

**Appendix 2. Summary of included studies with outcomes**

| Author                          | Year | Country   | Study design               | Outcomes   | Barriers and facilitators   |
|---------------------------------|------|-----------|----------------------------|--|---|
| <b>Viral hepatitis patients</b> |      |           |                            |  |   |
| McMahon et al <sup>1</sup>      | 2000 | USA       | Prospective cohort         | HCC diagnosed in 32 participants, AFP elevated in 97% of these; mean age at diagnosis 24 years. 83% detected through surveillance were at a resectable stage; 5-year survival rate 42%   | n/r   |
| Leykum et al <sup>2</sup>       | 2007 | USA       | Retrospective chart review | For all HCPs: 22% of patients were screened prior to HCC diagnosis; all screen-identified HCC was detected at early stages; improved survival for screened patients: Average survival: 19.8 months vs 8.5 months. Decreased risk of HCC death associated with PCP care delivered in a tertiary setting (unadjusted: HR 1.47, 95%CI 1.01, 2.14), but no associations in adjusted analysis | Barriers: Care from a non-hepatology clinic   |
| Sarkar et al <sup>3</sup>       | 2012 | USA       | Retrospective cohort       | 67% screened in first year after HBV diagnosis; 47% in second year, 24% in 10th year. HCC diagnosed in 51 patients. Screened patients more likely to be diagnosed at an early stage of HCC (79% vs 19%) and receive curative treatment (71% vs 30%). Median survival was associated with curative treatment (HR 0.3, 95% CI: 0.1–0.9).   | Predictors of surveillance: Attendance at a liver clinic, female, age 40–64 years, cirrhosis, recent HBV diagnosis<br>High ALT negatively associated with surveillance  |
| Sarkar et al <sup>4</sup>       | 2014 | USA       | Retrospective cohort       | Imaging within 18 months: 56% overall; 73% for PCPs vs 92% for gastroenterologists<br><br>Imaging + AFP: 49% overall; PCPs 65% vs gastroenterologists 87%<br><br>AFP only: PCPs 13% vs 5%  | n/r   |
| Wu et al <sup>5</sup>           | 2014 | USA       | Retrospective cohort       | 55% received surveillance at least once per 15 months; 35% ≤ every 15 months (mean surveillance interval 3.9 years); 10% received no surveillance. Greater odds of timely HCC surveillance when managed by a gastroenterologist versus PCP: OR 6.87 (95% CI: 4.5, 9.7)   | Non-adherence in primary care settings: 26% patient factors, 74% physician failure to order<br><br>Non-adherence in gastroenterology specialist settings: 88% patient factors, 12% physician failure to order   |
| Allard et al <sup>6</sup>       | 2017 | Australia | Retrospective cohort       | Follow-up 4.5 years: 'good adherence' 27%, suboptimal adherence 43%, poor adherence 30%  | Half the patients having regular viral load tests had suboptimal/poor adherence suggesting a different barrier for US (ie availability of pathology within the clinic)<br><br>Surveillance at recommended intervals was more likely in patients receiving antiviral treatment, more recently diagnosed, having regular viral load tests |

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| O'Leary et al <sup>7</sup>     | 2018 | Australia | Quasi-experimental                                   | Receipt of 2 US over 12 months: Baseline: 26%; Post-implementation: 88%; Controls: 10%   | n/r  |
| DeSilva et al <sup>8</sup>     | 2022 | USA       | Quasi-experimental                                   | 6 months prior to baseline (ie introduction of the intervention): Surveillance uptake: intervention (PCP) group 27%, GI 22%; PCP: 3%<br><br>6 months subsequent to introduction of intervention: intervention (PCP) group 34%, GI 15%; PCP: 2%   | n/r  |
| Burman et al <sup>9</sup>      | 2014 | USA       | Cross-sectional survey and clinical audit            | HCP survey: 96% of HCPs reported regular HCC surveillance in the centre; 43% were not familiar with recommendations<br><br>Audit: 51% of patients had some form of surveillance in preceding 12 months; of these, 51% had AFP, 13% imaging, 36% AFP + imaging  | Barriers: HCP characteristics: older provider age, >25% Asian patients in the practice<br><br>Facilitators: HCP characteristics: provider of Asian ethnicity, higher HBV/HCC knowledge, positive provider attitude towards surveillance  |
| Gowda et al <sup>10</sup>      | 2017 | USA       | Mixed methods  | Adherence to surveillance recommendations: 15% of patients had US surveillance at 6- to 12-month intervals<br><br>No statistical difference on surveillance adherence rates for provider type, however PCP had a slightly lower rate   | Barriers: Under-recognition of chronic HBV, infrequent patient visits, lack of continuity of care, inadequate development of patient-PCP trust relationship, patients not following up with US   |
| Davila et al <sup>11</sup>     | 2010 | USA       | Retrospective cohort of patients and their providers | Overall: 17% patients had regular surveillance, 38% inconsistent<br><br>Regular surveillance group: 52% US + AFP; 46% AFP, 2% US<br><br>9.8% of cirrhosis + ALD patients screened; 29% of cirrhosis + HBV/HCV; 32% of cirrhosis + ALD + HCV/HBV; 5% of cirrhosis only  | All HCPs: Patients receiving surveillance were more likely to be younger, female or Chinese, higher income and education. Patients seen by a gastroenterologist alone or also a PCP were five times more likely to be screened regularly |
| Patwardhan et al <sup>12</sup> | 2011 | USA       | Retrospective cohort                                 | Overall, 51% received recommended surveillance. Surveillance in context of ≥12-monthly follow-up with gastroenterologist: 67% of patients screened. For primary care only patients: 23% were screened  | Facilitators: Being seen ≥ annually by a gastroenterologist  |
| Del Poggio et al <sup>13</sup> | 2015 | Italy     | Quasi-experimental                                   | Pre-intervention: 35% diagnosed through surveillance, post-intervention 55%. HCC diagnosed at early stage (BCLC-A) increased from 48% to 64% in intervention group, and from 38% to 43% in the control. 5-year survival increased in the intervention group: 20% to 40%; in the control group this remained unchanged: 20% | n/r  |

