Hexavalent vaccines indicators

Table of contents

Burden & epidemiology

Number of new cases per year (last 3-5 years)

NOT RELEVANT FOR CURRENT DECISIONS - PLEASE CONSULT THE RELEVANT WHO POSITION PAPERS. 1, 2, 3, 4, 5, 6, 7, 8 For disease burden for relevant diseases (at least D,T,P) countries can consult the WHO JRF data for their country, or subregion per WHO JRF. 9

Proportion of the population affected by the disease or infected with the antigen

NOT RELEVANT FOR CURRENT DECISIONS - PLEASE CONSULT THE RELEVANT WHO POSITION PAPERS. 1, 2, 3, 4, 5, 6 For disease burden for relevant diseases (at least D,T,P) countries can consult the WHO JRF data for their country, or subregion per WHO JRF. 10

Serogroup or serotype distribution (for serogroup- or serotype-specific vaccines)

NOT RELEVANT FOR CURRENT DECISIONS - PLEASE CONSULT THE RELEVANT WHO POSITION PAPERS 1, 2, 3, 4, 5, 6, 7, 8

Number of deaths from the disease per year

NOT RELEVANT FOR CURRENT DECISIONS - PLEASE CONSULT THE RELEVANT WHO POSITION PAPERS 1, 2, 3, 4, 5, 6

Case Fatality ratio (number of deaths / number of new cases, in %)

NOT RELEVANT FOR CURRENT DECISIONS - PLEASE CONSULT THE RELEVANT WHO POSITION PAPERS

Outbreak, epidemic or pandemic risk

Diphtheria, though largely controlled in many regions thanks to vaccination, outbreaks are still reported today, especially in populations with low immunization coverage, high mobility, or poor living conditions. 11 Diphtheria outbreaks have been reported in various settings, including refugee camps in Asia, and among asylum seekers in Europe. 12, 13

Tetanus is generally rare in areas with high vaccination coverage, and since it is acquired from environmental sources, it does pose a risk for outbreaks. 14

Pertussis has a well-documented history of causing outbreaks, even in populations with high vaccination coverage. Recent trends show that pertussis continues to have significant outbreak

potential worldwide, affecting both children and adults, and posing particular risks to infants. [15], [16]

Hepatitis B has significant potential for outbreaks, especially in settings with poor infection control or low vaccination coverage. Outbreaks of hepatitis B have been documented in both healthcare and community settings, and the virus remains a persistent public health threat in many regions. [17], [18]

Prior to widespread vaccination, small outbreaks or clusters of cases of Hib disease have been noted in day-care centres and there were reports of nosocomial transmission in hospitals. The risk of Hib disease was also higher in larger families. [19]

The risk of poliovirus outbreaks and localised epidemics remains significant in areas with low vaccination coverage, fragile health systems, or gaps in immunization campaigns, particularly in regions experiencing conflict or displacement. Wild poliovirus (WPV) is endemic to Afghanistan and Pakistan, while vaccine-derived poliovirus (cVDPV) outbreaks have been reported in 20 countries in 2024. There is a rising risk of outbreaks of cVDPV2 since the global switch to bivalent oral poliovirus vaccine (bOPV). Although the global pandemic potential is low due to widespread immunity and effective vaccines, lapses in immunization and surveillance have led to the detection of poliovirus in environmental samples in previously polio-free countries. [6], [7], [8], [20]

Contribution of the vaccine to achievement of the national, regional or global disease goals

There are no established global elimination goals for Diphtheria or Pertussis (some countries have defined control goals for Diphtheria)

The Maternal and Neonatal Tetanus Elimination (MNTE) initiative, launched by the World Health Organization (WHO) in 1989, initially aimed to eliminate neonatal tetanus by 1995. As of June 2024, 47 out of 59 priority countries have achieved MNTE status, significantly reducing neonatal tetanus cases by 89% and deaths by 84% since 2000. Vaccination is the cornerstone of the strategy. Immunizing women of reproductive age with tetanus toxoid-containing vaccines (TTCVs) has been the primary driver of this reduction. [21], [22]

There is a clear and internationally recognized goal to eliminate hepatitis B as a public health threat. The World Health Organization (WHO) has set a target to achieve hepatitis B elimination by 2030, aiming for a 90% reduction in new infections and a 65% reduction in deaths.

Vaccination is the single most important tool in the global effort to eliminate Hepatitis B. Widespread and timely hepatitis B vaccination, especially starting at birth, dramatically reduces new infections, chronic disease, and deaths from liver complications. The prevalence of hepatitis B surface antigen (HBsAg) in children under 5 dropped from 4.7% before vaccination to 1.3% by 2015, thanks to universal vaccination programs in 189 countries. 23, 24, 25

While no formal global Hib elimination goal is set by WHO, elimination of invasive Hib disease is considered biologically and programmatically possible, and has been achieved in some countries through high vaccination coverage. After the introduction of Hib conjugate vaccines, countries like the US, UK, and Canada saw a reduction in Hib disease incidence by over 95%, with some regions achieving near elimination of invasive Hib disease in children under five years old. More than 90% of countries have included Hib vaccines in their national immunization programs, resulting in significant global decreases in Hib disease, though complete eradication has not yet been achieved. 26, 27

Polio vaccination has reduced poliomyelitis cases by over 99.9% globally since the launch of the Global Polio Eradication Initiative in 1988. Coordinated immunization campaigns have led to the certification of polio-free status in the Americas (1994), the Western Pacific (2000), Europe (2002), and Africa (2020). Globally, the vaccines (Polio mono and multivalent and IPV-containing combination vaccines) have brought the world closer to eradicating wild poliovirus, which is now confined to Afghanistan and Pakistan. In addition, they play a critical role in controlling outbreaks of vaccine-derived poliovirus (cVDPV). 28, 29, 30, 31, 32

