Vaccine 37 (2019) 4133–4139

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

# Are providers' recommendation and knowledge associated with uptake of optional vaccinations among children? A multilevel analysis in three provinces of China

Jie Chang [a,b], Zhiyuan Hou [c], Hai Fang [d], Qingyue Meng [d,*]

[a] Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmacy, Xi'an Jiaotong University, Xi'an 710061, China
[b] Center for Drug Safety and Policy Research, Xi'an Jiaotong University, Xi'an 710061, China
[c] School of Public Health, National Key Laboratory of Health Technology Assessment (National Health Commission), Collaborative Innovation Center of Social Risks Governance in Health, Fudan University, Shanghai 200032, China
[d] China Center for Health Development Studies, Peking University, Beijing 100191, China

ARTICLE INFO

*Article history:*
Received 6 August 2018
Received in revised form 13 May 2019
Accepted 24 May 2019
Available online 4 June 2019

ABSTRACT

*Background:* Immunization services providers play a crucial role in the successful implementation of immunization, particularly for new vaccines. Several childhood vaccinations that are important for public health are not included in the National Immunization Programme in China, although they are available as optional and self-paid vaccines. Their coverage remains low.
*Objective:* To examine the association between providers' knowledge and recommendations of optional vaccines, as well as other supply- and demand-side factors, and their uptake among children.
*Methods:* A cross-sectional study, that included an in-person questionnaire survey for parents of children under-3 years and a self-administrative questionnaire survey for their vaccination services providers, was conducted in 36 townships or sub-districts in three provinces of China in 2013. Using a sample of 1791 household from 30 townships or sub-districts, we applied multilevel logistic analyses to examine the factors associated with the uptake of optional vaccines based on a hierarchal framework that combined demand-side and supply-side factors.
*Results:* Coverage of optional childhood vaccinations varied across small areas. Supply- and demand-side factors were both associated with the uptake of these vaccines. Immunization services providers' recommendations and their knowledge about optional vaccination were positively and significantly associated with uptake. Children were more likely to receive the vaccines if they lived in communities with higher immunization worker density or larger immunization clinics. Several demand-side psychological factors about childhood vaccination were also associated with optional vaccinations.
*Conclusions:* Promoting immunization services providers to conduct evidence-based recommendations about some important childhood optional vaccinations and enhancing their knowledge regarding optional vaccinations and communication skills are useful strategies to increase the coverage of these vaccinations.



## 1. Introduction

Immunization is critical for reducing the burden of vaccine-preventable diseases in children [1], and it is highly cost-effective [2]. However, although more vaccines have been made available to protect against infections caused by Haemophilia Influenza B (Hib), influenza, rotavirus, pneumococcus, and varicella [3], these newer vaccines are currently underused in children in many middle-income countries [4]. In most of these countries, including China, traditional Expended Program on Immunization (EPI) vaccines are generally well managed to the birth cohorts through national programs, however, with a lack of financially and technically external assistance and non-eligibility for discounted procurement prices, the introduction of newer vaccines in these countries is relatively lagging behind donor-funded low-income countries and wealthier countries [4,5]. The coverage of those vaccines is, therefore, limited [4].

China's EPI was established in 1978, initially providing four types of basic vaccines against tuberculosis, polio, measles, diphtheria, tetanus, and pertussis [6]. The program then has expanded to integrate hepatitis B vaccine in 2002, and to include vaccines

* Corresponding author.
*E-mail address:* qmeng@bjmu.edu.cn (Q. Meng).

https://doi.org/10.1016/j.vaccine.2019.05.070
0264-410X/

against meningococcal meningitis, Japanese encephalitis, hepatitis A, rubella and mumps in 2007 [6]. In 2005, a State Council's guidance categorized vaccines into two categories with different vaccination policies [7]. EPI vaccines are belonging to the first category, which is government purchased and provided free of charge. The second category is vaccines not covered by EPI, which are fully paid by families out-of-pocket and optional.

China has a birth cohort of about 18 million births each year [8], however, as aforementioned, several newly available childhood vaccines, including vaccines against Hib, influenza, rotavirus, pneumococcus, and varicella-zoster virus, are not covered by the EPI [9–12]. These vaccines are important for children's health in China. For example, among children under-5 years, China accounts for 14% and 5.1% of the global burden of Hib infections and deaths, respectively [13], and 12% and 3.6% of Streptococcus pneumoniae infections and deaths, respectively [14]. And 40% of acute gastroenteritis hospitalizations in children under-5 years has been estimated to attributed to rotavirus infection in China [15]. Families can seek to purchase these vaccination services at immunization clinics which are generally held in township hospitals (THs) in rural areas and community health centres (CHCs) in urban areas. THs and CHCs are China's community platforms for public health services delivery with easy access to most residents [16]. However, recent reports showed the coverage of optional vaccinations is well below optimal levels in China [10–12,17–19], even in the most developed regions [10,17–19]. As such, a deeper understanding of the determinants of uptake of optional vaccines in China is warranted, which would help to develop strategies to promote their use.

Much of the existing global literature on determinants of childhood vaccination only focus on demand-side factors, including parents' demographics, socioeconomic status, vaccine-related knowledge, attitudes and beliefs, and the child's gender, birth order and other characteristics [20–23]. Previous studies have also shown that supply-side factors are critical determinants of vaccination coverage, such as the density of health workers, facility vaccine supply, immunization service providers' recommendation [24–30]. However, there is a lack of studies worldwide using an ecological design to examine demand-side and supply-side influences on childhood vaccination combinedly, and there is no study of this type in China. Therefore, using household data linked to an assessment of immunization services providers' performance and other supply-side factors, the present study applied the multilevel approach to study childhood optional vaccination determinants based on demand- and supply-side framework.

