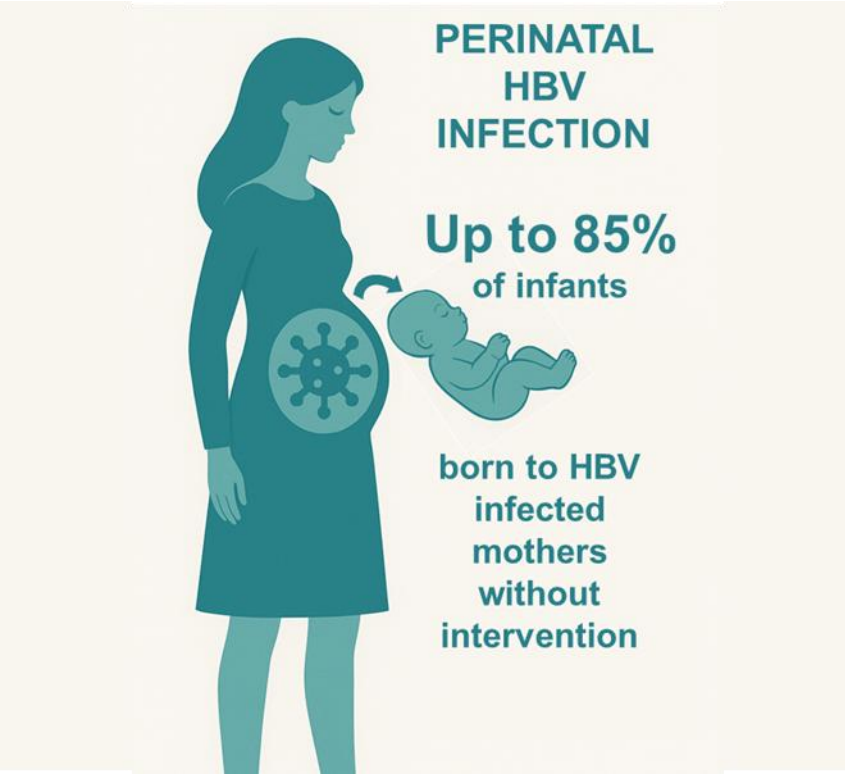
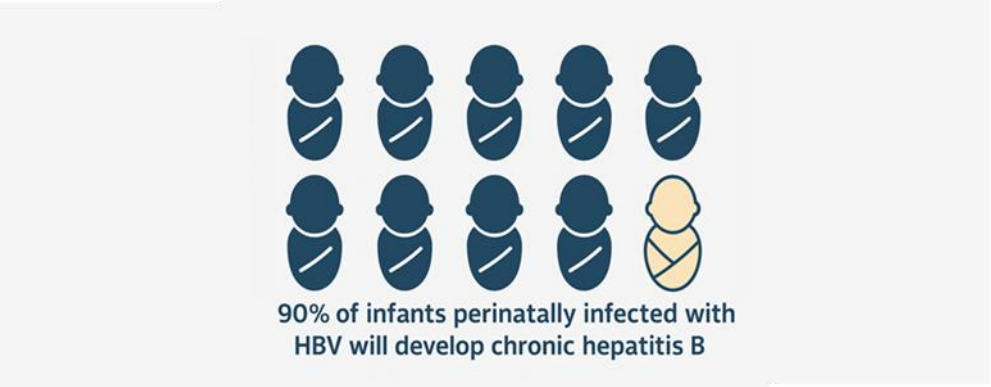
Hepatitis B Birth Dose Vaccination

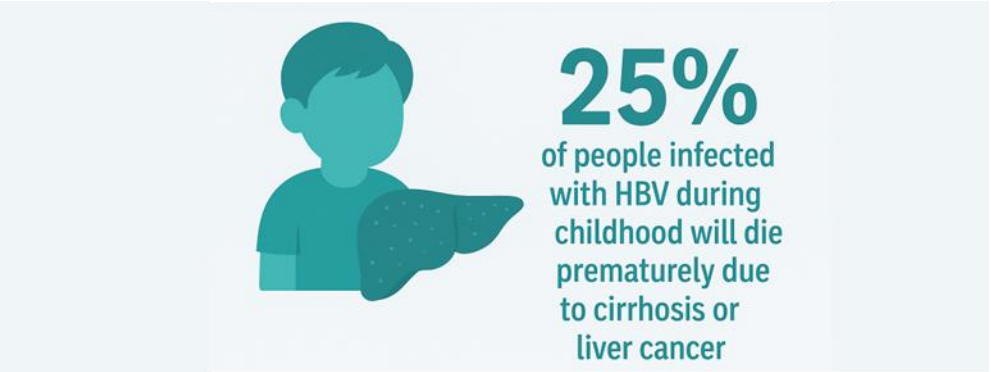
CDC Advisory Committee for Immunization Practices Meeting

September 18, 2025

Perinatal HBV transmission, which accounts for most infections globally, results in severe health consequences.







HBV = hepatitis B virus. Schillie S. MMWR Recomm Rep. 2018

*Image(s) generated by ChatGPT 5.0 (OpenAI), August 2025. Content originated as data from scientific publications and was transformed into an image via text prompts

Hepatitis B in the U.S. — a Tale of two Epidemiologies

- **Up to 2.4 million persons estimated to have hepatitis B in the United States[1]**
  - 50% unaware of their infection[2]
- **Persons born outside the U.S.[1,3]**
  - Chronic infection since childhood
  - Account for ~70% of all chronic infections
- **14,400 estimated acute hepatitis B cases in the U.S. in 2023[4]**
  - Unvaccinated persons with behavioral risk factors
  - Highest rates among adults aged 40-59 years
  - Adults have higher clearance rates and lower risk for chronic infection[5]

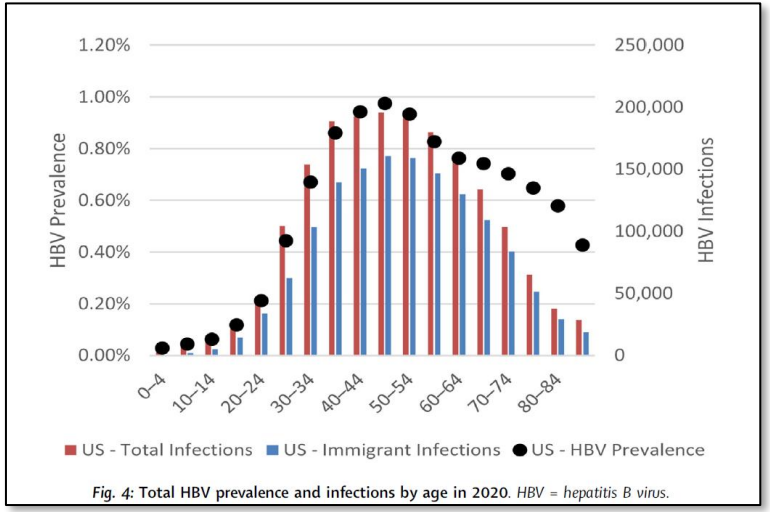


Fig. 4: **Total HBV prevalence and infections by age in 2020.** *HBV = hepatitis B virus.*

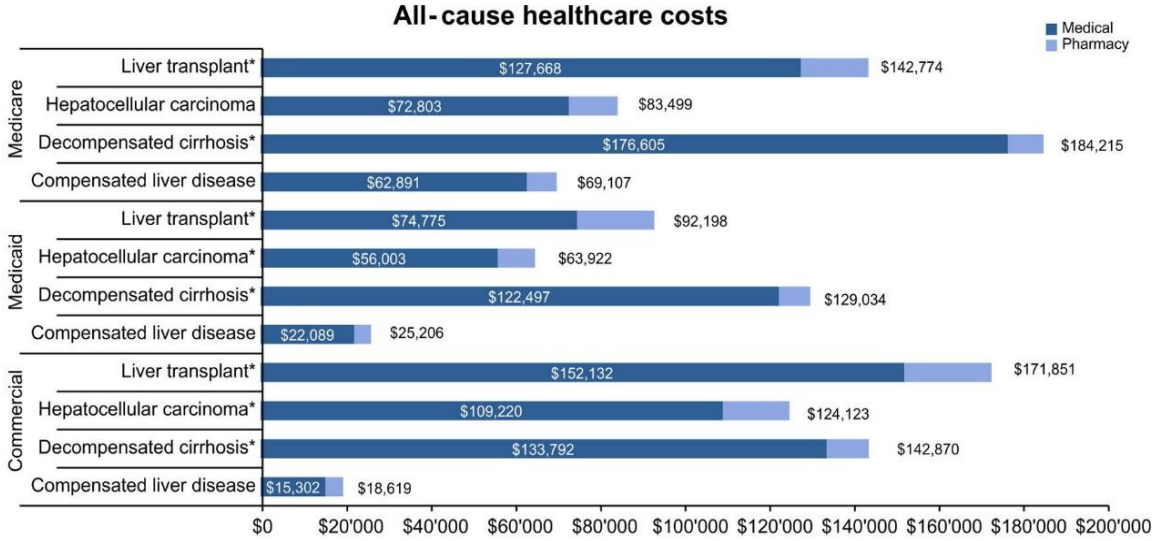
Source: Razavi-Shearer D, et al. The Lancet Regional Health Americas 2023.

1. Wong et al. Hepatology 2021; 2. Bixler et al. Hepatol Commun. 2023; 3. Razavi-Shearer D, et al. The Lancet Regional Health Americas 2023; 4. https://www.cdc.gov/hepatitis-surveillance-2023/about/index.html; 5. Chapter 10: Hepatitis B | Pink Book | CDC

Chronic HBV infection results in high lifetime healthcare costs.

