

Preplanned Studies

Coverage of the Combined DTaP-IPV/Hib Vaccine Among Children Aged 2–18 Months — 9 PLADs, China, 2019–2021

Li Li^{1,2,&}; Hui Liang^{3,&}; Yifan Song^{1,2}; Zhaonan Zhang^{1,2}; Jing An⁴; Ning Li⁵; Huifeng Sun⁶; Ying Bao⁷; Leijin Mao⁸; Lin Ding⁹; Jie Yan¹⁰; Zhiguo Wang¹¹; Lei Cao^{1,2}; Jiakai Ye^{1,2}; Wenzhou Yu^{1,2,#}

Summary

What is already known on this topic?

In China, there is limited data available on the use and coverage of the non-program, combined diphtheria, tetanus toxoid, acellular pertussis adsorbed, inactivated poliovirus and haemophilus influenzae type b (DTaP-IPV/Hib) pentavalent vaccine, and its role as a substitute for the separately administered standalone program vaccines.

What is added by this report?

We evaluated the use and coverage of the pentavalent vaccine in nine provincial-level administrative divisions (PLADs) spanning eastern, central, and western China from 2019 to 2021. Initial use and coverage were low, but demonstrated annual growth albeit with regional and urban-rural discrepancies. The pentavalent vaccine was increasingly substituted for standalone vaccines over the course of this period.

What are the implications for public health practice?

Parents in China are increasingly opting to replace the standard program vaccines with voluntarily purchased combination vaccines, particularly the pentavalent vaccine. The development of combination vaccines should thus be promoted in China, as it could enhance utilization and coverage rates, and decrease the economic burden.

Childhood vaccination plays a crucial role in shielding children from severe and potentially fatal infectious diseases. The main hurdles to childhood immunization encompass an increasing number of vital vaccines advised for young children, the discomfort tied to multiple injections, parental worries about the frequency of vaccination appointments and injection-associated pain, and the need to maintain high vaccination coverage. Combination vaccines present a solution, as they protect against multiple diseases via fewer injections, making the vaccination process more convenient for both parents and healthcare providers.

This also enhances adherence to the vaccination schedule, a factor that is paramount in sustaining high levels of population immunity (1).

Vaccines featuring a combination of diphtheria, tetanus, and pertussis (DTP) are extensively utilized globally. In 2022, around 110 million infants, constituting approximately 84% of the worldwide birth cohort, were administered three doses of a DTP-inclusive vaccine (2). These DTP-inclusive vaccines comprise DTaP, DTP-Hib (DTP integrated with a *Haemophilus influenzae* type b component), and the pentavalent DTP-inclusive vaccines, such as DTP, IPV, and Hib or hepatitis B components. The only existing pentavalent vaccine in China is Sanofi's DTaP-IPV/Hib vaccine, Pentaxim, which was licensed in the country in 2010 (3).

The DTaP-IPV/Hib vaccine serves as a suitable replacement for the DTP and IPV vaccines in the National Immunization Program (NIP) and further expands the spectrum of the NIP vaccines with the addition of the non-NIP Hib vaccine. This leads to a substantial reduction in the number of injections and visits needed for complete vaccination of children within the first two years of life. So far, studies on the pentavalent vaccine within the domestic context have been primarily concentrated on its immunogenicity and safety, with little emphasis on coverage and the ratio of its usage relative to other DTP-containing vaccines — a concept known as the substitution rate. This data are crucial for precise vaccine procurement. Thus, this paper aims to analyze usage, coverage, and the market penetration of the pentavalent vaccine in China.

The study was conducted across 9 provincial-level administrative divisions (PLADs) in China, as classified in the China Statistical Yearbook 2021. These include Jiangsu, Zhejiang, and Shandong provinces in the East; Anhui, Hubei, and Hunan provinces in the Central region; and Sichuan, Guizhou, and Gansu provinces in the West. The suggested schedule for the DTaP-

IPV/Hib vaccine involves a primary series of three doses given either at 2, 3, and 4 months of age, or at 3, 4, and 5 months of age. This regimen is then followed by a booster dose at 18 months.

