Preplanned Studies

Coverage of 13-Valent Pneumococcal Conjugate Vaccine Among Children 0–15 Months of Age — 9 Provinces, China, 2019–2021

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Summary

What is already known on this topic?

Limited data exist regarding the coverage of the 13-valent pneumococcal conjugate vaccine (PCV13) in China. A lack of official statistics, coupled with an insufficient body of published literature, hinders the accurate depiction of the current situation.

What is added by this report?

This study investigated the utilization of PCV13 and estimated its coverage in nine provinces across eastern, central, and western China between 2019 and 2021. Despite an annual increase in PCV13 usage during this period, the overall coverage remained suboptimal.

What are the implications for public health practice?

Consideration should be given to incorporating vaccines into the Expanded Program of Immunization, reducing vaccine prices, and addressing the vaccination coverage gap between eastern and western regions when there is an adequate supply of PCV13, particularly with domestic vaccines.

Streptococcus pneumoniae (Spn) infection can lead to invasive pneumococcal diseases (IPD), such as meningitis, bacteremia, and pneumonia, predominantly affecting children. The disease burden and economic impact on families and society are substantial. Among individuals without underlying health conditions, children under 2 years of age demonstrate the highest susceptibility to IPD (*1*). In China in 2017, an estimated 218,200 severe IPD cases and 8,000 IPD deaths occurred in children <5 years old (*2*). In 2019, the World Health Organization (WHO) classified pneumococcal conjugate vaccine (PCV) as a "very high priority" vaccine and advised its integration into national immunization programs worldwide (*3*). An estimated 400,000 child deaths and 54.6 million *Streptococcus pneumoniae*-associated illnesses could be averted annually if 13-valent pneumococcal conjugate vaccine (PCV13) was implemented in all countries (*4*). As of now, 160 countries have incorporated PCV into their national immunization programs (NIP) (*5*).

Evaluating current PCV13 vaccination coverage is crucial to inform decisions regarding the vaccine's introduction in China. However, there is a lack of data on the coverage of non-immunization program vaccines within the country. Official statistics are unavailable, and the limited published literature fails to accurately represent the existing situation. To analyze the utilization, coverage, and trends associated with PCV13, this study examined PCV13 usage data and estimated PCV13 coverage across nine provinces in eastern, central, and western China from 2019 to 2021.

In this study, nine provinces in the eastern, central, and western regions of China were selected for analysis. These provinces, as categorized in the China Health Statistical Yearbook, include Jiangsu, Zhejiang, and Shandong in the east; Anhui, Hubei, and Hunan in the central region; and Sichuan, Guizhou, and Gansu in the west. In China, the PCV13 vaccine is not part of the national immunization program and is administered voluntarily with informed consent. Three versions of the PCV13 vaccine are currently available in China: PCV13-CRM197, which is conjugated to the non-toxic diphtheria toxin mutant (CRM197); PCV13-TT, conjugated to tetanus toxoid (TT); and PCV13-TT/DT, conjugated to both TT and diphtheria toxoid (DT). Table 1 provides detailed information regarding the available PCV13 vaccines and their approved and recommended primary series and booster dose schedules.

Data from the provincial Immunization Information System (IIS) were utilized to ascertain the number of children born in 2019, 2020, and 2021 within the study setting. By examining IIS vaccination records, we determined the number of children in each of these three years who received at least one dose of PCV13

TABLE 1. Pneumococcal conjugate vaccines currently available in China.

Item	PCV13- CRM197	PCV13-TT	PCV13-TT/DT
Manufacturer	Pfizer Ireland Pharma	Yuxi Walvax Bio-Tech Co.	Beijing Minhai Bio-Tech Co.
Approved age range	6 weeks to 15 months*	6 weeks to 5 years	
Number of doses in recommended schedules	4 doses	1 to 4 doses (depend on the age of the first dose)	
Recommended schedules	Three-dose primary series (2, 4, and 6 months of age), 4–8 week intervals, the first dose can be given at 6 weeks One booster dose at 12 to 15 months In principle, the first dose should be given before 5 months of age, the three primary series doses should be completed before 6 months of age.	Infants from 6 weeks to 6 months of age: 3-dose primary series, 1- or 2-month intervals, and 1 booster dose at 12 to 15 months Infants 7 to 11 months of age: 2 doses of primary series at least 2 months apart and 1 booster dose after 12 months Children 12–23 months of age: 2 doses at least 2 months apart Children 2 to 5 years old: 1 dose	

