衞生防護中心
Centre for Health Protection

Cancer Expert Working Group on Cancer Prevention and Screening (CEWG)

Recommendations on Prevention and Screening for Liver Cancer For Health Professionals

Local epidemiology

Liver cancer, including malignant neoplasm of the liver and intrahepatic bile ducts, was the fifth commonest cancer in Hong Kong, ranking fourth among males and 12th among females in 2022.[1] There were 1,612 reported liver cancer cases recorded (1,173 in males and 439 in females), accounting for 4.6% of all new cases.[1] The overall age-standardised incidence rate (ASIR) * was 9.2 per 100,000 standard population, with rates of 15.1 for males and 4.1 for females.[1]

2. In 2022, there were 1,412 liver cancer deaths (1,005 males and 407 females) making it the third leading cause of cancer deaths (third among males and fifth amongst females), constituting 9.6% of all cancer deaths.[1] The overall age-standardised mortality rate (ASMR)* was 7.1 per 100,000 standard population, with 11.6 for males and 3.2 for females.[1]

3. Both the ASIR and ASMR for liver cancer in Hong Kong were substantially higher than those in Western countries (e.g. Australia and United States), but lower than those in Mainland China and neighbouring

*Rates are standardised to the Segi's World Standard Population (1960).

regions like Republic of Korea and Singapore.

4. Hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for about 90% of all new cases.[2] Among 1,286 HCC patients recorded in 2022, nearly half (49.5%) were diagnosed at an early stage (stage I or II), while 44.3% were at an advanced stage (stage III or IV), and 6.2% were unstaged.[1]

5. Survival rates remain poor even in high-income countries. According to a survival study conducted by the Hong Kong Cancer Registry in 2024 involving nearly 22,000 liver cancer patients diagnosed between 2010 and 2021, the overall 5-year survival for liver cancer during this period was 29.5%.[2] Among 9,654 HCC patients for which stage data were compiled between 2016 and 2021, the 5-year survival rates for early-stage and advanced-stage HCC were 58.8% and 8.7%, respectively.[2]

Risk factors for Hepatocellular carcinoma

6. HCC is a complex disease with multiple potential causes and cofactors. Approximately 70-90% of HCC patients have a history of chronic liver disease and cirrhosis.[3] Significant risk factors include:

(i) **Hepatitis B Virus (HBV)**

Chronic HBV infection is the most important risk factor for HCC.[3,4,5,6,7,8] Individuals with chronic HBV infection have more than a 10-fold increased risk of developing HCC than uninfected individuals,[5] with a lifetime risk estimated at 10-25%.[9] In Hong Kong, chronic HBV accounts for 73.6% of HCC cases in 2022.[1] The Population Health Survey (PHS) 2020-2022 found that 6.2% of individuals aged 15-84 tested positive for hepatitis B surface antigen (HBsAg), with the highest prevalence (8.4%) in age group of 35-54, while rates were much lower in younger age groups (0.3% for age 15-24; 1.5% for age 25-34), reflecting the effectiveness of the universal childhood hepatitis B vaccination programme implemented in Hong Kong since the 1980s.[10]

(ii) **Hepatitis C Virus (HCV)**

HCV is an established risk factor and is the leading cause of HCC, especially in Western countries.[3,4,5,6,7,8] Patients with cirrhosis caused by HCV have a 17-fold higher risk of developing HCC compared to those with only HCV infection, although this risk varies with the degree of HCV-related liver fibrosis.[3] In Hong Kong, 8.2% of HCC cases were attributed to HCV infection in 2022.[1] According to PHS 2020-2022, approximately 17,000 people have hepatitis C.[11] The overall prevalence of viremic HCV infection (positive for HCV RNA) among PHS participants aged 15-84 was 0.26%, and this rate has remained consistently low in the local population over the past few decades.[10,11] Furthermore, coinfection with HBV and HCV can increase the risk of developing HCC and accounted for 0.4-3% of HCC cases in Hong Kong.[3,12]

