Factors associated with and screening models of national immunization programme vaccine series completion among preschool children in Fujian Province, south-eastern China

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ABSTRACT

Background: An effective method for the rapid identification of vulnerable preschool children at risk of not completing the national immunization programme (NIP) vaccine series in China is still lacking.
Methods: A cross-sectional study involving 772 preschool children born between September 1 2009 and August 31, 2011 was conducted in 2015 in Fujian Province, south-eastern China. The data were collected by face-to-face interviews with the parents or guardians of the children using a standard questionnaire.
Results: Children who received the first dose of a hepatitis B vaccine (HepB) less than 24 h after birth and those who received one or more doses of surrogate for-fee vaccines (SFVs) were more likely to complete the NIP vaccine series with adjusted odds ratios (ORs) of 3.12 (95% confidence interval [CI]: 1.19–8.23) and 4.74 (1.41–15.90), respectively. The cut-off value of the prediction score for the completion of the NIP vaccine series was 92.5%, and the sensitivity, specificity, and positive and negative predictive values were 87.5%, 47.1%, 11.4% and 98.0%, respectively.
Conclusions: The receipt of a timely first dose of HepB and one or more doses of SFVs were associated with and good predictors of NIP vaccine series completion by preschool children in Fujian, China.

Introduction

China has expanded the national immunization programme (NIP) since 2008, resulting in the inclusion of 11 vaccines series (22 doses) preventing 12 infectious diseases in children [1]. To improve the coverage of the NIP vaccine series, many measures and policies, such as the routine coverage surveillance system [2,3], the free-vaccine policy [4–6], and supplementary immunization activities [7–9], have been undertaken and have been shown to be successful. However, there are still some factors that prevent vulnerable children from finishing the NIP vaccine series.

Under the current immunization service model, most parents or guardians take their children to be vaccinated with the NIP vaccines at township level hospitals according to the NIP vaccine schedule. The most substantial problems with child vaccination are that the vaccine providers have no way to identify target children (e.g.,

migrant children) and there is a lack of active and effective vaccination reminders for target children, leading to the completion of the NIP vaccine series to a large extent relying on parental awareness and family economics [10,11]. We previously found that children who received surrogate for-fee vaccines (SFVs, refers to vaccines that should be paid for but can be replaced by the corresponding free NIP vaccines, e.g., the inactivated polio vaccine is an SFV and can be a substituted for the oral live attenuated polio vaccine) or who are administered their first dose of hepatitis B vaccine in a timely manner and whose parents have higher education levels were more likely to complete the NIP vaccine series [12–14]. However, some limitations existed in these studies. First, no confounders were controlled for in probing the association between the timely initiation of the first dose of the hepatitis B vaccine and the completion of the NIP vaccines series, which might exaggerate the impact of the timely administration of the first dose of the hepatitis B vaccine on the completion of the NIP vaccine series [13]. Second, school children and those about to enter school were studied together, which might have neutralized the impact of checking the immunization card at admission on the NIP vaccine series completion rates [12,14].

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Fig. 1. Location of Fujian in China.

According to the NIP vaccine schedule, 19 doses of the 10 NIP vaccines should be finished before the enrolment in school of children ≥3 years old, of which 17 doses of 9 NIP vaccines should be completed before the age of 2 years [15]. Admission checks of immunization cards has been proven to be an effective method of helping school children to obtain their missing vaccines [12]. However, an effective predictive model is still lacking to screen for vulnerable children, such as children not yet in school, especially those ≤2 years old who should have already completed most of the doses and vaccines (89.5% of the doses and 90% of vaccines should be finished before their enrolment in school).

Early screening for vulnerable children such as those not yet in school to administer their missing vaccines is important so they receive prophylaxis against diseases protected against by the NIP vaccines, preventing potential epidemics. We therefore conducted a cross-sectional study of children not yet in school to evaluate the factors influencing the completion of the NIP vaccine series and to construct a model with those influential factors to predict the completion of the NIP vaccine series in Fujian, China.

