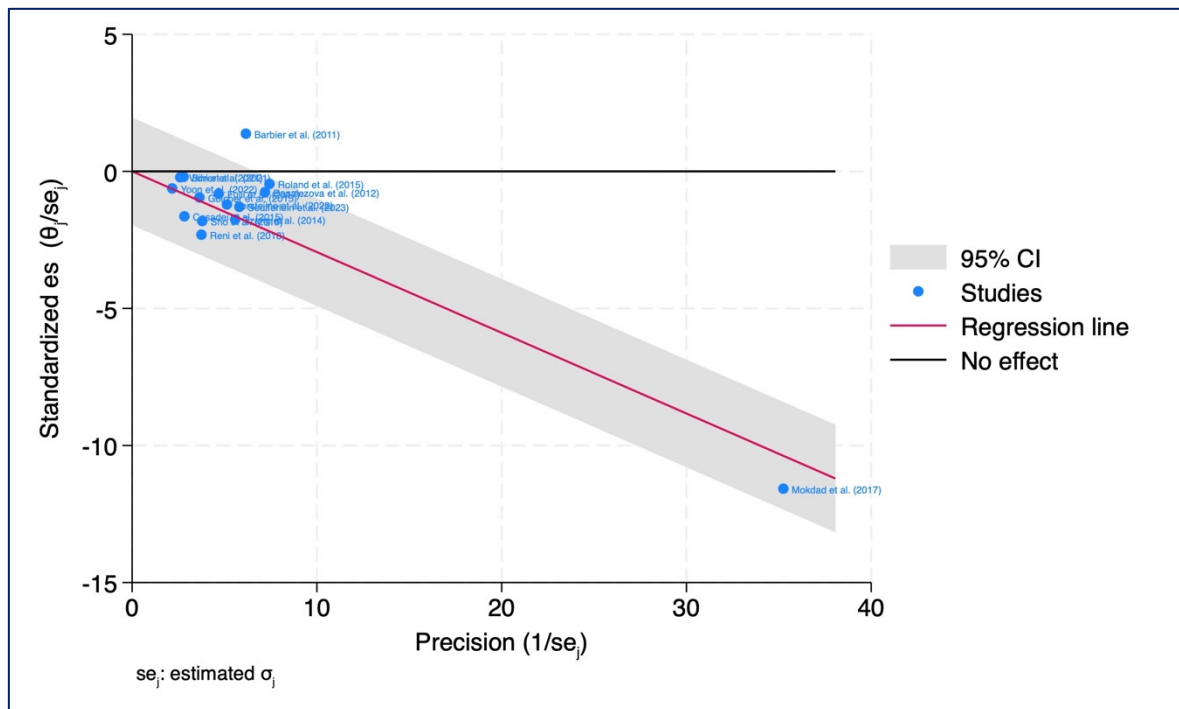


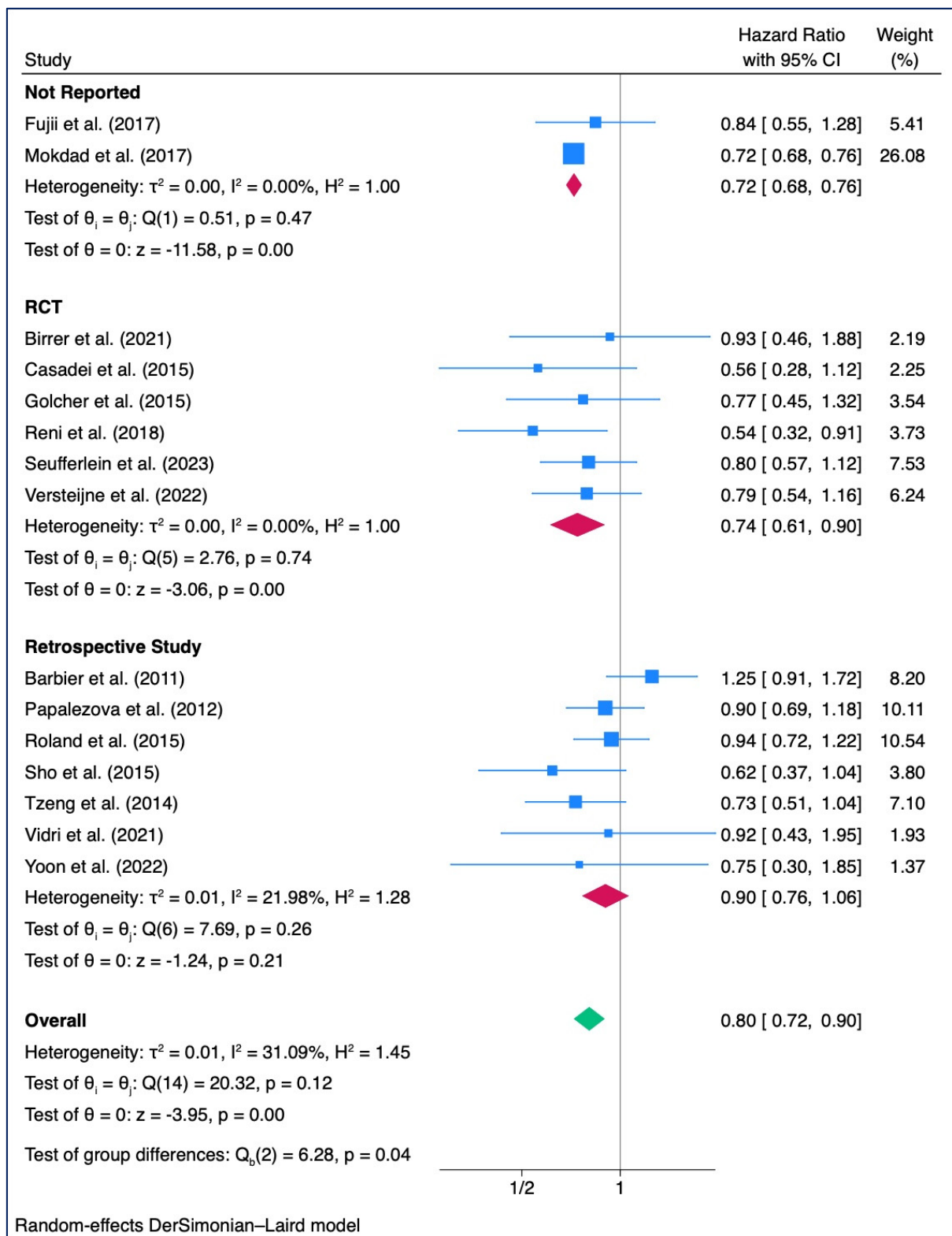
**Table S1. Studies Characteristics.**

Author	Neoadjuvant Regimen	Adjuvant Chemotherapy	Gender (Male/Female)	Age *
Barbier et al. (2011)	5 FU + Cisplatin + RT Upfront Surgery	None 5 FU or Gem	NR	NAT: 65 (39-81) US: 64 (37-79)
Birrer et al. (2021)	Gem + Oxaliplatin Upfront Surgery	Gem Gem	NR	NR
Casadei et al. (2015)	Gem 6 weeks + (Gem+RT) 6 weeks Upfront Surgery	Gem Gem	NAT: 8/10 US: 14/6	NAT: 71.5 (51- 78) US: 67.5 (48-79)
Fujii et al. (2017)	5 FU + Oteracil and Gimeracil + S-1 RT Upfront Surgery	Gem or Capecitabine Gem + Capecitabine	NAT: 21/19 US: 146/87	NAT: 65 (36-79) US: 67 (35-88)
Golcher et al. (2015)	Gem + Cispatin + RT Upfront Surgery	Gem Gem	NAT: 17/16 US: 18/15	NAT: 62.5 (33- 76) US: 65.1 (46-73)
Mokdad et al. (2017)	Chemotherapy (NR)  Upfront Surgery	-  -	NAT: 1044/961 US: 3150/2865	NAT: 18-55: 340, 55-64: 650; 65-74: 729; ≥ 75: 286; US: 18-55: 985; 55-64: 1972; 65- 74: 2222; ≥ 75: 836
Papalezova et al. (2012)	5-FU + RT Upfront Surgery	Gem 5FU	NAT: 75/69 US: 49/43	NAT: 64 ± 12 US: 65 ± 12
Reni et al. (2018)	Capecitabine + Gem + Cisplatin + Epirubicin Upfront Surgery	Capecitabine + Gem + Cisplatin + Epirubicin Capecitabine + Gem + Cisplatin + Epirubicin	NAT: 25/7 US: 13/17	NAT: 64 (39-75) US: 68 (49-75)