Abbreviation: PVC=pneumococcal conjugate vaccine; CRM=cross reacting material; TT=tetanus toxoid; DT=diphtheria toxoid.
* PCV13-CRM197 was suitable for children aged 6 weeks to 15 months in 2016–2022, the age range for vaccination has been extended to 6 weeks – 5 years in April 2023.

during their first 12 months of life. Additionally, we assessed the number of children who completed the primary series of PCV13 vaccinations within the same age range and the number of children who were administered a booster dose of PCV13 between 12–15 months of age. Adherence to primary series and booster dose schedules was assessed in accordance with the recommendations outlined in Table 1.

For each study year, 3 immunization coverage rates were computed: 1) the proportion of children who received at least one dose during their first year of life in the study year, calculated by dividing the number of children receiving ≥1 dose by the number of children born within the study year; 2) the proportion of children who completed a full primary series during their first year of life in the study year, calculated by dividing the number of children receiving the full primary series by the total number of children born within the same year; and 3) the proportion of children who received a booster dose between 12 and 15 months of age within the study year, calculated by dividing the number of children administered the booster dose by the total number of children born within that study year.

Data were compiled and analyzed using Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA) to determine the three vaccination rates. These rates were examined based on province, region, and urban/rural settings. The number of PCV13 doses administered annually was compared in a year-to-year manner within the study timeframe.

Over the course of three years, a total of 22,560,400 children were born within the study setting, subsequently enrolled in the IISs, and included in this research. Table 2 provides a breakdown of the administered doses by both study province and year. A consistent increase in PCV13 utilization was observed across all provinces annually. Specifically, from 2019 to 2020, there was a 43.54% increase in PCV13 use, with the highest increase observed in Shandong Province (92.63%) and the lowest in Zhejiang Province (20.21%). Furthermore, between 2020 and 2021, a 44.24% increase in PCV13 use was reported, in which Shandong Province exhibited the highest increase (80.20%) and Jiangsu Province, the lowest (19.78%).

Table 3 shows coverage by outcome, province, and year. Coverage of ≥1-dose, primary series, and booster doses consistently increased on an annual basis across all provinces and regions, showing significant differences by province. The coverage for ≥1-dose was 12.05% in 2019, 21.99% in 2020, and 35.44% in 2021; primary series coverage levels reached 5.99%, 12.30%, and 16.13%; and booster dose coverage levels attained 3.25%, 9.15%, and 14.52%. In 2021, the highest ≥1-dose coverage was in the eastern region (Zhejiang) at 59.57%, while the lowest was in the western region (Gansu) at 6.03%. The rate of ≥1-dose coverage was 2.09 times higher in the east (17.17%) than in the west (8.21%) in 2019, 2.63 times higher in the east (34.56%) than in the west (13.12%) in 2020, and 2.46 times higher in the eastern region (51.19%) than in the western region (20.79%) in 2021.

Table 4 shows coverage by province, region, year, and urban/rural status. Coverage demonstrated an annual increase and was consistently higher in urban areas compared to rural areas, though with a decreasing disparity. In 2019, coverage of ≥1-dose was 3.16 times higher in urban areas (16.61%) than rural areas

TABLE 2. PCV13 use in 9 provinces in China, 2019–2021 (million doses).

Province	2019	2020	2021	The year-on-year growth rate in 2020 (%)	The year-on-year growth rate in 2021 (%)
Jiangsu	33.48	44.49	53.29	32.91	19.78
Zhejiang	53.95	64.86	78.61	20.21	21.19
Anhui	12.51	20.53	30.68	64.16	49.44
Shandong	18.12	34.90	62.89	92.63	80.20
Hubei	10.56	15.83	20.36	49.92	28.64
Hunan	12.99	23.29	37.68	79.30	61.82
Sichuan	22.41	30.15	51.58	34.51	71.10
Guizhou	4.46	7.25	12.80	62.39	76.63
Gansu	1.67	2.93	4.38	75.53	49.30
Total	170.15	244.23	352.27	43.54	44.24

Abbreviation: PCV13=13-valent pneumococcal conjugate vaccine.

TABLE 3. PCV13 vaccination coverage among children aged 0–15 months in 9 provinces of China, 2019–2021.