(iii) **Cirrhosis**

Cirrhosis is an important risk factor for HCC. It develops when normal liver tissue is replaced by fibrosis due to long-term liver damage and it is clinically diagnosed usually by non-invasive tests such as liver function test and imaging.[3,5,6,7,8, 13] Various conditions can cause cirrhosis, including chronic viral hepatitis, chronic alcohol abuse acquired, inherited metabolic diseases, and genetic hemochromatosis.[6] Cirrhosis, regardless of its aetiology, increases the risk of HCC, with an annual incidence of 2-4%.[5,14] About one-third of cirrhotic patients will develop HCC during their lifetime,[6] and worldwide, 85% to 95% of HCC cases are attributed to cirrhosis.[5,7,8]

7. Other risk factors include metabolic dysfunction-associated fatty liver disease (MAFLD) (previously known as non-alcoholic fatty liver disease (NAFLD)),[15,16,17] diabetes mellitus,[18,19] obesity and high waist circumference,[20,21] alcohol consumption,[4,22,23] tobacco smoking,[4,23,24] exposure to aflatoxins,[4,25] family history of liver cancer,[26] and demographic factors (increasing age and male gender).[9,27]

8. Globally, the prevalence of MAFLD-related HCC is likely to increase concomitantly with the growing obesity epidemic.[8,15] In the United States, a large retrospective cohort study found that HCC incidence was

significantly higher in NAFLD patients (hazard ratio [HR] = 7.62; 95% confidence interval [CI] 5.76-10.09) and the risk was the highest in NAFLD patients with cirrhosis. [16] A local epidemiological study reported that 27.3% of the Chinese population aged 18-70 has NAFLD, with 3.7% of those having advanced fibrosis.[28]

Primary prevention

9. Primary prevention of HCC can be achieved with the following measures:

(i) **Prevent HBV and HCV infections**

Universal vaccination against HBV in newborns is highly effective in preventing HBV infection, and consequently reducing HCC.[5,7,8,9,29] In Hong Kong, universal neonatal vaccination programme has been implemented since 1988, along with the supplementary Primary 6 vaccination programme introduced in 1998, and the coverage for birth dose of hepatitis B vaccine among babies was consistently >99% in the past decade.[30,31] Supplementary Primary 6 vaccination programme was introduced in 1998 and overall the coverage for three doses of hepatitis B vaccine has been maintaining at very high level over 98%.[30,31]

To reduce the risk of mother-to-child transmission (MTCT) of HBV, hepatitis B immunoglobulin have been administered to babies born to HBsAg-positive mothers since the 1980s in Hong Kong.[30] Since 2020, maternal antiviral prophylaxis is recommended for pregnant women with high HBV DNA viral load (>200 000 IU/mL) to further minimise the MTCT risk of HBV.[32]

To date, there is no vaccine or other prophylaxis available against HCV. The best way to prevent HCV, same for HBV, is avoiding the risky behaviours, such as practising safer sex and never sharing needles or syringes.

(ii) **Adopt healthy lifestyles**

Avoiding alcohol consumption, quitting smoking or non-smokers should never start smoking significantly reduces HCC risk.[23, 33] Individuals

should maintain a healthy body weight through a balanced diet and regular physical activity, as mounting evidence associates obesity, diabetes, and MAFLD with increased HCC risk.[15,16,17,18,19,20,21] Furthermore, to minimise health risk from aflatoxins, people are advised to maintain a diverse diet, avoid consuming food that looks mouldy or damaged, and make sure that foods are stored properly.[34]

(iii) **Antiviral therapy**

Direct-acting antivirals (DAAs) is highly effective at clearing over 95% of HCV infections.[35] Patients treated with DAAs who achieved sustained virologic response was associated with a 76% reduction in HCC risk compared to those did not achieve SVR.[36] Antiviral treatment is also effective in inhibiting HBV replication and reducing the risk of developing cirrhosis and liver cancer.[29]

10. In sum, to reduce the risk for developing HCC, general public are recommended to:

(i) Vaccinate against HBV and prevent HBV/HCV infection by practising safer sex and never sharing needles or syringes

(ii) Adopt healthy lifestyle (no smoking, avoid alcohol consumption, have healthy diet and regular physical activities to maintain healthy body weight)

(iii) Avoid food source of aflatoxins, such as mouldy peanuts and grains

(iv) People with chronic HBV or HCV infection should consult their doctors to determine the need for antiviral treatment