In particular, the primary interest of this study was to explore the relationship between immunization services providers' recommendations and knowledge about optional vaccinations and children's uptake of these vaccines in China. Although, at a population level, previous studies have found that the geographical density of health workers is a predictor of higher coverage of routine childhood immunizations [24,25], and at the individual level, studies showed that providers' influence increased the likelihood of being vaccinated [26–29], to our best knowledge, this relationship might not have been established yet using a multilevel study design. The findings might be powerful to speak to policymakers in developing interventions to promote uptake from supply-side in a cost-effective manner.

Secondly, China has over sixty million children left behind at home communities by their migrant worker parents [31], and evidence shows the negative impact of parental migration on children's vaccination who are left-behind in China [32,33]. Hence, we had an interest to conduct a subsample analysis stratified by whether being left-behind children and to compare the results between left-behind children and non-left-behind children. This finding might provide some reference for tailored and targeted interventions aiming at improving uptake among left-behind children.

## 2. Methods

### 2.1. Design and sampling

A cross-sectional study that included an in-person questionnaire survey for parents of children under-3 years and a self-administrative questionnaire survey for their vaccination services providers was conducted in 36 townships or sub-districts in three provinces of China in 2013. The survey provinces, namely Jiangsu, Hubei and Gansu, are located in the eastern, central and western regions of China respectively. These three provinces have different levels of socio-economic development, with Jiangsu's GDP per capita ranked high, Hubei's in the middle, and Gansu's low [34].

Within each province, we used a multistage stratified random sampling to recruit households. We first selected two rural counties and one urban district (equivalent administrative division to county), stratified by socio-economic development status. Second, we randomly selected four townships in each county and sub-districts (equivalent administrative division to township) in each district, giving eight townships and four sub-districts in total in each province. Third, within each township or sub-district, we selected three villages or communities at random. Finally, in each village or community, 20 households with a child under-3 years were randomly selected. In total, this gave a planned sample size of 2160 households in 108 villages or communities in 36 townships/sub-districts, with 60 households in each township or sub-district. The actual number of sampled households was 2176. The parents or grandparents of the children in the sampled households were interviewed face-to-face using a structured questionnaire with a focus on the youngest child. The information about the use of optional vaccine doses was recorded by the survey enumerators from children's vaccination cards.

At the same time, a self-administrative questionnaire was used to collect information about the characteristics of immunization services providers at the 36 surveyed THs/CHCs (In China, each township or sub-district is equipped with only one TH/CHC, respectively. Therefore, we surveyed one THs/CHCs in each of the 36 survey townships/sub-districts). Data from a total of 150 immunization services providers were included in the analyses. Institution questionnaires yielded information of THs/CHCs about optional vaccination services, including the availability of the vaccines, staffing, and equipment.

All of the respondents consented to participate in the survey. The study received ethics approval from the Institutional Review Board of Peking University Health Science Center.

### 2.2. Measures

#### 2.2.1. Outcome: self-paid vaccination status

We defined four dichotomous outcomes: (1) uptake of at least one dose of self-paid vaccines, (2) uptake of at least one dose of Hib vaccines, (3) uptake of at least one dose of rotavirus vaccines, (4) uptake of one dose of varicella vaccine.

#### 2.2.2. Providers' recommendation, knowledge, and other supply-side variables

THs/CHCs are the primary community platforms for children to receive both EPI and optional vaccinations in China. We constructed a range of supply-side factors linking to characteristics of THs/CHCs, including knowledge and recommendation practices about optional vaccinations among immunization services providers at THs/CHCs, the physical space of immunization clinic that

held at THs/CHCs and staffing at THs/CHCs, and local economic development level (operationalized as the percentage of households above the national average disposable income per capita in each township/sub-district).

Immunization services providers' knowledge and usual practice on recommending optional vaccinations were measured using the questionnaire administered to staff affiliated to the surveyed THs/CHCs. A synthetic index of knowledge about optional vaccinations was produced from the responses to 12 questions (see Supplementary 1) and coded 1–12, with a high value indicating better knowledge. The frequency with which immunization services providers recommended optional vaccinations to caregivers was measured by a question "How often do you recommend some optional vaccines to parents when they were taking their children to uptake EPI vaccines?" The answer options are as follows: 1 = Never, 2 = Seldom, 3 = Occasionally, 4 = Often, 5 = Always. We calculated the means of the two measures at township or sub-district level.

*2.2.3. Demand-side variables*

Besides parental education level, household affordability of optional vaccines, and the child's characteristics (age, gender, whether they had siblings, whether they are left-behind children), we considered a set of measures of parental concern about optional vaccinations, which have been shown to be important psychological influencing factors in parental vaccination decisions [20–22,35]. Concerns about the monetary costs, needle pain, and safety of optional vaccinations were measured by one question respectively: "To what extent do you feel the vaccine prices are generally too high/vaccination is painful/vaccination is unsafe, and you do not want to vaccinate your child with an optional vaccine?", with a five-point Likert-type scale response (1 = Not at all, 2 = A little, 3 = A moderate amount, 4 = Somewhat large, 5 = Very large). Parental attitude towards providers' recommendation was measured by the question "To what degree do you agree with the statement — I'm willing to accept provider's recommendation about optional vaccination?" with a five-point response scale (1 = Strongly disagree, 2 = Disagree, 3 = Unsure, 4 = Agree, 5 = Strongly agree). In addition, the household affordability of optional vaccines

*2.3. Statistical analyses*

In the analysis, we firstly excluded a total of 361 (16.7%) sampled children and information from 18 immunization providers from six rural townships in Gansu Province. Because the THs in these six townships were not equipped to provide any optional vaccines and have no previous experience of providing these vaccines at the time of the survey. And then we removed 9 children's information due to data about covariates were missing. In the remaining sample, we further removed the data of 15 children aged below 2 months because the first possible dose of a self-paid vaccine is administered at the age of 2 months in China, like the first dose of Hib vaccine and rotavirus vaccine [36,37]. Thus the analyses for the outcome (1), (2) and (3) were confined to children of 2–36 months old. The analyses for the outcome (4)—receipt of varicella vaccine—were further restricted to children of 12–36 months old, because the first dose of varicella vaccine is recommended for children aged above12 months [38]. To compare the levels of self-paid vaccination across districts, we calculated the age-adjusted proportions with 95% confidence intervals for the four outcomes at township or sub-district level.

