

Supplementary Materials

Green tea consumption and hepatocellular carcinoma: a meta-analysis lacking evidence for a protective effect

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Supplementary Materials for:

Green Tea Consumption and Hepatocellular Carcinoma: A Meta-Analysis Lacking Evidence for a Protective Effect

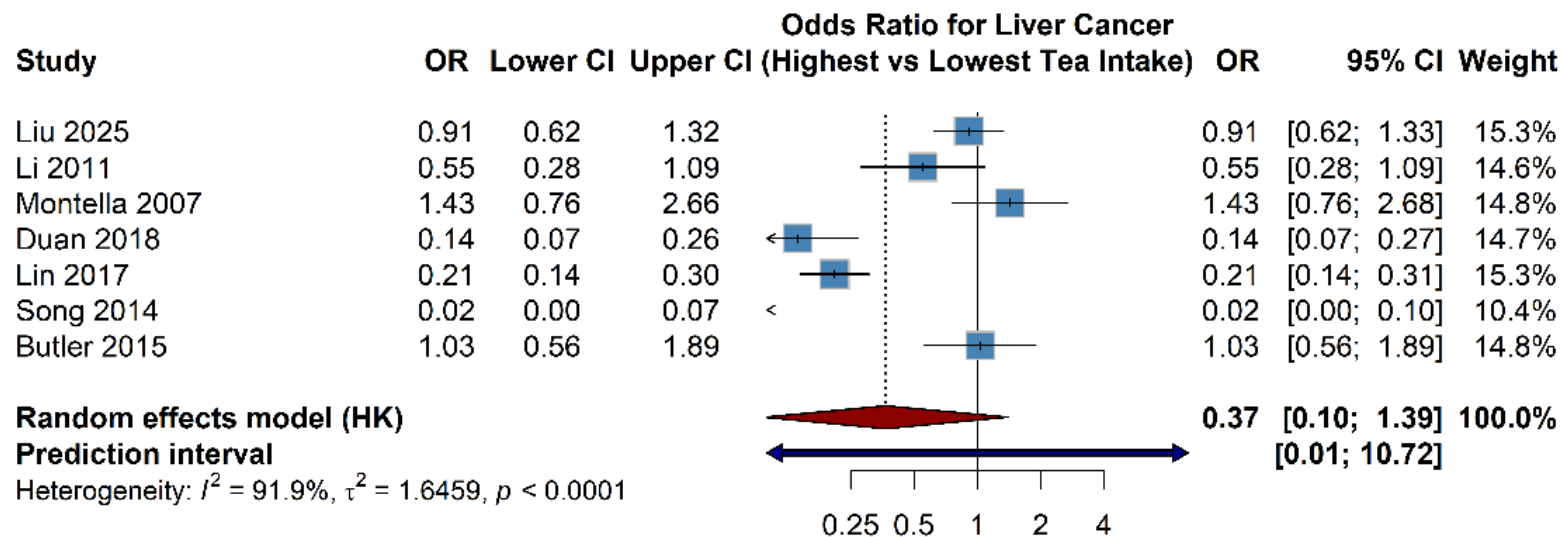
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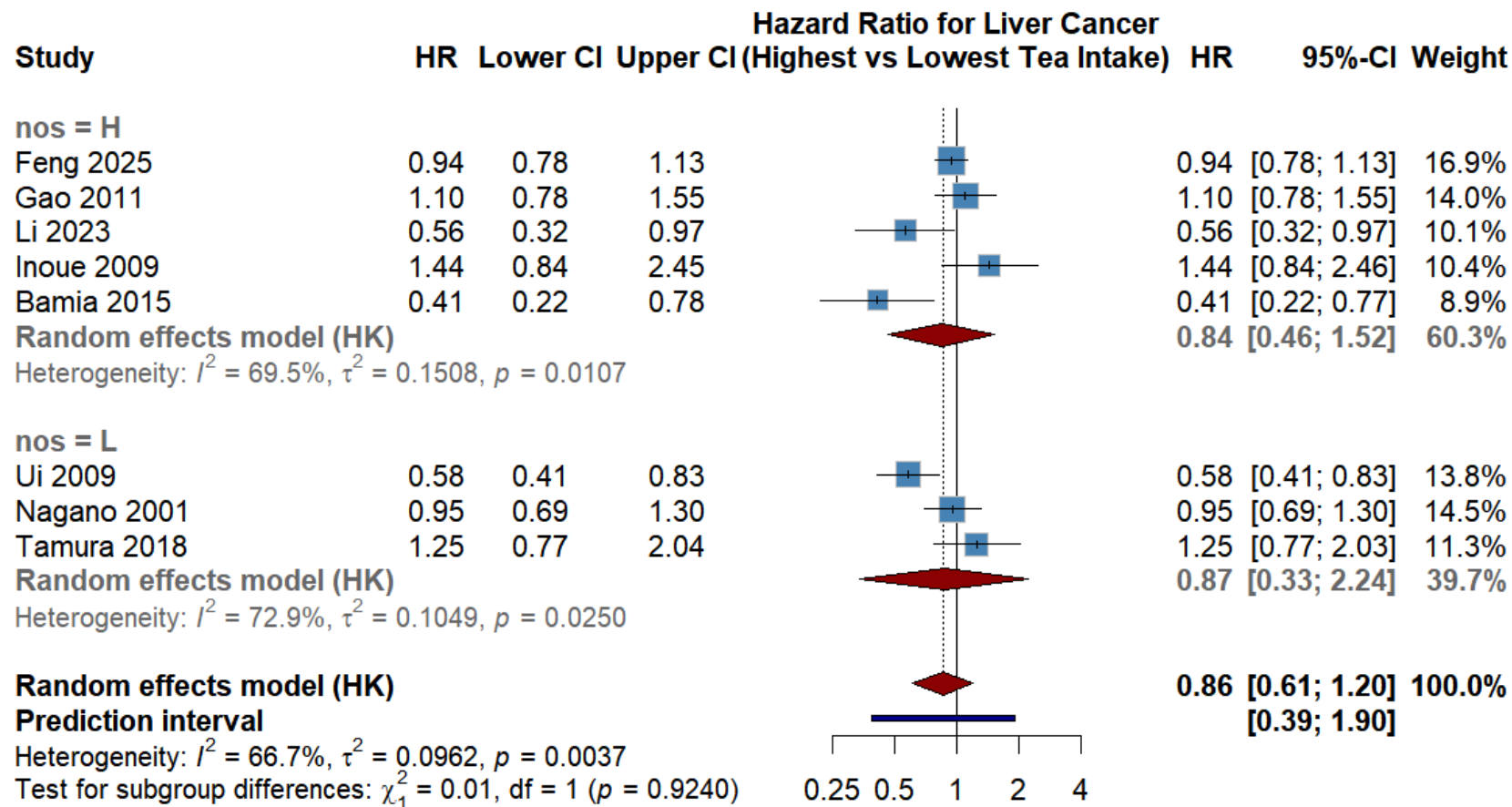
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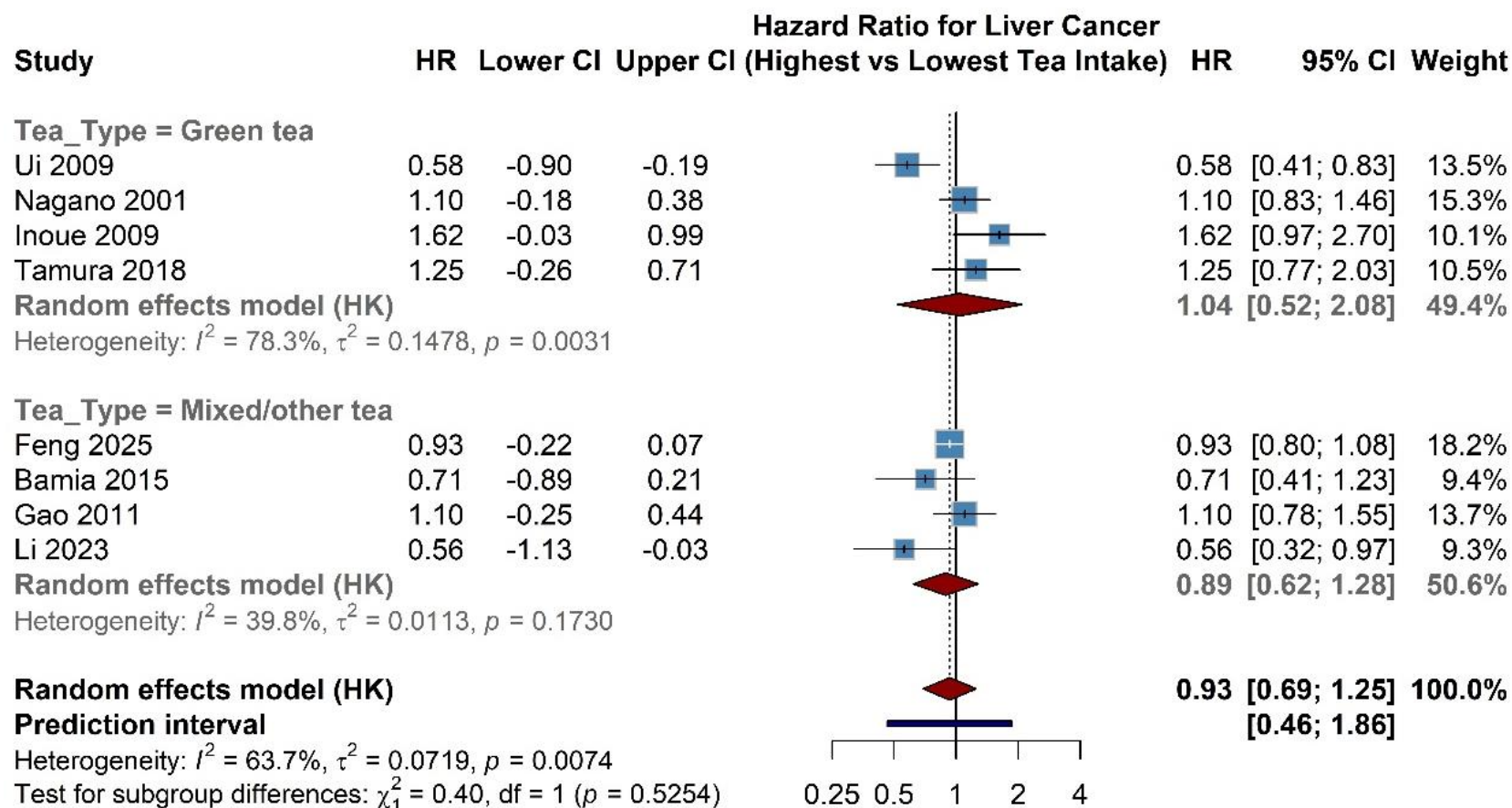
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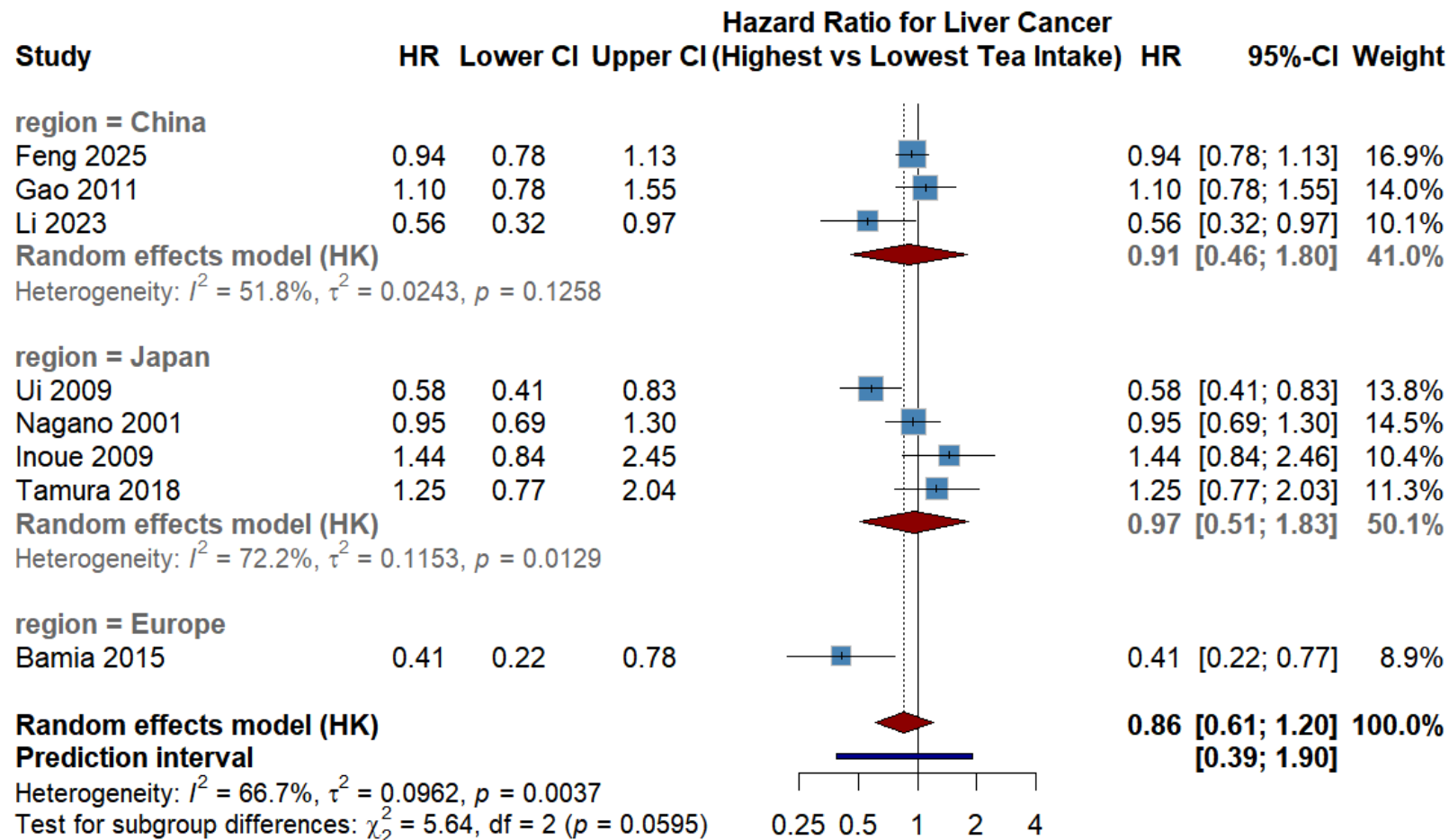
Supplementary Figure 1. Forest plot of the association between tea consumption and risk of liver cancer in Case-control studies. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; OR: odds ratio.