Roland et al. (2015)	Gem of 5 FU + RT Upfront Surgery	Gem (10%) Gem ± RT	NAT: 126/96 US: 43/42	NAT: 64 (35-86) US: 64 (40-85)
Seufferlein et al. (2023)	Gem + Abraxane Upfront Surgery	Gem	NAT: 34/25 US: 37/22	NAT: 65 (48-82); US: 68 (41-88)
Sho et al. (2015)	Gem + RT or Capecitabine Upfront Surgery	WHF + Gem or Gem alone WHF + Gem	NAT: 24/20 US: 32/24	NAT: 66.4 ± 8.5 US: 69.7 ± 9.1
Tzeng et al. (2014)	Gem + Cis + RT Upfront Surgery	- Gem	NAT: 61/54 US: 30/22	NAT: 65.5 (38- 79) US: 61.9 (25-79)
Verstaijne et al. (2022)	Gem + RT Upfront Surgery	Gem Gem	NAT: 64/55 US: 74/53	NAT: 66 (59.71) US: 67 (60-73)
Vidri et al. (2021)	Chemotherapy (NR) Upfront surgery	NR	NAT: 600/518; US: 1304/1502	NAT: 63.4 (10.0); US: 69.0 (10.9)
Yoon et al. (2022)	Gem + 5-FU + Leucovorin, Irinotecan + Oxaplatin  Upfront Surgery	Gem + 5-FU + Leucovorin, Irinotecan + Oxaplatin Gem + 5-FU + Leucovorin, Irinotecan + Oxaplatin	NAT: 21/14; US: 73/94	NAT: 67.0 (58- 73); US: 60 (56-70)

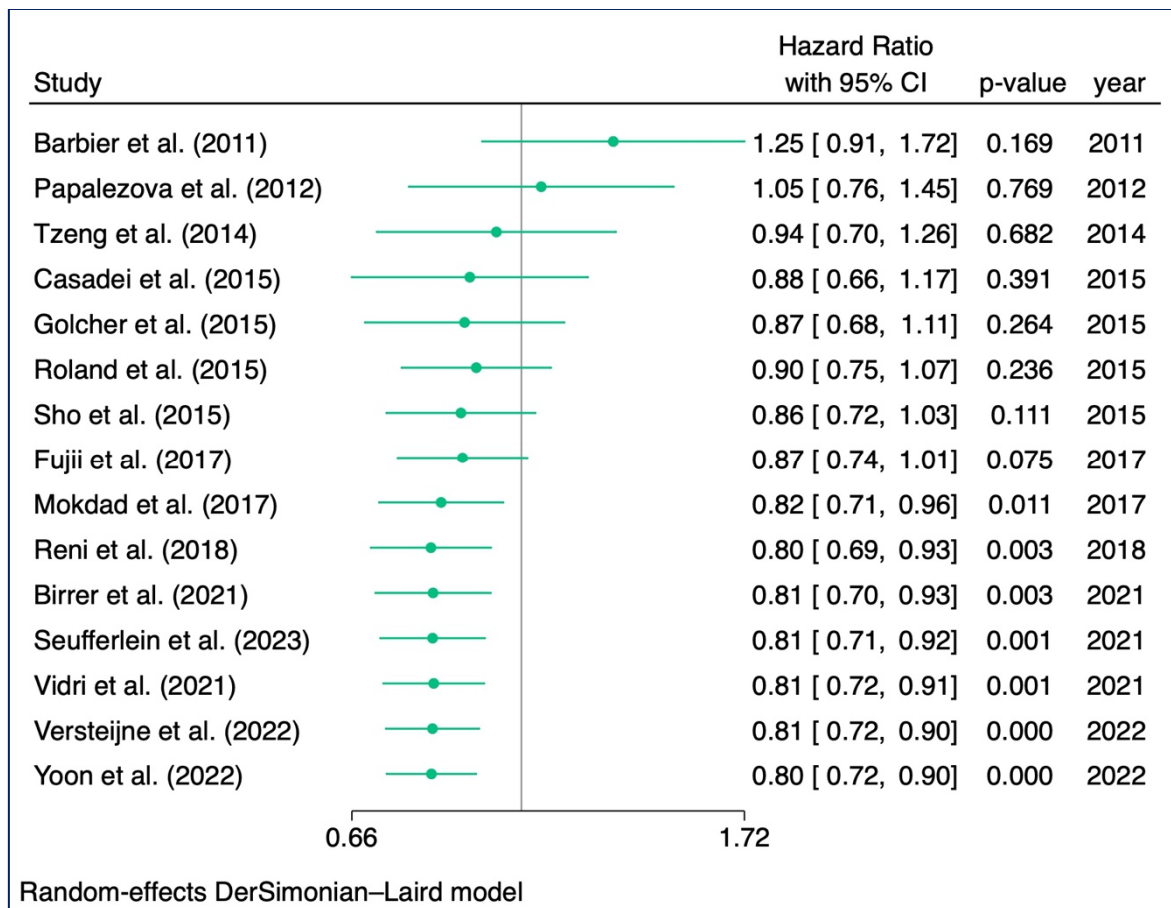
\* Age is reported as median (range) or mean ± standard deviation – Gem: gemcitabine; 5-FU: 5-fluorouracil; NAT: Neoadjuvant Therapy; US: US – NR: Not reported



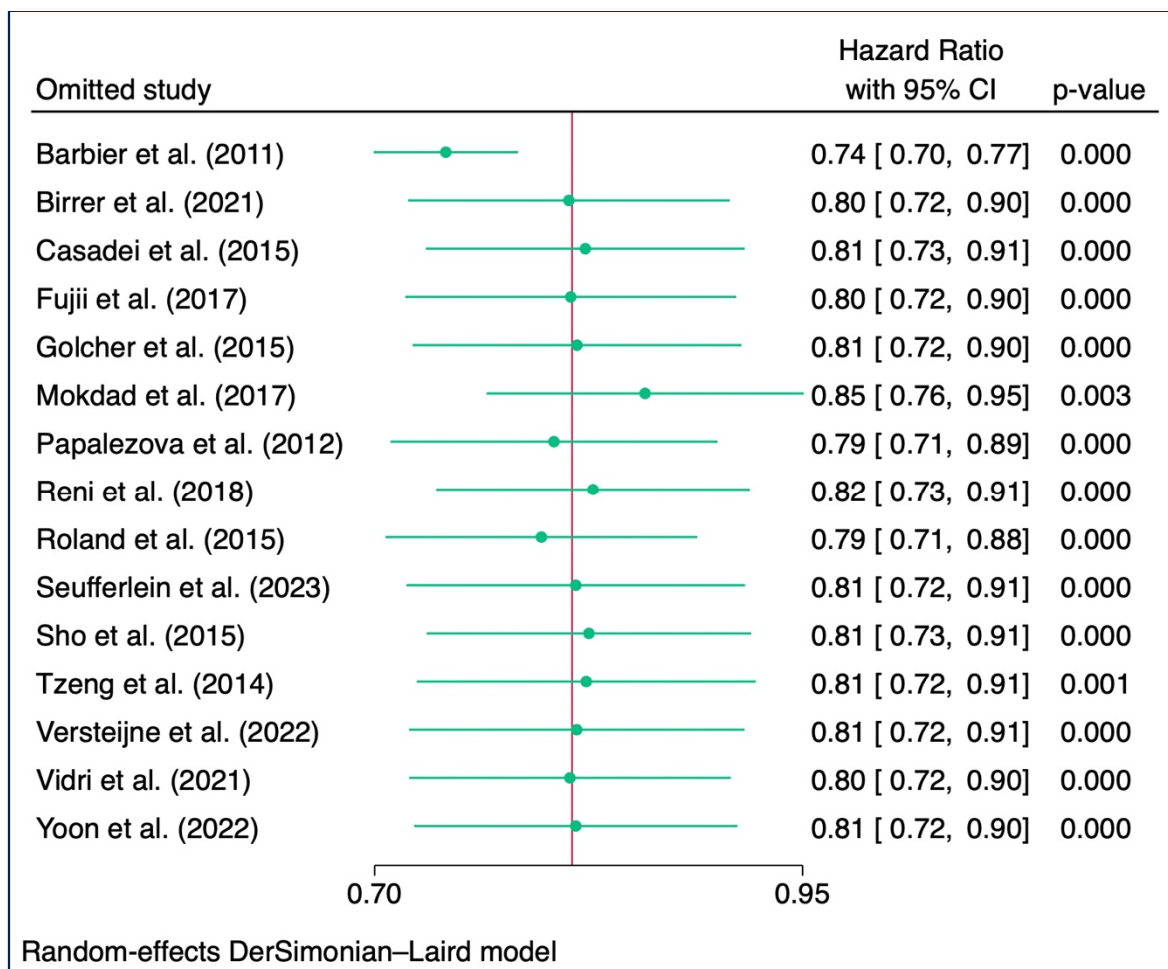
**Figure S1.** Overall Survival: Galbraith Plot.