Back to table of contents

Benefits of the intervention

Serogroup or serotype coverage by vaccines considered (for serogroup- or serotype-specific vaccines)

Serogrouping is not a relevant concept for diphtheria, tetanus, pertussis, or hepatitis B in the context of vaccine coverage

There are 6 serotypes of Haemophilus influenzae (a to f) of which type b was the commonest

cause of severe disease in children. Disease due to other serotypes and non-typeable Haemophilus influenzae can cause disease. 33, 34, 35, 36, 5

Poliovirus exists in three distinct serotypes: types 1, 2, and 3. Immunity to one serotype does not confer protection against the others, necessitating vaccines that target all three (trivalent vaccine). All the available Hexavalent vaccines contains all the three Polio serotypes. 6, 37

Efficacy and effectiveness estimates (e.g. against infection, disease, hospitalization, death), including in different populations

Clinical studies consistently show that hexavalent vaccines are highly effective in generating protective immune responses against all six targeted diseases35, 38, 39, 40, 41, 42, 43, 44, 45 :

- Diphtheria - Nearly all children achieve seroprotective antibody levels after vaccination and booster doses with non-inferior protection compared to monovalent or pentavalent vaccines. 39
- Tetanus - 100% seroprotection rates reported post-booster; strong and persistent antibody responses with no evidence of reduced efficacy compared to monovalent or other combination vaccines. 39
- Pertussis - High seroconversion rates (94–95% for Bordetella pertussis, 77–87% for pertussis toxin). Head-to-head studies and clinical trials confirm that the immune response to pertussis antigens in hexavalent vaccines is non-inferior to that of other licensed combination vaccines, including pentavalent and monovalent formulations. Some differences in antibody levels (e.g., anti-pertussis toxin, anti-pertactin) exist, but these have not shown clear clinical relevance. Hexavalent vaccines may contain either whole cell pertussis (wP) or acellular pertussis (aP) antigens, which influence immunogenicity and reactogenicity profiles, with aP generally associated with lower reactogenicity. 45
- Hepatitis B - >99% seroprotection post-booster with no significant reduction compared to the monovalent vaccine. 42
- Hib - 96–100% achieve protective antibody levels post-primary and booster doses. There is some evidence that Hib conjugate vaccine in combination with acellular pertussis (DTaP-Hib) induces a lower antibody response than Hib conjugate in combination with whole cell pertussis (DTwP-Hib) or separately administered DTaP and Hib conjugate vaccines. 44
- Poliomyelitis - 98–100% seroprotection for all three poliovirus types post-booster. Non inferiority (as measures by antibody titers) has been demonstrated for wP containing Hexavalent and IPV/OPV. 40, 41, 43

Duration of protection and waning of immunity in general and risk groups

The duration of protection varies by disease component, but evidence shows that these vaccines provide strong initial immunity and long-lasting immune memory, especially when booster doses are included . 1, 2, 3, 4, 5, 6, 46, 47, 48, 49, 50, 51, 52, 53 .

Diphtheria - Data on the duration of seroprotection from 2 large representative population studies from the Netherlands, using a complete 3-dose primary series plus 3-dose booster series prior to adolescence, indicate that this schedule results in very high seroprevalence above the threshold for basic protection (≥0.01 IU/mL) up to 39 years of age and potentially longer. 1, 48, 51

Tetanus - Data from serological studies suggest that a primary series of 3 TTCV doses in infancy plus a booster during the second year of life will provide 3–5 years of protection. A further booster dose (e.g. in early childhood) provides protection into adolescence, and another booster during adolescence induces immunity that lasts through much of adulthood, providing protection to women of reproductive age. 2, 47, 51

Pertussis - Whereas little is known about the duration of protection following pertussis vaccination in LMICs countries, several studies in HICs show that protection wanes after 4-12 years. 3, 46

Hepatitis B - In a study in Alaska, USA, a 3-dose vaccination schedule prevented all clinically appparent and chronic HepB infection for at least 30 years. 4, 49, 50, 52

Hib - Although there is some evidence of a decrease over time in the proportion of Hib vaccine recipients with antibody levels higher than the set thresholds, there is only limited evidence to suggest that this decline is associated with an increase in clinical disease. 5, 51

Poliomyelitis - The exact duration of immunity following a complete IPV series is not fully determined; however, it is believed to confer protection for many years. 6

Back to table of contents

Safety of the intervention

Type, including severity, consequences and frequency of short- and long-term adverse events following vaccination

Combination vaccines are used extensively in routine immunization programs (i.e. pentavalent, measles and rubella) and are a very safe and effective way to provide recommended vaccines with fewer injections.