Annual costs of treating a patient with less severe hepatitis B: **$25,308–$93,935** (2025 USD)

Annual cost of treating a patient requiring a liver transplant: **$174,282–$324,849** (2025 USD)



*p <0.01 compared to compensated liver disease (total costs) for each insurance type; 2015 US dollars
Compensated liver disease: 98% non-cirrhotic CHB; 2% compensated cirrhosis

HBV = hepatitis B virus

Nguyen MH, Burak Ozbay A, Liou I, Meyer N, Gordon SC, Dusheiko G, Lim JK. Healthcare resource utilization and costs by disease severity in an insured national sample of US patients with chronic hepatitis B. J Hepatol. 2019 Jan;70(1):24-32

Original estimates converted from 2015 USD to 2025 USD using https://www.bls.gov/data/inflation_calculator.htm

Hepatitis B birth dose vaccination and immune globulin (HBIG) substantially reduce the risk of mother-to-child transmission.

EARLIER BIRTH DOSE VACCINATION HAS GREATER EFFECTIVENESS

Setting	Time after birth vaccinated	Number of Children	% HBsAg+
Palau	> 3 days ≤ 3 days	30 323	6.7% 0.6%
Micronesia	> 3 days ≤ 3 days	78 217	2.6% 0.0%
Indonesia	> 7 days ≤ 7 days	656 1717	3.0% 1.4%

Schillie S. MMWR Recomm Rep. 2018; Beasley RP et al. Lancet. 1983; Lee C et al. 2006; Beasley RP et al. 1977; Armstrong GL. Pediatrics. 2001;
Mahoney. Pac Hth Dialog 1996; Ruff TA. The Journal of Infectious Diseases. 1995
*Image(s) generated by ChatGPT 5.0 (OpenAI), August 2025. Content originated as data from scientific publications and was transformed into an image via text prompts

Hepatitis B vaccines

- **Two single-antigen hepatitis B vaccines are FDA-approved for use from birth through adulthood; dosing varies by age group[1]**
  - Recombivax HB (1986)
  - Engerix-B (1989)

- **Safety**
  - The Institute of Medicine's Immunization Safety Review and the WHO's Global Advisory Committee on Vaccine Safety concluded that hepatitis B vaccine is both safe and effective.[1,2,3]

1.Poland GA et al, NEJM, 2004. 2. Stratton K et al, Immunization Safety Review, National Academies Press, 2002. 3. Global Advisory Committee on Vaccine Safety, Wkly Epidemiol Rec, 2002.

Hepatitis B vaccination is a multidose series, with increasing seroprotection among infants after each dose.

- **Hepatitis B vaccination recommendations on child and adolescent immunization schedule – United States, 2025**

Vaccine and other immunizing agents	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos
Hepatitis B (HepB)	1st dose	←2nd dose→			←3rd dose→			

- **In addition to the immediate benefit of providing postexposure prophylaxis to the newborn, the hepatitis B birth dose serves as the first dose of the infant vaccination series.***

- **Among healthy infants, the 3-dose hepatitis B vaccine series produces a protective antibody response (anti-HBs ≥10 mIU/mL) in approximately:**
  - ~25% of infants after the first dose,
  - ~63% of infants after the second dose, and
  - ~95% of infants after the third dose.

https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html (accessed 8/18/25);
*Except for pre-term infants weighing <2,000 grams born to women known to be HBsAg positive.
Schillie, S. et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 67, 1-31 (2018).

For decades, ACIP has recommended universal hepatitis B screening for pregnant women and birth dose vaccination for infants born to women who are HBsAg(+) or HBsAg status unknown.

ACIP hepatitis B screening recommendations for pregnant women and perinatal postexposure recommendations for infants, United States

Recommendation	Current?	Date of Initial Recommendation	Date Recommendation Superseded or Modified
Perinatal strategies			
Screening and testing for pregnant women			
Universal HBsAg screening in first trimester	Yes	1988[1]	
Test for HBsAg later in pregnancy for risk behaviors or acute hepatitis	Yes	1988[1]	
Test for HBsAg at delivery if status is unknown	Yes	1988[1]	
Post-exposure prophylaxis for infants born to HBsAg (+) pregnant women			
Administer HBIG within 12 hours of birth and HepB vaccine simultaneously or within 7 days of birth	No	1984[2]	1987[3]
Administer HBIG and HepB vaccine at birth*	No	1987[3]	1988[1]
Administer HBIG and HepB vaccine within 12 hours of birth*	Yes	1988[1]	
Infants born to HBsAg status unknown pregnant women			
In populations where screening is not feasible, administer HepB vaccine within 12 hours of birth*	No	1991[4]	2018[5]
Administer HepB vaccine and HBIG within 12 hours of birth*	Yes	2018[5]	

Modified from Bixler PHR 2023, Suppl Table 2. ACIP = Advisory Committee on Immunization Practices; HBIG = hepatitis B immune globulin; HepB, hepatitis B vaccine.
*Only single-antigen HepB vaccine should be used for the birth dose. Note: All hepatitis B birth dose vaccinations are considered to be the first dose of the infant series except among pre-term infants weighing <2,000 grams who are born to mothers who are HBsAg positive.

1.CDC. MMWR Morb Mortal Wkly Rep 37, 341-346, 351 (1988). 2.CDC. MMWR Morb Mortal Wkly Rep 33, 285-290 (1984). 3. CDC. Update on hepatitis B prevention. MMWR Morb Mortal Wkly Rep 36, 353-360, 366 (1987). 4.CDC. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Recomm Rep 40, 1-25 (1991). 5. Schillie, S. et al. MMWR Recomm Rep 67, 1-31 (2018).
6. Mast, E. E. et al. MMWR Recomm Rep 54, 1-31 (2005). 7. Bixler D, et al. Public Health Rep. 2023 Jun 9

For decades, ACIP has recommended that the first dose of universal infant hepatitis B vaccination among infants born to HBsAg(-) women occur close to birth.

ACIP hepatitis B infant vaccination recommendations, United States

Recommendation	Current?	Date of Initial Recommendation	Date Recommendation Superseded or Modified
Infant vaccination strategies			
Universal HepB vaccine before leaving the birth hospital* or within 2 months of age	No	1991[4]	2005[6]
Universal HepB vaccine at the birth hospital*	No	2005[6]	2018[5]
Universal HepB vaccine within 24 hours of birth*	Yes	2018[5]	

Modified from Bixler PHR 2023, Suppl Table 2.
ACIP = Advisory Committee on Immunization Practices; HBIG = hepatitis B immune globulin; HepB, hepatitis B vaccine.
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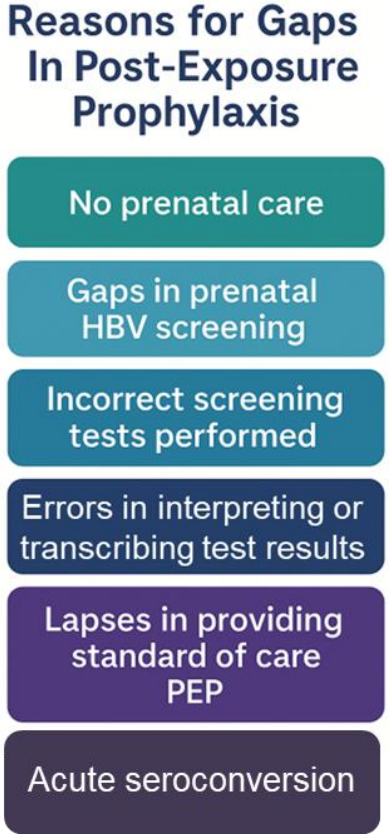
Note: All hepatitis B birth dose vaccinations are considered to be the first dose of the infant series except among pre-term infants weighing <2,000 grams who are born to mothers who are HBsAg positive.

1.CDC. MMWR Morb Mortal Wkly Rep 37, 341-346, 351 (1988). 2.CDC. MMWR Morb Mortal Wkly Rep 33, 285-290 (1984). 3. CDC. Update on hepatitis B prevention. MMWR Morb Mortal Wkly Rep 36, 353-360, 366 (1987). 4.CDC. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Recomm Rep 40, 1-25 (1991). 5. Schillie, S. et al. MMWR Recomm Rep 67, 1-31 (2018). 6. Mast, E. E. et al. MMWR Recomm Rep 54, 1-31 (2005). 7. Bixler D et al. Public Health Rep. 2023 Jun 9

HBV infections are missed among some pregnant women and can result in catastrophic outcomes.



