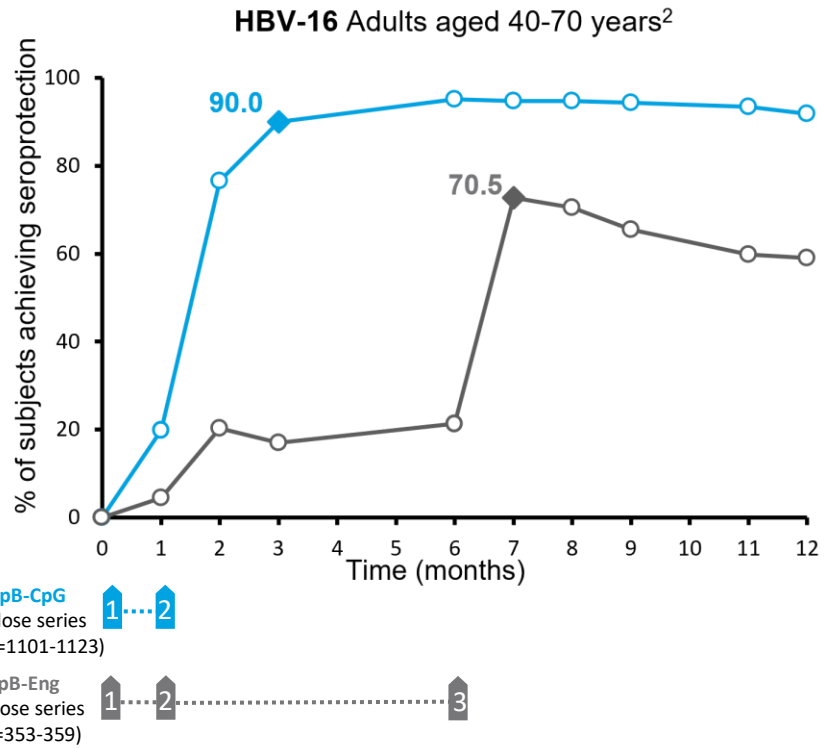
Vaccine	Test	Correlate of protection	Reference(s)
Diphtheria	Toxin neutralization	0.01–0.1 IU/mL	[14]
Hepatitis A	ELISA	10 mIU/mL	[15]
Hepatitis B	ELISA	10 mIU/mL	[16]
Hib polysaccharides	ELISA	1 mcg/mL	[17]
Hib conjugate	ELISA	0.15 mcg/mL	[18]
Influenza	HAI	1/40 dilution	[19]
Lyme	ELISA	1100 EIA U/mL	[20]
Measles	Microneutralization	120 mIU/mL	[7]
Pneumococcus	ELISA; opsonophagocytosis	0.20–0.35 mcg/mL (for children); 1/8 dilution	[21, 22]
Polio	SN	1/4–1/8 dilution	[23]
Rabies	SN	0.5 IU/mL	[24]
Rubella	Immunoprecipitation	10–15 mIU/mL	[25, 26]
Tetanus	Toxin neutralization	0.1 IU/mL	[27]
Varicella	SN; gpELISA	≥1/64 dilution; ≥5 IU/mL	[28, 29]

NOTE. gp, glycoprotein; HAI, hemagglutination inhibition; Hib, *Haemophilus influenzae* type b; SN, serum neutralization.

1. Schillie S, et al. *MMWR Recomm Rep* 2018;67(No. RR-1):1–31. DOI: http://dx.doi.org/10.15585/mmwr.rr6701a1 **2.** Vaccines, CID, 2008:47 (August 1) **3.** Bruce MG, et al. *Hepatology 2022.* PMID:35320592 https://doi. org/10.1002/hep.32474.

Seroprotection Rates in HBV-10 and HBV-16





Seroprotection defined as having anti-HBs Ab ≥10 mIU/mL

◆ Primary Endpoint
○ Measured Timepoint

1. Halperin S, et al. *Vaccine.* 2012;30:2556-2563. **2.** Heyward WL, et al. *Vaccine.* 2013;31:5300-5305.

HBV-23: Seroprotection in Prespecified Hyporesponsive Populations

Adults 18–70 Years of Age

	HepB-CpG N	HepB-Eng N	Peak SPR (%)*	
			HepB-CpG	HepB-Eng
Total population	4,376	2,289	95.4%	81.3%
Non-diabetes	3,762	1,968	96.2%	83.9%
Diabetes	640	321	90.0%	65.1%
18 – 29 years	174	99	100.0%	93.9%
30 – 39 years	632	326	98.9%	92.0%
40 – 49 years	974	518	97.2%	84.2%
50 – 59 years	1,439	758	95.2%	79.7%
60 – 70 years	1,157	588	91.6%	72.6%
Men	2,203	1,150	94.5%	78.8%
Women	2,173	1,139	96.4%	83.8%
Obese	2,165	1,076	94.7%	75.4%
Non-obese	2,208	1,212	96.1%	86.6%
Smoker	1,371	711	95.9%	78.6%
Non-smoker	3,005	1,578	95.2%	82.4%

