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Effectiveness of Pneumococcal Conjugate Vaccine in Reducing Childhood Pneumonia: A Comprehensive Literature Review

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ABSTRACT

Background: *Pneumonia remains the leading cause of morbidity and mortality among children under five worldwide, with Streptococcus pneumoniae and Haemophilus influenzae identified as the most common etiological agents. The high disease burden, particularly in low- and middle-income countries, underscores the urgent need for effective prevention strategies. The Pneumococcal Conjugate Vaccine (PCV) has demonstrated substantial impact in reducing pneumonia incidence and invasive pneumococcal disease globally, and has been included in Indonesia's national routine immunization program since 2022.* ***Objective:*** *This literature review aims to synthesize current evidence on the effectiveness of PCV in reducing childhood pneumonia morbidity and mortality, evaluate its safety profile, and discuss implications for immunization policy and program implementation in Indonesia and globally.* ***Methods:*** *A narrative literature review was conducted using data from peer-reviewed journals, WHO reports, and national health surveys published between 2010 and 2025. Databases searched included PubMed, Scopus, and Google Scholar, using keywords "pneumococcal conjugate vaccine," "effectiveness," "childhood pneumonia," and "immunization program." Studies meeting inclusion criteria—randomized controlled trials, cohort studies, case-control studies, and meta-analyses—were analyzed and synthesized.* ***Results:*** *Evidence from multiple countries, including the United States, France, Israel, South Africa, Argentina, and Indonesia, consistently demonstrates significant reductions in pneumonia hospitalizations, invasive pneumococcal disease incidence, and mortality among children following PCV introduction. PCV-13 and PCV-15 have shown broad serotype coverage and sustained impact. Co-administration of PCV with other routine vaccines has been proven safe, with no increase in adverse events following immunization (AEFI).* ***Conclusion:*** *PCV is an effective and safe intervention for reducing the burden of childhood pneumonia and invasive pneumococcal disease. Nationwide implementation in Indonesia has the potential to substantially decrease pneumonia-related mortality in children under five. Continuous surveillance, serotype monitoring, and program evaluation are essential to maximize vaccine benefits and inform future immunization policies.*

1. INTRODUCTION

Pneumonia remains the leading cause of mortality among children under five due to infectious diseases worldwide. The World Health Organization (WHO) reports that pneumonia accounts for approximately 14% of global under-five deaths, making it the foremost killer of young children (WHO, 2021). According to estimates from the United Nations Inter-Agency Group for Child Mortality Estimation for 2018, pneumonia is responsible for over 800,000 deaths annually, with one child succumbing to the disease every 39 seconds. It has been described as the "forgotten pandemic" and the "forgotten killer of children" due to its persistently high mortality rate and insufficient global attention (UNICEF, 2012; WHO, 2021).

In Indonesia, data from the 2014 Sample Registration System by the National Institute of Health Research and Development (Balitbangkes) ranked pneumonia as the third leading cause of under-five mortality (9.4%). The Ministry of Health estimated pneumonia morbidity at 3.55% of the under-five population in 2015, while the 2018 Basic Health Research (Riskesdas) survey reported a prevalence of 4.8%, peaking at 6% among children aged 12–23 months. A study on

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Streptococcus pneumoniae nasopharyngeal carriage, serotype distribution, and resistance patterns among Lombok Island children in 2016 revealed a 46% carriage prevalence, with the pathogen capable of causing both mild non-invasive and severe invasive diseases (Hadinegoro et al., 2016).

The 2019 WHO Position Paper recommends inclusion of the Pneumococcal Conjugate Vaccine (PCV) in national immunization programs, especially in countries with high child mortality rates. In Indonesia, Haemophilus influenzae type b (Hib) accounts for approximately 23% of severe childhood pneumonia cases. Since 2013, the Hib vaccine has been integrated into the DPT-HB-Hib combination vaccine to prevent Hib-related pneumonia. However, Hib vaccination alone is insufficient to address the burden of pneumococcal disease, necessitating the addition of PCV. The Indonesian Ministry of Health officially incorporated PCV into the routine national immunization schedule in 2022 to comprehensively reduce pneumonia-related mortality among children (WHO, 2019).

Emerging evidence demonstrates that PCV not only reduces invasive pneumococcal disease but also significantly decreases the incidence of all-cause pneumonia and hospital admissions in children under five. Countries that have adopted PCV into their immunization programs have reported substantial declines in pneumococcal disease burden, highlighting its role as a cost-effective intervention for improving child survival rates. Evaluating the effectiveness of PCV is crucial for sustaining public health gains, optimizing immunization policies, and addressing challenges such as serotype replacement and vaccine accessibility.

