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Supplementary Table 1. Search strategy

<i>Search strategy of Pubmed</i>	
#1	((((((Carcinoma[ti] OR tumor[ti] OR cancer[ti] OR neoplasm[ti])) AND (Liver[ti] OR hepatocellular[ti] OR hepatic[ti]))) OR (Hcc[ti] OR hepatoma[ti])) OR "Liver Neoplasms"[Mesh]) OR "Carcinoma, hepatocellular"[Mesh])
# 2	((("Mass Screening"[Mesh]) OR "Early Detection of Cancer"[Mesh]) OR (screening[ti] OR screen[ti] OR screened[ti] OR surveillance[ti] OR "early detection"[ti]))
#3	((((((("Tomography, X-Ray Computed"[Mesh]) OR ("Computed tomography"[ti] OR "CT"[ti]))) OR (((DCP[ti] OR "Des-gamma carboxyprothrombin"[ti] OR PIVKA*[ti] OR PIVKA-II[ti] OR "PIVKA II"[ti] OR "Protein induced by vitamin K absence*[ti])) OR (AFP-L3[ti] OR "AFP L3"[ti] OR "Lens culinaris agglutinin-reactive alpha-fetoprotein"[ti] OR "lectin-bound AFP"[ti] OR "L3 fraction"[ti] OR "L3-fraction"[ti] OR "glycosylated AFP"[ti]))) OR (("alpha-Fetoproteins"[Mesh]) OR (alpha-fetoproteins[ti] OR alpha-fetoprotein[ti] OR "alpha fetoprotein"[ti] OR AFP[ti] OR alpha-1-fetoprotein[ti] OR "alpha1fetoprotein"[ti] OR "alpha 1 fetoprotein"[ti] OR alpha-fetoglobulin[ti] OR "alpha fetoglobulin"[ti]))) OR ((("Magnetic Resonance Imaging"[Mesh]) OR ("Magnetic resonance imaging"[ti] OR "MRI"[ti]))) OR (((ultrason*[ti] OR ultrasound*[ti] OR ultrasonography[ti] OR echograph*[ti] OR echotomograph*[ti] OR doppler*[ti] OR B-mode[ti] OR B-scan[ti] OR grey*scale[ti] OR sonogram[ti] OR sonography[ti]))) OR "Ultrasonography"[Mesh])))
#4	#2 and #3
#5	#1 and #4
#6	(Animals[Mesh] NOT humans[Mesh])
#7	#5 NOT#6
<i>Search strategy of Embase</i>	
#1	(liver:ti OR hepatocellular:ti OR hepatic:ti) AND (carcinoma:ti OR tumor:ti OR cancer:ti OR neoplasm:ti) OR hcc:ti OR hepatoma:ti OR 'liver neoplasms'/exp OR 'hepatocellular carcinoma'/exp
# 2	screening:ti OR screen:ti OR screened:ti OR surveillance:ti OR 'early detection':ti OR 'mass screening'/exp OR 'early detection of cancer'/exp
#3	ultrason*:ti OR ultrasound*:ti OR ultrasonography:ti OR echograph*:ti OR echotomograph*:ti OR doppler*:ti OR 'b mode':ti OR 'b scan':ti OR grey*scale:ti OR 'sonogram':ti OR sonogram:ti OR 'sonography':ti OR sonography:ti OR 'ultrasonography'/exp OR 'alpha-fetoproteins':ti OR 'alpha-fetoprotein':ti OR 'alpha fetoprotein':ti OR afp:ti OR 'alpha-1-fetoprotein':ti OR 'alpha1fetoprotein':ti OR 'alpha 1 fetoprotein':ti OR 'alpha fetoglobulin':ti OR 'alpha-fetoproteins'/exp OR 'afp l3':ti OR 'lens culinaris agglutinin-reactive alpha-fetoprotein':ti OR 'lectin-bound afp':ti OR 'l3 fraction':ti OR 'l3-fraction':ti OR 'glycosylated afp':ti OR dcp:ti OR 'des-gamma carboxyprothrombin':ti OR pivka*:ti OR 'pivka ii':ti OR 'protein induced by vitamin k absence':ti OR 'computed tomography':ti OR 'ct':ti OR 'tomography, x-ray computed'/exp

