

## Preplanned Studies

# Vaccination Coverage, Timeliness and Adverse Events Following Immunization in Children with Medical Conditions — Shandong Province, China, 2023

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## Summary

### What is already known about this topic?

Children with medical conditions who remain undervaccinated are at risk of vaccine-preventable diseases.

### What is added by this report?

In a multicenter retrospective study of 24,966 children with medical conditions, the median coverage of 10 National Immunization Program vaccines reached 97.33%, whereas timely completion was 89.21%. Children with brain, immune, or congenital disorders exhibited significantly lower vaccination coverage than those with other medical conditions. Post-diagnosis delays exceeded those before diagnosis. Overall adverse events following immunization rate was 23.7/100,000 doses administered.

### What are the implications for public health practices?

Research on the vaccination of children with brain, immune system, and congenital disorders is imperative. Integration of advanced practices will enhance the vaccination rate.

coverage for the 10 National Immunization Program vaccines was 97.33%, and the median timely completion rate was 89.21%. Children with brain, immune system, or congenital disorders had lower vaccination coverage than those with other medical conditions. Vaccination delay was greater after diagnosis of a medical condition than before. Overall 147 AEFIs were reported, corresponding to 23.7/100,000 doses administered, and 95.92% of the reports were common vaccine reactions.

**Conclusion:** Although the overall vaccination coverage was high among children with medical conditions, significant delays occurred, particularly among children with brain, immunological, or congenital disorders. The safety profile of the vaccine was acceptable. Tailored immunization strategies, carefully monitored and informed by domestic and international experiences, may help optimize vaccine protection in children with medical conditions.

## ABSTRACT

**Introduction:** Children with medical conditions are at increased risk of vaccine-preventable disease outcomes. Evaluating vaccination coverage will support tailored vaccination strategies in China.

**Methods:** This multicenter retrospective study included children from seven hospitals in three cities of Shandong Province. Subjects were 1–6-year-olds with medical conditions. Demographic and diagnostic data were obtained from hospital information systems, and vaccination and adverse events following immunization (AEFI) data were obtained from the Chinese National Immunization Information System (CNIIS).

**Results:** Among 24,966 children, the median

Vaccination coverage is an important indicator of the effectiveness of immunization programs for preventing vaccine-preventable diseases. The *Healthy Children Action Enhancement Plan (2021–2025)*, issued by China's National Health Commission states that maintaining program vaccine coverage at >90% is an objective for ensuring children's health (1). According to the Chinese National Immunization Information System (CNIIS), the overall reported coverage of program vaccines exceeded 99% in 2021 (2). However, overall coverage does not necessarily reflect the vaccination status of an important child population: children with medical conditions. Immunization programs ensure that vaccination services are provided to all children, including those with medical conditions.

Children with medical conditions may have

physiological or disease states that make them vulnerable to an increased risk of infection or more severe illness from a vaccine-preventable disease, and medical conditions can influence the safety and effectiveness of vaccination. Underimmunized children with medical conditions are at a higher risk of vaccine-preventable infections and severe outcomes than otherwise healthy children (3). China's National Health Commission issued the *Childhood Immunization Schedule for National Immunization Program Vaccines — China (Version 2021)*, which sets the standard of care for immunization and includes a section on vaccinations for children with medical conditions (4).

Previous studies on vaccination coverage in children with medical conditions in China have included specific subpopulations or small-scale studies in hospital vaccination consultation clinics. Our study focused on children with medical conditions who had been seen in any of the seven hospitals in the three cities in Shandong Province. This study aimed to describe vaccination coverage and timeliness by type of medical condition and to evaluate reported adverse events following immunization (AEFI) among children with medical conditions to provide evidence for immunization strategies for children with medical conditions in China.

We conducted a retrospective study in seven municipal hospitals in Jinan, Jining, and Weifang, Shandong Province, China. Subjects were children who met the following criteria: 1) born between 2016–2021 (age-range 1–6 years), 2) visited a participating hospital as an outpatient or inpatient, 3) had their medical history documented, and 4) had a medical condition consistent with diagnostic categories in *Childhood Immunization Schedule for National Immunization Program Vaccines — China (version 2021)*: prematurity/low birth weight, allergy, born to a mother living with human immunodeficiency virus (HIV), immune function abnormality, and other medical conditions. Demographic and diagnostic information were obtained from the information systems of the seven hospitals: date of birth, sex, medical condition, and date of diagnosis of medical condition. The vaccine type, dose number, vaccination date, and AEFI reports were extracted from the CNIIS in April 2023.

The study included 10 vaccines in China's National Immunization Program (NIP): Bacillus Calmette-Guérin (BCG), hepatitis B (HepB), poliovirus vaccine (PV), diphtheria, tetanus, and pertussis combination

vaccine (DTaP), diphtheria-tetanus (DT), measles-containing vaccine (MCV), group A meningococcal polysaccharide vaccine (MPSV-A), group A and group C meningococcal polysaccharide vaccine (MPSV-AC), Japanese encephalitis vaccine, live (JE-L), and Hepatitis A vaccine, live (HepA-L), or their substituted equivalents. Vaccination coverage was defined as the proportion of age-eligible children who received a specific vaccine at the time of data collection. Coverage compares the vaccinations children receive with the vaccinations they should receive according to the 2021 schedule. Children who had not received the corresponding dose at the time of data collection were considered unvaccinated. Timely vaccination is defined as the proportion of vaccine doses administered within the recommended age range specified in the 2021 vaccination schedule. For example, the first dose of MCV administered between 8 and 12 months is timely, whereas the first dose administered after 12 months is not timely. Vaccination rates by age group are shown in [Supplementary Table S1](#) (available at <https://weekly.chinacdc.cn/>).

Statistical analyses were performed using the SPSS software (version 21.0; IBM Corp., Armonk, NY, USA). Coverage was calculated based on age and medical conditions. The timeliness of vaccination before the diagnosis of the medical condition was compared with the timeliness after diagnosis. Data are presented as percentages for counts and as medians with interquartile ranges [M (IQR)] for non-normally distributed continuous data. AEFI incidences are per 100,000 doses administered. The Mann–Whitney U test was used to assess differences between groups for non-normal continuous data. The significance level was  $P < 0.05$ .

**Table 1** shows the characteristics of the 24,966 children with medical conditions. The median age was 4.68 years; 52% of the patients were boys. Medical conditions included hematological disorders (40.27%), organic or functional brain disorders (23.34%), allergic disorders (15.64%), prematurity/low birth weight (10.45%), immunological disorders (5.44%), and congenital disorders (3.89%).