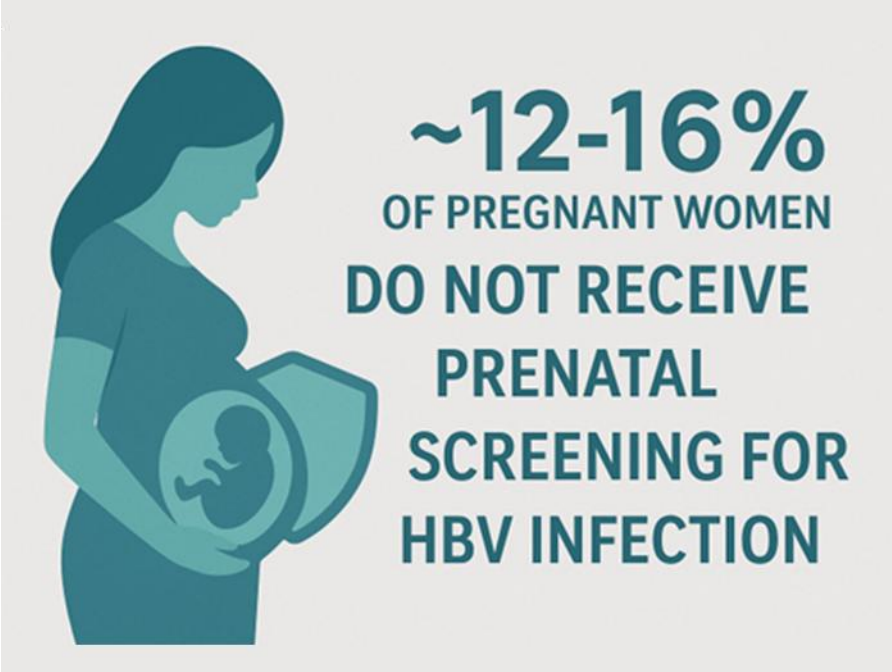
Michigan, 1999
"On December 14, 1999, a previously healthy 3-month-old infant was admitted to a hospital with diarrhea and jaundice, and acute hepatic failure attributed to HBV infection was diagnosed. The infant died on December 17, 1999. The infant had not received her first dose of hepatitis B vaccine until age 2.5 months.

The infant's mother was found to be HBsAg-positive at the first of 10 prenatal visits. However, the prenatal-care record provided to the birth hospital indicated that the mother was hepatitis-negative. Neither the provider nor the laboratory reported the mother's test results to MDCH as required by law."

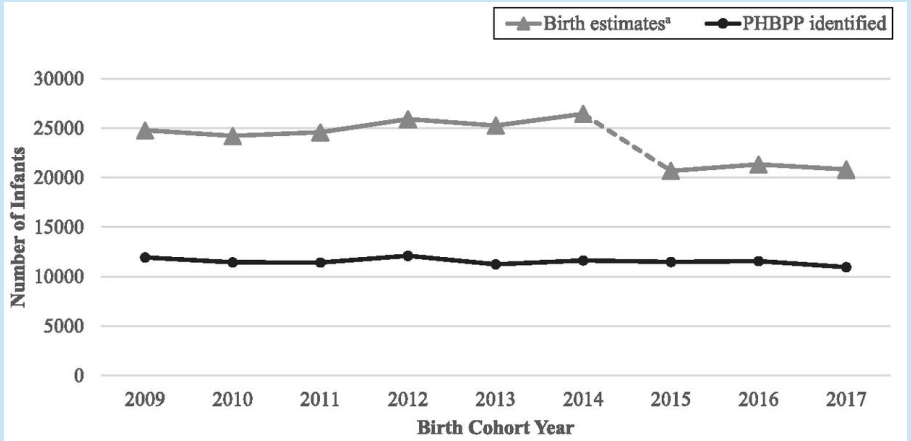
The Immunization Action Coalition documented *more than 500 transmissions of HBV in these types of situations* from 1999 to 2002

HBV = hepatitis B virus; PEP = post-exposure prophylaxis.
Schillie et al. MMWR Recomm Rep. 2018 Jan 12;67(1):1-31.
Willis, B.C., et al., Pediatrics, 2010. 125(4): p. 704-11.
CDC. MMWR Morb Mortal Wkly Rep. 2001 Feb 16;50(6):94-7.
Nolt D, et al. Pediatrics. 2022 Feb 1;149(2)

Hepatitis B birth dose vaccination serves as a critical safety net against gaps in protection against perinatal HBV infection.



The National Perinatal Hepatitis B Prevention Program identifies less than half of infants estimated to be born to HBV infected mothers



Koneru et al. Pediatrics. 2021 Mar;147(3):e20201823.
Pham et al. Am J Prev Med. 2023 Jul;65(1):52-59.
Kolasa et al. Pediatr Infect Dis J. 2017 Jul;36(7):e175-e180.
Martin JA, Osterman MJK. Natl Vital Stat Rep. 2023 May;72(4):1-14. PMID: 37252688.
Koneru A, et al. Pediatrics. 2021 Mar;147(3):e20201823.
Image(s) generated by ChatGPT 5.0 (OpenAI), August 2025. Content originated as data from scientific publications and was transformed into an image via text prompts

Unvaccinated infants remain at risk of non-perinatal HBV acquisition.

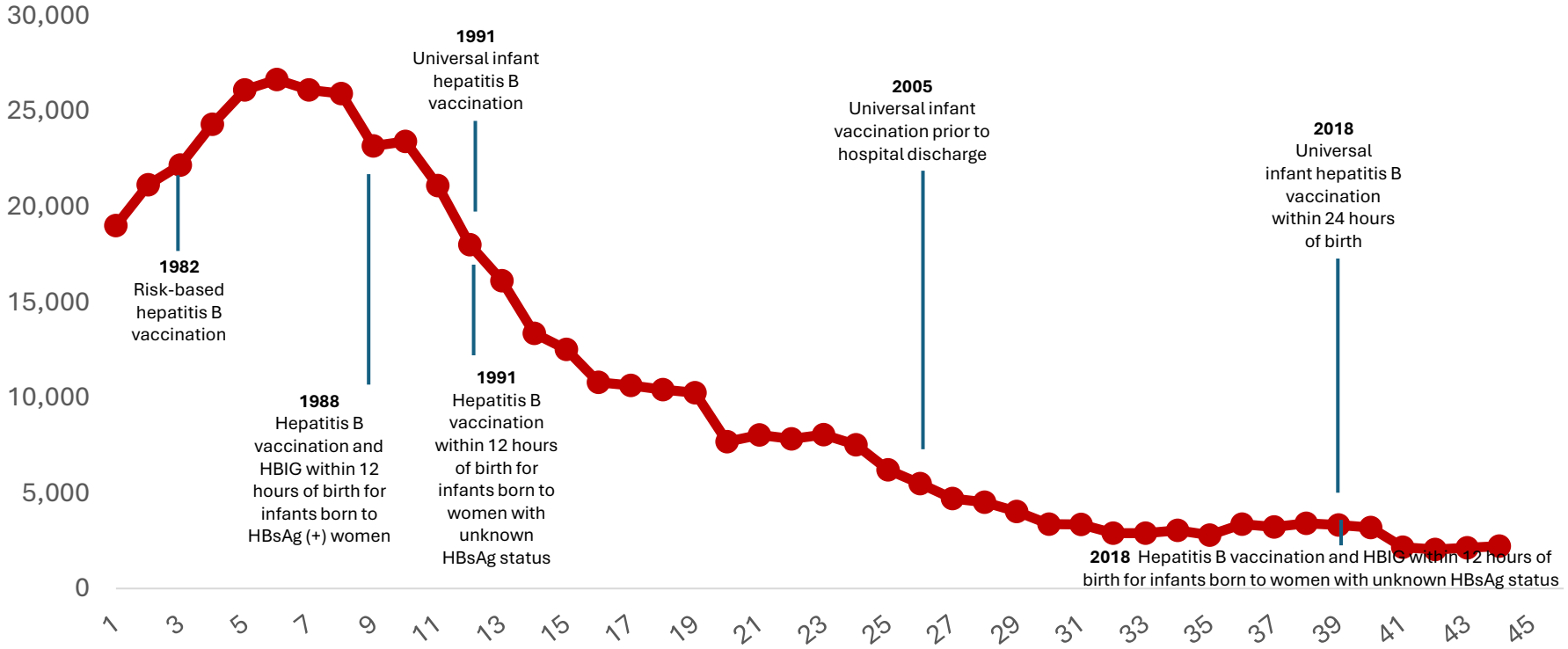
- HBV transmission occurs through percutaneous or mucosal exposure to infectious blood or body fluids
- **HBV can remain viable for over 7 days on environmental surfaces** at room temperature.[1]
- **Household and Community Transmission:** Unvaccinated children living with a person with chronic HBV infection in a household or community setting are at risk for becoming infected.
  - Prior to HepB BD, some U.S.-born children born to immigrant mothers without HBV infection had hepatitis B prevalences of 7–11%[2,3] attributable to community or household exposures.
- In the United States, up to 2.4 M people are estimated to have hepatitis B[4], and about **50% of people with hepatitis B are unaware of their infection**[5].
- Children who receive HepB BD have higher rates of hepatitis B childhood vaccine series completion and had a positive impact on rates of being up to date for other age-appropriate vaccines [6,7,8]

HBV = hepatitis B virus. HepB BD = hepatitis B birth dose vaccination.

1. Bond et al, Lancet. 1981; *2.* Franks et al, N Engl J Med. 1989; 3. Hurie et al, Pediatrics. 1992; 4. Wong et al, Hepatology. 2021; 5. Bixler et al, Hepatology Communications; 2023. 6. Yusuf HR, *et al,* JAMA. 2000 Aug 23-30;284(8):978-83 8; 7. Mast, E. E. *et al, MMWR Recomm Rep* **54**, 1-31 (2005). 8. Mennito SH, Darden PM.. J Pediatr. 2010 Apr;156(4):618-22.

Hepatitis B vaccination has been the cornerstone of hepatitis B control for decades and has brought the U.S. within reach of elimination.