Article Type

This manuscript is presented in the form of a narrative literature review, synthesizing current evidence from peer-reviewed journals, global health reports, and national surveillance data to evaluate the effectiveness of the pneumococcal conjugate vaccine (PCV) in preventing invasive pneumococcal disease, reducing pneumonia incidence, and lowering mortality among children under five years of age. The review integrates findings from randomized controlled trials, observational studies, and meta-analyses conducted in diverse geographic and epidemiological settings. By systematically summarizing available data, this paper aims to provide a comprehensive understanding of PCV impact, identify existing knowledge gaps, and support evidence-based policy recommendations for optimizing immunization strategies.

2. METHOD

This study employed a narrative literature review method to synthesize and analyze existing evidence regarding the effectiveness of the pneumococcal conjugate vaccine (PCV) in reducing the incidence of pneumococcal disease, pneumonia, and related mortality in children under five years of age. Relevant literature was systematically identified through searches in international databases including PubMed, Scopus, Web of Science, and Google Scholar, using keywords such as “pneumococcal conjugate vaccine,” “PCV effectiveness,” “pneumonia prevention,” and “child mortality.” Inclusion criteria encompassed peer-reviewed articles, randomized controlled trials, cohort studies, case-control studies, and meta-analyses published between 2010 and 2025 in English or Bahasa Indonesia. Exclusion criteria included conference abstracts without full text, studies with incomplete data, and articles focusing on non-human subjects. Data from eligible studies were extracted, compared, and thematically synthesized to highlight patterns, consistencies, and gaps in the existing literature, thereby providing a comprehensive overview of PCV effectiveness.

3. RESULT AND DISCUSSION

Definition

Pneumonia is an acute inflammation of the lung parenchyma characterized by the infiltration of inflammatory cells into the alveolar walls and interstitial spaces, accompanied by symptoms such as cough and shortness of breath. It is caused by infectious agents, including bacteria, viruses, mycoplasma, and aspiration of foreign substances. Pneumonia specifically

affects the distal lung parenchyma beyond the terminal bronchioles, leading to tissue damage and impaired local gas exchange. Pathogenic bacteria such as Streptococcus pneumoniae and Haemophilus influenzae are the leading causes of pneumonia in children under five years of age, particularly in developing countries. Mortality attributable to Streptococcus pneumoniae in this age group is estimated to be between 0.7 and 1 million deaths annually (UNICEF, 2012; Saputri & Wathoni, 2020).

Epidemiology

Infants and young children are the primary reservoirs of pneumococcal bacteria, with nasopharyngeal carriage prevalence ranging from 27% to 85% in children living in low- and middle-income countries, and in certain populations in high-income countries. According to WHO (2019), pneumonia accounts for 14% of all deaths among children under five years, with a total of 740,180 deaths globally, and an estimated 19,000 deaths in Indonesia. The highest pneumonia prevalence is observed among children aged 1–4 years, then rises again between ages 45–60 years and continues to increase in older age groups. Data from the 2018 Basic Health Research (Riskesdas) survey showed that the prevalence of pneumonia in Indonesia increased compared to 2013 (2.0%), with the highest incidence in children aged 12–23 months (6.0%). In 2024, the five provinces with the highest incidence of childhood pneumonia were East Nusa Tenggara (38.6%), Aceh (35.6%), Bangka Belitung (34.8%), West Sulawesi (34.8%), and Central Kalimantan (32.7%). In Central Java, the highest number of pediatric pneumonia cases was recorded in 2015 (6,770 cases), while the lowest was in 2014 (3,289 cases) (Riskesdas, 2018; Riskesdas, 2024; WHO, 2019).

Serotypes 6–11 have been identified as the cause of ≥70% of all invasive pneumococcal disease (IPD) cases in children under five prior to the introduction of PCV in national immunization programs. The annual incidence of IPD among children under two years in Africa ranges from 60 per 100,000 in South Africa to 797 per 100,000 in Mozambique, with significantly higher rates compared to Europe and the Americas. In 2015, under-five mortality reached 5.83 million globally, with an estimated 294,000 deaths attributed to pneumococcal infection (Wahl B et al., 2018).