Diphtheria, tetanus and pertussis combination vaccines (DTP) have been in use since the 1940s. Most recently, this DTP combination has been used as the basis for the development of combination vaccines containing additional vaccine
antigens such as hepatitis B and Haemophilus influenzae type b, resulting in pentavalent vaccine, or with the additional IPV, resulting in hexavalent vaccine.
None of these combination vaccines has produced any adverse events that had not been observed with the individual components and currently used combination vaccines have excellent safety records. 6, 28, 54

Back to table of contents

Values and preferences

Perception of the target population on the risk of disease

Perception of the risk of diptheria, tetatnus, pertussis, hepatitis B, Hib and poliomyelitis among target populations varies significantly depending on local disease prevalence, cultural beliefs and awareness levels. 55, 56, 57, 58, 59, 60, 61, 62

For diphtheria, studies report that factual knowledge of the disease is generally low, yet the risk is often perceived as high during outbreaks or in regions with recent cases. In many high-income countries, diphtheria is considered a rare threat, leading to decreased awareness and sometimes

lower perceived urgency to vaccinate. [56]

Perception of the risk of tetanus tends to be higher than diphtheria due to its high case-fatality and association with wounds and childbirth, especially neonatal tetanus in low-resource settings. [56, 57]

Parents of young infants and healthcare workers usually recognize pertussis as a serious illness, given its potential severity in infants. For instance, in Georgia 81% of women believed pertussis, would be serious during pregnancy while 92% believed pertussis would be serious to their infants. [58]

For hepatitis B, awareness and perceived risk vary greatly by region. In a study among pregnant women in Uganda, perceived risk was low. [59]

Haemophilus influenzae type b (Hib) disease is often under-recognized by the public, particularly in regions where widespread vaccination has nearly eliminated severe cases like meningitis and pneumonia. [57]

In regions where polio remains endemic, such as Afghanistan and Pakistan, the public is often more aware of the disease's dangers due to its ongoing presence. However, challenges like misinformation, cultural resistance, and distrust in vaccination programs can undermine risk perception, even in high-risk areas. Conversely, in polio-free regions, the perceived risk of polio is generally low, as the disease is no longer part of the collective memory. This complacency can lead to gaps in vaccination coverage, as seen in recent outbreaks of vaccine-derived poliovirus (cVDPV) in previously polio-free countries such as the United Kingdom and Israel. [55, 60, 61]

Back to table of contents

Acceptability to stakeholders

Acceptability of the vaccine and of vaccination against the disease

The acceptability of child combination vaccination including DTP, HepB, Hib and polio vaccination varies globally, influenced by factors such as cultural beliefs, misinformation, relationships between parents and healthcare professionals, and perceived disease risk.

In South Africa and Timor-Leste, general acceptance of immunization was observed, but with limited disease-specific knowledge. DTP vaccine acceptance was high among parents in France (85%) and India (98%).
Pertussis vaccine acceptance in countries such as the United Kingdom, Italy, Ireland, Australia, West Germany and Russia has been influenced by adverse events and to lesser extent the low effectiveness of selected wP vaccines.

In polio endemic regions, vaccine resistance has been linked to misconceptions about vaccine safety and cultural opposition, despite awareness of the disease's severity. Conversely, in polio-free countries, vaccine acceptability is generally high, though complacency has led to gaps in coverage, as evidenced by recent vaccine-derived poliovirus (cVDPV) outbreaks in the United Kingdom and Israel. Addressing these challenges, global initiatives led by WHO, UNICEF, and the Global Polio Eradication Initiative (GPEI) have prioritized public education and community engagement to sustain vaccination acceptance and achieve eradication goals. 60, 63, 64, 65, 66

Back to table of contents

Financing & funding

Estimated financial cost of materials per vaccine dose (syringes, needles, safety box) (in USD)

Cost of syringes: UNICEF procurement 0.028$ to 0.065$ depending on supplier and product / PAHO RF procurement 0.028$ to 0.048$ depending on supplier and product. [67]

Cost of safety boxes: UNICEF procurement, a box of 25 safety boxes (each with a 5-liter capacity) is about $20.26, resulting in approximately $0.81 per safety box. Each 5-liter safety box can hold around 100 syringes, leading to a disposal cost of approximately $0.008 per syringe. [68, 69]

Estimated vaccine financial cost per dose (in USD)

In Gavi-supported countries, Serum Institute of India (SII) has offered a price of $2.85 per dose in the 10 dose presentation for hexavalent vaccines (wP). [70]
For fully self-financing countries and those eligible under Gavi's Middle-Income Countries (MICs) Approach, the cost of SII's hexavalent vaccine is $3.00 per dose. [71]
For fully self-financing MICS, the cost of hexavalent vaccines (aP containing) is on average $28.8 per dose. [72]

The UNICEF price for the pentavalent vaccine is $0.85-$1.26 per dose for Gavi supported-countries depending on supplier and presentation . [73]
The PAHO price is $1.18 per dose (wP) and ranges between $18.33 and $21.54 for vaccines with aP depending on supplier and presentation. [74]
For fully self-financing MICS, the cost is $1.25-$2.29 per dose (DTwP-HepB-Hib). [72]

UNICEF prices for the IPV vaccine for countries assessing Gavi prices range between $1.25 and $2.8 depending on supplier and presentation. [75]
UNICEF price for self-procuring MICs is €3.1 per dose. [75]
The PAHO price ranges between $1.25 and $5.5 per dose. [74]
For fully self-financing MICS, the cost ranges from $2.23 to $10.66 per dose. [72]

Estimated financial cost per person vaccinated (in USD)

In European countries with vaccine procurement through public tenders the price per child vaccinated with standard vaccines ranged from €59 to €117 when using pentavalent and from €98 to €220 when using hexavalent vaccines, both with aP. 76
A 2022 a study focused on Peru estimated the total cost of fully vaccinating a child with the hexavalent vaccine (DTaP-HB-Hib-IPV) at $126.42, compared to $116.27 under the existing schedule using the current scheme (DTwP-HB-Hib + IPV + OPV). 77

Cost-effectiveness ratio

While hexavalent vaccines may have higher upfront costs, they can help reduce adverse events, logistical challenges, and overall societal burdens, offering potential economic and practical benefits for immunization programs, as demonstrated by studies from countries including Peru (wP pentavalent compared to aP hexavalent), Argentina (wP pentavalent compared to aP hexavalent), Colombia (aP compared to wP hexavalent vaccines), and South Korea (DTaP-IPV-Hib-HepB compared to DTaP-IPV/Hib). 78, 79, 80, 81, 82, 83, 84

Is there a Gavi programme to support the introduction of this vaccine? If a Gavi programme is available, what support is available to countries?