Reported cases of acute hepatitis B and key ACIP vaccination recommendations among infants, United States, 1980-2023



HBIG = Hepatitis B immune globulin; CDC NNDSS Viral Hepatitis Surveillance (https://www.cdc.gov/hepatitis/php/statistics-surveillance/index.html);
†From 1991–2010 all case classifications included (i.e., confirmed, probable, suspect, unknown); from 2011–2023 only confirmed cases included
Bixler D, Roberts H, Panagiotakopoulos L, Nelson NP, Spradling PR, Teshale EH. Public Health Rep. 2023 Jun 9

Rescinding Universal HepB BD vaccination recommendations among infants born to HBsAg (-) women may result in more cases of perinatal HBV infection.

Potential Risks of Rescinding Universal HepB BD Recommendations

Increased cases of perinatal HBV transmission

Increased administrative complexity and failure points for providers and health systems

Lack of safety net given gaps in access to prenatal care, HBV screening, and HBIG access

Disproportionate harm to patients without insurance or low healthcare engagement

Lower rates of hepatitis B childhood vaccine series completion

Higher lifetime healthcare costs from missed opportunities to prevent and eliminate hepatitis B

Potential Benefits of Rescinding Universal HepB BD Recommendations

Reductions in rare cases of hepatitis B birth dose vaccination adverse events

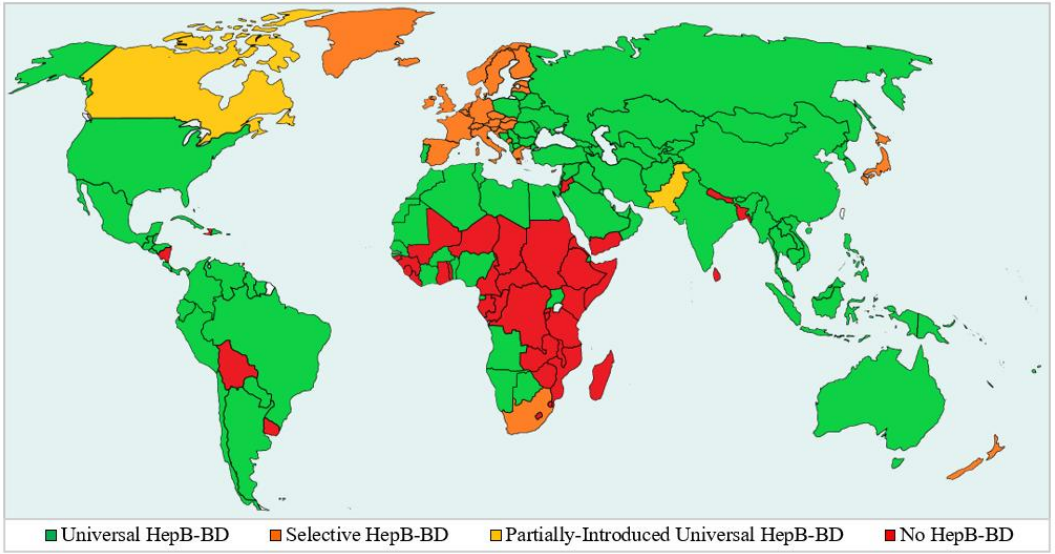
HepB BD = hepatitis B birth dose vaccination; adverse events listed in the section 'Vaccine Safety' in Schillie S. MMWR Recomm Rep. 2018 (page 11)

Request to CDC from ACIP Chair

- Survey of HepB vaccine recommendations in developed countries, including the United States, Canada, all EU countries, UK, Norway, Switzerland, Iceland, Australia, New Zealand, South Korea and Japan. Specifically,
  - At what age is the first dose recommended for:
    (i) children to HepB positive mothers, and for
    (ii) other children?
  - Also, in these countries, what is the prevalence of HepB infection in pregnant women?

Global hepatitis B birth dose vaccination policies

Hepatitis B vaccine birth dose vaccination policy by country, 2025[1]



Universal HepB-BD:
Hepatitis B vaccine recommended for all newborns.

Selective HepB-BD:
Hepatitis B vaccine recommended only to newborns born to HBsAg(+) women.

Partially-Introduced Universal HepB-BD:
Hepatitis B vaccine recommendations among newborns varies by geographic location within the country (at least one jurisdiction recommends universal HepB-BD).

HepB-BD = hepatitis B birth dose vaccination.

1. Provincial and territorial routine and catch-up vaccination schedule for infants and children in Canada - Canada.ca ; Hepatitis B vaccine – NHS; Vaccine Scheduler | ECDC; 9. Hepatitis B – Health New Zealand | Te Whatu Ora; Introduction of Hepatitis B vaccine; Hepatitis B | The Australian Immunisation Handbook; 20240220_Immunization_Schedule_english.pdf; National Immunization Program for children | Policy&Services : KDCA; Hepatitis B

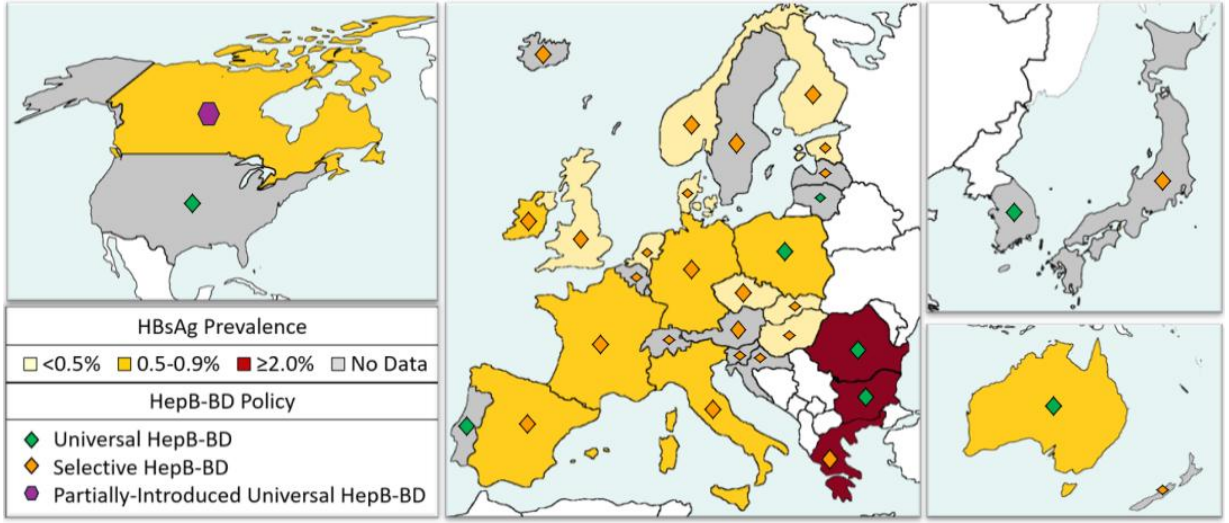
Hepatitis B first dose vaccination schedule in selected countries*

Age at first dose	Number of countries
At what age is the first dose recommended for children born to HBsAg (+) women? (N=38)	
Before discharge from the hospital, or within 24 hours of birth	36
Ideally within 24 hours of birth but no later than 7 days after birth	1 (Ireland)
Within 48 hours of birth (majority of newborns are vaccinated within 24 hours)	1 (Denmark)
At what age is the first dose recommended for children born to HBsAg (-) women?	
Countries that provide a universal HepB-BD (N=8)	
Same schedule as children born to HBsAg (+) women	7
Ideally within 24 hours but no later than 7 days after birth	1 (Australia)
Countries that provide selective HepB-BD and universal infant hepatitis B vaccination policy (N=26)	
At the age of 2 months	18
At the age of 3 months	6
At the age of 12-13 years	1 (Hungary)
Varies by province (2 months; 11 or 12 years)	1 (Canada)

Sources: Provincial and territorial routine and catch-up vaccination schedule for infants and children in Canada - Canada.ca ; Hepatitis B vaccine – NHS; Vaccine Scheduler | ECDC; 9. Hepatitis B – Health New Zealand | Te Whatu Ora; The Australian Immunisation Handbook; 20240220_Immunization_Schedule_english.pdf; National Immunization Program for children | Policy&Services : KDCA; Hepatitis B

* United States, Canada, all EU/EEA countries, UK, Norway, Switzerland, Iceland, Australia, New Zealand, South Korea and Japan.

Prevalence of hepatitis B among pregnant women in selected countries*



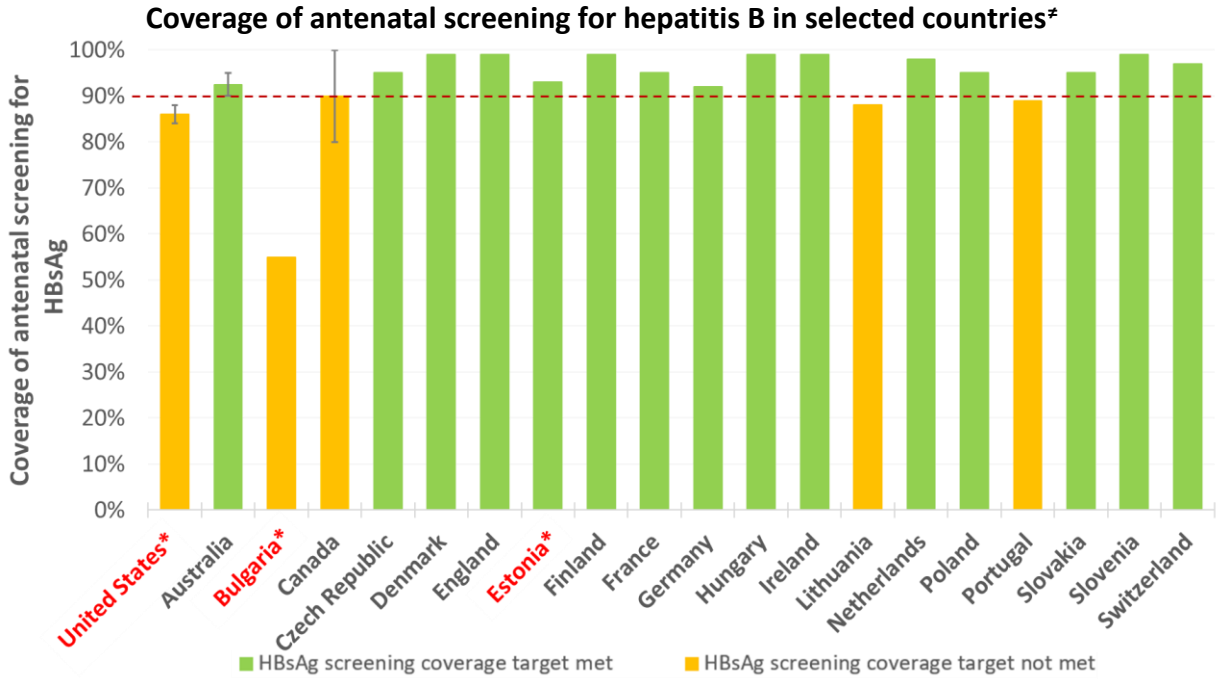
- Only 6 of 38 selected countries* have national registries to track hepatitis B screening in pregnant women and estimate prevalence on an annual basis

