




RESEARCH ARTICLE

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# Vaccination coverage and immunization safety among children with special health status in Chongqing, China

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## ABSTRACT

Vaccination of children with special health status has become one of the most urgent issues in China. We aim to evaluate vaccination coverage and safety as well as its associated factors among children with special health status in China during 2016–2020. We conducted a retrospective cohort review of all children with special health status recorded in the Electronic Immunization Registries System in Chongqing, China, between 2016 and 2020. Univariate and multivariate logistic regression analyses were used to analyze the influence factors. Among the 2,175 children with special health status enrolled in the study, the overall vaccination coverage rate was lower than that among the general population, and the incidence of adverse event in them following immunization was very rare. Children with congenital heart disease were better vaccinated (aOR = 1.508–6.331), while most of the jaundice children had missed vaccination (aOR = 0.441–0.556). The purchase of vaccine compensation insurance was associated with higher completion rate of basic immunization for Bacillus Calmette-G vaccine (aOR = 1.706, 95% CI: 1.249–2.329) and rotavirus vaccine (aOR = 1.346, 95% CI: 1.061–1.708). Children with special health status can be safely vaccinated. However, the vaccination coverage in these huge and vulnerable group is too low to protect them from vaccine-preventable diseases through immunization. More researches and interventions should be conducted to ensure a higher vaccination rate among the children with special health status.

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## Introduction

With the help of Expanded Programme on Immunization (EPI), the vaccination rate of EPI vaccines among healthy children in China has reached 99%.<sup>1</sup> However, the immune status of children with special health status, such as preterm infants, and children with immune-compromising medical conditions or other physiological and pathological conditions, is still unknown.<sup>1</sup> These children are deemed as special groups with increased risk of vaccine-preventable diseases. Previous studies have shown that to decide whether to vaccinate children with special health status is a difficult task for vaccination workers.<sup>2</sup> According to the 2011–2020 Global Vaccine Action Plan, immunization is recommended to all people because it is one of the most successful and cost-effective public health interventions.<sup>1–4</sup> The annual incidence of premature infants is 7% in China according to the National Health and Wellness Committee, which means there are a huge number of children with special health status.<sup>2,5</sup> Despite demonstrations of effectiveness and safety, vaccine uptake in these special groups is lower than expected even in developed countries with well-established vaccination strategies in place.<sup>4,6,7</sup> Due to ambiguous instructions on vaccination for children with these special health statuses in China and the fear of vaccine safety-related issues, many special health statuses are mistakenly considered as contraindications for vaccination, which may lead to a low vaccination rate in these groups.<sup>2,8,9</sup> As a result, vaccination of

children with special health status has become one of the most urgent issues in China.

In order to improve the vaccination coverage in children with special status and establish herd immunity, a number of expert consensus and recommendations have been issued in China in recent 5 years, and they have become practical guidelines for vaccinators. Since then, some vaccinators have gradually begun to vaccinate children with special health status. Nonetheless, many still suspect that special health status is a predisposition to Adverse Events Following Immunization (AEFI).<sup>3,10</sup> It is likely that children with special health status do not complete their immunization schedule.<sup>10</sup> Consequently, a further national instruction on Chinese immunization procedures has been published in 2021, which points out that certain diseases, such as premature birth, infectious diseases and jaundice, should not be regarded as contraindications or precautions for vaccination.<sup>11</sup> However, just as many other countries which do not monitor or report vaccination coverage in groups at risk, the national scale data at individual level are still unavailable in the Chinese national immunization recording system presently.<sup>4,12,13</sup> That is to say, little is known about the extent of age-appropriate immunizations and the actual immunization safety in this sub-population. An evidence-based evaluation of vaccines to ease the mental pressure of parents and vaccine providers is imperative.

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Chongqing is a municipality located in the southwest part of China with a population of 33 million. In the last ten years, rapid progress has been made to develop a municipal level Electronic Immunization Registries System (EIRS) in Chongqing. Vaccinators are required to input electronic information of children and vaccine into EIRS. Based on the data from the National AEFI Information System (CNAEFIS), death monitoring system (DMS), vaccine compensation insurance purchase system (VCIPS) and EIRS in Chongqing Municipality, it is possible to comprehensively analyze the data of vaccination coverage and safety for children with special health status. Starting from 2016, some vaccination clinics began to try to provide vaccination services for children with special health status, and any untoward medical occurrence which follows immunization will be recorded in CNAEFIS, even if these events does not necessarily have a causal relationship with the usage of the vaccine. Given the importance of vaccination for this vulnerable group, we evaluate the vaccination status and safety among children with special health status and determine the factors affecting the vaccination status from 2016 to 2020 in Chongqing, China.

## Methods

### Study design and setting

A retrospective study of medical records from 2016 was conducted. For each child, the collected data included the demographic characteristics (e.g., sex, birth weight, gestational age, birth order, and premature or not), the immunization status data, safety data (AEFI), survival status, and vaccine compensation insurance purchases. All data were fully anonymized, and the study was approved by the Ethics Institutional Review Board of Chongqing Municipal Center for Disease Control and Prevention (Project No: CQCDCLS (2021)006).

The data on immunization status were obtained from EIRS in Chongqing. It is a population-based lifespan immunization information system for all residents in Chongqing. Since 2013, all the people immunized in Chongqing were directly recorded in EIRS. The health status of newborns was recorded in EIRS within one month after birth, while the vaccination status was accurately recorded at the time of vaccination. To ensure that all children eligible for vaccination are recorded in the system, all children's vaccination records must be checked before they are allowed to enroll in kindergartens and primary schools since 2005. Therefore, the record in EIRS can be considered to comprise all people who have been immunized since the establishment of EIRS in Chongqing.

The safety data in this study were acquired from CNAEFIS, a national post-marketing vaccine safety monitoring system based on passive reporting.<sup>14</sup> In this system, an AEFI case is defined as a reaction or event following vaccination that is suspected to be related to the vaccine administration. The AEFI surveillance covers all vaccines marketed in mainland China, and more than 90% of vaccination clinics in Chongqing report AEFIs to CNAEFIS. In order to analyze factors that influence vaccination status, the information on vaccine compensation insurance purchases and deaths data were collected from the vaccine compensation insurance purchase system and

death monitoring system, respectively. Through the unique national identification number of each child, all the data of the same person were matched. After the data matching, the national identification number of all children were deleted in the database, and hence the personal information could not be identified after data collection.