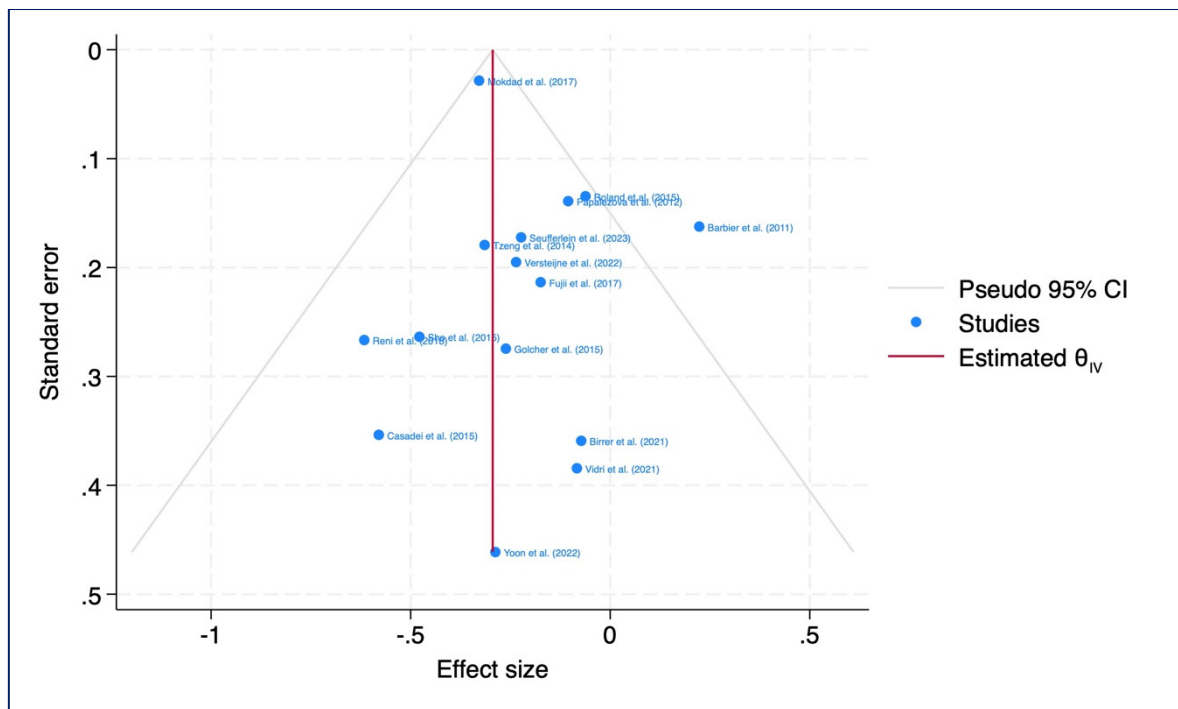
**Figure S2.** Overall Survival: Subgroup analysis related to study design—(RCT = 6, retrospective studies = 7, Study design Not Reported = 2).



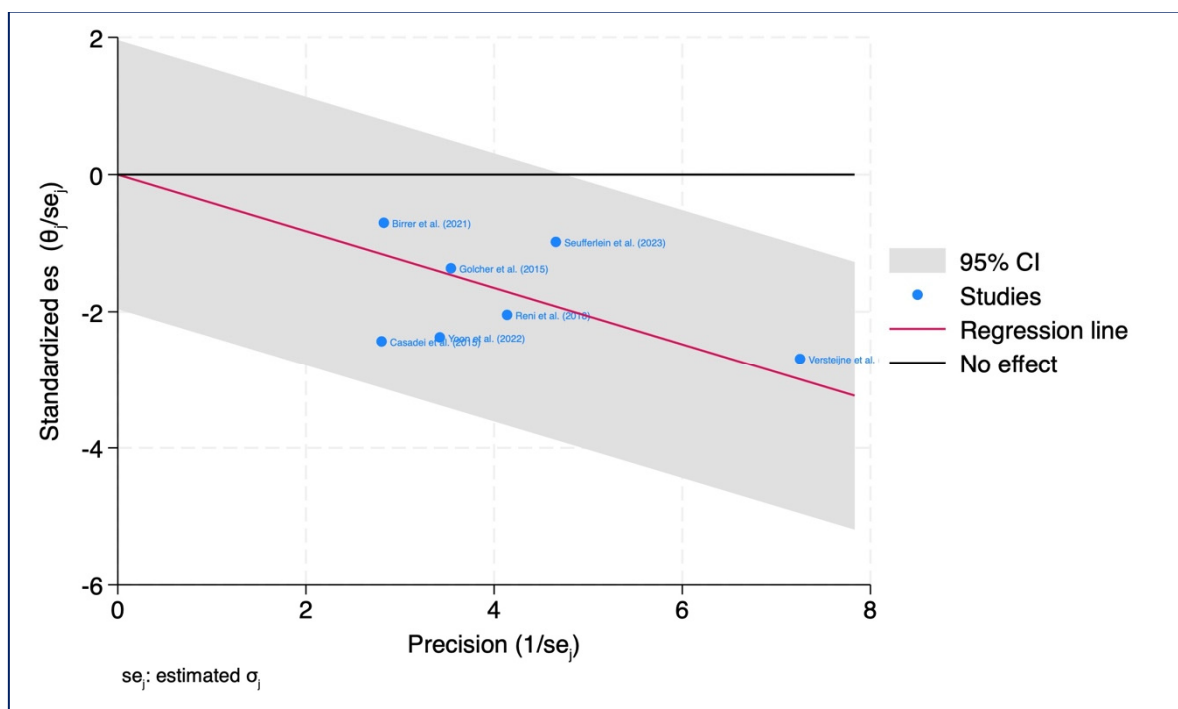
**Figure S3.** Overall Survival: Cumulative analysis per year.