We sourced the annual birth cohort sizes between 2017 and 2021, along with vaccination histories during 2019–2021, from the provincial Immunization Information Systems (IISs). Please refer to [Supplementary Material](https://weekly.chinacdc.cn/) (available at <https://weekly.chinacdc.cn/>) for detailed information. Utilizing the vaccination records from the IIS, we were able to establish the annual administration of doses for the pentavalent vaccine and other DTP-containing vaccines. Moreover, we quantified the number of children who had received at least one dose of the pentavalent vaccine, those who completed a primary series of the pentavalent vaccine, and those who were administered a booster dose of the pentavalent vaccine.

The percentage of age-appropriate children who received one or more doses of the pentavalent vaccine was calculated by dividing the number of children receiving at least one dose by the total number of children born over a twelve-month period, spanning from the final two months of the preceding year to the first ten months of the study year. Similarly, the percentage completion of the full primary series among age-appropriate children was derived by dividing the number of children who finished the primary series by the number of children born over a period of twelve months, spanning from the last four months of the preceding year to the first eight months of the study year. The booster administration rate among 18-

month-old children was calculated by taking the ratio of the number of children who received a booster dose to the total number of children born during a eighteen-month period from the last six months of the year before the preceding year to the first six months of the preceding year. The annual usage rate of pentavalent vaccine doses per 100 newborns was established by dividing the quantity of pentavalent vaccine doses administered in a particular study year by the count of newborns in that same study year. We also determined the percentages of the pentavalent vaccine among all DTP-containing vaccines administered in the years 2019, 2020, and 2021.

The data were scrutinized utilizing Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA) to discern patterns of utilisation and coverage on an annual basis and by geographical divisions such as province, region, and urban/rural classifications.

Over the span of 2019 to 2021, a total of 6.79 million doses of the pentavalent vaccine were administered. [Table 1](#) illustrates the dosage rates per 100 newborns, categorized by PLAD, region, and year. Zhejiang commanded the highest vaccine utilization each year, with Guizhou pulling up the rear in 2019 and 2020, and Gansu being the most deficient in 2021. Notably, every PLADs demonstrated an annual growth in the use of the pentavalent vaccine. The use of the pentavalent vaccine per 100 newborns notably surged by 54.66% from 2019 to 2020, and by 24.13% from 2020 to 2021. Anhui observed the most significant advancement, whereas Gansu's growth remained sluggish. In terms of regional comparisons,

TABLE 1. Use of pentavalent vaccine in nine PLADs of China, 2019–2021 (expressed as doses per 100 newborns).

PLADs	2019	2020	2021	Year-on-year growth rate in 2020 (%)	Year-on-year growth rate in 2021 (%)
Eastern Region	37.42	61.23	78.41	63.63	28.05
Jiangsu	33.04	57.24	76.82	73.25	34.21
Zhejiang	64.57	98.12	122.41	51.98	24.75
Shandong	21.71	36.32	45.79	67.33	26.06
Central Region	23.07	34.48	43.81	49.50	27.06
Anhui	14.17	25.54	40.19	80.27	57.35
Hubei	31.30	45.70	61.38	46.00	34.31
Hunan	16.00	25.06	32.99	56.62	31.62
Western Region	19.73	28.47	35.48	44.29	24.63
Sichuan	33.78	49.28	63.06	45.88	27.97
Guizhou	6.03	10.08	12.66	67.16	25.59
Gansu	7.86	10.62	12.21	35.15	15.02
Total	28.81	44.56	55.32	54.66	24.13

Abbreviation: PLADs=provincial-level administrative divisions.

the eastern region consistently reported the highest dosage rates, approximately double that of its western counterpart.