We linked supply-side data to demand-side data. This matching was performed at township/sub-district level. To assess both demand- and supply-side determinants of optional vaccination while accounting for the hierarchical nature of the data, we constructed 2-level mixed-effect logistic regressions (random intercept approach) to model the probability of the four dichotomous optional vaccination outcomes, with demand-side variables at the individual level and supply-side variables at township/sub-district-level. We clustered standard errors at township/sub-district level. To control for any changes over time cross townships/sub-districts, we included a fixed-effect interaction term of child's age and the identification variable of townships/sub-districts in the regressions. Estimated coefficients were presented as odds ratios (ORs) with 95% confident intervals for interpretation. All analyses were performed with Stata 14.0 (StataCorp LP, College Station, TX).

## 3. Results

The final sample included in multi-level analysis comprised 1791 households. Samples from the six rural townships of Gansu Province that did not have the capability to provide optional vaccines were excluded from the analytical part. Table 1 shows the descriptive statistics for the sample used for multi-level analyses. Of a total of 1791 under-3-year children with an average age of 1.14 years (standard deviation (SD): 1.43), 57.7% were boys, and 22.5% were left-behind children whose parents were both migrant workers. The average household annual income of this analyzed sample was 72849.8 China Yuan (SD: 126190.9).

In the sample used for multi-level analysis, 59.4% [1063/1791] of children aged 2–36 months had received at least one type of optional vaccination. Only 36.2% [648/1791] and 20.3% [364/1791] of children aged 2–36 months had received at least one dose of Hib and rotavirus vaccine, and 42.9% [429/1001] of children aged 12–36 months had been immunized against varicella. Among the 150 immunization workers at THs and CHCs, the mean recommendation frequency score was 3.19 (SD: 0.68), and the mean knowledge score was 7.94 (SD: 1.88). Regarding parental psychological measures, the mean score for concern about the price, concern about needle pain, concern about vaccination safety, and attitude towards recommendation were 1.88 (SD: 1.12), 1.27 (SD: 0.63), 1.74 (SD: 1.04), and 3.88 (SD: 1.02), respectively.

Fig. 1 shows the age-adjusted coverage for the uptake of at least one optional vaccine and uptake of at least one dose of vaccine against Hib, rotavirus, and varicella across the thirty townships and sub-districts. There was substantial variation in coverage, from 0% in some districts in Gansu Province to over 90% in some districts in Hubei Province.

Table 2 shows the results of the multivariate regression analyses. Immunization services providers' recommendation frequency was significantly associated with vaccination status in all four models with considerable effect size (at least one dose of vaccine OR = 4.29 $p < 0.0001$; Hib vaccine OR = 3.08 $p < 0.0001$; rotavirus vaccine OR = 3.56 $p < 0.0001$; varicella vaccine OR = 1.78 $p = 0.0091$). Providers' knowledge was also a significant predictor of uptake of at least one dose of optional vaccines and Hib vaccine (at least one dose of optional vaccine OR = 1.31 $p = 0.0417$; Hib vaccine OR = 1.22 $p = 0.0738$; rotavirus vaccine OR = 1.13 $p = 0.0293$; varicella vaccine OR = 1.16, $p = 0.0698$). The density of immunization worker and the physical space of the immunization clinics were also associated with vaccination status. In our sample for analysis, the likelihood of uptake of the rotavirus vaccine among children living in urban areas was significantly lower than the counterparts of rural areas. Several demand-side factors, such as parental concern about vaccine price, and attitude towards providers' recommendations, were significantly associated with vaccination uptake. Left-behind children were less likely to be vaccinated against Hib and rotavirus. When the analysis was stratified according to whether the child is left-behind children, the results were generally consistent (see Table S1 in Supplementary