### Study population

Starting from 2016, vaccination clinics in Chongqing municipality began to provide vaccination services to children with special health status. Therefore, the target population in this study consisted of all the children with a special health status in EIRS with the following inclusion criteria: (1) born between 1 January 2016 and 31 December 2020; and (2) the health status recorded in the system indicating that more observation was required after vaccination. All the profiles of eligible cases in EIRS were obtained on 1 October 2021 to ensure that all the children in the study had reached the age for measles vaccination (8 months after birth)-one of the most important indicators of vaccine coverage in China. As a comparison, the vaccination rate of the children without special health status in EIRS was obtained, too.

### Data source and variables

According to the Chinese National Immunization Programme schedule, the routine vaccination coverage indicators refer to the percentage of children who have received vaccines recommended in the Expanded Programme on Immunization (EPI), which includes one dose of Bacillus Calmette-G vaccine (BCG) after birth; three doses of hepatitis B vaccine (HepB) at birth, 1 month, and 6 months of age; three doses of polio vaccine (two doses of inactivated poliovirus vaccine and one dose of live oral poliovirus vaccine) at 2 months, 3 months, and 4 months of age; three doses of diphtheria-tetanus-pertussis-containing (DTP) vaccine at 3 months, 4 months, and 5 months of age; one dose of measles-containing vaccine (MCV) at 8 months of age; two dose of Group A meningococcal polysaccharide vaccine (MPSV-A) at 6 months and 9 months of age; and one dose of Japanese encephalitis vaccine (JEV) at 8 months of age.<sup>15</sup> If EPI vaccines are replaced by equivalent non-EPI vaccines, children are also considered to be fully vaccinated for those vaccines. For the Children over 12 months of age, if they have received BCG before 4 months and the rest EPI vaccines before 12 months of age, they will be classified as up to date (UTD). Considering that the children with special health status were vulnerable to many other diseases, the completion of non-EPI vaccines is also taken into account according to the vaccine instructions, which includes the following immunizations before 12 months of age: 3 doses of Haemophilus influenza type-b vaccine (Hib), 3 doses of rotavirus vaccine (ROV), 1 dose of varicella vaccine (VarV), 2 doses of enterovirus 71 (EV71), at least 1 dose of influenza vaccine (InfV), and 3 doses of pneumococcal conjugate vaccine (PCV13-valent).

## Statistical analysis

Statistical analysis was performed using the statistical software SPSS 26.0 (International Business Machines Corporation, Armonk, USA). Immunization status and safety data were presented as numbers and percentages in children with/without special health status first. Then, depending on the traditional classification of vaccination contraindication, children were classified into 7 groups with different special health statuses: history of infectious diseases (HID), jaundice, congenital heart disease (CHD), premature birth, surgical diseases (SD), immunological disease (ID) and chronic disease (CD). Among them, the HID, jaundice, CHD and premature birth used to be considered contraindications for a long time, which caused a high incidence of measles in these groups in a child hospital of Chongqing in 2014, and hence they are analyzed separately in our study; SD refers to children with congenital malformations, intestinal obstruction and other surgical diseases; ID refers to children who have autoimmune diseases, asthma, allergic diseases, or are in immunosuppression state due to medication; and CD refers to children with chronic diseases that require long-term medication but are not accompanied by abnormal immune functions.<sup>16</sup>

The vaccine coverage rates among groups of different health statuses were also compared. Demographics and vaccination coverage rate for each vaccine were stratified according to health status groups. Proportion of the groups was compared by Chi-square tests. Univariate and multivariate logistic regression were used to compare the proportional differences in factors associated with vaccination coverage. Significance tests were two-tailed, and  $P$  values  $<0.05$  were considered statistically significant.

## Results

### Characteristics of the population

From 1 January 2016 to 31 December 2020, 2,175 children with special health status and 1,694,875 children without

special health status were recorded and verified in EIRS. The number and proportion of children with special health status recorded in EIRS are increasing year by year (Figure 1). The vaccination coverage rates for each vaccine for children with and without special health status are shown in Figure 2. Considering that the target population of this study is only a sample of the national population, the 95% confidence intervals of vaccination coverage rates were also calculated. Except for the 1st and 2nd dose of hepatitis B vaccine, the coverage rate of all vaccines among children with special health status are lower.

2,175 children with special health status recorded in EIRS represent people who meet the criteria for vaccination according to the immunization guidelines and are willing to be vaccinated at least once, and a total 14,068 doses of vaccines have been administered. Children with different special health statuses do show hesitancy toward certain vaccines. Therefore, the vaccination rates between different subgroups in this cohort were compared to identify the key factors for vaccine hesitancy. The distribution of the special health status among them is shown in Figure 3, and the characteristics of these children are reported in Table 1. There were 245 children with a history of infectious diseases (11.3%), 633 with jaundice or jaundice history (29.1%), 81 with a history of surgery (3.7%), 91 with immunological disease (4.2%), 777 with congenital heart disease (35.7%), 125 with premature birth (5.7%) and 223 with chronic disease (10.3%). 54.2% of the children were male, 75.2% had a normal birth weight, 66.6% were the first born of their mother, and 61.9% did not purchase the vaccine compensation insurance. Only 3 (0.1%) of them reported a history of AEFI, corresponding to a rate of 21.3 per 100,000 doses, all of which were common reactions. As the disease progresses, 0.1% of the children died. The vaccine compensation insurance was the only factor that showed statistically significant difference in groups of different special health status.