Per protocol population
Seroprotection defined as antibody concentration ≥10 mIU/mL

*Peak SPR was measured at Week 24 for HepB-CpG and Week 28 for HepB-Eng. Peak SPRs were statistically significantly higher for HepB-CpG compared to HepB-Eng for all group comparisons, $p < 0.0000001$

Jackson S, et al. *Vaccine.* 2018;36(5):668-674.

HBV-10: Solicited Local and Systemic Reactions

PERCENTAGES OF SUBJECTS WHO REPORTED LOCAL AND SYSTEMIC REACTIONS WITHIN 7 DAYS OF VACCINATION

	HepB-CpG		HepB-Eng		
	Post-Dose		Post-Dose		
Reaction	**1**	**2**	**1**	**2**	**3**
Local	N=1810	N=1798	N=605	N=603	N=598
Injection-site Pain	38.5%	34.8%	33.6%	24.7%	20.2%
Injection-site Redness	4.1%	2.9%	0.5%	1.0%	0.7%
Injection-site Swelling†	2.3%	1.5%	0.7%	0.5%	0.5%
Systemic	N=1784	N=1764	N=596	N=590	N=561
Fatigue	17.4%	13.8%	16.7%	11.9%	10.0%
Headache	16.9%	12.8%	19.2%	12.3%	9.5%
Malaise	9.2%	7.6%	8.9%	6.5%	6.4%
Fever‡	1.1%	1.5%	1.8%	1.7%	1.8%

The most common (>10%) local reaction following HepB-CpG vaccination was injection site pain (39%), and the most common systemic reactions were fatigue (17%) and headache (17%)

*Redness and swelling ≥2.5 cm.
†Oral temperature ≥100.4F (38.0C).

Halperin S, et al. *Vaccine.* 2012;30:2556-2563.

HBV-16: Solicited Local and Systemic Reactions

PERCENTAGES OF SUBJECTS WHO REPORTED LOCAL AND SYSTEMIC REACTIONS WITHIN 7 DAYS OF VACCINATION

	HepB-CpG		HepB-Eng		
	Post-Dose		Post-Dose		
Reaction	**1**	**2**	**1**	**2**	**3**
Local	N=1952	N=1905	N=477	N=464	N=448
Injection-site Pain	23.7%	22.8%	18.4%	15.9%	13.8%
Injection-site Redness	0.9%	0.7%	0.6%	0.2%	0.2%
Injection-site Swelling†	0.9%	0.6%	0.6%	0.6%	0.2%
Systemic	N=1923	N=1887	N=472	N=459	N=438
Fatigue	12.6%	10.8%	12.8%	12.1%	9.4%
Headache	11.8%	8.1%	11.9%	9.5%	8.5%
Malaise	7.7%	7.0%	8.6%	7.1%	5.1%
Myalgia	8.5%	6.4%	9.6%	8.0%	4.5%
Fever‡	0.6%	0.6%	0.6%	0.9%	0.7%

The most common (>10%) local reaction following HepB-CpG vaccination was injection site pain (23%), and the most common systemic reactions were fatigue (13%) and headache (12%)

*Redness and swelling ≥2.5 cm.
†Oral temperature ≥100.4F (38.0C).

Heyward WL, et al. *Vaccine.* 2013;31:5300-5305.