Table 2 presents the annual coverage of the pentavalent vaccine by PLAD and region. An incremental yearly increase was observed in every PLADs and region for ≥ 1 -dose, full primary series, and booster shots. The provincial-specific increase, however, varied. In 2019, the coverage for ≥ 1 dose was 11.25%, increasing to 18.74% in 2021. The full primary series covered 7.75% in 2019 and extended to 13.42% in 2021. Booster coverage grew from 1.37% in 2019 to 10.13% in 2021. Jiangsu consistently recorded the highest coverage for ≥ 1 dose every year. The lowest coverage rates for the same were seen in Guizhou in 2019 and 2020, and Gansu in 2021. The highest coverage for ≥ 1 -dose, full primary series, and booster shots were invariably found in the eastern region. In 2021, the eastern region's coverage of ≥ 1 -dose was 1.77 times higher than the central region (27.84% *vs.* 15.77%), and 2.97 times higher than the western region (9.38%).

Figure 1 shows progressively increasing coverage year-by-year, consistently demonstrating higher coverage in urban areas in comparison to rural zones. In 2019, the coverage in urban locales stood at 16.33%, while in 2021 this figure rose to 26.22%. Correspondingly, in rural areas the coverage was considerably lesser at 4.91% in 2019, increasing

marginally to 9.45% in 2021. The PLAD registering the pre-eminent coverage in both urban and rural regions was Jiangsu, whilst Gansu observed the least coverage. The graphs incorporate a 45-degree line, symbolizing parity between urban and rural coverage — with areas experiencing higher urban coverage plotted above the line. The plotted trajectories approach lines indicative of equivalence, signaling a progression towards urban-rural equilibrium.

Table 3 displays a progressive increase in pentavalent vaccine administration from 1.83 million doses in 2019, 2.35 million in 2020 to 2.61 million doses in 2021, reflecting an average annual growth rate of 19.32%. The majority of these doses were utilized in the eastern region, with the western region utilizing the least amount. Additionally, the table provides a proportion (%) of DTP-containing doses that were substituted with pentavalent doses, identified as the “pentavalent substitution rate”, by PLAD, region, and year. The substitution rate markedly increased from 7.61% in 2019 to 13.83% in 2021. While the eastern region reported the highest substitution rate in 2019, and the central region the lowest, the western region consistently reported the lowest rates in 2020 and 2021. Notably, an exception to the increasing trend was observed in Gansu, with a drop in substitution rates from 2.52% in 2019 to 1.82% in 2020, followed by a subsequent increase to 2.89% in 2021.

TABLE 2. Percentage of pentavalent vaccine coverage among children aged 2–18 months in nine PLADs of China, 2019–2021.

PLADs	2019			2020			2021		
	At least one dose	Full primary series	Booster dose	At least one dose	Full primary series	Booster dose	At least one dose	Full primary series	Booster dose
Eastern Region	16.02	10.82	1.75	22.30	15.72	8.47	27.84	18.73	14.33
Jiangsu	25.13	9.00	1.09	37.82	14.88	7.33	48.54	18.50	12.79
Zhejiang	21.30	18.88	3.53	25.93	25.32	14.42	30.43	29.25	23.72
Shandong	6.05	6.60	1.09	8.36	9.32	5.22	10.65	10.88	8.68
Central Region	7.81	5.33	1.16	11.55	8.04	4.25	15.77	10.62	6.93
Anhui	5.31	3.88	0.49	7.59	6.78	2.86	11.30	9.93	6.99
Hubei	10.37	8.14	2.00	12.67	11.32	6.03	16.33	14.66	9.30
Hunan	8.09	4.37	1.12	14.52	6.52	4.10	19.72	7.95	4.87
Western Region	7.70	5.70	0.99	8.52	8.26	4.33	9.38	9.02	7.43
Sichuan	13.34	9.92	1.78	14.61	14.42	7.60	16.45	15.93	13.00
Guizhou	2.22	1.71	0.24	3.09	2.70	1.26	3.44	3.22	2.36
Gansu	2.99	1.98	0.36	3.15	2.77	1.52	3.41	3.00	2.35
Total	11.25	7.75	1.37	15.04	11.25	6.05	18.74	13.42	10.13

Abbreviation: PLADs=provincial-level administrative divisions.

