A mathematical model of hepatitis B virus transmission and its application for vaccination strategy in China

Shoujun Zhao, Zhiyi Xu and Ying Lu

Background
Before universal infant immunization against hepatitis B virus (HBV) in 1986 China was a region endemic for HBV infection. The prevalence of HBV infection in the population was about 60% and the proportion of chronic HBV carriers around 10%. These HBV carriers could progress to chronic hepatitis B, cirrhosis, and primary hepatocellular carcinoma. Since 1976, large-scale sero-surveys of HBV infection have been carried out and a lot of data have been collected.

Method
This paper describes a mathematical model developed to predict the dynamics of HBV transmission and to evaluate the long-term effectiveness of the vaccination programme. We used a compartment model expressed by a set of partial differential equations based on the characteristics of HBV infection.

Results
All parameters, expressed in the model as a non-linear function of age and time since vaccination, were estimated using sero-survey data. The model fits well with both pre-vaccination and post-vaccination sero-surveys. The observed and estimated age-specific prevalence rates of HBV infection and HBV carriage agree with each other. According to our model, if all newborns are vaccinated according to schedule, the rate of HBV carriage will decline sharply over time to 0.2% in 70 years. By then, the ratio of acute hepatitis B will be less than 0.5% and the ratio of chronic hepatitis B will be around 5%.

Conclusions
The results suggest that HBV infection in China can be controlled in just one generation, and eventually eliminated. Our model shows that vaccination coverage is the most important indicator for the elimination of HBV transmission. The higher the vaccination coverage, the better the long-term effectiveness of immunization. Thus, the key to controlling and eliminating HBV transmission in China is to find ways to immunize all infants throughout the country, especially in poor, rural areas.

Keywords
Hepatitis B, compartment models, differential equation, epidemiology, infectious diseases, hepatitis B vaccination, immunization strategy

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In China and other Asian countries, hepatitis B virus (HBV) infection has been a major public health problem. The prevalence of HBV infection in China was around 60% and the proportion of chronic HBV carriers as high as 10%. Before the vaccination programme, these HBV carriers could progress to chronic hepatitis B, cirrhosis, and primary hepatocellular carcinoma. The development of the hepatitis B vaccine was a landmark in the control and elimination of HBV infection in humans. In China prior to 1986, most HBV infections occurred in infancy and early childhood. In 1986, China implemented a large-scale programme to immunize all newborns against HBV. This programme has resulted in enormous social and economic benefits. In children under 10 years old, the proportion carrying HBV has decreased to 0.53% in Shanghai. In some rural areas HBV carriage has been reduced to 1–2%, as long as all newborns are vaccinated with a low dose programme (10μg × 3) according to the schedule. However, the long-term effectiveness of the programme in China still needs to be evaluated. It is very important to understand changes in the dynamics of HBV transmission following implementation of
the programme, and the ways that best control and eliminate HBV infection in the population throughout China. The aim of this study was to establish a mathematical model for HBV transmission dynamics so it can be used for predicting the long-term effectiveness of the immunization programme and help in selecting optimal strategies for nationwide HBV immunization.

**Materials and Methods**

**A compartment model**

A compartment mathematical model expressed by a set of first-order partial differential equations was developed. Based on the characteristics of HBV transmission, the population was divided into five compartments: (1) susceptibles \( S(a,t) \); (2) latent period \( L(a,t) \); (3) temporary HBV carriers \( T(a,t) \); (4) chronic HBV carriers \( C(a,t) \); and (5) the immune \( I(a,t) \). Here ‘a’ represents the age and ‘t’ represents the length of follow-up. Of the five stages, compartments 3 and 4 are infectious. According to the natural history of HBV, a susceptible subject acquires HBV by direct contact with a temporary HBV carrier state. More specifically, the model parameters were defined as follows:

- \( \lambda(a,t) \): the force of infection.
- \( \alpha \): the rate of transition from latent period to temporary HBV viraemia.
- \( \beta(a) \): the risk of transient viraemia progressing to chronic HBV carrier state.
- \( \epsilon \): the rate of transition from temporary HBV viraemia to immune per time unit.
- \( \nu(a) \): the rate of HBV clearance in chronic HBV carriers.
- \( \tau(a) \): the mortality rate of HBV related diseases.
- \( \mu(a) \): the age-specific mortality rate of non-HBV related diseases.
- \( V_c(a,t) \): the effectiveness of hepatitis B vaccine immunization.