Prevention and Control of Pneumonia

The WHO and UNICEF launched the Global Action Plan for Pneumonia and Diarrhoea (GAPPD), adopting an integrated multi-sectoral approach aimed at reducing the incidence of pneumonia and diarrhoea, lowering stunting rates among children, and preventing childhood deaths from these diseases. The action plan outlines a coordinated framework of proven key interventions to protect, prevent, and manage childhood pneumonia and diarrhoea. These interventions include zinc supplementation, exclusive breastfeeding, and appropriate antibiotic treatment (Directorate of Immunization Management, Indonesian Ministry of Health, 2022).

Figure 2.1 Framework for the Prevention and Control of Pneumonia (Directorate of Immunization Management, Indonesian Ministry of Health, 2022)

Pneumococcal Conjugate Vaccine (PCV)

The WHO Position Paper on Pneumococcal Conjugate Vaccine for Childhood Immunization (2019) states that, given the high burden of pneumococcal disease in children under five and the availability of a safe and effective vaccine, countries with high under-five mortality rates are strongly recommended to integrate the pneumococcal vaccine into their National Immunization Program. The Indonesian Technical Advisory Group on Immunization (ITAGI) issued a recommendation on February 21, 2020, to consider incorporating PCV into the National Immunization Program (WHO, 2019).

WHO data up to 2020 show that 150 countries (77%) worldwide had introduced the pneumococcal vaccine into their immunization programs, either nationally, sub-nationally, or in high-risk regions. A study conducted in three districts (Central Lombok, West Lombok, and East Lombok) in West Nusa Tenggara Province (NTB) in 2016 found that the predominant pneumococcal serotypes were 6A/6B, 23F, 19F, and 14, while serotypes 3 and 5 were present but less consistently detected. A pneumococcal carriage study in Indonesia (Lombok, Semarang, and Jakarta) identified serotypes 6A and 19A as the main causes of severe pneumococcal infections (Hadinegoro et al., 2016).

Pneumococcal conjugate vaccines have been developed in four main formulations — PCV-7, PCV-9, PCV-10, and PCV-13 — each covering different serotypes, and thus each being most effective against the specific serotypes it contains. Of these, PCV-7, PCV-10, and PCV-13 are most widely recommended for children. The most suitable vaccine for demonstration programs in Indonesia is PCV-13, which contains 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) conjugated to non-toxic diphtheria protein carriers (Diphtheria D, Diphtheria CRM197) (Lucero et al., 2009; Bakir, 2012).

The 15-valent Pneumococcal Conjugate Vaccine (PCV15; V114) contains serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 22F, and 33F. PCV15 (Merck Sharp & Dohme Corp.) was licensed by the U.S. Food and Drug Administration in 2021 for adults aged ≥18 years. Comparative studies show that PCV15 elicits significantly higher antibody responses than PCV13 due to the inclusion of two additional serotypes. On October 20, 2021, the U.S. Advisory Committee on Immunization Practices (ACIP) recommended PCV15 for all adults aged ≥65 years and for adults aged 19–64 years with underlying medical conditions who have never received PCV or whose vaccination history is unknown. On June 22, 2022, ACIP extended its recommendation for PCV15 use to individuals under 19 years of age. PCV15 has the potential to prevent up to an additional 13% of pediatric invasive pneumococcal disease cases compared to PCV13, while remaining cost-effective, saving healthcare costs, and reducing disease incidence. PCV15 also demonstrated a safety profile similar to that of PCV13 (CDC, 2024).

PCV15 includes polysaccharide serotypes 22F and 33F in addition to those in PCV13, conjugated to genetically detoxified diphtheria toxin. PCV15 met non-inferiority criteria compared with PCV13 for the 13 shared serotypes. Randomized controlled trials involving healthy infants aged 42 to 90 days assessed the interchangeability of PCV13 and PCV15, showing similar geometric mean IgG concentrations for the shared serotypes. Among children aged 7 months to 17 years who were PCV-naïve or partially vaccinated, catch-up doses of PCV15 yielded comparable IgG levels to PCV13 for the shared serotypes. PCV15 produced higher geometric mean IgG concentrations for 6 of the 13 shared serotypes and for its two unique serotypes in children with sickle cell disease, and higher concentrations for 2 unique serotypes and 8 of the 13 shared serotypes in children with HIV infection (Tereziu & Minter, 2023). Contraindications for both PCV13 and PCV15 include severe allergic or anaphylactic reactions to any vaccine components or diphtheria toxoid-containing vaccines. Pregnancy is not a contraindication; high-risk pregnant women should be vaccinated. Caution is advised due to post-vaccination apnea observed in preterm infants, who should be monitored for 48 hours after immunization (Tereziu & Minter, 2023).