Prevention and control of viral hepatitis in Hong Kong

11. In 2018, the Government established the Steering Committee on Prevention and Control of Viral Hepatitis (SCVH),[37] and in 2020, the SCVH formulated the *Hong Kong Viral Hepatitis Action Plan 2020-2024*, with reference to the World Health Organization (WHO)'s recommendations, providing a comprehensive strategy with four strategic axes, namely awareness, surveillance, prevention and treatment, with a view to eliminating viral hepatitis as a public health threat.[30] Furthermore, *the Chief Executive's 2024 Policy Address* announced that a risk-based hepatitis B screening and management programme via District Health Centers and family doctors will commence within 2025.[38]

Screening and surveillance for HCC

Target population and risk prediction scores

12. Hepatocellular carcinoma often remains asymptomatic until reaching advanced stages and the prognosis is largely dependent on the stage at which the tumour is detected. Early detection and treatment of HCC has potential of reducing morbidity and mortality. In Hong Kong, HBV and HCV infection are responsible for approximately about 74% and 8% of HCC cases, respectively.[1] While various risk prediction scores (such as The Chinese University-HCC Score (CU-HCC),[39] Liver Stiffness Measurement HCC Score (LSM-HCC),[40] PAGE-B Score,[41] etc.) have been developed to estimate the risk of HCC, there is a lack of large-scale trials to compare and assess their effectiveness. Continued research in this area would be warranted. There is currently a lack of evidence to support HCC screening for the general population at average risk. Surveillance is recommended to be focused on individuals at risk of developing HCC, specifically those with pre-existing liver diseases, including chronic HBV or HCV infections, and liver cirrhosis irrespective of its aetiology.

Accuracy of HCC screening / surveillance tools

13. Common screening/surveillance tests for liver cancer include ultrasound, alpha-fetoprotein, computed tomography and magnetic resonance imaging. Emerging serum biomarkers, such as protein induced by vitamin K absence or antagonist-II (PIVKA-II, also known as des-gamma-carboxy prothrombin (DCP)) and plasma cell-free DNA (cfDNA), are also being studied for HCC surveillance in high-risk groups.

Ultrasound

14. Abdominal ultrasound has been widely used for liver imaging, and is a non-invasive method for HCC surveillance in chronic HBV patients. A meta-analysis of 32 studies comprising 13,367 cirrhosis patients showed that ultrasound alone has a pooled sensitivity of 84% (95% CI 76%–92%) for detecting HCC at any stage, but lower at 47% (95% CI 33%–61%) for detecting early-stage HCC.[42] Its effectiveness can be affected by operator expertise and patient-specific factors such as liver disease severity.[43]

Alpha-fetoprotein (AFP) testing

15. Alpha-fetoprotein is the most widely used serum biomarker for HCC detection, but it has relatively low sensitivity for HCC when used alone. At a cut-off level of 20ng/mL, AFP shows a sensitivity of 39%-65%, a specificity of 76%-94%, and a positive predictive value of 9%-50% for detecting HCC among cirrhotic patients.[44] The sensitivity of AFP was 52% when the diameter of tumour was >3 cm, but decreased to 25% for tumours <3 cm, indicating the low sensitivity of AFP limits its potential as a single screening tool for HCC.[45] It has been reported that about 30%-40% of HCC patients are AFP-negative, leading to a considerable rate of misdiagnosis and missed diagnosis.[7]

Combined ultrasound and AFP testing

16. Combining ultrasound and AFP testing for HCC surveillance in high-risk groups is generally considered superior to using either method alone. When comparing with ultrasound alone, the sensitivities of ultrasound with AFP were significantly higher, 97% (95% CI 91%-99%) for detection of HCC at any stage and 63% sensitivity (95% CI 48%-75%) for early HCC detection, respectively.[42] However, this combination was associated with decreased specificity, with 84% (95% CI 77%–89%) for ultrasound plus AFP versus [vs.] 92% (95% CI 85%–96%) for ultrasound alone.[42]

Computed tomography (CT) and magnetic resonance imaging (MRI)

17. Studies suggested CT or MRI has higher sensitivity for detecting HCC compared to ultrasound alone. A meta-analysis of 40 studies involving 3,624 patients with chronic liver disease showed that the overall sensitivity of MRI was significantly higher than that of multidetector CT (80% vs. 68%, p= .0023).[46] However, using MRI and CT would incur higher cost and manpower implication to specialists for interpretation. There is limited evidence on the cost-effectiveness of routine CT/MRI use for screening or surveillance.