The five compartments and model variables are illustrated in Figure 1. More specifically, the model parameters were defined as the following: \( \lambda(a,t) \) is the force of infection; \( \alpha \) is the rate of transition from latent period to temporary HBV viraemia; \( \beta(a) \) is the risk of transient viraemia progressing to chronic HBV carriage; \( \epsilon \) is the rate of transition from temporary HBV viraemia to immune per time unit; \( \nu(a) \) is the rate of HBV clearance in chronic HBV carriers; \( \tau(a) \) is the mortality rate of HBV related diseases; \( \mu(a) \) is the age-specific mortality rate of non-HBV related diseases; \( V_c(a,t) \) is the effectiveness of hepatitis B immunization. These parameters must satisfy the following partial differential equations (1):

\[
\begin{align*}
\frac{\partial S(a,t)}{\partial a} + \frac{\partial S(a,t)}{\partial t} &= -[\lambda(a,t) + V_c(a,t) + \mu(a)] \cdot S(a,t) \\
\frac{\partial L(a,t)}{\partial a} + \frac{\partial L(a,t)}{\partial t} &= \lambda(a,t) \cdot S(a,t) - [\alpha + \mu(a)] \cdot L(a,t) \\
\frac{\partial T(a,t)}{\partial a} + \frac{\partial T(a,t)}{\partial t} &= \alpha \cdot L(a,t) - [\beta(a) + \epsilon + \mu(a)] \cdot T(a,t) \\
\frac{\partial C(a,t)}{\partial a} + \frac{\partial C(a,t)}{\partial t} &= \beta(a) \cdot T(a,t) - [\nu(a) + \tau(a) + \mu(a)] \cdot C(a,t) \\
\frac{\partial I(a,t)}{\partial a} + \frac{\partial I(a,t)}{\partial t} &= V_c(a,t) - \epsilon \cdot T(a,t) + \nu(a) \cdot C(a,t) - \mu(a) \cdot I(a,t)
\end{align*}
\]
Epidemiological data sets

Data from the following studies were used in this paper to estimate the model parameters. More detailed descriptions of these studies are given in the Appendix.

1. A cross-sectional sero-epidemiological survey of HBV markers in 10 484 subjects, aged 0–70 years in four provinces (Hebei, Hunan, Heilongjiang and Henan) of China, in 1985.1,26
5. Age-specific mortality rates in China 1990.23,30
6. Ten-year follow-up studies of vaccination effectiveness data in newborn babies were used to evaluate the precision of the model prediction.7–10

All the parameters in the model were estimated by the maximum likelihood method based on the data from the above epidemiological surveys.31,32

Results

Estimation of model parameters

Parameter \( \lambda(a,t) \), the force of HBV infection, is the instantaneous per capita rate for susceptibility of acquiring the infection at age \( a \) and time \( t \). At the start of vaccination (\( t = 0 \)), this parameter, \( \lambda(a,0) \), can be derived based on data set 1. The estimating parameter equation of \( \lambda(a,0) \) is:

\[
\lambda(a,0) = \begin{cases} 
0.13074116 - 0.01362531a + 0.00046463a^2, & 0 \leq a \leq 47.5, \\
0.00000489a^3, & a > 47.5 
\end{cases}
\]

The estimated prevalence of HBV infection coincided well with the field survey data (Table 1, \( \chi^2 = 8.6497 \), d.f. = 10, \( P = 0.5656 \)). Figure 2a shows the parameter \( \lambda(a,0) \). It peaked in infancy and early childhood, declined rapidly with age, dropped to a low level at age 15 and remained at that level afterwards.1,26 The peak has mainly been associated with maternal-infant transmission and improperly sterilized needles and syringes in China.1,4–6,33

Parameter \( \alpha \) is designated as the rate of transition from latent period to temporary HBV viraemia. Assuming that the rate per time unit for a shift from latent to temporary viraemia is constant for the entire latent period, the average time of the shift should be \( 1/\alpha \).17–19 There are two ways of leaving the latent state; either moving to temporary viraemia or dying of other diseases. Thus, this parameter was calculated based on the average latent time, \( 1/\alpha \), and the mortality rate, \( m(a) \). The estimated average latent time was 1.5 months.

