

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Detailed Methods

The Population, Intervention, Comparison, Outcomes, and Study (PICOS) framework was used to structure the initial search strategy (**eTable 1**), and the methodology for the subsequent systematic review reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A systematic literature review was performed in PubMed (MEDLINE) as well as the proceedings of the American Society of Clinical Oncology (ASCO) and American Society for Radiation Oncology (ASTRO) annual meetings. We reviewed the reference lists of included publications along with relevant review articles retrieved from the electronic searches to identify other potentially relevant studies that could have been missed. The initial search strategy was as follows: “hepatic” OR “liver” AND “carcinoma” OR “cancer” OR “malignancy” OR “neoplasm” AND “prospective” OR “randomized” OR “trial”. Searches were conducted by multiple authors and included reports published in the English language before November 1, 2023. If a trial had been updated, the publication with the most updated data was included. Conflicts were resolved via direct discussion between the authors.

Studies were eligible if they met the following inclusion criteria: (1) patient population representing nonmetastatic HCC (studies with < 5% of patients with metastases were included as these studies were felt to measure the relevant population of interest), (2) randomized phase II or phase III trials with protocol-mandated surgical management, locoregional therapy (LRT) as defined by the NCCN¹ or other national guidelines² (RFA, MWA, TAE, [DEB-J]TACE, TARE, RT, HAIC) in at least one arm (including studies of adjuvant treatment), and (3) reported data sufficient for quantitative meta-analysis for PFS, OS, or both. Exclusion criteria were as follows: (1) studies comparing variants of the same class of therapy, (2) publications involving a placebo control comparator, (3) trials with planned subtotal and/or incomplete locoregional treatment, (4) reports of incomplete studies or those which were assessed as having high risk of bias identified by the study investigators, and (5) data reported solely in meta-analyses, reviews, surveys, press releases, letters, and book chapters. Each study was assessed for bias using the Cochrane RoB2 tool³ as shown in **eFigure 1**.

Data Extraction

From each study, extracted data included the first author's name, study year, country of enrollment, baseline trial cohort composition, trial design, treatment regimens, number of patients, as well as a measure of treatment effect for the comparison (i.e., hazard ratios [HR]) for overall survival (OS) and progression free survival (PFS). When HRs were not reported and Kaplan-Meier curves with corresponding risk tables were reported, WebPlotDigitizer version 4.6 was used to extract survival data and estimate the HR. When PFS was not reported, composite endpoints of survival and disease recurrence were utilized for the PFS endpoint. As this study focused exclusively on randomized trials, unadjusted, intention-to-treat analyses were utilized.

eReferences

1. Network NCC. Hepatocellular Carcinoma (Version 2.2023). 2023. Accessed November 22, 2023, 2023. https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf
2. Kudo M, Kawamura Y, Hasegawa K, et al. Management of Hepatocellular Carcinoma in Japan: JSH Consensus Statements and Recommendations 2021 Update. *Liver cancer*. Jun 2021;10(3):181-223. doi:10.1159/000514174
3. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. doi:10.1136/bmj.d5928

eTable 1. PICOS Framework Summary

PICOS Framework Utilized for Analysis 1	
Participants	Nonmetastatic hepatocellular carcinoma ineligible for liver transplant*
Interventions	Any locoregional therapy for treatment of HCC: 1. surgery without adjuvant therapy, 2. surgery with adjuvant therapy, 3. radiofrequency ablation (RFA), 4. microwave ablation (MWA), 5. radiotherapy (RT), 6. hepatic arterial infusion (HAI) chemotherapy, 7. transarterial chemoembolization (TACE), 8. transarterial radioembolization (TARE), 9. bland embolization (TAE),
Comparisons	Prospective randomized comparisons of any locoregional therapy compared against another locoregional therapy or a systemic therapy option
Outcomes	Progression Free Survival (PFS) and/or Overall Survival (OS)
Study design	Randomized, controlled phase II or III trials
PICOS Framework Utilized for Analysis 2	
Participants	Nonmetastatic hepatocellular carcinoma ineligible for liver transplant*
Interventions	1. Locoregional therapy alone 2. Systemic therapy alone 3. A protocol treatment utilizing a combination of locoregional therapy and systemic therapy
Comparisons	Prospective randomized comparisons of any of the above interventions or combinations thereof
Outcomes	Progression Free Survival (PFS) and/or Overall Survival (OS)
Study design	Randomized, controlled phase II or III trials
* Trials with < 5% metastatic patients will be included as it is felt that such trials will meaningfully represent the sought after effect estimates	

eTable 2. Baseline Characteristics of Evaluable Studies

Study	Country	Patient per arm (n)	Median Age	Sex by Arm (M/F)	Tumor Size	Child-Pugh Score	Viral Hepatitis Etiology	Serum AFP (ng/mL)	Surgical Candidate	Prior Treatment
Ng et al. 2017	China	109, 109	55; 57	89/20; 86/23	< 4 cm	A	Any	58; 63.5	Yes	None
Xia et al. 2020	China	120, 120	50; 50	107/13; 109/11	< 4 cm, number < 3	A	Any	70; 73	Yes	Partial Hepatectomy
Feng et al. 2012	China	84, 84	51; 47	79/5; 75/9	< 4 cm, number < 3	A or B	HBV	215.5; 262.8	Yes	None
Huang et al. 2010	China	115, 115	55.9; 56.7	85/30; 79/36	< 5 cm, number < 3	A or B	HBV	NR	Yes	None
Takamaya et al. 2022	Japan	151, 150	68; 69	112/38; 108/43	< 3 cm, number < 3	A	Any	NR	Yes	None
Comito et al. 2022	Italy	21, 19	75; 75	15/6; 15/4	BCLC Stage A/B	A or B	Any	NR	No	Prior TACE
Romero et al. 2023	Multinational	12, 16	69; 62	10/2; 14/2	< 6 cm total, number < 3	A	Any	8; 5	No	None
Kim et al. 2021	Korea	72, 72	60; 61.5	61/11; 59/13	< 3 cm, number < 2	A	HBV	4.9; 5.1	No	Prior resections permitted
Bush et al. 2023	United States	35, 39	61.7; 59.6	27/8; 26/13	< 5 cm, number < 3	A or B	Any	NR	No	None

Yoon et al. 2018	Korea	45, 45	55; 55	77/13; 39/6	1 measurable lesion	A	Any	667; 1496	No	None
Chow et al. 2018	Multinational	182, 178	59.5; 57.7	147/35; 151/27	BCLC Stage B/C	A or B	Any	NR	No	< 2 prior Hepatic/ directed therapies permitted
Vilgrain et al. 2017	France	174, 206	66;65	212/25; 202/20	BCLC Stage C	A or B	Any	87;80	No	Prior resections permitted
Zheng et al. 2022	China	32, 32	56;55	30/2; 31/1	inoperable HCC	A	Any	310; 655	No	No prior HAI or systemic therapy
He et al. 2019	China	125, 122	49; 49	111/14; 112/10	inoperable HCC	A	Any	5922; 6666	No	None
Ikeda et al. 2016	Japan	66, 42	64; 66	56/9; 32/9	inoperable HCC	A or B	Any	188; 223.5	No	No prior HAI or systemic therapy
Kondo et al. 2019	Japan	36, 34	70.9; 72	27/6; 28/7	Any HCC deemed to have limited benefit from surgery	A or B	Any	216; 67.3	No	All prior treatment permitted, 4/week washout
Giorgio et al. 2016	Italy	49, 50	71;72	37/12; 36/14	< 5 cm, number < 3, with PVT	A	Any	83;80	No	None
Li et al. 2021	China	159, 156	53; 54	134/24; 141/15	BCLC Stage A/B	A	Any	NR	Yes	None

Peng et al. 2023	China	170, 168	54; 56	139/31; 132/36	Locally advanced	A	Any	55,979; 31,752	No	Prior resection s permitted
Dawson et al. 2022	United States	85, 92	66	NR	BCLC Stage B/C	A	Any	NR	No	Prior resection s permitted
Ricke et al. 2019	Multinational	216, 208	66; 66	181/31; 177/30	BCLC Stage A/C	A or B	Any	NR	No	Prior resection s or liver/directed therapies (>3 months) permitted
Qin et al. 2023	Multinational	334, 334	62; 60	289/53, 281/51	BCLC Stage B/C	A or B	Any	NR	No	Prior curative treatment
Kudo et al. 2011	Multinational	229, 229	69; 70	174/55; 160/69	< 10 lesions; < 70 mm in greatest dimension	NR	Any	NR	No	Prior local therapy
Kudo et al. 2018	Multinational	444, 444	66.2; 65.4	363/81; 364/80	BCLC Stage A/C	A	Any	NR	No	Prior Local therapy
Kudo et al. 2014	Multinational	249, 253	57;59	206/43; 216/37	< 4 lesions, one measured >5 cm	B or C	Any	NR	No	No prior treatment
Tak et al. 2018	Multinational	354, 347	NR	267/87; 263/84	BCLC Stage A/B	A or B	Any	NR	No	No prior treatment
Bruix et al. 2015	Multinational	556, 558	58;60	451/105; 461/97	Single lesion < 5 cm or 3 lesions < 3 cm	A or B	Any	6; 5.6	Yes	Prior resection or ablation

