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RESEARCH PAPER

Hepatitis B vaccination among 1997-2011 birth cohorts in rural China: the potential for further catch-up vaccination and factors associated with infant coverage rates

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ABSTRACT

Hepatitis B vaccination rates in China have recently increased. This study aimed to investigate infant vaccination coverage for birth cohorts from 1997 to 2011 in rural regions and to assess catch-up vaccination potential. We used questionnaire-based interviews from a cross-section of 6,529 individuals from seven provinces. Logistic regression analyses were used to model two measures of infant vaccination status, namely, birth dose within 24 hours and three doses within the first year of life. During interviews, individuals' vaccination status and vaccination plan were recorded. Unvaccinated individuals without plans for future vaccination were presented with a hypothetical offer of free vaccination and indirect cost compensation. Institutional birth rates were higher than vaccination rates, but both increased over time. Vaccination coverage rates were not significantly associated with sex. Infant vaccination coverage was positively associated with a mother's educational level, household income level, knowledge of transmission routes, and perceived duration of protection obtained through vaccination. Vaccination status at the time of the survey showed the occurrence of catch-up vaccinations, but a notable percentage of individuals remained unvaccinated and had no plans for future vaccination. Of these individuals, approximately 50% were prepared to accept vaccination if offered free of charge.

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hepatitis B vaccination; vaccination coverage; immunization; socioeconomic status

Background

In China, the hepatitis B virus (HBV) causes the death of approximately 300,000 individuals annually.[1] The most severe health problems relate to sequelae of chronic infections, most importantly cirrhosis and liver cancer. The likelihood of developing a chronic infection is inversely related to age at the time of infection: approximately 90% for newborns, 30% for young children, and 6% for children older than five years.[2]

Chinese health authorities' efforts to curb HBV transmission prioritized infant vaccination in accordance with World Health Organization recommendations.[2-4] The infant vaccination schedule consists of a birth dose within 24 hours and two additional doses within the following six months.[5,6] This vaccination scheme effectively prevents mother-to-child transmission, which is the primary transmission route in high-endemic regions, and provides lifelong protection.[7-9]

The Chinese HBV vaccination policy has undergone substantial changes.[3,10,11] In 1992, the Ministry of Health recommended infant immunization, and parents were required to cover the expenses. Since 2002, the HBV vaccine has been offered for free under the national Expanded Program on Immunization (EPI), although parents were required to pay service fees. Since 2005, infant vaccination was offered at no cost.[10] Alongside these developments, extensive efforts to improve maternal health, including reduction of home births,[12,13] have helped to promote HBV vaccination.[14] Additional substantial efforts to prevent HBV infection have been made, including improved staff training, development of local vaccination delivery strategies, and increase in public awareness regarding HBV infection.[15-17] Nationwide, the number of infants who have received timely immunization has steadily increased, from approximately 60% in 2000 to 99% in 2009.[18] As a result, the infection rate among infants has reduced from approximately 10% in 1992 to 1.0% in 2006.[19-21] Catch-up vaccination has been recommended and performed at the national level, although additional efforts still appear to be required in rural areas.[9,10,19,22-25]

This study aimed to investigate the HBV vaccination coverage for the birth cohorts from 1997 to 2011, including many children who were born before the infant vaccination program achieved high implementation rates. We also intended to add to existing knowledge regarding the development of the Chinese HBV vaccination program for infants and to assess catch-up vaccination potential. We obtained data through a cross-sectional, questionnaire-based household survey in the rural areas of seven provinces. Our data supplemented previous studies based on nationwide sero-surveys,[4,21] administrative data at the county level,[11] or a combination of different data sources.[10] This approach also has a wider scope than household surveys from more limited geographical regions.[22]

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Supplemental data for this article can be accessed here.

Results

Table 1 shows the development of institutional birth rates and infant vaccination coverage rates. The rate of institutional births increased from 64.5% for the period 1997–1999 (i.e., the sample proportion was 0.645) to 81.6% for 2010–2011. The percentage of newborns who received the first HBV vaccination dose within 24 hours after birth increased from 50.4% for 1997–1999 to 84.0% for 2010–2011, while an additional 3.7–5.1% received the first dose within 48 hours. The percentage of infants receiving the third dose within the first year of life was 2.1–5.1% lower than the percentage of those receiving the first dose within the first 24 hours.