**Table 2** shows vaccination coverage and timely vaccination by vaccine dose and year of life. Median coverage was 97.33%. The most frequently missed vaccine was MPSV-AC<sub>2</sub>, with a coverage of 61.39%, followed by DT at 70.12%. Coverage for all other vaccines exceeded 92%, and HepB<sub>1</sub> was the highest at 99.66%. Median timely coverage was 89.21%, ranging from 61.39% for MPSV-AC<sub>2</sub> to 97.79% for HepB<sub>2</sub>.

TABLE 1. Characteristics of children with medical conditions in Shandong Province, China, 2023.

| Characteristic                           | N      | Proportion (%) |
|------------------------------------------|--------|----------------|
| Age (years)                              |        |                |
| 1                                        | 668    | 2.68           |
| 2                                        | 4,159  | 16.66          |
| 3                                        | 4,617  | 18.49          |
| 4                                        | 4,596  | 18.41          |
| 5                                        | 6,010  | 24.07          |
| ≥6                                       | 4,916  | 19.69          |
| Sex                                      |        |                |
| Male                                     | 12,982 | 52.00          |
| Female                                   | 11,984 | 48.00          |
| Medical condition                        |        |                |
| Hematologic disorders                    | 10,054 | 40.27          |
| Anemia                                   | 9,881  | 39.58          |
| Leukemia                                 | 173    | 0.69           |
| Organic or functional brain disorders    | 5,827  | 23.34          |
| Seizures                                 | 2,504  | 10.03          |
| Epilepsy                                 | 1,693  | 6.78           |
| Purulent meningitis                      | 762    | 3.05           |
| Viral encephalitis                       | 371    | 1.49           |
| Incomplete brain development             | 281    | 1.13           |
| Other                                    | 216    | 0.87           |
| Allergic diseases                        | 3,904  | 15.64          |
| Allergic dermatitis                      | 2,804  | 11.23          |
| Allergic rhinitis                        | 634    | 2.54           |
| Eczema                                   | 267    | 1.07           |
| Anaphylactic reactions                   | 162    | 0.65           |
| Other                                    | 37     | 0.15           |
| Prematurity/low birth weight             | 2,609  | 10.45          |
| Prematurity                              | 2,067  | 8.28           |
| Low birth weight                         | 542    | 2.17           |
| Immunological disorders                  | 1,359  | 5.44           |
| Kawasaki disease                         | 1,000  | 4.01           |
| Allergic purpura                         | 318    | 1.27           |
| Immunodeficiency/Immunocompromised State | 41     | 0.16           |
| Congenital disorders                     | 972    | 3.89           |
| Congenital thyroid disease               | 415    | 1.66           |
| Phenylketonuria                          | 197    | 0.79           |
| Congenital heart disease                 | 185    | 0.74           |
| Methylmalonic acidemia                   | 100    | 0.40           |
| Other                                    | 75     | 0.30           |
| Other Medical Conditions                 | 241    | 0.97           |

TABLE 2. Vaccination coverage and timeliness by vaccine dose and year of life among children with medical conditions in Shandong Province, China, 2023.

| Vaccine doses        | Vaccination coverage proportion (%) / Vaccination timeliness proportion(%) |             |             |             |             |             |             |
|----------------------|----------------------------------------------------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                      | 1 year                                                                     | 2 years     | 3 years     | 4 years     | 5 years     | 6 years     | Overall     |
| BCG                  | 98.50/84.88                                                                | 99.25/89.66 | 99.31/87.42 | 99.37/91.51 | 99.22/94.61 | 99.21/95.28 | 99.25/91.76 |
| HepB <sub>1</sub>    | 99.70/56.44                                                                | 99.78/65.35 | 99.74/68.90 | 99.72/79.85 | 99.63/85.97 | 99.45/86.62 | 99.66/77.59 |
| HepB <sub>2</sub>    | 99.40/96.86                                                                | 99.59/98.27 | 99.55/96.90 | 99.50/97.65 | 99.47/98.12 | 99.31/98.07 | 99.48/97.79 |
| HepB <sub>3</sub>    | 95.81/90.12                                                                | 97.96/90.65 | 98.25/87.07 | 98.37/90.14 | 98.54/91.93 | 98.54/93.02 | 98.28/90.66 |
| PV <sub>1</sub>      | 98.95/96.41                                                                | 99.52/97.88 | 99.44/96.62 | 99.54/97.63 | 99.47/97.00 | 99.31/97.44 | 99.44/97.26 |
| PV <sub>2</sub>      | 97.75/94.61                                                                | 98.92/95.77 | 98.94/93.55 | 99.15/95.34 | 99.08/94.41 | 98.96/95.20 | 98.98/94.81 |
| PV <sub>3</sub>      | 94.76/90.87                                                                | 97.98/91.13 | 98.18/88.56 | 98.50/90.84 | 98.62/86.69 | 98.52/89.52 | 98.29/89.21 |
| PV <sub>4</sub>      | –                                                                          | –           | –           | –           | 90.42/86.46 | 94.26/89.97 | 92.15/88.04 |
| DTaP <sub>1</sub>    | 98.35/95.06                                                                | 99.30/96.87 | 99.18/94.43 | 99.15/95.91 | 99.25/96.76 | 99.10/97.05 | 99.17/96.20 |
| DTaP <sub>2</sub>    | 96.26/92.96                                                                | 98.46/93.58 | 98.61/90.82 | 98.46/90.14 | 98.84/94.04 | 98.72/94.41 | 98.57/92.69 |
| DTaP <sub>3</sub>    | 94.31/88.92                                                                | 97.62/88.43 | 97.77/83.34 | 97.89/80.90 | 98.22/88.77 | 98.29/90.17 | 97.89/86.54 |
| DTaP <sub>4</sub>    | –                                                                          | 92.04/85.86 | 94.67/84.99 | 95.39/82.64 | 95.49/79.12 | 96.64/88.04 | 94.96/83.86 |
| DT                   | –                                                                          | –           | –           | –           | –           | 70.12/70.12 | 70.12/70.12 |
| MCV <sub>1</sub>     | 96.71/92.37                                                                | 97.23/92.38 | 97.31/90.75 | 97.67/86.77 | 96.74/92.75 | 97.46/93.92 | 97.24/91.44 |
| MCV <sub>2</sub>     | –                                                                          | 93.41/90.74 | 95.28/90.99 | 96.13/89.69 | 94.98/88.85 | 96.18/92.84 | 95.23/90.55 |
| MPSV-A <sub>1</sub>  | 97.01/91.32                                                                | 97.74/90.48 | 96.90/84.56 | 96.61/87.64 | 96.61/88.92 | 96.99/87.51 | 96.94/87.92 |
| MPSV-A <sub>2</sub>  | 93.56/89.67                                                                | 95.09/89.69 | 93.70/85.51 | 93.76/87.32 | 93.71/88.25 | 94.51/89.30 | 94.10/88.06 |
| MPSV-AC <sub>1</sub> | –                                                                          | –           | –           | 93.17/91.56 | 94.68/91.11 | 95.46/90.42 | 94.48/91.03 |
| MPSV-AC <sub>2</sub> | –                                                                          | –           | –           | –           | –           | 61.39/61.39 | 61.39/61.39 |
| JE-L <sub>1</sub>    | 94.01/81.89                                                                | 96.66/81.53 | 97.29/76.18 | 97.54/78.15 | 97.90/83.58 | 97.93/81.96 | 97.42/80.51 |
| JE-L <sub>2</sub>    | –                                                                          | –           | 91.57/88.56 | 94.30/89.12 | 94.58/88.49 | 95.73/90.74 | 94.11/89.20 |
| HepA-L               | –                                                                          | 92.23/83.87 | 95.54/84.51 | 95.78/80.18 | 95.89/79.65 | 96.42/86.82 | 95.28/82.85 |

