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MAJOR ARTICLE

Survey of Hepatitis B Vaccination Coverage and Surface Antibody–Positive Rates in People Aged 1–59 Years in 2006 and 2024

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Background. Implementing hepatitis B vaccination is an important strategy to reduce hepatitis B virus infection and disease burden. Suboptimal adult hepatitis B vaccination coverage limits the further reduction of hepatitis B virus infection.

Methods. A multistage stratified random sampling method was adopted to survey the permanent population aged 1–59 in 2006 and 2024. We calculated the vaccination coverage rate, hepatitis B surface antibody (HBsAb)–positive rate, rate difference, and their 95% confidence intervals (CIs) of the 2 survey populations, and used the 95% CI and χ^2 test to determine whether the difference in rate was statistically significant.

Results. Six hundred twenty-three people were surveyed in 2006 and 606 people were surveyed in 2024. From 2006 to 2024, the hepatitis B vaccination coverage among people aged 1–59 years increased from 54.1% to 78.9%, and the HBsAb-positive rate increased from 46.2% to 57.6%. There was no significant difference in vaccination coverage in the population <15 years of age, but the antibody-positive rate increased significantly. The vaccination coverage rate of the 15–59 age group increased significantly, but there was no statistical difference in the antibody positivity rate of the 15–49 age group, and the antibody positivity rate of the 50–59 age group increased significantly.

Conclusions. Hepatitis B vaccination coverage among adults was still insufficient. Hepatitis B vaccine-mediated immunity was low in adults aged 30–49 years. It is recommended to update the guidelines for hepatitis B vaccination of adults in China, cancel the assessment of risk factors and prevaccination serological screening, and emphasize universal vaccination of all unvaccinated adults to increase coverage.

Keywords. adults; hepatitis B; positive rates; surface antibody; vaccination coverage.

Hepatitis B virus (HBV) is a serious global public health threat that causes acute and chronic liver disease, significantly increasing the global burden of disease and mortality rates [1, 2]. More than 1.5 million new preventable HBV infections continue to occur each year, with an estimated global burden of chronic HBV infection of 296 million people, and >820 000 people die prematurely each year from liver cancer and cirrhosis [3–6]. In response to the serious public health threat posed by viral hepatitis, the World Health Organization (WHO) proposed the "Global Health Sector Viral Hepatitis Strategy 2016–2021" in 2016 [7]. The strategy calls for the elimination of viral hepatitis as a public health threat by 2030 (defined as a 90% reduction in the incidence of new infections and a 65% reduction in mortality) [7]. However, progress in further reducing acute hepatitis B cases has stagnated in recent years [8]. Progress on the indicators must be accelerated to achieve the 2030 target.

The hepatitis B vaccine is the most economical and effective means to block the spread of HBV [9, 10]. Perinatal and early postnatal transmission is the leading cause of chronic hepatitis infection, so newborn and infant vaccination is a key intervention to prevent HBV infection [11]. According to WHO recommendations, 190 countries in the world have included hepatitis B vaccination in their national childhood immunization programs [5]. China is the country with the highest burden of HBV infection [12]. China has included the hepatitis B vaccine in its child immunization program since 1992 and has provided free vaccination to all newborns since 2002. Routine birth-dose hepatitis B vaccination has rapidly reduced perinatal HBV transmission, with global prevalence among children <5 years of age declining from 4.7% in the early 1990s to 1.3% in 2015 [11]. Compared with the prevaccine era, chronic HBV infection in China had declined by 90% among children <15 years of

Received 27 July 2024; editorial decision 30 September 2024; accepted 02 October 2024; published online 5 October 2024

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https://doi.org/10.1093/ofid/ofae589

age and by 97% among children <5 years of age in 2014 [13]. The contribution of childhood hepatitis B vaccination to controlling HBV infection and reducing the burden of HBV-related liver disease is enormous [14].