PIVKA-II

18. A meta-analysis of 27 studies with 7,507 HCC cases and 5,399 controls demonstrated that combining PIVKA-II and AFP improved sensitivity but not specificity (82%) compared to either test alone: 82% and 85% for PIVKA-II plus AFP vs. 65% and 88% for AFP alone; and vs. 69% and 89% for PIVKA-II alone, respectively. The area under the curve also increased with the

combination (0.90) compared to PIVKA-II (0.88) and AFP (0.75).[47] In Hong Kong, a pilot programme from 2022 to 2023 tested PIVKA-II combined with AFP in public hospitals involving patients who were HBV carriers, had advanced fibrosis or cirrhosis, and/ or had a high suspicion for HCC with elevated AFP or abnormal imaging findings.[48] After the clinical audit of 165 patients who underwent PIVKA-II testing, pooled analysis showed an overall sensitivity of 85.7%, specificity of 96.2%, and a positive predictive value of 50%.[48]

19. In 2023, a panel of 17 Asia-Pacific experts reached a consensus on the clinical usefulness and value of PIVKA-II for HCC surveillance and treatment monitoring. Their consensus statements include: *"PIVKA-II in combination with AFP improves the detection of HCC, including small sized tumours (≤3 cm), compared to either biomarker alone."* and *"PIVKA-II is valuable in the detection of HCC in AFP-negative HCC patients."*[49] These consensus statements are similar to the recommendations by the HCC Surveillance Expert Meeting convened by the Hong Kong Association for the Study of Liver Diseases in 2023, which recommended PIVKA-II in combination with AFP, for special patient populations (such as those with cirrhosis, normal AFP levels, and non-viral aetiologies of chronic liver disease) and the use of biomarkers (PIVKA-II and AFP) cannot serve as a substitute for semiannual liver ultrasound in HCC surveillance.[48]

Cell-free DNA

20. There is also growing interest in utilising liquid biopsies for early detection of HCC. Research indicated that detection of fragmentation patterns of cfDNA provided good differentiation between patients with and without HCC, suggesting the potential use of cfDNA as a non-invasive test for detecting HCC.[50,51] Nevertheless, further research is needed.

Efficacy, effectiveness and benefits of HCC screening / surveillance

Ultrasound and AFP testing

21. Evidence supports HCC surveillance with ultrasound in combination with AFP testing in high-risk patients improving early HCC detection and reducing mortality. A large-scale randomised controlled trial (RCT) in Shanghai (1992–1997) involved 18,156 people aged 35–39 with HBV

infection, randomised to either semiannual screening with AFP testing and ultrasound or usual care (control).[52] Among those diagnosed with HCC, the screened group had significantly higher survival rates at 1, 3, and 5 years (66%, 53%, 46%) compared to the control group (31%, 7%, 0%).[52] HCC mortality was reduced by 37% in the screened group (83.2 vs. 131.5 per 100,000; mortality rate ratio 0.63; 95% CI 0.41–0.98), despite suboptimal study adherence (58%) reported in the screened group.[52]

22. The WHO conducted an evidence review on surveillance strategies for early detection of HCC in individuals with chronic HBV and found that 6-monthly ultrasound and AFP screening compared with no intervention reduced disease-specific mortality (OR=0.57; 95% CI 0.37–0.89), while 6-monthly AFP alone did not show a significant effect.[29] The 5-year survival rate was higher for those receiving 6-monthly ultrasound and AFP screening compared to no intervention (31% vs. 23%; p= .03).[29] Although the total number of new HCC cases detected was not statistically significant, HCC was detected significantly earlier in terms of stage and with smaller lesion sizes (<3 cm or <5 cm in diameter) with both 6-monthly ultrasound and AFP (OR=11.2; 95% CI 6.7–18.7) and >6-monthly screening (OR=2.1; 95% CI 1.4–3.2), as well as with 6-monthly AFP alone, compared to no intervention.[29]