Lencioni et al. 2016	Multinational	154. 153	64.5; 63	135/19; 126/27	BCLC Stage B	A	Any	NR	No	No prior local therapy
Meyer et al. 2017	United Kingdom	157. 156	65; 68	139/18; 138/18	1 measurable lesion	A	Any	23; 25	No	No prior local therapy
Brown et al. 2016	United States	51, 50	68; 65	37/14; 41/9	Okuda Stage I or II	A or B	Any	NR	No	NR
Wang et al. 2018	China	140, 140	52.6, 54.2	109/31; 121/19	NR	A or B	HBV	NR	Yes	No prior treatment
Li et al. 2023	China	143, 143	50; 54	136/21; 139/19	NR	A or B	Any	164; 189	N/A	Prior resection
Sun et al. 2019	China	26, 26	49.6; 51.1	24/2; 24/2	BCLC Stage A or B	A	HBV	NR	N/A	Prior resection
Li et al. 2020	China	78, 78	53.0; 53.0	58/20; 61/17	NR	A	Any	27.7; 50.2	N/A	Prior resection
Chen et al. 2013	China	34, 34	48.9; 50.8	24/10; 25/9	BCLC Stage A or B	A	Any	579; 612	N/A	Prior resection
Rong et al. 2020	China	61, 58	53.1; 55.5	44/1; 31/9	BCLC Stage 0 or A	NR	Any	NR	Yes	No prior treatment
Shi et al. 2022	China	38. 38	56.2; 55.7	33/5; 36/2	BCLC Stage 0 or A	NR	Any	NR	N/A	Prior Resection
Wei et al. 2018	China	125, 125	44, 48.5	106/10; 106/12	BCLC Stage A	A or B	Any	NR	N/A	Prior resection
Vietti Violi et al. 2018	Multinational	73, 71	68; 65	59/12; 62/11	< 3 lesions all < 3 cm in diameter	A or B	Any	NR	No	No prior treatment

Abbreviations: HCC = Hepatocellular Carcinoma, BCLC = Barcelona Cancer Liver Clinic, TACE = transarterial chemoembolization, HAI = hepatic artery infusion. NR = not reported.

eTable 3. Select Outcomes of Evaluable Studies

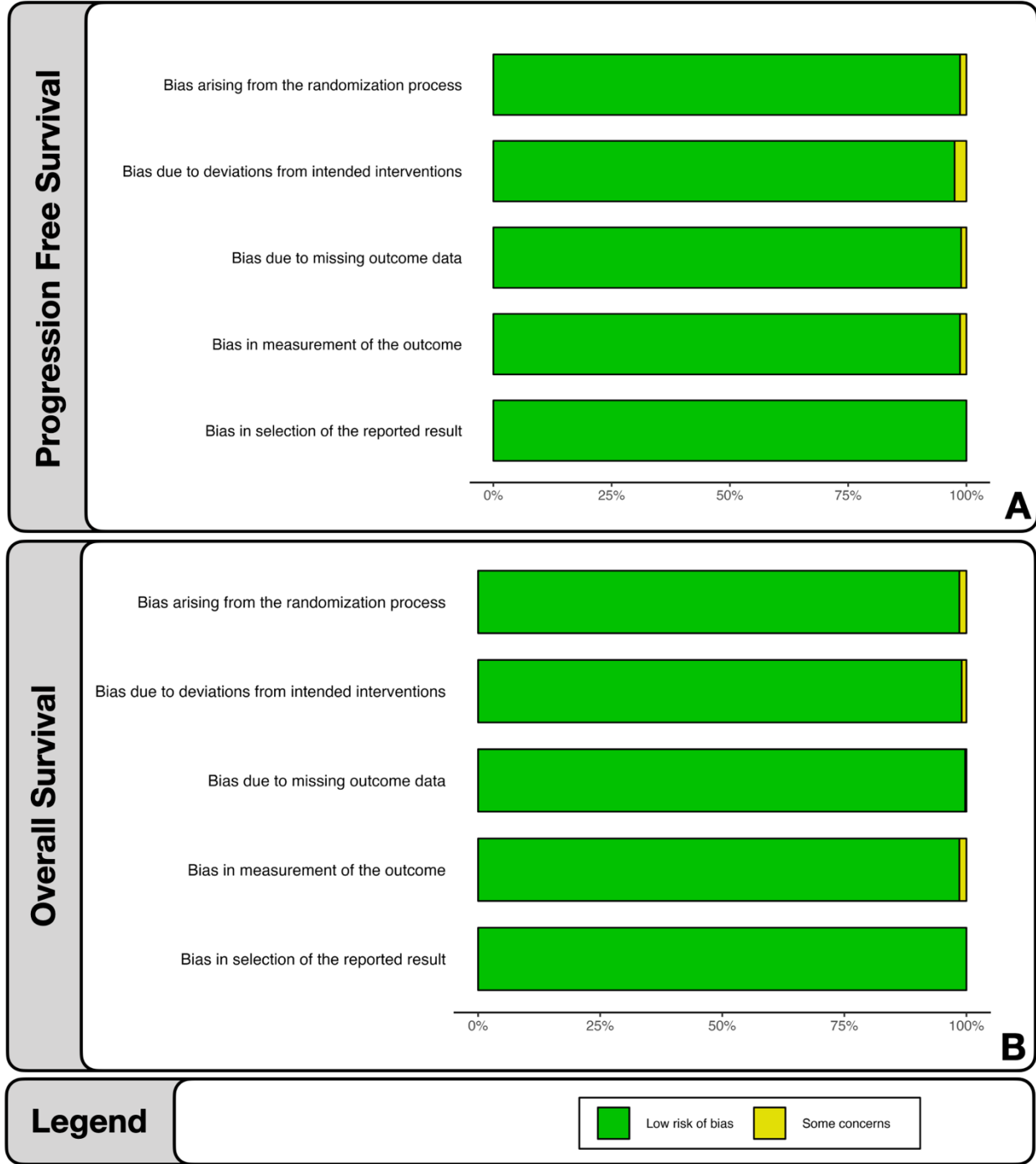
Study	Arm 1	Arm 2	Median Follow-Up (months)	Primary Outcome	Included in Analysis 1 PFS	Included in Analysis 1 OS	Included in Analysis 2 PFS	Included in Analysis 2 OS
Ng et al. 2017	RFA	Surgery	93	Tumor recurrence	No	No	Yes	Yes
Xia et al. 2020	RFA	Surgery	44.3	OS	No	No	Yes	Yes
Feng et al. 2012	RFA	Surgery	36	OS	No	No	Yes	Yes
Huang et al. 2010	RFA	Surgery	37.1, 46.4	OS	No	No	Yes	Yes
Takamaya et al. 2022	RFA	Surgery	59.9, 60.5	RFS	No	No	Yes	No
Comito et al. 2022	TACE	RT (30-75 Gy in 3-10 fx)	20	LC	No	No	Yes	Yes
Romero et al. 2023	TACE-DEB	SBRT (54 Gy in 3 fractions)	28.1	TTP	No	No	No	Yes
Kim et al. 2021	PBT (66 Gy in 10 fractions)	RFA	51.6, 50.7	LPFS	No	No	Yes	Yes
Bush et al. 2023	PBT (70.2 Gy in 15 fractions)	TACE	30	OS	No	No	Yes	No
Yoon et al. 2018	Sorafenib	TACE + EBRT (45 Gy in 15-18 fractions)	35	PFS	Yes	Yes	Yes	Yes
Chow et al. 2018	Sorafenib	TARE	NR	OS	Yes	Yes	Yes	Yes
Vilgrain et al. 2017	Sorafenib	TARE	25.7, 30.1	OS	Yes	Yes	Yes	Yes
Zheng et al. 2022	Sorafenib	Sorafenib + 5FU/Oxaliplatin HAI	25.0, 16.4	OS	Yes	Yes	Yes	Yes

He et al. 2019	Sorafenib	Sorafenib + FOLFOX HAI	28	OS	Yes	Yes	Yes	Yes
Ikeda et al. 2016	Sorafenib	Sorafenib + CDDP	NR	OS	No	Yes	No	Yes
Kondo et al. 2019	Sorafenib	CDDP HAI + Sorafenib	NR	OS	No	Yes	No	Yes
Giorgio et al. 2016	Sorafenib	Sorafenib + RFA	NR	OS	No	Yes	No	No
Li et al. 2021	TACE	FOLFOX HAI	NR	OS	No	No	Yes	Yes
Peng et al. 2023	Lenvatinib	TACE + Lenvatinib	17	OS	Yes	Yes	Yes	Yes
Dawson et al. 2022	Sorafenib	Sorafenib + SBRT	13.2	OS	Yes	Yes	Yes	Yes
Ricke et al. 2019	Sorafenib	TARE + Sorafenib	9.4, 6.6	OS	No	Yes	No	Yes
Qin et al. 2023	Surgery	Surgery + Atezolizumab + Bevacizumab	33	OS	Yes	Yes	Yes	Yes
Kudo et al. 2011	TACE + Sorafenib	TACE	NR	TTP	No	Yes	No	No
Kudo et al. 2018	TACE + Orantinib	TACE	NR	OS	Yes	Yes	No	No
Kudo et al. 2014	TACE + Brivanib	TACE	16.6	OS	No	Yes	No	No
Tak et al. 2018	RFA + Dox	RFA	NR	PFS	Yes	Yes	No	No
Bruix et al. 2015	Surgery + Sorafenib	Surgery	8.5	RFS	Yes	Yes	Yes	No