Note: “–” means that the corresponding vaccine dose is not scheduled for this age group per the NIP, and thus no vaccination coverage or timeliness was calculated.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=diphtheria-tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=group A and group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L=hepatitis A vaccine, live.

The timely administration rate for HepB<sub>1</sub> among 1-year-old group was notably low at 56.44%. For children aged 5 years, timely coverage of DTaP<sub>4</sub> was the lowest at 79.12%. In the 6-year-old group, timely vaccination rates were low: 70.12% for DT and 61.39% for MPSV-AC<sub>2</sub>.

Figure 1 shows vaccine coverage following diagnosis, stratified by medical condition. Children with brain, immunological, and congenital disorders had lower vaccination rates, particularly for vaccines recommended for older children. Vaccine doses recommended for older-age children had lower coverage than other vaccine doses. MPSV-AC<sub>2</sub> had the lowest coverage, and DT coverage was lower in children with congenital and brain disorders. Vaccines

administered early in life had higher coverage across all medical conditions.

We compared timely vaccination before vs after the diagnosis of medical conditions. Among children with hematologic diseases, brain diseases, and allergic diseases (Supplementary Tables S2–S4, available at <https://weekly.chinacdc.cn/>), patterns were similar: early doses (e.g., BCG, HepB<sub>1–2</sub>, PV<sub>1–2</sub>, DTaP<sub>1–2</sub>) were generally delayed by approximately 1–5 months. For preterm/low birth weight infants (Supplementary Table S5, available at <https://weekly.chinacdc.cn/>), there were notable delays in birth doses: BCG was delayed from birth to 1 month, and HepB<sub>1</sub> was postponed from birth to 35 days. For children with immunological diseases (Supplementary Table S6,