Province	2019			2020			2021		
	At least 1 dose	Full vaccination of primary series	Booster	At least 1 dose	Full vaccination of primary series	Booster	At least 1 dose	Full vaccination of primary series	Booster
Eastern Region	17.17	8.46	4.54	34.56	20.30	13.84	51.19	23.26	17.06
Jiangsu	10.43	6.20	1.51	31.78	31.25	12.88	43.95	33.00	15.41
Zhejiang	27.49	16.55	10.81	41.01	22.80	21.42	59.57	25.80	25.52
Shandong	14.40	4.03	2.07	31.45	9.50	8.34	50.15	13.31	11.45
Central Region	8.71	3.82	2.21	15.24	6.92	5.93	30.04	13.15	10.98
Anhui	13.60	3.68	1.76	22.11	6.57	5.10	46.96	13.65	12.70
Hubei	4.61	3.77	2.87	9.90	8.10	7.15	20.00	16.37	13.23
Hunan	6.69	3.99	2.21	11.56	6.50	5.98	21.70	10.42	7.82
Western Region	8.21	4.90	2.53	13.12	8.03	6.04	20.78	10.04	8.10
Sichuan	13.40	7.58	4.16	22.26	12.79	10.21	33.21	16.45	14.13
Guizhou	2.66	2.02	0.96	4.14	3.42	2.30	10.75	4.13	3.13
Gansu	2.06	1.78	0.23	2.83	2.52	0.52	6.03	4.28	1.17
Total	12.05	5.99	3.25	21.99	12.30	8.96	35.44	16.13	12.47

Abbreviation: PCV13=13-valent pneumococcal conjugate vaccine.

(5.25%), in 2020, it was 2.73 times higher in urban areas (29.01%) than in rural areas (10.59%), and in 2021, it was 2.20 times higher in urban areas (44.50%) than in rural areas (20.17%).

DISCUSSION

In October 2016, Pfizer's PCV13 was licensed in China, followed by the domestic PCV13 in December 2019 and June 2021. A supply shortage occurred during this period, indicating that accelerating the continued production and supply of PCV13 could help improve vaccination coverage (*6*). The present study demonstrated that the number of PCV13 doses administered and the resulting coverage increased annually from 2019 to 2021 in nine Chinese provinces. Furthermore, the coverage was higher in urban settings compared to rural areas. In 2021, 35.44% of infants received at least one PCV13 dose, 16.13% completed a full primary series, and 12.47% obtained a booster dose. The highest coverage was observed in eastern China and the lowest in the western region. In addition to regional disparities in coverage, significant province-level differences were also identified.

Prior researches on PCV13 coverage in China

TABLE 4. Urban and rural vaccination coverage of PCV13 among children aged 0–15 months in 9 provinces of China, 2019–2021.

Region	2019				2020				2021			
	Urban		Rural		Urban		Rural		Urban		Rural	
	Number of vaccinations (×10,000)	Coverage rate (%)	Number of vaccinations (×10,000)	Coverage rate (%)	Number of vaccinations (×10,000)	Coverage rate (%)	Number of vaccinations (×10,000)	Coverage rate (%)	Number of vaccinations (×10,000)	Coverage rate (%)	Number of vaccinations (×10,000)	Coverage rate (%)
Eastern region	38.91	21.03	8.65	9.40	62.40	41.89	12.13	18.20	75.90	59.68	17.46	31.63
Jiangsu	6.65	11.36	2.00	8.21	16.29	33.88	4.51	25.96	19.42	46.88	5.21	35.67
Zhejiang	16.98	28.99	6.02	23.98	22.06	44.94	5.83	30.81	25.33	61.17	8.62	55.31
Shandong	15.28	22.49	0.63	1.48	24.05	46.43	1.79	5.89	31.15	70.24	3.63	14.52
Central region	17.56	13.27	2.42	2.50	25.25	21.45	4.84	6.08	35.27	39.22	9.18	15.81
Anhui	9.98	20.98	1.61	4.28	13.66	30.57	3.28	10.27	17.91	58.55	6.28	30.03
Hubei	2.73	7.42	0.05	0.21	4.80	15.56	0.05	0.30	7.89	30.92	0.08	0.53
Hunan	4.85	10.11	0.76	2.12	6.79	16.09	1.51	5.11	9.47	28.01	2.82	12.36
Western region	10.79	12.31	3.20	3.86	14.42	16.94	5.96	8.49	20.58	26.07	8.80	14.10
Sichuan	8.90	18.51	3.08	7.45	11.76	26.37	5.75	16.89	14.22	36.40	8.22	28.84
Guizhou	1.39	5.10	0.09	0.31	2.03	7.17	0.18	0.71	5.16	18.00	0.51	2.12
Gansu	0.50	4.04	0.03	0.19	0.63	5.14	0.03	0.29	1.20	10.69	0.07	0.70
Total	67.26	16.61	14.26	5.25	102.07	29.01	22.93	10.59	131.75	44.50	35.44	20.17