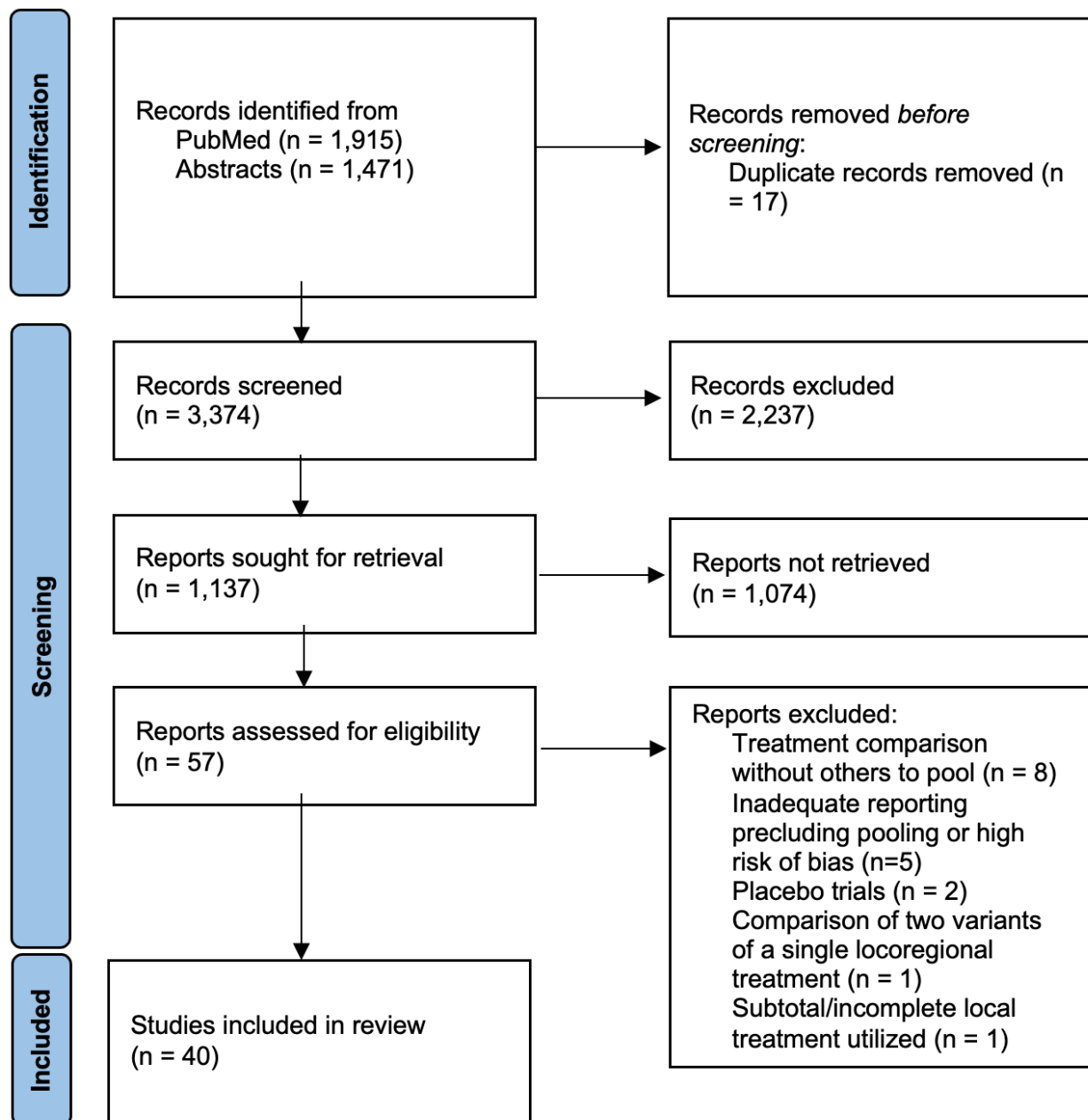
Lencioni et al. 2016	TACE-DEB + Sorafenib	TACE-DEB	9.1	TTP	No	Yes	No	No
Meyer et al. 2017	TACE-DEB + Sorafenib	TACE-DEB	21	PFS	Yes	Yes	No	No
Brown et al. 2016	TAE	TACE-DEB	34	RTT	No	No	Yes	Yes
Wang et al. 2018	Surgery	Surgery + TACE	44.1	RFS	Yes	Yes	Yes	Yes
Li et al. 2023	Surgery	Surgery + FOLFOX HAI	23.7	DFS	Yes	Yes	Yes	Yes
Sun et al. 2019	Surgery	Surgery + EBRT (50 Gy/25 fx)	12	OS	Yes	Yes	Yes	Yes
Li et al. 2020	Surgery	Surgery + RAI	55.9	RFS	Yes	Yes	Yes	Yes
Chen et al. 2013	Surgery	Surgery + I-125 BT	47.6	TTP	Yes	Yes	Yes	Yes
Rong et al. 2020	Surgery	Surgery + EBRT (60 Gy/ 30 fx)	NR	RFS	Yes	Yes	Yes	Yes
Shi et al. 2022	Surgery	Surgery + SBRT (35 Gy/ 5 fx)	52	DFS	Yes	Yes	Yes	Yes
Wei et al. 2018	Surgery	Surgery + TACE	37.5	DFS	Yes	Yes	Yes	Yes
Vietti Violi et al. 2018	MWA	RFA	26	LC	No	No	No	Yes

Abbreviations: RFA = radiofrequency ablation, EBRT = external beam radiation therapy, SBRT = stereotactic body radiation therapy, PBT = proton beam therapy, Gy= Gray (SI), fx = fraction, TACE = transarterial chemoembolization, TARE = transarterial radiofrequency embolization, 5FU = 5-fluorouracil, DEB = drug-eluting bead, FOLFOX = folinic acid, fluorouracil, and oxaliplatin, HAI = Hepatic arterial infusion, CDDP = cisplatin, LEN= lenvatinib, RFS = recurrence free survival, NR = not reported, LC = local control, RTT = Response to treatment, TTP = time to progression, LPFS = locoregional progression free survival, OS = overall survival, PFS = progression free survival,