Parameter \( b(a) \), the risk of temporary HBV viraemia progressing to chronic HBV carriage, described the relationship between age of infection and development of chronic HBV carriage. Based on data set 2, we estimated the parameter equation as follows (Table 2, \( \chi^2 = 4.14 \), d.f. = 5, \( P = 0.5296 \)):

\[
P(a,0) = 1 - \exp\left[ -\int_0^a \lambda(a,0)da \right]
\]

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\[
b(a) = 0.706004\exp(-0.78771a) + 0.084648
\]

The risk was a function of age and was very high in infancy but remained at a low level after 5 years of age (Figure 2b).27,28,34 There are three ways of leaving the state of temporary HBV viraemia: becoming immune, or a chronic HBV carrier and death from the causes other than HBV related diseases. Let \( e \) be the rate of transition from temporary HBV viraemia to immune.

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### Table 1
Comparison of values estimated by parameter equation 3 with observed prevalence of hepatitis B virus (HBV)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Observations No.</th>
<th>HBV infection No.</th>
<th>Age-specific estimated prevalence of HBV</th>
<th>HBV infection estimated by model No.</th>
<th>Prevalence estimated by model</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>131</td>
<td>20</td>
<td>0.1527</td>
<td>15.29</td>
<td>0.1167</td>
</tr>
<tr>
<td>1–2</td>
<td>229</td>
<td>50</td>
<td>0.2183</td>
<td>48.04</td>
<td>0.2098</td>
</tr>
<tr>
<td>2–3</td>
<td>542</td>
<td>152</td>
<td>0.2804</td>
<td>154.28</td>
<td>0.2847</td>
</tr>
<tr>
<td>3–4</td>
<td>506</td>
<td>188</td>
<td>0.3715</td>
<td>199.70</td>
<td>0.3947</td>
</tr>
<tr>
<td>4–5</td>
<td>551</td>
<td>256</td>
<td>0.4555</td>
<td>258.00</td>
<td>0.4682</td>
</tr>
<tr>
<td>5–6</td>
<td>469</td>
<td>256</td>
<td>0.3458</td>
<td>242.92</td>
<td>0.5180</td>
</tr>
<tr>
<td>6–7</td>
<td>1289</td>
<td>725</td>
<td>0.5625</td>
<td>733.88</td>
<td>0.5693</td>
</tr>
<tr>
<td>7–8</td>
<td>1113</td>
<td>698</td>
<td>0.6271</td>
<td>668.11</td>
<td>0.6003</td>
</tr>
<tr>
<td>8–9</td>
<td>898</td>
<td>524</td>
<td>0.5835</td>
<td>548.48</td>
<td>0.6108</td>
</tr>
<tr>
<td>9–10</td>
<td>887</td>
<td>565</td>
<td>0.6370</td>
<td>549.11</td>
<td>0.6191</td>
</tr>
<tr>
<td>10–11</td>
<td>972</td>
<td>590</td>
<td>0.6070</td>
<td>616.57</td>
<td>0.6343</td>
</tr>
<tr>
<td>11–12</td>
<td>672</td>
<td>457</td>
<td>0.6801</td>
<td>442.06</td>
<td>0.6578</td>
</tr>
<tr>
<td>12–13</td>
<td>507</td>
<td>364</td>
<td>0.7180</td>
<td>346.81</td>
<td>0.6841</td>
</tr>
<tr>
<td>13–14</td>
<td>1718</td>
<td>1211</td>
<td>0.7049</td>
<td>1213.30</td>
<td>0.7062</td>
</tr>
</tbody>
</table>

\( \chi^2 = 8.6497 \), d.f. = 10, \( P = 0.5656 \).
of the transient viraemia. Thus, the average time of a transition is $1/\epsilon$. This parameter was calculated based on $1/\epsilon$, $\beta(a)$ and $\mu(a)$. The estimated average time of transition was 3 months.\(^{16-19}\)

