Proceedings of ICMMGH 2027 Symposium: Clinical OMICS for Drug Discovery and Personalized Medicine
DOI: 10.54254/2753-8818/2027.MB39186

Hepatitis B Vaccine as a Primary Prevention Strategy for Cancer: Mechanisms, Outcomes and Model Extension

Qingyang Xia

RCF Experimental School, Beijing, China
Xiaqingyang@rdfzcygj.cn

Abstract. Vaccination against Hepatitis B can prevent liver cancer by preventing chronic infection of the liver. This paper reviews the role of hepatitis B virus (HBV) in hepatocellular carcinoma, cancer prevention via vaccination, and lessons learned from China's experience for other cancer-prevention programmes. HBV promotes cancer by inducing chronic inflammation in the host, integrating viral DNA into the host's DNA, and altering cell regulation through viral proteins. China's childhood vaccination programme has reduced infections among young children significantly. Extended data from the Qidong trial have also indicated a decrease in primary liver cancer; however, due to a small number of cancer cases, the exact extent remains unknown. Comparison with human papillomavirus (HPV) vaccination shows that the biological principle can be applied to infections, but delivery needs to match the age and circumstances of the target population. China's addition of HPV vaccination to the national programme in 2025 is a policy change. Disease spread can be effectively prevented through timely vaccination, accessible medical services, and ongoing care for high-risk groups.

Keywords: Hepatitis B virus, Hepatitis B vaccination, Hepatocellular carcinoma, Primary prevention, Human papillomavirus

1. Introduction

A vaccine given in infancy can prevent cancer that would have developed decades later. Hepatitis B vaccination is a typical case; it can prevent infection with the hepatitis B virus (HBV), a major cause of hepatocellular carcinoma (HCC), the most common primary liver cancer [1]. After the spread of infant vaccinations in China, there was a significant drop in childhood hepatitis B [2]. The connection to cancer prevention is biologically plausible, but demonstrating reductions in infection and cancer requires different types of evidence.

How does HBV vaccination prevent cancer, what has been shown in China in this regard, and to what extent can this approach be applied to HPV vaccination? Both vaccines can prevent diseases that lead to cancer and are therefore suitable for comparison [3, 4]. Success will also depend on when people are vaccinated and how the services reach them. Therefore, the discussion will connect biological mechanisms with infection surveys, cancer outcomes and vaccination policies, and not assume that vaccine availability will lead to effective prevention programmes.

© 2026 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2027.MB39186

2. HBV carcinogenesis and the protective mechanism of vaccination

2.1. How HBV contributes to liver cancer

Age of infection for HBV significantly affects the prognosis of the disease. Most infected adults recover; up to 90% of infants infected at birth or during infancy have chronic infections, and the corresponding risk in adults is about 5% [5]. Chronic infection allows the virus and the immune response to affect the liver over many years. Therefore, prevention of infection at birth is relatively more urgent, although liver cancer generally presents at an older age.

Much of the liver damage in chronic hepatitis B is caused by an immune reaction to infected liver cells. Repeated injury stimulates replacement of damaged cells. Inflammation causes DNA damage, and continuous cell division leads to an accumulation of genetic errors. Fibrosis and cirrhosis can occur in this environment, increasing the risk of cancer [1].

HBV can also affect the host genome more directly. Fragments of viral DNA may be incorporated into the DNA of hepatocytes. Sung and his colleagues have identified recurrent integrations at cancer-related genes in sequencing studies and have also observed increased expression of these genes in tumours [6]. Therefore, integration can change the regulation of growth; however, an insertion does not automatically lead to cancer in a cell.

Viral proteins are also a type of altered-cell-regulation agent. HBx modifies gene expression and signals to regulate cell growth and death. These effects are associated with inflammatory injury and alterations in the host genome over time. Cirrhosis is a relatively common cause; however, HBV-related HCC can occur without cirrhosis [1]. Thus, disease progression does not necessarily follow a sequence in which all infections must pass through cirrhosis before cancer develops.

