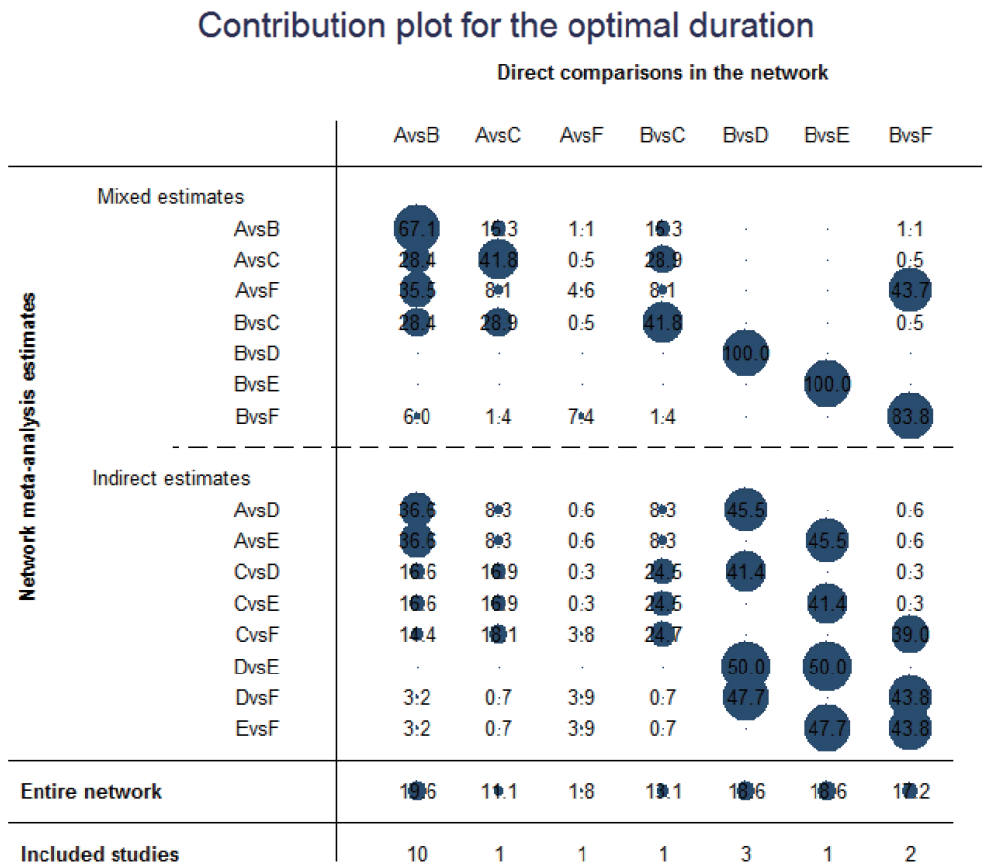
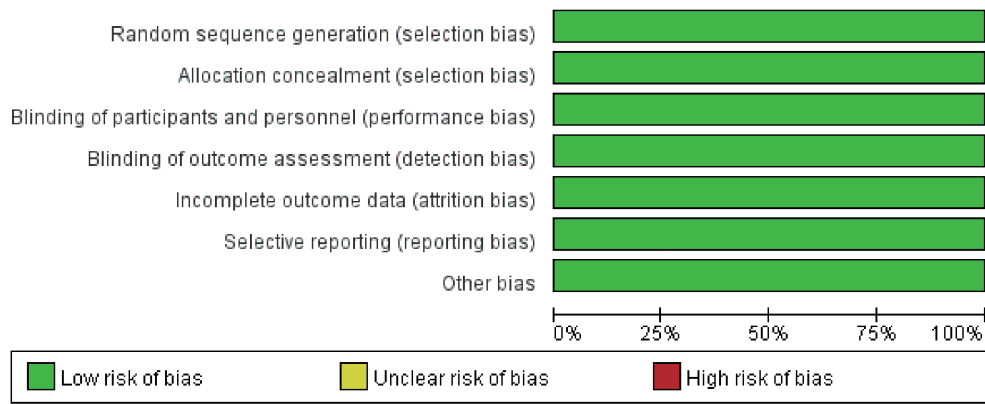


**Figure S1** Inconsistency plot for the optimal duration of adjuvant trastuzumab network. Two triangular loops were found in the six comparisons. The  $P_{(A-B-F)}$  was 0.067, and the  $P_{(A-B-C)}$  was 0.321. A, observation; B, T-12 months; C, T-24 months; F, T-9 weeks; and T, trastuzumab.