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| Beste et al <sup>14</sup>                | 2015 | USA     | Quasi-experimental   | 'Adequate' surveillance was 28% for intervention site vs 18% at control sites  | n/r  |
| Ahmed Mohammed et al <sup>15</sup>       | 2017 | USA     | Retrospective cohort | 14% received 100% of biannual surveillance, 16% received 75–99%, 29% received 50–74%, 21% received 25–49% 13% received 1–24%, 7% received no surveillance  | For 26 patients not receiving surveillance: 50% were recommended by a specialist but not implemented by PCP or patients did not attend; 26% due to a failure in discharge planning; 15% specialist diagnosed cirrhosis but did not recommend surveillance; 8% diagnosis made by radiologist/pathologist but not recorded in clinical notes |
| Atiq et al <sup>16</sup>                 | 2017 | USA     | Retrospective cohort | Over three years 26.3% had $\geq 3$ US, 1.6% had $\geq 6$ US<br>70% of HCC detected at an early stage vs 40% with no surveillance<br>23% of patients eligible for curative treatment vs 0% not receiving surveillance  | n/r  |
| Singal et al <sup>17</sup>               | 2017 | USA     | Retrospective cohort | Surveillance over 2 years: 2% received consistent surveillance, 33% inconsistent surveillance and 65% no surveillance  | Compared with HCV patients, HBV patients were more likely to receive surveillance and patients with ALD cirrhosis and NASH were less likely. Receipt of any surveillance was associated with care from a gastroenterologist/hepatologist   |
| Goldberg et al <sup>18</sup>             | 2017 | USA     | Retrospective cohort | Up-to-date with surveillance over median of 4.7 years: 18% for US/MRI/CT   | Small association between numbers of US and PCP visits. Number of specialty visits associated with increased odds of US, independent of PCP visits   |
| Singal et al <sup>19</sup>               | 2019 | USA     | Randomised trial     | Surveillance over 2 years: Mailed US outreach: 18%; mailed US outreach + patient navigation: 23%, usual care: 7%. HCC diagnosed in 1.8% of outreach/navigation, 1.0% of outreach, 2.3% of usual care   | Stronger effect of intervention for patients with Child-Pugh class B and those not in receipt of hepatology care   |
| Rodriguez Villalvazo et al <sup>20</sup> | 2020 | USA     | Retrospective cohort | Patients living $>60$ miles away were less likely to be screened (any imaging) (HR 0.83; 95% CI: 0.79, 0.88) compared with those living 10–30 miles away (HR 1.05; 95% CI: 1.00, 1.11). Patients living in large/small rural towns or isolated areas less likely to receive surveillance | Increased travel time to a VA medical centre was associated with reduced surveillance  |
| Yeo et al <sup>21</sup>                  | 2021 | USA     | Retrospective cohort | Surveillance across all HCPs: 6–12 months: 8.8%, 12–24 months: 25.3%, $>24$ months: 40.5%, no testing: 45.4%. Being seen by a PCP negatively associated with surveillance: OR 0.48; 95% CI: 0.46, 0.52   | n/r  |

