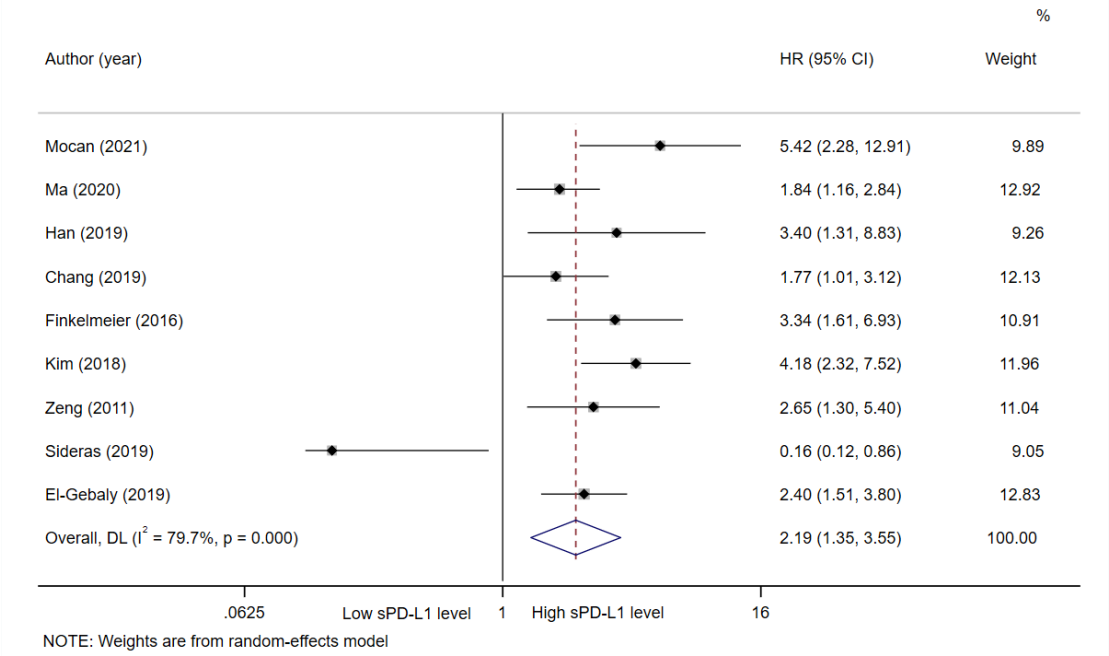
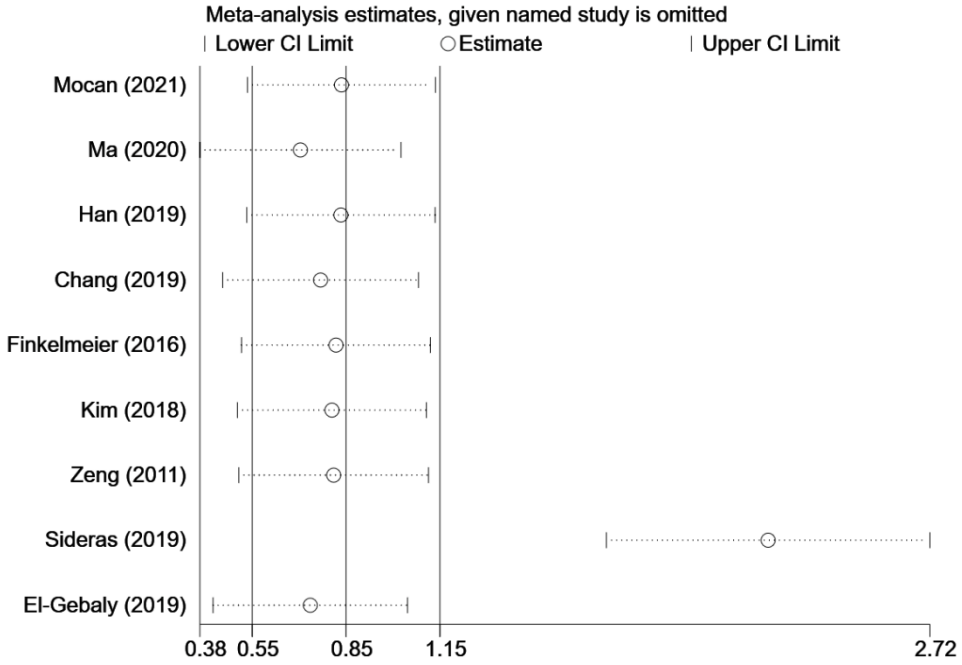
Supplementary Information