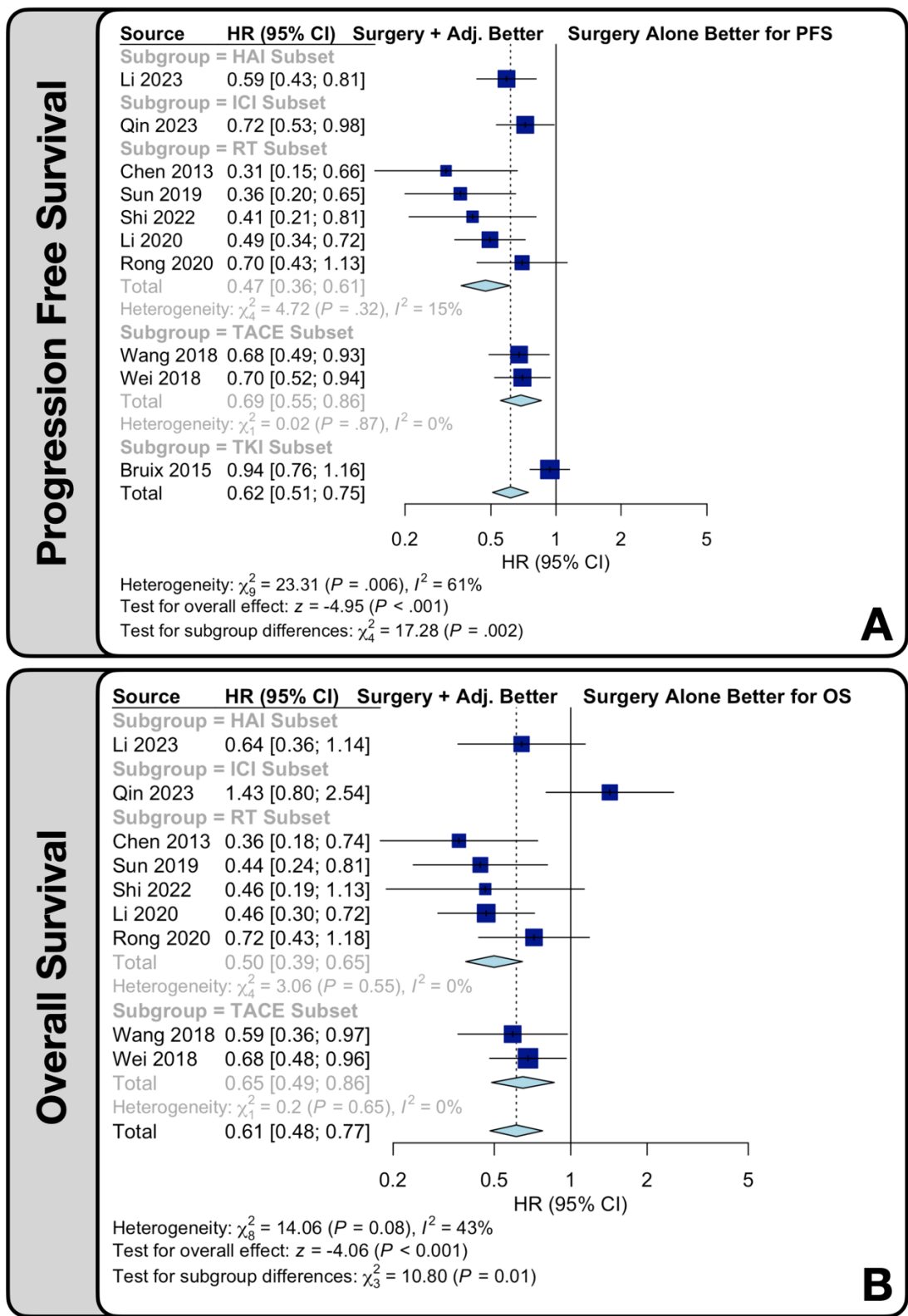
eFigure 1. Risk of Bias Assessment



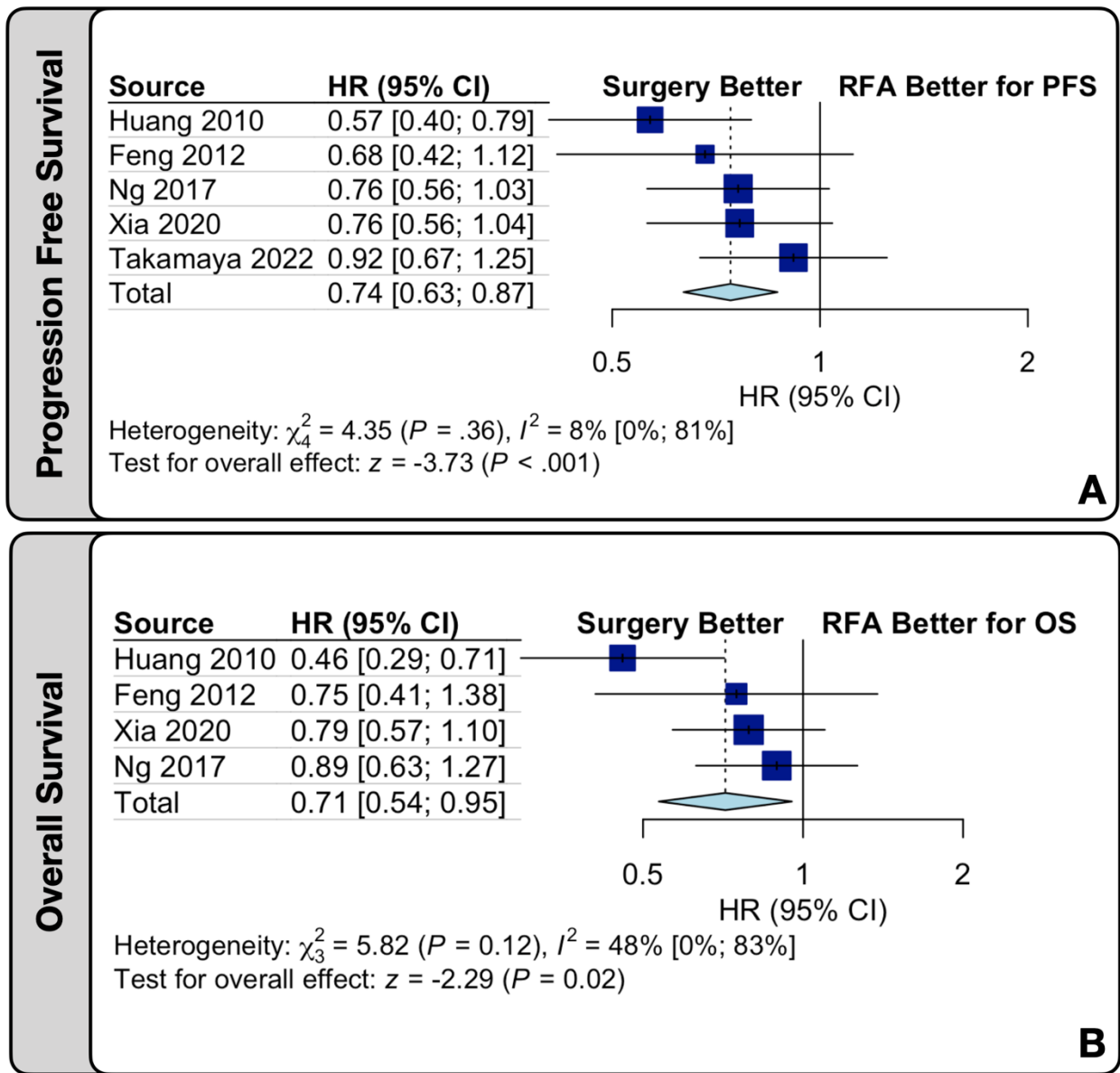
eFigure 2. PRISMA Flowchart of Study Selection



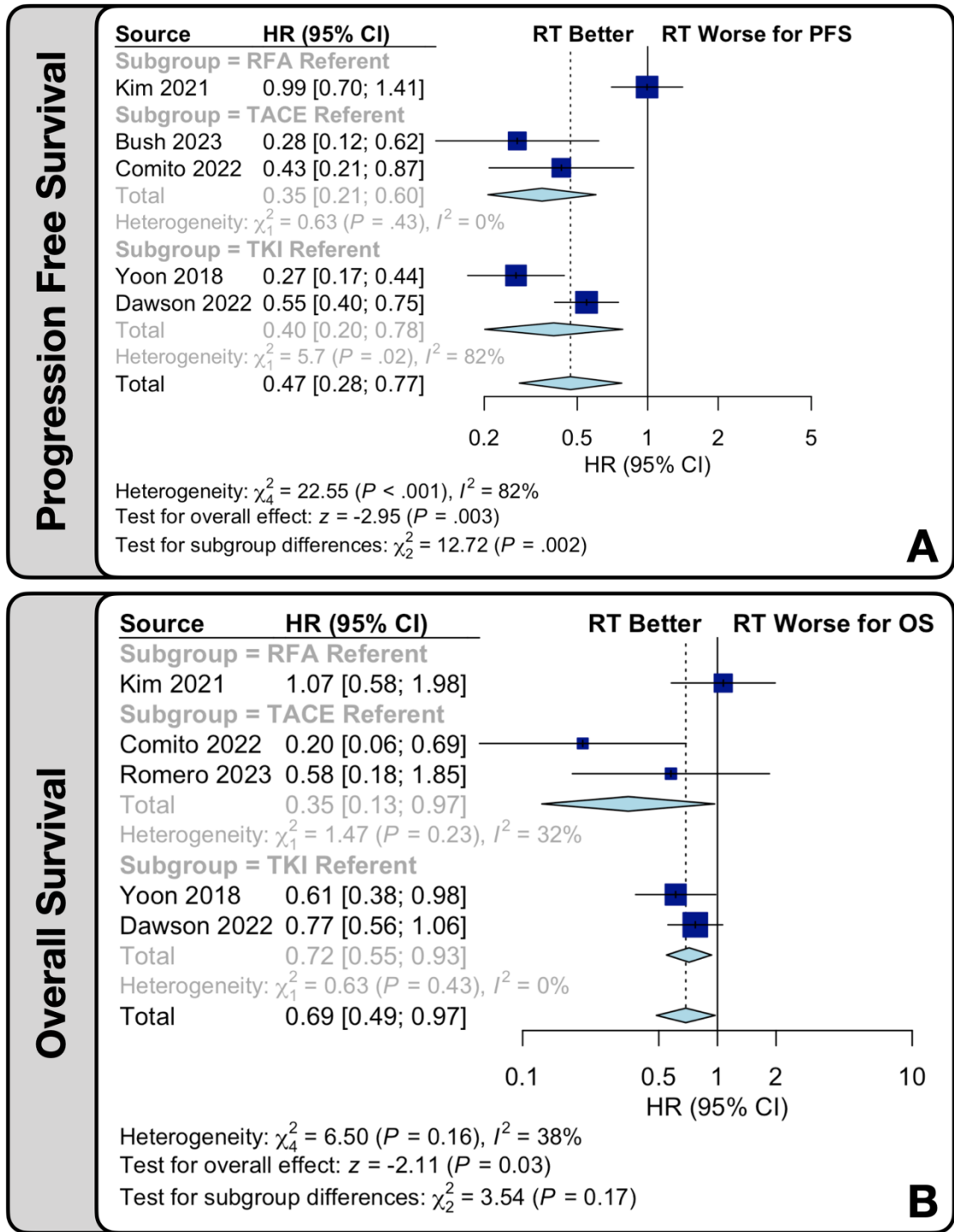
eFigure 3. Surgery ± Adjuvant. Forest plots of studies comparing surgery with surgery plus additional LRT methods given in the adjuvant setting with corresponding meta-analytic estimates.