2.2. How hepatitis B vaccination achieves primary prevention

Recombinant hepatitis B vaccines contain hepatitis B surface antigen (HBsAg), a viral surface protein produced by genetic engineering. They contain no infectious HBV particles and cannot cause hepatitis B infection. Exposure to this antigen induces the production of anti-HBs antibodies and establishes immunity [3]. This allows the immune system to recognise a viral component without the host becoming infected with HBV.

After re-exposure to HBV, anti-HBs can bind with the virus to prevent damage to liver cells (hepatocytes). Immune memory provides an enhanced response after a fall in circulating antibodies. Prevention of chronic infection can stop the continuous damage to the liver and viral changes in the host's genome [3]. Cancer benefits arise from the prevention of the underlying disease; vaccines do not directly target cancer cells. Therefore, protection should be established in time to prevent chronic infection.

3. Practical effectiveness and limitations of hepatitis B vaccination for cancer prevention in China

3.1. Construction and implementation of China's national immunisation programme

China's infant vaccination program developed in stages. In 1992, the government started to organise free vaccinations for newborns across the country. In 2002, hepatitis B vaccines were added to the national immunization schedule. In 2025, all remaining vaccine and service fees were abolished. The regular schedule is to give doses at birth, one month and six months, and the birth dose should

DOI: 10.54254/2753-8818/2027.MB39186

be given within 24 hours [7]. Removing both the vaccine and service fees reduced the financial burden on families for timely vaccination.

Birth dose is only one method for preventing mother-to-child transmission. Infants need to complete the vaccination programme, and babies born to HBsAg-positive mothers are also given hepatitis B immunoglobulins for immediate antibody protection [7]. Pregnant women with a high viral load may need antiviral prophylaxis according to current recommendations [8]. Protection therefore depends on the mother's infection status, timely delivery of care and completion of the schedule. Even with antibody-based passive immunity, infants born to mothers with a high viral load may still acquire HBV infection [5].

The national survey reports on changes in childhood infections. Prevalence of HBsAg among children aged 1-4 years dropped from about 10% in 1992 to 0.96% in 2006 and 0.32% in 2014, and the 2020 survey reported 0.30% [7, 9]. HBsAg is a marker of active infection, and the population surveys have shown the success of China's prevention programme. However, they did not wait for each child to get cancer. Fewer infections indicate a smaller group at long-term risk of HBV infection, and a reduction in cancer requires separate follow-up data.

3.2. Evidence of cancer prevention and remaining risks

The Qidong Hepatitis B Intervention Study provides extended data support. In this cluster-randomised trial in Jiangsu, 39,292 newborns were randomised to the vaccination group and 34,441 to the control group between 1985 and 1990. Follow-up in 2013 found an estimated 84% protective effect for primary liver cancer, and the 95% confidence interval was 23%–97% [10]. The wide confidence interval indicates that the observed number of cancer cases remained limited. Moreover, 67.8% of controls later received catch-up vaccination at ages 10–14. This result supports the prevention of liver cancer in young adults in that area; it is not an estimate of the reduction in all liver cancers across China.

Routine vaccination cannot eliminate the virus or reverse existing liver damage in people with chronic HBV infection [3]. Antiviral treatment and reasonable HCC follow-up are still required for eligible patients [8]. Hepatitis B vaccination offers no protection against other risk factors for liver cancer, such as hepatitis C, excessive alcohol consumption, metabolic liver disease, and aflatoxin exposure [1]. Preventing HBV can reduce one of several risk factors, but it does not make the liver immune to cancer.

Antibody decline is not the same as a loss of immunity. Immune memory can last for several decades after a successful primary course, and routine boosters are generally not needed for immunocompetent individuals [11, 12]. Failure to respond to the initial vaccine is a different problem. Post-vaccination tests are only for groups that require follow-up care based on the results, such as infants of infected mothers and some immunocompromised patients [5]. A reduced antibody level years after vaccination is not, by itself, considered vaccine failure.