- The remaining 32 countries (including the United States), do not have national registries to track hepatitis B screening during pregnancy; when available, prevalence estimates from these countries are based on surveys or studies.

* United States, Canada, all EU/EEA countries, UK, Norway, Switzerland, Iceland, Australia, New Zealand, South Korea and Japan.

Hepatitis B in England 2024 - GOV.UK; Hepatitis B and C in Pregnancy and Children: A Canadian Perspective – PMC; Evidence brief - prevention of hepatitis B and C in Europe and the UK; Uptake of perinatal immunoprophylaxis for infants born to women with a record of hepatitis B in Victoria (2009–2017) – ScienceDirect; Updated-National Hepatitis Elimination Profile- Switerland-July2023_0.pdf; Gaps in Prenatal Hepatitis B Screening and Management of HBsAg Positive Pregnant Persons in the U.S., 2015–2020 - PMC

EU, UK and other countries with selective hepatitis B birth dose vaccination have higher hepatitis B prenatal screening coverage than in the United States



EU = European Union; UK = United Kingdom.

***No universal healthcare coverage**

≠2023 data except for the following countries: Lithuania, 2021; United States, 2015-2019; France, Germany, and Poland, data >5 but <10 years old.

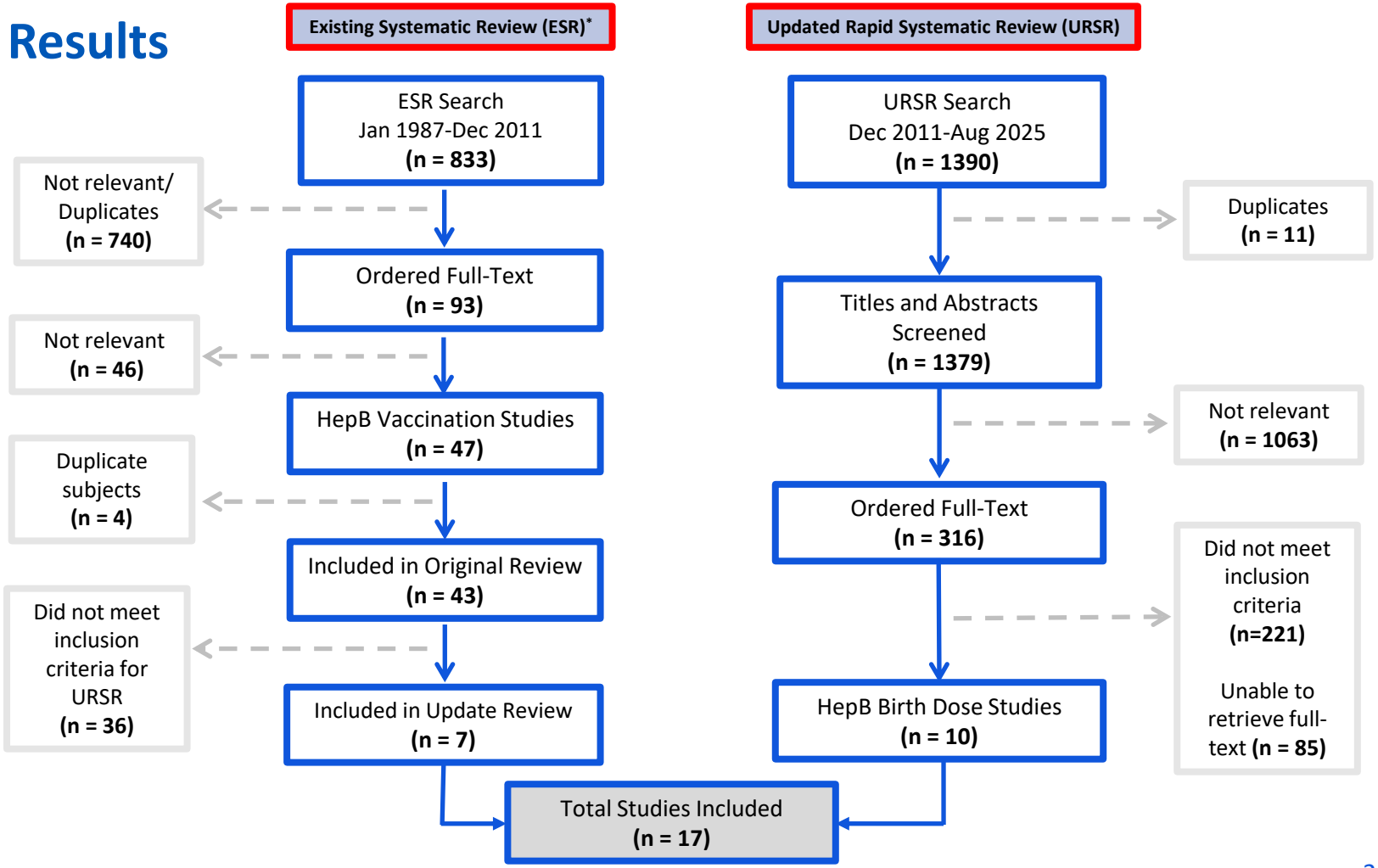
No data is publicly available for Austria, Belgium, Croatia, Cyprus, Greece, Iceland, Italy, Japan, Latvia, Lichtenstein, Luxembourg, Malta, New Zealand, Norway, Romania, South Korea, Spain, or Sweden.

Hepatitis B in England 2024 - GOV.UK; Hepatitis B and C in Pregnancy and Children: A Canadian Perspective – PMC; Evidence brief - prevention of hepatitis B and C in Europe and the UK; Uptake of perinatal immunoprophylaxis for infants born to women with a record of hepatitis B in Victoria (2009–2017) – ScienceDirect; Updated-National Hepatitis Elimination Profile- Switerland-July2023_0.pdf; Gaps in Prenatal Hepatitis B Screening and Management of HBsAg Positive Pregnant Persons in the U.S., 2015–2020 - PMC

Request to CDC from ACIP Chair

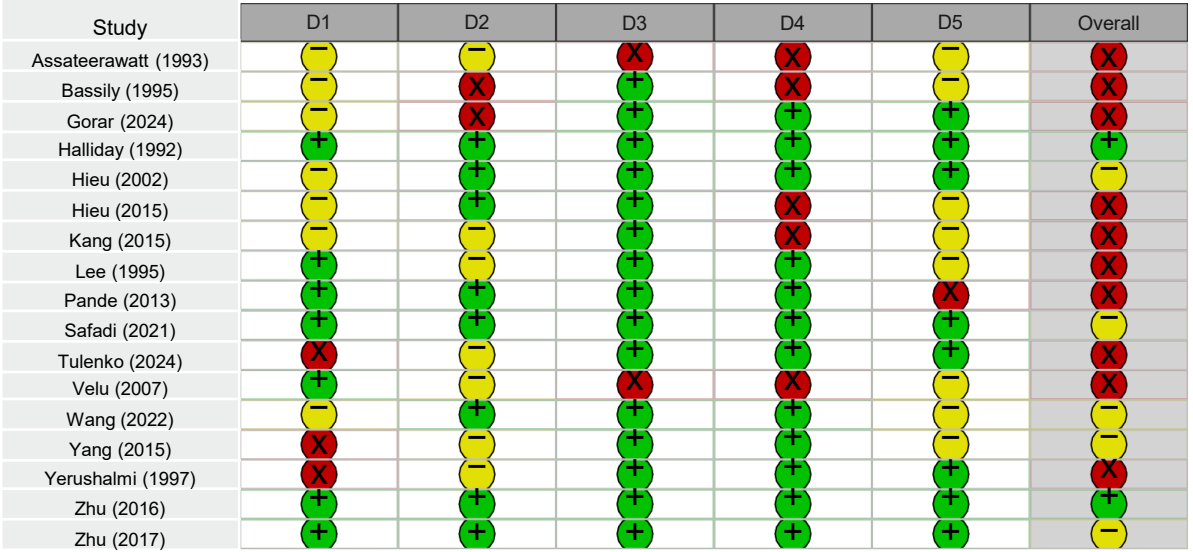
- Results from randomized trials concerning the administration of the HepB vaccine within 24 hours of birth, with all results stratified by the HepB infection status of the mother. Include both efficacy data and adverse events, including all-cause morbidity and mortality. For children whose mothers are HepB negative, present results for all children combined as well as stratified by pre-mature birth and birth weight. If randomized data is lacking for any of the requested populations, please mention that.