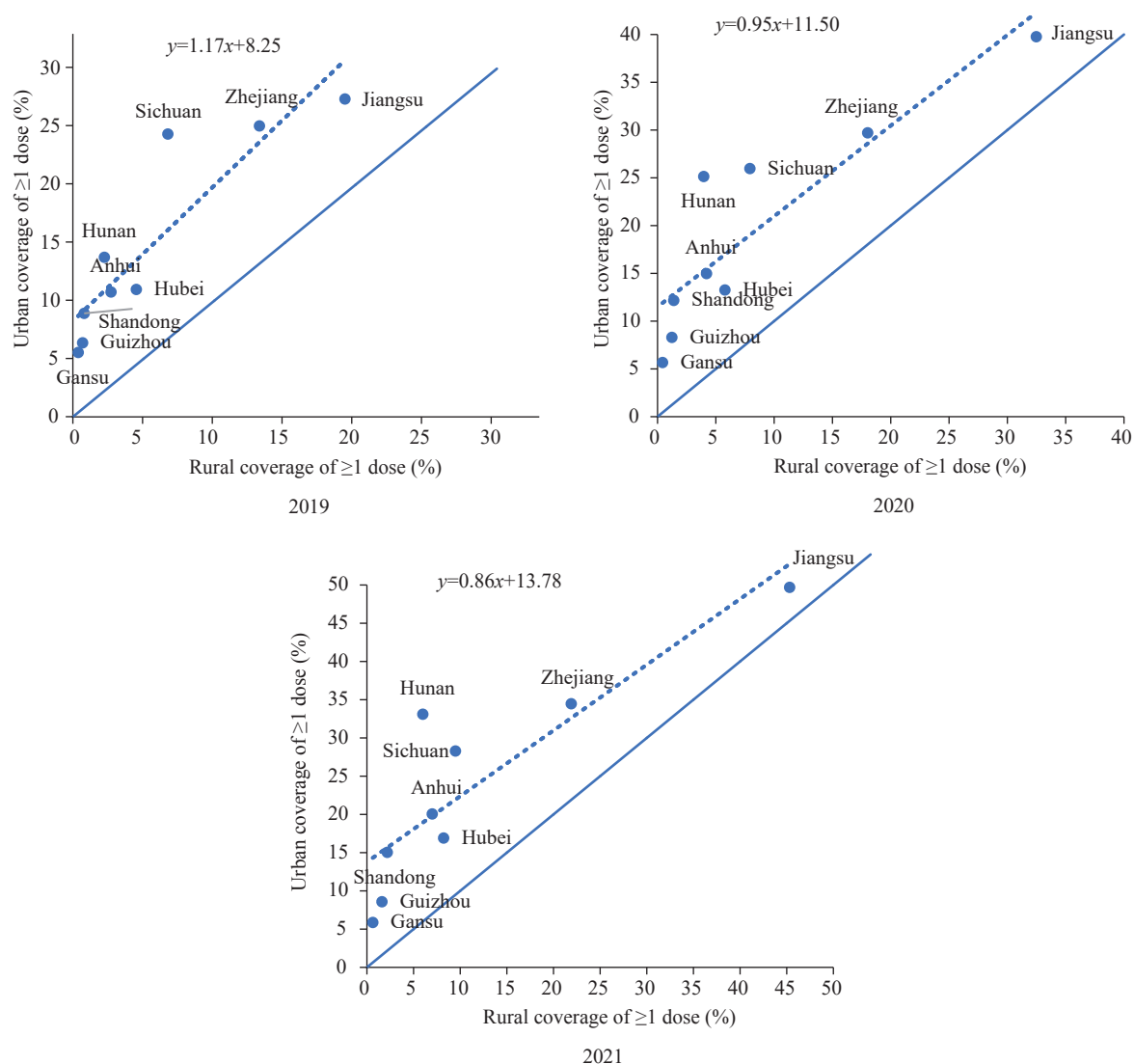


FIGURE 1. Pentavalent vaccine coverage among children aged 2–18 months in urban and rural areas in nine PLADs of China, 2019–2021.