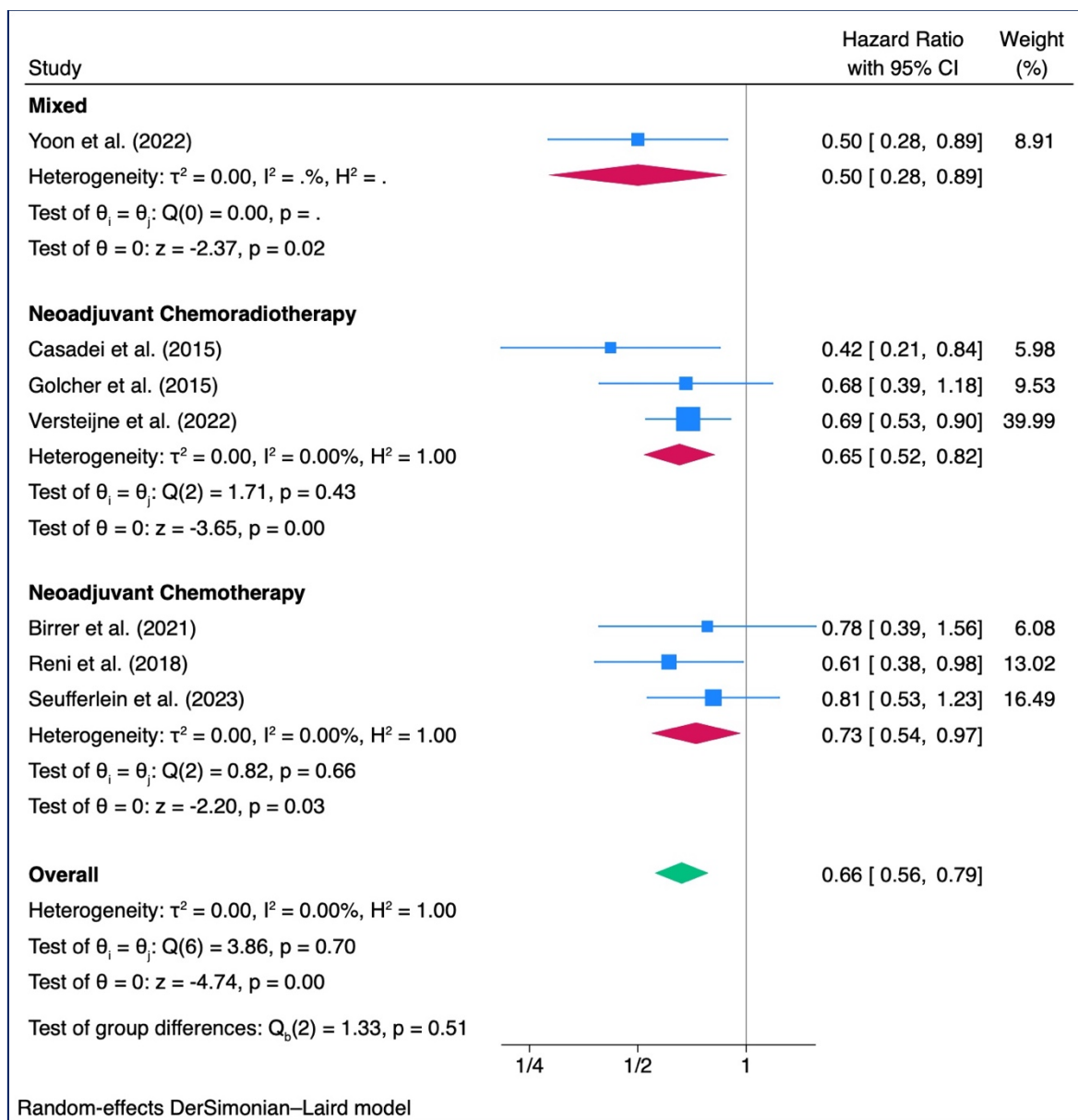
**Figure S4.** Overall Survival: Leave-one-out analysis.



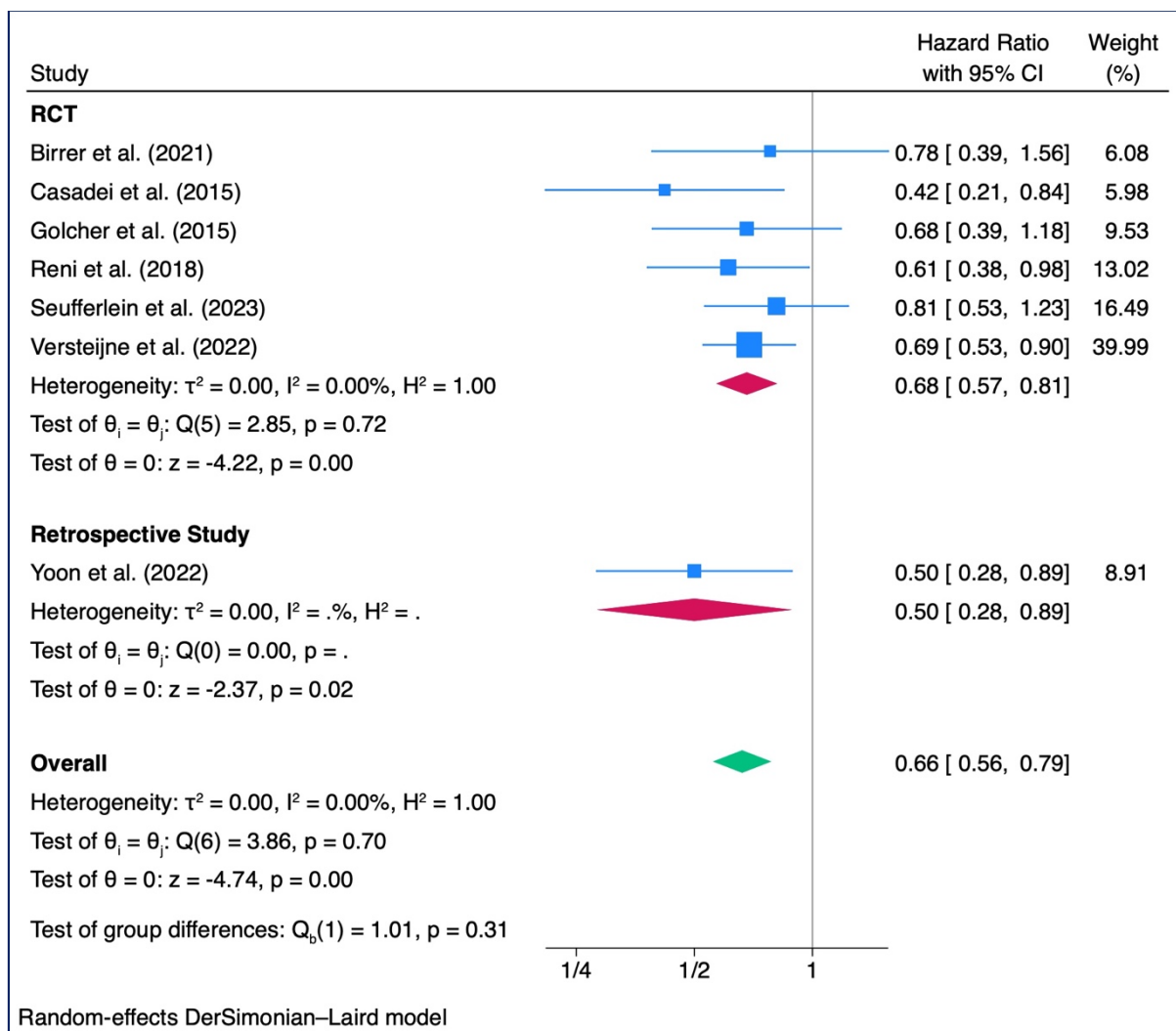
**Figure S5.** Overall Survival: Funnel plot for publication bias.