Search Results



*Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. Vaccine. 2013 May 17;31(21):2506-16. doi: 10.1016/j.vaccine.2012.12.012. Epub 2012 Dec 17.

Summary of Cochrane risk of bias assessments* for studies in existing and updated rapid systematic reviews (n=17)



Study	D1	D2	D3	D4	D5	Overall
Assateerawatt (1993)	−	−	X	X	−	X
Bassily (1995)	−	X	+	X	−	X
Gorar (2024)	−	X	+	+	+	X
Halliday (1992)	+	+	+	+	+	+
Hieu (2002)	−	+	+	+	+	−
Hieu (2015)	−	+	+	X	−	X
Kang (2015)	−	−	+	X	−	X
Lee (1995)	+	−	+	+	−	X
Pande (2013)	+	+	+	+	X	X
Safadi (2021)	+	+	+	+	+	−
Tulenko (2024)	X	−	+	+	+	X
Velu (2007)	+	−	X	X	−	X
Wang (2022)	−	+	+	+	−	−
Yang (2015)	X	−	+	+	−	−
Yerushalmi (1997)	X	−	+	+	+	X
Zhu (2016)	+	+	+	+	+	+
Zhu (2017)	+	+	+	+	+	−

Judgment of Risk of Bias

- High
- Some concerns
- Low

Domains:

D1: Bias due to randomization.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing data.
D4: Bias due to outcome measurement.
D5: Bias due to selection of reported result.

*Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; 366: l4898.

Intervention Characteristics (n=17)

Characteristic		# of Studies Reporting (%)
Intervention Study Type	Efficacy trials	2 (11.8%)
	Timing of vaccination	1 (5.9%)
	Product or formulation differences	8 (47.1%)
	Dose and schedule	4 (23.5%)
	HBIG co-intervention	2 (11.8%)
Vaccine Administered*	Engerix	7 (41.2%)
	Recombivax	1 (5.9%)
	Other	14 (82.3%)
Vaccine Dose*	10 µg	13 (76.4%)
	20 µg	2 (5.9%)
	Other	6 (35.2%)
Vaccination Schedule	0, 1, 6 months	11 (64.7%)
	0, 1, 2, 12 months	1 (5.9%)
	Other	5 (29.4%)

Abbreviations: µg, micrograms; HBIG hepatitis B immune globulin

*Not mutually exclusive

Efficacy Trials (n=2)

Hepatitis B vaccine series first administered at birth achieved high levels of seroprotection.

HepB vaccine

Author (year)	Comparison Arms	Maternal Status	Seroprotection		% Difference	Risk of Bias
			Intervention	Comparator		
Assateerawatt (1993)	20 mcg + HBIG vs. 20 mcg	HBsAg positive and HBeAg positive	26/26 (100%)	22/23 (95.7%)	4.3 pct pts	High

Comparative efficacy

Author (year)	Comparison Arms	Maternal Status	Seroprotection		% Difference	Risk of Bias
			Intervention	Comparator		
Hieu (2002)	Hepavax vs. Engerix	HBsAg positive	49/52 (94.2%)	45/52 (86.5%)	7.7 pct pts	Some concern

Abbreviations: HBeAg, hepatitis B virus e-antigen; HBsAg, hepatitis B surface antigen; mcg, micrograms

Seroprotection: Anti-HBs ≥10 mIU/mL at least 1-2 month after the final dose in the vaccine series or between 9-12 months of age.

Efficacy Trials (n=2)

Among infants born to HBsAg positive mothers, hepatitis B birth dose vaccine demonstrated efficacy in the prevention of perinatal transmission.

HepB vaccine vs. no vaccine*

Author (year)	Comparison Arms	Maternal Status	Infant HBsAg Positive Cases		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Assateerawatt (1993)	20 mcg vs. no vaccine*	HBsAg positive and HBeAg positive	3/22 (13.6%)	34/40 (85.0%)	**0.16 (0.06, 0.46)**	High
Assateerawatt (1993)	20 mcg + HBIG vs. no vaccine*	HBsAg positive and HBeAg positive	1/25 (4.0%)	34/40 (85.0%)	**0.05 (0.01, 0.32)**	High

Comparative efficacy

Author (year)	Comparison Arms	Maternal Status	Infant HBsAg Positive Cases		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Hieu (2002)	Hepavax vs. Engerix	HBsAg positive	1/53 (1.9%)	2/52 (3.8%)	0.49 (0.05, 5.25)	Some concerns

Abbreviations: HBeAg, hepatitis B virus e-antigen; HBsAg, hepatitis B surface antigen; mcg, micrograms

*Vaccine refusals

Efficacy Trial (n=1)
Hepatitis B birth dose resulted in few systemic adverse events.

Comparative efficacy

Author (year)	Comparison Arms	Maternal Status	Systemic Adverse Events		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Hieu (2002)	Hepavax vs. Engerix	HBsAg positive	2/53 (3.8%)	2/52 (3.9%)	0.98 (0.14, 6.71)	Some concerns

Note: majority of adverse events were reported as mild fever

Abbreviations: HBeAg, hepatitis B virus e-antigen; HBsAg, hepatitis B surface antigen; mcg, micrograms

Timing of Vaccination Trial (n=1)*

Among infants born to HBsAg negative mothers, high level of seroprotection and no significant difference in adverse events reported between the intervention and comparison groups.

- **Intervention:** received 2.5µg Recombivax vaccine at birth, 2 months, and 6 months
- **Comparator:** received 3 doses of 2.5µg Recombivax vaccine seroprotection at the end of the study, starting at 18 months
- **Maternal status:** HBsAg negative
- **Risk of bias assessed:** High
- **Outcomes:**
  - *Seroprotection:*
    - 91.0% (162/178) of intervention group achieved seroprotection 1 month after the final dose of the vaccine series
  - *Adverse events:*
    - Localized symptoms: I: 5/178 (2.8%); C: 3/191 (1.6%)→ RR = 1.77 (95% CI: 0.43, 7.29); RD = 1.2%
    - Systemic symptoms: I: 10/178 (5.6%); C: 4/191 (2.1%)→ RR = 2.59 (95% CI: 0.83, 8.12); RD = 3.5%
- **Summary:**
  - Over 9 in 10 newborn infants in the intervention group achieve seroprotection.
  - Among infants born to HBsAg negative mothers, there was **no significant difference in adverse events reported between the intervention and comparison groups.**

Abbreviations: C, comparison group; HBsAg, hepatitis B surface antigen; I, intervention group; RR, risk ratio; RD, risk difference (absolute)

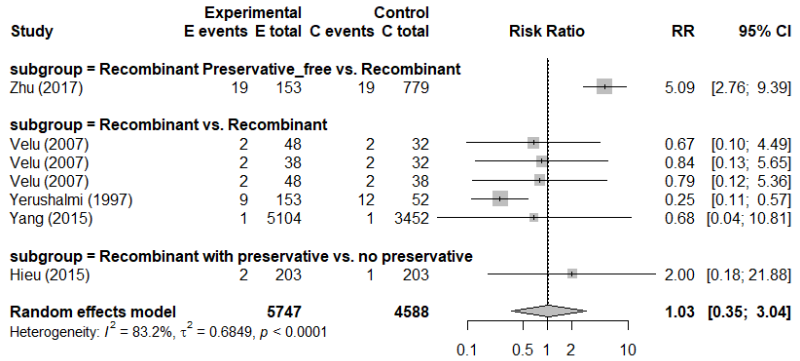
*Bassily, S.,Kotkat, A.,Gray, G.,Hyams, K. C.,Brown, F. M.,Imam, I. Z.,Arthur, R.. Comparative study of the immunogenicity and safety of two dosing schedules of hepatitis B vaccine in neonates. *Am J Trop Med Hyg.* 1995. 53:419-22.

Product or Formulation Trials

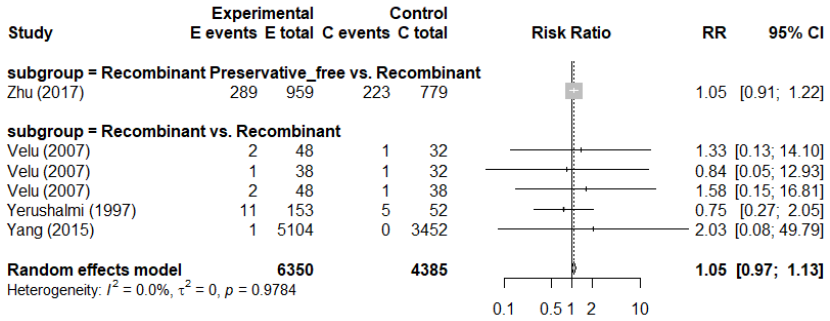
Hepatitis B vaccine series beginning at birth among infants born to HBsAg positive or negative women

- **Seroprotection (n=7)**
  - Achieved **high levels** of seroprotection among infants in both intervention (89%-99%) and comparison groups (71%-98%).
- **Efficacy (n=4)**
  - Among HBsAg positive women, demonstrated **equivalent efficacy** in the prevention of perinatal transmission between intervention and comparison groups
- **Adverse events (n=5)**
  - Hepatitis B birth dose resulted in **few local or systemic adverse events** among infants in intervention and comparison groups

Local Symptoms (n=5)



Systemic Symptoms (n=4)



Seroprotection studies: Halliday, 1992; Hieu, 2015; Safadi, 2021; Velu, 2007; Yerulshami, 1997; Zhu, 2016; Zhu 2017.