HepB-CpG Safety Profile Compared to HepB-Eng in Three Pivotal Clinical Trials With Up to 12 Months of Follow-Up

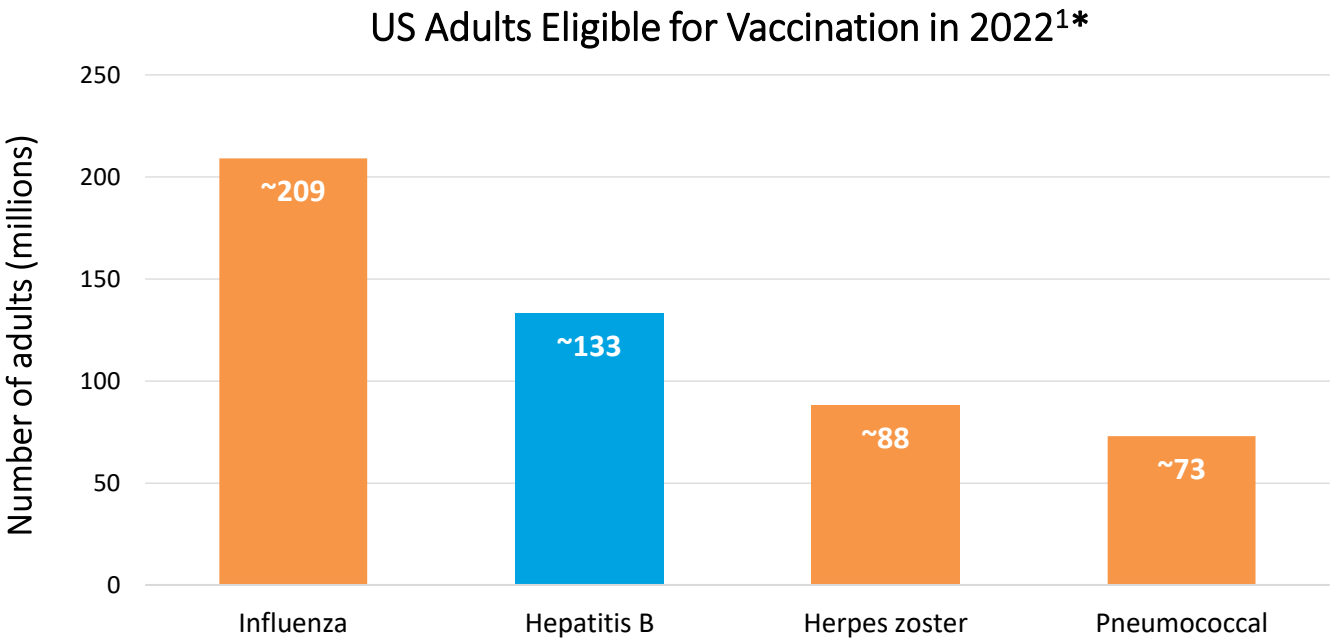
Percentage of subjects with an unsolicited adverse event

			Unsolicited Adverse Event*		Serious Adverse Event	Immune-mediated Adverse Event*
HBV-10	HepB-CpG (N=1810)	Within 28 days of any injection	42.0%	Within 7 months of the first vaccine dose	1.5%	0.2%
	HepB-Eng (N=605)		41.3%		2.1%	0.7%
HBV-16	HepB-CpG (N=1968)	Within 28 days of any injection	35.4%	Within 12 months of the first vaccine dose	3.9%	0.2%
	HepB-Eng (N=481)		36.2%		4.8%	0.0%
HBV-23	HepB-CpG (N=5587)	Within 28 days of any injection	20.1%	Within 13 months of the first vaccine dose	6.2%	0.1%
	HepB-Eng (N=2781)		20.1%		5.3%	0%

*For HBV-23, only unsolicited, medically attended adverse events (i.e., those for which a subject sought medical care) were captured.

HEPLISAV-B [package insert]. Emeryville, CA: Dynavax Technologies Corporation; 2023.

Hepatitis B Vaccines Are Likely to Become the Second Most Widely Used Adult Vaccines in Healthcare Systems