Parameter $\lambda(a)$ is designated as the rate of HBV clearance in chronic HBV carriers. A follow-up study (data set 3) had shown that there were significant differences in the rates of reversion from HBV carrier to negativity among different age groups. The rate after age 50 is much higher than before 50. No reversion was observed in people 0–4 years old. A low reversion level was observed in people 5–45 years old. A high rate of reversion in the elderly has not been reported in the literature and can be explained by the sudden decrease in HBV carriers after age 50. It also provides an interpretation for self-limitation of chronic HBV infection proposed by Szmuness (Figure 2c).\(^{22}\)

Parameter $\tau(a)$ is the mortality rate of HBV related diseases, such as chronic hepatitis B, cirrhosis, and primary hepatocellular carcinoma, among the chronic HBV carriers. It was estimated using the data of age-specific mortality rates from data set 4 (Figure 2d).\(^{29}\)

Parameter $\mu(a)$ is the age-specific mortality rate of non-HBV related diseases. It was estimated using the age-stratified death notification data (data set 5).\(^{23,30}\)

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**Table 2** Comparison of values estimated by parameter equation 4 with observed data

<table>
<thead>
<tr>
<th>Age group</th>
<th>HBV infection</th>
<th>HBsAg(^a) carrier</th>
<th>Carriers estimated by model</th>
<th>$\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>No.</td>
<td>Ratio</td>
<td>No.</td>
<td></td>
</tr>
<tr>
<td>0–77</td>
<td>77</td>
<td>61</td>
<td>0.7922</td>
<td>60.88</td>
</tr>
<tr>
<td>1–47</td>
<td>47</td>
<td>13</td>
<td>0.2766</td>
<td>14.16</td>
</tr>
<tr>
<td>2–62</td>
<td>62</td>
<td>10</td>
<td>0.1613</td>
<td>8.03</td>
</tr>
<tr>
<td>5–74</td>
<td>74</td>
<td>5</td>
<td>0.0676</td>
<td>6.41</td>
</tr>
<tr>
<td>10–74</td>
<td>54</td>
<td>5</td>
<td>0.0926</td>
<td>4.57</td>
</tr>
<tr>
<td>20–46</td>
<td>25</td>
<td>4</td>
<td>0.1600</td>
<td>2.12</td>
</tr>
<tr>
<td>30–54</td>
<td>30</td>
<td>4</td>
<td>0.1333</td>
<td>2.54</td>
</tr>
<tr>
<td>40–62</td>
<td>46</td>
<td>2</td>
<td>0.0435</td>
<td>3.89</td>
</tr>
<tr>
<td>Total</td>
<td>415</td>
<td>104</td>
<td>0.2506</td>
<td>102.59</td>
</tr>
</tbody>
</table>

\(^a\) Hepatitis B virus surface antigen. 

$\chi^2 = 4.14$, d.f. = 5, $P = 0.5296$. 

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**Figure 2** Model parameters estimated using the data from sero-epidemiological surveys
Finally, parameter $V_c(a,t)$ is the effectiveness of hepatitis B vaccine immunization at age $a$ and time $t$ and was estimated based on dataset 6,8–10

**Model evaluation**

Based on the parameters estimated above, we calculated all the probabilities in the model (1), including $S(a,t)$, $L(a,t)$, $T(a,t)$, $C(a,t)$ and $I(a,t)$, at age $a$ and time $t$, by the integral of the partial differential equations. These estimates fit the dynamics of HBV transmission in the population during the pre-vaccination period. The observed and estimated values for the age-specific prevalence rates of HBV and for the proportion of HBV carriers in the population were all very close and the model corresponded well with the sero-epidemiological surveys (Figure 3) before the vaccination programme. It is interesting to show that the model successfully simulated not only the age-specific HBV carrier rates observed in the 1985 sero-surveys in four provinces, but also those observed in the 1978 sero-surveys among 176,068 subjects in all 29 provinces of China (Figure 3b).1,2

We applied the following formula proposed by Anderson13,15 to estimate the force of the HBV infection after vaccination:

$$\lambda(a,t) = \int_0^a \beta(a',a) [T(a',t) + C(a',t)] da'$$

(5)

Different WAIFW (Who Acquires Infection From Whom) matrices were created to determine the term $\beta(a',a)$, and the best WAIFW matrix which predicted the age-specific proportions of HBV infection and carriers at baseline and after vaccination for 10 years, was selected (Figures 3 and 4). Because $\lambda(a,t)$ is concomitant with the mass vaccination year by year, the dynamics of HBV transmission can be simulated under the model 1. The model-predicted proportions of HBV carriers in the population were in agreement with the proportions observed among randomly sampled vaccinated children (Figure 4).