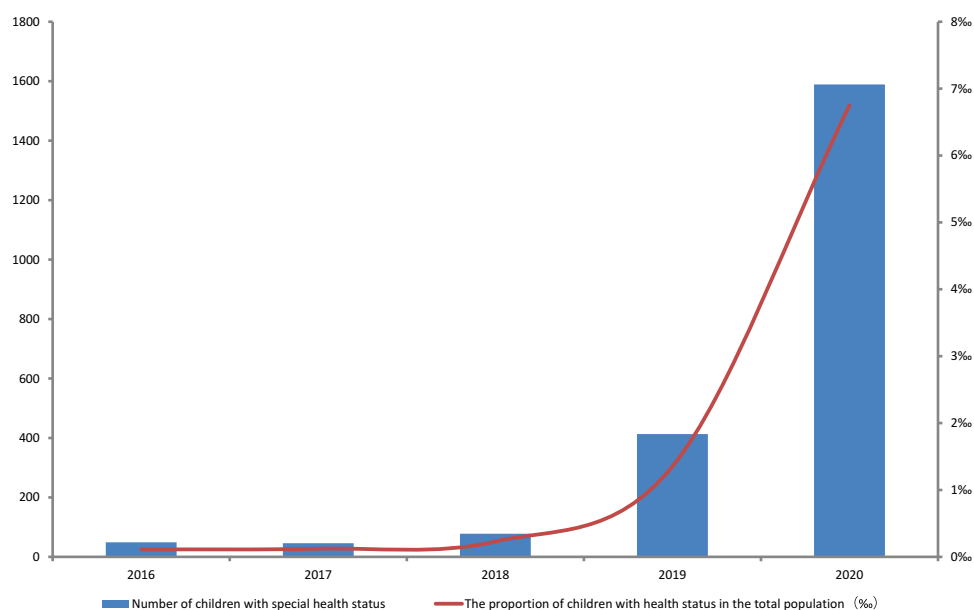
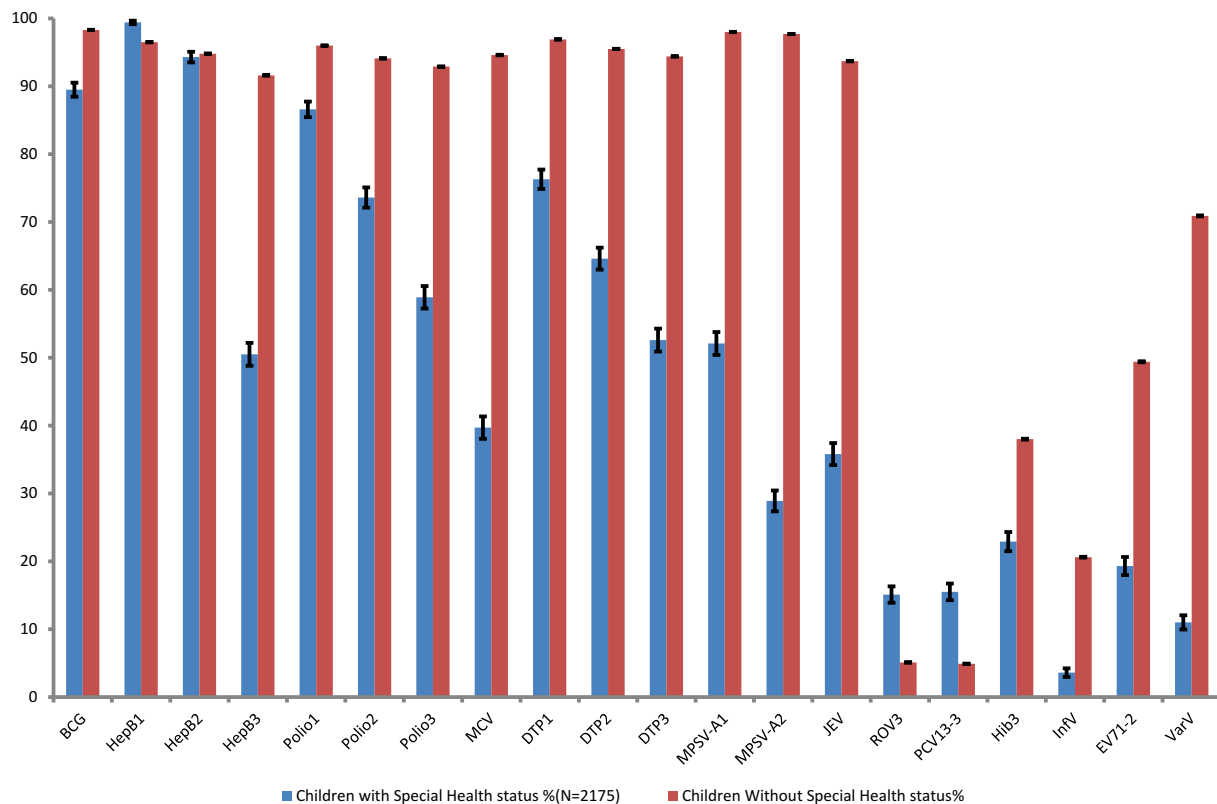


Figure 1. The number and proportion of children with special health status recorded in EIRS.



**Figure 2.** Vaccination coverage rates for the individual vaccines in children with and without special health status. The confidence intervals of the vaccination coverage rates among the general population are too small to be shown for its large sample size (1,694,875).

## Vaccination status

### Vaccination coverage

Table 2 shows the coverage rate of each vaccine in children with different special health statuses. In the seven different subgroups, HepB3 coverage was lower in the HID, jaundice, and premature groups, polio 1,2,3 coverage were all lower in the ID group, and MCV coverage was lower in the jaundice, premature, and CD groups. The coverage of DTP1,2,3, MPSV-A1,2 and JEV were all lower in the jaundice group. This study also calculated the completion of basic immunization of non-EPI vaccine. Compared with other subgroups, CHD group had the highest vaccination rate of all vaccines except for BCG and HepB, and children with jaundice or a history of jaundice were less likely to be vaccinated with HepB3, MCV, DTP1,2,3, MPSV-A, JEV, and all of the non-EPI vaccines.