DISCUSSION

Our analysis of real-world data reveal that between 2019 and 2021, the use and coverage of the pentavalent vaccine increased annually across nine PLADs in China. The number of pentavalent vaccine doses used per 100 newborns and the corresponding coverage levels were highest in the eastern region, followed by the central and western regions, although substantial variations were observed at the provincial level. While the pentavalent coverage was consistently higher in urban areas compared to rural areas, we noted a decreasing disparity between the two. Over the years, a growing trend towards the substitution of pentavalent vaccine in place of separately administered standalone vaccines was detected.

Our findings align with previous research. A study conducted in Anhui (4) demonstrated that the coverage for pentavalent vaccination escalated from 2015 to 2020, recording a coverage of 6.11% for 2–3 year olds and 8.51% for 1–2 year olds. These percentages are parallel to our Anhui records in 2019 and 2020, which were 5.31% and 7.59%, respectively. Furthermore, a cross-sectional survey carried out in Hainan (5) during December 2022 and January 2023 reported DTaP-IPV/Hib vaccination rates of 24.4% for at least one dose, 18.5% for the primary series, and 16.0% for the booster dose. Our findings for the eastern region in 2021 showcased similar rates, with at least one dose at 27.84%, the primary series at 18.73%, and the booster at 14.33%.

The inclusion of DTP-containing pentavalent

TABLE 3. Usage and substitution rates (%) of pentavalent vaccine in nine PLADs of China, 2019–2021.

PLADs	2019		2020		2021		Annual growth rate of doses (%)
	Number of Pentavalent (×10,000 dose)	Substitution rate (%)	Number of Pentavalent (×10,000 dose)	Substitution rate (%)	Number of Pentavalent (×10,000 dose)	Substitution rate (%)	
Eastern Region	105.99	9.97	136.01	14.71	149.40	19.26	18.73
Jiangsu	27.36	10.04	37.43	13.63	42.99	18.60	25.35
Zhejiang	52.92	20.03	66.14	28.96	71.55	34.69	16.28
Shandong	25.71	4.88	32.44	7.69	34.86	10.30	16.44
Central Region	40.68	5.48	53.10	8.05	61.22	11.04	22.68
Anhui	10.00	3.90	15.16	6.67	19.74	10.26	40.50
Hubei	19.22	8.70	22.95	11.80	25.05	15.41	14.16
Hunan	11.46	4.33	14.99	6.31	16.43	8.24	19.74
Western Region	36.36	6.07	45.88	6.87	49.96	9.02	17.22
Sichuan	30.14	9.55	37.09	12.64	40.35	15.43	15.70
Guizhou	4.13	2.06	6.10	2.70	6.67	3.51	27.08
Gansu	2.09	2.52	2.69	1.82	2.94	2.89	18.60
Total	183.03	7.61	234.99	10.43	260.58	13.83	19.32

Abbreviation: PLADs=provincial-level administrative divisions.

vaccines in immunization schedules has been a long-standing practice in countries such as the United States and the United Kingdom (6–7). In several low and lower-middle-income countries, this vaccine has been incorporated into their immunization programs, facilitated by Gavi support. In Kenya, the success of the immunization program is often gauged by the coverage percentage for the third dose of the pentavalent vaccine (8). For instance, in Afghanistan in 2018, first-dose and third-dose coverages for 12–23-month-old children were reported at 94.0% and 82.3% respectively (9). However, in China, the pentavalent vaccine is not included in the NIP and is, hence, not subsidized by the government. Parents who wish for their children to receive this vaccine must bear the cost themselves. The out-of-pocket expenses associated with non-program vaccines often contribute to their lower uptake (10).