**Table 1**
Summary statistics of the sample used for analyses.

| Supply- and demand-side characteristics | Measurements | Number and Percentage | | Mean (SD) |
|---|---|---|---|---|
| | | No. | % | |
| *Supply-side (Community and THs/CHCs) characteristics(n = 30)* | | | | |
| Immunization providers' average recommendation frequency score at THs/CHCs | Continuous | NA | NA | 3.19 (0.68) |
| Immunization providers' average knowledge score about optional vaccination at THs/CHCs | Continuous | NA | NA | 7.94 (1.88) |
| Space of vaccination clinics (square metres) | Continuous | NA | NA | 139.73 (108.49) |
| Staffing of immunization workers | | | | |
| More than 1 immunization workers per 10,000 population in the township/sub-district | 1 = Yes, 0 = No | 16 | 53.33 | NA |
| Less than 1 immunization workers per 10,000 population in the township/sub-district | 1 = Yes, 0 = No | 14 | 46.67 | NA |
| Urban/rural status | | | | NA |
| Urban areas | 1 = Yes, 0 = No | 12 | 40.00 | NA |
| Rural areas | 1 = Yes, 0 = No | 18 | 60.00 | NA |
| Percentage of households above the national average disposable income per capita[a] | Continuous | NA | NA | 28.63 (28.67) |
| *Demand-side (Household- and individual-level) characteristics (n = 1791)* | | | | |
| Mother's education | | | | |
| <Junior high school | 1 = Yes, 0 = No | 192 | 10.72 | NA |
| Junior high school or senior high school | 1 = Yes, 0 = No | 1093 | 61.03 | NA |
| >Senior high school | 1 = Yes, 0 = No | 506 | 28.25 | NA |
| Household affordability of optional vaccines[b] | | | | NA |
| Affordable | 1 = Yes, 0 = No | 1625 | 90.73 | NA |
| Unaffordable | 1 = Yes, 0 = No | 166 | 9.27 | NA |
| Left-behind children status | | | | NA |
| Being left-behind children | 1 = Yes, 0 = No | 403 | 22.50 | NA |
| Not being left-behind children | 1 = Yes, 0 = No | 1388 | 77.50 | NA |
| Gender of the child | Continuous | | | NA |
| Boy | 1 = Yes, 0 = No | 1034 | 57.73 | NA |
| Girl | 1 = Yes, 0 = No | 757 | 42.27 | NA |
| Whether have siblings | | | | NA |
| Being only child | 1 = Yes, 0 = No | 1191 | 66.50 | NA |
| Not being only child | 1 = Yes, 0 = No | 600 | 33.50 | NA |
| Age of the child (year) | Continuous | NA | NA | 1.14 (1.43) |

Notes:
SD = standard deviation. NA = not applicable.
[a] The national average annual disposable income per capita in 2013 was 18310.8 China Yuan, according to China Statistical Yearbook 2014 [Available from: http://www.stats.gov.cn/tjsj/ndsj/2014/zk/html/Z0601e.htm].
[b] The household affordability of the optional vaccines was operationalized as whether the price of one dose of Hib vaccine accounted for less than 10% of the monthly income of a surveyed household. According to the authors' data, Hib vaccines were the most commonly used optional vaccines at the time of our survey in 2013, and the uptake price across different regions in China is about 125 China Yuan for one dose in 2013. The cut-off value of 10% was chosen referred to previous drug affordability studies.

2). And we found a larger effect size of provider's recommendation on the uptake of the three specific types of optional vaccines among left-behind children, as opposed to the non-left-behind group.

## 4. Discussion

We revealed large disparities in childhood optional vaccination coverage cross areas in China. We found that immunization services providers' knowledge and recommendations were significantly associated with increased optional vaccinations among children. This result was robust to a wide range of controls from both demand- and supply-side based on a hierarchical structure, and held across specific vaccinations (against Hib, rotavirus, and varicella) and stratified groups (left-behind children and non-left-behind children). Meanwhile, several demand-side psychological factors about childhood vaccination were associated with optional vaccinations, which is consistent with previous studies [20–23,35].

The study is uniquely valuable. Although recent studies using the multilevel approach have examined some regional level and supply-side determinants of vaccination coverage, such as regional socioeconomic and religious background [39,40], availability of health centres and health workers [39], and types of health personnel in vaccination services [41], none of these has explored the effects of more specific indicators of service quality—such as knowledge and recommendation practices of immunization workers, availability of specific vaccines, the infrastructure of immunization clinics—on vaccination coverage. Moreover, as most implementation research focused on vaccines that incorporated in EPI or other public-funded programs, few of them have focused on optional and self-paid childhood vaccinations. Given that many important childhood vaccines are optional and self-paid in many middle-income countries [4,5]. We believe that the policy implication of the current work is valuable for China, and might also be useful for other countries with a similar situation.

Childhood vaccinations require interaction between immunization services providers and parents. Our finding regarding the association between providers' recommendation and children's vaccination status supports the theory of health belief model [27,42], which suggests that a cue to action, such as professional's recommendation, could trigger the adoption of health behaviours. This is also in agreement with previous studies which showed respondents who reported that healthcare providers had recommended were more likely to have been immunized [26–28]. The positive association between providers' knowledge about optional vaccinations and coverage of these vaccinations is in line with previous research that found immunization services providers' vaccine-related attitudes and beliefs may influence parents' corresponding attitudes [43]. As in many other countries [26,43], healthcare providers are the main source of vaccine-related information for parents in China—in our survey, around 90% of respondents used them for information about optional vaccinations,