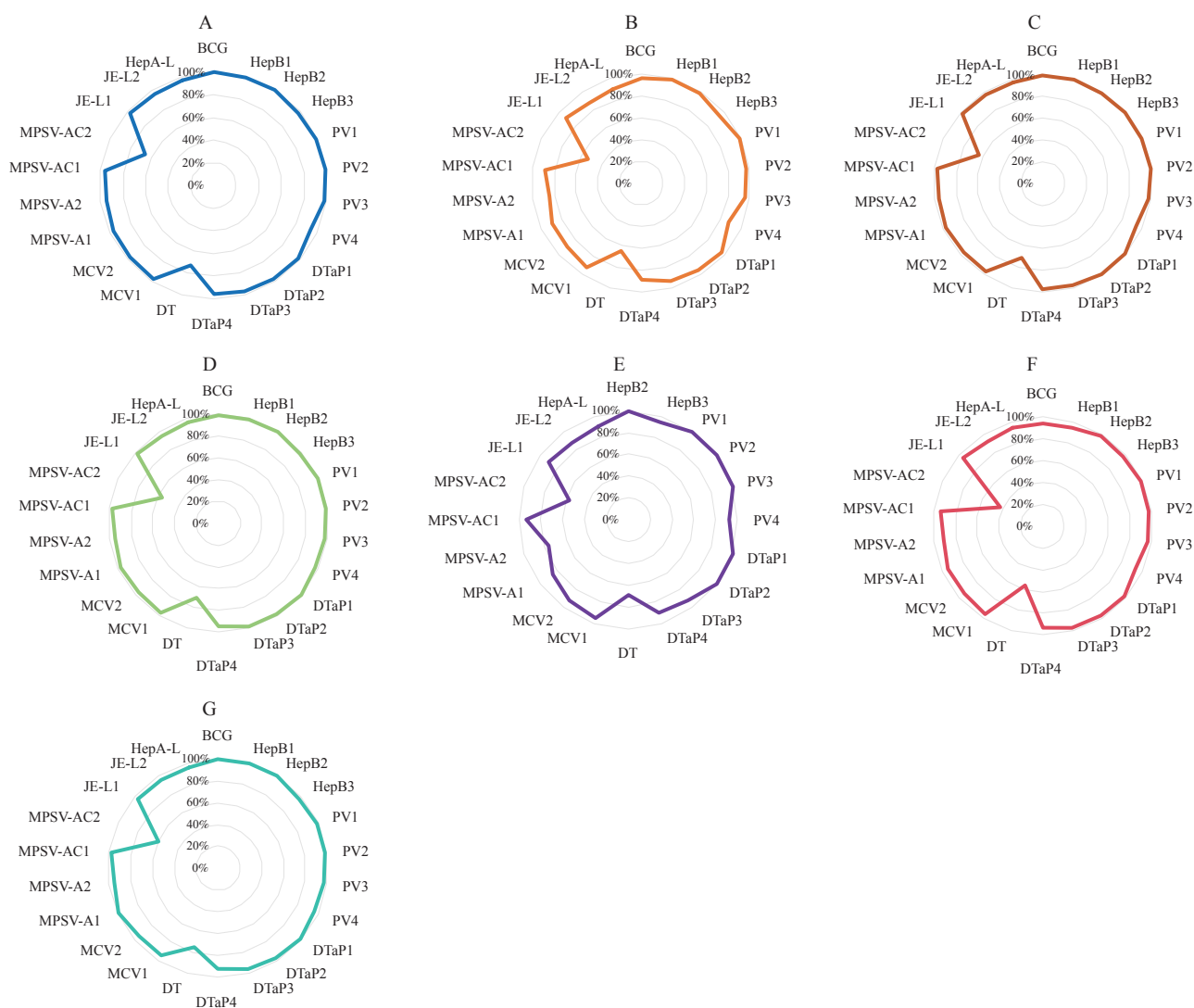


FIGURE 1. Post-medical-condition-diagnosis, disease-specific vaccination coverage (%) among children with medical conditions in Shandong Province, China, 2023. (A) hematological disorders; (B) organic or functional brain disorders; (C) allergic diseases; (D) prematurity/low birth weight; (E) immunological disorders; (F) congenital disorders; (G) other diseases. Note: Panel (E) (immunological disorders): no valid data for BCG and HepB<sub>1</sub>, as none of the enrolled subjects were diagnosed with immunological disorders prior to the primary vaccination age of these two vaccines.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=diphtheria-tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=group A and group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L=hepatitis A vaccine, live.

available at <https://weekly.chinacdc.cn/>), vaccines such as HepB<sub>3</sub>, PV<sub>1-3</sub>, and DTaP<sub>1-3</sub> were delayed to 12–17 months, while HepA-L was postponed until 24 months. Among children with congenital disorders (Supplementary Table S7, available at <https://weekly.chinacdc.cn/>), a few vaccine doses such as BCG and HepB<sub>1</sub> had significant delays.

Overall, 620,256 vaccinations in the study population and 147 AEFI cases were reported,

corresponding to 23.7 per 100,000 doses; 141 (95.92%) AEFIs reports were for common vaccine reactions; four (2.72%) were for rare vaccine reactions: two thrombocytopenic purpura, one febrile convulsion, and one epilepsy case; one coincidental event and one unclassified case were also reported. All 147 AEFIs were reported as doses administered after the diagnosis of a medical condition. The highest AEFI reporting rate was for low birth weight/preterm infants



(54.09 per 100,000 doses), followed by immunological disorders (33.47 per 100,000 doses), brain disorders (25.10 per 100,000 doses), allergic diseases (22.53 per 100,000 doses), hematologic disorders (17.18 per 100,000 doses), and congenital disorders (4.38 per 100,000 doses) ( $P < 0.001$ ).

## DISCUSSION

Our study on vaccination coverage, timeliness, and AEFI in 24,966 children with medical conditions found that the overall coverage of the 10 NIP vaccines was high at 97%. Coverage was highest for vaccines recommended for administration during infancy but was lower for vaccine doses recommended for older ages. In contrast to high overall coverage, timely vaccination was lower at 89%, and vaccination was more delayed after a medical condition was diagnosed compared with before a medical condition was diagnosed. The AEFI reporting rate for vaccines administered to children with medical conditions was 23.7 per 100,000 doses, and more than 95% of the AEFI reported in our study were common vaccine reactions. Tailored immunization strategies that are carefully monitored and informed by domestic and international research and experience may help optimize vaccine protection in children with medical conditions.

The patterns of ultimate vaccination coverage found in this special population of children in Shandong are similar to those reported in a 2023 study conducted in Shandong by Zhang et al. (5). The infant coverage levels in our study ranged from 92% to >99%, compared with 90% to >99% in the 2023 study. Among the 6-year-olds in our study, coverage was over 94% for all vaccines, except MPSV-AC<sub>2</sub> and DT, which are recommended for 6-year-olds.

Vaccines should be administered at the recommended age, or as soon as possible if the recommended age is missed (4). In contrast to the 97% coverage ultimately achieved in the study participants, the median timely vaccination rate was lower at 89%. Vaccination is delayed more after a medical condition diagnosis than before diagnosis, especially in children with organic or functional brain disorders, immunological disorders, and congenital disorders. Preterm/low-birthweight infants experience postponement of birth doses. The most pronounced delays occurred in children with immunological disorders, in whom key primary-series vaccines were deferred by over 12 months beyond the recommended

age. Children with hematological disorders, brain disorders, or allergic conditions had moderate delays. Delays in vaccination after a medical diagnosis may reflect parental or provider concerns or the presence of precautions (6–7). Our finding of an AEFI reporting rate of 23.7 per 100,000 doses compares favorably with the AEFI rate of 44.18 per 100,000 doses for vaccines administered to the general population (8). In China, immunization providers screen for contraindications and precautions, assess the health of vaccine recipients, and obtain informed consent from parents or guardians before vaccination (9).

This study had several implications. The high overall coverage of these 10 program vaccines, combined with the relatively low AEFI rate, implies that immunization providers are doing a good job vaccinating children with medical conditions and are using good immunization practices to screen for contraindications and precautions. Additional research is needed to determine vaccine- and medical-condition-specific reasons for delays in vaccination and to develop tailored immunization strategies to safely minimize delays. Evidence-based condition-specific vaccination guidelines can provide immunization providers confidence in their vaccination practices to protect children with medical conditions from vaccine-preventable diseases (10).

Our study has some limitations. First, the selection of participants was limited to three cities in Shandong Province, which limits representativeness. Second, only children with medical conditions were included in the study without external concurrent healthy controls. We compared the vaccinations this special population received with the vaccinations they should receive according to the schedule, and we compared the timeliness of vaccination in a self-controlled manner to show the association between medical condition diagnosis and vaccination delay. Future studies on the factors associated with delays due to medical conditions will likely require concurrent external control groups. Third, the study data were sourced from registry data, and the reasons for delayed or omitted vaccinations were not captured. Fourth, AEFI data are from passive reports, which underestimate AEFI incidence and are influenced by reporting behavior.

In conclusion, although children with medical conditions ultimately achieved high vaccination coverage, significant delays occurred, especially among children with brain, immunological, or congenital disorders, and for doses scheduled for older ages. The

safety profile of the NIP vaccines in children under medical conditions was acceptable. Tailored immunization strategies, carefully monitored and informed by domestic and international experiences, may help optimize vaccine protection in children with medical conditions.

**Conflicts of interest:** No conflicts of interest.

**Ethical statement:** Approved by the Institutional Ethics Committee of the Chinese Center for Disease Control and Prevention. The requirement for individual informed consent was waived for this retrospective study that used registry data. (approval number 202207).