In December 2023, Gavi opened a funding window for eligible countries to switch from pentavalent to hexavalent vaccine, including assistance in assessing financial, logistical, and programmatic implications to determine suitability for their specific contexts. Operational support is also available to facilitate the introduction of the hexavalent vaccine into national immunization programs. 85, 70

Back to table of contents

Market (feasibility)

Available vaccines, licensing status, prequalification status, presentation, formulation, dosage and route of administration

4 Hexavalent vaccines are available, 3 of which contains acellular pertussis and one whole-cell pertussis. Three of those vaccines come in a fully liquid ready for use formulation, one has the Hib component lyophilised and requires reconstitution. Vial and prefilled syringe presentations are available. Only 2 of those vaccines are WHO prequalified (one of the aP-containing and the wP-containing). 86

Back to table of contents

Service delivery (feasibility)

Number of doses and timing of administrations

There are several schedule options with hexavalent vaccine. The schedule recommendation for hexavalent consists of 3 primary doses, starting as early as 6 weeks of age, with a minimum interval of 4 weeks between doses.
Many countries are following a pentavalent schedule of 3 primary doses at 6, 10 and 14 weeks. In this case, the pentavalent vaccine can be substituted by the hexavalent vaccine at the same age.
Countries that are currently following other pentavalent schedule options, can continue to maintain their schedules if they switch to hexavalent vaccine. Some schedules include, but are not limited to, primary doses given at 8, 12 and 16 weeks (equal to 2, 3 and 4 months of age) or, 8, 16 and 24 weeks (equal to 2, 4 and 6 months of age). In these cases, pentavalent vaccine can be substituted by the hexavalent vaccine at the same age. 87, 88 . For hexavalent vaccines, a 3-dose schedule is adequate when initiated at ≥6 weeks of age and with a minimum of 4 weeks interval between doses. 88

Back to table of contents

Logistics (feasibility)

Cold chain volume required per vaccine dose (in cm3)

For those vaccines that have vial presentation (3 out of 4) the cold-chain space requirements varies between 2.11 and 11.32 cm3/vial [86]

Back to table of contents

Sources

1a.1b.1c.1d.1e.1f.
Diphtheria vaccine: WHO position paper, August 2017. Weekly Epidemiological Record. 2017; 92(31): 417–435.

2a.2b.2c.2d.2e.2f.
Tetanus vaccine: WHO position paper, February 2017. Weekly Epidemiological Record. 2017; 92(6): 53–76.

3a.3b.3c.3d.3e.3f.
Pertussis vaccine: WHO position paper, August 2015. Weekly Epidemiological Record. 2015; 90(35): 433–460.

4a.4b.4c.4d.4e.4f.
Hepatitis B vaccines: WHO position paper, July 2017. Weekly Epidemiological Record. 2017; 92(27): 369–392.

5a.5b.5c.5d.5e.5f.5g.
Haemophilus influenzae type b (Hib) vaccine: WHO position paper, July 2013. Weekly Epidemiological Record. 2013; 88(39): 413–426.

6a.6b.6c.6d.6e.6f.6g.6h.6i.

Polio vaccines: WHO position paper, June 2022. Weekly Epidemiological Record. 2022; 97(25): 277–296.7.

7a.7b.7c.
Wild poliovirus count. In: Global Polio Eradication Initiative [website]. Geneva: Global Polio Eradication Initiative; 2025 (https://polioeradication.org/wild-poliovirus-count/, accessed 24 June 2025).

8a.8b.8c.
Circulating vaccine-derived poliovirus count. In: Global Polio Eradication Initiative [website]. Geneva: Global Polio Eradication Initiative; 2025 (https://polioeradication.org/circulating-vaccine-derived-poliovirus-count/, accessed 24 June 2025).

9.
Global immunization data. In: World Health Organization [website]. Geneva: World Health Organization; n.d. (https://immunizationdata.who.int/global?topic=Reported-cases-and-incidence&location=, accessed 11 July 2025).

10.
Global immunization data. In: World Health Organization [website]. Geneva: World Health Organization; n.d. (https://immunizationdata.who.int/global?topic=&location=, accessed 11 July 2025).

11.
Centers for Disease Control and Prevention (no date). Diphtheria: Chapter 1. In: Surveillance Manual. Atlanta: CDC. Available at: https://www.cdc.gov/surv-manual/php/table-of-contents/chapter-1-diphtheria.html (accessed 1 July 2025).

12.
Fatihatun R, Adnan N, Laila N (2024). Diphtheria outbreak in Serang City, Banten, Indonesia, 2024: epidemiological investigation and response. J Teknol Kesehat Borneo. doi:10.30602/jtkb.v5i2.354.

13.

Brockhaus L, Urwyler P, Leutwyler U, Würfel E, Vasconcelos M, Goldenberger D et al. (2024). Diphtheria in a Swiss asylum seeker reception centre: outbreak investigation and evaluation of testing and vaccination strategies. Int J Public Health. doi:10.3389/ijph.2024.1606791.

14.
Finkelstein P, Teisch L, Allen C, Ruiz G (2017). Tetanus: a potential public health threat in times of disaster. Prehosp Disaster Med. 32:339–342. doi:10.1017/S1049023X17000012.

15.
Khalil A, Samara A, Campbell H, Ladhani SN, Amirthalingam G (2024). Recent increase in infant pertussis cases in Europe and the critical importance of antenatal immunizations: we must do better…now. Int J Infect Dis. 146:107148. doi:10.1016/j.ijid.2024.107148.