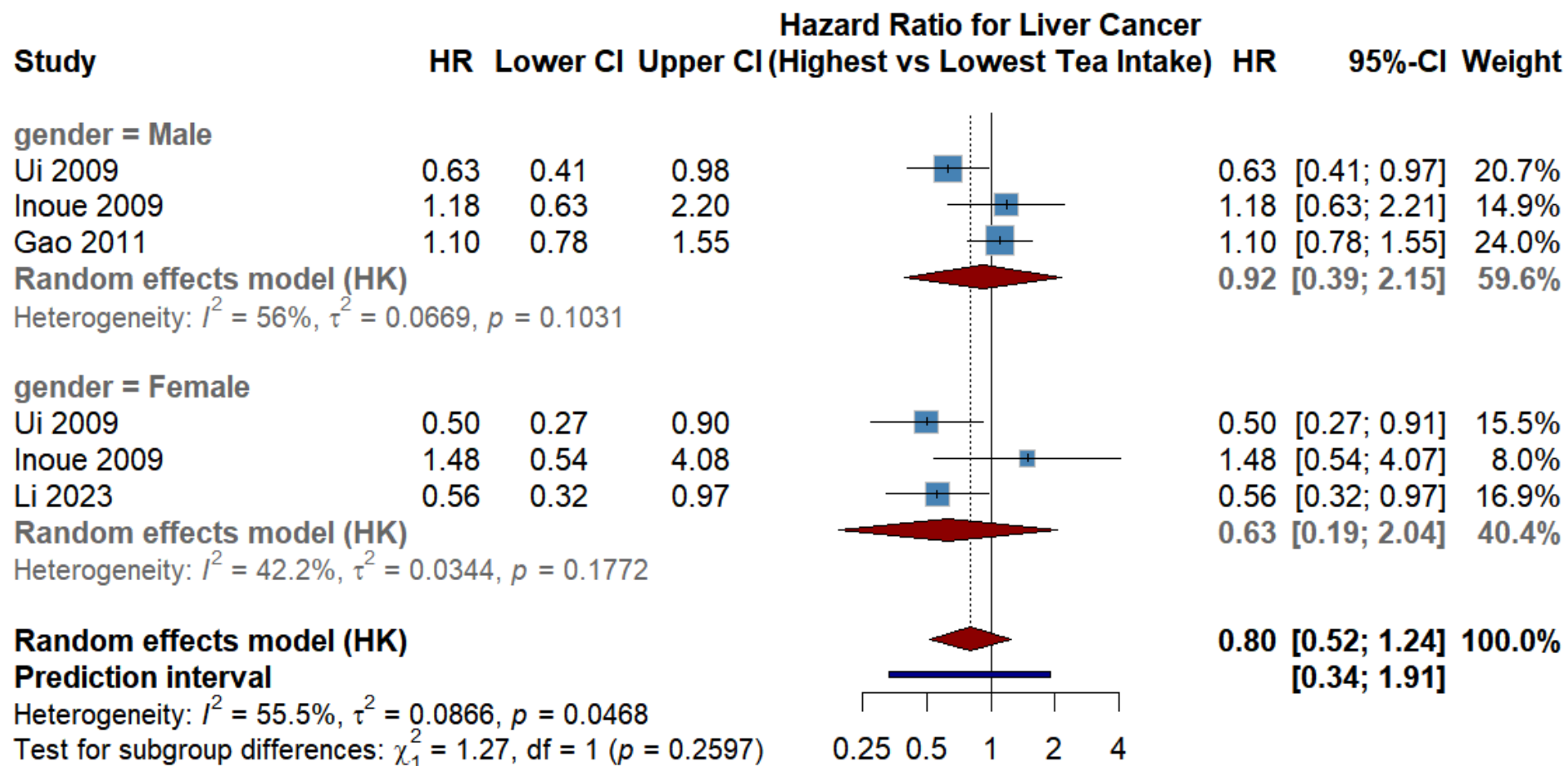
Supplementary Figure 2. Forest plot stratified by NOS scores in cohort study. Random-effects models were fitted using the HKSJ method. NOS scores: ≥ 8 = H (high quality); 7.5 = M (medium quality); ≥ 6 and < 7.5 = L (low quality). CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio; NOS: Newcastle-Ottawa scale.