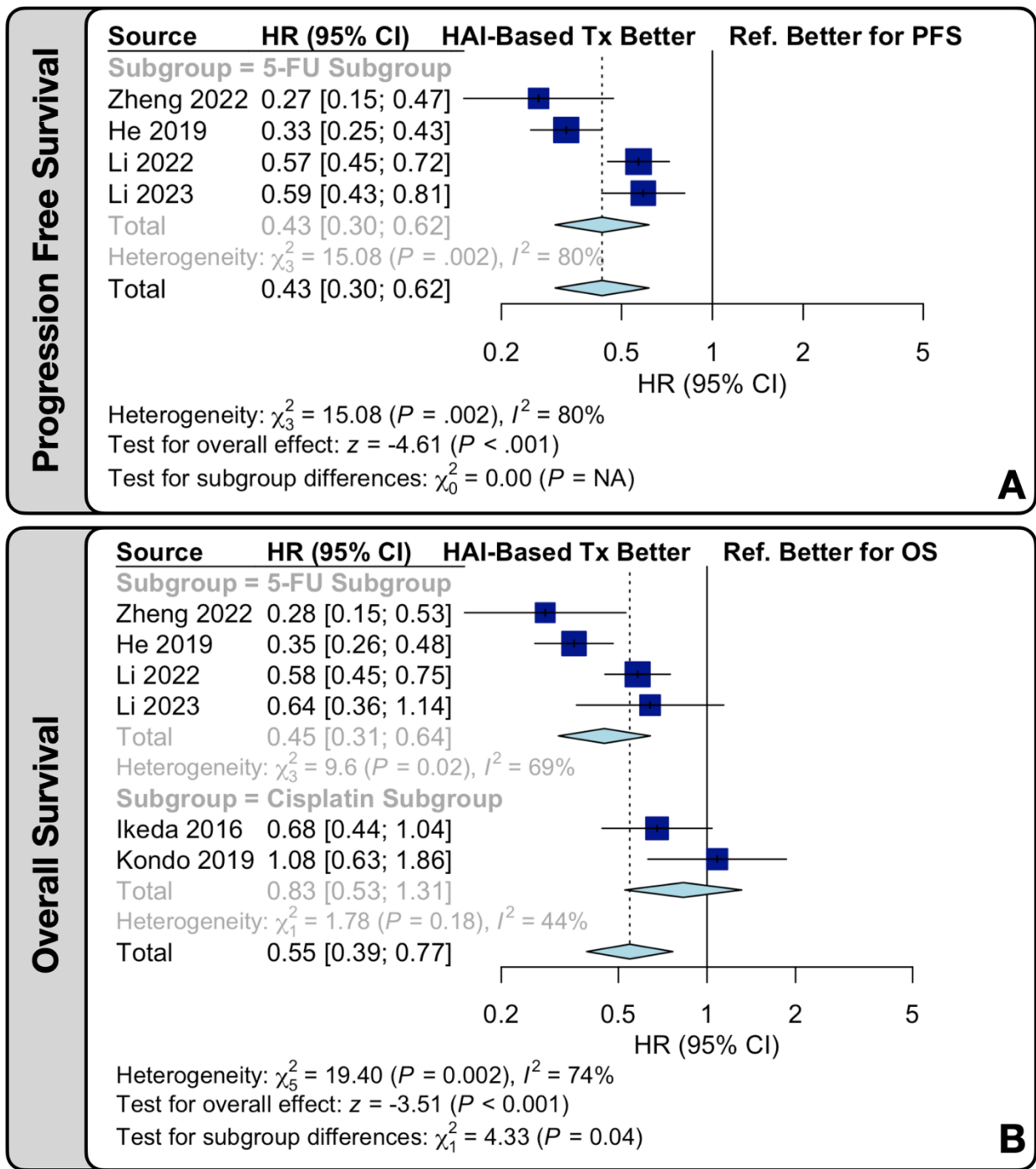
eFigure 4. Surgery vs RFA. Forest plots of studies comparing surgery with radiofrequency ablation (RFA) with corresponding meta-analytic estimates.



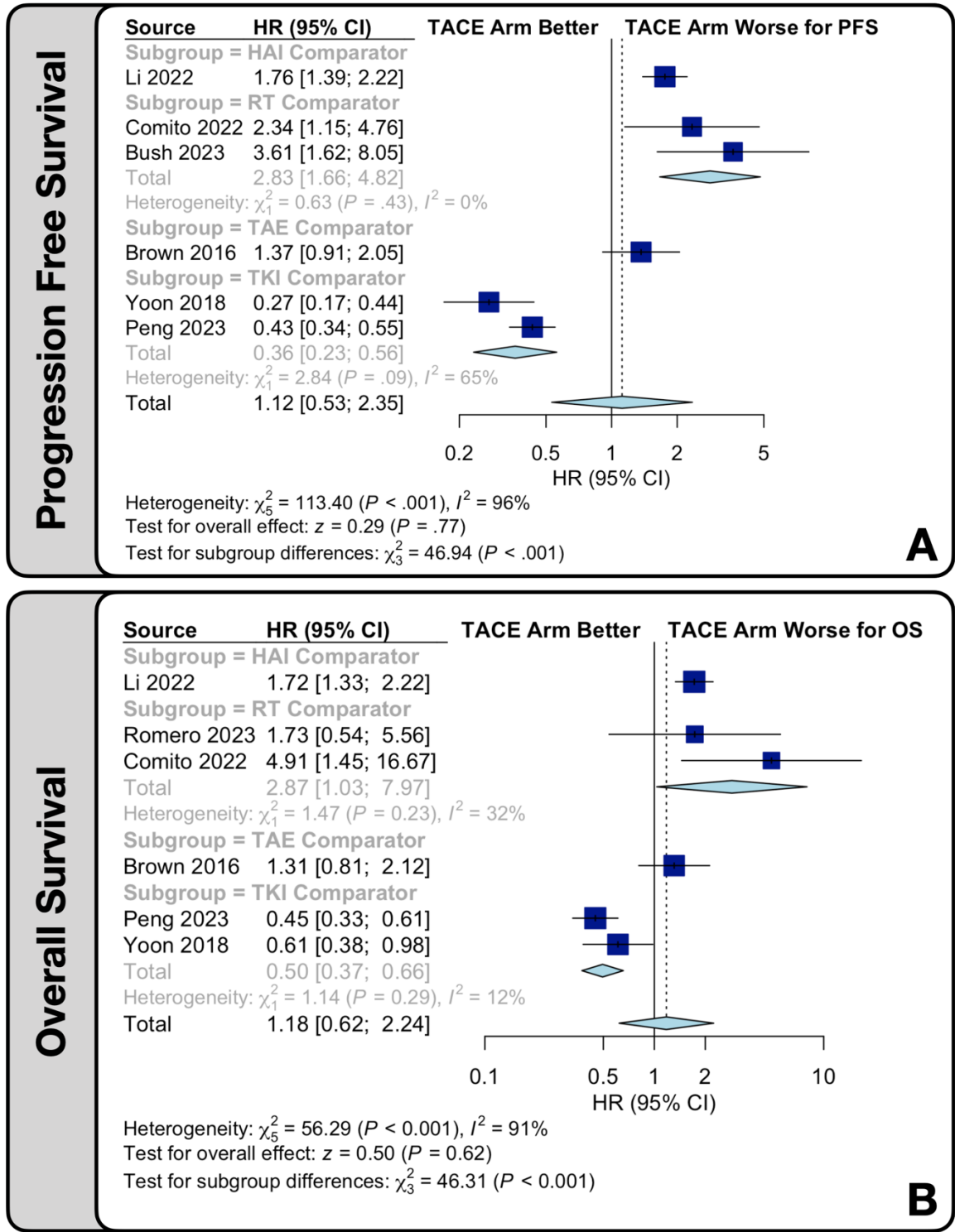
eFigure 5. RT vs. Other. Forest plots of studies comparing radiotherapy (RT) with other locoregional therapies by subgroup with corresponding meta-analytic estimates.



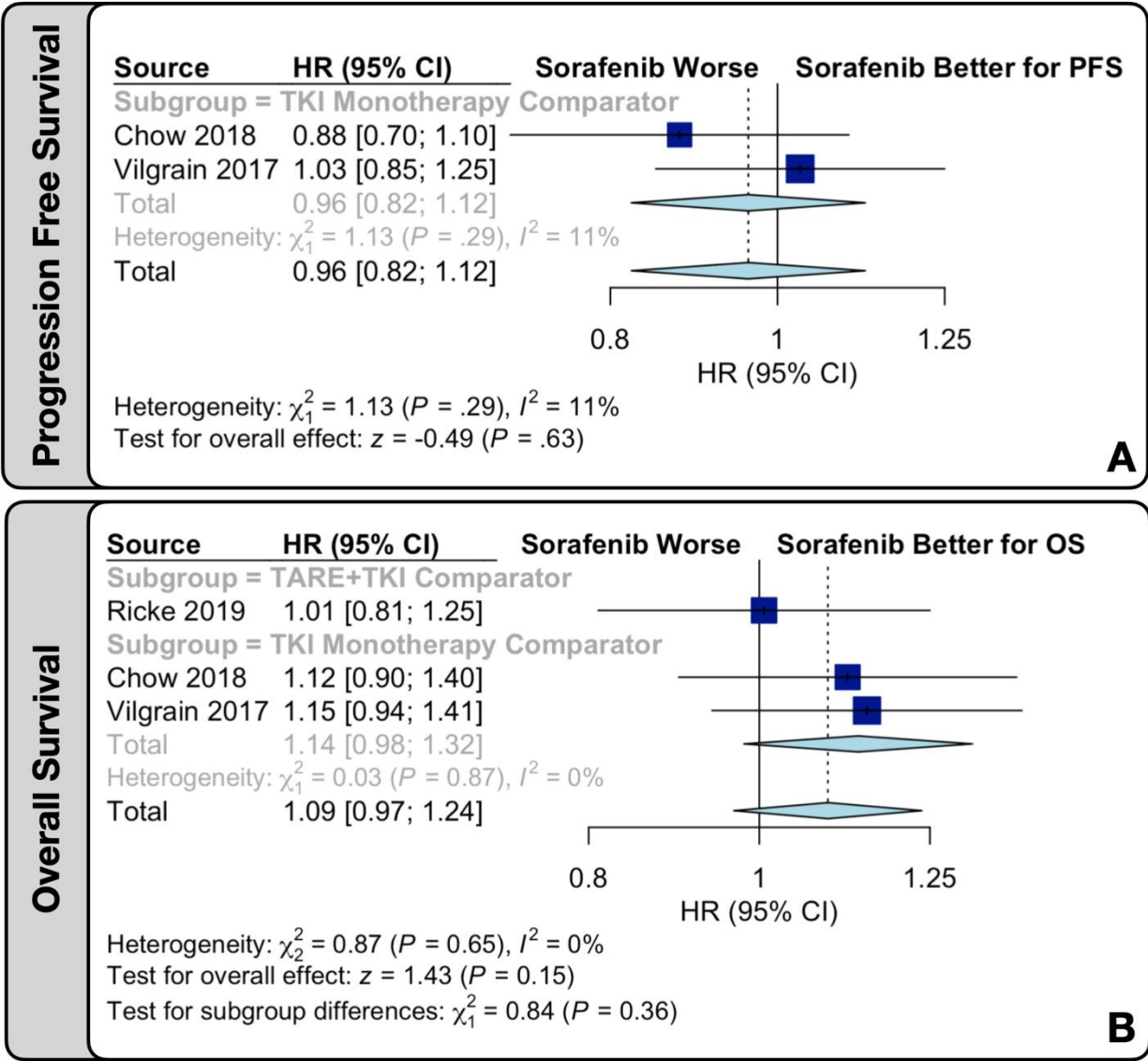
eFigure 6. HAI vs Other. Forest plots of studies comparing hepatic arterial infusion (HAI) chemotherapy-based treatments with comparators by subgroup with corresponding meta-analytic estimates.