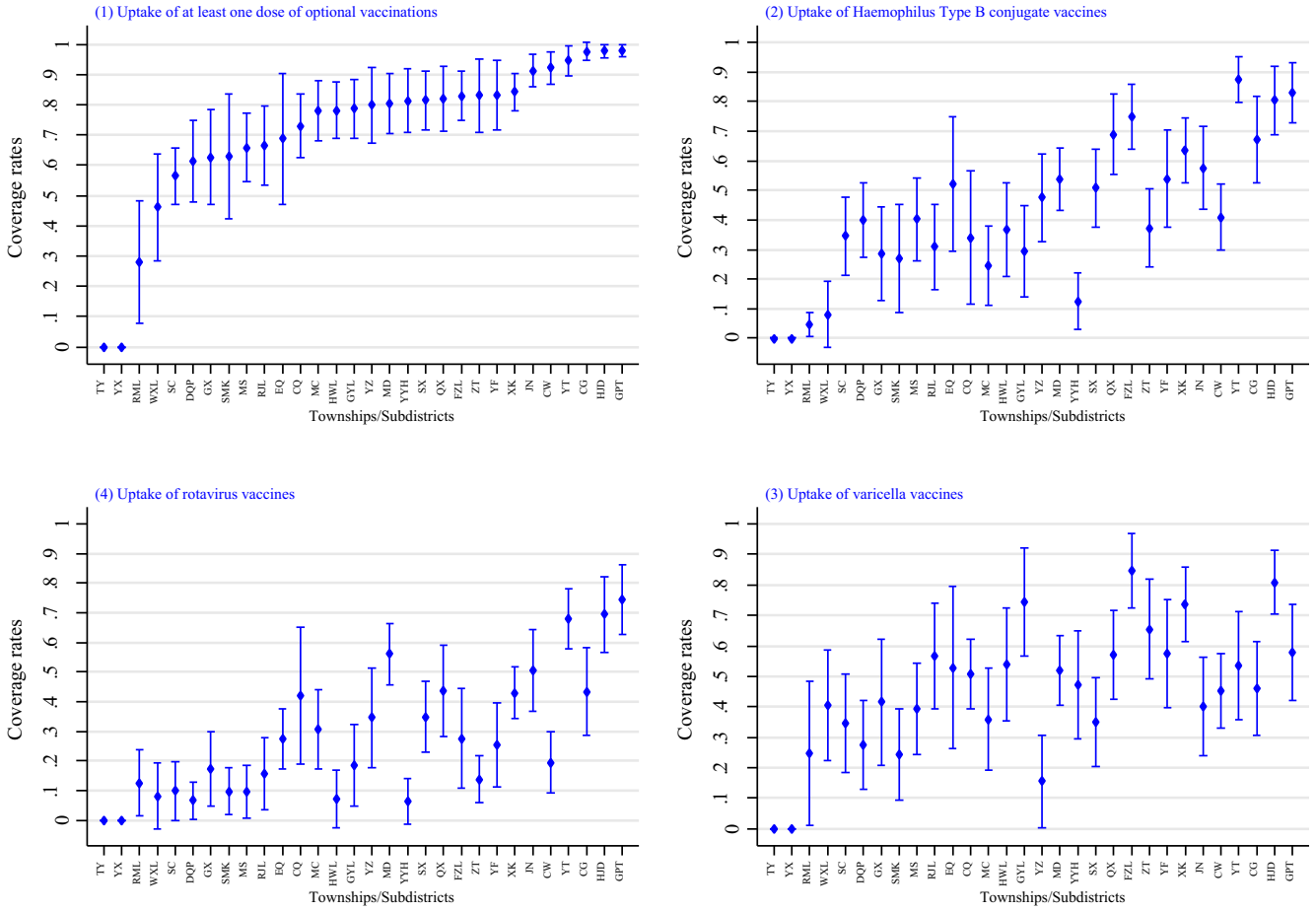


**Fig. 1.** Age-adjusted coverage rates for optional vaccination coverage by townships/sub-districts. (1) uptake of at least one dose of optional vaccines, (2) uptake of at least of one dose of Hib vaccines, (3) uptake of at least one dose of rotavirus vaccines, (4) uptake of varicella vaccine, across 36 surveyed towns/streets. The dots represent estimates of coverage rates, and the horizontal bars around the dots represent 95% confidence interval. Urban areas in Gansu Province includes RML, WXL, GYL, FZY. Rural areas in Gansu Province includes TY, YX. Urban areas in Hubei Province includes ZT, CW, YF, EQ. Rural areas in Hubei Province includes HJD GPT, YT, CG, DQP, YZ, MS, JN. Urban areas in Jiangsu Province includes HWL, RJL, YYH, SMK. Rural areas in Hubei Province includes MC, SX, QX, SC, CQ, GX, XK, MD.

trusted them, and were willing to follow their recommendations [35]. Providers with better knowledge and correct attitudes and beliefs about optional vaccinations might pass more relevant information to parents and therefore be a positive influence on their decision-making.

The results point to the opportunity to increase optional vaccination coverage by encouraging immunization services providers to recommend these vaccinations. It is also important that providers should be trained to communicate effectively with parents, because research shows that improving the quality of provider-parent communication in discussions about vaccines plays a critical role in the success of childhood vaccination programs [44], particularly for new vaccines [45].

The subsample analyses generally suggested a provider's recommendation has a larger effect on the three specific types of optional vaccination status in the left-behind children. Given left-behind children are mostly taken care by grandparents [31], who are generally lower educated with lesser health literacy as compared with the younger parents, our finding implied that an external motivator, such as a health professional's suggestion, might play a stronger role on them, while the influence might be comparatively weaker in China's younger and better-educated parents. In a background that Chinese parents' vaccine confidence is at stake due to several vaccine safety events in more recent years [46–48], the result suggests that evidence-based risk and benefit communication should be regarded as an essential skill for all immunization workers in communities, which could be helpful for them to educate parents about sensible attitudes on childhood vaccination. This requires not only communication skill, but also sufficient expertise. Hence, training aiming at enhancing immunization workers' knowledge level is extremely warranted at a national level.

Of the demand-side factors, we found parental attitudes towards providers' recommendations were significantly and positively associated with uptake, which echoed with the supply-side results discussed above. We also found that parental concern about the cost was significantly and negatively associated with uptake, which is consistent with previous studies conducted in China [35,49].