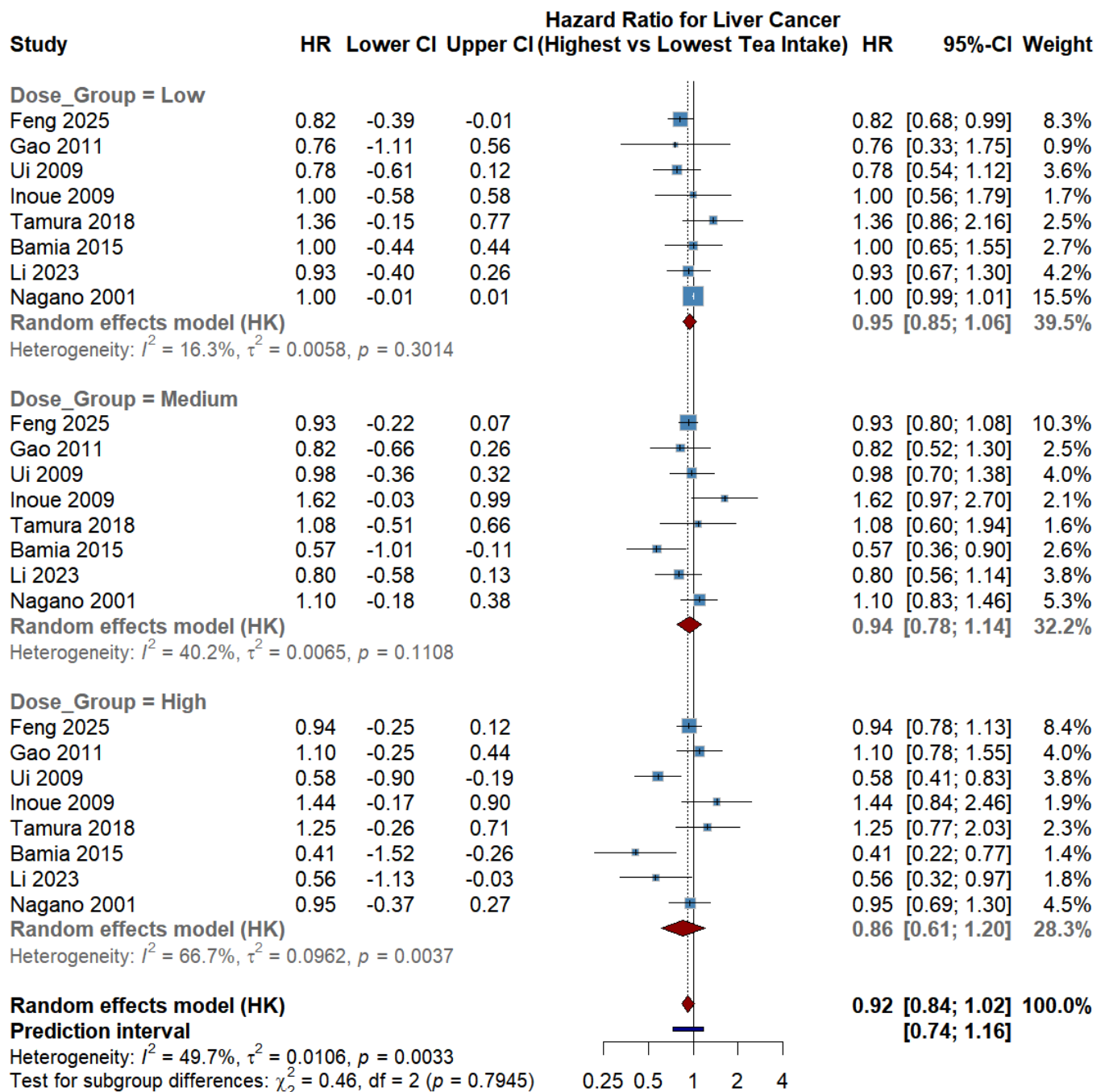
Supplementary Figure 3. Forest plot stratified by tea type in cohort study. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.



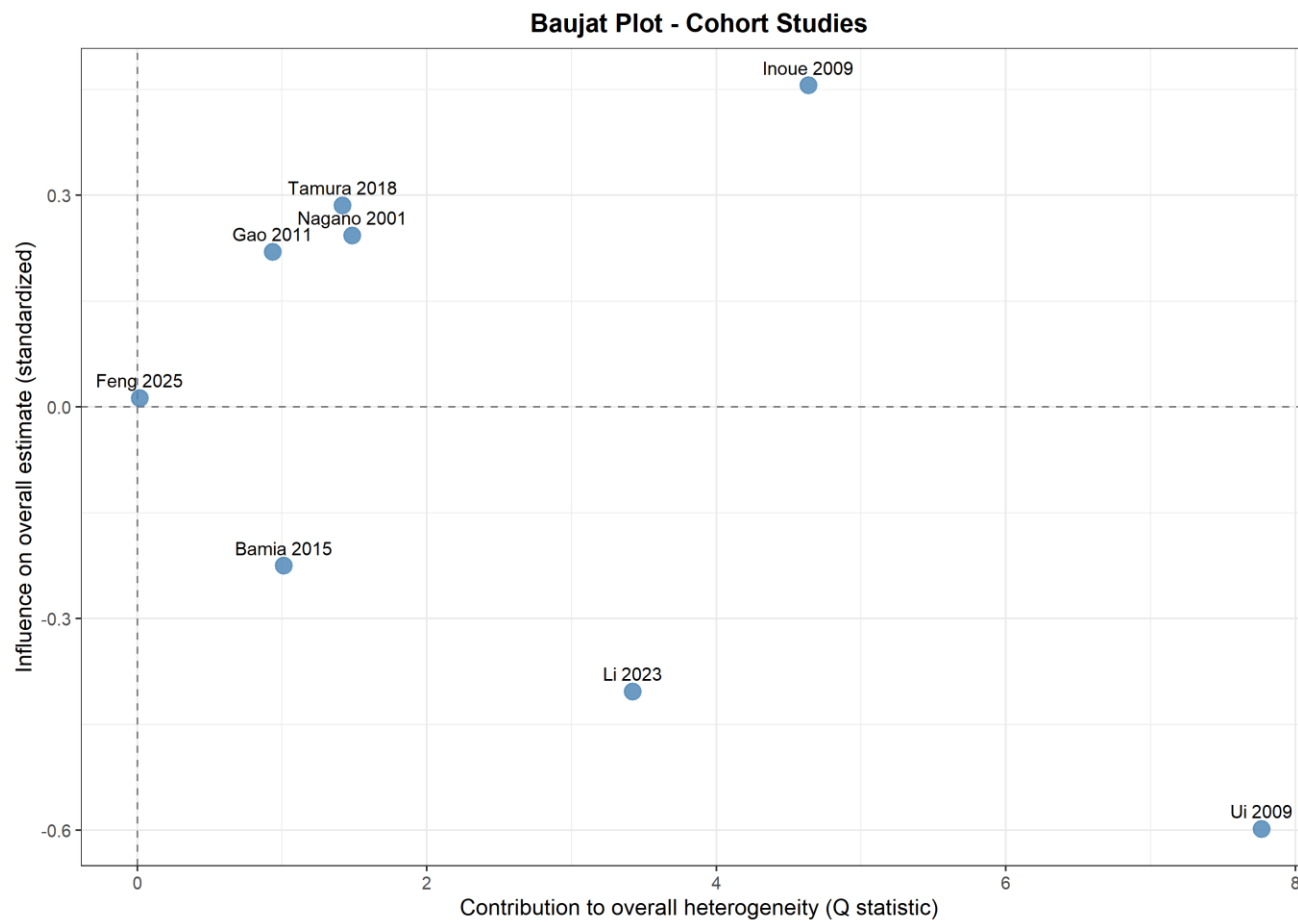
Supplementary Figure 4. Forest plot stratified by geographic region in cohort study. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.



Supplementary Figure 5. Forest plot stratified by sex in cohort study. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

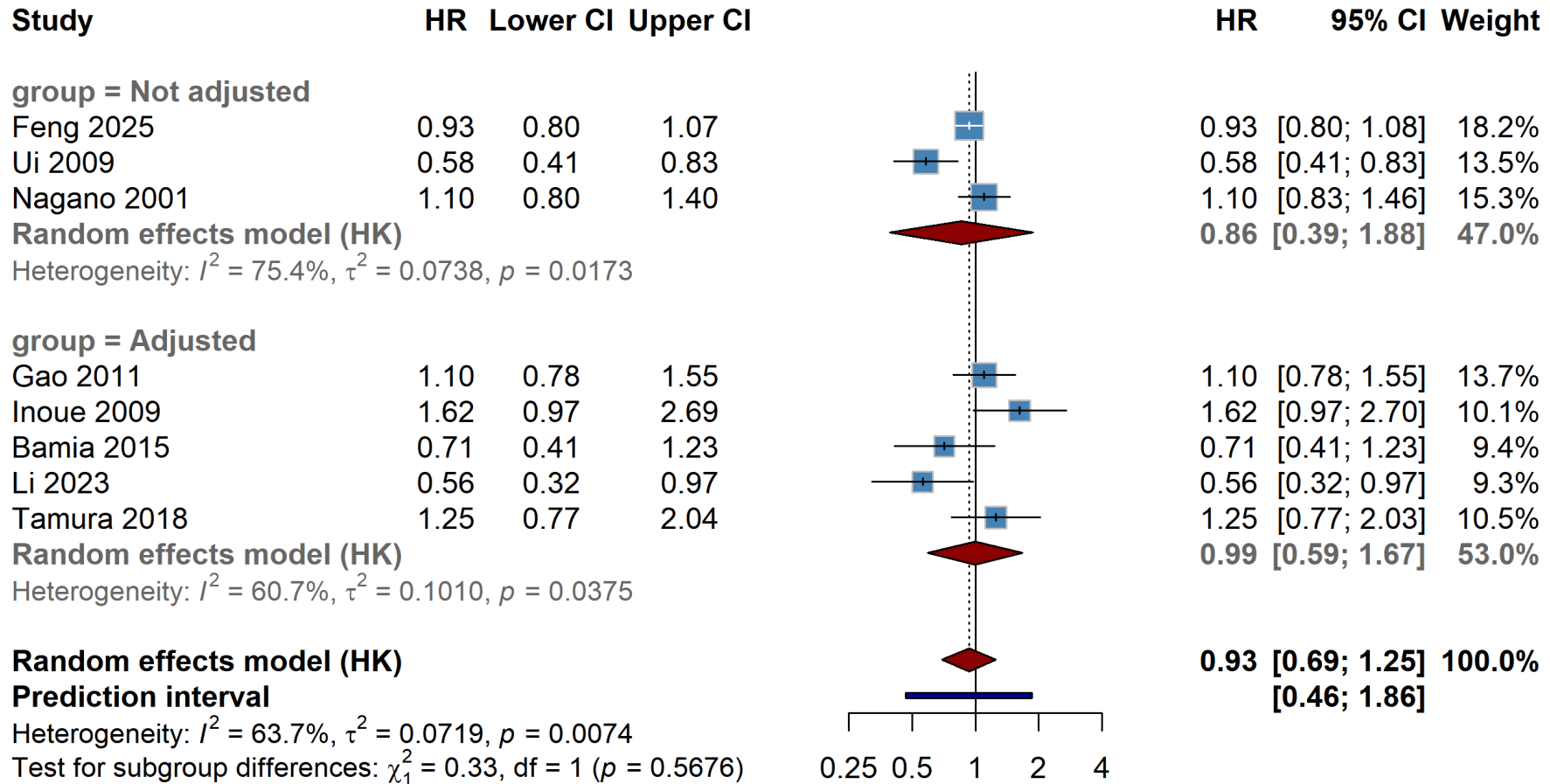


Supplementary Figure 6. Forest plot stratified by dose in cohort study. Dose subgroups were stratified by exposure levels using the within-study tertile method, with no cross-study standardization of dose units. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