16.
Bricks LF, Vargas-Zambrano JC, Macina D (2024). Epidemiology of pertussis after the COVID-19 pandemic: analysis of the factors involved in the resurgence of the disease in high-, middle-, and low-income countries. Vaccines (Basel). 12(12):1346. doi:10.3390/vaccines12121346.

17.
Lanini S, Puro V, Lauria F, Fusco F, Nisii C, Ippolito G (2009). Patient to patient transmission of hepatitis B virus: a systematic review of reports on outbreaks between 1992 and 2007. BMC Med. 7:15. doi:10.1186/1741-7015-7-15.

18.
Lee C, Emeto T, Walsh N (2022). Prevalence of hepatitis B virus amongst refugees, asylum seekers and internally displaced persons in low- and middle-income countries: a systematic review. J Viral Hepat. 30:4–18. doi:10.1111/jvh.13770.

19.
Shane AL, Pickering LK (2012). Infections associated with group childcare. In: Cherry JD, Demmler-Harrison GJ, Kaplan SL, Steinbach WJ, Hotez PJ, editors. Principles and practice of pediatric infectious diseases. 4th ed. Philadelphia: Elsevier Saunders; 2012:24–32.e6. doi:10.1016/B978-1-4377-2702-9.00102-1.

20.

Namageyo-Funa A, Greene SA, Henderson E, et al. (2024). Update on Vaccine-Derived Poliovirus Outbreaks — Worldwide, January 2023–June 2024. MMWR Morb Mortal Wkly Rep. 2024;73:909–916. DOI: http://dx.doi.org/10.15585/mmwr.mm7341a1

21.

Maternal and neonatal tetanus elimination (MNTE). In: World Health Organization [website]. Geneva: World Health Organization; no date (https://www.who.int/initiatives/maternal-and-neonatal-tetanus-elimination-%28mnte%29, accessed 24 June 2025).

22.

Jones CE, Yusuf N, Ahmed B, Kassogue M, Wasley A, Kanu FA (2024). Progress toward achieving and sustaining maternal and neonatal tetanus elimination — worldwide, 2000–2022. MMWR Morb Mortal Wkly Rep. 73:614–621. DOI: http://dx.doi.org/10.15585/mmwr.mm7328a1.

23.

Chen D (2009). Hepatitis B vaccination: the key towards elimination and eradication of hepatitis B. J Hepatol. 50(4):805–816. https://doi.org/10.1016/j.jhep.2009.01.002.

24.

Al-Busafi S, Alwassief A (2024). Global perspectives on the hepatitis B vaccination: challenges, achievements, and the road to elimination by 2030. Vaccines. 12. https://doi.org/10.3390/vaccines12030288.

25.

Zhao H, Zhou X, Zhou Y (2020). Hepatitis B vaccine development and implementation. Hum Vaccin Immunother. 16:1533–1544. https://doi.org/10.1080/21645515.2020.1732166.

26.

Slack M, Esposito S, Haas H, Mihályi A, Nissen M, Mukherjee P, Harrington L (2020). Haemophilus influenzae type b disease in the era of conjugate vaccines: critical factors for successful eradication. Expert Rev Vaccines. 19:903–917. https://doi.org/10.1080/14760584.2020.1825948.

27.

Gilsdorf J (2021). Hib vaccines: their impact on Haemophilus influenzae type b disease. J Infect Dis. 224:S321–S330. https://doi.org/10.1093/infdis/jiaa537.

28a.28b.
Frequently asked questions and considerations for the introduction of hexavalent vaccine DTwP-HepB-Hib-IPV in routine immunization programmes. In: World Health Organization [website]. Geneva: World Health Organization; 2024 (https://www.technet-21.org/en/resources/guidance/frequently-asked-questions-and-considerations-for-the-introduction-of-hexavalent-vaccine-dtwp-hepb-hib-ipv-in-routine-immunization-programmes-june-2024, accessed 24 June 2025).

29.
World Health Organization (2022). Polio vaccines: WHO position paper – June 2022. Wkly Epidemiol Rec. 97(25):277–296. Available at: https://www.who.int/publications/m/item/polio-vaccines-who-position-paper-june-2022 (accessed 24 June 2025).

30.
Global Polio Eradication Initiative website. In: Global Polio Eradication Initiative [website]. Geneva: Global Polio Eradication Initiative; no date (https://polioeradication.org/, accessed 24 June 2025).

31.
Poliomyelitis: Fact sheet. In: World Health Organization [website]. Geneva: World Health Organization; no date (https://www.who.int/news-room/fact-sheets/detail/poliomyelitis, accessed 24 June 2025).

32.
Poliomyelitis overview. In: Centers for Disease Control and Prevention [website]. Atlanta: CDC; no date (https://www.cdc.gov/polio/index.html, accessed 24 June 2025).

33.
Shuel M, Hoang L, Law DKS, Tsang R (2011). Invasive Haemophilus influenzae in British Columbia: non-Hib and non-typeable strains causing disease in children and adults. Int J Infect Dis. 15:e167–e173. doi:10.1016/j.ijid.2010.10.005.

34.
Knuf M et al. (2021). Hexavalent vaccines: what can we learn from head-to-head studies? Vaccine. 39(41):6025–6036. doi:10.1016/j.vaccine.2021.08.086.

35a.35b.
Boisnard F, Manson C, Serradell L, Macina D (2023). DTaP-IPV-HB-Hib vaccine (Hexaxim): an update 10 years after first licensure. Expert Rev Vaccines. 22:1196–1213. doi:10.1080/14760584.2023.2280236.