23. A systematic review of 47 studies with 15,158 cirrhotic patients, of whom 6,284 (41.4%) had HCC detected by surveillance revealed that HCC surveillance (using ultrasound with or without AFP) was associated with improved early stage detection (OR=2.08; 95% CI 1.80–2.37) and curative treatment rates (OR=2.24; 95% CI 1.99–2.52).[53] Additionally, HCC surveillance was associated with significantly prolonged survival (OR=1.90; 95% CI 1.67–2.17), which remained significant in the subset of studies adjusting for lead-time bias.[53]

Potential harms of HCC screening / surveillance

24. Routine HCC surveillance can lead to false-positive results from AFP tests or ultrasounds detecting non-HCC small lesions, such as regenerative nodules in cirrhotic livers, which may not progress to cancer, resulting in unnecessary interventions and associated physical harms, and increasing healthcare costs. In a retrospective cohort study of 680 cirrhosis patients undergoing HCC surveillance over three years, surveillance-related physical

harms were observed in 187 patients (27.5%), and most harm was mild to moderate.[54] In another prospective cohort of 614 cirrhosis patients with ≥1 surveillance over 18 months, 8.8% had physical harms related to false-positive findings with most being mild.[55]

Recommended surveillance interval

3-month versus 6-month surveillance interval

25. A multicenter RCT in France and Belgium compared the effectiveness of ultrasound in cirrhotic patients every 3 months *versus* every 6 months. The results showed no difference in either HCC incidence (11.9% vs. 12.3%, p= .13) or in the prevalence of tumours ≤30 mm in diameter (79% vs. 70%, p= .30) observed between the two groups.[56]

6-month versus 12-month surveillance interval

26. A systematic review demonstrated a significantly higher sensitivity for early HCC detection with ultrasound every 6 months than with annual surveillance (70% vs. 50%; p = .001).[57] Additionally, a meta-analysis of five retrospective cohort studies comparing the effectiveness of ultrasonography surveillance every 6 months versus every 12 months found that early HCC detection rates were significantly higher in the 6-month group compared to the 12-month group, with a RR of 1.17 (95% CI 1.08–1.26, I^2=0). The 5-year survival rate was also significantly higher for the 6-month group (RR=1.39; 95% CI 1.07–1.82, I^2=63.8%).[8]

Recommended age for HCC screening / surveillance

27. Most international and Asian guidelines for HCC surveillance do not specify an age range, focusing instead on risk factors such as chronic HBV/HCV infection, cirrhosis, or a family history of HCC. However, the *2022 China guideline for liver cancer screening* recommends initiating HCC surveillance at age 40 for high-risk groups, including those with chronic HBV/HCV or cirrhosis, and discontinuing at age 74 or when life expectancy is <5 years. For patients with liver cirrhosis, the *China guideline* imposes no age limits for starting or stopping surveillance.[8]

Cost-effectiveness of HCC screening / surveillance

28. Currently, there is no evidence suggesting that screening for HCC among general population at average risk provides has an overall benefit greater than harm or is effective/cost-effective. Overseas studies suggested that HCC surveillance targeting high-risk patients, such as those with cirrhosis or chronic hepatitis B or C, would be cost-effective by semiannual ultrasound, with or without AFP testing whilst surveillance using CT or MRI would be less cost-effective.[5,8,29,58,59,60]

29. A Markov modelling study compared surveillance strategies of ultrasound alone, combined ultrasound and AFP, and no surveillance in cirrhosis patients.[60] Based on the assumptions of HCC incidence >0.4% per year, semiannual surveillance adherence >19.5%, and a willingness-to-pay threshold of USD100,000 per quality-adjusted life year, combined ultrasound and AFP was found to be the most cost-effective strategy for HCC surveillance compared with ultrasound alone or no surveillance.[60] Additionally, studies on the cost-effectiveness of strategies combining other biomarkers (such as PIVKA-II, AFP-L3 or cfDNA) for HCC surveillance remains limited.