**Prediction of long-term effectiveness of hepatitis B vaccination**

Since the model can fit HBV transmission dynamics before and after vaccination, we utilized it to predict the long-term effectiveness of hepatitis B immunization and to depict the transmission dynamics of HBV in the population.

The proportion of HBV carriers in a vaccinated cohort will decrease sharply depending on both the coverage of immunization and the doses received by infants,7–10,35,36 If all newborn babies are immunized according to the schedule set in Shanghai, the proportion of HBV carriage in immunized children will decrease to 0.53%.7,8,10,37 In some urban or rural areas with the low dose schedules, the proportion will also decrease to a low level of 1–2%.9,10 Table 3 shows the predicted proportions of HBV carriers following the immunization programme with 100% coverage in the population and Figure 5 illustrates the dynamics of HBV carriers. The majority of HBV carriers will shift gradually in age from children to the elderly and fade away in 70 years. After the vaccination programme has been implemented for 70 years, the average HBV carrier rate will decrease to 0.2%. Since the HBV carrier state lasts for many years and the annual rate of HBV clearance in chronic carriers less than 50 years old was as low as 1–2%, the reduction in the HBV carrier rate among those unvaccinated adults will remain until all carriers die. Of course, if a new drug can be developed to cure chronic HBV carriage, the time it takes to control HBV transmission will be shorter than our estimates.

To assess the impact of vaccination on the future incidence of acute and chronic hepatitis B, we defined two incidence ratios for acute and chronic hepatitis B as functions of age and time since vaccination. The incidence of acute disease can be considered as a linear function of proportion of new acute HBV infection. The incidence of chronic hepatitis B is a function of proportion of chronic HBV carriers because almost all attacks of chronic hepatitis B were a reactivation of the chronic carrier status.16,17

![Figure 3](image3.png)  
**Figure 3** Prevalence of hepatitis B virus (HBV) infection and HBV carriage rate by age

![Figure 4](image4.png)  
**Figure 4** Hepatitis B virus carriage rate in vaccinated children
The first ratio is the incidence ratio of acute hepatitis B, \( R_{a_1,a_2:t} \). It is defined as the number of acute cases in the age range from \( a_1 \) to \( a_2 \) at time \( t \) divided by the corresponding number of acute cases at \( t = 0 \), the baseline before vaccination. Mathematically,

\[
R_{a_1,a_2:t} = \frac{\int_{a_1}^{a_2} T(a,t)da}{\int_{a_1}^{a_2} T(a,0)da} \quad (6)
\]

The range in equation (6) has been defined as \( a_1 = 10 \) and \( a_2 = 45 \), because the peak of the incidence curve for acute hepatitis B was observed in the age interval 10–45 years old. Incidence in other age groups is very low.\(^{16,17}\) The \( R_{a_1,a_2:t} \) at time \( t \) with different vaccination coverage is shown in Figure 6. It decreases steeply at the beginning of the hepatitis B vaccination programme. The higher the vaccination coverage level, the steeper the decrease. The decrease slows down in a few years after the start of the vaccination programme. At a coverage rate of 100\%, the ratio will be reduced from 1 to less than 0.5% 70 years from the start of the vaccination programme.

The incidence ratio of chronic hepatitis B, \( R_{c_1,c_2:t} \) is defined as the number of chronic HBV carriers in the age range from \( c_1 \) to \( c_2 \), at time \( t \) divided by the corresponding number of chronic HBV carriers at \( t = 0 \), the baseline before vaccination. Mathematically

\[
R_{c_1,c_2:t} = \frac{\int_{c_1}^{c_2} C(a,t)da}{\int_{c_1}^{c_2} C(a,0)da} \quad (7)
\]