	OR 'magnetic resonance imaging':ti OR 'mri':ti OR 'magnetic resonance imaging'/exp
#4	#2 and #3
#5	#1 and #4
#6	[humans]/lim AND ('english':la OR 'chinese':la)
#7	#5 and #6
<i>Search strategy of the Cochrane library</i>	
#5	#1 MeSH descriptor: [Liver Neoplasms] explode all trees #2 MeSH descriptor: [Carcinoma, Hepatocellular] explode all trees #3 Hcc:ti or hepatocellular:ti (Word variations have been searched) #4 ((Carcinoma or tumor or cancer or neoplasm) and (Liver or hepatocellular or hepatic)):ti (Word variations have been searched) #5 #1 or #2 or #3 or #4
#9	#6 MeSH descriptor: [Mass Screening] explode all trees #7 MeSH descriptor: [Early Detection of Cancer] explode all trees #8 (Screening or screen or screened or surveillance or "early detection"):ti (Word variations have been searched) #9 #6 or #7 or #8
#15	#10 MeSH descriptor: [Ultrasonography] explode all trees #11 (ultrason* or ultrasound* or ultrasonography or echograph* or echotomograph* or doppler* or 'b mode' or 'b scan' or grey*scale or 'sonogram' or sonogram or 'sonography' or sonography):ti (Word variations have been searched) #12 #10 or #11 #13 MeSH descriptor: [alpha-Fetoproteins] explode all trees #14 (alpha-fetoproteins or alpha-fetoprotein' or 'alpha fetoprotein' or afp or 'alpha 1 fetoprotein' or 'alpha 1 fetoprotein' or 'alpha fetoglobulin'):ti (Word variations have been searched) #15 #13 or #14 #16 (AFP-L3 or "AFP L3" or "Lens culinaris agglutinin-reactive alpha-fetoprotein" or "lectin-bound AFP" or "L3 fraction" or "L3-fraction" or "glycosylated AFP"):ti (Word variations have been searched) #17 (DCP or "Des-gamma carboxyprothrombin" or PIVKA* or PIVKA-II or "PIVKA II" or "Protein induced by vitamin K absence*"):ti (Word variations have been searched) #18 ("Magnetic resonance imaging" or "MRI"):ti (Word variations have been searched) #19 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees #20 #18 or #19 #21 MeSH descriptor: [Tomography, X-Ray Computed] explode all trees #22 ("Computed tomography" or "CT"):ti (Word variations have been searched) #23 #21 or #22 #24 #12 or #15 or #16 or #17 or #20 or #23

#26	#24 AND #9
#27	#5 AND#26
<i>Search strategy of Clinicaltrials.gov</i>	
	liver cancer OR liver neoplasm OR liver tumour OR liver carcinoma OR hepatocellular carcinoma OR hepatic cancer OR hepatic carcinoma OR HCC screen OR surveillance OR 'early detection of cancer' OR 'mass screening' Applied Filters: ☐ Completed
<i>Search strategy of Web of science</i>	
	((TI=(Liver OR hepatocellular OR hepatic) AND TI=(Carcinoma OR tumor OR cancer OR neoplasm)) OR TI=(Hcc OR hepatoma)) AND (TI=(screening OR screen OR screened OR surveillance OR "early detection")) AND (TI=("Tomography, X-Ray Computed" OR "Computed tomography" OR "CT" OR DCP OR "Des-gamma carboxyprothrombin" OR PIVKA* OR PIVKA-II OR "PIVKA II" OR "Protein induced by vitamin K absence*" OR AFP-L3 OR "AFP L3" OR "Lens culinaris agglutinin-reactive alpha-fetoprotein" OR "lectin-bound AFP" OR "L3 fraction" OR "L3-fraction" OR "glycosylated AFP" OR alpha-fetoproteins OR alpha-fetoprotein OR "alpha fetoprotein" OR AFP OR alpha-1-fetoprotein OR "alpha1fetoprotein" OR "alpha 1 fetoprotein" OR alpha-fetoglobulin OR "alpha fetoglobulin" OR "Magnetic Resonance Imaging" OR "Magnetic resonance imaging" OR "MRI" OR ultrason* OR ultrasound* OR ultrasonography OR echograph* OR echotomograph* OR doppler* OR B-mode OR B-scan OR grey*scale OR sonogram OR sonography))
<i>Search strategy of Google scholar</i>	
	allintitle: (("liver cancer" OR "liver neoplasm" OR "liver tumour" OR "liver carcinoma" OR "hepatocellular carcinoma" OR "hepatic cancer" OR "hepatic carcinoma" OR "HCC") AND ("screen" OR "surveillance" OR "early detection"))