When comparing uptake across different regions, the optional vaccines coverage rates of townships/sub-districts in Gansu, a western province, were much lower than the rates of surveyed communities from comparatively wealthier areas (central and eastern regions). This huge gap in optional vaccination coverage is much larger than the difference in EPI vaccination among regions. China's 5th National Health Service Survey (NHSS) [50] shows the basic EPI vaccination coverage in children had generally reached universal across eastern, central, and western China in 2013 (see supplementary 3). Although there were still slight differences in the coverage percentage across regions in the 5th NHSS, which might reflect large disparities in the number of unimmunized children given China's large birth cohort, a clear trend

**Table 2**
Supply- and demand-side factors associated with the uptake of optional vaccinations.

| | Multivariable, multilevel regressions estimates presented as odds ratio (95% confidence interval) | | | |
|---|---|---|---|---|
| | (1) Any optional vaccines | (2) Hib vaccines | (3) Rotavirus vaccines | (4) Varicella vaccines |
| *Supply-side variables* | | | | |
| Immunization providers' average frequency of recommendation at the TH/CHC | 4.29 (2.25–8.19)*** | 3.08 (1.87–5.08)*** | 3.56 (2.20–5.75)*** | 1.78 (1.16–2.75)*** |
| Immunization providers' average knowledge about optional vaccination at the TH/CHC | 1.31 (1.01–1.69)** | 1.22 (0.98–1.52)* | 1.13 (1.01–1.26)** | 1.16 (0.99–1.35)* |
| Space of vaccination clinics# | 2.02 (0.97–4.20)* | 1.44 (0.84–2.47) | 1.43 (0.93–2.20) | 1.30 (0.91–1.86) |
| Immunization worker density## | 1.91 (0.72–5.03) | 1.54 (0.73–3.25) | 2.53 (1.26–5.10)*** | 1.89 (1.15–3.12)** |
| Community socioeconomic status### | 1.76 (0.30–10.20) | 0.66 (0.12–3.60) | 1.17 (0.37–3.72) | 1.24 (0.44–3.50) |
| Urban areas | 0.38 (0.10–1.38) | 0.34 (0.11–1.09)* | 0.20 (0.08–0.49)*** | 1.53 (0.62–3.81) |
| *Demand-side variables* | | | | |
| Parental concern about the cost | 0.85 (0.77–0.94)*** | 0.87 (0.75–1.00)** | 0.89 (0.75–1.04) | 0.82 (0.72–0.92)*** |
| Parental concern about needle pain | 1.05 (0.86–1.28) | 1.05 (0.86–1.29) | 1.10 (0.82–1.47) | 1.02 (0.83–1.26) |
| Parental concern about vaccine safety | 0.98 (0.86–1.12) | 1.00 (0.86–1.17) | 0.97 (0.80–1.16) | 1.07 (0.90–1.26) |
| Parental attitude towards recommendation | 1.35 (1.18–1.55)*** | 1.20 (1.03–1.40)** | 1.08 (0.90–1.30) | 1.03 (0.90–1.19) |
| Mother's educational attainment | | | | |
| <Junior high school | | | | |
| Junior high school or senior high school | 1.14 (0.66–1.97) | 1.22 (0.84–1.77) | 1.02 (0.74–1.40) | 1.14 (0.73–1.77) |
| > Senior high school | 0.94 (0.51–1.72) | 1.01 (0.58–1.77) | 0.69 (0.38–1.26) | 0.93 (0.47–1.81) |
| Household affordability of optional vaccines | 0.99 (0.62–1.59) | 1.35 (0.95–1.91)* | 1.59 (0.93–2.73)* | 1.18 (0.58–2.38) |
| Boy child | 1.05 (0.84–1.32) | 0.86 (0.69–1.08) | 1.13 (0.87–1.46) | 1.40 (1.04–1.88)** |
| Child age (year) | 4.92 (2.37–10.22)*** | 1.98 (0.89–4.44)* | 2.59 (1.91–3.52)*** | 1.78 (1.15–2.75)*** |
| Only child without siblings | 1.16 (0.78–1.74) | 1.06 (0.78–1.44) | 1.51 (1.09–2.09)** | 1.19 (0.76–1.84) |
| Left-behind children | 0.81 (0.51–1.30) | 0.62 (0.41–0.96)** | 0.55 (0.40–0.76)*** | 1.08 (0.75–1.56) |
| Interaction term between child age and community identifier variable | 0.99 (0.98–1.01) | 1.00 (0.99–1.01) | 1.00 (0.99–1.00) | 1.00 (1.00–1.01) |
| Observations | 1791 | 1791 | 1791 | 1001 |
| Number of groups | 30 | 30 | 30 | 30 |
| Community-level variance | 27.81% | 19.63% | 14.30% | 5.55% |
| Individual-level variance | 72.19% | 80.37% | 85.70% | 94.45% |

Notes:
# Physical space of vaccination clinics measured in square metres was log-transformed.
## Density of immunization workers was dichotomized into more than 1 immunization workers per 10,000 population versus less than 1 immunization workers per 10,000 population.
### Operationalized and measured as the percentage of surveyed households above the national average disposable income per capita in a township/sub-district.
* Significance level: $p < 0.1$.
** Significance level: $p < 0.05$.
*** Significance level: $p < 0.01$.

towards lower EPI vaccination coverage in western China, as shown in previous waves of NHSS [51], had been no longer observable. This comparison of regional disparities between optional vaccination coverage and EPI vaccination coverage also points to the needed efforts in further lowering the inequality in children's healthcare utilization across different regions in China.

This study had several limitations. First, in the analyses on Hib and rotavirus vaccinations, we only studied the uptake of at least of one dose, instead of full vaccination, because we didn't further collect information of uptake doses for the optional vaccines required multiple doses during our survey. Second, the current study was not designed to determine any causality, and further studies with an experimental design would be needed for this.

## 5. Conclusions

We found that the large variations in coverage of optional childhood vaccinations across regions could be attributed to both supply- and demand-side factors. The immunization services providers' knowledge and recommendations about optional vaccinations also play a key role. Therefore, besides strategies such as to improve availability of optional vaccines at community immunization platforms, to remove the economic barriers, and to educate parents, promoting immunization services providers to conduct evidence-based recommendations about some important childhood optional vaccinations and enhancing their communication skills and knowledge regarding optional vaccinations are also useful strategies to increase the coverage of these vaccinations.