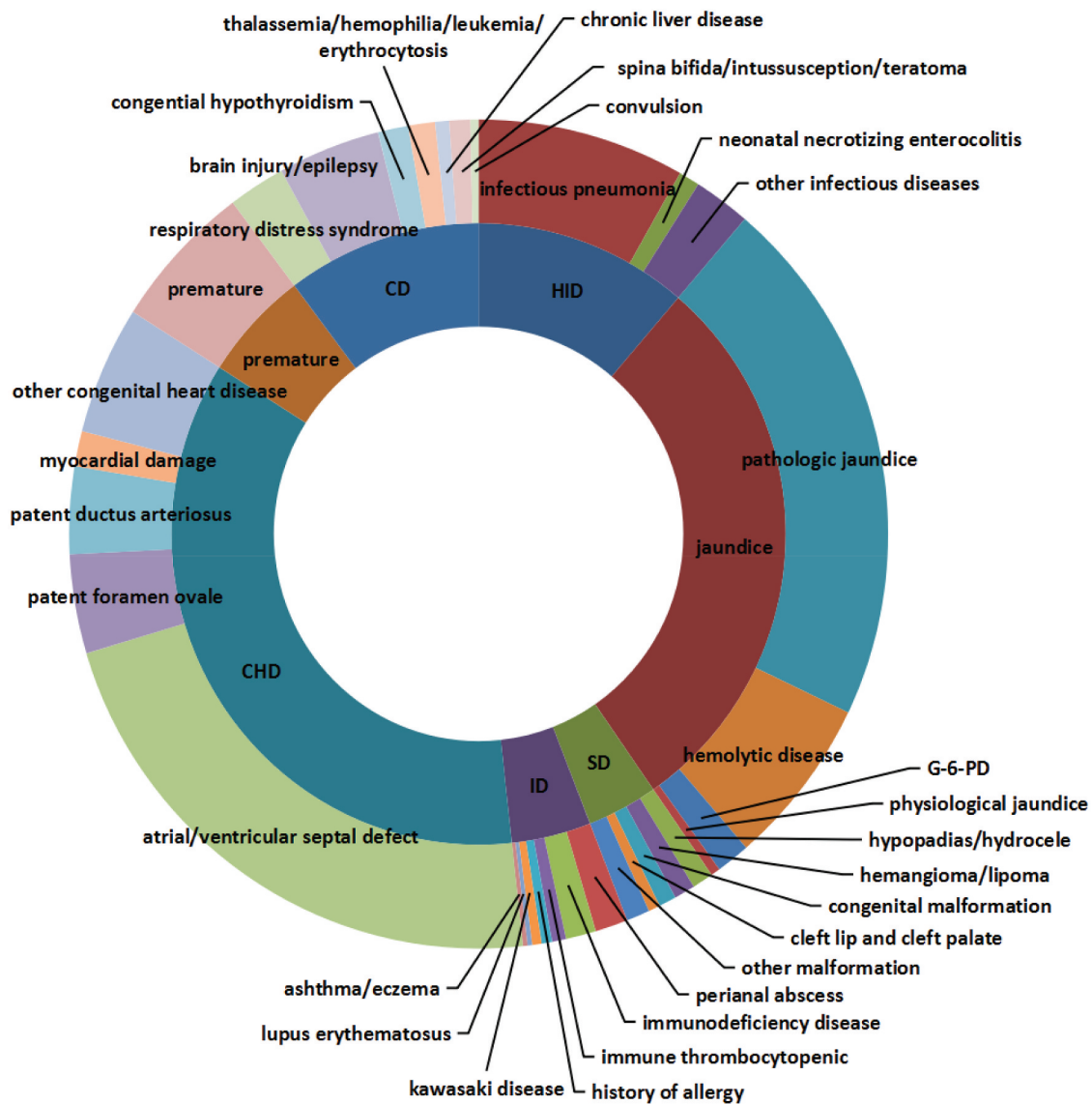
### Vaccination up-to-date status

There were 1824 children older than 12 months. As shown in Table 3, compared with the HID group, these children with a history of jaundice were significantly ( $P < .05$ ) less likely to be UTD for all the EPI vaccines except for BCG. Compared with the HID group, the BCG UTD rate was lower in the SD ( $OR = 0.501$ , 95%  $CI: 0.281-0.894$ ), CHD ( $OR = 0.553$ , 95%  $CI: 0.382-0.801$ ) and CD ( $OR = 0.624$ , 95%  $CI: 0.398-0.980$ ) groups, the HepB UTD rate was lower in the jaundice group ( $OR = 0.482$ , 95%  $CI: 0.345-0.675$ ), the Polio vaccine UTD rate was lower in the in the jaundice group ( $OR = 0.591$ , 95%  $CI: 0.415-0.841$ ), the MCV UTD rate was lower in the jaundice ( $OR = 0.539$ , 95%

$CI: 0.385-0.756$ ) and CD groups ( $OR = 0.634$ , 95%  $CI: 0.424-0.949$ ), the DTP UTD rate was lower in the in the jaundice group ( $OR = 0.590$ , 95%  $CI: 0.422-0.825$ ), and the JEV UTD rate was lower in the premature birth ( $OR = 0.474$ , 95%  $CI: 0.336-0.668$ ) and CD groups ( $OR = 0.501$ , 95%  $CI: 0.331-0.759$ ). Overall, the jaundice ( $OR = 0.533$ , 95%  $CI: 0.372-0.765$ ), the SD ( $OR = 0.533$ , 95%  $CI: 0.288-0.983$ ), and the CD groups ( $OR = 0.541$ , 95%  $CI: 0.348-0.842$ ) were less likely to be up to date.

### Influencing factors of vaccination

Several variables were correlated with the coverage of each vaccine and the demographic and health status in the univariate analysis. All variables with  $P < .20$  in the univariate analysis were input into an initial logistic multivariable regression model followed by a backward selection procedure that retained variables with  $P < .05$  to create a final multivariable model. In the multivariate analysis, four factors – birth weight, parity, vaccine compensation insurance, and health status – remained independently associated with vaccination status after controlling covariates (Table 4). Most of the children with jaundice missed vaccination (a $OR = 0.441-0.556$ ), while most of children with CHD were immunized (a $OR = 1.508-6.331$ ). The SD was associated with a higher completion rate of basic immunization of PCV13 (a $OR = 2.669$ , 95%  $CI: 1.431-4.980$ ) and InfV (a $OR = 16.279$ , 95%  $CI: 1.872-141.581$ ). Premature birth was associated with a lower completion rate of basic immunization of EV71 (a $OR = 0.378$ , 95%  $CI: 0.184-$



**Figure 3.** The group distribution of the children's special health status. HID history of infectious diseases, CHD congenital heart disease, SD surgical diseases, ID immunological disease and CD Chronical disease.