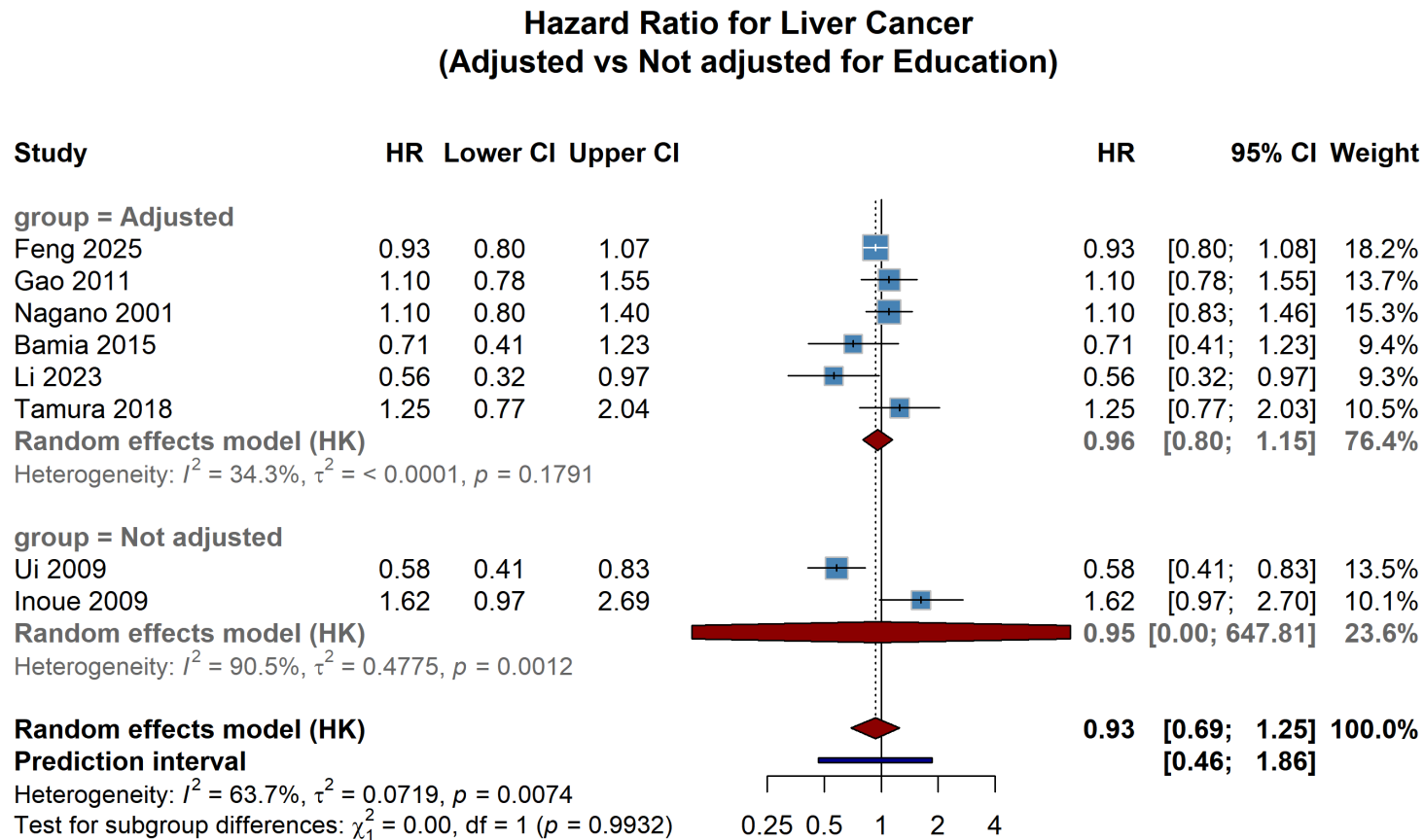


Supplementary Figure 7. Baujat plot for cohort studies. The x-axis shows the contribution to overall heterogeneity (Q statistic); the y-axis shows the standardized influence on the pooled estimate. Random-effects models were fitted using the HKSJ method. HKSJ: Hartung-Knapp-Sidik-Jonkman.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Diabetes)

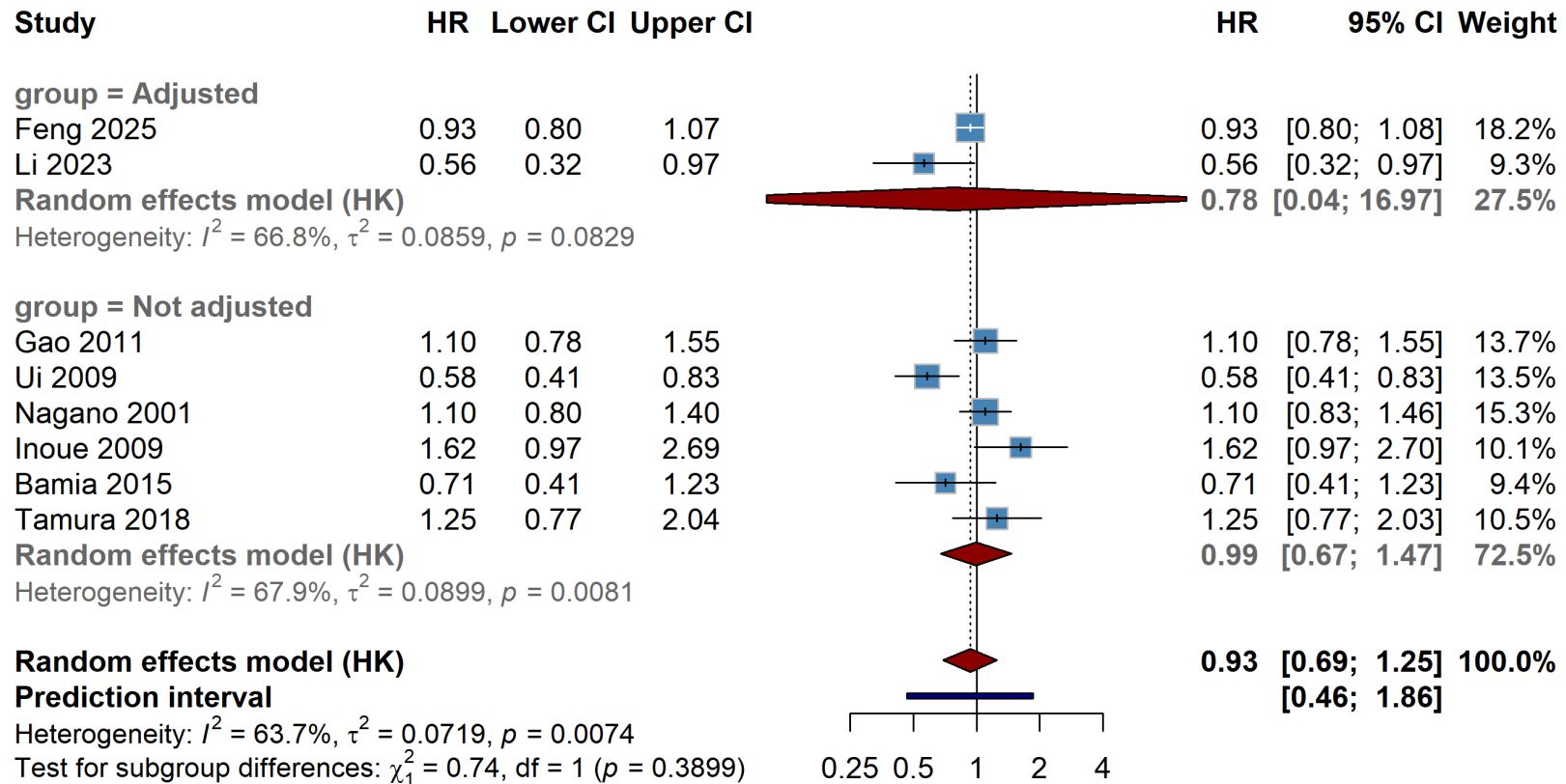


Supplementary Figure 8. Subgroup analysis stratified by adjustment for diabetes. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.