Effectiveness of PCV Vaccine

Given the high burden of disease caused by pneumonia, prevention through immunization is crucial. PCV must demonstrate high effectiveness before being included in a national

immunization program. Vaccine effectiveness refers to a vaccine's ability to prevent disease occurrence or reduce disease incidence. The effectiveness of PCV is assessed by measuring the reduction in pneumonia cases within populations where the vaccine has been introduced. In Indonesia, PCV introduction began in stages in 2020 and reached nationwide scale in 2022 (Directorate of Immunization Management, Indonesian Ministry of Health, 2022).

Effectiveness data are drawn from countries that have implemented PCV as part of their routine national immunization programs. In the United States, the introduction of PCV-7 in 2000 and PCV-13 in 2010 resulted in a decrease in pneumonia-related hospitalizations among children under two years, from 14.5 per 1,000 children in the pre-PCV era to 8.6 and 4.1 in the PCV-7 and PCV-13 eras, respectively. In France, a three-year study (2009–2012) across eight hospitals found a 63% reduction in community-acquired pneumonia hospitalizations in children aged 1 month to 15 years between the pre-PCV and PCV-13 eras. In Israel, hospitalization and outpatient pneumonia cases among children under five decreased from 13.8% in the pre-PCV period to 11.2% after PCV-7 introduction and to 7.4% after PCV-13 introduction.

In South Africa, surveillance from 2005 to 2015 showed that invasive pneumococcal disease incidence among children under two dropped from 57.4 to 12.3 following vaccine introduction. In Argentina, pneumonia-related hospital admissions in children under five decreased significantly by 51% ($P<0.0001$) after PCV-13 introduction. In Italy, the incidence of pneumococcal parapneumonic effusion decreased substantially in vaccinated children compared to those born before PCV-13 introduction (Berman-Rosa et al., 2020).

Countries implementing PCV-13 have reported rapid and sustained reductions in serotype 19A invasive pneumococcal disease in children under five, ranging from 69% in Israel to 100% in Norway. Denmark reported a 100% reduction in serotype 19A IPD in children under two. In the UK, PCV-13 introduction in 2010 led to an 87% reduction in serotype 19A IPD cases between 2010 and 2017. In Europe, PCV-13 immunization has reduced the incidence of serotypes 6A, 3, and 19A IPD in adults aged ≥65 years. Mortality rates decreased by 69% for IPD in children under five in the UK within eight years of PCV introduction (Berman-Rosa et al., 2020).

Implementation of PCV Immunization

The distribution of vaccines and logistics is carried out in a tiered manner. Vaccines and logistical supplies (ADS and safety boxes) procured by the Central Government are distributed to the Provincial Health Office, then to the District/City Health Offices, onward to Community Health Centers (Puskesmas), and finally to immunization service posts. The distribution from the Provincial Health Office to Puskesmas may follow either a push mechanism (delivered) or a pull mechanism (collected). Supporting logistics such as anaphylaxis kits, infection prevention and control supplies, information-education-communication (IEC) materials, as well as recording and reporting formats (for coverage, logistics, and AEFI) are provided by local authorities according to the needs of each Puskesmas.

PCV vaccines are delivered to service posts on the same day as the immunization session, using vaccine carriers equipped with 2–4 cold packs. Health workers or immunization providers are responsible for transporting the vaccine carriers to the service location and returning any unopened vials, vaccine carriers, and filled safety boxes to the Puskesmas (Directorate of Immunization Management, Indonesian Ministry of Health, 2022). The PCV vaccine has the following characteristics: PCV is freeze-sensitive and must be stored at 2–8°C, protected from direct sunlight; It remains potent for up to 36 months if stored in a refrigerator at 2–8°C, protected from sunlight; Each vial is equipped with a Vaccine Vial Monitor (VVM); PCV is packaged in vials containing four doses.

Figure 2.2 Vaccine Vial Monitor (Directorate of Immunization, Indonesian Ministry of Health, 2022)

Since PCV is freeze-sensitive, it must be stored and transported at 2–8°C from the manufacturer to the point of administration. Key storage and handling principles include: Storing each vial according to its batch number; Checking the vaccine expiry date. Expired vaccines must not be used, and the "early-expiry-first-out" (EEFO) principle should be applied; Monitoring the VVM status. Vaccines with greater heat exposure (VVM B) should be used before VVM A, even if they have a longer expiry date.