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| Toyoda et al <sup>22</sup>   | 2006 | Japan   | Retrospective cohort   | Tertiary-based surveillance: 33% of HCC diagnosed at BCLC 1, 36% at Stage 2; 53% Class A Child-Pugh. PCP surveillance: 13% of HCC diagnosed at BCLC 1, 31% at stage 2; 46% Class A Child-Pugh. No surveillance: 4% of HCC diagnosed at Stage 1, 16% at Stage 2; 34% Class A Child-Pugh.<br><br>Survival 2001–04: Surveillance in tertiary and primary care: 5-year survival 36%, for no surveillance 19%. | n/r   |
| Nguyen et al <sup>23</sup>   | 2007 | USA     | Cross-sectional survey | Any surveillance undertaken in high-risk patients: Gastroenterologists: 100%; internal medicine: 88%; family practice: 84.2%  | Facilitators: Knowledge that prevalence of CHB is higher in Asian Americans, surveillance reduces mortality, is cost-effective, non-surveillance represents malpractice   |
| Ferrante et al <sup>24</sup> | 2008 | USA     | Cross-sectional survey | Self-report: 25% reported they would order AFP or abdominal imaging for HBV patients with abnormal LFTs   | HBV patients, surveillance rates (self-reported) were higher in female PCPs and in group practice (vs individual practice [29%])<br><br>HCV patients, doctors in academic settings more likely to screen for HCC (41%)  |
| Khalili et al <sup>25</sup>  | 2011 | USA     | Cross-sectional survey | 88% self-reported using abdominal imaging and AFP 6- to 12-monthly<br><br>66% (of all providers) screened ≥75% of HBV patients for HCC, and 94% self-reported HCC surveillance for HBV patients<br><br>27% were unfamiliar with guidelines  | Barriers: Lack of imaging resources (59%), unclear guidelines (35%); difficulty accessing specialty care (35%), costs to patients (31%), poor patient adherence (54%), lack of insurance (49%)  |
| El-Serag et al <sup>26</sup> | 2013 | USA     | Cross-sectional survey | 71% self-reported surveillance in line with recommendations. HCPs working in gastroenterology/hepatology specialities were more likely to recommend guideline-concordant HCC surveillance than other groups   | Barriers: Limited knowledge of HCC surveillance recommendations, lack of availability HCC treatment services<br><br>Facilitators: Experience with management of HCV patients  |
| Han et al <sup>27</sup>      | 2014 | USA     | Qualitative            | n/r   | Barriers: Patients too busy with work, language and culture barriers, limited awareness of CHB, CHC and HCC surveillance, cost<br><br>Facilitators: Follow-up of surveillance closer to the community (ie distance), ongoing care provided by the PCP, community support of the PCP, patient navigators of the same ethnicity |

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| McGowan et al <sup>28</sup>           | 2015 | USA     | Cross-sectional survey | PCPs caring for patients with cirrhosis, 45% recommended surveillance   | Barriers: Patient factors: poor adherence, financial constraints, lack of insurance<br>Facilitators: Evidence to support surveillance, PCP knowledge of HCC treatment modalities   |
| Dalton-Fitzgerald et al <sup>29</sup> | 2015 | USA     | Cross-sectional survey | Self-reported surveillance: Median annual US surveillance 65%, median biannual surveillance 15%. 86% used US ± AFP<br><br>US-based surveillance conducted by ~33% biannually and ~67% annually  | Barriers: 68% stated not being up-to-date with guidelines; communication difficulties with patients about surveillance (56%), more pressing clinical issues (52%)  |
| Mukhtar et al <sup>30</sup>           | 2017 | USA     | Cross-sectional survey | Half of the participants reported surveillance >75% of CHB patients; AFP and US the most frequent used  | Barrier: Practicing within a safety net system<br>Facilitator: PCPs with >25% of patients speaking English as a second language (OR 4.26; 95% CI: 1.76, 10.30)   |
| Fitzgerald et al <sup>31</sup>        | 2018 | USA     | Cross-sectional survey | 92% responded surveillance should be carried out using US; and 64% reported this should occur every 6–12 months<br><br>For HBV patients, 68% recommended surveillance; 78% responded that HBV patients from China and Africa should be screened   | Barriers: Provider: lack of clear guidelines (49%), competing healthcare priorities (45%), time constraints (35%), lack of referral options (32%)<br><br>Patient barriers: lack of awareness of HCC risk (85%), cost/lack of insurance (70%) |
| Simmons et al <sup>32</sup>           | 2019 | USA     | Cross-sectional survey | 67% conducted surveillance, 33% referred to specialist care for this<br><br>Of those ordering surveillance: >90% US ± AFP. CT/MRI more commonly used for patients with NASH/obesity or decompensated cirrhosis. 36.8% reported not performing surveillance in healthy patients aged >80 years with compensated cirrhosis. 62% screened HCV patients without cirrhosis | Barriers: PCPs not being up to date with recommendations (42%), not considered role of PCP (29%), limited clinical time (14%), other clinical priorities (12%), communication difficulties (10%)   |

AFP,  $\alpha$ -fetoprotein; ALD, alcoholic liver disease; ALT, alanine transaminase; BCLC, Barcelona Clinic level cancer; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CI, confidence interval; CT, computed tomography; GI, gastroenterologist; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCP, healthcare provider; HCV, hepatitis C virus; HR, hazard ratio; LFT, liver function test; MRI, magnetic resonance imaging; NASH, non-alcoholic steatohepatitis; n/r, not reported; OR, odds ratio; PCP, primary care provider; US, ultrasound; VA, Veterans Affairs.

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