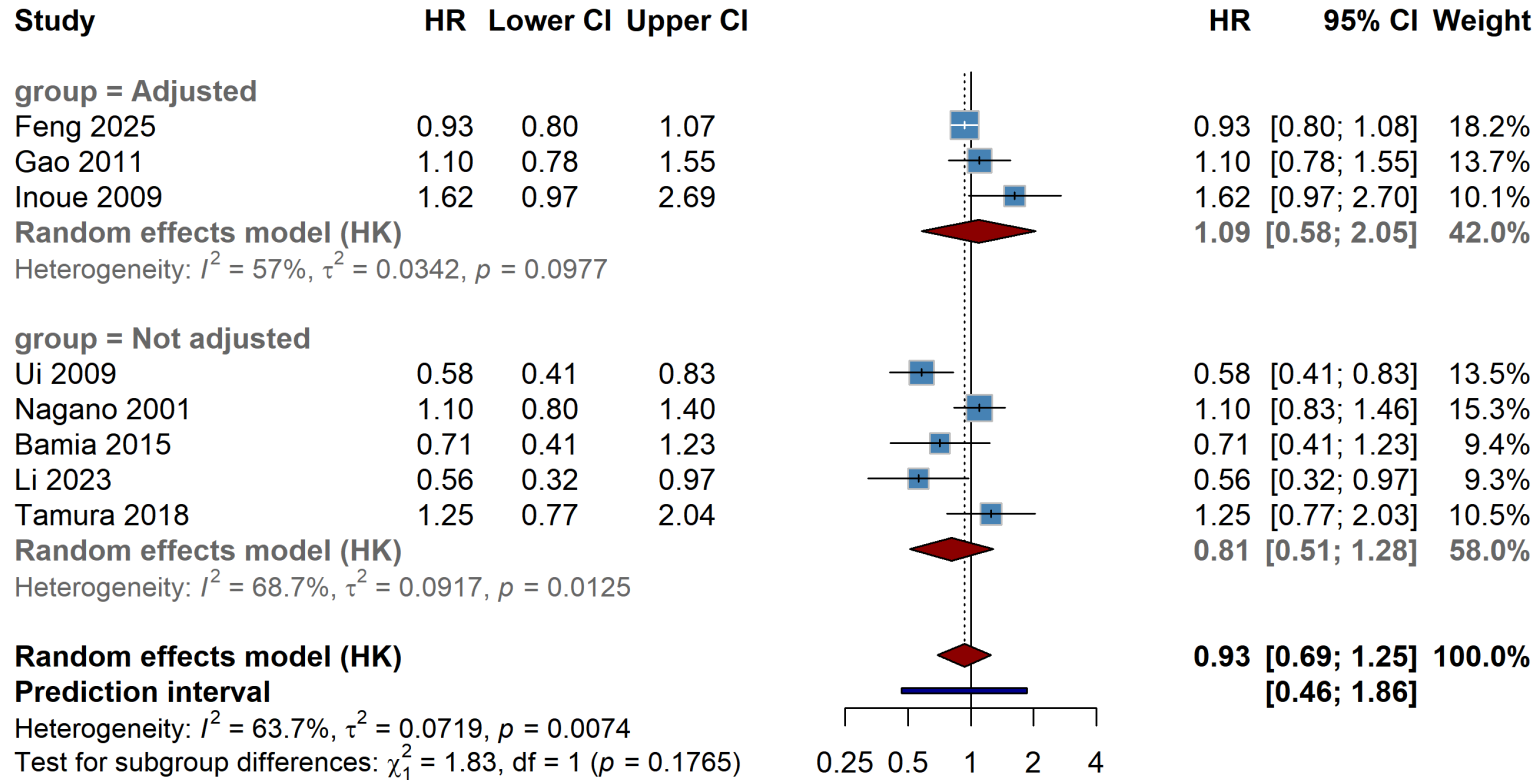
Supplementary Figure 9. Subgroup analysis stratified by adjustment for education. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Family History)



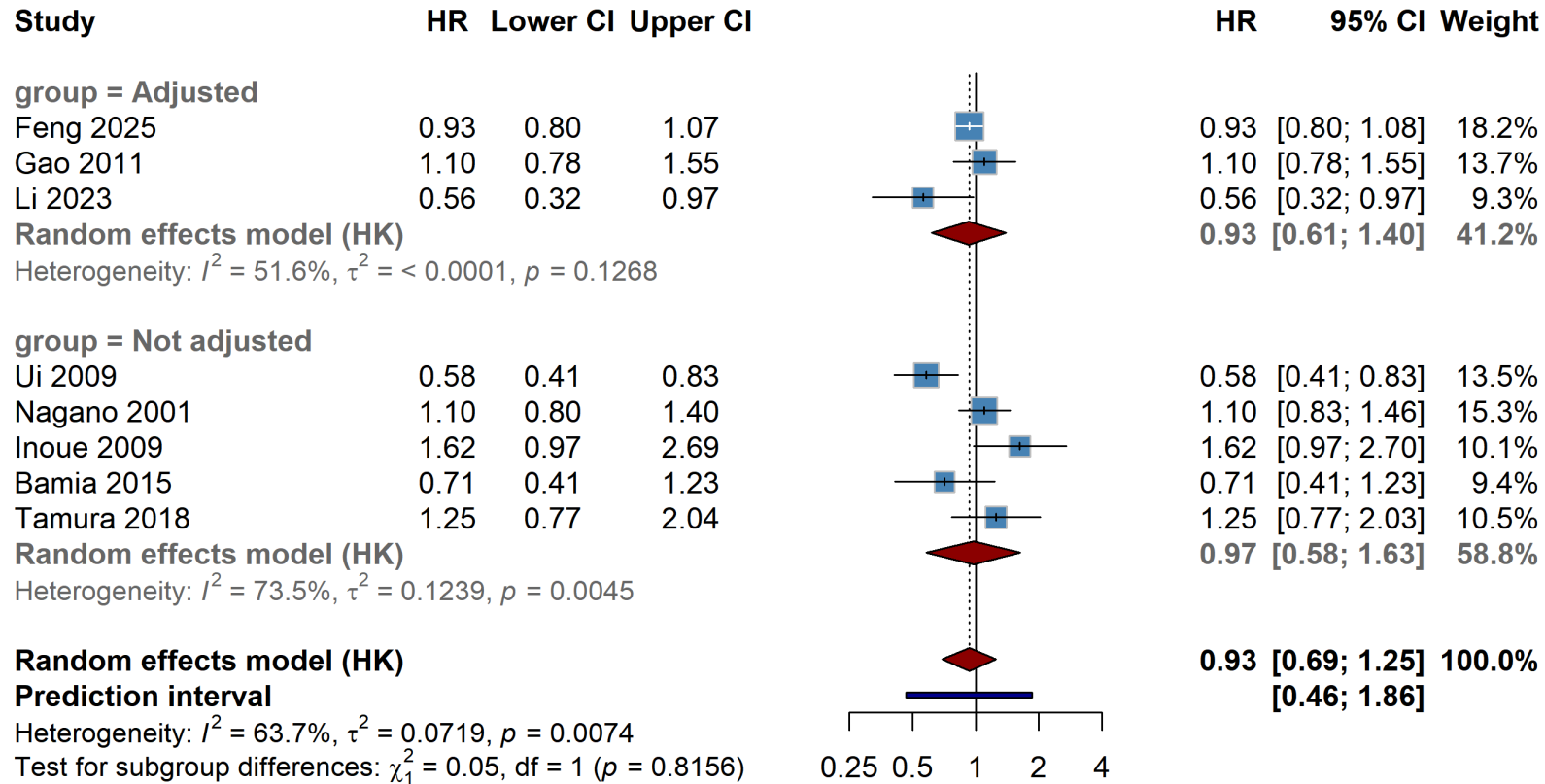
Supplementary Figure 10. Subgroup analysis stratified by adjustment for family history. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for HBV)



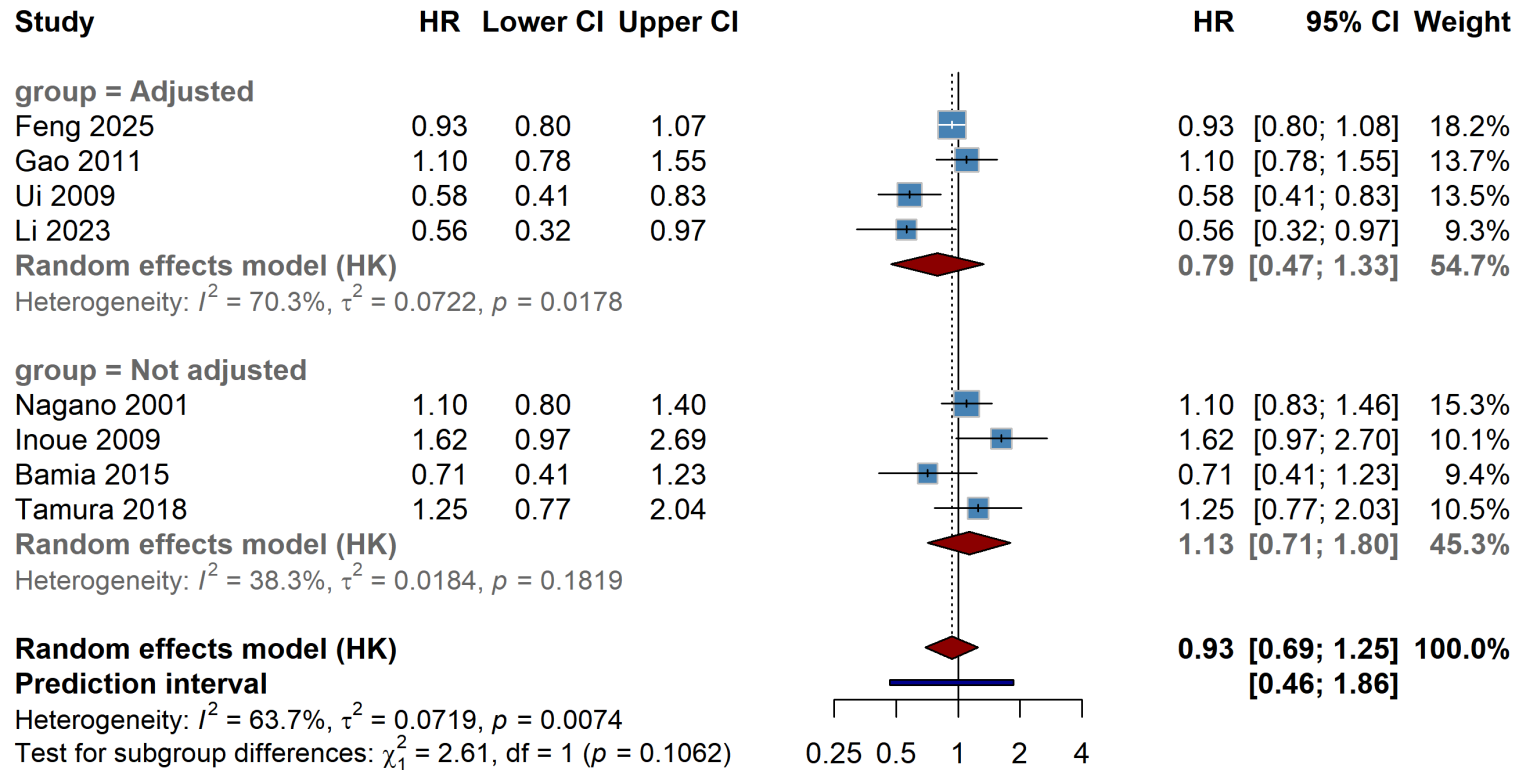
Supplementary Figure 11. Subgroup analysis stratified by adjustment for HBV. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HBV: hepatitis B virus; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Income)