International guidelines on HCC screening / surveillance

30. International guidelines, including the American Association for the Study of the Liver Diseases,[7] the European Association for the Study of the Liver,[6] the Asian Pacific Association for the Study of the Liver,[5] and the WHO,[29] recommend semiannual surveillance for HCC in at-risk individuals. While the definition of high-risk groups varies slightly among health agencies, people with cirrhosis, chronic HBV or HCV infection are generally considered as at increased risk of developing HCC. Most Asian HCC practice guidelines, including those from China, also recommend routine HCC surveillance every six months for high-risk groups, which include people with chronic hepatitis B or C infection and liver cirrhosis.[8,61,62,63,64] Most international guidelines recommend the combined use of ultrasound and AFP testing for HCC surveillance,[5,7,8,62,63,64,65,66] while guidelines from Japan and Taiwan also suggest the use of PIVKA-II in clinical settings for surveillance.[63,64] Details of these HCC surveillance guidelines are summarised in **Annex**.

International practices on HCC screening / surveillance

31. HCC screening or surveillance programmes have been introduced in some East Asian countries where HCC is more prevalent, such as China, Japan and South Korea. In Mainland China, HCC surveillance by ultrasound and AFP are offered to patients with chronic HBV infections under three cancer screening projects.[8] In Japan, HCC surveillance targeting high risk patients by ultrasound and three tumour markers (AFP, PIVKA-II and AFP-L3) has been implemented to eligible individuals under national health insurance.[67] In South Korea, HCC surveillance by combined abdominal ultrasonography and AFP testing are offered every six months for individuals aged 40 and over who are HBsAg-positive or anti-HCV positive or have liver cirrhosis.[68]

Conclusion

32. Most of the causes and associated risk factors for HCC are preventable and primary prevention of HCC remains the most important in reducing morbidity and mortality from HCC. In addition to HBV vaccination to prevent HBV infection, it is also advised to adopt a healthy lifestyle (including no smoking, avoiding alcohol consumption, regular physical activity and healthy diet to maintain healthy body weight) to prevent HCC and other cancers as well as other major non-communicable diseases. Patients with chronic viral hepatitis should seek medical advice if antiviral treatment is needed.

33. Currently, there is no evidence in supporting HCC screening among general population at average risk. Screening for HCC for general population at average risk is not recommended.

34. In view of local epidemiology and overseas evidences, patients with high risk of developing HCC (including chronic HBV infection, chronic HCV infection, cirrhosis irrespective of its aetiology) are recommended to seek medical advice on surveillance for HCC by combined ultrasound and AFP every 6 months.

35. There is lack of evidence in supporting routine use of CT or MRI as a cost-effective screening strategy.

36. There are emerging serum biomarkers, such as PIVKA-II, which in combination with AFP has shown higher sensitivity compared to AFP alone. In Hong Kong, their current indication for HCC surveillance is mainly on an individualised clinical basis for selected patient groups. Further research particularly on their cost-effectiveness as compared with AFP / ultrasound would be useful in delineating their role in routine application in HCC surveillance in high-risk individuals.

Revised recommendations by CEWG

37. Taking local epidemiology, emerging scientific evidence, overseas screening recommendations and screening practices into consideration, the CEWG revised the recommendations on HCC prevention and screening / surveillance which were endorsed by the Cancer Coordinating Committee at its 20th meeting on 3 June 2025. The recommendations for the local population are given below.

Prevention
1. Universal hepatitis B vaccination to newborns is effective in preventing chronic hepatitis B virus infection. 2. All individuals are recommended to adopt a healthy lifestyle (including no smoking, avoid alcohol consumption, have regular physical activities and healthy diet to maintain healthy body weight) as well as avoid food source of aflatoxins. 3. People with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection are recommended to seek medical advice periodically to determine whether antiviral treatment is needed.
For asymptomatic population at average risk
4. Routine screening for liver cancer, including ultrasound or alpha-fetoprotein (AFP) testing, is NOT recommended for asymptomatic population at average risk.
For asymptomatic persons at increased risk
5. Persons with chronic HBV, HCV infection or liver cirrhosis regardless of the cause are at increased risk of hepatocellular carcinoma. Persons at increased risk should seek advice from doctors regarding regular surveillance every 6 months with ultrasound and AFP testing.