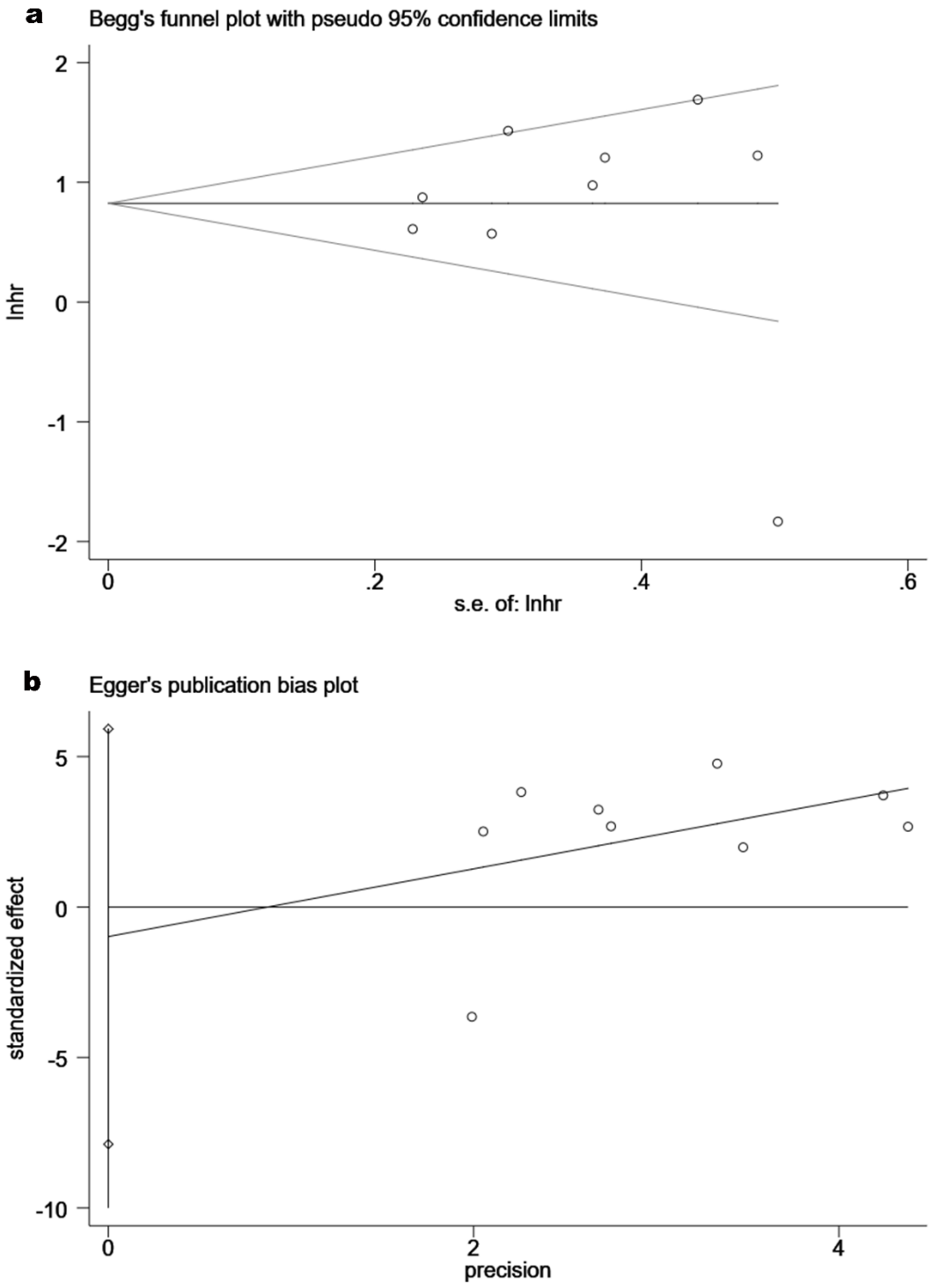
Inventory of Supplementary Information



supplementary Fig. 1: Forest plot of sPD-L1 and OS in hepatocellular carcinoma. CI confidence interval, HR hazard ratio, OS overall survival, sPD-L1 soluble programmed cell death ligand-1