However, universal immunization does not cover a large number of adults, limiting further reductions in HBV infection. Adults are at high risk of contracting HBV through sexual contact, intravenous injection, invasive treatment, blood exposure, etc. The Advisory Committee on Immunization Practices (ACIP) noted that half of acute hepatitis B cases in the United States (US) in 2019 were in patients aged 30–49 years, and cases in adults aged ≥40 years are rising, with the number of reported cases in adults aged 40–49 years increasing from 1.9 per 100 000 people in 2011 to 2.7 per 100 000 people in 2019 [8]. A study on the changing trend of the hepatitis B epidemic in China showed that from 1990 to 2017, the main population groups with hepatitis B have shifted to the adult population, and the reported incidence of hepatitis B in the adult population has been on the rise [15]. Recent trends in hepatitis B incidence indicate a high burden of hepatitis B disease among adults. This highlights the importance of adult hepatitis B vaccination. It suggests that while we are doing a good job in controlling hepatitis B in children, we also need to take measures to strengthen hepatitis B vaccination in adults and reduce new HBV infections in adults.

Hepatitis B vaccination can effectively generate protective immunity against HBV infection. Immunity to HBV infection depends on the presence of hepatitis B surface antibody (HBsAb) after completion of vaccination. Studies have shown that vaccine-induced HBsAb levels decline rapidly within the first year after vaccination and continue to decline with age, even becoming undetectable in serum samples decades later [16]. The serological survey in 2006 showed that the positive rate of HBsAb was 66.1% in the population aged 1–4 years and 48.8% in the population aged 50–59 years.

To understand the changes in hepatitis B vaccination coverage and HBsAb-positive rate in the population aged 1–59 in the past 18 years, we surveyed in 2024 using the same method as the 2006 Chinese Viral Hepatitis Survey and compared the results of the 2 surveys, aiming to monitor the status of hepatitis B vaccination and the immunity to HBV infection in the population and to provide a reference for achieving the goal of eliminating hepatitis B by 2030.

METHODS

Data Sources

The hepatitis B vaccination history of children <15 years old was obtained from the records of the China Immunization Information System, and the hepatitis B vaccination history of people ≥15 years old was obtained from their recollections. To obtain as accurate and thoughtful responses as possible, we scheduled a reasonable survey time in advance before the survey, optimized the survey content, and minimized interference. The 2006 survey data came from the China Viral Hepatitis Serological Epidemiological Survey Database.

Methodology of the Survey

Multistage stratified random sampling was used in both surveys. Two counties were randomly selected, and 2 townships were selected from each county. In the selected townships, 2 survey points were randomly selected based on the community (village) unit. According to the list of households provided by the survey points, random survey households were selected to carry out household surveys. The resident population aged 1–59 years was divided into 6 age groups: 1–4, 5–14, 15–29, 30–39, 40–49, and 50–59.

Calculation of the Sample Size for the 2024 Survey

According to the results of the 2006 hepatitis B serum epidemiological survey of people aged 1–59 years in Quzhou, the coverage rate of hepatitis B vaccination was 54%, and the HBsAb positivity rate was 46%. The sample size formula was $N = Z^2[P(1 - P)] / d^2 \times deff$, where Z was the test statistic, taken as 1.96; P was the antibody positivity rate, taken as 46%; the permissible error d was 0.06; the design effect deff was taken as 2; and the estimated sample size in 2024 was 530. The sample size was enlarged to 583 individuals, taking into account a 10% lost visit rate.

HBsAb Testing

Peripheral venous blood (3 mL) was extracted and serum was isolated for HBsAb detection. The samples in both investigations were tested with the kit of Beijing Wantai Biopharmaceutical Co, Ltd. Enzyme-linked immunosorbent assay was used for detection. According to the manufacturer's instructions, the critical value is equal to the mean optical density (A) of the negative control wells × 2.1, and if the A value of the negative control wells is <0.05, it will be calculated as 0.05; samples with A values greater than or equal to the critical value are judged as positive. In 2006, the samples were tested by the Chinese Center for Disease Control and Prevention, and the microparticle enzyme immunoassay test reagent of Abbott was used for reverification. The samples in 2024 were tested by the Zhejiang Provincial Center for Disease Control and Prevention using internal control quality control serum (included with the kit) for quality control, and all experimental results were within control.