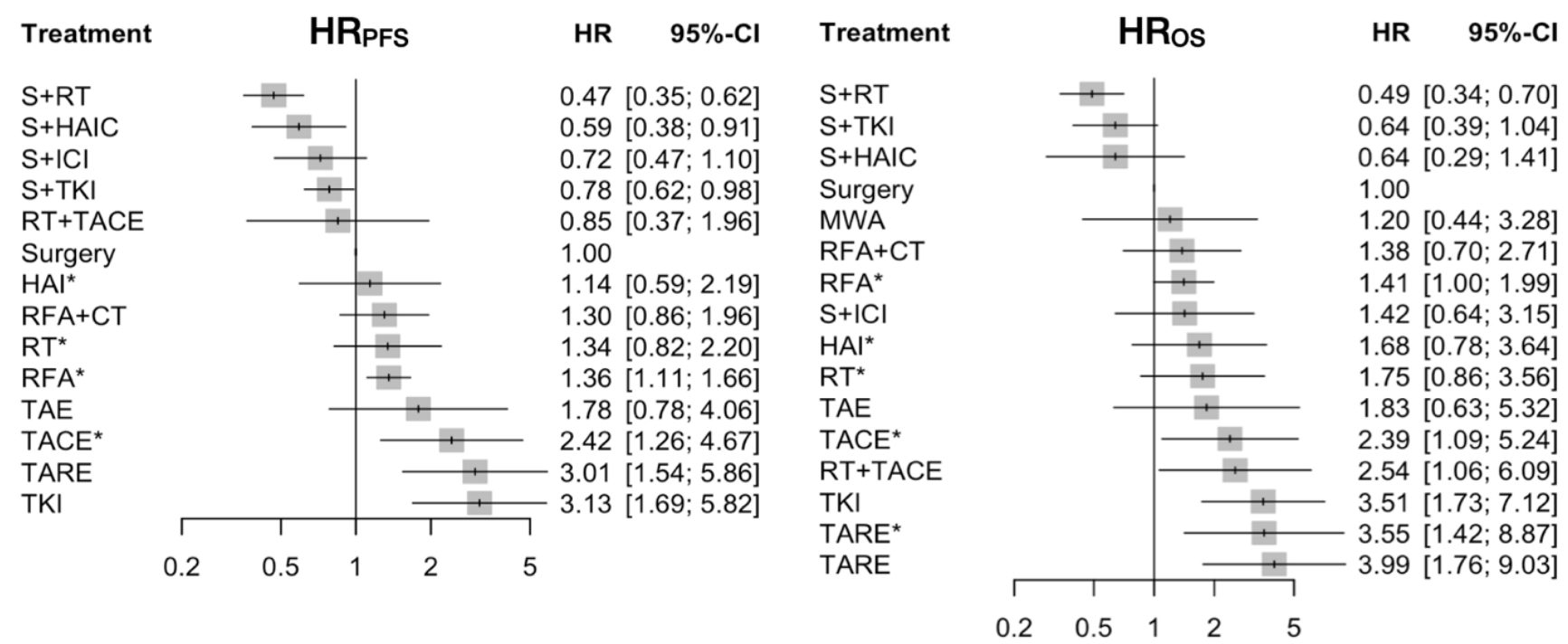
eFigure 7. TACE vs. Other. Forest plots of studies comparing trans-arterial chemoembolization (TACE) comparators by subgroup with corresponding meta-analytic estimates.



eFigure 8. TARE vs TKI-Based Therapy. Forest plots of studies comparing trans-arterial radioembolization (TARE) comparators by subgroup with corresponding meta-analytic estimates.



eFigure 9. Network Meta-Analysis. Forest plot of a comparative efficacy estimates on the endpoints of PFS and OS against the referent of surgery from a network meta-analysis.



* Asterisk denotes locoregional therapy with or without additional treatments.

eAppendix

RESULTS

The Comparative Role of Systemic and Locoregional Therapy (LRT)

Systemic Therapy ± LRT

Pooling studies that investigated locoregional intensification of systemic therapy with RFA, RT, HAIC, or embolization-based methods⁴⁻¹¹ showed that local intensification improved PFS (HR 0.40 [95% CI: 0.30-0.52]; $p < 0.001$) and OS (HR 0.56 [95% CI: 0.40-0.81]; $p = 0.02$) (**eAppendix Figure 1A**). Heterogeneity was observed in both analyses ($Q_{df=3} = 8.26$, $p = 0.04$ for PFS and $Q_{df=7} = 51.93$, $p < 0.001$ for OS). A subgroup analysis (**eAppendix Figure 2**) including a HAIC subgroup and another subgroup comprised of other forms of LRT was conducted, and the benefit of local intensification remained consistent across subgroups on both outcomes of PFS (both $p < 0.001$) and OS (both $p < 0.05$).

LRT ± Systemic Therapy

Pooling studies that investigated the addition of systemic therapy to LRT¹²⁻¹⁹ showed an improvement in PFS (HR 0.90 [95% CI: 0.82-0.98], $p = 0.02$), but no corresponding improvement in OS (HR 1.00 [95% CI: 0.90-1.11], $p > 0.99$) (**eAppendix Figure 1B**). No significant heterogeneity was observed for PFS ($Q_{df=4} = 3.66$, $p = 0.45$) or OS ($Q_{df=7} = 3.24$, $p = 0.86$) between treatment class comparisons (**eAppendix Figure 3**).

LRT vs. Systemic Therapy

Pooling trials that compared local therapy alone to systemic therapy²⁰⁻²² did not detect a difference in PFS or OS between classes (**eAppendix Figure 1C**). As significant heterogeneity was observed ($Q_{df=2} = 25.72$, $p < 0.001$ for PFS and $Q_{df=2} = 6.07$, $p = 0.048$ for OS), subgroup analysis was conducted. The heterogeneity was a result of the inclusion of a single trial that showed a large benefit of intensive local treatment with TACE+RT over sorafenib²². In contrast, the other studies^{20,21} comparing TARE to sorafenib showed no significant evidence of a difference between arms (**eAppendix Figure 4**).

A network meta-analysis was done showing a consistent ordinality of results (**eAppendix Figure 5**)

DISCUSSION

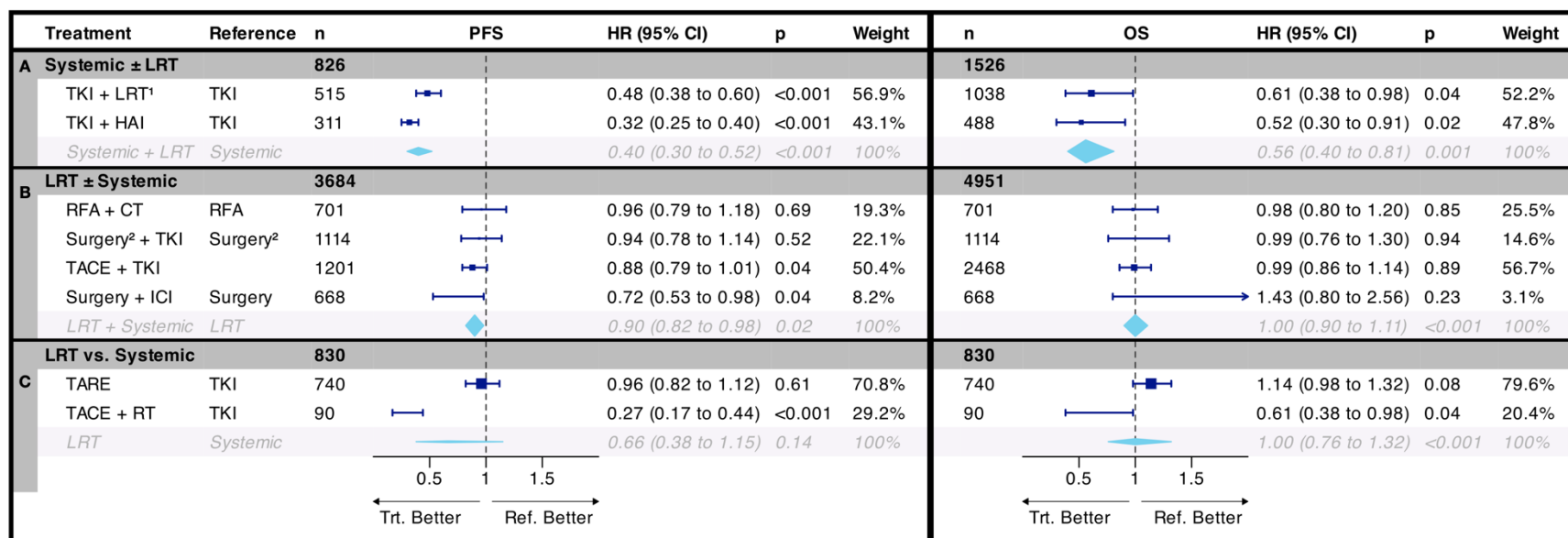
The Comparative Role of Systemic and Locoregional Therapy (LRT)

The comparative efficacy of systemic therapy alone versus LRT alone in practice observed may be a result of the baseline disease features between trials or differences in the efficacy of various LRTs, given the high heterogeneity observed. Intuitively, systemic therapy serves to improve extrahepatic control while LRT improves intrahepatic control, as observed in SARAH²¹. Thus, future work utilizing baseline imaging and patient factors to weigh the competing risk of intra- versus extrahepatic progression may be important to determine which of these two should be considered a higher priority when clinicians are faced with such a decision in a patient eligible for both.