In the birth cohorts dating from 1997 to 2011, the male-to-female ratio was 1.107 (3,430 males and 3,099 females, 95% confidence interval (CI); 1.053, 1.161). For children born before the implementation of EPI (from 1997 to 2001), 53.5% of males and 52.1% of females received the first vaccination dose within 24 hours after birth, which is an insignificant difference in proportions (p = 0.536). After implementation of EPI (from 2001 to 2011), these rates had increased (77.0% for males, 75.8% for females, p = 0.355).

There was no significant difference between sexes regarding completed vaccinations in the first year of life. For the cohorts born from 1997 to 2001, 49.9% of males and 48.4% of females (p = 0.526) have completed vaccinations in the first year of life. For the cohorts from 2002 to 2009, these percentages were 70.3% and 72.0%, respectively, (p = 0.238).

Table 2 presents descriptive statistics for the independent variables. For the true transmission route index, the relative frequency of scores (0–5) was 0.296, 0.111, 0.184, 0.156, 0.124, and 0.130, implying that 29.6% of the respondents were unable to identify any actual transmission route. For the false transmission route index, the relative frequency of scores (0–2) was 0.452, 0.341, and 0.207.

The results from the two logistic regression analyses are presented in Table 3. All coefficients that were statistically significant (5% level) in the Timely Birth dose model were also significant in the Completed Vaccination model. Two additional coefficients were significant in the Completed Vaccination model (migration; birth year, 2001). All coefficients that were significant in both models had the same sign, and the largest difference in size was for Institutional Birth, which was notably higher in the Timely Birth Dose model (0.873) than in the Completed Vaccination model (0.528). All significant coefficients were positive, except for the negative effect of migration in the Completed Vaccination model. The similar logistic regression models estimated for three sub-groups (individuals born in the periods 1998–2001, 2002–2005, and 2006–2009) are reported in the online supplement. These results showed a similar pattern to the overall sample (Table 3), but the effects of the explanatory variables tended to be more significant for the older sub-group (1998–2001) than for the more recent sub-group.

Participants were asked whether they had received immunization at the time of the survey (Table 4). Overall, 83.4% answered: "yes, all doses"; 7.4% answered: "some, but not all doses"; 3.4% answered: "no"; and 5.8% answered: "do not know" (n = 6529). The combined percentage of people completely or partially vaccinated tended to increase gradually over time, while the percentage of unvaccinated or uncertain decreased.

Among individuals who had answered "some, but not all doses" (n = 481), 71.9% stated that they intended to be vaccinated in the future. Among individuals who answered "no" (n = 212) or "do not know" (n = 376), 43.9% and 45.5% of them, respectively, stated that they intended to be vaccinated in the future.

The sub-group of unvaccinated participants without future vaccination plans consisted of 85 individuals. If the vaccine were offered for free, 49.4% of respondents indicated that they would accept the free vaccine offer. This percentage increased when a compensation of 10 Yuan (64.7%) or 40 Yuan (68.2%) was offered, while higher compensation amounts did not increase willingness for vaccination.

Discussion

Numerous studies on the development of the Chinese HBV vaccination program have been undertaken. Notable contributions include three nationwide sero-surveys, a PhD thesis by Fuqiang Cui, and an evaluation of the Gavi vaccine alliance supportive efforts in the implementation of the HBV vaccine.[4,10,11,19,21] Studies have mainly focused on vaccination programs involving infants and young children, which is reasonable due to the elevated risk of severe consequences of HBV infections for these age groups. HBV vaccination for adults in rural areas has also been studied by our group, and HBV vaccinations in a large sero-survey among married men born in 1991 or earlier have also been examined.[26,27]

The current study adds to this literature by offering an independent source of information on the rural population. Previous studies have reported associations between socio-economic factors and HBV vaccine status, in other countries and in China,[28,29] as well as measures of Chinese parents' HBV related knowledge.[30] We are not aware of Chinese studies that have measured associations between HBV infant vaccination status and a similar variety of independent variables (income, parents' education, and knowledge level). It has