Statistical Analysis

Data analysis of both surveys was performed using SPSS 17.0 software to calculate the vaccination coverage rate, HBsAb positivity rate, rate difference, and their 95% confidence intervals (CIs), and the 95% CI and χ^2 test were used to determine

Variable	The year 2006 (n=623)			The year 2024 (n=606)			Between-group difference, % (95% CI)
	Number of people surveyed	Number of people vaccinated	Vaccination coverage rate, % (95% CI)	Number of people surveyed	Number of people vaccinated	Vaccination coverage rate, % (95% CI)	
Sex							
Male	295	161	54.6 (48.9–60.3)	274	197	71.9 (66.5–77.3)	17.3 (9.5–25.1)
Female	328	176	53.7 (48.2–59.1)	332	281	84.6 (80.7–88.5)	31.0 (24.3–37.6)
Age, y							
1–4	118	118	100	125	125	100	0.0 (0.0–0.0)
5–14	193	188	97.4 (95.1–99.7)	168	167	99.4 (98.2–100)	2.0 (-0.5–4.5)
15–29	52	30	57.7 (43.8–71.6)	161	134	83.2 (77.4–89.1)	25.5 (10.9–40.2)
30–39	80	1	1.3 (0–3.7)	51	24	47.1 (32.9–61.2)	45.8 (31.9–59.7)
40–49	98	0	0	53	17	32.1 (19.1–45.1)	32.1 (19.5–44.6)
50–59	82	0	0	48	11	22.9 (10.6–35.2)	22.9 (11.0–34.8)
Total	623	337	54.1 (50.2–58.0)	606	478	78.9 (75.6–82.1)	24.8 (19.7–29.9)

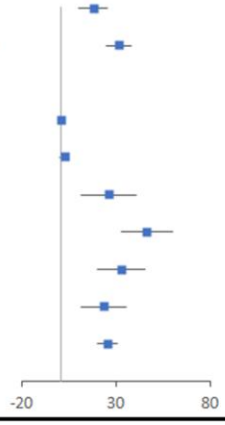

Figure 1. Changes of hepatitis B vaccination coverage rate in healthy people aged 1–59 years in Quzhou, China, in 2006 and 2024. Vaccination coverage among people of different age groups decreased with age. Compared with 2006, the vaccination rates of both males and females aged 1–59 years in the 2024 survey increased, and the difference was statistically significant. Except for people <15 years old, the vaccination rates of other age groups have increased, and the differences are statistically significant. Abbreviation: CI, confidence interval.

whether the difference in rates was statistically significant. All statistical analyses were 2-tailed, with an α of 5% used.

RESULTS

Overall Results

Six hundred twenty-three people aged 1–59 years were surveyed in 2006, and 606 people aged 1–59 years were surveyed in 2024.

Vaccination Coverage Survey

Three hundred thirty-seven people were vaccinated in 2006, giving a coverage rate of 54.1% (n = 623). There was no statistically significant difference in vaccination rates between the sexes ($P = .818$). The vaccination coverage rate for people aged 1–14 years was 98.4% (306/311), and the vaccination coverage rate for people ≥30 years of age was 0.4% (1/260).

A total of 478 people were vaccinated in 2024, giving a coverage rate of 78.9% (n = 606). The vaccination rate of females was higher than that of males, and the difference was statistically significant. Vaccination coverage among people of different age groups decreased with age. The vaccination rate for people aged ≥30 years was 34.2% (52/152).

Compared with 2006, the vaccination rates of both males and females aged 1–59 years in the 2024 survey increased, and the difference was statistically significant. Except for people <15 years old, the vaccination rates of other age groups increased, and the differences were statistically significant. The changes in hepatitis B vaccination coverage are shown in Figure 1.

HBsAb Positivity Rate

In 2006, 288 people were positive for HBsAb, with a positivity rate of 46.2% (n = 623). There was no statistically significant difference in antibody positivity rate between the sexes ($P = .703$). The antibody positivity rate in the age group 1–4 years was higher than that in the age group 5–14 years, and the difference was statistically significant.

In 2024, 349 people were positive for HBsAb, with a positivity rate of 57.6% (n = 606). The positive rate of antibody in females was higher than that in males, and the difference was statistically significant. The antibody positivity rate of people <30 years old decreased with age, and the difference between age groups was statistically significant. There was no statistical difference in the antibody-positive rate among age groups ≥30 years ($P = .354$).