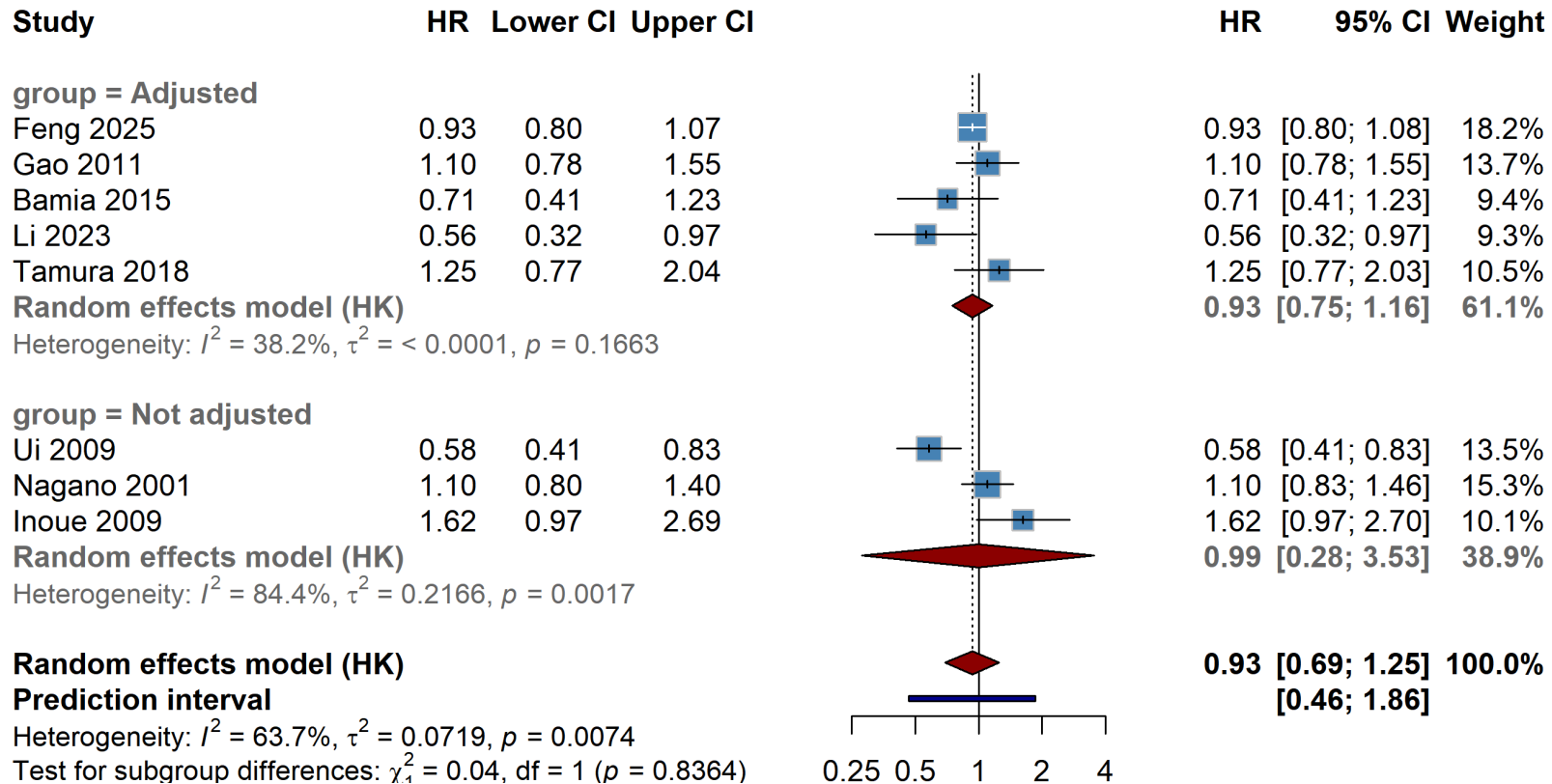
Supplementary Figure 12. Subgroup analysis stratified by adjustment for income. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Liver Disease)



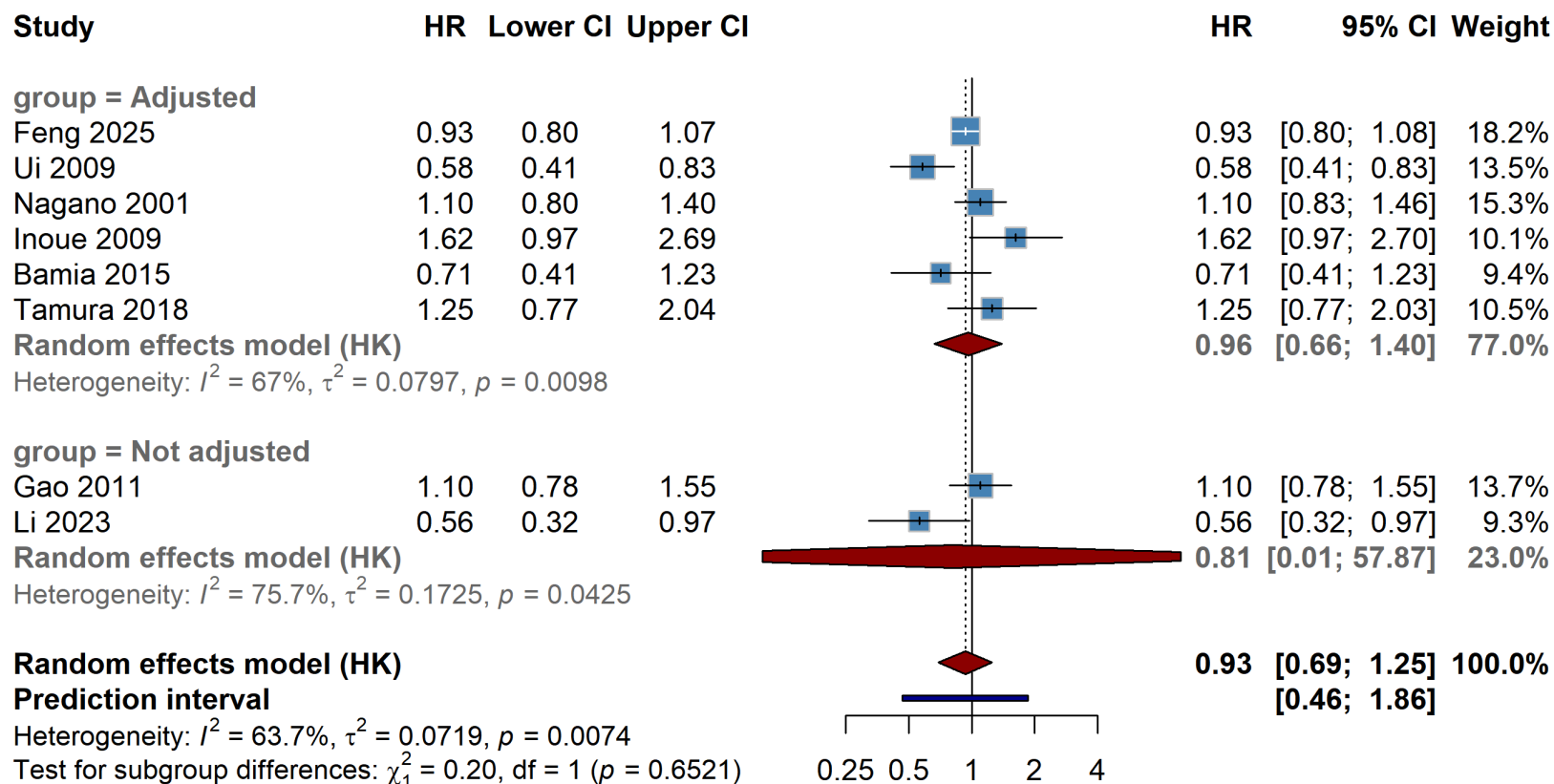
Supplementary Figure 13. Subgroup analysis stratified by adjustment for liver disease. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Physical Activity)