Table 1. Institutional births and infant hepatitis B vaccination coverage according to time after birth.*

		Institutional births	1st dose within 24 hours	1st dose within 48 hours	3rd dose within first year
Birth year	N	Percentage (%)	Percentage (%)	Percentage (%)	Percentage (%)
1997–1999	1168	64.5 (61.6, 67.2)	50.4 (47.5, 53.3)	54.6 (51.7, 57.5)	45.5 (42.6, 48.4)
2000–2002	1119	68.6 (65.8, 71.3)	59.6 (56.7, 62.5)	63.3 (60.4, 66.1)	57.5 (54.5, 60.4)
2003–2005	1240	72.2 (69.6, 74.7)	71.4 (68.8, 73.9)	75.1 (72.6, 77.5)	67.7 (65.1, 70.3)
2006–2007	1004	77.2 (74.5, 79.8)	76.6 (73.8, 79.2)	80.9 (78.3, 83.3)	73.1 (70.2, 75.8)
2008–2009	1065	81.4 (78.9, 83.7)	81.3 (78.8, 83.6)	85.6 (83.4, 87.7)	76.2 (73.6, 78.8)
2010–2011	702	81.6 (78.6, 84.4)	84.0 (81.1, 86.7)	89.2 (86.6, 91.4)	-

*Percentages according to birth year groups with 95% confidence intervals (in parentheses). Confidence intervals were calculated using the binomial distribution (exact).

Table 2. Variable definitions and descriptive statistics for regression variables (N = 5,625).

Variables	Definitions	Mean[a]	SD[b]
Institutional birth	Child born at township, county, or a higher-level hospital	.732	
Birth year 1997	Born in 1997	.053	
Birth year 1998	Born in 1998	.067	
Birth year 1999	Born in 1999	.064	
Birth year 2000	Born in 2000	.064	
Birth year 2001	Born in 2001	.055	
Birth year 2002	Born in 2002	.061	
Birth year 2003	Born in 2003	.059	
Birth year 2004	Born in 2004	.064	
Birth year 2005	Born in 2005	.073	
Birth year 2006	Born in 2006	.081	
Birth year 2007	Born in 2007	.078	
Birth year 2008	Born in 2008	.084	
Birth year 2009	Born in 2009	.087	
Birth year 2010	Born in 2010	.080	
Birth year 2011	Born in 2011	.031	
Male	Male	.525	
Father's education level	Education level, range 1-7[c]	2.88	.84
Mother's education level	Education level, range 1-7[c]	2.64	.87
Migration	At least one parent is a migrant worker	.418	
Income group 1	Income in 1st quintile[d]	.231	
Income group 2	Income in 2nd quintile[d]	.219	
Income group 3	Income in 3rd quintile[d]	.161	
Income group 4	Income in 4th quintile[d]	.207	
Income group 5	Income in 5th quintile[d]	.182	
True transmission route ind.	No. of identified true transmission routes; range, 0–5	2.09	1.76
False transmission route ind.	No. of identified false transmission routes; range, 0–2	.76	.77
Perceived protection 1	Vaccine is unknown or protection lasts <1 year	.379	
Perceived protection 2	Protection lasts between 1 and 5 years	.369	
Perceived protection 3	Protection lasts between 5 and 10 years	.106	
Perceived protection 4	Protection lasts between 10 and 20 years	.048	
Perceived protection 5	Protection lasts for more than 20 years	.099	

[a]Dichotomous variables have a value of 1 when the responses corresponded to the statements in the definitions column and a value of 0 otherwise (e.g., if a boy was born at home, then Male = 1 and Institutional birth = 0). Hence, the mean values of dichotomous variables represent sample proportions.
[b]SD is the standard deviation, for numerical variables.
[c]Education level, in increasing order: no schooling; primary school and below; junior middle school; senior middle school or technical school; junior college; undergraduate; postgraduate.
[d]The cut-off points were 2,750, 4,400, 6,667, and 10,000 Yuan per year.