36.
Vesikari T, Borrow R, Da Costa X, Richard P, Eymin C, Boisnard F, Lockhart S (2017). Concomitant administration of a fully liquid, ready-to-use DTaP-IPV-HB-PRP-T hexavalent vaccine with a meningococcal serogroup C conjugate vaccine in infants. Vaccine. 35(3):452–458. doi:10.1016/j.vaccine.2016.11.053.

37.
Centers for Disease Control and Prevention (CDC) (no date). Polio vaccines [website]. Atlanta: CDC. Available at: https://www.cdc.gov/polio/vaccines/index.html (accessed 24 June 2025).

38.
Dakin A, Borrow R, Arkwright P (2022). A review of the DTaP-IPV-HB-PRP-T Hexavalent vaccine in pediatric patients. Expert Rev Vaccines. 22:104–117. doi:10.1080/14760584.2023.2161519.

39a.39b.39c.
Wanlapakorn N, Sarawanangkoor N, Srimuan D, Thatsanathorn T, Thongmee T, et al. (2024). Antibody persistence to diphtheria toxoid, tetanus toxoid, Bordetella pertussis antigens, and Haemophilus influenzae type b following primary and first booster with pentavalent versus hexavalent vaccines. Hum Vaccin Immunother. 20. doi:10.1080/21645515.2024.2352909.

40a.40b.
Knuf M, Haas H, García-Corbeira P, Turriani E, Mukherjee P, et al. (2021). Hexavalent vaccines: what can we learn from head-to-head studies? Vaccine. doi:10.1016/j.vaccine.2021.08.086.

41a.41b.
Sharma H, Parekh S, Pujari P, Shewale S, Desai S, et al. (2024). A randomized, active-controlled, multi-centric, phase-II clinical study to assess safety and immunogenicity of a fully liquid DTwP-HepB-IPV-Hib hexavalent vaccine (HEXASIIL®) in Indian toddlers. Vaccine. 42(26):126380. doi:10.1016/j.vaccine.2024.126380.

42a.42b.

Steiner M, Ramakrishnan G, Gartner B, Van Der Meeren O, Jacquet J, et al. (2010). Lasting immune memory against hepatitis B in children after primary immunization with 4 doses of DTPa-HBV-IPV/Hib in the first and 2nd year of life. BMC Infect Dis. 10:9. doi:10.1186/1471-2334-10-9.

43a.43b.
Sanchez L, Rungmaitree S, Kosalaraksa P, Jantarabenjakul W, Leclercq J, Yaiprayoon Y, Midde VJ, Varghese K, Mangarule S, Noriega F (2023). Immunogenicity and safety of a hexavalent DTwP-IPV-HB-PRPT vaccine versus separate DTwP-HB-PRPT, bOPV, and IPV vaccines administered at 2, 4, 6 months of age concomitantly with rotavirus and pneumococcal conjugate vaccines in healthy infants in Thailand. Pediatr Infect Dis J. 42(8):711–718. doi:10.1097/INF.0000000000003975.

44a.44b.
Haemophilus influenzae type b (Hib) vaccine: WHO position paper, July 2013. Weekly Epidemiological Record. 2013;88(39):413–426.

45a.45b.
Patterson J, Kagina BM, Gold M, Hussey GD, Muloiwa R (2018). Comparison of adverse events following immunisation with acellular and whole-cell pertussis vaccines: a systematic review. Vaccine. 36:6007–6016. doi:10.1016/j.vaccine.2018.08.022.

46a.46b.
Wendelboe, A.M., et al. (2005) ‘Duration of immunity against pertussis after natural infection or vaccination’, Pediatric Infectious Disease Journal, 24(Suppl. 5), pp. S58–S61.

47a.47b.
Borrow, R., Balmer, P. and Roper, M.H. (2007) The immunologic basis for immunization: module 3: tetanus. Geneva: World Health Organization. Available at: http://apps.who.int/iris/bitstream/10665/43687/1/9789241595551_eng.pdf (accessed 30 June 2025).

48a.48b.
Swart, E.M., et al. (2016) ‘Long-term protection against diphtheria in the Netherlands after 50 years of vaccination: results from a seroepidemiological study’, PLoS ONE, 11(2), e0148605. doi: 10.1371/journal.pone.0148605.

49a.49b.
Bruce, M.G., et al. (2016) ‘Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose’, Journal of Infectious Diseases, 214, pp. 16–22. doi: 10.1093/infdis/jiw144.

50a.50b.
Wanlapakorn, N., Sarawanangkoor, N., Srimuan, D., Thatsanathorn, T., Klinfueng, S. and Poovorawan, Y. (2024) ‘Persistence of hepatitis B surface antibody until 7 years of age following administration of hexavalent and pentavalent vaccines in children at 2, 4, 6, and 18 months’, Vaccine: X, 20. doi: 10.1016/j.jvacx.2024.100561.

51a.51b.51c.51d.
Wanlapakorn, N., Sarawanangkoor, N., Srimuan, D., Thatsanathorn, T., Thongmee, T. and Poovorawan, Y. (2024) ‘Antibody persistence to diphtheria toxoid, tetanus toxoid, Bordetella pertussis antigens, and Haemophilus influenzae type b following primary and first booster with pentavalent versus hexavalent vaccines’, Human Vaccines & Immunotherapeutics, 20. doi: 10.1080/21645515.2024.2352909.