Supplementary 2. Risk-of-bias assessment in individual studies

Supplementary Table 2.1 Risk-of-bias assessment of RCT(CROB)

Included studies	①	②	③	④	⑤	⑥	⑦	Total
Comparing different screening intervals								
Trinchet.et al ^[1]	1	1	0	0	1	1	NA	4/7
Wang, J. H.et al ^[2]	1	0	1	0	1	1	0	4/7
Comparing different screening modalities								
Pocha.et al ^[3]	1	1	NA	NA	1	1	NA	4/7
Rhee.et al ^[4]	1	NA	0	0	1	1	NA	3/7
Kudo.et al ^[5]	1	1	NA	NA	1	1	NA	4/7

Notes: ① =Random sequence generation, ② = Allocation concealment, ③ =Blinding of participants and personnel, ④ = Blinding of assessment, ⑤ =complete outcome data, ⑥ =selective reporting, ⑦=other bias, 1= low risk, 0=high risk, NA= not available

Supplementary Table 2.2 Risk-of-bias assessment of cohort study (NOS scale)

Included studies	selection				Comparability	Outcome			Total
	①	②	③	④	⑤	⑥	⑦	⑧	
Comparing different screening intervals									
Del Poggio.et al ^[6]	1	1	1	1	1	1	1	0	8/9
Khalili.et al ^[7]	1	1	1	1	1	1	1	1	8/9
Santi.et al ^[8]	1	1	1	1	2	1	1	1	9/9
Trevisani.et al ^[9]	1	1	0	1	2	1	1	1	8/9
Wu CY.et al ^[10]	1	1	1	1	2	1	1	0	8/9
Song JJ ^[11]	0	1	0	1	1	0	1	0	4/9
Comparing different screening modalities									
Kim.et al ^[12]	1	0	1	1	1	1	1	1	7/9
Kim.et al ^[13]	1	1	1	1	1	1	1	1	8/9

Notes: NOS=Newcastle-Ottawa Scale, ①=Representativeness of the exposed cohort, ②= Selection of the non exposed cohort, ③=Ascertainment of exposure, ④= Demonstration that outcome of interest was not present at start of study, ⑤=Comparability of cohorts on the basis of the design or analysis, ⑥=Assessment of outcome, ⑦= Follow-up long enough for outcomes to occur, ⑧=Adequacy of follow-up of cohorts.

Supplementary Table 3. Results of Sensitivity analysis

Outcomes	RR（95%CI）	Low-quality studies excluded
6-month screening intervals vs 12-month screening intervals (Cohort studies)		
5-year survival rate	(1) Before exclude	Song JJ.et al.2016 ^[11]
	1.39(1.07-1.82)	
	(2) After exclude	
	1.19 (1.13-1.26)	
Notes: RR= risk ratio		