0.777) and JEV ( $aOR = 0.551$ , 95%  $CI: 0.342-0.899$ ). The status of chronic diseases was associated with a lower completion rate of basic immunization of JEV ( $aOR = 0.623$ , 95%  $CI: 0.422-0.921$ ) and a higher completion rate of basic immunization of Hib ( $aOR = 1.772$ , 95%  $CI: 1.146-2.738$ ).

Multivariate analysis showed that parity was associated with BCG vaccination status ( $aOR = 0.433$ , 95%  $CI: 0.243-0.771$ ). The higher birth weight was associated with a lower completion rate of basic immunization of PCV13 ( $aOR = 0.635$ , 95%  $CI: 0.473-0.853$ ) and ROV ( $aOR = 0.697$ , 95%  $CI: 0.529-0.919$ ). The purchase of vaccine compensation insurance was associated with a higher completion rate of basic immunization of BCG ( $aOR = 1.706$ , 95%  $CI: 1.249-2.329$ ) and ROV ( $aOR = 1.346$ , 95%  $CI: 1.061-1.708$ ).

## Discussion

The correlation between chronic illness and immunization status in China is inconclusive. Most earlier studies are limited

to specific subpopulations or vaccines.<sup>17</sup> This study characterizes the general immunization status of children with special health status in Chongqing, China, based on data at individual level. At the present moment, there is no such data available at national scale, and our study on the municipal scale represents the most comprehensive study of such kind in China, which provides an evidence-based assurance to ease the concerns on vaccination risks.

Children with special health status comprise a large population in China. For instance, the cumulative prevalence of asthma among children under 14 years old in cities was 3.02% nationwide in 2010, and the majority of them can be safely vaccinated according to the state-recommended schedule.<sup>11,17</sup> However, although twenty-three percent of parents reported that their adolescent had asthma,<sup>5,18</sup> but only 2 children with asthma were recorded in our study. That is to say, only a small portion of children with special health status were vaccinated and recorded in EIRS accordingly. As a result, although the vaccination rate among children with special

**Table 1.** The characteristics of the study population (n = 2,175).

variables	N(%)	Health status							$\chi^2$
		HID	jaundice	SD	ID	CHD	Premature	CD	
sex									
Male	1178(54.2)	136(55.5)	345(54.5)	42(51.9)	47(51.6)	415 ( 53.4)	66(52.8)	127 ( 57.0)	1.583
Female	997(45.8)	109(44.5)	288(45.5)	39(48.1)	44 ( 48.4)	362 ( 46.6)	59(47.2)	96 ( 43.0)	
Birth weight									
<2500g	445(20.5)	29(11.8)	26(4.1)	12(14.8)	18(19.8)	192(24.7)	88(70.4)	80(35.9)	360.312
2500–4000g	1635(75.2)	204(83.3)	579(91.5)	67(82.7)	65(71.4)	555(71.4)	36(28.8)	129(57.8)	
>4000g	95(4.4)	12(4.9)	28(4.4)	2(2.5)	8(8.8)	30(3.9)	1(0.8)	14(6.3)	
History of AEFI									
Yes	3(0.1)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(0.1)	1(0.8)	1(0.4)	6.994
No	2172(99.9)	245(100.0)	633(100.0)	81(100.0)	91(100.0)	776(99.9)	124(99.2)	222(99.6)	
parity									
1	1410(66.6)	173(70.9)	410(65.0)	55(68.8)	50(64.1)	499(66.2)	77(61.6)	146(71.6)	15.275
2	621(29.3)	61(25.0)	201(31.9)	24(30.0)	24(30.8)	225(29.8)	39(31.2)	47(23.0)	
>3	85(4.0)	10(4.1)	20(3.2)	1(1.3)	4(5.1)	30(4.0)	9(7.2)	11(5.4)	
vaccine compensation insurance									
Yes	829(38.1)	93(38.0)	265(41.9)	31(38.3)	33(36.3)	262(33.7)	45(36.0)	100(44.8)	14.789*
No	1346(61.9)	152(62.0)	368(58.1)	50(61.7)	59(63.7)	515(66.3)	80(64.0)	123(55.2)	
Survival status									
live	2172(99.9%)	245(100.0)	633(100.0)	81(100.0)	91(100.0)	774(99.6%)	125(100.0)	223(100.0)	5.405
dead	3(0.1%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	3(0.4%)	0(0.0%)	0(0.0%)	

\*  $P < .05$ ; \*\*  $P < .001$ .**Table 2.** Vaccination coverage of vaccines in the study population (n = 2,175).