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## SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Chinese childhood immunization schedule with minimum and recommended upper vaccination ages and study age groups.

| Vaccine | Dose | Minimum age to administer per schedule | Recommended upper age range to administer per schedule | Age Group of Participants |         |         |         |         |         |
|---------|------|----------------------------------------|--------------------------------------------------------|---------------------------|---------|---------|---------|---------|---------|
|         |      |                                        |                                                        | 1 year                    | 2 years | 3 years | 4 years | 5 years | 6 years |
| BCG     | 1    | Birth                                  | 3 months                                               | √                         | √       | √       | √       | √       | √       |
| HepB    | 1    | Birth                                  | 24 hours of birth                                      | √                         | √       | √       | √       | √       | √       |
|         | 2    | 1 month                                | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 3    | 6 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
| PV      | 1    | 2 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 2    | 3 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 3    | 4 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 4    | 4 years                                | 5 years                                                | ×                         | ×       | ×       | ×       | √       | √       |
| DTaP    | 1    | 3 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 2    | 4 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 3    | 5 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 4    | 18 months                              | 24 months                                              | ×                         | √       | √       | √       | √       | √       |
| DT      | 1    | 6 years                                | 7 years                                                | ×                         | ×       | ×       | ×       | ×       | √       |
| MCV     | 1    | 8 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 2    | 18 months                              | 24 months                                              | ×                         | √       | √       | √       | √       | √       |
| MPSV-A  | 1    | 6 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 2    | 9 months                               | 18 months                                              | √                         | √       | √       | √       | √       | √       |
| MPSV-AC | 1    | 3 years                                | 4 years                                                | ×                         | ×       | ×       | √       | √       | √       |
|         | 2    | 6 years                                | 7 years                                                | ×                         | ×       | ×       | ×       | ×       | √       |
| JE-L    | 1    | 8 months                               | 12 months                                              | √                         | √       | √       | √       | √       | √       |
|         | 2    | 2 years                                | 3 years                                                | ×                         | ×       | √       | √       | √       | √       |
| HepA-L  | 1    | 18 months                              | 24 months                                              | ×                         | √       | √       | √       | √       | √       |

Note: √ Coverage assessed in this study; × Not Applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB=hepatitis B vaccine; PV=poliovirus vaccine; DTaP=diphtheria, tetanus, and pertussis combination vaccine; DT=diphtheria-tetanus vaccine; MCV=measles-containing vaccine; MPSV-A=group A meningococcal polysaccharide vaccine; MPSV-AC=group A and group C meningococcal polysaccharide vaccine; JE-L=Japanese encephalitis vaccine, live; HepA-L=hepatitis A vaccine, live.



SUPPLEMENTARY TABLE S2. Vaccination time before and after diagnosis in children with hematological disorders.

| Vaccine doses        | Before diagnosis       |                           | After diagnosis        |                           | Mann-Whitney U test | P      |
|----------------------|------------------------|---------------------------|------------------------|---------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time M (IQR)* | Number of vaccinations | Vaccination time M (IQR)* |                     |        |
| BCG                  | 8,853                  | 0 (0–0)                   | 1,123                  | 3 (2–5)                   | –70.762             | <0.001 |
| HepB <sub>1</sub>    | 8,937                  | 0 (0–1)                   | 1,072                  | 110 (73–164)              | –55.457             | <0.001 |
| HepB <sub>2</sub>    | 8,289                  | 1 (1–1)                   | 1,707                  | 4 (2–6)                   | –60.532             | <0.001 |
| HepB <sub>3</sub>    | 5,820                  | 6 (6–7)                   | 4,097                  | 8 (6–10)                  | –45.384             | <0.001 |
| PV <sub>1</sub>      | 7,868                  | 2 (2–2)                   | 2,136                  | 4 (2–6)                   | –40.553             | <0.001 |
| PV <sub>2</sub>      | 7,275                  | 3 (3–4)                   | 2,694                  | 5 (4–9)                   | –42.479             | <0.001 |
| PV <sub>3</sub>      | 6,365                  | 5 (4–6)                   | 3,550                  | 8 (5–11)                  | –47.684             | <0.001 |
| PV <sub>4</sub>      | 126                    | 4 (4–4)                   | 4,130                  | 4 (4–4)                   | –4.306              | <0.001 |
| DTaP <sub>1</sub>    | 7,578                  | 3 (3–3)                   | 2,403                  | 4 (3–7)                   | –37.738             | <0.001 |
| DTaP <sub>2</sub>    | 6,929                  | 4 (4–5)                   | 3,006                  | 6 (5–9)                   | –41.859             | <0.001 |
| DTaP <sub>3</sub>    | 5,936                  | 6 (5–7)                   | 3,940                  | 8 (6–12)                  | –46.524             | <0.001 |
| DTaP <sub>4</sub>    | 827                    | 18 (18–19)                | 8,642                  | 19 (18–20)                | –7.091              | <0.001 |
| DT                   | 5                      | 6 (6–6)                   | 1,523                  | 6 (6–6)                   | –                   | –      |
| MCV <sub>1</sub>     | 4,801                  | 8 (8–8)                   | 5,043                  | 8 (8–9)                   | –17.107             | <0.001 |
| MCV <sub>2</sub>     | 905                    | 18 (18–18)                | 8,587                  | 18 (18–19)                | –3.962              | <0.001 |
| MPSV-A <sub>1</sub>  | 5,454                  | 6 (6–7)                   | 4,379                  | 7 (6–10)                  | –31.585             | <0.001 |
| MPSV-A <sub>2</sub>  | 2,960                  | 10 (9–11)                 | 6,651                  | 11 (10–13)                | –28.901             | <0.001 |
| MPSV-AC <sub>1</sub> | 279                    | 3 (3–3)                   | 5,827                  | 3 (3–3)                   | –1.929              | 0.054  |
| MPSV-AC <sub>2</sub> | 5                      | 6 (6–6)                   | 1,391                  | 6 (6–6)                   | –                   | –      |
| JE-L <sub>1</sub>    | 3,874                  | 9 (8–10)                  | 5,982                  | 10 (9–11)                 | –27.443             | <0.001 |
| JE-L <sub>2</sub>    | 524                    | 2 (2–2)                   | 7,211                  | 2 (2–2)                   | –2.383              | 0.017  |
| HepA-L               | 774                    | 19 (19–20)                | 8,719                  | 20 (19–21)                | –5.204              | <0.001 |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L=Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.