The HBsAb positivity rate of the surveyed population in 2024 increased by 11.4% compared with 2006, and the difference was statistically significant. The antibody-positive rate of females in 2024 was higher than that in 2006, and the difference was statistically significant. The antibody-positive rate in people <15 years old and people aged 50–59 years increased, and the difference was statistically significant. There was no statistically significant difference in antibody-positive rates among people aged 15–49 years. The changes in HBsAb-positive rate are shown in Figure 2.

Variable	The year 2006 (n=623)			The year 2024 (n=606)			Between-group difference, % (95% CI)
	Number of people surveyed	Antibody-positive number	Antibody-positive rate, % (95% CI)	Number of people surveyed	Antibody-positive number	Antibody-positive rate, % (95% CI)	
Sex							
Male	295	134	45.4 (39.7–51.1)	274	138	50.4 (44.4–56.3)	4.9 (-3.3–13.1)
Female	328	154	47.0 (41.5–52.4)	332	211	63.6 (58.4–68.8)	16.6 (9.1–24.1)
Age, y							
1–4	118	78	66.1 (57.4–74.8)	125	112	89.6 (84.2–95.0)	23.5 (13.4–33.6)
5–14	193	65	33.7 (27.0–40.4)	168	95	56.5 (49.0–64.1)	22.9 (12.8–32.9)
15–29	52	19	36.5 (23.0–50.1)	161	53	32.9 (25.6–40.3)	-3.6 (-18.6–11.3)
30–39	80	37	46.3 (35.1–57.4)	51	29	56.9 (42.8–70.9)	10.6 (-6.8–28.1)
40–49	98	49	50.0 (39.9–60.1)	53	28	52.8 (38.9–66.7)	2.8 (-13.9–19.5)
50–59	82	40	48.8 (37.7–59.8)	48	32	66.7 (52.8–80.5)	17.9 (0.7–35.1)
Total	623	288	46.2 (42.3–50.2)	606	349	57.6 (53.6–61.5)	11.4 (5.8–16.9)

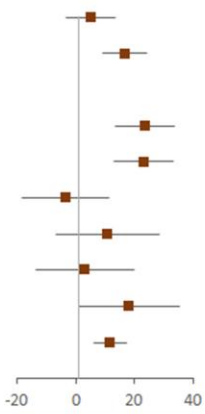

Figure 2. Changes of hepatitis B surface antibody–positive rate in healthy people aged 1–59 years in Quzhou, China, in 2006 and 2024. The antibody-positive rate of females in 2024 was higher than that in 2006, and the difference was statistically significant. The antibody-positive rate in people <15 years old and people aged 50–59 years increased, and the difference was statistically significant. There was no statistically significant difference in antibody-positive rates among people aged 15–49 years. Abbreviation: CI, confidence interval.

DISCUSSION

Eliminating HBV by 2030 is an important global health milestone [3]. The WHO strongly recommends hepatitis B vaccination as the most effective tool for eliminating HBV. Realizing the full potential of vaccines is key to achieving elimination. Universal vaccination of the entire population is the cornerstone of the strategy to eliminate and ultimately eradicate HBV [17]. The Chinese Center for Disease Control and Prevention issued hepatitis B vaccination guidelines for adults in 2011, encouraging adults, especially those with risk factors, to receive hepatitis B vaccine [18]. ACIP updated its risk factor–based hepatitis B vaccination guidelines in 2022 to recommend vaccination for all adults aged 19–59 years, and those aged ≥60 years with risk factors [8]. But even with the WHO and ACIP recommendations, hepatitis B vaccination rates among adults are far from optimal, with less than a third of US adults reporting having received the hepatitis B vaccine in 2018 [19]. Comprehensive data on hepatitis B vaccination coverage in China, especially for adults, are scarce. A systematic review provided data showing that the hepatitis B vaccination coverage rate for adults in China from 2011 to 2021 was 26.27% [20]. Quzhou participated in the seroepidemiology of viral hepatitis in China as a national investigation site in 2006. Survey data from Quzhou in 2006 showed that the vaccination coverage rate for adults was far from ideal, with only 0.4% of people aged 30–59 years covered. From 2006 to 2024, the hepatitis B vaccination coverage among people aged 1–59 years increased significantly due to the expansion of the birth-dose hepatitis B vaccination population. However, the vaccination rate for people aged 30–59 years in 2024 was only 34.2%, which is similar to the 30% hepatitis B vaccination coverage for adults aged ≥19 years in the US in 2018 [19].