**Figure S6.** Disease Free-Survival: Galbraith Plot.

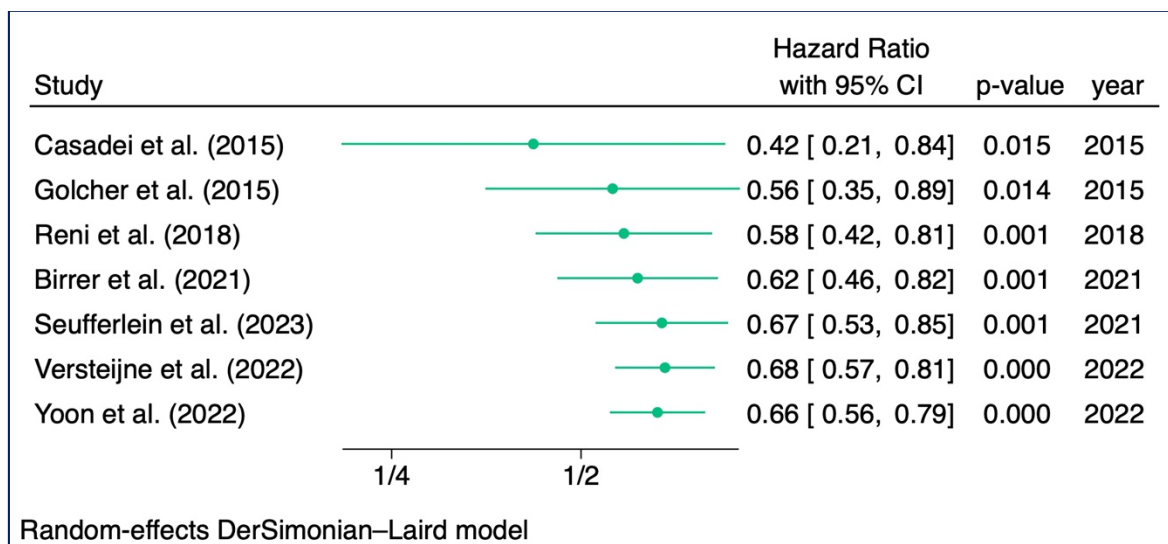


**Figure S7.** Disease Free Survival (n = 7): Forest plot—Subgroup analysis related to use of neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy.