4. Comparison with HPV vaccination and conditions for wider use

4.1. What the HBV and HPV models share

HBV and HPV vaccines both aim to prevent cancer caused by these infections before they occur. Nevertheless, their oncogenic mechanisms differ. Persistent high-risk HPV infection causes cervical cancer mainly by altering the control of cell growth via viral proteins, such as E6 and E7 [13]. HBV-associated liver cancer also presents as chronic liver injury and regeneration. HPV vaccines use

DOI: 10.54254/2753-8818/2027.MB39186

virus-like particles to stimulate protective antibodies, and WHO recommends vaccination for girls aged 9-14 years before likely exposure through sexual contact [4]. Both programs are time-sensitive, but the suitable vaccination window is different.

Parental surveys indicate the reasons why adolescents are not vaccinated despite the availability of vaccines. Huang and others compared the surveys in Zhejiang in 2018 and 2023. Parents' reasons for not vaccinating their daughters included a lack of knowledge, vaccine shortages, safety concerns, and cost [14]. The results are only for this province and cannot be applied nationwide. The surveys also occurred before the policy change.

As of November 10, 2025, China added HPV vaccination to the national immunisation plan and offered eligible 13-year-old girls two free doses of the bivalent vaccine six months apart [15]. Public funds now support both infant HBV and adolescent HPV vaccinations. The other question is how to reach the eligible girls and complete the program on time. Funding commitments can broaden coverage but do not guarantee even distribution of coverage in different regions or a decrease in cancer incidence among newly eligible people.

4.2. Practical obstacles to the promotion of vaccine cancer prevention model

The first obstacle is that the cause of infection must be preventable. Plummer and others estimated that 15.4% of all new cancers globally in 2012 were caused by infectious factors [16]. There are also bacteria and parasites in this figure that the current vaccines cannot prevent. An infectious cause must be determined, an effective vaccine must be developed, and people must be vaccinated before exposure. Therefore, the HBV experience offers a reference only for certain cancers and does not constitute a general cancer-vaccine solution.

Vaccine delivery should be adapted for older target age groups. Maternity services offer a convenient opportunity for HBV vaccination at birth. The adolescent HPV programme needs to arrange for identifying eligible girls, obtaining parental consent and recording doses. China's implementation plan links health and education services and organises vaccinations at designated institutions [17]. The lesson of HBV is to include prevention in regular health examinations. Adolescent services do not need to replicate the organisation of newborn care.

4.3. Social value and public health education

Vaccination, screening and treatment are at different stages of disease occurrence. People with established HBV infection need assessment for treatment and cancer surveillance according to risk. Women still need cervical cancer screening after HPV vaccination because the vaccines do not cover all types of oncogenic HPV [4, 8]. Program evaluation needs to take into account the following differences: Timeliness of dose and completion rate are indicators of service delivery; infection prevalence shows an earlier biological outcome; cancer incidence is a later one. These indicators help show which parts of the prevention program are effective and which need to improvement.

5. Conclusion

Hepatitis B vaccination reduces the risk of liver cancer by preventing chronic hepatitis and subsequent damage to the liver cells caused by prolonged viral disruption of cell regulation. China's childhood infection surveys and the Qidong cancer follow-up study also support this hypothesis. Together, they promote early vaccination as a type of cancer prevention, but not all prevented

DOI: 10.54254/2753-8818/2027.MB39186

infections will lead to cancer, and the full scope of the national cancer benefit has not yet been realised.

The transferable principle is the prevention of a causal infection at the appropriate time. The actualisation of this will require an effective vaccine, continuous access and services for the target group. China has added HPV vaccination to the national programme, and eligible 13-year-old girls can now access the service through designated institutions. Vaccination should therefore be integrated with screening and treatment for high-risk groups in ongoing cancer-prevention efforts.

References

[1] Levrero, M., & Zucman-Rossi, J. (2016). Mechanisms of HBV-induced hepatocellular carcinoma. *Journal of Hepatology, 64*(1 Suppl), S84–S101. doi:10.1016/j.jhep.2016.02.021.