Table 3. Logistic regression models for infant HBV vaccination status.

	Timely Birth Dose[a]			Completed Vaccination[b]		
	Coef.	Std. err.	P	Coef.	Std. err.	P
Institutional birth	0.873	0.070	0.000	0.528	0.071	0.000
Birth year 1998	0.154	0.165	0.351	0.248	0.164	0.130
Birth year 1999	0.086	0.167	0.607	0.236	0.165	0.153
Birth year 2000	0.410	0.168	0.015	0.463	0.165	0.005
Birth year 2001	0.221	0.174	0.203	0.650	0.172	0.000
Birth year 2002	0.615	0.172	0.000	0.774	0.169	0.000
Birth year 2003	0.930	0.178	0.000	1.002	0.173	0.000
Birth year 2004	0.891	0.174	0.000	0.953	0.169	0.000
Birth year 2005	1.018	0.171	0.000	1.233	0.168	0.000
Birth year 2006	1.075	0.167	0.000	1.203	0.163	0.000
Birth year 2007	1.299	0.176	0.000	1.403	0.169	0.000
Birth year 2008	1.222	0.171	0.000	1.514	0.169	0.000
Birth year 2009	1.370	0.174	0.000	1.261	0.164	0.000
Birth year 2010	1.383	0.178	0.000			
Birth year 2011	1.824	0.258	0.000			
Male	0.017	0.063	0.790	−0.058	0.063	0.360
Father's education level	0.008	0.045	0.859	−0.009	0.046	0.840
Mother's education level	0.269	0.045	0.000	0.235	0.045	0.000
Migration	−0.052	0.065	0.418	−0.165	0.065	0.011
Income group 2	0.432	0.092	0.000	0.459	0.093	0.000
Income group 3	0.364	0.101	0.000	0.486	0.102	0.000
Income group 4	0.489	0.097	0.000	0.537	0.097	0.000
Income group 5	0.458	0.101	0.000	0.459	0.101	0.000
True transmission route index	0.166	0.022	0.000	0.148	0.022	0.000
False transmission route index	−0.043	0.050	0.388	−0.032	0.050	0.525
Perceived protection 2	0.279	0.074	0.000	0.354	0.074	0.000
Perceived protection 3	0.373	0.113	0.001	0.482	0.113	0.000
Perceived protection 4	0.674	0.169	0.000	0.739	0.167	0.000
Perceived protection 5	0.507	0.120	0.000	0.643	0.119	0.000
Constant	−2.128	0.186	0.000	−2.051	0.187	0.000

The dependent variables were dichotomous. Coefficients (coef.), standard errors (Std.err), and two-sided p-values are reported.
[a]Basis outcome: had not received the first dose within 24 hours after birth (n = 5,625).
[b]Basis outcome: had not received completed vaccination within the first year of life (n = 5,001).

not been assessed previously to what extent there is a willingness for still unvaccinated children to participate in a continuation of the catch-up vaccination, but our group has made corresponding investigations for unvaccinated adults.[27]

Regarding infant vaccination, our results indicate that the HBV vaccination coverage rates and the rate of institutional births increased rapidly. In the early years (1997–2002), institutional birth rates tended to be higher than the timely birth dose rates, implying that birth at the hospital was not sufficient to begin the HBV immunization schedule. This finding is consistent with reports suggesting that health workers were initially reluctant to vaccinate children who were "perceived to be sick, weak, or of low birth weight".[17] Additional information concerning the relationship between HBV vaccination and place of birth has been reported by other studies.[12,15,16,19,31,32] Our results for the timely birth dose correspond well with the findings of the most recent national sero-survey, in particular for the younger cohorts, while our results show a consistently lower rate of completed vaccination in the first year of life.[21] Given that urban areas, where the vaccine was more readily available and coverage rates tended to be higher than in rural areas, were not part of our survey, it is likely that our coverage estimates would be lower than the national estimates.[15-17] One reason that may partly explain why there were more pronounced differences concerning completed vaccinations than for timely birth doses is that the former have higher indirect costs per vaccination dose than the latter.