Our study identified distinct geographical and urban-rural variations over the years. In 2021, for instance, the eastern region administered 2.21 times the number of pentavalent vaccine doses for every 100 newborns compared to the western region (78.41 *vs.* 35.48), and Zhejiang province utilized 10.03 times the doses for every 100 newborns relative to Gansu province (122.41 *vs.* 12.21). These discrepancies illuminate disparities between more and less-developed regions, as well as wealthier and poorer regions in China. In every province, we noted consistently higher vaccine coverage among urban children compared to

their rural counterparts, although the disparities have been progressively diminishing over time. A multitude of factors influenced parental preference for non-NIP vaccines, with vaccine cost and family income proving being major determinants of acceptance (11). Given the high cost of the pentavalent vaccine in China — a four-dose series being priced at 2,488 Chinese Yuan in Hainan, families in less developed, remote, and rural areas may encounter notable limitations (5). However, children in such areas have an elevated demand for combination vaccines to augment vaccination rates and to decrease the number of necessary clinic visits, thus saving the time parents spend taking their children to vaccination clinics.

The Pentavalent vaccine, an alternative to independent vaccines for DTaP, IPV, and oral polio, is part of China's NIP. It additionally includes the non-program Hib vaccine. From 2019 to 2021, usage of the pentavalent doses surged in the PLADs under study, and the substitution of the pentavalent vaccine for standalone vaccines saw an annual increase of approximately 3%. Furthermore, the preference for pentavalent vaccines among parents has been on an upward trend, despite a recent downturn in birth numbers. As the demand for combination vaccines may persistently rise, fostering research and innovation in their development within China is crucial (12).

This study is subject to some limitations. The count of administered pentavalent vaccines hinged on provincial IIS data, which may be slightly deficient due

to unsuccessful data uploads or discrepancies. Nonetheless, China's vaccine management law mandates comprehensive traceability of vaccines, resulting in a minuscule proportion of incomplete records. To mitigate the deficiencies of IIS data, we utilized estimated birth population numbers as denominators for the computation of coverage. We have confidence in the reliability of our findings, given their alignment with prior research, as mentioned above.

Our study poses queries which warrant further investigation. It is crucial to identify the contributing factors behind regional and urban-rural disparity in pentavalent vaccine coverage via observational studies. Experimental studies may be essential to test viable measures to minimize these disparities. Additionally, research focused on maintaining high coverage and analyzing the cost-effectiveness of combined vaccines could justify their inclusion in the NIP.

In conclusion, we observed a progressive increase in the use, coverage, and replacement of the pentavalent vaccine among children aged 2 to 18 months. The pentavalent vaccine's market share has been consistently growing. However, the overall coverage of the pentavalent vaccine remains modest, with variations seen across different regions, provinces, and city size. Parental preference for the pentavalent vaccine is made evident by their willingness to purchase it out-of-pocket over standalone vaccines.

Conflicts of interest: No conflicts of interest.

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* Corresponding author: Wenzhou Yu, yuwz@chinacdc.cn.

¹ National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, Beijing, China; ² National Immunization Program, Chinese Center for Disease Control and Prevention, Beijing, China; ³ Zhejiang Center for Disease Control and Prevention, Hangzhou City, Zhejiang Province, China; ⁴ Gansu Center for Disease Control and Prevention, Lanzhou City, Gansu Province, China; ⁵ Hubei Center for Disease Control and Prevention, Wuhan City, Hubei Province, China; ⁶ Shandong Center for Disease Control and Prevention, Jinan City, Shandong Province, China; ⁷ Sichuan Center for Disease Control and

Prevention, Chengdu City, Sichuan Province, China; ⁸ Anhui Center for Disease Control and Prevention, Hefei City, Anhui Province, China; ⁹ Guizhou Center for Disease Control and Prevention, Guiyang City, Guizhou Province, China; ¹⁰ Hunan Center for Disease Control and Prevention, Changsha City, Hunan Province, China; ¹¹ Jiangsu Center for Disease Control and Prevention, Nanjing City, Jiangsu Province, China.

* Joint first authors.