Abbreviation: PCV=pneumococcal conjugate vaccine.

primarily relied on estimates derived from modeling. In 2017, the estimated primary series coverage for children under five years old in China was a mere 1.3% (*4*). Based on the latest PCV coverage rates reported by the World Health Organization/United Nations Children's Fund Joint Reporting Form on Immunization (JRF), the European Region demonstrated the highest final-dose coverage (82%) in 2021. In contrast, the Americas, Africa, Eastern Mediterranean, Southeast Asia, and Western Pacific regions reported final-dose coverage levels of 74%, 66%, 54%, 29%, and 19%, respectively (*7*). Within the JRF, Australia reported a final-dose coverage of 96.27%, while the United States, France, and India indicated coverage rates of 92.0%, 91.8%, and 69.3%, respectively (*7*).

Despite observing annual increases, our study found that coverage levels for both primary series and booster doses remained below 20% by the end of the study period. In China, the "3+1" immunization schedule, consisting of a 3-dose primary series and one booster dose, is recommended for PCV13. Schedules involving multiple doses can negatively impact vaccination timeliness, decrease the willingness to vaccinate, and make completing all recommended doses a challenge. WHO and several developed countries suggest reducing the PCV13 schedules to "3+0" or "2+1" to enhance coverage and achieve greater population immunity through improved compliance with a simplified schedule (*8*).

In the United Kingdom, the implementation of a "2+1" immunization program resulted in 92.0% [95% confidence interval (*CI*): 81.7%–96.7%] IPD protection against PCV7 serotypes and 72.7% (95% *CI*: 31.1%–89.9%) protection against the six additional serotypes in PCV13 (*9*). Furthermore, meningitis caused by vaccine serotypes nearly disappeared in children fully immunized with PCV13 after nine years of employing a "3+0" schedule in Australia (*10*).

We discovered that PCV13 coverage rates were highest in the eastern regions and lowest in the western regions. This finding contrasts with the regional distribution of IPD burden, in which incidence, morbidity, and mortality rates are highest in the less economically developed western regions due to the natural environment and relatively weaker healthcare conditions (*2*). Vaccination rates in both urban and rural areas have increased annually; however, coverage among urban children remains significantly higher compared to rural children, with the disparity gradually decreasing.

In China, PCV13 is not included in the immunization program, and its cost poses a significant barrier to utilization. Completing a four-dose series in China requires an out-of-pocket expenditure of 1,900–2,800 Chinese Yuan (CNY). The high price may contribute to the low affordability in central and western provinces as well as rural areas of China, leading to a prominent issue of vaccine inequity (*10*–*11*). The WHO recommends that all countries introduce PCV into their national childhood immunization programs, particularly in developing countries where safe and effective PCV vaccination has demonstrated significant progress in reducing IPD-related morbidity and mortality (*5*). A study conducted in China estimated that incorporating PCV13 into the National Immunization Program (NIP) could result in a birth cohort gaining 3.58 million quality-adjusted life years (QALYs) and averting 147,500 associated deaths, with a net benefit of 13.5 billion CNY (*12*).

Our study presents several limitations. First, despite utilizing official vaccination records, the data were sourced from provincial IISs, encompassing only those children with enrollment in the IIS and possessing vaccination histories. Consequently, we could not acquire data for children lacking IIS enrollment, which may result in an overestimation of PCV13 vaccination rates. Additionally, data constraints hindered our ability to determine the birth cohort immunization rate, allowing us to solely provide an approximation of PCV13 coverage.

In conclusion, the utilization and coverage of PCV13 among children aged 0–15 months in China have demonstrated a consistent upward trend. However, significant issues persist, including regional coverage disparities and vaccination rates substantially below the global average. Several challenges hinder the improvement of PCV13 coverage in China, such as high vaccine costs for non-program vaccines, complex vaccination schedules, limited vaccine supply, and the recent licensing of domestic vaccines.

We recommend incorporating PCV13 into the National Immunization Program to reduce its price, enhance coverage, mitigate regional disparities, and promote equitable access to the vaccine.

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