Our male-to-female ratio of 1.112 appears high compared to the natural ratio of 1.04–1.05. High male-to-female ratios in China have been reported previously[33,34] and may result from a combination of sex-selective abortion and mistreatment of girls.[35-37] To the extent that neglect of girls may have been common, this could have resulted in a lower vaccination coverage for girls than for boys. However, in our sample regions, our findings suggest that HBV vaccination coverage

Table 4. Vaccination status at the time of the survey.*

		Completed immunization	Partial immunization	Uncertain	No immunization
Birth year	N	Percentage (%)	Percentage (%)	Percentage (%)	Percentage (%)
1997–1999	1,273	74.9 (72.5, 77.3)	7.7 (6.3, 9.3)	9.5 (7.9, 11.3)	7.9 (6.4, 9.5)
2000–2002	1,154	82.6 (80.3, 84.7)	6.4 (5.1, 8.0)	6.3 (5.0, 7.9)	4.7 (3.5, 6.1)
2003–2005	1,272	88.3 (86.4, 90.0)	4.6 (3.5, 5.9)	4.9 (3.8, 6.2)	2.3 (1.5, 3.3)
2006–2007	1,027	91.0 (89.1, 92.7)	2.4 (1.6, 3.6)	5.0 (3.7, 6.5)	1.6 (0.9, 2.5)
2008–2009	1,085	91.2 (89.3, 92.8)	3.8 (2.7, 5.1)	3.9 (2.8, 5.2)	1.2 (0.6, 2.0)

*Percentages according to birth year groups with 95% confidence intervals (in parentheses). Confidence intervals were calculated using the binomial distribution (exact).

rates did not vary greatly between sexes, neither before nor after the implementation of EPI.

The two logistic regression models had similar coefficients, with three notable exceptions. First, the effect of Institutional Birth was higher for the timely birth dose (0.873) than for the Completed Vaccination model (0.528). Thus, Institutional Birth increased the likelihood of recommended vaccination, but more so for the birth dose than for the complete vaccination schedule. Second, having migrant workers as parents did not affect the likelihood of a timely birth dose, but it reduced the likelihood of completed vaccination. Third, the positive effects of the income group variables, implying lower coverage in the lowest income group, were more pronounced in the Completed Vaccination model.

These differences may have resulted from differences in indirect vaccination costs (travel costs or lost working time for parents). In cases the birth dose was available at the local birth clinic, the indirect costs would be negligible. In contrast, administration of the third dose required a separate trip to the vaccination site and in particular, poor or migrant parents could consider this additional need as less pressing than the need for assistance at the time of birth.

In both models, the birth cohort coefficients showed an increasing trend in vaccination coverage while sex (male) was an insignificant factor. The father's educational level was insignificant, but the mother's educational level was positively associated with the vaccination coverage. The true transmission route index showed significantly positive effects, suggesting that more accurate knowledge of transmission routes (recognizing true transmission routes) helped to increase vaccination rates. The causality for such an association may also be inversely related, that is, families with fully vaccinated children learned more about HBV transmission during the vaccination process. The perceived protection variables tended to be positively associated with higher coverage rates. However, only 10.3% perceived that protection lasts more than 20 years (Table 2), which is the most correct alternative, suggesting that the information provided to parents during the vaccination process could be improved.

As with our previous study involving adults, we attempted to measure the effects of economic barriers associated with vaccination (i.e., user fees for vaccination, time spent on traveling or waiting at the vaccination site, and travel costs). However, this aspect of statistical modeling proved difficult to measure precisely. This was most likely due to the EPI increasing efforts to reach children who otherwise should travel long distances, thus generating a trend confounding our estimated effects of traveling time and costs. Moreover, for the more recent birth cohorts, the majority of respondents reported no user fees, while some reported high vaccination fees, indicating that the latter had chosen expensive imported vaccines rather than the free of charge, domestically produced vaccines. Unlike our study in adults, for which the HBV vaccination policy has developed less rapidly, we were unable to obtain reliable estimates for direct and indirect costs for infant vaccination. Thus, we omitted these variables from our analysis, but this did not notably affect the estimated coefficients reported in Table 3.