Efficacy studies: Halliday, 1992; Velu, 2007; Safadi, 2021; Zhu 2017.

*Local symptoms may include injection site pain, soreness, redness, swelling in the arm where the shot was given; alternatively, investigators may report under a general grouping of “local adverse events”.

Systemic symptoms may include fever, excessive crying, rash, irritability, vomiting, diarrhea, loss of appetite, drowsiness; alternatively, investigators may report under a general grouping of “systemic adverse events”.

Dose and Schedule Trials (n=4)
Among infants born to HBsAg positive or negative women, hepatitis B birth dose vaccine schedule is seroprotective

Author (year)	Comparison Arms	Maternal Status	Seroprotection		Percent difference	Risk of Bias
			Intervention	Comparator		
Lee (1995)	5 mcg vs. 2.5 mcg	HBsAg negative	261/279 (94.0%)	271/308 (88.0)	6.0 pct pts	High
Kang (2015)	10 mcg vs. 5 mcg	All negatives + positives	169/177 (95.5%)	166/173 (96.0%)	-0.5 pct pts	High
Tulenko (2024)	4 doses vs. 3 doses	HBsAg negative	24/28 (85.7%)	26/28 (93.0%)	-7.3 pct pts	High
Gorar (2024)	HepB BD vax vs. standard schedule (no BD)	HBsAg negative	116/121 (96.0%)	57/97 (59.0%)	37.0 pct pts	High

Dose and Schedule Trials (n=2)
Among infants born to HBsAg positive or negative women, hepatitis B birth dose vaccine schedule has high efficacy

Author (year)	Comparison Arms	Maternal Status	Infant HBsAg Positive Cases		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Kang (2015)	10 mcg vs. 5 mcg	All negatives + positives	4/90 (4.4%)	6/90 (6.7%)	0.67 (0.19, 2.28)	High
Tulenko (2024)	4-dose series vs. 3-dose series	HBsAg negative	0/28	0/28	1.00 (0.02, 48.7)	High

Dose and Schedule Trials: Safety Outcomes (n=1)
Among infants born to HBsAg positive or negative women, hepatitis B birth dose vaccine schedule resulted in few local or systemic adverse events

Author (year)	Comparison Arms	Maternal Status	Local Adverse Events		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Kang (2015)	10 mcg vs. 5 mcg	All negatives + positives	1/253 (0.4%)	2/253 (0.8%)	0.50 (0.05, 5.48)	High

Author (year)	Comparison Arms	Maternal Status	Systemic Adverse Events		Risk Ratio (95% CI)	Risk of Bias
			Intervention	Comparator		
Kang (2015)	10 mcg vs. 5 mcg	All negatives + positives	8/253 (3.2%)	7/253 (2.8%)	1.14 (0.42, 3.10)	High

Evidence Gap / Limitations

Evidence Gap:

- **Lack of placebo-controlled trials assessing efficacy**
  - This is not surprising as it is unethical to withhold a proven, safe and effective intervention (i.e., hepatitis B vaccination) simply to include a placebo group
- **Paucity of evidence reporting outcomes for preterm/LBW/ELBW infants, as well as morbidity and mortality for all infants**

Limitations:

- Heterogeneous reporting of timepoints and definitions
- Many of the studies were done before the wide application of the CONSORT statement*, which seeks to improve reporting of randomized controlled trials (RCTs)
- Most of the RCTs (59%) assessed had a high risk of overall bias primarily due to the randomization and measurement of outcomes

Abbreviations: LBW, low birth weight; ELBW, extremely low birth weight.

*Hopewell S, Chan A, Collins GS, et al. CONSORT 2025 Statement: Updated Guideline for Reporting Randomized Trials. JAMA. 2025;333(22):1998–2005. doi:10.1001/jama.2025.4347

Conclusion

- **Based on the included body of evidence:**
  - Hepatitis B birth dose induces high seroprotection and efficacy
  - Hepatitis B birth dose vaccine is safe
  - Head-to-head comparisons of various hepatitis B recombinant vaccine products, doses, and schedule show no meaningful differences in reported outcomes in efficacy and safety

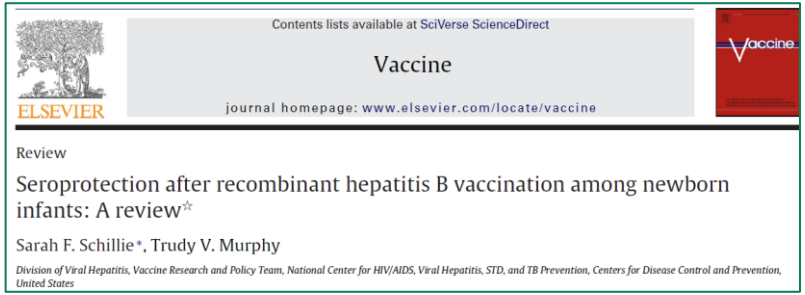
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 cdc.gov
Follow us on X (Twitter) @CDCgov & @CDCEnvironment

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

Background Slides

Search for Evidence

- Identified an existing systematic review focused on HepB vaccination among newborns*
  - Used the Schillie review as a starting point
  - Search period: 1/1/1987 – 12/16/2011
- Conducted an updated rapid systematic review using a similar search strategy
  - Search period: 12/17/2011 – 8/14/2025
- Electronic databases searched:
  - Medline (OVID)
  - Embase (OVID)



*Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. Vaccine. 2013 May 17;31(21):2506-16.

Existing Systematic Review*

- **Objective:** To summarize seroprotection and immunogenicity of recombinant hepatitis B vaccines administered within the first 30 days of life
- **Search Period:** January 1, 1987 to December 16, 2011
- **Databases:** Medline (via PubMed) and Embase (OVID)
- **Key Inclusion Criteria:** studies reporting seroprotective response to monovalent recombinant HepB vaccine administered to infants within ≤30 days
- **Key Exclusion Criteria:**
  - When seroprotection was assessed in conjunction with administration of other vaccines
  - When a combination vaccine containing hepatitis B vaccine was administered
  - When vaccine was not administered intramuscularly
  - When seroprotection was not reported within 3 months of the final dose

*Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. Vaccine. 2013 May 17;31(21):2506-16.

Updated Rapid Systematic Review: Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Newborn infants receiving a HepB vaccine at birth (i.e., ≤24 hours old at dose 1)	• Non-English language articles • Animal studies
• Randomized controlled trial • Monovalent HepB vaccine administered within ≤24 hours of birth; co-administration of HepB immune globulin (HBIG) is permitted	• Combination infant vaccines at birth, when the HepB component's contribution or timing cannot be isolated • No extractable data on maternal status; for HBsAg(-) mothers, no data for total group and none for prematurity/birth-weight strata • No outcome of interest reported • Results not stratified by intervention arm
• Provided comparative data regarding the safety and effectiveness of Hep immunization strategies, such as delayed HepB vaccination (>24 hrs. after birth) or no HepB vaccination; other vaccination schedule	• Nonrandomized/observational designs; RCTs where all arms initiate vaccine >24 hours after birth without a ≤24-hour comparator

• Outcomes include any of the following:
  • HBV infection
  • Chronic HBV infection
  • Seroprotection
  • Seroconversion
  • Safety outcomes
  • All-cause morbidity
  • All-cause mortality
	• Preprints
	• Conference abstracts
	• Editorial/Commentary
	• Letter to the Editor

List of Outcomes

Outcome Type	Outcome Definition	Included in ESR?	Included in URSR?
Efficacy	• HBsAg and/or HBV DNA positivity	Yes	Yes
Seroprotection	• Anti-HBs ≥10 mIU/mL at least 1-2 month after the final dose in the vaccine series or between 9-12 months of age.	Yes	Yes
Safety	• Local/systemic adverse events*	Yes	Yes
Morbidity	• Severe illness • Hospitalization	N/R	Yes
Mortality	• Death	N/R	Yes

Abbreviations: anti-HBs, antibody to hepatitis B surface antigen; ESR, existing systematic review; URSR, updated rapid systematic review; HBsAg, hepatitis B surface antigen; HBV DNA, hepatitis B virus deoxyribonucleic acid. N/R = not reported

*Local symptoms may include injection site pain, soreness, redness, swelling in the arm where the shot was given. Alternatively, investigators may report under a general grouping of “local adverse events”; systemic symptoms may include fever, excessive crying, rash, irritability, vomiting, diarrhea, loss of appetite, drowsiness. Alternatively, investigators may report under a general grouping of “systemic adverse events.”

Risk of Bias Assessment

- **Cochrane Risk of Bias, version 2 (RoB 2)** [1]
  - Used to assess risk of bias in RCTs
    - Bias related to:
      - randomization process
      - Deviation from intended intervention
      - Missing outcome data
      - Measurement of outcome
      - Selection of reported results
  - **RoB 2 overall judgement options:** low risk, some concerns, high risk

Cochrane Methods Bias

Trusted evidence.
Informed decisions.
Better health.

[1]Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; 366: l4898.