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Annex

Summary of selected international guidelines for HCC screening / surveillance in high risk groups

Organisation	Year	Definition of high risk groups	Screening tool	Screening interval
World Health Organization[29]	2024	• People with ➢ Cirrhosis, regardless of age or other risk factors ➢ Family history of HCC • If no family history of HCC or evidence of cirrhosis, people older than 40 years and with HBV DNA level >20,000 IU/mL	Ultrasound and AFP testing	Every 6 months
American Association for the Study of Liver Diseases[7]	2023	• Patients with ➢ Child-Turcotte-Pugh A or B cirrhosis, any etiology ➢ Child-Turcotte-Pugh C cirrhosis on the liver transplant waitlist • Non-cirrhotic chronic HBV carriers: man from endemic country age >40 years, woman from endemic country age >50 years, persons from Africa at earlier age, family history of HCC, PAGE-B score ≥10	Ultrasound and AFP testing	Every 6 months
Cancer Council Australia[69]	2023	People with • Hepatitis B who are at higher risk (based on age and background) • Liver cirrhosis • Liver cirrhosis and hepatitis C (even if cured) • Waiting for a liver transplant • Other long-term liver problems	Ultrasound, with or without AFP testing	Every 6 months
National Comprehensive Cancer Network (NCCN)[65]	2023	• Patients with Cirrhosis due to: HBV/ HCV, alcohol, NAFLD, other causes • HBV carriers without cirrhosis • Following patients are at additional risk: Carriers with family history of HCC, Asian men aged ≥40 years, Asian women aged ≥50 years, African/North American Blacks	Ultrasound and AFP testing	Every 6 months
National Institute for Health and Care Excellence (NICE), United Kingdom[70,71]	2023	Adults with chronic hepatitis B • People with significant fibrosis (METAVIR stage ≥F2 / Ishak stage ≥3) or cirrhosis • People without significant fibrosis or cirrhosis if older than 40 and has family history of HCC and HBV DNA ≥20,000 IU/mL	Ultrasound and AFP testing	Every 6 months
	2017	People with cirrhosis who do not have HBV infection	Ultrasound, with or without AFP testing	Every 6 months

Organisation	Year	Definition of high risk groups	Screening tool	Screening interval
Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan[64]	2023	High-risk patients with chronic HBV, HCV, and with cirrhosis	Ultrasound and tumour markers (such as AFP and/or PIVKA-II)	Every 6 months
		Extremely high-risk patients (particularly those diagnosed with chronic HBV/HCV-related cirrhosis) and/or patients whose liver is difficult to image with ultrasonography	Combine regular screening methods with dynamic CT or MRI or gadoxetic acid-enhanced MRI	Every 6-12 months
China guideline for liver cancer screening (Beijing)[8]	2022	Patients with • Cirrhosis, regardless of the cause • Chronic HBV and/or HCV infection, and aged ≥40 years	Ultrasound and AFP testing	Every 6 months
Korean Liver Cancer Association and National Cancer Centre Korea[62]	2022	Patients with chronic hepatitis B, chronic hepatitis C, and liver cirrhosis	Ultrasound and AFP testing	Every 6 months
Japan Society of Hepatology[63]	2021	High-risk group: HBV/HCV-associated chronic hepatitis and cirrhosis of other etiologies	Ultrasound and tumour marker (AFP, AFP-L3, and PIVKA-II)	Every 6 months
		Extremely high-risk group: HBV/HCV-related cirrhosis	Ultrasound and tumour marker (AFP, AFP-L3, and PIVKA-II)	Every 3-4 months
			Dynamic CT or MRI (optional)	Every 6 months
Academy of Medicine, Singapore[66]	2019	Hepatitis B carrier or individuals with liver cirrhosis	Ultrasound and AFP testing	Every 6 months
European Association for the Study of the Liver[6]	2018	• Cirrhotic patients, Child-Pugh stage A and B • Cirrhotic patients, Child-Pugh stage C awaiting liver transplantation • Non-cirrhotic HBV patients at intermediate or high risk of HCC (PAGE-B score ≥10) • Non-cirrhotic F3 patients, regardless of aetiology may be considered for surveillance based on an individual risk assessment	Ultrasound	Every 6 months
Asian Pacific Association for the Study of the Liver[5]	2017	• Cirrhotic hepatitis patients • Non-cirrhotic chronic HBV carriers who are / have: Asian females >50 years, Asian males >40 years, Africans ages >20 years, family history of HCC	Ultrasound and AFP testing	Every 6 months

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