SUPPLEMENTARY TABLE S3. Vaccination time before and after diagnosis in children with organic or functional brain disorders.

| Vaccine doses        | Before diagnosis       |                           | After diagnosis        |                           | Mann-Whitney U test | P      |
|----------------------|------------------------|---------------------------|------------------------|---------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time M (IQR)* | Number of vaccinations | Vaccination time M (IQR)* |                     |        |
| BCG                  | 5,659                  | 0 (0–0)                   | 132                    | 3 (1–8)                   | –32.955             | <0.001 |
| HepB <sub>1</sub>    | 5,706                  | 0 (0–1)                   | 106                    | 97 (45–246)               | –18.502             | <0.001 |
| HepB <sub>2</sub>    | 5,172                  | 1 (1–1)                   | 623                    | 2 (1–5)                   | –29.854             | <0.001 |
| HepB <sub>3</sub>    | 4,314                  | 6 (6–7)                   | 1,349                  | 7 (6–10)                  | –19.799             | <0.001 |
| PV <sub>1</sub>      | 4,882                  | 2 (2–3)                   | 898                    | 3 (2–6)                   | –23.725             | <0.001 |
| PV <sub>2</sub>      | 4,657                  | 3 (3–4)                   | 1,079                  | 5 (3–8)                   | –23.542             | <0.001 |
| PV <sub>3</sub>      | 4,410                  | 5 (4–6)                   | 1,265                  | 7 (5–12)                  | –24.392             | <0.001 |
| PV <sub>4</sub>      | 457                    | 4 (4–4)                   | 2,010                  | 4 (4–4)                   | –10.422             | <0.001 |
| DTaP <sub>1</sub>    | 4,722                  | 3 (3–3)                   | 1,025                  | 4 (3–7)                   | –24.033             | <0.001 |
| DTaP <sub>2</sub>    | 4,523                  | 4 (4–5)                   | 1,163                  | 5 (4–10)                  | –23.834             | <0.001 |
| DTaP <sub>3</sub>    | 4,283                  | 6 (5–7)                   | 1,347                  | 8 (6–13)                  | –23.800             | <0.001 |
| DTaP <sub>4</sub>    | 2,558                  | 19 (18–20)                | 2,721                  | 20 (18–23)                | –16.353             | <0.001 |
| DT                   | 11                     | 6 (6–6)                   | 770                    | 6 (6–6)                   | –                   | –      |
| MCV <sub>1</sub>     | 4,110                  | 8 (8–8)                   | 1,467                  | 8 (8–9)                   | –13.858             | <0.001 |
| MCV <sub>2</sub>     | 2,736                  | 18 (18–18)                | 2,585                  | 18 (18–20)                | –15.803             | <0.001 |
| MPSV-A <sub>1</sub>  | 4,201                  | 7 (6–8)                   | 1,310                  | 8 (6–11)                  | –16.500             | <0.001 |
| MPSV-A <sub>2</sub>  | 3,683                  | 10 (10–12)                | 1,593                  | 12 (10–15)                | –18.271             | <0.001 |
| MPSV-AC <sub>1</sub> | 1,028                  | 3 (3–3)                   | 2,605                  | 3 (3–3)                   | –5.426              | <0.001 |
| MPSV-AC <sub>2</sub> | 11                     | 6 (6–6)                   | 631                    | 6 (6–6)                   | –                   | –      |
| JE-L <sub>1</sub>    | 3,945                  | 9 (9–10)                  | 1,611                  | 10 (9–14)                 | –18.137             | <0.001 |
| JE-L <sub>2</sub>    | 1,846                  | 2 (2–2)                   | 2,771                  | 2 (2–2)                   | –11.871             | <0.001 |
| HepA-L               | 2,486                  | 19 (19–21)                | 2,837                  | 20 (19–23)                | –12.625             | <0.001 |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L= Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.

SUPPLEMENTARY TABLE S4. Vaccination time before and after diagnosis in children with allergic diseases.

| Vaccine doses        | Before diagnosis       |                              | After diagnosis        |                              | Mann-Whitney U test | P      |
|----------------------|------------------------|------------------------------|------------------------|------------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time<br>M (IQR)* | Number of vaccinations | Vaccination time<br>M (IQR)* |                     |        |
| BCG                  | 3,864                  | 0 (0–0)                      | 19                     | 6 (1–18)                     | –                   | –      |
| HepB <sub>1</sub>    | 3,876                  | 0 (0–1)                      | 16                     | 220 (101–520)                | –                   | –      |
| HepB <sub>2</sub>    | 3,710                  | 1 (1–1)                      | 181                    | 1 (1–3)                      | –12.320             | <0.001 |
| HepB <sub>3</sub>    | 3,069                  | 6 (6–7)                      | 809                    | 6 (6–8)                      | –7.608              | <0.001 |
| PV <sub>1</sub>      | 3,551                  | 2 (2–2)                      | 339                    | 2 (2–4)                      | –8.170              | <0.001 |
| PV <sub>2</sub>      | 3,392                  | 3 (3–4)                      | 494                    | 4 (3–6)                      | –8.999              | <0.001 |
| PV <sub>3</sub>      | 3,168                  | 5 (4–6)                      | 705                    | 6 (5–9)                      | –13.270             | <0.001 |
| PV <sub>4</sub>      | 462                    | 4 (4–4)                      | 1,532                  | 4 (4–4)                      | –5.338              | <0.001 |
| DTaP <sub>1</sub>    | 3,460                  | 3 (3–3)                      | 432                    | 3 (3–4)                      | –7.200              | <0.001 |
| DTaP <sub>2</sub>    | 3,282                  | 4 (4–5)                      | 600                    | 5 (4–7)                      | –8.494              | <0.001 |
| DTaP <sub>3</sub>    | 3,040                  | 6 (5–7)                      | 832                    | 7 (5–10)                     | –11.827             | <0.001 |
| DTaP <sub>4</sub>    | 1,779                  | 19 (18–20)                   | 1,994                  | 19 (18–20)                   | –4.704              | <0.001 |
| DT                   | 19                     | 6 (6–6)                      | 682                    | 6 (6–6)                      | –                   | –      |
| MCV <sub>1</sub>     | 2,800                  | 8 (8–8)                      | 1,021                  | 8 (8–8)                      | –3.596              | <0.001 |
| MCV <sub>2</sub>     | 1,840                  | 18 (18–18)                   | 1,896                  | 18 (18–19)                   | –4.442              | <0.001 |
| MPSV-A <sub>1</sub>  | 2,960                  | 7 (6–7)                      | 889                    | 7 (6–9)                      | –11.746             | <0.001 |
| MPSV-A <sub>2</sub>  | 2,466                  | 10 (10–12)                   | 1,328                  | 11 (10–13)                   | –10.714             | <0.001 |
| MPSV-AC <sub>1</sub> | 888                    | 3 (3–3)                      | 1,889                  | 3 (3–3)                      | –3.131              | 0.002  |
| MPSV-AC <sub>2</sub> | 15                     | 6 (6–6)                      | 618                    | 6 (6–6)                      | –                   | –      |
| JE-L <sub>1</sub>    | 2,645                  | 9 (9–10)                     | 1,223                  | 9 (9–11)                     | –11.276             | <0.001 |
| JE-L <sub>2</sub>    | 1,345                  | 2 (2–2)                      | 1,967                  | 2 (2–2)                      | –5.927              | <0.001 |
| HepA-L               | 1,729                  | 19 (19–21)                   | 2,036                  | 20 (19–21)                   | –5.650              | <0.001 |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L= Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.