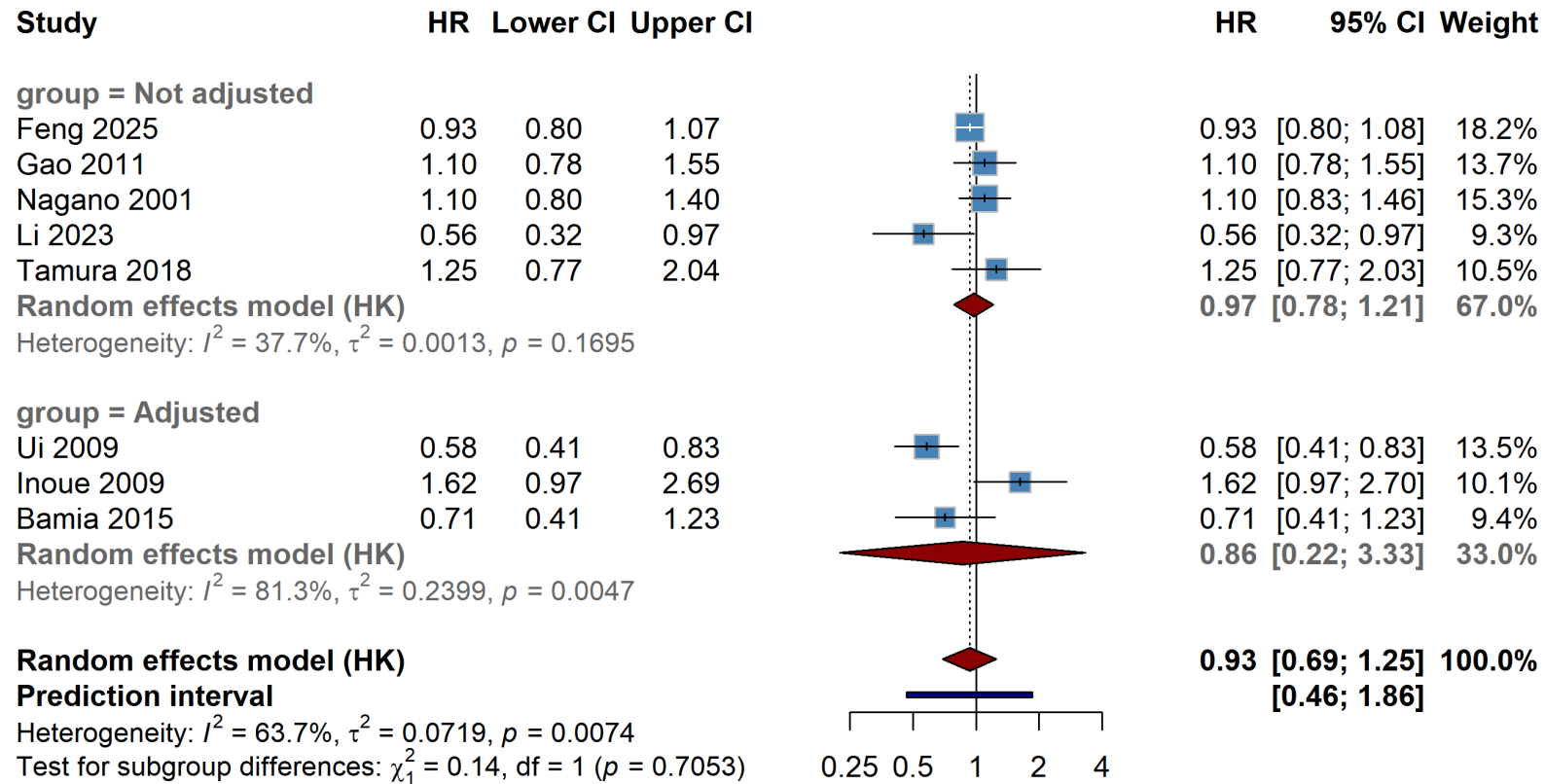
Supplementary Figure 14. Subgroup analysis stratified by adjustment for physical activity. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Sex)



Supplementary Figure 15. Subgroup analysis stratified by adjustment for sex. Random-effects models were fitted using the HKSJ method. CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Hazard Ratio for Liver Cancer (Adjusted vs Not adjusted for Coffee)

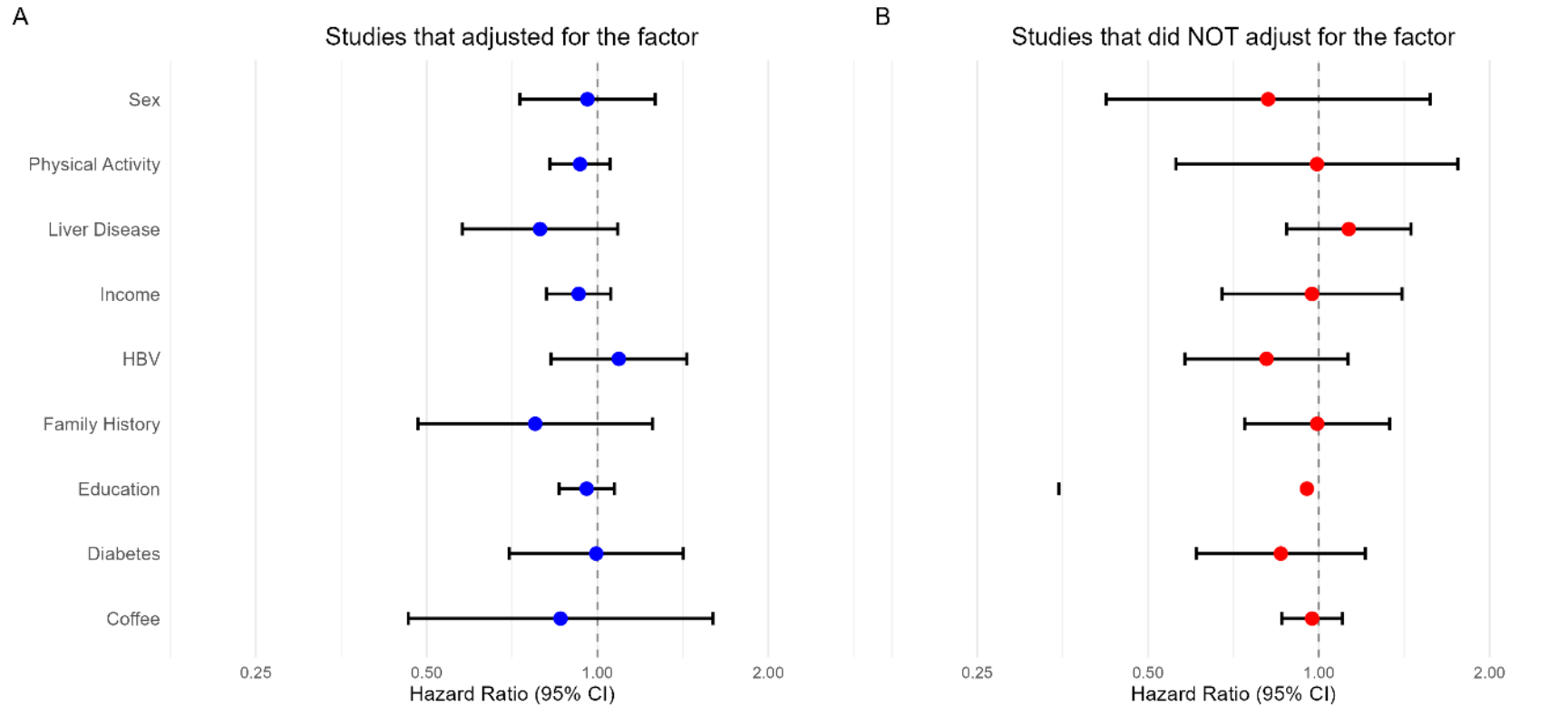


Supplementary Figure 16. Subgroup analysis stratified by adjustment for coffee. Random-effects models were fitted using the HKSJ method.

CI: Confidence intervals; HKSJ: Hartung-Knapp-Sidik-Jonkman; HR: hazard ratio.

Subgroup analysis stratified by adjustment for potential confounders

Left: Adjusted for the factor; Right: Not adjusted



Supplementary Figure 17. Composite forest plot of subgroup analyses stratified by adjustment for each potential confounder. (A) studies adjusted for the factor; (B) studies not adjusted for the factor. Subgroups containing only one study are not shown in the forest plot. CI: Confidence intervals.

Supplementary Table 1. Literature search strategy

Database	Search strategy	His
PubMed	((“Liver Neoplasms”[Mesh] OR “Hepatocellular Carcinoma”[Mesh]) AND (“Tea”[Mesh] OR “Tea, Green”[Mesh] OR “Tea, Black”[Mesh])) OR ((liver cancer OR hepatoma OR hepatic neoplasm) AND (tea OR green tea OR black tea OR tea polyphenol OR catechin))	1,195
embase	('liver cell carcinoma'/exp OR 'hepatocellular carcinoma'/exp OR 'liver neoplasm'/exp OR 'liver cancer':ab,ti OR 'hepatoma':ab,ti OR 'hepatic neoplasm':ab,ti OR 'hepatic cancer':ab,ti) AND ('tea'/exp OR 'green tea'/exp OR 'black tea'/exp OR 'oolong tea'/exp OR 'tea polyphenol':ab,ti OR 'catechin':ab,ti OR 'epigallocatechin gallate':ab,ti OR 'tea':ab,ti OR 'green tea':ab,ti OR 'black tea':ab,ti OR 'oolong tea':ab,ti)	165
Cochrane Library	([mh “Liver Neoplasms”] OR [mh “Carcinoma, Hepatocellular”] OR (liver cancer OR hepatoma OR hepatic neoplasm):ti,ab,kw) AND ([mh “Tea”] OR [mh “Tea, Green”] OR [mh “Tea, Black”] OR (tea OR green tea OR black tea OR tea polyphenol OR catechin):ti,ab,kw)	41
SinoMed	#1 "Liver Neoplasms"[Unweighted: Explode] OR "Hepatocellular Carcinoma"[Unweighted: Explode] OR "Liver Cancer"[Common Fields: Smart] OR "Hepatocellular Carcinoma"[Common Fields: Smart] OR "Malignant Liver Tumor"[Common Fields:	839

	Smart] #2 "Tea"[Unweighted: Explode] OR "Green Tea"[Unweighted: Explode] OR "Black Tea"[Unweighted: Explode] OR "Tea Polyphenols"[Common Fields: Smart] OR "Catechins"[Common Fields: Smart] #3 #1 AND #2	
CNKI	(SU='Liver Neoplasms' OR SU='Liver Cancer' OR SU='Hepatocellular Carcinoma' OR SU='Malignant Liver Tumor' OR SU='hepatocellular carcinoma' OR SU='liver cancer' OR SU='hepatoma') AND (SU='Tea' OR SU='Green Tea' OR SU='Black Tea' OR SU='Tea Polyphenols' OR SU='Catechins' OR SU='tea' OR SU='green tea' OR SU='black tea' OR SU='catechin')	128
Wanfang	Title/Keyword:(Liver Neoplasms OR Liver Cancer OR Hepatocellular Carcinoma OR Malignant Liver Tumor OR hepatocellular carcinoma OR liver cancer OR hepatoma) AND Title/Keyword:(Tea OR Green Tea OR Black Tea OR Tea Polyphenols OR Catechins OR tea OR green tea OR black tea OR catechin)	500

Search date: from database inception to December 15, 2025, for all databases.