Based on the availability of the reported RCTs, we explored to see if the comparative efficacy of each treatment class (LRT, systemic therapy, or both) was congruent with known patterns of failure. Because many patients die of local disease burden and/or critical liver dysfunction rather than from metastatic disease, it was hypothesized that locoregional control is an important management priority for patients, and the differential efficacy of various LRTs was also discerned herein. First, we found evidence that the addition of LRT to systemic therapy likely improves both PFS and OS. This is consistent with the observation that the most significant pattern of failure in transplant-ineligible patients is local^{23,24}, and therefore, locoregional intensification may improve the disease-free interval for such patients. Given that the leading cause of death in patients with HCC is disease-related^{25,26}, this has the potential to translate into improved OS, as was observed herein. He et al.⁶ showed that only 4% of patients demonstrated an intra-hepatic overall response rate (partial or complete) with sorafenib monotherapy, and, although novel immunotherapy agents have demonstrated an improved

local activity of systemic therapy, the ORR continues to indicate suboptimal local control at approximately 15%²⁷-20%²⁸ for immunotherapy alone and approximately 25-30% for immunotherapy in combination²⁹. Based on the available evidence, the observed PFS benefit from the inclusion of LRT appears to translate to an improvement in OS, highlighting the importance of effective locoregional control in patients with non-metastatic HCC.

Additionally, our findings suggest that the addition of systemic therapy to LRT also improves PFS. This may occur via one of two mechanisms: (1) a decrease in distant metastases or (2) a decrease in intrahepatic foci outside the LRT volume, a failure pattern which may be more frequent than in-volume recurrence³⁰. This increase in treatment intensity, however, did not translate into an improvement in OS. It is possible that because patients who fail LRT will almost always continue to be candidates for systemic therapy as disease progresses, there is little survival benefit to early systemic therapy. This contrasts with the prior case of upfront locoregional intensification of systemic therapy where patients may often lose eligibility to receive local ablation due to intrahepatic or extrahepatic progression, thus potentially missing the opportunity to experience the benefit of the addition of this form of treatment in their lifespan.

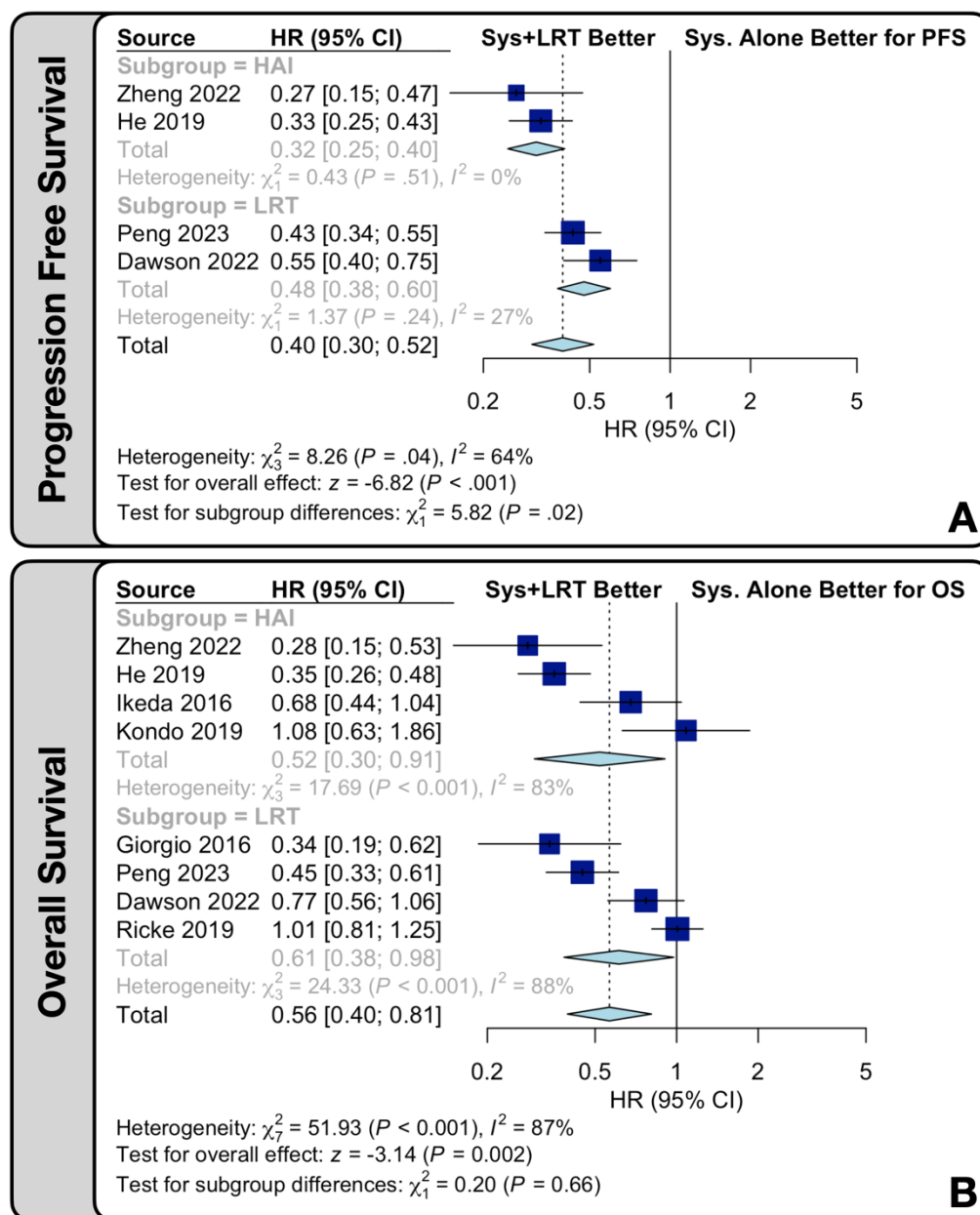


eAppendix Figure 1. Forest plots for the first analysis comparing classes of therapy.

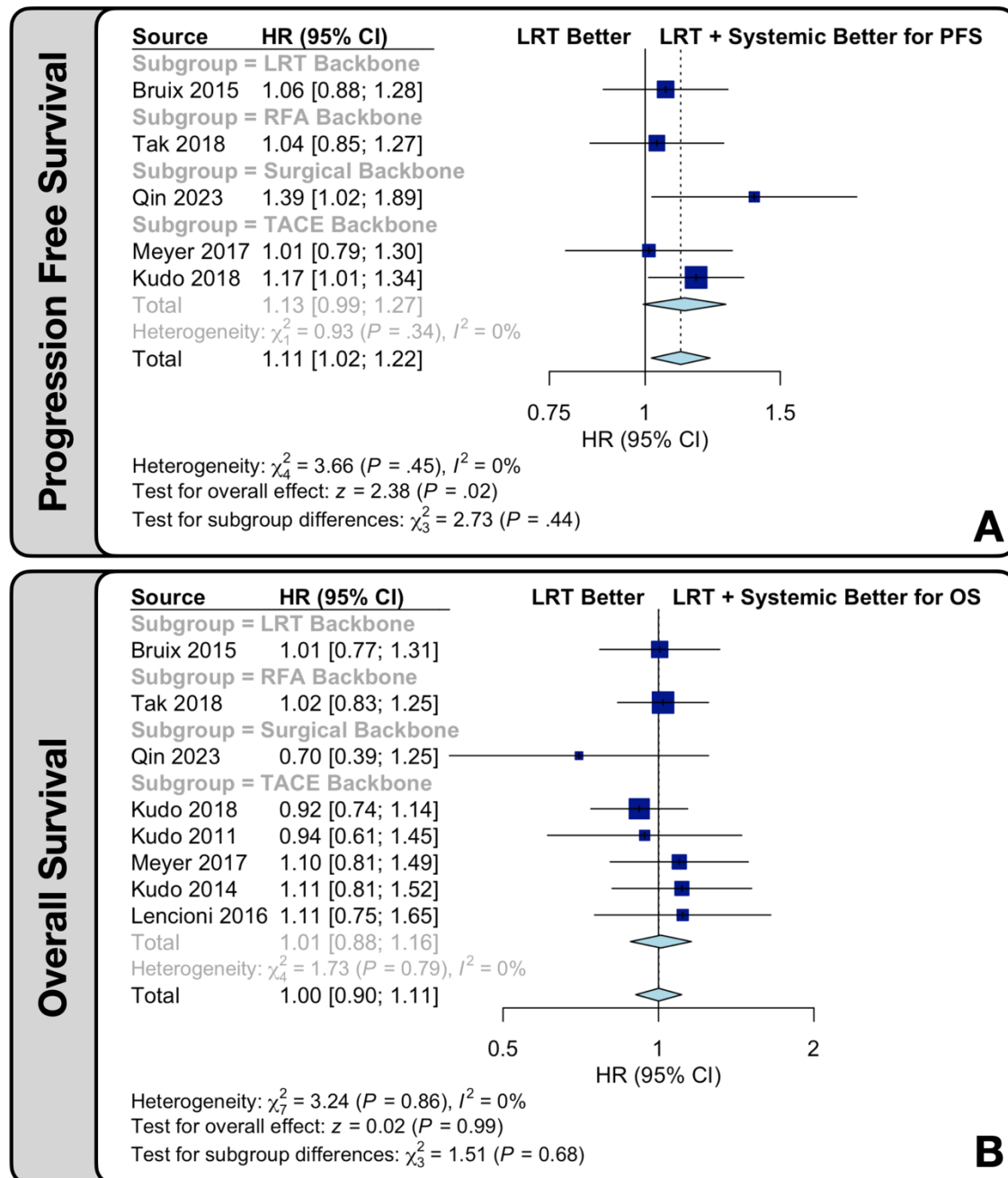
¹ LRT consisting of RFA, SBRT, TACE, and TARE