SUPPLEMENTARY TABLE S5. Vaccination time before and after diagnosis in children with premature birth or low birth weight.

| Vaccine doses        | Before diagnosis       |                           | After diagnosis        |                           | Mann-Whitney U test | P      |
|----------------------|------------------------|---------------------------|------------------------|---------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time M (IQR)* | Number of vaccinations | Vaccination time M (IQR)* |                     |        |
| BCG                  | 85                     | 0 (0–0)                   | 2,487                  | 1 (1–3)                   | –12.348             | <0.001 |
| HepB <sub>1</sub>    | 183                    | 0 (0–0)                   | 2,419                  | 35 (8–68)                 | –21.659             | <0.001 |
| HepB <sub>2</sub>    | –                      | –                         | 2,572                  | 2 (1–4)                   | –                   | –      |
| HepB <sub>3</sub>    | –                      | –                         | 2,536                  | 7 (6–9)                   | –                   | –      |
| PV <sub>1</sub>      | –                      | –                         | 2,573                  | 3 (2–4)                   | –                   | –      |
| PV <sub>2</sub>      | –                      | –                         | 2,557                  | 4 (3–6)                   | –                   | –      |
| PV <sub>3</sub>      | –                      | –                         | 2,536                  | 6 (4–8)                   | –                   | –      |
| PV <sub>4</sub>      | –                      | –                         | 192                    | 4 (4–4)                   | –                   | –      |
| DTaP <sub>1</sub>    | –                      | –                         | 2,570                  | 3 (3–5)                   | –                   | –      |
| DTaP <sub>2</sub>    | –                      | –                         | 2,552                  | 5 (4–7)                   | –                   | –      |
| DTaP <sub>3</sub>    | –                      | –                         | 2,535                  | 6 (5–9)                   | –                   | –      |
| DTaP <sub>4</sub>    | –                      | –                         | 2,158                  | 19 (18–20)                | –                   | –      |
| DT                   | –                      | –                         | 79                     | 6 (6–6)                   | –                   | –      |
| MCV <sub>1</sub>     | –                      | –                         | 2,523                  | 8 (8–9)                   | –                   | –      |
| MCV <sub>2</sub>     | –                      | –                         | 2,176                  | 18 (18–19)                | –                   | –      |
| MPSV-A <sub>1</sub>  | –                      | –                         | 2,531                  | 7 (6–9)                   | –                   | –      |
| MPSV-A <sub>2</sub>  | –                      | –                         | 2,462                  | 11 (9–13)                 | –                   | –      |
| MPSV-AC <sub>1</sub> | –                      | –                         | 473                    | 3 (3–3)                   | –                   | –      |
| MPSV-AC <sub>2</sub> | –                      | –                         | 63                     | 6 (6–6)                   | –                   | –      |
| JE-L <sub>1</sub>    | –                      | –                         | 2,531                  | 9 (9–11)                  | –                   | –      |
| JE-L <sub>2</sub>    | –                      | –                         | 1,278                  | 2 (2–2)                   | –                   | –      |
| HepA-L               | –                      | –                         | 2,181                  | 19 (19–21)                | –                   | –      |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L=Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.

SUPPLEMENTARY TABLE S6. Vaccination time before and after diagnosis in children with immunological disorders.

| Vaccine doses        | Before diagnosis       |                              | After diagnosis        |                              | Mann-Whitney U test | P      |
|----------------------|------------------------|------------------------------|------------------------|------------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time<br>M (IQR)* | Number of vaccinations | Vaccination time<br>M (IQR)* |                     |        |
| BCG                  | 1,353                  | 0 (0–0)                      | 3                      | –                            | –                   | –      |
| HepB <sub>1</sub>    | 1,355                  | 0 (0–0)                      | 2                      | –                            | –                   | –      |
| HepB <sub>2</sub>    | 1,345                  | 1 (1–1)                      | 10                     | –                            | –                   | –      |
| HepB <sub>3</sub>    | 1,210                  | 6 (6–7)                      | 132                    | 13 (9–19)                    | –17.158             | <0.001 |
| PV <sub>1</sub>      | 1,328                  | 2 (2–2)                      | 28                     | 14 (8–17)                    | –11.029             | <0.001 |
| PV <sub>2</sub>      | 1,295                  | 3 (3–4)                      | 58                     | 14 (8–20)                    | –12.665             | <0.001 |
| PV <sub>3</sub>      | 1,230                  | 5 (4–6)                      | 115                    | 17 (11–25)                   | –16.693             | <0.001 |
| PV <sub>4</sub>      | 241                    | 4 (4–4)                      | 449                    | 4 (4–4)                      | –5.500              | <0.001 |
| DTaP <sub>1</sub>    | 1,303                  | 3 (3–3)                      | 50                     | 12 (7–17)                    | –13.434             | <0.001 |
| DTaP <sub>2</sub>    | 1,256                  | 4 (4–5)                      | 91                     | 15 (11–21)                   | –16.164             | <0.001 |
| DTaP <sub>3</sub>    | 1,202                  | 6 (5–7)                      | 133                    | 16 (12–23)                   | –17.392             | <0.001 |
| DTaP <sub>4</sub>    | 802                    | 19 (18–20)                   | 467                    | 23 (19–29)                   | –15.784             | <0.001 |
| DT                   | 4                      | –                            | 232                    | 6 (6–6)                      | –                   | –      |
| MCV <sub>1</sub>     | 1,152                  | 8 (8–8)                      | 181                    | 15 (10–19)                   | –20.048             | <0.001 |
| MCV <sub>2</sub>     | 845                    | 18 (18–19)                   | 442                    | 21 (18–27)                   | –16.648             | <0.001 |
| MPSV-A <sub>1</sub>  | 1,178                  | 7 (6–8)                      | 133                    | 14 (11–18)                   | –16.013             | <0.001 |
| MPSV-A <sub>2</sub>  | 1,035                  | 10 (10–12)                   | 201                    | 18 (14–21)                   | –17.386             | <0.001 |
| MPSV-AC <sub>1</sub> | 452                    | 3 (3–3)                      | 526                    | 3 (3–3)                      | –3.092              | <0.001 |
| MPSV-AC <sub>2</sub> | 4                      | –                            | 186                    | 6 (6–6)                      | –                   | –      |
| JE-L <sub>1</sub>    | 1,107                  | 9 (9–10)                     | 218                    | 17 (13–24)                   | –19.326             | <0.001 |
| JE-L <sub>2</sub>    | 663                    | 2 (2–2)                      | 456                    | 2 (2–2)                      | –11.332             | <0.001 |
| HepA-L               | 780                    | 19 (19–21)                   | 479                    | 24 (20–30)                   | –15.951             | <0.001 |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L=Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.