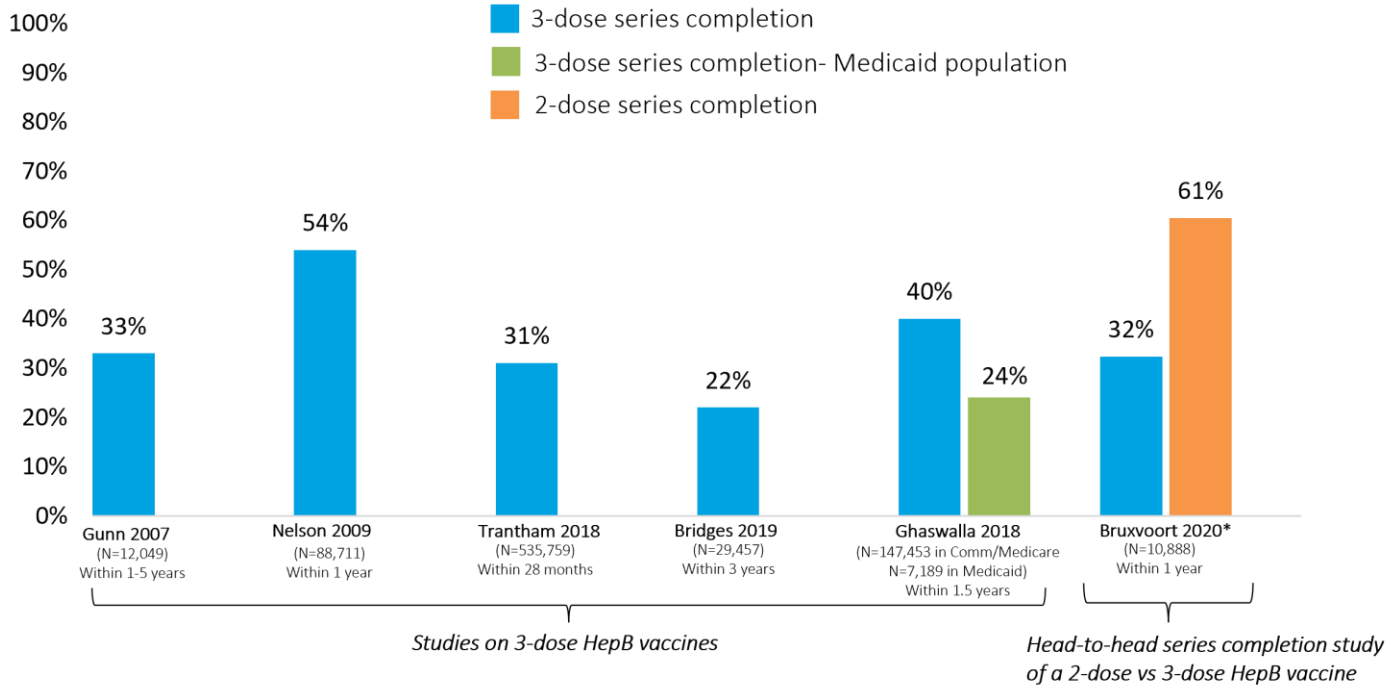


*Covid vaccines were excluded from this analysis. Adults eligible for influenza vaccines calculated from population aged 18+ in 2022; adults eligible for hepatitis B vaccines included general population aged ≤59 years and at-risk adults aged 19+ years calculated based on CDC ACIP assessment[2], converted to patient numbers using compliance data from Nelson et al.[3]

ACIP, Advisory Committee on Immunization Practices.

1. Data on file. Dynavax Technologies Corporation; 2022. **2.** Weng MK, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(13):477-483. **3.** Nelson JC, et al. *Am J Public Health*. 2009;99(suppl 2):S389-S397.

HepB Vaccine Series Completion Rates

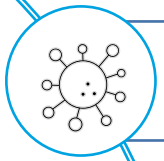


For most people, seroprotection is not achieved until the series is completed

*At 3 months following recommended dosing schedule, 44.7% of HepB-CpG initiators and 26.1% of HepB-alum initiators completed the series

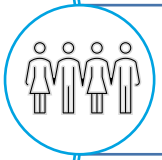
1. Gunn RA, et al. *Sex Transm Dis.* 2007;34(9):663-668. **2.** Nelson J, et al. *Am J Public Health.* 2009;99:S389-S397. **3.** Trantham L, et al. *Vaccine.* 2018;36(35):5333-5339. **4.** Bridges CB, et al. *Vaccine.* 2019;37(35):5111-5120. **5.** Ghaswalla PK, et al. *Hum Vaccin Immunother.* 2018;14(11):2780-2785. **6.** Bruxvoort K, et al. *JAMA Netw Open.* 2020;3(11):e2027577. **7.** Mast EE, et al. *MMWR Recomm Rep.* 2006;55(RR-16):1-33.

Conclusion



Hepatitis B (HepB) is a serious, potentially life-threatening vaccine-preventable disease and is associated with considerable morbidity and mortality

The stated goal of public health authorities is HepB elimination by 2030, and prevention is the key to achieving this goal



ACIP shifted from a risk-based recommendation to a universal recommendation for adults 19 through 59 years of age. Adults aged 60 and older with risk factors should be vaccinated and those without risk factors may receive vaccination.

HepB-CpG is the 2-dose HepB vaccine, which may help support implementation efforts by improving series completion

Factors impacting successful implementation of updated HepB recommendations: Patient Identification, Minimizing Missed Opportunities, Strong Provider Recommendation, and Focusing on Series Completion