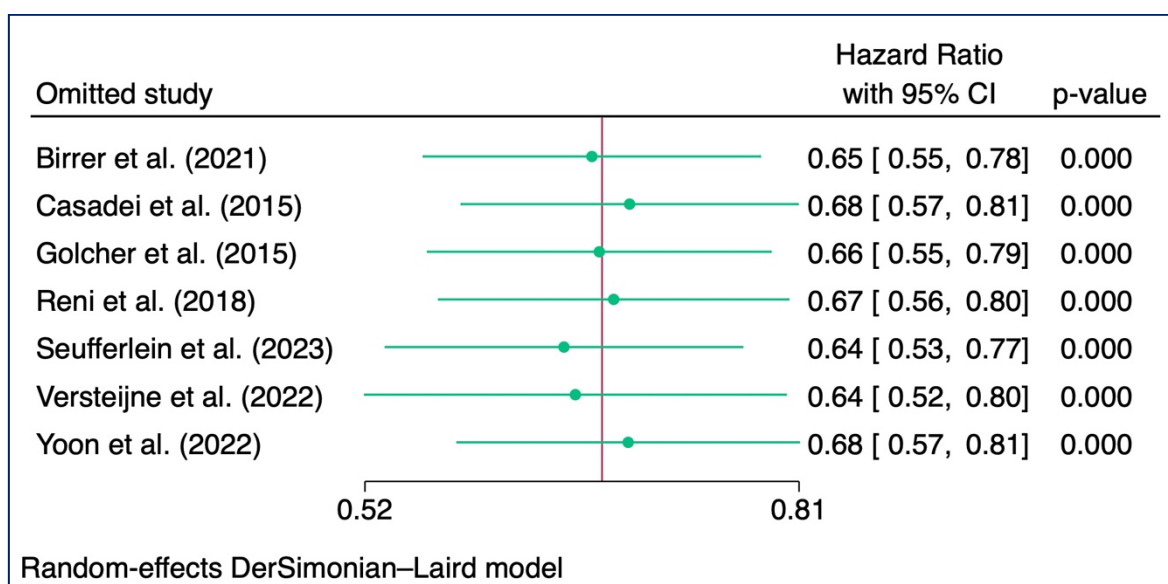


**Figure S8.** Disease Free Survival—Subgroup analysis related to study design (RCT = 6, retrospective studies = 1).

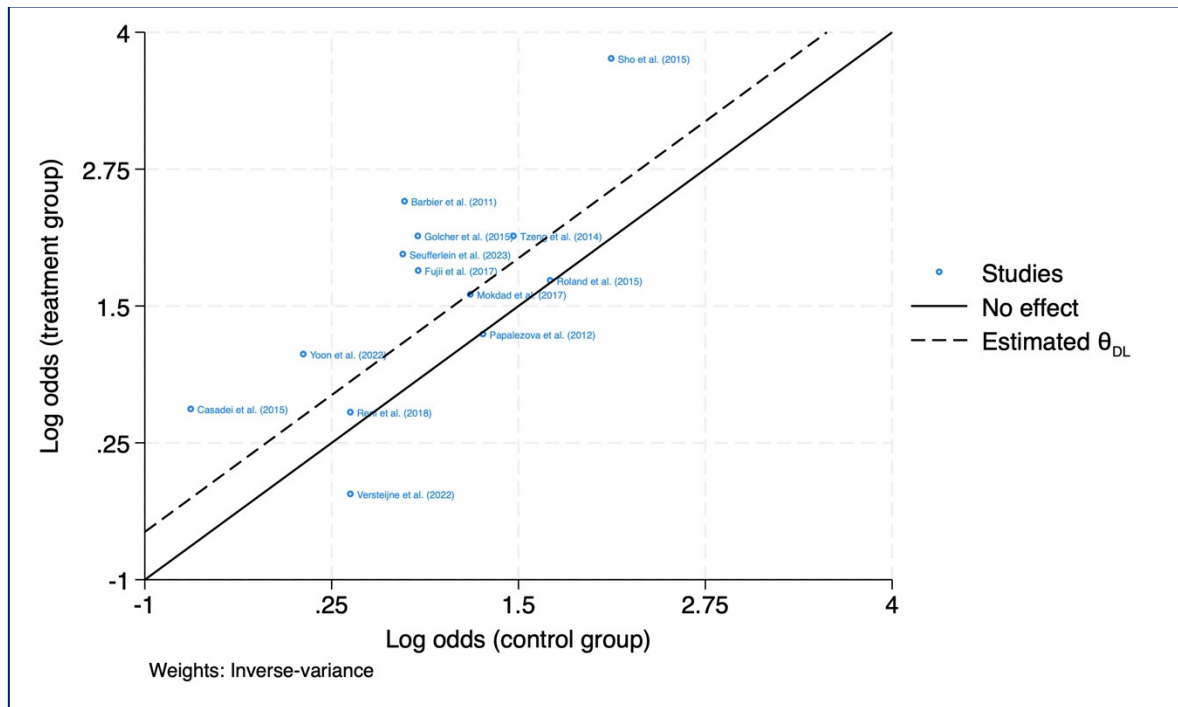




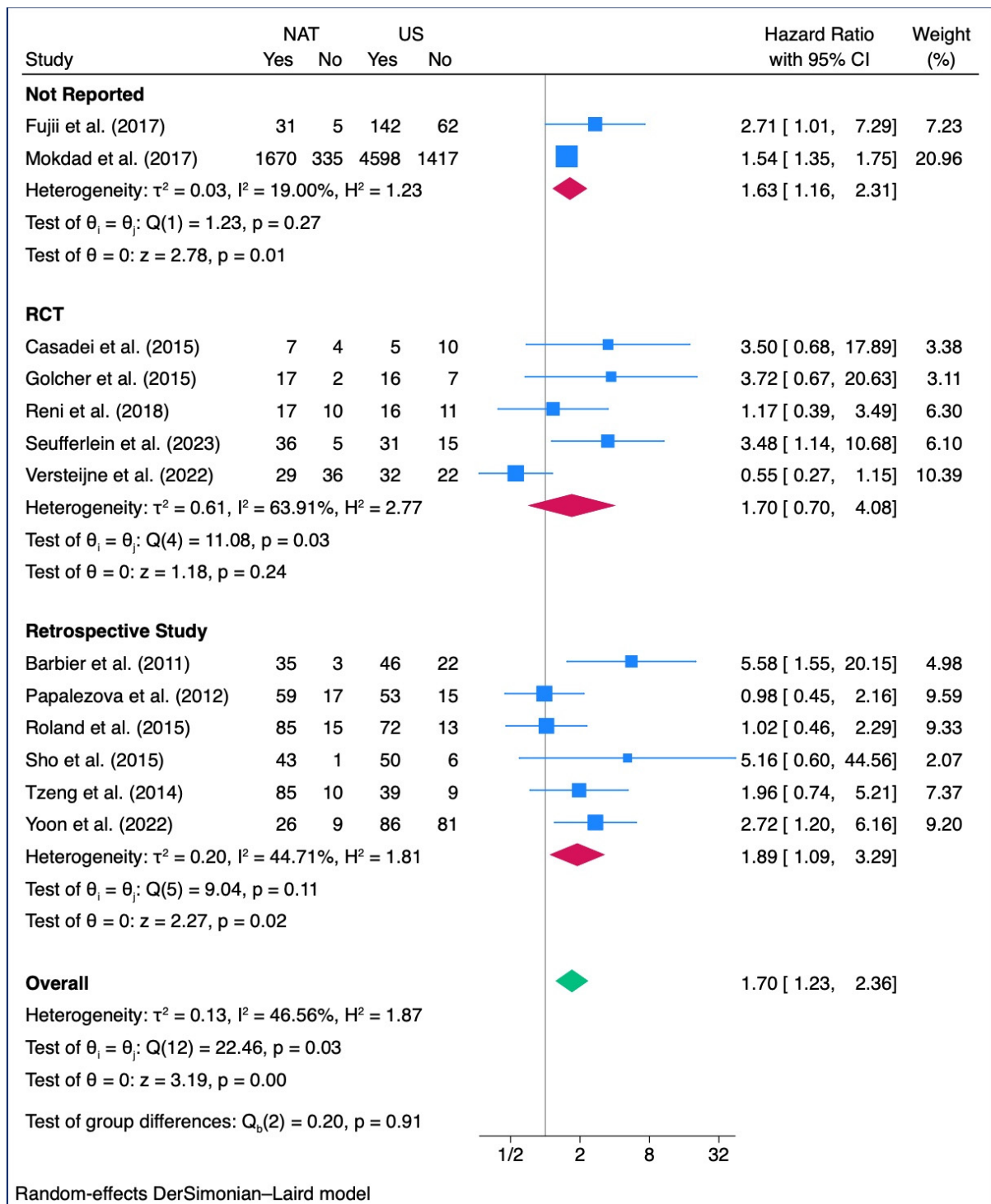
**Figure S9.** Disease Free Survival: Cumulative Meta-Analysis.



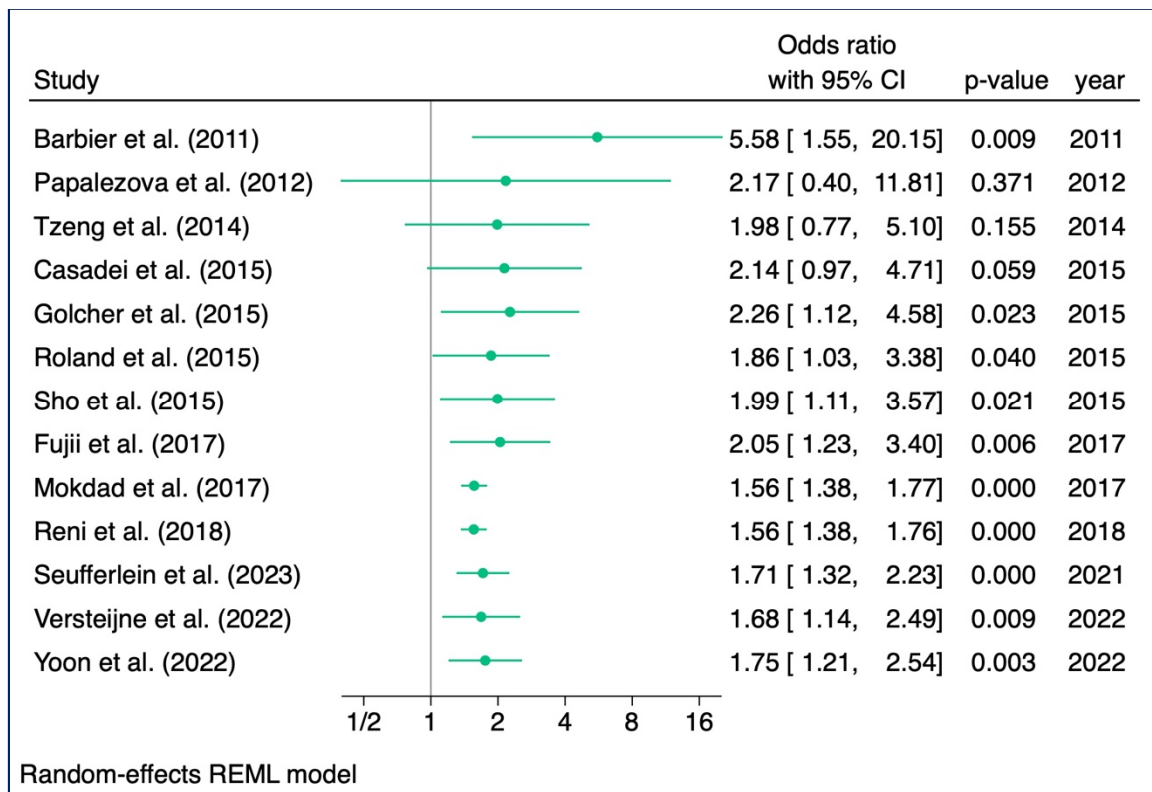
**Figure S10.** Disease Free Survival: Leave-one-out analysis.



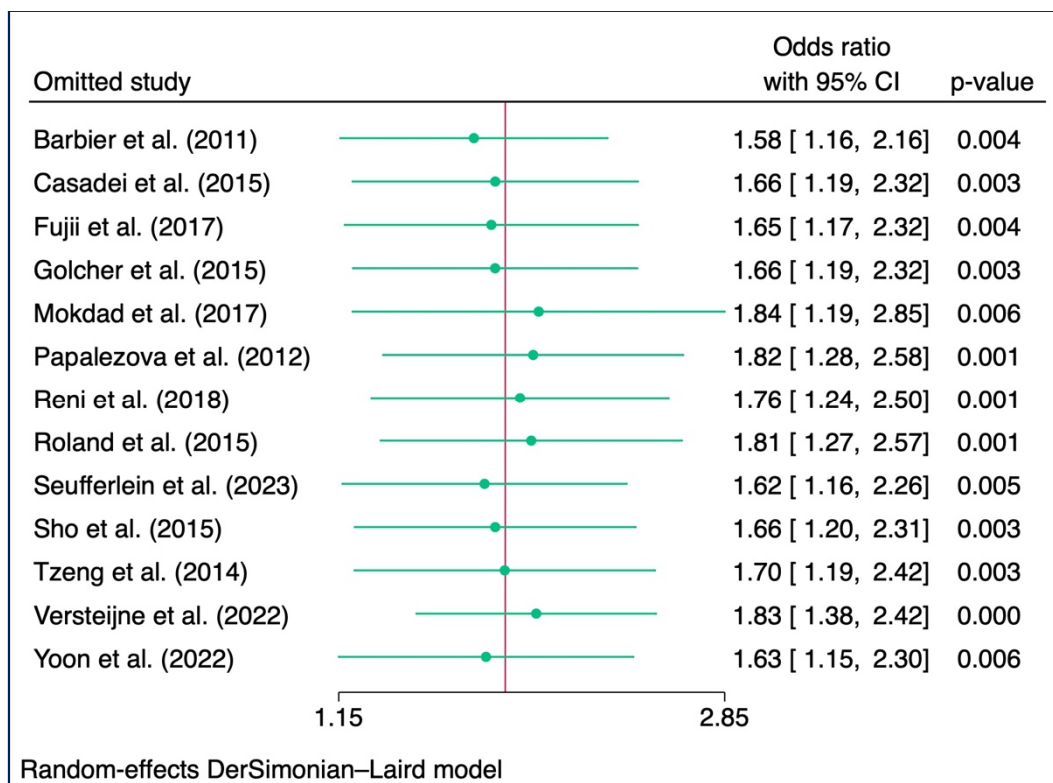
**Figure S11.** R0 Rate: L'Abbè Plot for R0 Rate Studies.