supplementary Fig. 2: Sensitivity analysis of sPD-L1 and OS in hepatocellular carcinoma. CI confidence interval, sPD-L1 soluble programmed cell death ligand-1, OS overall survival



supplementary Fig. 3: Assessment of publication bias for this meta-analysis using Begg's test and Egger's test. (**a**) Begg's test for OS of sPD-L1 (**b**) Egger's test for OS of sPD-L1. lnhr the ln of HR, s.e. standard error, sPD-L1 soluble programmed cell death ligand-1, OS overall survival

supplementary Table 1 Database-specific search strategy for PubMed

P (population)	Keywords searched for in All Fields	hepatocellular carcinoma **OR** hepatocarcinoma **OR** hepatomas **OR** HCC **OR** liver carcinoma **OR** liver cell carcinoma **OR** liver cancer
	MeSH headings	carcinoma, hepatocellular [MeSH]
I (intervention)	Keywords searched for in All Fields	sPD-1 **OR** soluble programmed death-1 **OR** sPD-L1 **OR** soluble programmed death-ligand 1 **OR** sB7-H1
	MeSH headings	none
Additional limits	Limit to English language only	

supplementary Table 2 Subgroup meta-analysis of prognostic role of sPD-L1 for OS in HCC after treatment

Factor	No. of study	No. of patients	HR (95%CI)	P-value	Heterogeneity	
					I^2(%)	P-value
OS						
Total	9	979	2.19 (1.35-3.55)	0.001	79.7	< 0.001
Ethnicity						
Asian	5	477	2.47 (1.74-3.51)	< 0.001	38.2	0.166
Non-Asian	4	502	1.68 (0.51-5.60)	0.396	90.8	< 0.001
Study style						
Prospective study	4	474	3.34 (2.36-4.73)	< 0.001	19.2	0.294
Retrospective study	5	505	1.43 (0.66-3.10)	0.367	84.5	< 0.001
Treatment						
Multiple therapies	5	583	1.67 (0.71-3.93)	0.244	87.7	< 0.001
Monotherapy	4	396	2.39 (1.60-3.55)	< 0.001	49.1	0.117
Method of detection						
ELISA	7	750	2.19 (1.16-4.11)	0.015	84.4	< 0.001
Other methods	2	229	2.07 (1.33-3.22)	0.001	0.0	0.384
Cutoff value of sPD-L1						
Less than average	6	665	2.12 (0.95-4.76)	0.067	87.0	< 0.001
Greater than average	3	314	2.22 (1.61-3.05)	< 0.001	0.0	0.618
Follow-up times						
2 years or longer	3	287	3.14 (1.94-5.08)	< 0.001	27.3	0.253
Less than 2 years or NR	6	692	1.75 (0.89-3.44)	0.106	85.3	< 0.001

HCC Hepatocellular carcinoma, CI confidence interval, HR hazard ratio, OS overall survival, sPD-L1 soluble programmed cell death ligand-1

supplementary Table 3 Quality assessment of studies by checklist (based on Newcastle-Ottawa Scale)

study	Selection				Comparability	outcome			score
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cases and controls on the basis of the design or analysis	Assessment of outcome	follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Na et al;2021	★	★	★	★	★	★	☆	★	**7**
Mocan et al;2021	★	★	★	★	★	★	★	★	**8**
Ma et al;2020	★	★	★	★	★	★	☆	☆	**6**
Han et al;2019	★	★	★	★	★	★	★	★	**8**
El-Gebaly et al;2019	★	★	☆	★	★	☆	☆	★	**5**
Sideras et al;2019	★	★	★	★	☆	☆	☆	☆	**4**
Chang et al;2019	★	★	★	★	★★	★	★	☆	**8**
Kim et al;2018	☆	★	★	★	★★	★	☆	☆	**6**
Li et al;2017	★	★	☆	★	★	★	★	☆	**6**
Finkelmeier et al;2016	★	★	★	★	★	★	☆	☆	**6**

Zeng et al;2011	★	★	☆	★	★	★	☆	☆	**5**

★Asterisk means that the study is satisfied the item, ☆ asterisk means the opposite situation. A score ≤5 is considered low quality, and >5 can be considered high quality.

Supplementary PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review and meta-analysis.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of	20	For all outcomes considered (benefits or harms),	6

individual studies		present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6-7
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097