## 6. Contributors

JC and QM conceived of the research question and designed the study. JC did the statistical analyses, literature analysis, interpreted the results and wrote the article. QM, ZH and HF contributed extensively to the study design, results interpretation and the revision of the manuscript. QM supervised the study. All authors read and approved the final manuscript.

## Declaration of Competing Interest

None declared.

## Acknowledgements

This study was supported by the National Health Commission of P. R. China. Jie Chang acknowledges support from the National Natural Science Foundation of China (71503196) and the China Postdoctoral Science Foundation (2015M580862, 2016T90935). The authors also thank Quanle Li, Yun Feng, Jingshan Zheng, Dahai Yue, Qiong Wu, Yang Sun, and Qing Wang for their invaluable effort and support that made this study possible.

## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.05.070.

## References


[1] Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2015;385 (9966):430–40.

[2] Ozawa S, Mirelman A, Stack ML, Walker DG, Levine OS. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: a systematic review. Vaccine 2012;31(1):96–108.

[3] WHO, UNICEF, World Bank. State of the world's vaccines and immunization, 3rd ed. Geneva: World Health Organization; 2009. [Available from: https://www.who.int/immunization/sowvi/en/].

[4] Kaddar M, Schmitt S, Makinen M, Milstien J. Global support for new vaccine implementation in middle-income countries. Vaccine 2013;31(Suppl 2): B81–96.

[5] Makinen M, Kaddar M, Molldrem V, Wilson L. New vaccine adoption in lower-middle-income countries. Health Policy Plann 2012;27(suppl 2):ii39–49. https://doi.org/10.1093/heapol/czs036.

[6] Zheng J, Zhou Y, Wang H, Liang X. The role of the China experts advisory committee on immunization program. Vaccine 2010;28(Suppl 1):A84–7.

[7] State Council. Regulation about vaccine supply and vaccination management. [Available from: http://www.gov.cn/zhengce/content/2016-04/25/content_5067597.htm].

[8] National Bureau of Statistics of China. China statistical yearbook; 2017. [Available from: http://www.stats.gov.cn/tjsj/ndsj/2017/indexch.htm].

[9] Yu H, Yang W, Varma JK. To save children's lives, China should adopt an initiative to speed introduction of pneumonia vaccines. Health Aff (Millwood) 2012;31(11):2545–53.

[10] Hu Y, Luo S, Tang X, Lou L, Chen Y, Guo J. Comparative assessment of immunization coverage of migrant children between national immunization program vaccines and non-national immunization program vaccines in East China. Hum Vaccin Immunother 2015;11(3):761–8.

[11] Zhang X, Syeda ZI, Jing Z, et al. Rural-urban disparity in category II vaccination among children under five years of age: evidence from a survey in Shandong, China. Int J Equity Health 2018;17(1):87.

[12] Zheng J, Cao L, Guo S, Wang AKL, Yu W, Yuan P, Jiang K, Zhang G, Cao L, Wang H. Survey on the immunization status Of non-EPI vaccines among children aged 1 to 2 years in China (in Chinese).. Chin J Vaccines Immun 2012;18 (3):233–7.

[13] Watt JP, Wolfson LJ, O'Brien KL, et al. Burden of disease caused by Haemophilus influenzae type b in children younger than 5 years: global estimates. Lancet 2009;374(9693):903–11.

[14] O'Brien KL, Wolfson LJ, Watt JP, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet 2009;374(9693):893–902.

[15] Wu D, Yen C, Yin ZD, et al. The public health burden of rotavirus disease in children younger than five years and considerations for rotavirus vaccine introduction in China. Pediatr Infect Dis J 2016;35(12):e392–8.

[16] The Asia Pacific Observatory on Health Systems and Policies. People's Republic of China Health System Review, 2015. Health Systems in Transition 2015;5(7). [Available from: http://www.searo.who.int/entity/asia_pacific_observatory/publications/hits/hit_china/en/].

[17] He Q, Wang M, Xu J, Zhang C, Wang H, Zhu W, et al. Rotavirus vaccination coverage among children aged 2–59 months: a report from Guangzhou, China. PLoS One 2013;8(6):e68169.

[18] Wagner AL, Sun X, Montgomery JP, Huang Z, Boulton ML. The impact of residency and urbanicity on *Haemophilus influenzae* Type b and pneumococcal immunization in Shanghai Children: a Retrospective Cohort Study. PLoS One 2014;9(5):e97800.

[19] Hu Y, Chen Y, Zhang B, Li Q. An evaluation of voluntary varicella vaccination coverage in Zhejiang Province, East China. Int J Environ Res Public Health 2016;13(6):560.

[20] Rainey JJ, Watkins M, Ryman TK, Sandhu P, Bo A, Banerjee K. Reasons related to non-vaccination and under-vaccination of children in low and middle income countries: findings from a systematic review of the published literature, 1999–2009. Vaccine 2011;29(46):8215–21.

[21] Favin M, Steinglass R, Fields R, Banerjee K, Sawhney M. Why children are not vaccinated: a review of the grey literature. Int Health 2012;4(4):229–38.

[22] Brown KF, Kroll JS, Hudson MJ, Ramsay M, Green J, Long SJ, et al. Factors underlying parental decisions about combination childhood vaccinations including MMR: a systematic review. Vaccine 2010;28(26):4235–48.

[23] Bish A, Yardley L, Nicoll A, Michie S. Factors associated with uptake of vaccination against pandemic influenza: a systematic review. Vaccine 2011;29 (38):6472–84.