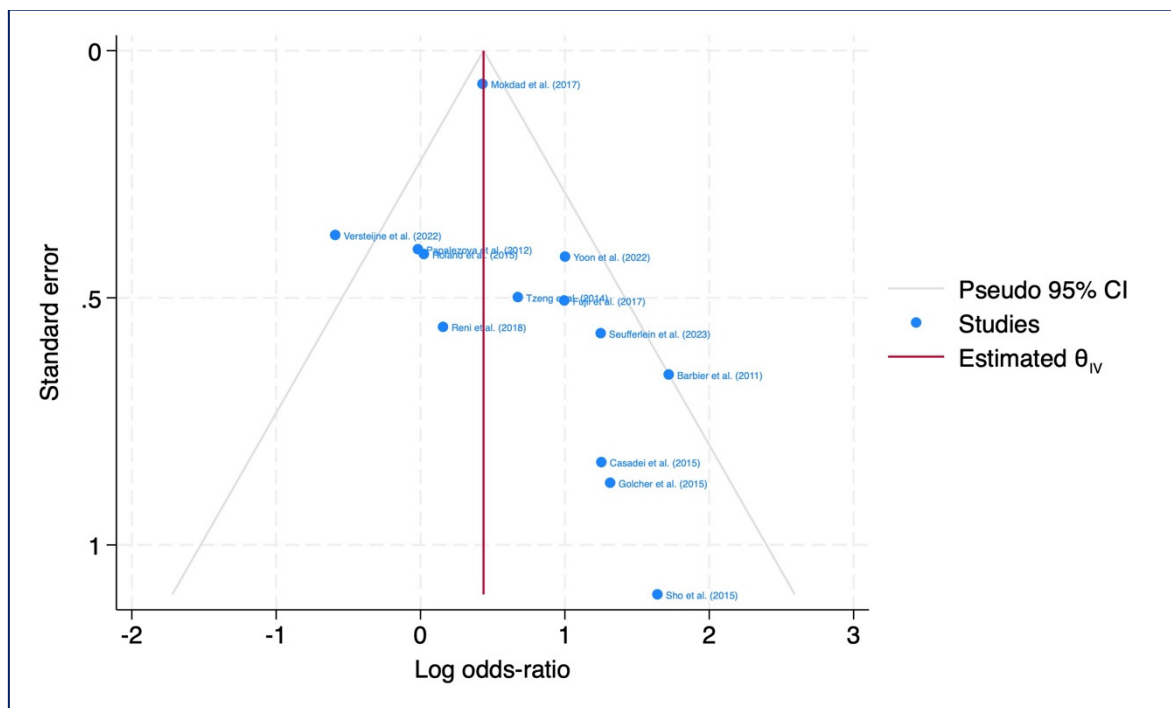
**Figure S12.** R0 Rate—Subgroup analysis related to study design (RCT = 5, retrospective studies = 6, Study design Not Reported = 2).



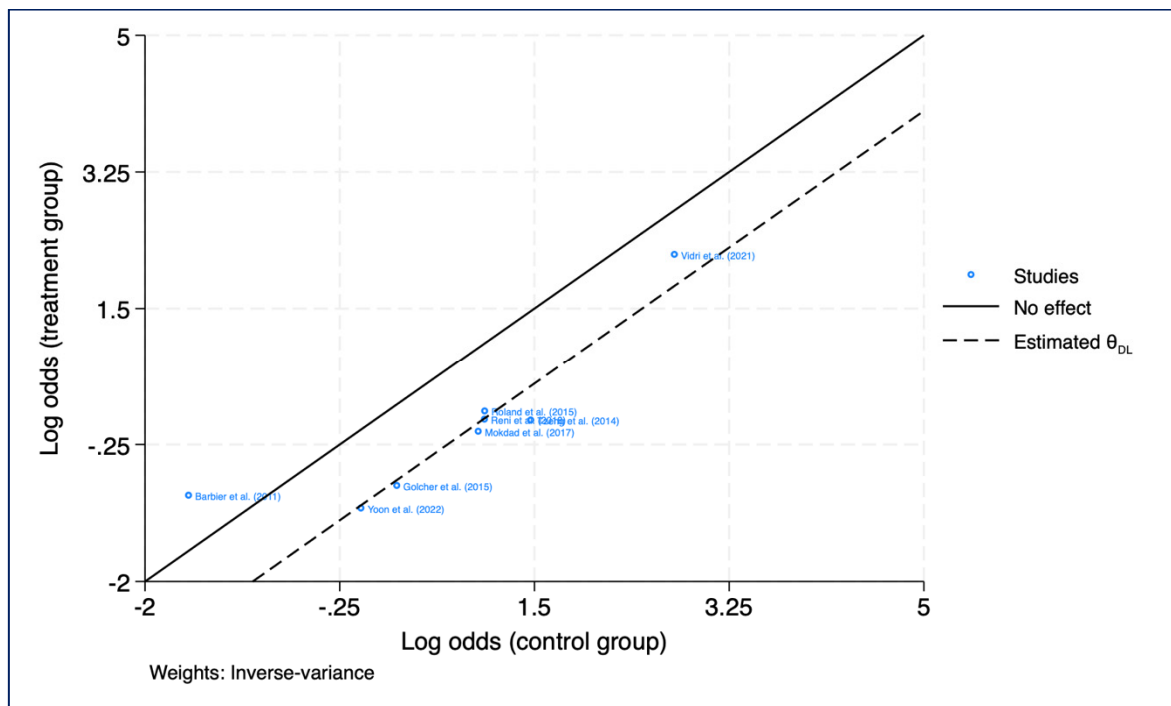
**Figure S13.** R0 Rate (n = 13): Cumulative Meta-Analysis.



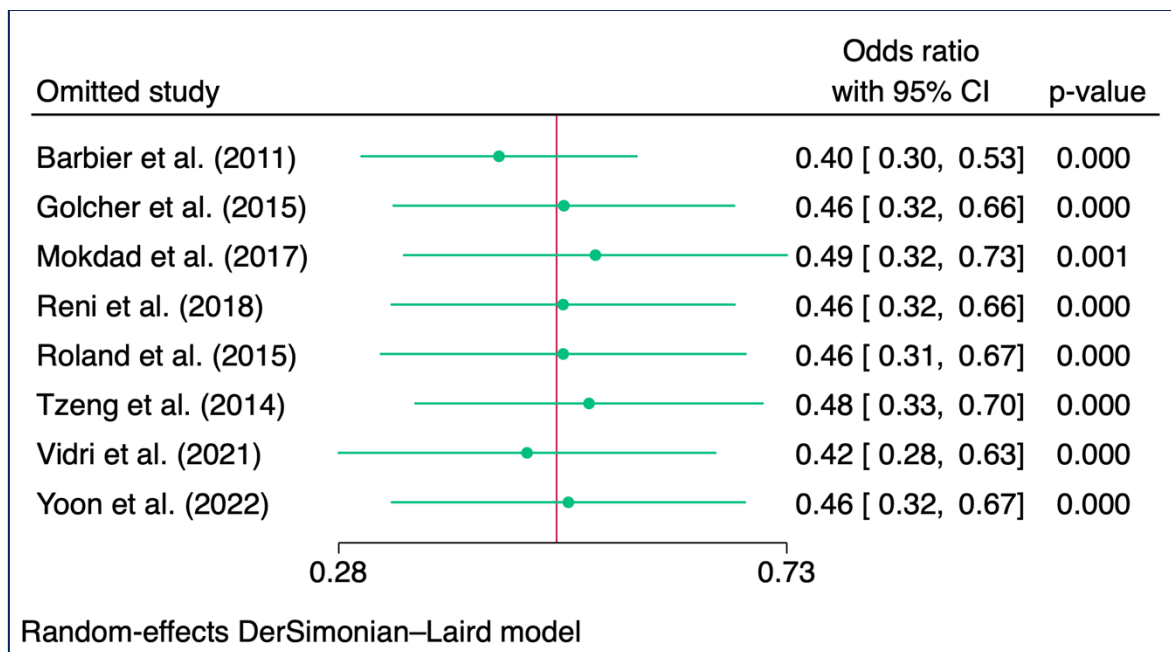
**Figure S14.** R0 Rate (n = 13): Leave-one-out Analysis.