Supplementary Table 2. Quality evaluation criteria of included study

Newcastle-Ottawa Scale (NOS) Quality Assessment Criteria for Cohort Studies			
Dimension	Item	Criteria	Score
Selection (4 points)	1. Representativeness of the exposed cohort	Randomly selected community/occupational cohort (1 point); Selected high-risk cohort (0.5 points); Not described (0 points)	
	2. Selection of the non-exposed cohort	From the same community as the exposed cohort (1 point); From a different source (0.5 points); Not described (0 points)	
	3. Ascertainment of tea exposure	Food frequency questionnaire (FFQ) assessing type, duration, and amount (1 point); Only “yes/no” for tea consumption (0.5 points); Not described (0 points)	
	4. Demonstration that outcome was not present at start of study	Clearly excluded participants with liver cancer at baseline (1 point); Not described (0 points)	
Comparability (2 points)	1. Control for confounding factors	Adjusted for HBsAg/HCV infection, smoking, and alcohol consumption (1 point); Adjusted for ≥ 1 other factors (e.g., cirrhosis, diabetes) (1 point); No adjustment (0 points)	
Outcome (3 points)	1. Assessment of liver cancer outcome	Based on pathological diagnosis or imaging combined with serological markers (1 point); Based solely on hospital	

		records (0.5 points); Not described (0 points)	
	2. Length of follow-up	Follow-up ≥ 5 years (1 point); 3-5 years (0.5 points); < 3 years (0 points)	
	3. Adequacy of follow-up	Loss to follow-up $< 20\%$ and outcomes reported (1 point); Loss to follow-up 20%-30% (0.5 points); Loss to follow-up $> 30\%$ (0 points)	
Newcastle-Ottawa Scale (NOS) Quality Assessment Criteria for Case-Control Studies			
Dimension	Item	Criteria	Score
Selection (4 points)	1. Adequacy of case definition	Primary liver cancer confirmed by pathological diagnosis or imaging combined with serological markers (1 point); Based solely on self-report/hospital records (0 points)	
	2. Representativeness of cases	Consecutive cases from multiple hospitals/communities (1 point); Single-center cases or representativeness not described (0 points)	
	3. Selection of controls	Community controls (from the same area as cases) (1 point); Hospital-based non-liver cancer controls (0.5 points); Not described (0 points)	
	4. Definition of controls	Clearly defined as having no history of liver cancer (1 point); History of liver cancer not specified (0 points)	

Comparability (2 points)	1. Control for confounding factors	Adjusted for HBsAg/HCV infection, smoking, and alcohol consumption (1 point); Adjusted for ≥ 1 other factors (e.g., cirrhosis, diabetes) (1 point); No adjustment (0 points)	
Exposure (3 points)	1. Ascertainment of tea exposure	Food frequency questionnaire (FFQ) assessing type, duration, and daily intake (1 point); Only “yes/no” for tea consumption (0.5 points); Not described (0 points)	
	2. Same method of ascertainment for cases and controls	Same method used for both cases and controls (1 point); Different methods used (0 points)	
	3. Non-response rate	Non-response rates are the same for cases and controls or both $<10\%$ (1 point); Non-response rates differ but described (0.5 points); Not described (0 points)	

Note: Studies with a total score of ≥ 8 were considered high quality (H), those with a score of 7.5 were considered medium quality (M), those with a score of ≥ 6 and <7.5 were considered low quality (L), and studies with a score of <6 were excluded from the analysis. FFQ: Food frequency questionnaire; NOS: Newcastle-Ottawa scale.

Supplementary Table 3. Data extraction table

First author and publication year
Article type (1.case-control;2.cohort)
Follow-up duration (cohort/year)
Country of study subjects
Method of exposure ascertainment
Total sample size
Number of positive cases (liver cancer)/negative cases
NOS score
Diagnosis of liver cancer (pathology/medical records/imaging)
adjustment for confounding bias (① Age, ② Sex, ③ Education, ④ HBsAg/HBV, ⑤ HCV, ⑥ BMI, ⑦ Income, ⑧ Family history of liver cancer, ⑨ Physical activity, ⑩ Diabetes, ⑪ Cirrhosis, ⑫ Diet/energy, ⑬ Coffee intake, ⑭ Radiation, ⑮ ALT level, ⑯ Occupation, ⑰ Gallstones.)
Representativeness of the population
Tea drinking frequency
Years of tea drinking (years)
Years since stopping tea drinking
Daily tea drinking duration
Tea consumption (ml/week)
Water temperature when drinking tea (1.boiled; 2.high temperature;3.warm;4.cold)
Water temperature for brewing tea
Source of water for brewing tea
Type of tea (1. green tea; 2.red tea; 3.mix; 4.unsure)
Mean age

ALT: Alanine aminotransferase; BMI: body mass index; HBV: hepatitis B virus;

HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus.

Supplementary Table 4. Leave-one-out sensitivity analysis for the primary cohort studies

Excluded study	Pooled HR	95%CI	<i>P</i>
Feng 2025	0.928	0.642 - 1.341	0.638
Gao 2011	0.905	0.636 - 1.286	0.512
Ui 2009	1.002	0.780 - 1.287	0.986
Nagano 2001	0.902	0.633 - 1.285	0.502
Inoue 2009	0.878	0.662 - 1.166	0.305
Bamia 2015	0.956	0.683 - 1.339	0.756
Li 2023	0.978	0.725 - 1.319	0.860
Tamura 2018	0.897	0.642 - 1.253	0.457
Overall (none excluded)	0.932	0.697 - 1.244	0.527

All pooled estimates were derived from random-effects models using restricted maximum likelihood (REML) to estimate the between-study variance (τ^2). Confidence intervals and P-values were calculated using the Knapp-Hartung (HK) adjustment to more appropriately account for the uncertainty in the heterogeneity estimate. CI: Confidence intervals; HK: Knapp-Hartung; HR: Hazard Ratio; REML: restricted maximum likelihood.

Supplementary Table 5. Adjusted covariates and reported effect estimates with 95% confidence intervals of the cohort studies

Author, year	Exposure contrast reported	Effect estimate used in Figure 2	NOS score	Main adjustment factors															Other adjustments*
				Age	Sex	Education	HBV/HCV infection	BMI	Income	Family history	Physical activity	Diabetes	Cirrhosis/chronic liver disease	energy intake	Coffee	Gallstones	Smoking	Alcohol	
Feng 2025	>26g/week vs never tea drinking	HR 0.93 (0.80-1.07)	9	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓			✓	✓	Region; Marital Status; Hypertension
Ui 2009	≥5 Cups/Day vs <1Cup/Day	HR 0.58 (0.41-0.83)	7	✓	✓								✓	✓	✓		✓	✓	City; Time
Nagano 2001	≥5 Times/Day vs ≤1 Time/Day	RR 1.10 (0.80-1.40)	7	✓	✓	✓		✓									✓	✓	Region, Radiation exposure
Inoue 2009	≥500ml/Day vs <3 Cups/Day	HR 1.62 (0.97-2.69)	9	✓	✓		✓	✓				✓			✓		✓	✓	Center, ALT level
Bamia 2015	250-360 ml/d vs Non-Tea Drinking	HR 0.71 (0.41-1.23)	8	✓	✓	✓		✓			✓	✓		✓	✓		✓	✓	Other adjustments
Gao 2011	≥40g/Month vs never tea drinking	HR 1.10 (0.78-1.55)	8	✓		✓	✓	✓	✓		✓	✓	✓	✓			✓	✓	Region; Marital Status; Hypertension
Li 2023	Cumulative Any Tea Consumption >30kg vs never tea drinking	HR 0.56 (0.32-0.97)	9	✓		✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	City; Time
Tamura 2018	≥4 Times/Day vs never tea drinking	HR 1.25 (0.77-2.04)	7	✓	✓	✓		✓			✓	✓		✓			✓	✓	Region

*“Other adjustments” include additional covariates not listed in the main adjustment columns. CI: Confidence intervals; HR: hazard ratio.

Supplementary Table 6. Subgroup analysis stratified by adjustment status for potential confounders

Subgroup	Adjusted		Not adjusted		<i>P</i> for interaction
	No. of studies	HR (95%CI)	No. of studies	HR (95%CI)	
BMI	7	1.00 (0.85-1.18)	1	Not estimable	-
Coffee consumption	3	0.86 (0.46-1.60)	5	0.97 (0.86-1.10)	0.583
Diabetes	5	0.99 (0.70-1.42)	3	0.86 (0.61-1.21)	0.548
Education level	6	0.96 (0.86-1.07)	2	0.95 (0.35-2.61)	0.930
Family history	2	0.78 (0.48-1.25)	6	0.99 (0.74-1.33)	0.390
HBV infection	3	1.09 (0.83-1.44)	5	0.81 (0.58-1.13)	0.175
HCV infection	1	Not estimable	7	0.88 (0.71-1.09)	-
Income level	3	0.93 (0.81-1.06)	5	0.97 (0.68-1.40)	0.683
Liver disease	4	0.79 (0.58-1.09)	4	1.13 (0.88-1.45)	0.114
Physical activity	5	0.93 (0.82-1.05)	3	0.99 (0.56-1.76)	0.750
Sex	6	0.96 (0.73-1.26)	2	0.81 (0.42-1.57)	0.633

CI: Confidence interval; HR: hazard ratio.