Analyses and Presentation Decisions

Factor	Decision
Type of Analysis	Proportions for seroprotection; risk ratios for efficacy and safety outcomes
Time Point Used	***Seroprotection:*** first reported time point immediately following the last dose in a series ***Efficacy (against HBV infection)*:** latest available time point with ongoing intervention ***Safety outcomes:*** at birth or the closest time point immediately after the birth dose
Outcome Measure	Multiple outcome measures reported separately
Overall Effect Estimate Measure	Pooled random effect meta-analysis where possible
Multiple Intervention Arms	Intervention arms reported separately
Summary	Qualitatively compare summary estimates

Abbreviations: HBV, hepatitis B virus

Search Strategy: Medline (OVID)

1. exp Hepatitis B Vaccines/
2. (((Hepatitis B OR HepB OR Hep B OR HBV) ADJ5 vaccin*) OR HepB-BD OR Engerix-B OR Recombivax HB OR Hepavax-Gene).ti,ab,kf.
3. 1 OR 2
4. Exp Infant/
5. (Infant* OR newborn* OR new born* OR neonat* OR birth OR birth-dose*).ti,ab,kf.
6. 4 OR 5
7. Hepatitis B/im OR Hepatitis B Antibodies/ OR Hepatitis B Surface Antigens/
8. (seroprotection OR sero-protection OR immunogeni* OR immune response OR antibod*).ti,ab,kf.
9. 7 OR 8
10. Randomized Controlled Trials as Topic/
11. (random* OR RCT* OR clinical trial* OR clinical stud* OR controlled trial* OR double-blind* OR single-blind* OR placebo* OR control group*).ti,ab,kf,hw.
12. 10 OR 11
13. 3 AND 6 AND 9 AND 12
14. exp animals/ NOT exp humans/
15. 13 NOT 14
16. limit 15 to dt="20111217-20250814"
17. limit 16 to English language

Search Strategy: Embase (OVID)

1. exp Hepatitis B Vaccine/
2. (((Hepatitis B OR HepB OR Hep B OR HBV) ADJ5 vaccin*) OR HepB-BD OR Engerix-B OR Recombivax HB OR Hepavax-Gene).ti,ab,kf.
3. 1 OR 2
4. Exp Infant/
5. (Infant* OR newborn* OR new born* OR neonat* OR birth OR birth-dose*).ti,ab,kf.
6. 4 OR 5
7. Hepatitis B Antibody/ OR Hepatitis B Surface Antigen/
8. (seroprotection OR sero-protection OR immunogeni* OR immune response OR antibod*).ti,ab,kf.
9. 7 OR 8
10. "randomized controlled trial (topic)"/
11. (random* OR RCT* OR clinical trial* OR clinical stud* OR controlled trial* OR double-blind* OR single-blind* OR placebo* OR control group*).ti,ab,kf,hw.
12. 10 OR 11
13. 3 AND 6 AND 9 AND 12
14. exp animal/ NOT exp human/
15. 13 NOT 14
16. limit 15 to dc="20111217-20250814"
17. limit 16 to English language

List of Included Studies (n=17), Part I

References	Latest Follow-up Period (months)	Sample Size
• Assateerawatt, A.,Tanphaichitr, V. S.,Suvatte, V.,Yodthong, S.. Immunogenicity and efficacy of a recombinant DNA hepatitis B vaccine, GenHevac B Pasteur in high risk neonates, school children and healthy adults. Asian Pac J Allergy Immunol. 1993. 11:85-91.	12	100
• Bassily, S.,Kotkat, A.,Gray, G.,Hyams, K. C.,Brown, F. M.,Imam, I. Z.,Arthur, R.. Comparative study of the immunogenicity and safety of two dosing schedules of hepatitis B vaccine in neonates. Am J Trop Med Hyg. 1995. 53:419-22.	18	590
• Gorar, Z. A.,Butt, Z. A.. Impact of hepatitis B birth dose on immune response in Pakistani children: an open-label, non-inferiority randomized controlled trial, implications for achieving SDG target. Infectious Diseases. 2024. 56:1-10 .	5	296
• Halliday, M. L.,Kang, L. Y.,Rankin, J. G.,Coates, R. A.,Corey, P. N.,Hu, Z. H.,Zhou, T. K.,Yuan, G. J.,Yao, F. L.. An efficacy trial of a mammalian cell-derived recombinant DNA hepatitis B vaccine in infants born to mothers positive for HBsAg, in Shanghai, China. Int J Epidemiol. 1992. 21:564-73.	12	220
• Hieu, N. T.,Kim, K. H.,Janowicz, Z.,Timmermans, I.. Comparative efficacy, safety and immunogenicity of Hepavax-Gene and Engerix-B, recombinant hepatitis B vaccines, in infants born to HBsAg and HBeAg positive mothers in Vietnam: an assessment at 2 years. Vaccine. 2002. 20:1803-8.	24	105
• Hieu, N. T.,Sarnecki, M.,Tolboom, J.. The safety and immunogenicity of two hepatitis B vaccine formulations (thiomersal-free and thiomersal-containing) in healthy vietnamese infants: a phase III, prospective, single-blinded, randomized, controlled trial. Pediatric Infectious Disease Journal. 2015. 34:79-83.	7	408
• Kang, G.,Ma, F.,Chen, H.,Yang, Y.,Guo, S.,Wang, Z.,Liang, X.,Li, L.,Cui, F.,Zhang, L.. Efficacy of antigen dosage on the hepatitis B vaccine response in infants born to hepatitis B-uninfected and hepatitis B-infected mothers. Vaccine. 2015. 33:4093-9.	6	506
• Lee, S. S.,Lo, Y. C.,Young, B. W.,Wong, K. H.,Lim, W. L.. A reduced dose approach to hepatitis B vaccination for low-risk newborns and preschool children. Vaccine. 1995. 13:373-6.	12	587
• Pande C, Sarin SK, Patra S, Kumar A, Mishra S, Srivastava S, et al. Hepatitis B vaccination with or without hepatitis B immunoglobulin at birth to babies born of HBsAg-positive mothers prevents overt HBV transmission but may not prevent occult HBV infection in babies: a randomized controlled trial. J Viral Hepat. 2013 Nov;20(11):801-10.	24	259

List of Included Studies (n=17), Part II

References	Latest Follow-up Period (months)	Sample Size
• Safadi, R.,Khoury, T.,Saed, N.,Hakim, M.,Jamalia, J.,Nijim, Y.,Farah, N.,Nuser, T.,Natur, N.,Mahamid, M.,Amer, J.,Roppert, P. L.,Gerlich, W. H.,Glebe, D.. Efficacy of Birth Dose Vaccination in Preventing Mother-to-Child Transmission of Hepatitis B: A Randomized Controlled Trial Comparing Engerix-B and Sci-B-Vac. Vaccines. 2021. 9:01.	12	171
• Tulenko, S. E.,Ngimbi, P.,Mwandagalirwa, K.,Tabala, M.,Matondo, J.,Ntambua, S.,Mbonze, N.,Mbendi, C.,Luhata, C.,Jhaveri, R.,Edwards, J. K.,Becker-Dreps, S.,Moormann, A. M.,Kaba, D.,Yotebieng, M.,Parr, J. B.,Gower, E. W.,Thompson, P.. Immunogenicity of a Birth Dose of Hepatitis B Vaccine in Kinshasa, Democratic Republic of Congo: A Randomised, Controlled Trial. Journal of Viral Hepatitis. 2024. 31:795-807.	12	231
• Velu, V.,Nandakumar, S.,Shanmugam, S.,Jadhav, S. S.,Kulkarni, P. S.,Thyagarajan, S. P.. Comparison of three different recombinant hepatitis B vaccines: GeneVac-B, Engerix B and Shanvac B in high risk infants born to HBsAg positive mothers in India. World J Gastroenterol. 2007. 13:3084-9.	12	158
• Wang, H.,Fang, J. W.,Gu, Z. W.,Song, D. J.,Chen, Y.,Chen, G. D.,Zhao, B.,Sun, C.,Ma, Y.,Wang, K. X.,Shen, J. Q.,Yang, X. F.,Luo, Q.. Application of hepatitis B immunoglobulin in prevention of mother-to-child transmission of chronic hepatitis B in HBsAg- and HBeAg-positive mother. Journal of Obstetrics & Gynaecology. 2022. 42:877-882.	6	331
• Yang, S.,Ma, X.,Ni, H.,Zhou, S.,Hu, D.,Shi, H.,Chen, X.,Dong, H.,Xu, G.. Safety, immunization coverage and determinants of a new kind of Hepatitis B vaccine firstly applied in Ningbo, China. Human vaccines & Immunotherapeutics. 2015. 11:2819-26.	6	8556
• Yerushalmi, B.,Raz, R.,Blondheim, O.,Shumov, E.,Koren, R.,Dagan, R.. Safety and immunogenicity of a novel mammalian cell-derived recombinant hepatitis B vaccine containing Pre-S1 and Pre-S2 antigens in neonates. Pediatr Infect Dis J. 1997. 16:587-92.	12	205
• Zhu, F. C.,Sun, K. X.,Pan, H. X.,Yang, Z. H.,Lu, Y.,Liang, Z. L.,Liang, X. F.,Wang, F. Z.,Zeng, Y.,Li, J.. The immunogenicity in healthy infants and efficiency to prevent mother to child transmission of Hepatitis B virus of a 10mcg recombinant yeast-derived Hepatitis B vaccine (Hep-KSC). Vaccine. 2016. 34:2656-62.	6	1731
• Zhu, F.,Deckx, H.,Roten, R.,Michiels, B.,Sarnecki, M.. Comparative Efficacy, Safety and Immunogenicity of Hepavax-Gene TF and Engerix-B Recombinant Hepatitis B Vaccines in Neonates in China. Pediatric Infectious Disease Journal. 2017. 36:94-101.	12	1739