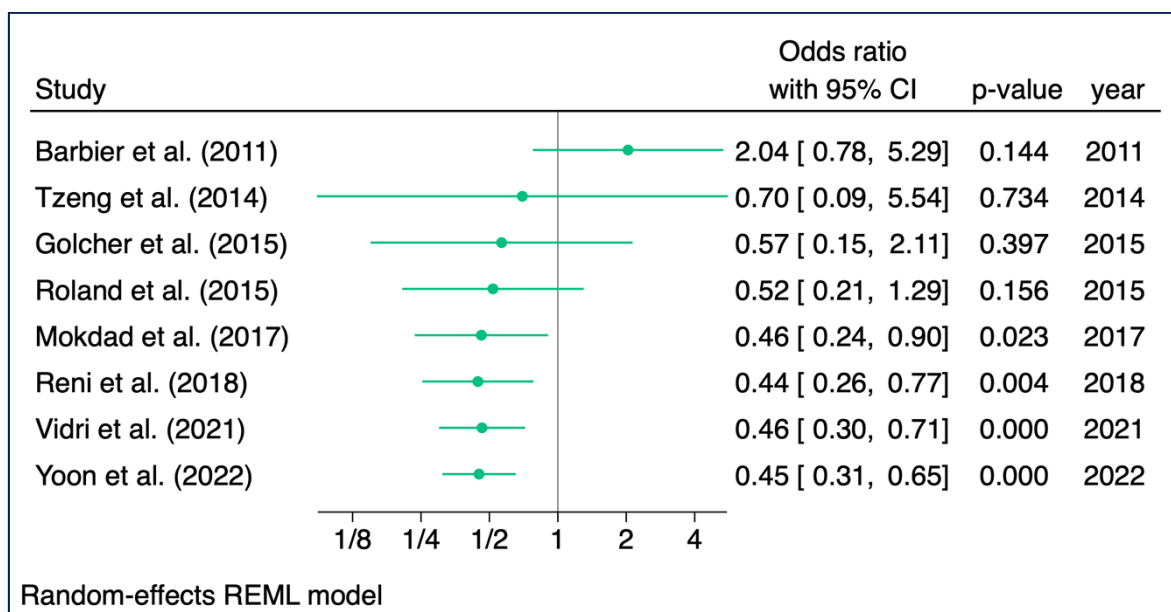
**Figure S15.** R0 Rate (n = 13): Funnel Plot—Publication Bias.



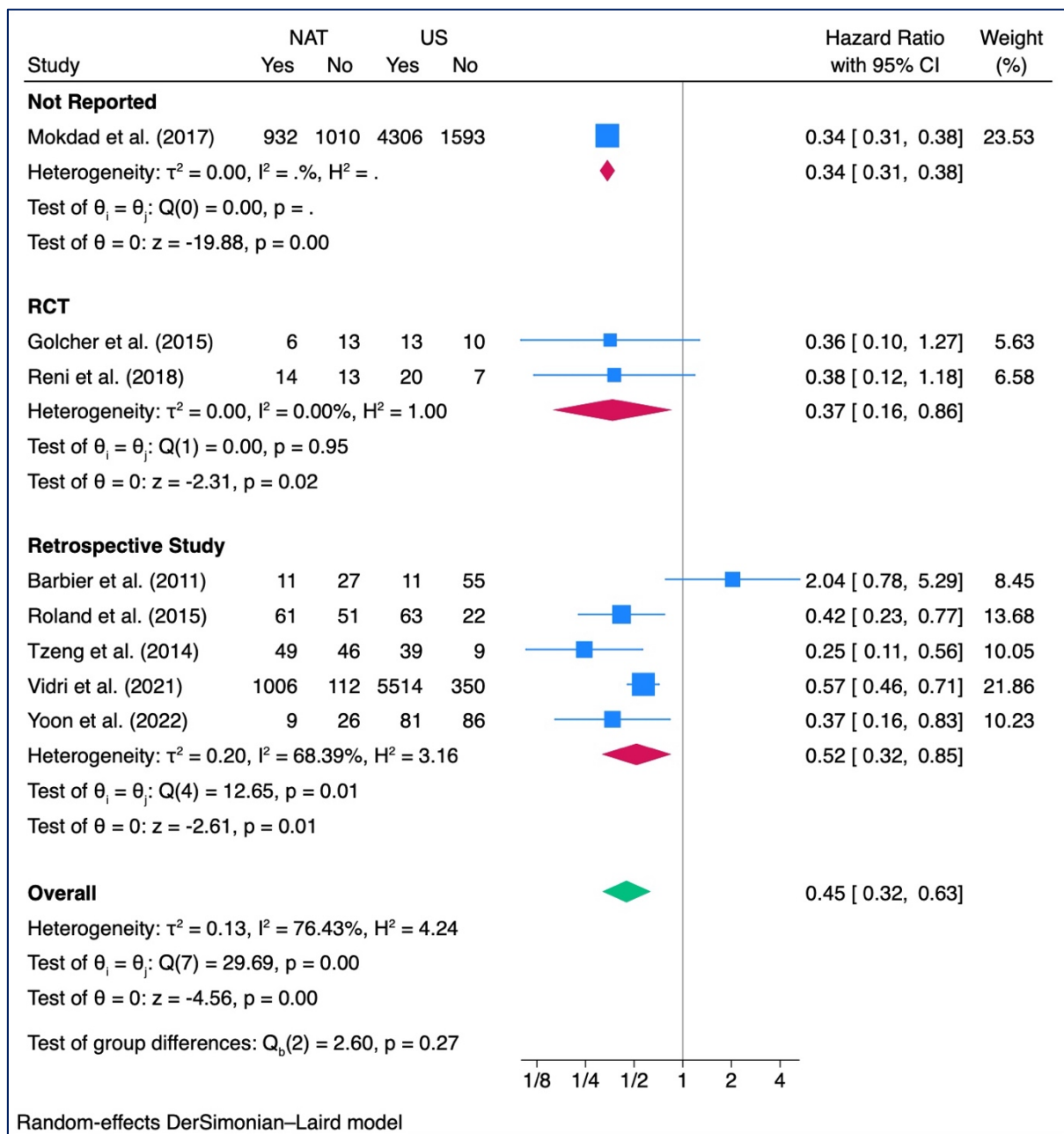
**Figure S16.** N+ Rate (n = 8): L'Abbé Plot—N+ Rate. Note: for Versteijne et al. 2022 data were extracted from the Versteijne et al. 2020.



**Figure S17.** N+ Rate (n = 8): Sensitive Analysis.



**Figure S18.** N+ Rate (n = 8): Cumulative meta-analysis.



**Figure S19.** N+ Rate—Subgroup analysis related to study design (RCT = 2, retrospective studies = 5, Study design Not Reported = 1).