[24] Anand S, Bärnighausen T. Health workers and vaccination coverage in developing countries: an econometric analysis. Lancet 2007;369 (9569):1277–85.

[25] Hu Y, Shen L, Guo J, Xie S. Public health workers and vaccination coverage in Eastern China: a health economic analysis. Int J Environ Res Public Health 2014;11(5):5555–66.

[26] Smith PJ, Kennedy AM, Wooten K, Gust DA, Pickering LK. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. Pediatrics 2006;118(5):E1287–92.

[27] Malosh R, Ohmit SE, Petrie JG, Thompson MG, Aiello AE, Monto AS. Factors associated with influenza vaccine receipt in community dwelling adults and their children. Vaccine 2014;32(16):1841–7.

[28] Pandolfi E, Marino MG, Carloni E, Romano M, Gesualdo F, Borgia P, et al. The effect of physician's recommendation on seasonal influenza immunization in children with chronic diseases. BMC Public Health 2012;12:984.

[29] Streng A, Seeger K, Grote V, Liese JG. Varicella vaccination coverage in Bavaria (Germany) after general vaccine recommendation in 2004. Vaccine 2010;28 (35):5738–45.

[30] Phillips DE, Dieleman JL, Lim SS, Shearer J. Determinants of effective vaccine coverage in low and middle-income countries: a systematic review and interpretive synthesis. BMC Health Serv Res 2017;17(1):681.

[31] Zhou C, Sylvia S, Zhang L, et al. China's left-behind children: impact of parental migration on health, nutrition, and educational outcomes. Health Aff (Millwood) 2015;34(11):1964–71.

[32] Ni ZL, Tan XD, Shao HY, Wang Y. Immunisation status and determinants of left-behind children aged 12–72 months in central China. Epidemiol Infect 2017;145(9):1763–72.

[33] Tang X, Geater A, McNeil E, Zhou H, Deng Q, Dong A, et al. Parental migration and children's timely measles vaccination in rural China: a cross-sectional study. Trop Med Int Health 2016;21(7):886–94.

[34] National Bureau of Statistics of China. China statistical yearbook 2014. [Available from: http://www.stats.gov.cn/tjsj/ndsj/2014/indexch.htm].

[35] Hou Z, Chang J, Yue D, Fang H, Meng Q, Zhang Y. Determinants of willingness to pay for self-paid vaccines in China. Vaccine 2014;32(35):4471–7.

[36] Li Y, Yue C, Wang Y, et al. Utilization pattern of Haemophilus influenza type b vaccine in eight provinces of China. Hum Vaccin Immunother 2018;14 (4):894–9.

[37] Cui S, Tobe RG, Mo X, Liu X, Xu L, Li S. Cost-effectiveness analysis of rotavirus vaccination in China: projected possibility of scale-up from the current domestic option. BMC Infect Dis 2016;16(1):677.

[38] Fu C, Wang M, Liang J, Xu J, Wang C, Bialek S. The effectiveness of varicella vaccine in China. Pediatr Infect Dis J 2010;29(8):690–3.

[39] Ghosh A, Laxminarayan R. Demand- and supply-side determinants of diphtheria-pertussis-tetanus nonvaccination and dropout in rural India. Vaccine 2017;35(7):1087–93.

[40] van Lier A, van de Kassteele J, de Hoogh P, Drijfhout I, de Melker H. Vaccine uptake determinants in The Netherlands. Eur J Public Health 2014;24 (2):304–9.

[41] Abebe DS, Nielsen VO, Finnvold JE. Regional inequality and vaccine uptake: a multilevel analysis of the 2007 Welfare Monitoring Survey in Malawi. BMC Public Health 2012;12:1075.

[42] Sturm LA, Mays RM, Zimet GD. Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections. J Dev Behav Pediatr 2005;26(6):441–52.

[43] Mergler MJ, Omer SB, Pan WK, Navar-Boggan AM, Orenstein W, Marcuse EK, et al. Association of vaccine-related attitudes and beliefs between parents and health care providers. Vaccine 2013;31(41):4591–5.

[44] Connors JT, Slotwinski KL, Hodges EA. Provider-parent Communication when discussing vaccines: a systematic review. J Pediatr Nurs 2017;33:10–5.

[45] Morin A, Lemaître T, Farrands A, Carrier N, Gagneur A. Maternal knowledge, attitudes and beliefs regarding gastroenteritis and rotavirus vaccine before implementing vaccination program: which key messages in light of a new immunization program? Vaccine 2012;30(41):5921–7.

[46] Yu W, Liu D, Zheng J, et al. Loss of confidence in vaccines following media reports of infant deaths after hepatitis B vaccination in China. Int J Epidemiol 2016;45(2):441–9.

[47] Qiu J, Hu H, Zhou S, Liu Q. Vaccine scandal and crisis in public confidence in China. Lancet 2016;387(10036):2382.

[48] Phillips N. Chinese vaccine scandal unlikely to dent childhood immunization rates. Nature 2018;560(7716):14–5.

[49] Zhang SK, Pan XF, Wang SM, Yang CX, Gao XH, Wang ZZ, et al. Perceptions and acceptability of HPV vaccination among parents of young adolescents: a multicenter national survey in China. Vaccine 2013;31(32):3244–9.

[50] Center for Health Statistics and Information of National Health and Family Planning Committee. An analysis report of the 5th national health services survey in China, 2013. Beijing: Peking Union Medical College Press; 2015.

[51] Center for Health Statistics and Information, Ministry of Health. An Analysis Report of National Health Services Survey in China; 2008. [Available from: http://www.nhc.gov.cn/mohwsbwstjxxzx/s8211/201009/49165.shtml].