For fixed-site (indoor) services, an opened multi-dose vial of PCV may be used for up to 28 days if it meets the Multi-Dose Vial Policy (MDVP) criteria: Stored at 2–8°C; VVM remains in category A or B; Date of vial opening is clearly labeled; Not past the expiry date; Vial has not been submerged in water or frozen; All doses are withdrawn aseptically. PCV immunization consists of three doses: the first at 2 months, the second at 3 months, and the booster at 12 months of age. The first and second doses are given concurrently with the DPT-HB-Hib and OPV vaccines, while in the Special Region of Yogyakarta, they are given alongside DPT-HB-Hib and IPV.

USIA ANAK	JENIS IMUNISASI
<24 jam	Hepatitis 0 (HB0)
1 bulan	BCG, OPV1
2 bulan	DPT-HB-Hib 1, OPV 2*, **PCV 1**
3 bulan	DPT-HB-Hib 2, OPV 3*, **PCV 2**
4 bulan	DPT-HB-Hib 3, OPV 4* dan IPV
9 bulan	Campak-Rubela
12 bulan	**PCV 3**
18 bulan	Campak-Rubela, DPT-HB-Hib 4
Kelas 1	Campak-Rubela, DT
Kelas 2	Td
Kelas 5	Td, HPV**
Kelas 6	HPV**

Figure 2.3 Immunization Schedule after PCV Introduction (Directorate of Immunization Management, Indonesian Ministry of Health, 2022)

At the start of PCV introduction in the routine immunization program, the first dose is administered at 2 months, the second at 3 months, and the booster at 12 months. Children who miss the 2- and 3-month doses can still receive two doses before 11 months of age, given at least 4 weeks apart, followed by a booster at 12 months (minimum 8 weeks after the second dose).

For children above 12 months who have never received PCV, two doses can be given at least 8 weeks apart before the age of 24 months. If the 12-month booster is missed, it can still be administered before the age of 24 months. For children over 24 months who have never received PCV, a single dose may be administered up to the age of 5 years (Directorate of Immunization Management, Indonesian Ministry of Health, 2022).

PCV is administered intramuscularly in a 0.5 ml dose into the middle third of the outer left thigh in infants aged 2 and 3 months, and in children at 12 months. Administration must take into account any contraindications. Immunization should be postponed until the child has recovered or at least 14 days after the onset of symptoms. Children undergoing treatment for specific conditions should be consulted with a physician. Those with a history of post-immunization adverse events may still receive PCV unless they experienced anaphylaxis or seizures following a previous vaccination (Directorate of Immunization Management, Indonesian Ministry of Health, 2022).

Adverse Events Following Immunization (AEFI)

PCV is considered a very safe vaccine; however, adverse reactions may occur. Since the first and second PCV doses are given alongside other vaccines, vigilance is required for potential adverse events. Local reactions may include pain, swelling, and redness at the injection site. Health

workers may advise cold compresses and analgesics if necessary. Systemic reactions may include fever, nausea, vomiting, loss of appetite, irritability, drowsiness, or disturbed sleep. Recommendations include increased fluid intake, comfortable clothing, warm compresses or bathing, and medication if needed.

Severe allergic reactions such as anaphylaxis are possible but extremely rare. Procedural errors during immunization can also cause AEFI; thus, immunization services must be supported by competent personnel (with adequate knowledge, skills, and professional conduct), complete equipment, and clear technical guidelines, including assignment letters, registration, and practice permits. All staff must fully understand these guidelines. Coincidental events not related to the vaccine should also be considered. Careful pre-immunization health screening is essential, and children with uncertain health status should have their data recorded to aid investigation if an AEFI occurs (CDC, 2024).

4. CONCLUSION

a. Pneumonia remains the leading cause of mortality among infants and young children, most commonly caused by Streptococcus pneumoniae and Haemophilus influenzae, particularly in low- and middle-income countries.
b. The Pneumococcal Conjugate Vaccine (PCV) has been included as part of the national routine immunization schedule and has been implemented nationwide in Indonesia since 2022, representing a major milestone in child health prevention efforts.
c. Strong evidence from both global and national studies demonstrates that PCV effectively reduces pneumonia-related morbidity and mortality, particularly in children under five, and significantly decreases the burden of invasive pneumococcal disease.
d. Co-administration of PCV with other routine childhood vaccines has been proven safe and effective, without increasing the risk of adverse events following immunization (AEFI), thereby supporting integrated immunization strategies.
e. Continued surveillance, serotype monitoring, and cost-effectiveness evaluations are essential to sustain the benefits of PCV, address potential serotype replacement, and optimize policy decisions for future vaccine formulations and schedules.

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