Subjects and methods

Survey design and data collection

The study was a part of a cross-sectional survey investigating the coverage of the NIP vaccine series at the township level in Fujian, China. Fujian is located on the southeast coast of China on the west side of the Taiwan Strait and has an area of 124 thousand square kilometres and a population of approximately 39 million. The province is divided into 10 cities, 88 counties, and 1058 towns (Fig. 1).

Details of the design and methods are described elsewhere [12]. Briefly, a township with a population less than 10,000 was merged with a neighbouring township to ensure an adequate sample size for the selection of children. Thirty-four townships were randomly selected from a total of the 1004 combined townships. The village where the township government was located and another four random villages were selected as investigation units. A list of children by home address number was enumerated in each survey unit, from which children were randomly recruited by lot quality assurance sampling. At least 42 children (10 in the village where the government was located and 8 in each of the other 4 villages) were sampled in each township to detect whether coverage with each of the NIP vaccines had reached 90% at the township level according to the inequality formula, where the significance level was set to 0.05, and the maximum number of unvaccinated children allowed was one [16,17].

A face to face interview with the parent or guardian was performed after obtaining their verbal consent. The basic data regarding the children, including residential area, gender, ethnicity, birthdate, birthplace and the parents' education levels, were collected. The children's vaccination histories were extracted from the vaccination certificates kept by the parents or from vaccination cards kept in the immunization clinic, when the vaccination certificate was missing. Children were considered unvaccinated if both the vaccination certificate and vaccination card were absent. Children less than 3 years old (born from September 1, 2010, to August 31, 2011) were included in this study.

Outcome and variable definition

Completion of the NIP vaccine series was defined as finishing the NIP vaccine series with the correct/appropriate intervals for different vaccines and/or doses. The NIP vaccine series for preschool children included 1 dose of bacillus Calmette-Guerin vaccine (BCG), 3 doses of hepatitis B vaccine (HepB), 3 doses of oral live attenuated polio vaccine (OPV), 4 doses of acellular pertussis diphtheria tetanus vaccine (DTaP), 2 doses of measles-containing vaccine (MV), 2 doses of group A meningococcal polysaccharide vaccine (MPSV-A), 1 dose of live attenuated hepatitis A vaccine (HepA), and the first dose of attenuated Japanese encephalitis vaccine (JEV) [12].

We derived new variables, namely, the timely initiation of the first dose of HepB and receipt of SFVs, from the time at which the child received their first dose of HepB and from their history of SFV immunizations, respectively. The timely initiation of the first dose of HepB was defined as the administration of the first dose of HepB within 24 h after the birth of a neonate [18]. Receipt of SFVs was defined as the administration of one or more doses of SFVs.

Table 1
Completion rates of NIP vaccine series by groups of different variables.

Variables	Number surveyed	NIP vaccine series completion		χ^2 value	P value
		No. completed	Completion rate (%)		
Initiation time of first dose of HepB				9.4	0.002
>24 h	34	27	79.41		
≤24 h	738	689	93.36		
History of SFV administration				8.57	0.003
No	613	560	91.35		
Yes	159	156	98.11		
Education level of mother				7.2	0.027
Junior school or less	558	509	91.22		
High and technical school	126	121	96.03		
College and above	88	86	97.73		
Education level of father				12.47	0.002
Junior school or less	526	476	90.49		
High and technical school	150	146	97.33		
College and above	96	94	97.92		
Gender				0.184	0.668
Male	421	392	93.11		
Female	351	324	92.31		
Nationality				26.87	<0.001
Han	758	708	93.4		
Minority	14	8	57.14		
Place of birth				5.74	0.057
County hospital or above	663	617	93.06		
Township hospital	107	98	91.59		
Home	2	1	50		
Residence type				6.46	0.040
Mountain area	430	390	90.7		
Hills	93	90	96.77		
Plain	249	236	94.78		