Patterns corresponding to the overall results in Table 3 were found for the sub-groups classified according to birth year (online supplement); however, for example, the income variables had more significant coefficients in the earlier sub-group (children born from 1998 to 2001) than in the recent sub-group (children born from 2006 to 2009). In our view, this was likely due to the development of vaccination policies that gradually reduced low-income household barriers to vaccination, thus rendering the HBV vaccine less expensive and universally available.

In the Chinese setting, catch-up HBV vaccination is clearly beneficial for immunized individuals, and also offers indirect protection to those who remain susceptible to HBV. In the age group of 15–29 years, the most recent national sero-survey, conducted in 2014,[21] reported that the prevalence of hepatitis B surface antigen (HbsAg, a marker of current infection, acute or chronic) and hapatitis B core antigen (anti-HBc, a marker of current or previous infection) was 4.4% and 22.5%, respectively. Thus, only 19.6% of people exposed to HBV (anti-HBc positive) were currently infected (HbsAg positive). In contrast, between 80% and 90% of children infected in their first year of life are generally expected to develop chronic infection. This may indicate that a notable portion of individuals aged between 15 and 29 years in 2014 had been infected after infancy. Catch-up HBV vaccination has been recommended as a general strategy where resources are available,[38] and where the tradeoff between costs and health benefits are likely to be in favor of HBV vaccination in China, even with relatively high existing coverage rates.[23]

In agreement with such recommendations, Chinese health authorities conducted a national catch-up HBV vaccination program from 2009 to 2011.[39,40]. This program succeeded in increasing the coverage rates, which can also be observed in our results. In the birth cohorts from 1997 to 1999, only 45.5% were completely vaccinated within the first year of life (Table 1), while 74.9% had completed vaccination at the time of the survey (Table 4). The coverage level was higher for the younger cohorts, but even for the 2008–2009 period, approximately 10% of children were not completely vaccinated. Overall, our results are comparable to a study conducted in

rural China in 2011 that found that 12% of children aged below 16 years had not been immunized.[22]

For children who had not been completely vaccinated, a willingness for further HBV vaccination was generally positive. Even for those who were unvaccinated and without plans for further vaccination, a relatively small monetary compensation to cover indirect costs would encourage more than two-thirds of them to become vaccinated. Similar results have been found for unvaccinated adults.[27]

Our study had three main limitations. First, our measure of vaccination status was potentially subject to recall bias because vaccination cards were not always available.[4,20–22] Second, the parents' educational levels, migration status and income were measured as of the time of survey (2011–2012) and not as of the time when their children were eligible for infant vaccination (1997–2011). For educational level, this difference in timing may have little effect, if most parents in rural areas reached their highest educational level before they had children. Third, we have reported unweighted results because the exact sampling weights were unknown and, thus, the results may not provide a fully accurate representation of the rural population in the sampled provinces.

Materials and methods

Study population and sampling procedure

We developed a questionnaire and performed a cross-sectional household survey using trained staff. The sample was obtained from 45 rural villages in seven provinces (Hainan, Hebei, Heilongjiang, Henan, Jiangsu, Ningxia, and Shandong). Stratification was performed at the county level (low, medium, or high level of economic development) and village level (short, medium, or long travel distance to vaccination site). The benefit of including more villages was balanced against the increased administrative costs of surveying more villages. In small villages, all households were invited, while in larger villages, households were selected randomly (probability proportional to size).

Contact with local health agencies and village leaders was established prior to the survey. A team from Shandong University coordinated and participated in data collection at all survey sites. Local students, familiar with local customs and dialects, were recruited and trained to support face-to-face interviews. The response rate was 82%, and the main reason for non-participation was that all family members had migrated to industrialized regions.

The questionnaire contained one section specifically aiming at children 15 years old or younger, who constituted our population of interest. This part of the questionnaire included items on child's place of birth, child vaccination according to the recommended schedule, and background variables such as parents' occupation and education level as of the time of survey. Questions were answered by a household member most familiar with the household situation, often with other household members present.