variables	Total N	N(%)	Health status							$\chi^2$
			HID	jaundice	SD	ID	CHD	premature	CD	
BCG	1946	89.5	226(92.2)	567(89.6)	69(85.2)	80(87.9)	691(88.9)	111(88.8)	202(90.6)	4.415
HepB1	2162	99.4	245(100.0)	630(99.5)	81(100.0)	90(98.9)	770(99.1)	124(99.2)	222(99.6)	3.880
HepB2	2051	94.3	235(95.9)	598(94.5)	73(90.1)	86(94.5)	725(93.3)	122(97.6)	212(95.1)	8.063
HepB3	1099	50.5	118(48.2)	193(30.5)	50(61.7)	55(60.4)	500(64.4)	58(46.4)	125(56.1)	172.830**
Polio1	1883	86.6	227(92.7)	542(85.6)	71(87.7)	72(79.1)	670(86.2)	111(88.8)	190(85.2)	13.685*
Polio2	1601	73.6	183(74.7)	402(63.5)	65(80.2)	63(69.2)	622(80.1)	96(76.8)	170(76.2)	54.183**
Polio3	1281	58.9	146(59.6)	280(44.2)	52(64.2)	57(62.6)	533(68.6)	69(55.2)	144(64.6)	91.610**
MCV	863	39.7	99(40.4)	157(24.8)	35(43.2)	45(49.5)	407(52.4)	40(32.0)	80(35.9)	119.441**
DTP1	1659	76.3	199(81.2)	442(69.8)	59(72.8)	65(71.4)	631(81.2)	100(80.0)	163(73.1)	32.235
DTP2	1404	64.6	158(64.5)	325(51.3)	55(67.9)	55(60.4)	574(73.9)	85(68.0)	152(68.2)	80.763**
DTP3	1145	52.6	124(50.6)	224(35.4)	46(56.8)	53(58.2)	507(65.3)	61(48.8)	130(58.3)	130.857**
MPSV-A 1	1133	52.1	122(49.8)	204(32.2)	51(63.0)	55(60.4)	501(64.5)	64(51.2)	136(61.0)	161.861**
MPSV-A 2	629	28.9	62(25.3)	108(17.1)	25(30.9)	29(31.9)	318(40.9)	25(20.0)	62(27.8)	104.857**
JEV	778	35.8	94(38.4)	136(21.5)	29(35.8)	36(39.6)	389(50.1)	32(25.6)	62(27.8)	138.401**
PCV13-3	338	15.5	30(12.2)	84(13.3)	22(27.2)	13(14.3)	128(16.5)	19(15.2)	42(18.8)	15.325*
EV71-2	419	19.3	46(18.8)	72(11.4)	21(25.9)	21(23.1)	215(27.7)	10(8.0)	34(15.2)	76.349**
ROV3	328	15.1	31(12.7)	89(14.1)	16(19.8)	12(13.2)	117(15.1)	19(15.2)	44(19.7)	7.045
InfV	78	3.6	1(0.4)	8(1.3)	5(6.2)	5(5.5)	49(6.3)	3(2.4)	7(3.1)	36.821**
VarV	239	11.0	15(6.1)	32(5.1)	6(7.4)	13(14.3)	153(19.7)	4(3.2)	16(7.2)	102.019**
Hib3	497	22.9	46(18.8)	98(15.5)	21(25.9)	28(30.8)	212(27.3)	25(20.0)	67(30.0)	41.264*

BCG = Bacillus Calmette-G vaccine, HepB = hepatitis B vaccine, Polio = poliovirus vaccine, DTP = diphtheria-tetanus-pertussis-containing vaccine, MCV = measles-containing vaccine, MPSV-A = Group A meningococcal polysaccharide vaccine, JEV = Japanese encephalitis vaccine, Hib = Haemophilus influenzae type-b vaccine, VarV = varicella vaccine; EV71-2= the second dose of enterovirus 71 vaccine, InfV = influenza vaccine, PCV13-3 = the third dose of 13 valent pneumococcal conjugate vaccine. ROV3= the third dose of rotavirus vaccine.

\*  $P < .05$ ; \*\*  $P < .001$ .

health status is increasing year by year as shown in [Figure 1](#), it is still not high from enough to protect these vulnerable groups through the immunization. Because it is difficult for the vaccinator to reach this population, how to benefit more children with special health status with vaccines has become a problem that must be considered in next step.

Because an individual would be registered as vaccinated as long as one vaccine dose was administered, the actual vaccination status among children with special health status is even more pessimistic. Different from the study in USA which indicates that children with special needs have a higher vaccination coverage than children without, our study shows a significantly lower level of vaccination coverage among the children with special health status than that among the general

population in Chongqing, China.<sup>6</sup> A low vaccination coverage may increase the risk of morbidity and mortality from vaccine-preventable diseases among those children.<sup>19–21</sup> Fortunately, having benefited from a large number of expert consensus and recommendations in recent 5 years, the incidence of AEFI is very rare; the reported rate of AEFI among children with special health status is only 21.3 per 100,000 doses which is lower than that among the general population (46.5 per 100,000).<sup>22</sup> Considering that many vaccinators cannot fully comprehend the expert consensus issued previously, we advocate a well-organized multi-intervention vaccination campaign for children with special health status and their parents, in which closer monitoring of vaccination status and optimizing practice recommendations for the immunization are two

**Table 3.** Vaccination up-to-date status in the study population (n = 1,824).

variables	UTD n (%)	Health status																				
		HID			jaundice			SD			ID			CHD			premature			CD		
		N(%)	OR(95% CI)	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	N(%)	OR(95% CI) <sup>a</sup>	
BCG	1309 (71.8)	156 (78.0)	1.0	372 (78.2)	1.009(0.677– 1.504)	48 (64.0)	0.501(0.281– 0.894)**	52 (69.3)	0.638(0.352– 1.155)	463 (66.2)	0.553 (0.382– 0.801)*	83 (80.6)	1.171(0.648– 2.116)	135 (68.9)	0.624(0.398– 0.980)*							
HepB3	981(53.8)	115 (57.5)	1.0	188 (39.5)	0.482(0.345– 0.675)**	45 (60.0)	1.109(0.646– 1.903)	47 (62.7)	1.241(0.719– 2.141)	410 (58.7)	1.049(0.7637– 1.441)	57 (55.3)	0.916(0.567– 1.479)	119 (60.7)	1.142(0.765– 1.706)							
Polio3	1176 (64.5)	139 (69.8)	1.0	275 (57.8)	0.591(0.415– 0.841)*	48 (64.0)	0.767(0.438– 1.344)	50 (66.7)	0.863(0.489– 1.523)	457 (65.4)	0.815(0.580– 1.146)	69 (67.0)	0.876(0.526– 1.459)	138 (70.4)	1.027(0.667– 1.580)							
MCV	772(42.3)	94(47.2)	1.0	155 (32.6)	0.539(0.385– 0.756)**	30 (40.0)	0.745(0.434– 1.277)	36 (48.0)	1.031(0.606– 1.755)	346 (49.5)	1.095(0.799– 1.501)	40 (38.8)	0.709(0.437– 1.151)	71(36.2)	0.634(0.424– 0.949)*							
DTP3	1033 (56.7)	118 (59.3)	1.0	220 (46.2)	0.590(0.422– 0.825)**	43 (57.3)	0.922(0.539– 1.580)	48 (64.0)	1.220(0.704– 2.115)	419 (59.9)	1.027(0.745– 1.416)	61 (59.2)	0.997(0.614– 1.618)	124 (63.3)	1.182(0.788– 1.773)							
JEV	666(36.5)	90(45.0)	1.0	133 (27.9)	0.474(0.336– 0.668)**	25 (33.3)	0.611(0.351– 1.065)	28 (37.3)	0.728(0.422– 1.255)	302 (43.2)	0.930(0.678– 1.276)	31 (30.1)	0.526(0.318– 0.872)*	57(29.1)	0.501(0.331– 0.759)*							
All UTD	509(27.9)	71(35.7)	1.0	108 (22.7)	0.533(0.372– 0.765)**	17 (22.7)	0.533(0.288– 0.983)*	21 (28.0)	0.707(0.395– 1.264)	220 (31.5)	0.834(0.600– 1.162)	27 (26.2)	0.645(0.381– 1.092)	45(23.0)	0.541(0.348– 0.842)*							

