

Hepatitis B screening to reduce liver cancer burden

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Epidemiology of liver cancer and hepatitis B infection

According to the 2021 statistics from the Hong Kong Cancer Registry, liver cancer is the fifth most commonly diagnosed cancer and the third leading cause of cancer-related mortality in Hong Kong.¹ Over the past few decades, the incidence of liver cancer in Hong Kong has exhibited an exceptionally declining trend, consistent with the overall decrease observed across Eastern Asia.^{2–5} However, the number of new liver cancer cases in Hong Kong has been increasing, primarily due to the ageing population.^{2,3} In addition to the heightened risk of liver cancer among older individuals, prognosis is often worsened by increased liver fragility and the presence of co-morbidities.⁶

Hepatocellular carcinoma (HCC) is the predominant histological type of liver cancer, causing the majority of liver cancer diagnoses and deaths.^{7,8} Cirrhosis of the liver precedes HCC development in most cases, acting as a driver through hepatocyte regeneration.^{9,10} Among the various causes of cirrhosis, chronic hepatitis B infection is the leading contributor to HCC.¹¹ The hepatitis B virus (HBV) infects only primates and can cause hepatocellular injury by damaging infected hepatocytes.¹² Moreover, HBV exhibits oncogenic potential by inducing genomic instability through its integration into the host genome.¹² Other risk factors for HCC include chronic hepatitis C virus (HCV) infection, dietary exposure to aflatoxin, excessive alcohol consumption, obesity, type 2 diabetes, and smoking.² However, the burden of liver cancer in Hong Kong is unlikely to be linked to HCV or aflatoxin exposure, considering the low prevalence of HCV and the rarity of aflatoxin contamination over the past decade.^{13,14}

The endemicity of hepatitis B in Hong Kong has declined from high-intermediate to intermediate-

low, with a significant reduction in seroprevalence of hepatitis B surface antigen (HBsAg) among various populations, including new blood donors and pregnant women.¹⁵ This success can be attributed to the implementation of a universal hepatitis B vaccination programme in 1988 for all newborns and the availability of antiviral treatments. Since the initiation of the vaccination programme, coverage of the third dose of the hepatitis B vaccine in children aged 3 to 5 years has consistently exceeded 99%.¹⁶ However, adults over the age of 30 years were not included in the universal neonatal hepatitis B vaccination programme; these individuals remain at high risk of hepatitis B infection because they lack immunological protection.² A recent study estimated that the overall HBsAg seroprevalence in Hong Kong remains as high as 7.2%.¹³ Therefore, a subsidised screening programme is urgently needed to protect the unvaccinated population from the risks of hepatitis B infection and liver cancer.

Existing screening practices and their challenges

Worldwide, the epidemiology of liver cancer is shifting due to expanded vaccination coverage for HBV and HCV, increasing prevalences of chronic diseases, and growing numbers of smokers and individuals consuming excessive amounts of alcohol.^{17,18} According to a global analysis,¹⁸ liver cancer was responsible for 529 202 new cases, 483 875 deaths, and 12.9 million disability-adjusted life years in 2021. These figures represent approximately 26% and 25% increases in liver cancer incidence and mortality, respectively, from 2010 to 2021.¹⁸ In 2021, the majority of liver cancer deaths were attributed to HBV (38%), followed by HCV (30%), alcohol (19%), metabolic dysfunction-associated steatotic liver disease (9%), and other causes (4%).¹⁸

The global burden of HBV remains substantial, with an estimated HBsAg prevalence of 3.9% in 2016, corresponding to nearly 291 million infections.¹⁹ However, only 10% (29 million) of these infections were diagnosed, and just 5% (4.8 million of 94 million eligible individuals) received antiviral therapy.¹⁹ The absolute number of liver cancer cases due to hepatitis B increased by 21%, and associated deaths rose by 17% from 2010 to 2021 globally.²⁰ The global age-standardised incidence rate for liver cancer due to hepatitis B declined, with an annual percentage change of -0.60% (95% uncertainty interval: -0.69% to -0.51%); the age-standardised death rate also decreased, with an annual percentage change of -0.98% (95% uncertainty interval: -1.24% to -0.72%).¹⁸

To reduce the prevalence and burden of HBV infection, two primary screening strategies have been proposed and implemented in various countries: universal screening and screening in higher-prevalence settings. In the United States, the Centers for Disease Control and Prevention updated its guidelines in 2023, recommending hepatitis B screening using three laboratory tests at least once in a lifetime for adults aged ≥ 18 years.²¹ Prior to this update, hepatitis B screening was recommended only for pregnant women and populations at increased risk of chronic HBV infection.²¹ This policy change was informed by a study demonstrating the cost-effectiveness of universal screening, particularly in settings with an undiagnosed chronic hepatitis B prevalence of 0.24% and annual antiviral treatment costs below US\$894.²² Universal screening also simplifies implementation by eliminating complex risk stratification, which is challenging for healthcare workers to effectively implement in real-world settings.²² Conversely, targeted screening may be more cost-effective in settings where the prevalence of undiagnosed HBsAg is very low ($<0.026\%$), often achievable through universal neonatal vaccination and high screening coverage.²² Targeted screening also requires fewer resources, making it more feasible in resource-limited contexts.²²