In equation (7), \( c_1 = 25 \) and \( c_2 = 70 \). Most chronic liver diseases were observed in adults \( \geq 25 \) years. The disease incidence in the younger age group was negligible.\(^{16,17}\) The \( R_{c_1,c_2:t} \) at time \( t \) with different vaccination coverage, is shown in Figure 7. It remained almost unchanged at the beginning of the vaccination programme, and dropped rapidly only after 25 years of immunization. Again, the decrease in the ratio

<table>
<thead>
<tr>
<th>Age group</th>
<th>Baseline</th>
<th>5 years</th>
<th>10 years</th>
<th>15 years</th>
<th>20 years</th>
<th>30 years</th>
<th>40 years</th>
<th>50 years</th>
<th>60 years</th>
<th>70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–</td>
<td>0.0400</td>
<td>0.0030</td>
<td>0.0027</td>
<td>0.0025</td>
<td>0.0023</td>
<td>0.0017</td>
<td>0.0012</td>
<td>0.0007</td>
<td>0.0003</td>
<td>0.0001</td>
</tr>
<tr>
<td>1–</td>
<td>0.0976</td>
<td>0.0074</td>
<td>0.0068</td>
<td>0.0063</td>
<td>0.0058</td>
<td>0.0044</td>
<td>0.0030</td>
<td>0.0018</td>
<td>0.0009</td>
<td>0.0003</td>
</tr>
<tr>
<td>2–</td>
<td>0.1171</td>
<td>0.0091</td>
<td>0.0083</td>
<td>0.0077</td>
<td>0.0071</td>
<td>0.0055</td>
<td>0.0038</td>
<td>0.0023</td>
<td>0.0011</td>
<td>0.0004</td>
</tr>
<tr>
<td>3–</td>
<td>0.1225</td>
<td>0.0097</td>
<td>0.0088</td>
<td>0.0082</td>
<td>0.0075</td>
<td>0.0059</td>
<td>0.0041</td>
<td>0.0025</td>
<td>0.0013</td>
<td>0.0005</td>
</tr>
<tr>
<td>4–</td>
<td>0.1241</td>
<td>0.0099</td>
<td>0.0090</td>
<td>0.0083</td>
<td>0.0077</td>
<td>0.0061</td>
<td>0.0043</td>
<td>0.0026</td>
<td>0.0014</td>
<td>0.0006</td>
</tr>
<tr>
<td>5–</td>
<td>0.1261</td>
<td>0.1132</td>
<td>0.0093</td>
<td>0.0086</td>
<td>0.0079</td>
<td>0.0064</td>
<td>0.0045</td>
<td>0.0028</td>
<td>0.0015</td>
<td>0.0006</td>
</tr>
<tr>
<td>6–</td>
<td>0.1246</td>
<td>0.1165</td>
<td>0.0093</td>
<td>0.0086</td>
<td>0.0079</td>
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<td>0.0047</td>
<td>0.0029</td>
<td>0.0016</td>
<td>0.0007</td>
</tr>
<tr>
<td>7–</td>
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<td>0.1176</td>
<td>0.0094</td>
<td>0.0086</td>
<td>0.0080</td>
<td>0.0066</td>
<td>0.0048</td>
<td>0.0031</td>
<td>0.0017</td>
<td>0.0007</td>
</tr>
<tr>
<td>8–</td>
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<td>0.1184</td>
<td>0.0096</td>
<td>0.0087</td>
<td>0.0081</td>
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is closely related to vaccination coverage. At 100% vaccination coverage, the ratio will be around 5% 70 years from the start of the vaccination programme.

Discussion and Conclusion

Hepatitis B virus is highly prevalent and control of HB is a major public health concern in China. Since the assays of HBV markers were developed, the prevalence and incidence rates as well as the age distribution of HBV infection and HBV carriage have remained very similar across most provinces of China for decades. This stable state, expressed as ‘equilibrium’ between the virus and human population, has provided good opportunities for using the mathematical models to study the disease’s dynamics.1,2

Much field data were accumulated and can be used to develop appropriate mathematical models. Results of several large-scale population studies based on sero-surveys as well as special follow-up studies were analysed, which allowed us to successfully estimate the model parameters. The correspondence of these parameters to the observed field data is demonstrated in Figures 2–4.