CI confidence interval, N number of children, n number of children with the characteristic, OR odds ratio, UTD up to date, children were classified as up to date if they had received BCG before 4 months and the other dose of vaccines before 12 months of age.

HID history of infectious diseases, CHD congenital heart disease, SD surgical diseases, ID immunological disease and CD Chronical disease.

BCG = Bacillus Calmette-G vaccine, HepB = hepatitis B vaccine, Polio = poliovirus vaccine, DTP = diphtheria-tetanus-pertussis-containing vaccine, MCV = measles-containing vaccine, MPSV-A = Group A meningococcal polysaccharide vaccine, JEV = Japanese encephalitis vaccine, Hib = Haemophilus influenza type-b vaccine, VarV = varicella vaccine, EV71-2= the second dose of enterovirus 71 vaccine, InfV = influenza vaccine, PCV13-3 = the third dose of 13 valent pneumococcal conjugate vaccine. ROV3= the third dose of rotavirus vaccine.

a Univariate logistic regression.

b All UTD include: all the children were included if they had received all the EPI vaccines on time (BCG before 4 months, and the other dose of vaccines before 12 months of age).

\* P < .05; \*\* P < .001.

**Table 4.** Adjusted odds (CI) of vaccination factors among study population<sup>a</sup>.

	BCG	Polio3	DTP3	HepB3	MCV	EV71-2	PCV13-3	ROV-3	InfV	MPSV-A2	JEV	VarV	Hib3
<2500g	-	-	-	-	-	-	1.0	1.0	-	-	-	-	-
2500–4000g	-	-	-	-	-	-	0.635(0.473–0.853)*	0.697(0.529–0.919)*	-	-	-	-	-
>4000g	-	-	-	-	-	-	0.861(0.480–0.853)	0.942(0.529–1.679)	-	-	-	-	-
1	1.0	-	-	-	-	-	-	-	-	-	-	-	-
2	0.848(0.624–1.154)	-	-	-	-	-	-	-	-	-	-	-	-
>3	0.433(0.243–0.771)*	-	-	-	-	-	-	-	-	-	-	-	-
No	1.0	-	-	-	-	-	-	1.0	-	-	-	-	-
Yes	1.706(1.249–2.329)**	-	-	-	-	-	-	1.346(1.061–1.708)*	-	-	-	-	-
HID	-	1.0	1.0	1.0	1.0	1.0	1.0	-	1.0	1.0	1.0	1.0	1.0
Jaundice	-	0.533(0.394–0.719)*	0.537(0.398–0.724)**	0.537(0.398–0.724)**	0.535(0.396–0.722)**	0.556(0.371–0.833)**	1.133(0.724–1.773)	-	3.158(0.393–25.390)	0.597(0.418–0.852)*	0.441(0.320–0.608)*	0.797(0.423–1.501)	0.798(0.542–1.176)
SD	-	1.224(0.727–2.062)	1.287(0.776–2.135)	1.287(0.776–2.135)	1.295(0.780–2.150)	1.525(0.844–2.757)	2.669(1.431–4.980)*	-	16.279(1.872–141.581)*	1.355(0.778–2.360)	0.896(0.532–1.511)	1.255(0.469–3.359)	1.524(0.843–2.755)
ID	-	1.154(0.702–1.895)	1.345(0.826–2.189)	1.345(0.826–2.189)	1.358(0.834–2.211)	1.308(0.729–2.345)	1.141(0.565–2.306)	-	9.566(0.980–93.388)	1.456(0.838–2.533)	1.049(0.641–1.718)	2.182(0.936–5.088)	1.880(1.084–3.259)*
CHD	-	1.508(1.119–2.033)*	1.824(1.362–2.443)**	1.824(1.362–2.443)**	1.841(1.374–2.467)**	1.663(1.163–2.377)*	1.347(0.876–2.071)	-	16.692(2.292–121.561)*	2.099(1.519–2.901)**	1.603(1.195–2.151)*	3.947(2.268–6.870)**	1.613(2.311)*
Premature	-	0.893(0.569–1.400)	0.908(0.578–1.428)	0.908(0.578–1.428)	0.916(0.582–1.441)	0.378(0.184–0.777)*	0.996(0.533–1.903)	-	5.920(0.609–57.551)	0.720(0.425–1.218)	0.551(0.342–0.899)*	0.565(0.180–1.769)	1.016(0.578–1.788)
CD	-	1.274(0.872–1.863)	1.343(0.928–1.944)	1.343(0.928–1.944)	1.333(0.920–1.931)	0.776(0.477–1.262)	1.452(0.866–2.435)	-	7.557(0.902–63.331)	1.190(0.783–1.809)	0.623(0.422–0.921)*	1.376(0.661–2.864)	1.772(1.146–2.738)*

CI confidence interval, N number of children, n number of children with the characteristic, OR odds ratio.

HID history of infectious diseases, CHD congenital heart disease, SD surgical diseases, ID immunological disease and CD Chronical disease.