[2] Cui, F., Shen, L., Li, L., Wang, H., Wang, F., Bi, S., et al. (2017). Prevention of chronic hepatitis B after 3 decades of escalating vaccination policy, China. *Emerging Infectious Diseases, 23*(5), 765–772. doi:10.3201/eid2305.161477.

[3] World Health Organization. (2017). Hepatitis B vaccines: WHO position paper – July 2017. *Weekly Epidemiological Record, 92*(27), 369–392.

[4] World Health Organization. (2022). Human papillomavirus vaccines: WHO position paper, December 2022. *Weekly Epidemiological Record, 97*(50), 645–672.

[5] Haber, P., & Schillie, S. (2024, May 9). Chapter 10: Hepatitis B. In *Epidemiology and Prevention of Vaccine-Preventable Diseases* [Internet]. Centers for Disease Control and Prevention. [cited 2026 Oct 6].

[6] Sung, W. K., Zheng, H., Li, S., Chen, R., Liu, X., Li, Y., et al. (2012). Genome-wide survey of recurrent HBV integration in hepatocellular carcinoma. *Nature Genetics, 44*(7), 765–769. doi:10.1038/ng.2295.

[7] Chinese Center for Disease Control and Prevention. Hepatitis B [Internet]. [cited 2026 Oct 6]. Chinese.

[8] World Health Organization. (2024). Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection [Internet]. World Health Organization. [cited 2026 Oct 6].

[9] Liang, X., Bi, S., Yang, W., Wang, L., Cui, G., Cui, F., et al. (2009). Epidemiological serosurvey of hepatitis B in China—declining HBV prevalence due to hepatitis B vaccination. *Vaccine, 27*(47), 6550–6557. doi:10.1016/j.vaccine.2009.08.048.

[10] Qu, C., Chen, T., Fan, C., Zhan, Q., Wang, Y., Lu, J., et al. (2014). Efficacy of neonatal HBV vaccination on liver cancer and other liver diseases over 30-year follow-up of the Qidong Hepatitis B Intervention Study: a cluster randomized controlled trial. *PLoS Med, 11*(12), e1001774. doi:10.1371/journal.pmed.1001774.

[11] Leuridan, E., & Van Damme, P. (2011). Hepatitis B and the need for a booster dose. *Clin Infect Dis, 53*(1), 68–75. doi:10.1093/cid/cir270.

[12] Van Damme, P., Dionne, M., Leroux-Roels, G., Van Der Meeren, O., Di Paolo, E., Salaun, B., et al. (2019). Persistence of HBsAg-specific antibodies and immune memory two to three decades after hepatitis B vaccination in adults. *J Viral Hepat, 26*(9), 1066–1075. doi:10.1111/jvh.13125.

[13] Bosch, F. X., Lorincz, A., Muñoz, N., Meijer, C. J. L. M., & Shah, K. V. (2002). The causal relation between human papillomavirus and cervical cancer. *Journal of Clinical Pathology, 55*(4), 244–265. doi:10.1136/jcp.55.4.244.

[14] Huang, Y., Ling, J., Zhao, X., Lv, Q., Wang, L., Wu, Q., et al. (2024). Are HPV vaccines well accepted among parents of adolescent girls in China? Trends, obstacles, and practical implications for further interventions: A five-year follow-up study. *Vaccines (Basel), 12*(9), 1073. doi:10.3390/vaccines12091073.

[15] World Health Organization. (2025, October 31). China takes historic step to protect women's health: HPV vaccine joins national immunization programme [Internet]. [cited 2026 October 6].

[16] Plummer, M., de Martel, C., Vignat, J., Ferlay, J., Bray, F., & Franceschi, S. (2016). Global burden of cancers attributable to infections in 2012: A synthetic analysis. *Lancet Global Health, 4*(9), e609–e616. doi:10.1016/S2214-109X(16)30143-7.

[17] Chinese Center for Disease Control and Prevention. (2025, October 30). Technical implementation plan for incorporating human papillomavirus vaccine into the national immunization program [Internet]. [cited 2026 October 6]. Chinese.