The model has simulated well, not only HBV transmission dynamics, but also the proportion of age-specific HBV carriers obtained from two large-scale, cross-sectional sero-surveys undertaken 7 years apart (Figure 3). It is also a powerful tool to study the impact of parameters on long-term vaccine effectiveness. It demonstrates that the HBV carrier rate, the most important parameter of the vaccine’s effectiveness, will fall from 10% to less than 0.2% 70 years after the start of the universal infant vaccination programme (Figure 5). Thus, long-term vaccination effectiveness is foreseeable and the disease is eradicable. The model also suggests that vaccination coverage is the most important parameter for vaccine effectiveness (Figures 5, 6, and 7). Compared to different vaccination strategies being applied in China, our model has shown that a low dose strategy with higher vaccination coverage and lower vaccine efficacy provided higher long-term effectiveness than a high dose strategy with lower coverage and higher efficacy.11

One limitation of this model, however, may be underestimation. The formula (2) indicated that the decreased number of infectious subjects in the post-vaccination period would result in a reduction in transmission of HBV infection. Thus, vaccine effectiveness should be higher than the vaccine efficacy. However, the formula did not completely consider the role of herd immunity, established after the universal immunization programme, in reducing infection transmission. This is especially important for a chronic infection. Therefore, this formula awaits further modification and improvement.

A universal infant hepatitis B immunization programme has been underway for more than 10 years in China. A set of administrative systems for the hepatitis B immunization programme has been well-established in most developed regions, especially in major cities. Most newborns are vaccinated according to the schedule. For example, in Shanghai, the vaccination coverage rate has remained at more than 95% in recent years, and the proportion of HBV carriage among vaccinated children has decreased to a very low level. In addition, disinfection of the medical instruments and syringes has also contributed to the reduction in HBV transmission. However, the hepatitis B immunization programme is different from those of other viral infectious diseases. Some infants, if they remain unvaccinated and are infected by HBV, will become chronic HBV carriers. They will be the new sources of infection, which will last for many years. These study results show that the goal of eliminating HBV transmission in some developed regions of China will be realized in just one generation.

In summary, this paper established a mathematical model to describe the epidemic dynamics of HBV infections. Based on several large-scale epidemiological surveys and follow-up studies, we estimated model parameters. The model corresponded with observed data and can be used to evaluate the long-term effectiveness of the vaccination programme and help determine the optimal strategy to reduce and eventually eliminate HBV infections.

Acknowledgement

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References

Conclusion
The prevalence of HBV infection and the proportion of HBV carriers in population were 58.16% and 10.09%, respectively. The age-specific prevalence of HBV infection as well as the age-specific proportion of HBV carriers was increased with age. It suggested HBV infection mainly occurs in infancy and early childhood.

References
1, 2, 6

1 A cross-sectional sero-epidemiological survey of HBV^a markers was carried out in four provinces of PR China in 1985, including two urban and three rural areas. A total of 10,484 subjects, about 15% of total civilian population of different age groups, were randomly selected for the HBV prevalence study.

2 A cross-sectional sero-epidemiological study on the distribution of HBV carriers was carried out in 1979. In all, 176,068 subjects from 29 provinces of PR China were randomly selected and tested.

3 A cohort of 3096 HBV susceptibles in different age groups was followed for one year, and 415 subjects were infected by HBV, those proceeding to HBV carriers were detected.

4 A cohort of 227 HBV carriers in different age groups was followed for 8 years and all the sero-reversions were tested annually.

5 A random sample of 613,939 subjects in four provinces was recruited and all disease and death reports for them were collected from 1984 to 1987.

6 A cohort of 14,775 subjects, immunized with hepatitis B vaccines at birth in 1986, were followed in five trial fields (Shanghai, Hebei, Hunan, Guangxi and Guangdong) for 10 years. The HBsAg, anti-HBs and anti-HBc were assayed annually for all subjects.

7 A cross-sectional sero-survey was carried out in 3193 subjects randomly selected from children 0–9 years old in Shanghai, who had received hepatitis B immunization at birth since 1986.

8 4825 subjects from 0–40 years old were recruited from Longan county of Guangxi Autonomous region in order to observe HBV-marker sero-prevalence after hepatitis B vaccination in 1995. The HBsAg, anti-HBs and anti-HBc were assayed for all subjects.

^a Hepatitis B virus.