Proposed programme overview

In the 2024 Policy Address, the Hong Kong Government announced plans to introduce a subsidised hepatitis B screening programme to prevent liver cancer.²³ Under this programme, District Health Centres and family doctors will provide risk-based hepatitis B screening and management through strategic purchasing.²³ The initiative aims to support Hong Kong in achieving the World Health Organization's viral hepatitis elimination goals²⁴ by increasing awareness among individuals unaware of their HBV infection. The programme will involve Hong Kong's 18 District Health Centres, which will offer simple blood tests. Family doctors will follow up with hepatitis B carriers, ensuring

consistent monitoring for this chronic and often asymptomatic condition, which can persist for 20 to 30 years.²³ The programme will adopt a risk-based screening approach, initially offering free screening to individuals with elevated risk of HBV infection, such as family members of hepatitis B patients, and subsequently expanding to other adults.²⁵ Additional high-risk groups, including people who inject drugs, individuals with human immunodeficiency virus, men who have sex with men, sex workers, and prison inmates, will be prioritised for testing.²⁵ Screening may also target specific age-groups to more effectively reduce severe morbidity and mortality.

Benefits of the proposed programme

The proposed programme offers several advantages. First, it will improve access to screening for individuals at high risk of HBV infection, addressing resource constraints in Hong Kong's healthcare system while enhancing clinical outcomes by prioritising vulnerable populations. Second, the programme has the potential to reduce liver cancer rates through early detection and intervention. Considering the strong association between HBV infection and liver cancer, this initiative could significantly alleviate the burden of both conditions. Finally, the programme will strengthen community healthcare by identifying at-risk individuals early, preventing progression to more severe disease, and reducing strain on the healthcare system.

Implementation considerations

Before implementing the proposed hepatitis B screening programme, three critical aspects must be carefully addressed and optimised to ensure its success.

First, it is essential to assess and address the training needs of healthcare providers. The shortage of healthcare professionals in Hong Kong, combined with increasing healthcare demand, has led to prolonged waiting times for medical services.²⁶ To enhance implementation readiness, targeted and comprehensive training programmes should be developed and delivered to healthcare providers prior to the programme's launch. This training should focus on equipping providers with the necessary knowledge, skills, and workflows to ensure the programme's efficiency and effectiveness while minimising disruptions to existing services.

Second, increased public awareness of hepatitis B is vital for efforts to achieve high participation rates in the screening programme. A 2010 telephone survey revealed suboptimal public awareness of hepatitis B in Hong Kong; approximately 45% of respondents were unaware that hepatitis B is the leading cause of chronic viral hepatitis, and 73% mistakenly believed

that the virus could be transmitted by consuming contaminated seafood.²⁷ Similarly, a 2020 study identified persistent deficiencies in knowledge, attitudes and behaviours regarding viral hepatitis, as well as low screening rates, highlighting the need for comprehensive educational initiatives.²⁸ These initiatives should utilise evidence-based strategies to correct misconceptions, enhance risk awareness, and promote positive health-seeking behaviours, consistent with the World Health Organization's viral hepatitis elimination targets.²⁸

Finally, robust evaluation mechanisms should be established to monitor and assess the programme's implementation and outcomes. Key metrics can include the proportion of the target population screened relative to the estimated need and the programme's cost-effectiveness, measured by comparing cost savings from early detection and treatment with total programme expenditures. Implementation science frameworks, such as process evaluation and logic models, can be established to identify barriers, facilitators, and contextual factors influencing outcomes. This approach facilitates ongoing refinement and scalability of the programme. A structured three-phase approach is recommended to develop effective implementation strategies. In the first phase, qualitative studies using the Consolidated Framework for Implementation Research can identify obstacles and facilitators to implementation.²⁹ The second phase involves designing tailored strategies based on the Consolidated Framework for Implementation Research-linked Expert Recommendations for Implementing Change to address barriers and enhance facilitators.³⁰ In the third phase, these strategies can be evaluated and refined through consensus-building methods, such as Delphi techniques.³¹

Conclusion

The rising burden of liver cancer, largely attributable to chronic hepatitis B infection, emphasises the pressing need for robust screening and prevention strategies. The proposed subsidised hepatitis B screening programme aims to identify at-risk individuals and facilitate early detection, ultimately reducing the community's liver cancer burden. By leveraging the resources of District Health Centres and family doctors, the programme seeks to enhance public awareness and expand access to screening, particularly for high-risk populations. Efforts to ensure adequate training for healthcare providers and improve public education regarding hepatitis B will be central to the programme's success. Based on careful planning, implementation, and evaluation, this initiative has the potential to substantially advance Hong Kong's progress toward achieving the World Health Organization's viral hepatitis elimination targets.

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All authors contributed to the editorial, approved the final version for publication, and take responsibility for its accuracy and integrity.

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