SUPPLEMENTARY TABLE S7. Vaccination time before and after diagnosis in children with congenital disorders.

| Vaccine Doses        | Before diagnosis       |                              | After diagnosis        |                              | Mann-Whitney U test | P      |
|----------------------|------------------------|------------------------------|------------------------|------------------------------|---------------------|--------|
|                      | Number of vaccinations | Vaccination time<br>M (IQR)* | Number of vaccinations | Vaccination time<br>M (IQR)* |                     |        |
| BCG                  | 888                    | 0 (0–0)                      | 76                     | 2 (1–5)                      | –23.070             | <0.001 |
| HepB <sub>1</sub>    | 911                    | 0 (0–0)                      | 57                     | 81 (41–256)                  | –13.200             | <0.001 |
| HepB <sub>2</sub>    | 450                    | 1 (1–2)                      | 513                    | 1 (1–3)                      | –6.074              | <0.001 |
| HepB <sub>3</sub>    | 256                    | 6 (6–7)                      | 687                    | 6 (6–8)                      | –2.147              | 0.032  |
| PV <sub>1</sub>      | 376                    | 2 (2–3)                      | 586                    | 2 (2–4)                      | –3.098              | <0.001 |
| PV <sub>2</sub>      | 316                    | 3 (3–5)                      | 636                    | 4 (3–6)                      | –2.648              | 0.008  |
| PV <sub>3</sub>      | 268                    | 5 (4–8)                      | 669                    | 5 (4–9)                      | –0.928              | 0.053  |
| PV <sub>4</sub>      | 23                     | –                            | 323                    | 4 (4–4)                      | –                   | –      |
| DTaP <sub>1</sub>    | 334                    | 3 (3–4)                      | 622                    | 3 (3–5)                      | –2.426              | 0.015  |
| DTaP <sub>2</sub>    | 288                    | 4 (4–6)                      | 659                    | 5 (4–7)                      | –1.959              | 0.050  |
| DTaP <sub>3</sub>    | 255                    | 6 (5–8)                      | 680                    | 6 (5–10)                     | –1.813              | 0.070  |
| DTaP <sub>4</sub>    | 134                    | 19 (18–21)                   | 753                    | 19 (18–21)                   | –1.797              | 0.072  |
| DT                   | 0                      | –                            | 67                     | 6 (6–6)                      | –                   | –      |
| MCV <sub>1</sub>     | 231                    | 8 (8–8)                      | 700                    | 8 (8–9)                      | –1.156              | 0.244  |
| MCV <sub>2</sub>     | 148                    | 18 (18–19)                   | 743                    | 18 (18–19)                   | –0.576              | 0.570  |
| MPSV-A <sub>1</sub>  | 235                    | 7 (6–9)                      | 675                    | 7 (6–9)                      | –0.032              | 0.974  |
| MPSV-A <sub>2</sub>  | 194                    | 11 (10–13)                   | 675                    | 11 (10–13)                   | –0.299              | 0.765  |
| MPSV-AC <sub>1</sub> | 54                     | 3 (3–3)                      | 481                    | 3 (3–3)                      | –1.540              | 0.123  |
| MPSV-AC <sub>2</sub> | 0                      | –                            | 51                     | 6 (6–6)                      | –                   | –      |
| JE-L <sub>1</sub>    | 223                    | 9 (9–11)                     | 708                    | 9 (9–11)                     | –0.747              | 0.455  |
| JE-L <sub>2</sub>    | 102                    | 2 (2–2)                      | 595                    | 2 (2–2)                      | –1.644              | 0.100  |
| HepA-L               | 134                    | 20 (19–22)                   | 757                    | 19 (19–22)                   | –1.829              | 0.067  |

Note: “–” means no enrolled subjects with a diagnosis occurring prior to the primary vaccination age, or that the Mann-Whitney U test was not applicable.

Abbreviation: BCG=Bacillus Calmette-Guérin vaccine; HepB<sub>1</sub>/HepB<sub>2</sub>/HepB<sub>3</sub>=Hepatitis B vaccine (1st/2nd/3rd dose); PV<sub>1</sub>/PV<sub>2</sub>/PV<sub>3</sub>/PV<sub>4</sub>=Poliovirus vaccine (1st/2nd/3rd/4th dose); DTaP<sub>1</sub>/DTaP<sub>2</sub>/DTaP<sub>3</sub>/DTaP<sub>4</sub>=Diphtheria, tetanus, and pertussis combination vaccine (1st/2nd/3rd/4th dose); DT=Diphtheria-Tetanus vaccine; MCV<sub>1</sub>/MCV<sub>2</sub>=Measles-containing vaccine (1st/2nd dose); MPSV-A<sub>1</sub>/MPSV-A<sub>2</sub>=Group A meningococcal polysaccharide vaccine (1st/2nd dose); MPSV-AC<sub>1</sub>/MPSV-AC<sub>2</sub>=Group A and Group C meningococcal polysaccharide vaccine (1st/2nd dose); JE-L<sub>1</sub>/JE-L<sub>2</sub>=Japanese encephalitis vaccine, live (1st/2nd dose); HepA-L= Hepatitis A vaccine, live.

\* HepB<sub>1</sub> is measured in days; PV<sub>4</sub>, DT, JE-L<sub>2</sub>, MPSV-AC<sub>1</sub>, and MPSV-AC<sub>2</sub> are measured in years; all other vaccine doses are measured in months.