52a.52b.
Avdičová, M., Crasta, P., Hardt, K. and Kovac, M. (2015) ‘Lasting immune memory against hepatitis B following challenge 10-11 years after primary vaccination with either three doses of hexavalent DTPa-HBV-IPV/Hib or monovalent hepatitis B vaccine at 3, 5 and 11-12 months of age’, Vaccine, 33(23), pp. 2727–2733. doi: 10.1016/j.vaccine.2014.06.070.

53.
Mangarule, S., Sapru, A., Bavdekar, A., Kawade, A., Lalwani, S., et al. (2023) ‘Antibody persistence following administration of a hexavalent DTwP-IPV-HB-PRPT vaccine versus separate DTwP-HB-PRPT and IPV vaccines and safety and immunogenicity of a booster dose of DTwP-IPV-HB-PRP~T administered with an MMR vaccine in healthy infants in India’, Pediatric Infectious Disease Journal, 42(12), pp. 1128–1135.

54.
GACVS report on hexavalent vaccines. In: World Health Organization [website]. Geneva: World Health Organization; 2005 (https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/hexavalent-vaccines, accessed 11 July 2025).

55a.55b.
Centers for Disease Control and Prevention (CDC) (no date). Polio Vaccine Questions and Answers. Available at: https://www.cdc.gov/vaccines/vpd/polio/public/index.html (accessed 30 June 2025).

56a.56b.56c.
Babandi, Z.S., Suleiman, A.G., Darma, M.A., Indabo, U.H., Shehu, S., Hamza, A.S., Henry, J., Umar, U.M., Ojediran, S.L., Amadu, L., Ibrahim, M.S. & Ejembi, C.L. (2024). Knowledge and Perception of Diphtheria among Residents of a Rural Community in Kaduna State, Northwest Nigeria. Journal of Community Medicine and Primary Health Care, 36, pp.111–123. https://doi.org/10.4314/jcmphc.v36i2.9

57a.57b.57c.
Hilton, S., Hunt, K. & Petticrew, M. (2007). Gaps in parental understandings and experiences of vaccine-preventable diseases: a qualitative study. Child Care Health Dev., 33(2), pp.170–179. doi:10.1111/j.1365-2214.2006.00647.x.

58a.58b.
Chamberlain, A.T., Seib, K., Ault, K.A., Orenstein, W.A., Frew, P.M., Malik, F., Cortés, M., Cota, P., Whitney, E.A.S., Flowers, L.C., Berkelman, R.L. & Omer, S.B. (2015). Factors Associated with Intention to Receive Influenza and Tetanus, Diphtheria, and Acellular Pertussis (Tdap) Vaccines during Pregnancy: A Focus on Vaccine Hesitancy and Perceptions of Disease Severity and Vaccine Safety. PLoS Currents. https://doi.org/10.1371/currents.outbreaks.d37b61bceebae5a7a06d40a301cfa819

59a.59b.
Nankya-Mutyoba, J., Aizire, J., Makumbi, F., Ocama, P. & Kirk, G.D. (2019). Hepatitis B virus perceptions and health seeking behaviors among pregnant women in Uganda: implications for prevention and policy. BMC Health Services Research, 19, 760. https://doi.org/10.1186/s12913-019-4516-0

60a.60b.60c.
Global Polio Eradication Initiative (GPEI) (no date). Polio Today: Endemic Countries. Available at: https://polioeradication.org/where-we-work/polio-endemic-countries/ (accessed 30 June 2025).

61a.61b.

Circulating vaccine-derived poliovirus count. In: Global Polio Eradication Initiative [website]. Geneva: Global Polio Eradication Initiative; no date (https://polioeradication.org/circulating-vaccine-derived-poliovirus-count/, accessed 24 June 2025).

62.
Al Bashar, L., Dube, E., Kandasamy, T., Zaini, N., Abdul Rahman, H., et al. (2023) ‘Parents’ and healthcare professionals’ perception toward the introduction of a new fully liquid hexavalent vaccine in the Malaysian national immunization program: a cross-sectional study instrument development and its application’, Frontiers in Immunology, 14. https://doi.org/10.3389/fimmu.2023.1052450.

63.
Global Polio Eradication Initiative (no date). Circulating vaccine-derived poliovirus count [website]. Geneva: Global Polio Eradication Initiative. Available at: https://polioeradication.org/circulating-vaccine-derived-poliovirus-count/ (accessed 24 June 2025).

64.
Bakhache, P., Yewale, V., Parikh, R., Clancey, G., Spickernell, G., Berlaimont, V. & Turriani, E. (2022). Diphtheria-tetanus-pertussis (DTP) vaccination: understanding the perspectives and expectations of parents and healthcare professionals in France and India. Human Vaccines & Immunotherapeutics, 18(1), 1961468. https://doi.org/10.1080/21645515.2021.1961468.

65.
Klein, N. P. (2014). Licensed pertussis vaccines in the United States: History and current state. Human Vaccines & Immunotherapeutics, 10(9), 2684–2690. https://doi.org/10.4161/hv.29576.

66.
Al Bashar, L., Dube, E., Kandasamy, T., Zaini, N., Abdul Rahman, H., et al. (2023) ‘Parents’ and healthcare professionals’ perception toward the introduction of a new fully liquid hexavalent vaccine in the Malaysian national immunization program: a cross-sectional study instrument development and its application’, Frontiers in Immunology, 14. https://doi.org/10.3389/fimmu.2023.1052450.

67.

UNICEF (2025). Auto-disable (AD) syringe price data. Available at: https://www.unicef.org/supply/documents/auto-disable-ad-syringe-price-data (accessed 30 June 2025).

68.
UNICEF (2025). Safety boxes price data. Available at: https://www.unicef.org/supply/documents/safety-boxes-price-data (accessed 30 June 2025).