The survey was performed between 2011 and 2012, over a 16-month period; however, for practical reasons the survey in each geographical area was completed within two to three weeks. Therefore, individuals born from 1996 to 2012 (n = 6,940) would be 15 years old or younger at the time of the survey, and that geographical sample weights differed for the youngest and oldest birth cohorts. To reduce the influence of varying sample weights, we limited the analyses of birth-related events to the birth cohorts from 1997 to 2011 (n = 6,529), while the analyses of subsequent events were limited to the 1997–2009 cohorts (n = 5,811).

We performed two logistic regression analyses for infant vaccination outcomes. Observations with missing values were excluded from these regressions, yielding effective sample sizes of 5,625 (1997–2011) and 5,001 (1997–2009). The coefficients in the logistic regressions can be translated to odds ratios using the anti-log. For instance, the coefficient of male sex in the completed vaccination model (−0.058) implies that the corresponding odds ratio is exp(−0.058) = 0.944. We also performed logistic regression analysis for three sub-groups, consisting of individuals born in three four-year periods, namely, 1998–2001, 2002–2005, and 2006–2009. Exact sample weights were unknown, and only unweighted analyses were performed. All statistical analyses were performed in Stata 13. The logistic regressions were estimated by maximum likelihood (Stata's logit procedure) and the statistical inference was based on the large sample theory (normal approximation).

Measures

We first investigated variables related to the infant vaccination program, including whether the child was born at home or at a hospital. It has been reported that "boy preference" is common in China; therefore, we tested whether there were significant sex differences in HBV vaccination.

Two dependent regression variables measured whether the child had received a first HBV vaccination dose within 24 hours after birth, and whether the child had received all three HBV vaccination doses in the first year of life. This information was obtained from vaccination cards or self-reports.

The independent regression variables are presented in Table 2. For each child, we recorded whether the place of birth was at an institution or at home (the variable "Institutional Birth"), birth year, and sex. We recorded the educational level of the parents and whether any of the parents were migrant workers living away from their family. Household per capita income was transformed into income groups.

Knowledge regarding HBV transmission was measured through interrogation of seven routes of HBV transmission to participants. Five alternatives were actual transmission routes (a child may be infected during birth if the mother was infected; use of unclean medical or dental equipment; unprotected sex; unhygienic practices of tattooing or ear-piercing; and sharing shaving equipment with an infected person) and two were false transmission routes (eating with HBV patients or HBV carriers; and mosquito or insect bites). One index counted the number of actual transmission routes correctly identified; a second index counted the number of false transmission routes erroneously identified.

Respondents' knowledge of the HBV vaccine was categorized into either one group unaware of the vaccine or believing that protection lasted for less than one year (Perceived protection 1), or four groups knowing about the vaccine but with various opinions about the duration of protection.

We also investigated the HBV vaccination status at the time of survey, and potential vaccination plans for those who were unvaccinated. For unvaccinated individuals without vaccination plans, a hypothetical situation was presented: "Suppose the vaccination was free and there was no service fee. Suppose also that you were offered a fixed sum reimbursement per dose to compensate for travel costs, lost working hours, and other inconveniences." A sequence of questions followed: "If the fixed sum reimbursement was X yuan per dose would you then take the vaccine?" where X was raised sequentially (values: 0, 10, 20, 40, 60, 80, 100) until the participants answered "Yes" or refused the highest offer. This part of the questionnaire was revised after initiating the survey in the Henan region; therefore, we excluded the initial responses from the Henan region.

Thus, in rural areas, substantial percentages of the 1997–2011 birth cohorts had not received infant HBV vaccinations as recommended. A catch-up vaccination program has improved coverage rates, but further vaccination efforts are still required. It is likely that most individuals who remained unvaccinated would accept a catch-up vaccination if it were offered.

Ethics and institutional approval

Participants were informed that participation was voluntary, and potentially sensitive questions were not included in the questionnaire. All study participants were informed that they could refuse to answer any questions. This project was conducted in accordance with the Statistics Law of the People's Republic of China, and has been reviewed and approved by the Medical Ethics Committee at the Shandong University School of Medicine (Grant No. 201001052).

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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Availability of materials and data

The dataset analyzed during the current study is available from Knut R. Wangen on reasonable request.

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