Since the population <15 years of age has received the birth dose of the hepatitis B vaccine in both surveys, the increase in vaccination coverage is mainly due to the increase in the age group ≥15 years. From 2006 to 2024, the 15–29 age group gradually entered the period of birth-dose hepatitis B vaccination, and the hepatitis B vaccination coverage increased from 57.7% to 83.2%, but there was still a gap with the under-15 age group. No one in the 30–59 age group received a birth dose of the vaccine in 2024, and although vaccination coverage increased significantly from 2006, only one-third received the hepatitis B vaccine, suggesting that the potential of the hepatitis B vaccine has not been fully realized. With the release of guidelines for adult hepatitis B vaccination, China's hepatitis B control strategy has shifted from focusing on child vaccination to taking both children and adults into consideration. However, the guidelines for adult hepatitis B vaccination that emphasize personal risk assessment are not ideal for improving adult vaccination coverage. Although guidelines encourage vaccination for adults, members of the public may shift their focus to the assessment of risk factors and choose to forgo vaccination when risk factors are low. ACIP now emphasizes that adults should be vaccinated against hepatitis B if they have not yet been vaccinated, regardless of associated risk factors. In

addition, prevaccination serological screening also hinders vaccination of adults. By testing the serological indicators of hepatitis B, it is possible to determine whether a person is infected or has been infected with HBV. Most people believe that only after the serological screening to confirm that they do not have the virus can they be vaccinated. However, serological testing is sometimes not readily available, and the lack of serological testing is therefore a barrier to vaccination. However, due to the safety of the hepatitis B vaccine, serological testing is not necessary before vaccination. In the absence of testing, vulnerable people should continue to be vaccinated. It is recommended to update the technical guidelines for adult vaccination in China, cancel the assessment of risk factors and prevaccination serological screening, and emphasize universal hepatitis vaccination for all unvaccinated adults to improve vaccination coverage.

From 2006 to 2024, the HBsAb positivity rate of hepatitis B in people aged 1–59 years has increased significantly, among which the positivity rate of people <15 years old and those aged 50–59 years has increased significantly. There was no statistical difference in the coverage rate of people <15 years old between the 2 surveys, but there was a significant difference in the HBsAb positivity rate. One of the reasons may be that the hepatitis B vaccines used in the 2 surveys were different. China began using blood-derived hepatitis B vaccine in 1992. In 1995, the blood-derived hepatitis B vaccine was discontinued and the genetically engineered hepatitis B vaccine began to be used. In 2009, the birth dose of hepatitis B vaccine was changed from 5 μg to 10 μg. In 2006, people aged <15 years used a blood-derived hepatitis B vaccine and a 5-μg genetically engineered hepatitis B vaccine, while in 2024, people under the age of 15 used a 10-μg genetically engineered hepatitis B vaccine. Previous studies have shown that the immune effect of genetically engineered vaccines is better than that of blood-derived vaccines [21], and the persistence of HBsAb at 5 years after initial vaccination with 10-μg hepatitis B vaccine is better than that with 5-μg hepatitis B vaccine [22]. Another reason may be the spontaneous booster behavior of parents for hepatitis B vaccination in recent years. Previous studies have shown that after successful immunization with the hepatitis B vaccine, even if the HBsAb level drops below the detection limit, the protective effect of the vaccine can still last for 30 years or even lifelong [17, 23, 24]. Even if the HBsAb level drops to the point where no antibodies can be detected, it does not necessarily mean that you are not protected, because the immune memory of the hepatitis B surface antigen can persist [5]. This scientific literature and advisory groups do not advocate routine HBV vaccine booster doses in fully vaccinated, healthy, and immunocompetent individuals [16, 23, 25–27]. However, due to the harm of hepatitis B infection and the increased awareness of disease prevention among parents in recent years, it is still common for parents to seek out hepatitis B vaccination booster programs when their children's health check-ups screen negative for HBsAb. Studies have shown that among individuals whose HBsAb levels dropped to inadequate levels, 94% achieved protective levels within 3 weeks after a booster dose [28]. Therefore, there was a significant difference in the antibody positivity rate among people <15 years of age with the same high vaccination coverage rate.