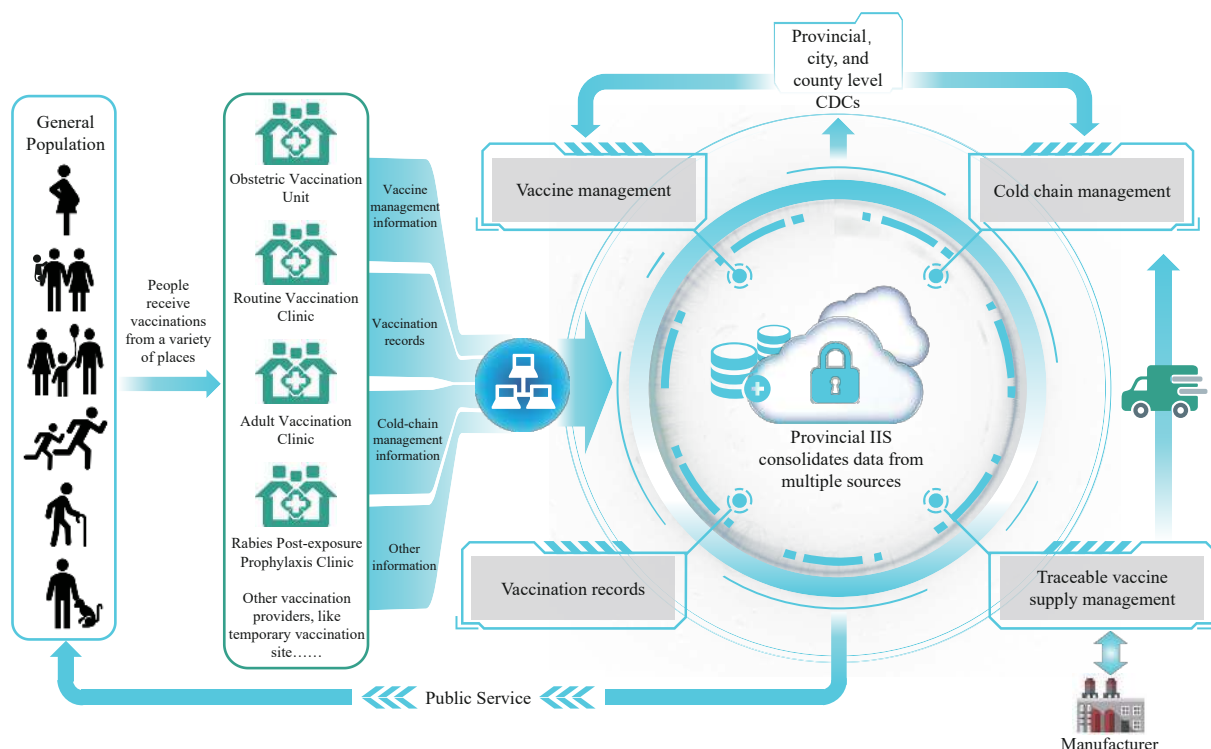
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SUPPLEMENTARY MATERIAL

Immunization Information Systems (IISs) are secure, computerized, population-based systems that gather and control vaccination data (1). In China, each provincial-level administrative division (PLAD) operates its own Provincial Immunization Information System (PIIS). As depicted in [Supplementary Figure S1](#), a PIIS consolidates data from various sources to carry out tasks such as management of vaccination records, vaccine handling, cold chain equipment and temperature observing information management, tracking of adverse events post-immunization, delivering public services, and overseeing user authentication along with permission management (2). The PIIS ensures the gathering, control, data interchange, sharing, and utilization of immunization-related information within the PLAD.



SUPPLEMENTARY FIGURE S1. Overview of the provincial immunization information system used for data collection and management of vaccination records in China.

Abbreviation: IIS=immunization information system.

Data for the Pentavalent vaccine and other DTP-containing vaccines utilized in our study were sourced from the immunization records of qualifying children across the IISs in the nine PLADs under study. Initially, a consensus on computation rules was reached via collaboration with provincial immunization experts. Subsequently, all PIISs uniformly applied these rules to ascertain both the number of individuals and the overall doses of each vaccine administered between 2019 to 2021. As a measure to ensure the validity of the calculation outcomes, these findings were reviewed and verified by the provincial experts.

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