69.
UNICEF (2025). Syringe and safety box bundles price data. Available at: https://www.unicef.org/supply/documents/syringe-and-safety-box-bundles-price-data (accessed 30 June 2025).

70a.70b.
Gavi (2023). Hexavalent vaccine programme information. Available at: https://www.gavi.org/our-support/guidelines/hexavalent-vaccine-programme-information (accessed 30 June 2025).

71.
UNICEF (2024). DTP-HepB-IPV-Hib vaccine prices [PDF]. Available at: https://www.unicef.org/supply/media/21171/file/DTP-HepB-IPV-Hib-vaccine-prices-05042024.pdf (accessed 30 June 2025).

72a.72b.72c.
World Health Organization (WHO) (2025). MI4A vaccine purchase data. Available at: https://www.who.int/teams/immunization-vaccines-and-biologicals/vaccine-access/mi4a/mi4a-vaccine-purchase-data (accessed 30 June 2025).

73.
UNICEF (2022). DTP-HepB-Hib-Penta vaccine prices [PDF]. Available at: https://www.unicef.org/supply/media/15346/file/DTP-HepB-Hib-Penta-vaccines-prices-27122022.pdf (accessed 30 June 2025).

74a.74b.
Pan American Health Organization (PAHO) (2025). Revolving fund vaccine prices. Available at: https://www.paho.org/en/documents/revolving-fund-vaccine-prices-2025 (accessed 30 June

2025).

75a.75b.
UNICEF (2024). IPV vaccine prices [PDF]. Available at: https://www.unicef.org/supply/media/22786/file/IPV-vaccine-prices-28102024.pdf (accessed 30 June 2025).

76.
Salo, H., Sakalauskaitė, M., Lévy-Bruhl, D., Lindstrand, A., Valentiner-Branth, P., Wichmann, O. & Puumalainen, T. (2023). Prices of paediatric vaccines in European vaccination programmes. Vaccine X, 15, 100392. doi:10.1016/j.jvacx.2023.100392.

77.
Seinfeld, J., Rosales, M.L., Sobrevilla, A. et al. (2022). Economic assessment of incorporating the hexavalent vaccine as part of the National Immunization Program of Peru. BMC Health Services Research, 22, 651. doi:10.1186/s12913-022-08006-1.

78.
Seinfeld, J., Rosales, M.L., Sobrevilla, A. & López Yescas, J.G. (2022). Economic assessment of incorporating the hexavalent vaccine as part of the National Immunization Program of Peru. BMC Health Services Research, 22(1), 651. doi:10.1186/s12913-022-08006-1.

79.
Olivera, I., Pérez, C.G., Lazarov, L., Lopez, E., Oddo, C. & Dibarboure, H. (2023). Cost minimization analysis of a hexavalent vaccine in Argentina. BMC Health Services Research, 23(1), 1067. doi:10.1186/s12913-023-10038-0.

80.
Romero, M., Góngora, D.-S., Caicedo, M.-L., Benchabane, D. & Lopez, J.-G. (2021). Cost-Minimization and Budget Impact Analysis of a Hexavalent Vaccine (Hexaxim®) in the Colombian Expanded Program on Immunization. Value in Health Regional Issues, 26, 150–159. doi:10.1016/j.vhri.2021.06.001.

81.

Min, S., Kwon, S.H., Lee, Y.W., Lee, J.M., Bae, E.J. & Lee, E.K. (2023). Estimating the Total Societal Cost of a Hexavalent Vaccine versus a Pentavalent Vaccine with Hepatitis B in South Korea. Vaccines (Basel), 11(5), 984. doi:10.3390/vaccines11050984.

82.
Olivera, M., Soto, J., Llamas, L.M., Reyes, N., Cid, M., et al. (2020) 'Valuing the cost of improving Chilean primary vaccination: a cost minimization analysis of a hexavalent vaccine', BMC Health Services Research, 20, p. 295. https://doi.org/10.1186/s12913-020-05115-7

83.
Aljunid, S.M., Ismail, A., Nor, N.M., Zafar, A., Suleiman, A., et al. (2022) 'Economic impact of switching from partially combined vaccine "Pentaxim® and hepatitis B" to fully combined vaccine "Hexaxim®" in the Malaysian National Immunization Program', BMC Health Services Research, 22, p. 34. https://doi.org/10.1186/s12913-021-07428-7

84.
Mogale, M., Burnett, R.J., Olivier, D., Mphahlele, J. (2014) 'Economic assessment of implementing Hexaxim® vaccine within the South African Expanded Programme on Immunisation (EPI-SA)', International Journal of Infectious Diseases, 21(Suppl.), pp. 1–460 (Abstract, 16th ICID).

85.
Gavi (2024). Gavi vaccine funding guidelines. Available at: https://www.gavi.org/news/document-library/gavi-vaccine-funding-guidelines (accessed 30 June 2025).

86a.86b.
Detailed information can be found in the vaccine comparison tables

87.
World Health Organization (WHO), UNICEF (2024). Frequently asked questions and considerations for the introduction of hexavalent vaccine DTwP-HepB-Hib-IPV in routine immunization programmes (June 2024) [web site]. Hexavalent_FAQs_EN_June 2024.pdf (https://www.technet-21.org/en/resources/guidance/frequently-asked-questions-and-considerations-for-the-introduction-of-hexavalent-vaccine-dtwp-hepb-hib-ipv-in-routine-immunization-programmes-june-2024, accessed 8 July 2025).

88a.88b.

Meeting of the Strategic Advisory Group of Experts on Immunization, March 2025: conclusions and recommendations. Weekly Epidemiological Record. 2022; 100(23): 219–238.