The SFVs contained inactivated polio vaccine (surrogate for OPV); acellular pertussis diphtheria tetanus and Haemophilus influenzae type B conjugate vaccine (surrogate for DTaP); acellular pertussis diphtheria tetanus, inactivated polio and Haemophilus influenzae type B conjugate vaccine (surrogate for DTaP and OPV); group A/C meningococcal conjugate vaccine (surrogate for MPSV-A); inactivated hepatitis A vaccine (surrogate for HepA); and inactivated Japanese encephalitis vaccine (surrogate for JEV). Children who received an SFV in accordance with the immunization schedule were identified as completing the corresponding NIP vaccine. The equivalencies between the SFV and the NIP vaccines were described in a previous study [12]. The study was part of a regular national public health surveillance activity and was exempt from ethical review [16,17]. Verbal consent was obtained from all parents or guardians before the administration of the questionnaire.

Statistical analysis

Chi-square or Fisher's exact tests were run to compare the differences between the groups of children who did and did not complete the NIP vaccine series. Multivariate logistic regression models with an enter method and a backward (conditional) method were fitted to estimate the odds ratios (ORs) and their 95% confidence intervals (CIs) for the completion of the NIP vaccine series.

Filtered variables in the backward conditional method were included in the logistic regression to predict the completion of the NIP vaccine series and generate a regression formula and a new variable of the probability of the completion of the NIP vaccine series for each child. A cut-off value for the predictive probability of completion of the NIP vaccine series was calculated using a receiver operating characteristic curve analysis. Permutations of the filtered variables were used to calculate the probabilities of

the completion of the NIP vaccine series and its predictive evaluation indexes (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV], etc.) using formulas in cases of various combinations of the filtered variables.

All statistical tests were conducted using IBM SPSS version 19.0 (IBM Corp., Armonk, NY, USA). A P value of <0.05 was considered statistically significant.

Results

Characteristics of the study population

A total of 772 children aged 2–3 years old was surveyed and included in the analysis. Among these children who had yet to enrol in school, 716 (92.3%) had finished the NIP vaccine series. Most of the children were of Han ethnicity (98.2%), had received a timely first dose of HepB (95.6%) and were born at county level and above hospitals (85.9%). More than half of the children were boys (54.5%). Only 20.6% of the subjects had received at least one dose of SFV (Table 1).

Factors associated with completion of the NIP vaccine series

Children who had received a timely first dose of HepB were more likely to complete the NIP vaccine series than those who had received a delayed first dose of HepB (93.4% vs. 79.4%, unadjusted OR = 3.65, 95% CI, 1.51–8.79). After controlling for the potential confounders in the logistic regression model with the enter method, the association was attenuated but remained significant, with an adjusted OR of 3.12 (1.19–8.23). Similarly, compared with children who did not receive an SFV, children who received at least of one dose of SFV had an increased likelihood of completing the NIP vac-

Table 2
Odds ratios and 95% confidence intervals for completion of the NIP in "Enter" and "Backward" logistic regression models.

Variables	Enter method model			Backward method model		
	P value	Odds ratios	95% confidence interval	P value	Odds ratios	95% confidence interval
Initiation time of the first dose of HepB						
>24 h		1.00			1.00	
≤24 h	0.02	3.12	1.19–8.23	0.01	3.61	1.45–8.98
History of SFV administration						
No		1.00			1.00	
Yes	0.01	4.74	1.41–15.90	0.01	4.46	1.36–14.63
Education level of mother						
Junior school or less	0.94	1.00				
High and technical school	0.99	1.01	0.35–2.92			
College and above	0.72	1.38	0.24–8.03			
Education level of father						
Junior school or less	0.09	1.00		0.02	1.00	
High and technical school	0.06	2.96	0.95–9.16	0.04	3.04	1.07–8.69
College and above	0.15	3.67	0.62–21.62	0.04	4.53	1.07–19.15
Gender						
Male		1.00				
Female	0.78	0.92	0.52–1.64			
Nationality						
Han		1.00			1.00	
Minority	<0.01	0.15	0.05–0.48	<0.01	0.14	0.04–0.41
Place of birth						
County hospital or above	0.43	1.00				
Township hospital	0.95	0.97	0.44–2.16			
Home	0.20	0.09	0.01–3.52			
Residence type						
Mountain area	0.16	1.00				
Hills	0.07	3.06	0.91–10.29			
Plain	0.41	1.33	0.67–2.64			

cine series, with crude and adjusted ORs of 4.92 (1.52–15.96) and 4.74 (1.41–15.90), respectively. However, ethnic minority children were less likely to complete the NIP vaccine series than children of Han ethnicity (57.1% vs. 93.4%, adjusted OR, 0.15, 95% CI, 0.05–0.48) (Tables 1, 2).