Reference

1. Trinchet JC, Chaffaut C, Bourcier V, Degos F, Henrion J, Fontaine H, et al. Ultrasonographic surveillance of hepatocellular carcinoma in cirrhosis: a randomized trial comparing 3- and 6-month periodicities. *Hepatology*. 2011;54:1987-97. doi: 10.002/hep.24545.
2. Wang JH, Chang KC, Kee KM, Chen PF, Yen YH, Tseng PL, et al. Hepatocellular carcinoma surveillance at 4-vs. 12-month intervals for patients with chronic viral hepatitis: A randomized study in community. *American Journal of Gastroenterology*. 2013;108:416-24. doi: 10.1038/ajg.2012.445.
3. Pocha C, Dieperink E, McMaken KA, Knott A, Thuras P, Ho SB. Surveillance for hepatocellular cancer with ultrasonography vs. computed tomography - A randomised study. *Aliment Pharmacol Ther*. 2013;38:303-12. doi: 10.1111/apt.12370. Epub 2013 Jun 10.
4. Rhee H, An C, Kim DY, Choi JY, Han KH, Kim MJ. Unenhanced MRI versus ultrasonography for hepatocellular carcinoma surveillance: Preliminary results of a prospective randomized trial (miracle-HCC). *Liver Cancer*. 2018;7:95. doi: 10.1159/000490877.
5. Kudo M, Ueshima K, Osaki Y, Hirooka M, Imai Y, Aso K, et al. B-Mode Ultrasonography versus Contrast-Enhanced Ultrasonography for Surveillance of Hepatocellular Carcinoma: A Prospective Multicenter Randomized Controlled Trial. *Liver Cancer*. 2019;8:271-80. doi: 10.1159/000501082.
6. Del Poggio P, Olmi S, Ciccarese F, Di Marco M, Rapaccini GL, Benvegnù L, et al. Factors That Affect Efficacy of Ultrasound Surveillance for Early Stage Hepatocellular Carcinoma in Patients With Cirrhosis. *Clinical Gastroenterology and Hepatology*. 2014;12:1927-33. doi: 10.1016/j.cgh.2014.02.025.
7. Khalili K, Menezes R, Kim TK, Yazdi LK, Jang HJ, Sharma S, et al. The effectiveness of ultrasound surveillance for hepatocellular carcinoma in a Canadian centre and determinants of its success. *Canadian Journal of Gastroenterology and Hepatology*. 2015;29:267-73. doi: 10.1155/2015/563893.
8. Santi V, Trevisani F, Gramenzi A, Grignaschi A, Mirici-Cappa F, Del Poggio P, et al. Semiannual surveillance is superior to annual surveillance for the detection of early hepatocellular carcinoma and patient survival. *J Hepatol*. 2010;53:291-7. doi: 10.1016/j.jhep.2010.03.010.
9. Trevisani F, De Notariis S, Rapaccini G, Farinati F, Benvegna L, Zoli M, et al. Semiannual and annual surveillance of cirrhotic patients for hepatocellular carcinoma: effects on cancer stage and patient survival (Italian experience). *Am J Gastroenterol*. 2002;97:734-44. doi: 10.1111/j.572-0241.2002.05557.x.
10. Wu CY, Hsu YC, Ho HJ, Chen YJ, Lee TY, Lin JT. Association between ultrasonography screening and mortality in patients with hepatocellular carcinoma: a nationwide cohort study. *Gut*. 2016;65:693-701. doi: 10.1136/gutjnl-2014-308786.
11. Song JJ, Lu wy, Zhao ZW, Fan XX, Tu JF, Ji JS. Association between ultrasound screening frequency and mortality in patients with hepatocellular carcinoma. *Chinese Medical Journal* 2016;(45):3652-5. doi: 10.3760/cma.j.issn.0376-2491.2016.45.009.
12. Kim JH, Kang SH, Lee M, Choi HS, Jun BG, Kim TS, et al. Improved detection of hepatocellular carcinoma by dynamic computed tomography in cirrhotic patients with chronic hepatitis B: A multicenter study. *J Gastroenterol Hepatol*. 2020;35:1795-803. doi: 10.1111/jgh.15046.
13. Kim JH, Kang SH, Lee M, Choi HS, Jun BG, Kim TS, et al. Individualized surveillance of chronic hepatitis B patients according to hepatocellular carcinoma risk based on PAGE-B scores. *Eur J Gastroenterol Hepatol*. 2021;33:1564-72. doi: 10.1097/meg.0000000000001870.