The vaccination coverage rate among people aged 30–49 years increased significantly in the 2 surveys, but there was no statistical difference in the antibody positivity rate. In 2006, people aged 30–49 years had not received the hepatitis B vaccine but had a higher HBsAb positivity rate, indicating that the antibodies in this group of people came from natural infection. In 2024, one-third of the 30–49 age group had received the hepatitis B vaccine. With the addition of immunity from the vaccine, the HBsAb-positive rate increased slightly, but there was no statistical difference. The increase of protective antibodies in adults is slow. On the one hand, HBsAb titers will weaken over time, leading to a lower positivity rate, but these people may already be immune to the infection. So, while there has been no significant increase in the number of antibody-positive people with evidence of protection, actual immunity to infection may have increased. On the other hand, the hepatitis B vaccine is less immunogenic in adults than in infants and children, and the ability of populations to induce protective immunity after hepatitis B vaccination declines with age [29]. The serum protection rate after hepatitis B vaccination is >95% in healthy infants, children, and young adults, ≥90% in people <49 years of age, and ≥80% in people <60 years of age [30]. This indicates that improving protective immunity among adults requires a higher vaccination coverage rate. The lack of significant increase in the proportion of adults with evidence of protective immunity also indicates that adult vaccination coverage is insufficient, vaccine-mediated immunity in the adult population is low, and most adults are not protected or not optimally protected. Adult hepatitis B vaccine coverage needs to be further improved to reduce HBV natural infection and horizontal transmission.

The HBsAb-positive rate among people aged 50–59 years in 2024 has increased significantly compared with 2006. This indicates that people in this age group have higher protective immunity, but since less than a quarter of people in this age group have been vaccinated, we cannot distinguish whether the enhanced immunity comes from natural infection or vaccination.

There are differences in HBsAb-positive rates among different age groups. The lowest rates of HBsAb positivity were in the age group 5–14 years in 2006 and in the age group 15–29 years in 2024. The antibody-positive rate of people <30 years of age

decreased significantly with the increase in age, indicating that the natural attenuation of antibodies was rapid after vaccination. A large population cohort study in Israel showed that only one-third of people vaccinated maintained protection 15 years later [27]. The HBsAb positivity rate was 33.7% in the age group 5–14 years in 2006 and 32.9% in the age group 15–29 years in 2024, consistent with the previous study. Both groups had completed birth-dose hepatitis B vaccination and had high vaccination coverage. On the one hand, antibody detection has experienced a long period of natural decay and titer decline; on the other hand, the existence of induced long-term protective immunity after vaccination effectively avoids natural infection and the immunity from natural infection is low, so the antibody-positive rate is lowest.

Females had higher vaccination coverage in 2024. It may be because females have a higher awareness of diseases and vaccines than males [31] and tend to be more concerned about their health [32], so they have a greater motivation to vaccinate against hepatitis B. HBsAb-positive rates were higher in females than males in 2024, which is consistent with a retrospective study in Japan [33]. This may be related to higher hepatitis B vaccination coverage in females.

There are limitations to this study. There is recall bias in collecting the hepatitis B vaccination history of adults, which affects the reliability of data analysis. The data in this study come from Quzhou, a city in eastern China, and cannot represent the whole of China.

Our study found that vaccination coverage among Chinese adults in 2024 remains inadequate, vaccine-mediated immunity in the adult population is low, and most adults are unprotected or not optimally protected. More effective intervention strategies and robust vaccination programs are needed to increase adult hepatitis B vaccination coverage in the future to ensure progress toward the goal of eliminating hepatitis B by 2030.

Notes

Author contributions. X. G. wrote the article and Z. Y. critically reviewed the article. C. Z., Q. F., and W. X. were involved in the epidemiological investigation and data analysis. All authors have agreed on the journal to which the article will be submitted and all agree to take responsibility for all aspects of the work.

Data availability. All data can be available upon request from the corresponding author.

Patient consent. Informed consent was obtained from all subjects involved in the study.

Ethical approval. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Quzhou Center for Disease Control and Prevention (approval number: IRB-2024-P-10).

Financial support. This work was supported by the Clinical Research Application Project of the Zhejiang Health Science and Technology Programme (award number 2022KY1354) and by the Chinese Foundation for Hepatitis Prevention and Control (award number YGFK20210019).

Potential conflicts of interest. All authors: No reported conflicts.

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