² Estimate derived from the STORM trial¹⁷ in which 900 of 1114 patients underwent surgery and the remaining 214 patients underwent other forms of loco-regional therapy. Given that the subgroup analysis revealed a very similar HR for PFS between the two groups and this study fulfilled the criteria for this analysis, these were pooled for this analysis. Of note, no subgroup analysis was reported for OS in this study.

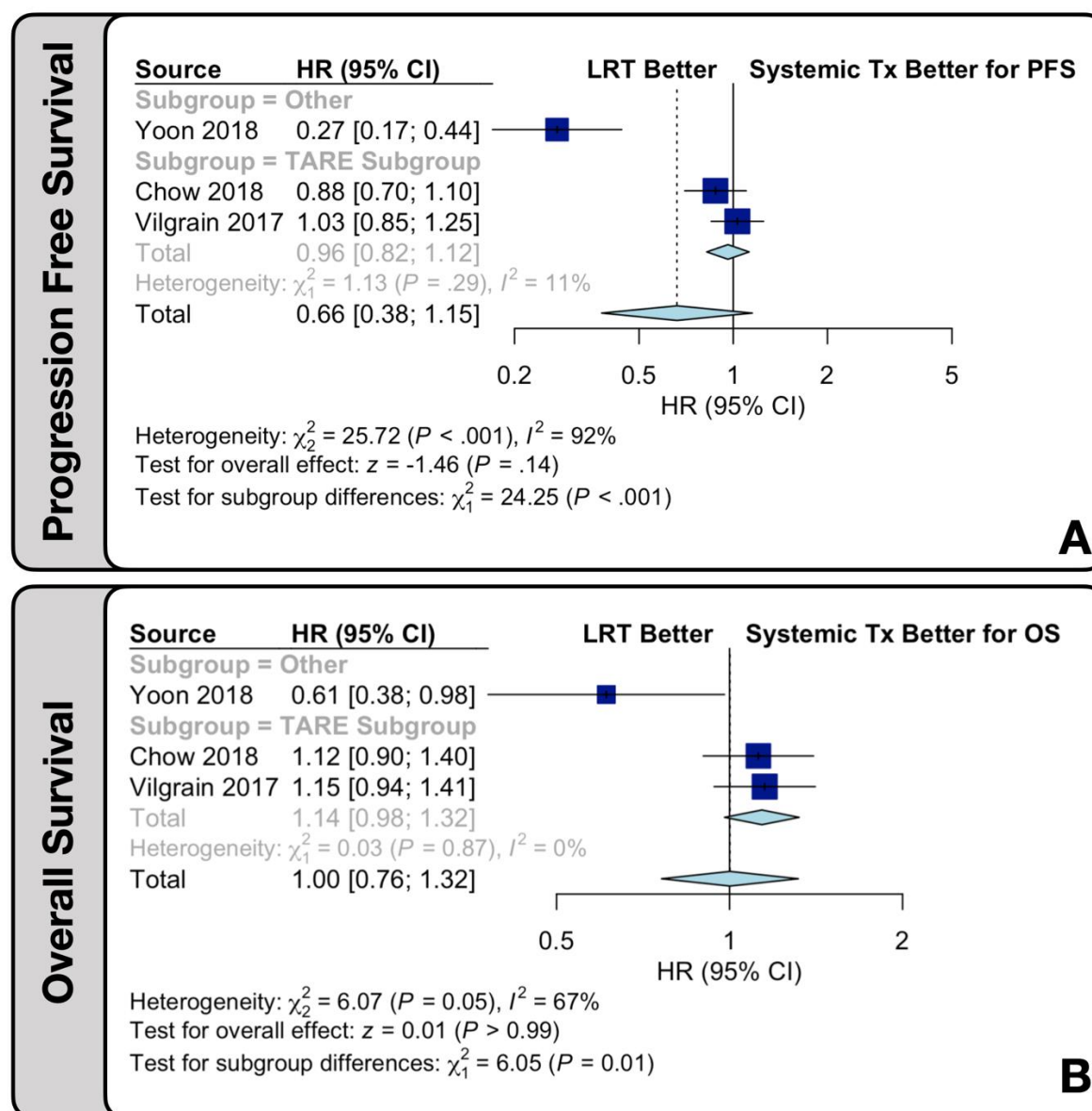
Abbreviations: TKI: tyrosine kinase inhibitor; LRT: locoregional therapy; HAI: hepatic arterial infusion chemotherapy; RFA: Radiofrequency ablation; CT: Chemotherapy; TACE: Transarterial chemoembolization; TARE: Transarterial radioembolization; RT: radiotherapy; Trt.: Treatment; Ref.: Reference treatment; CI: confidence interval; PFS: progression-free survival; OS: overall survival



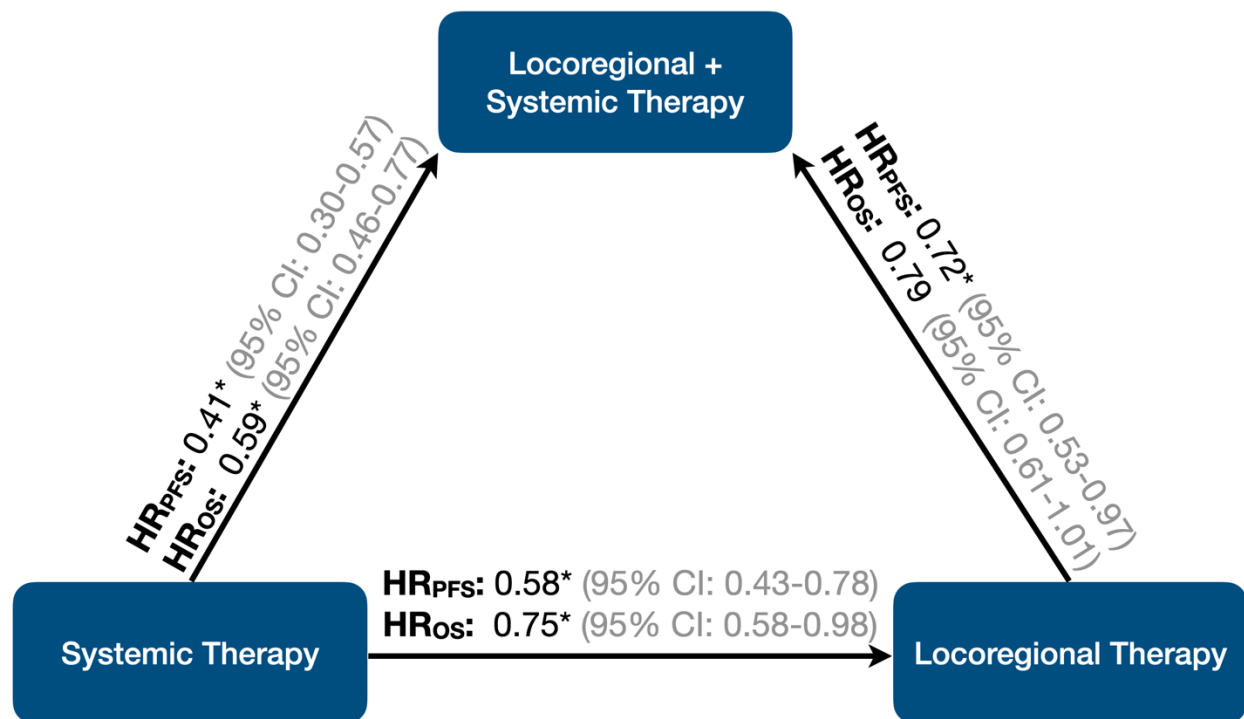
eAppendix Figure 2. Forest Plots Corresponding to the Meta-analysis of Systemic Therapy with or without Locoregional Therapy by Subgroup of Hepatic Arterial Infusion Chemotherapy Studies vs. Other Locoregional Therapy Studies.



eAppendix Figure 3. Forest Plots Corresponding to the Meta-analysis of Locoregional Therapy with or without Systemic Therapy by Subgroup of Locoregional Therapy Backbone.



eAppendix Figure 4. Forest Plots Corresponding to the Meta-analysis of Locoregional Therapy Compared with Systemic Therapy Alone by Subgroup.



eAppendix Figure 5. Effect Estimates Determined from a full network meta-analysis utilizing both Direct and Indirect Evidence. Arrow heads indicate the favored treatment (i.e., the one with better overall or progression free survival) of the comparison. Effect estimates which were significant at the 0.05 threshold are denoted with an asterisk (*).

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