In the logistic regression model with the backward (conditional) method, the variables of timely initiation of the first dose of HepB, a history of SFV immunization, the education level of the father, ethnicity, and types of the residence were eventually retained in the regression equation (Table 2). The final regression equation was

$$\log it(P) = 1.01 + 1.283 \times HepB + 1.495 \times SFV$$
$$+ 1.511 \times Education - 2.005 \times Ethnicity.$$

Predictive values of the combination of significant factors on NIP vaccine series completion

The cut-off value of the probability of completing the NIP vaccine series was 92.5%, with a significant area under the curve of 0.713 (P < 0.001), according to which 44.6% of the children were predicted to complete the NIP vaccine series, with a sensitivity, specificity, PPV, and NPV of 87.5%, 47.1%, 11.4% and 98.0%, respectively. According to the model, children who received a timely first dose of HepB and received an SFV, whose fathers had college education and above, and who were of Han ethnicity, had a 99.5% probability of completing the NIP vaccine series; the sensitivity and NPV both reached 100%. However, the specificity and PPV were low (2.5% and 7.4%, respectively), and only 2.3% of children were predicted to complete the NIP vaccine series. Among other combinations, the receipt of a timely first dose of HepB and the receipt of

an SFV appeared to be good prognosticators, with an NPV of 98.2% and coverage of 29.4% of the children (Table 3).

Discussion

As in our previous studies [12,13], we verified that the children who received a timely first dose of HepB and received an SFV, whose fathers had higher education levels, and who were of Han ethnicity were more likely to complete the NIP vaccine series. However, the results are more realistically responses to the associations between factors and NIP vaccine series completion among children about to enter school. For example, the association between a timely first dose of HepB and the completion of the NIP vaccine series was attenuated but remained significant after controlling for potential confounders, with an adjusted OR of 3.12 (1.19–8.23), while the crude OR was 3.24 (1.81–5.81) for the association in a previous study [13]. Moreover, the OR was further reduced to 2.70 (1.20–6.00) among a mixed group of children of school and preschool ages [12], which might demonstrate a positive effect of vaccination card inspection at the time of enrolment for school children on the completion of the NIP vaccine series.

The associations between factors that affect immunization and the completion of the NIP vaccine series may be attributed to the fact that these factors might be indicators of a better family economy, higher awareness of immunization and receipt of an earlier and more effective vaccination intervention, which are conducive to the completion of the NIP vaccine series by children [12,13,19–23].

The decision to receive an SFV or a corresponding NIP vaccine mainly depends on the family's economic affordability and the physical condition of the children. For example, OPV administration, especially the first dose of OPV vaccination, was associated

Table 3
Predictive values of combinations of factors that affect immunization on NIP completion.

Combination of the factors[a]				Percent (%)					
HepB first dose	Receipt of SFV	Father's education level	Nationality	Cut-off values of the prediction score of NIP vaccine series completion[b]	Percentage of children expected to finish the NIP vaccine series by the cut-off value	Screening evaluation index with the cut-off value			
						Sensitivity	Specificity	Positive predictive value	Negative predictive value
–	–	–	–	92.5[c]	44.6	87.5	47.1	11.4	98.0
1	1	1	1	99.5	2.3	100	2.5	7.4	100
1	1	1	0	96.4	44.0	87.5	46.5	11.3	97.9
1	1	0	1	97.8	29.4	92.9	31.1	9.5	98.2
1	0	1	1	97.8	7.0	98.1	8.2	8.2	98.1
0	1	1	1	98.2	7.0	98.2	7.4	7.7	98.1