BCG = Bacillus Calmette-G vaccine, HepB = hepatitis B vaccine, Polio = poliovirus vaccine, DTP = diphtheria-tetanus-pertussis-containing vaccine, MCV = measles-containing vaccine, MPSV-A = Group A meningococcal polysaccharide vaccine, JEV = Japanese encephalitis vaccine, Hib = Haemophilus influenza type-b vaccine, VarV = varicella vaccine; EV71-2= the second dose of enterovirus 71 vaccine, InfV = influenza vaccine, PCV13-3 = the third dose of 13 valent pneumococcal conjugate vaccine. ROV3= the third dose of rotavirus vaccine.

a Multivariate logistic regression using the forward likelihood ratio method, \*  $P < .05$ ; \*\*  $P < .001$ .

key components. We believe that this campaign will be effective, as several other studies have shown a significant increase in vaccine uptake as a result of similar approaches.<sup>23,24</sup>

In accordance with the study, it is observed that children with CHD are better vaccinated against major vaccine-preventable diseases (VPDs), which is probably because most researches in China are devoted to promoting vaccination in this subpopulation. However, the findings suggest that the jaundice group is at higher risk of VPDs because of the low vaccination rate. This group includes four kinds of diseases: pathologic jaundice, G-6-PD, physiological jaundice and hemolytic disease of newborn. Children with a history of jaundice are less likely to be vaccinated with HepB3, MCV, DTP1,2,3, MPSV-A, JEV and all of the non-EPI vaccine, and less likely to be UTD for all the EPI vaccines except for BCG. According to the multivariate analysis, most of the jaundice children have missed vaccination (aOR = 0.441–0.556). According to the expert consensus, children with physiological jaundice and G-6-PD can actually be vaccinated safely, and only the children with pathological jaundice need to be further evaluated for vaccination by identifying the cause of the condition.<sup>25</sup> The main causes of pathological jaundice are

infection, breastfeeding, hemolysis, and metabolism, and most of them are usually not contraindications for vaccination. This study also shows that the ID group has an immunization rate equal to the HID group, which indicates that the ID children can be vaccinated safely.

Emphasis should be put on the administration of live attenuated vaccines (BCG and MCV). The UTD rate of the BCG vaccine is lower in the SD, CHD, and CD groups. This is partly due to the early contraction of the disease, which delays BCG vaccination. However, such an unnecessary delay exposes these children to risk of tuberculosis for a long time. The MCV coverage rate is only 39.7%, particularly low in the jaundice group, but the CHD group is more likely to be immunized. For the non-EPI vaccines, the coverage rate of PCV13 and ROV are significantly higher than that among the general population, but Hib, InfV, EV71 and VarV are much lower as shown in Figure 2. Same as the pneumococcal vaccination, the InfV is also strongly recommended by the advisory Committee on Immunization practices (ACIP) in the United States, the Belgian National Immunization Technical Advisory Groups (NITAG), and other public health authorities.<sup>26–28</sup>

In addition to the health status, we have also analyzed the factors associated with insufficient vaccination coverage and



found that the birth weight, parity and vaccine compensation insurance are significant determinants of immunization of certain vaccines. A higher birth weight is associated with a lower completion rate of basic immunization of PCV13 (aOR = 0.635, 95% CI: 0.473–0.853) and ROV (aOR = 0.697, 95% CI: 0.529–0.919). This can be explained by the fact that the early treatment of these diseases has caused delaying or skipping of these vaccines. In accordance with a prior study<sup>[18]</sup>, we have observed that the purchase of vaccine compensation insurance is associated with a higher completion rate of basic immunization of BCG (aOR = 1.706, 95% CI: 1.249–2.329) and ROV (aOR = 1.346, 95% CI: 1.061–1.708). Owning a vaccine compensation insurance promotes the use of live attenuated vaccines in early life, which should be actively recommended for these children.<sup>29</sup>

The strength of this study is that it assesses the vaccination coverage of recommended vaccines in a large and diverse group of children at risk. Vaccination data at individual level in at-risk groups are scarce and often not monitored.<sup>4,13,30</sup> Available studies are often limited to a particular vaccine in a certain risk group. Second, the data are collected from the official information system of Chongqing, China, which ensures that all the vaccination data are recorded, and guaranteed the accuracy and authenticity of the data. The inclusion of the non-EPI vaccine, the data of the vaccine compensation insurance, and the data on the occurrence of AEFI and death also make the analysis more comprehensive.

However, there are some limitations to this study. First, we did not consider the factors associated with vaccinators. Vaccinators may cause the children with special health status to miss vaccination, possibly because the vaccinators are unaware of vaccination recommendations for this population and hence are overly concerned about potential risks associated with vaccines.<sup>31–33</sup> Reasons for under-vaccination of special groups include the fear of adverse outcomes or illness caused by vaccines, the inconvenience (and in some scenarios, the cost) of vaccination, and the unawareness of the need for vaccination or national recommendations. The results in this paper are a comprehensive reflection of these reasons, but more surveys need to be done next to identify which one of them is more influential.

## Conclusions

Our study provides an early insight into the actual vaccination status among children with special health status in China, and the result shows that this sub-population can be safely vaccinated. However, the vaccination coverage in these huge and vulnerable group is too low to protect them from vaccine-preventable diseases through immunization. It is discovered that children with jaundice are significantly less likely to be vaccinated than children with congenital heart disease. Interventions to address this issue should focus on the purchase of vaccine compensation insurance, which is found to promote the use of live attenuated vaccines in early life. More attentions should be paid to the neglected immunization problem among the children with special health status. We also strongly encourage further research on strategies to improve vaccination for these children in order to improve the uptake of vaccine.

## Author contributions

Conceptualization, Rongsheng Luan and Qing Wang; study design, Binyue Xu and Qing Wang; data analysis, Binyue Xu, Yi Zhang, Chao Zhou; data collection, Binyue Xu; data curation, Binyue Xu; writing – original draft preparation, Binyue Xu; writing – review and editing, Yi Zhang, and Qing Wang; visualization, Binyue Xu; supervision, Binyue Xu; project administration, Binyue Xu; funding acquisition, Binyue Xu. All authors involved in the discussion of results and have read and agreed to the published version of the manuscript.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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## Availability of data and materials

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to participant's privacy concerns.

## Ethics approval and consent to participate

This is a retrospective study of medical records with all data were fully anonymized. And the study is certified by the Ethics Institutional Review Board of Chongqing Municipal Center for Disease Control and Prevention (Project No: CQCDCLS (2021)006).

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