[a] HepB first dose ($1 \leq 24$ h; $0 > 24$ h), receipt of SFV (1 = yes; 0 = no), Father's education level (1 = college and above; 0 = junior school or less), nationality (1 = Han; 0 = minority).
[b] Probability of NIP completion was calculated using a regression equation with various combinations of factors that affect immunization. The equation of the probability of NIP completion was equal to EXP(1.01 + 1.283HepB + 1.495SFV + 1.511Education-2.005Ethnicity)/[EXP(1.01 + 1.283HepB + 1.495SFV + 1.511Education-2.005Ethnicity) + 1] × 100%.
[c] The cut-off value of the probability of NIP completion was set using a receiver operating characteristic curve analysis.

with an increased risk of vaccine-associated paralytic polio (VAPP), which may be avoided by inoculating with IPV instead of OPV [24,25]. However, IPV was not included in the NIP vaccine series until 2016 when domestic IPV has emerged on the market [15]. Children who chose to receive IPV before 2016 (the study was conducted in December 2013) had to pay RMB 630 per dose [12]. Therefore, only children from families with better economic conditions and/or children at risk of VAPP chose IPV instead of OPV. The characteristics of these children helped them complete the NIP vaccine series [12,22].

Previous studies have revealed that the timely initiation of the first dose of HepB is associated with a higher likelihood of completion of the Hep B series, HepB-DTaP-measles-containing vaccine series, the NIP vaccine series in China [4,13,14], and the vaccine series in the United States and Italy [26,27]. Generally, receiving a timely first dose of HepB might help emphasize the importance of the vaccine to parents. Awareness of the importance of vaccination could be further strengthened in areas with a high HBV endemic and promote their children's completion of subsequent vaccine series [28,29]. The relationship between education levels and vaccination is uncertain [30,31]. In our study, we found that higher education levels among fathers rather than mothers were associated with NIP vaccine series completion. This finding indicates that fathers' education has a greater impact on NIP vaccine series completion since fathers who have higher education levels may have a higher income, increased awareness of vaccination, and greater decision-making power over family events. The disparities in the NIP completion rates between minorities and those with a Han ethnicity may be attributed to the differences in economic status across the region, vaccination knowledge and faiths and beliefs of parents [32–34].

Immunization card inspections play a role in the completion of the NIP vaccine series by school age children. However, an effective screening pattern to quickly determine whether children have completed the NIP vaccine series is lacking for preschool children [35,36]. We screened for the completion of the NIP vaccine series by combining the significant factors that affect immunization and found that the receipt of a timely first dose of HepB and an SFV were good screening indicators of the completion of the NIP vaccine series among preschool Han children. In this model, 29.4% of preschool children were covered and were evaluated as negative for the lack of completion of the NIP vaccine series (positive means the lack of completion of the NIP vaccine series), with a high NPV of 98.2%, which means children who were screened as negative for the lack of completion of the NIP vaccine series had a 98.2% prob-

ability of completing the NIP vaccine series. Therefore, staff in the immunization clinics should pay more attention to those screen as positive for the lack of completion of the NIP vaccine series.

Our study has several limitations. First, the sample size was not large enough, which may limit the interpretation of some results. Second, we focused on factors related to recipients rather than the providers of the NIP vaccines, such as service levels of immunization clinics, the effects of adverse events following immunization, and the proportion of migrant children, which may also affect the NIP vaccination series [2,36–39]. Finally, the applicability of the screening model is still limited because of regional economic and vaccine policy differences [12].

In conclusion, children who received a timely first dose of HepB and an SFV, whose fathers had high education levels, and who were of Han ethnicity had an increased likelihood of completing the NIP vaccine series. Receipt of a timely first dose HepB and an SFV was a good screening model for the completion of the NIP vaccine series by preschool children in Fujian, China. Vaccine providers may screen preschool children for the lack of completion of the NIP vaccine series by the model.

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Competing interests

None declared.

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