**Figure S2** Contribution plot for the optimal duration of adjuvant trastuzumab. The numbers represent the weights as percentages (%). The size of each circle is proportional to the weights of the direct comparisons (horizontal axis). A, observation; B, T-12 months; C, T-24 months; D, T-6 months; E, T-12 weeks; F, T-9 weeks; and T, trastuzumab.



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Baselga 2012	+	+	+	+	+	+	+
Conte 2017	+	+	+	+	+	+	+
Earl 2019	+	+	+	+	+	+	+
Gianni 2014	+	+	+	+	+	+	+
Gianni 2016	+	+	+	+	+	+	+
Joensuu 2006	+	+	+	+	+	+	+
Joensuu 2018	+	+	+	+	+	+	+
Marc 2009	+	+	+	+	+	+	+
Martine 2005	+	+	+	+	+	+	+
Martine 2016	+	+	+	+	+	+	+
Mavroudis 2015	+	+	+	+	+	+	+
Perez 2011	+	+	+	+	+	+	+
Pivot 2019	+	+	+	+	+	+	+
Romond 2005	+	+	+	+	+	+	+
Schneider 2015	+	+	+	+	+	+	+
Slamon 2011	+	+	+	+	+	+	+

**Figure S3** Risk of bias summary of the RCTs included in the network meta-analysis. RCTs, randomized controlled trials.

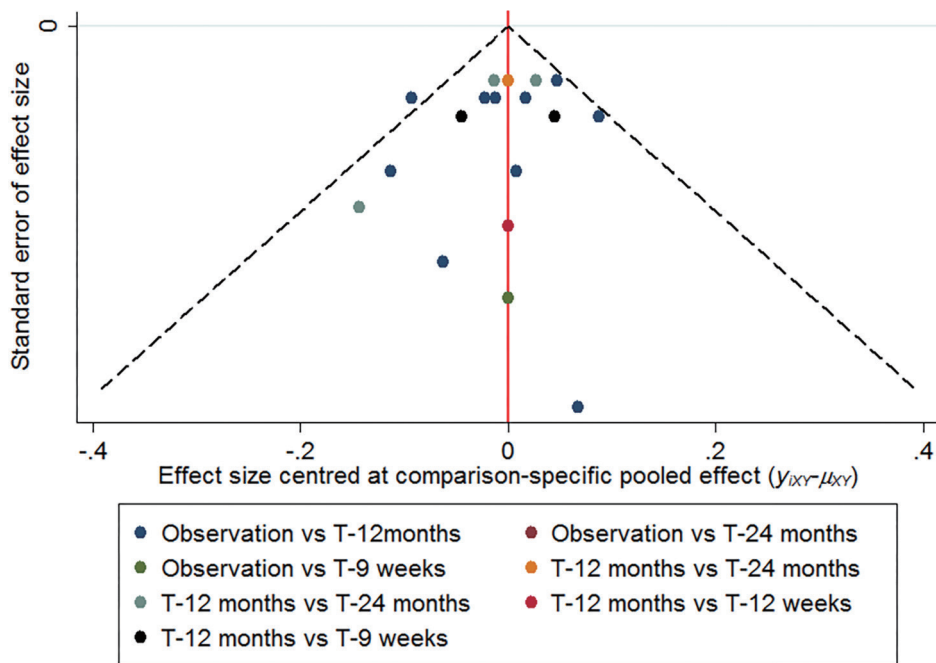


Figure S4 Comparison-adjusted funnel plot for the optimum duration of adjuvant trastuzumab. T, trastuzumab.

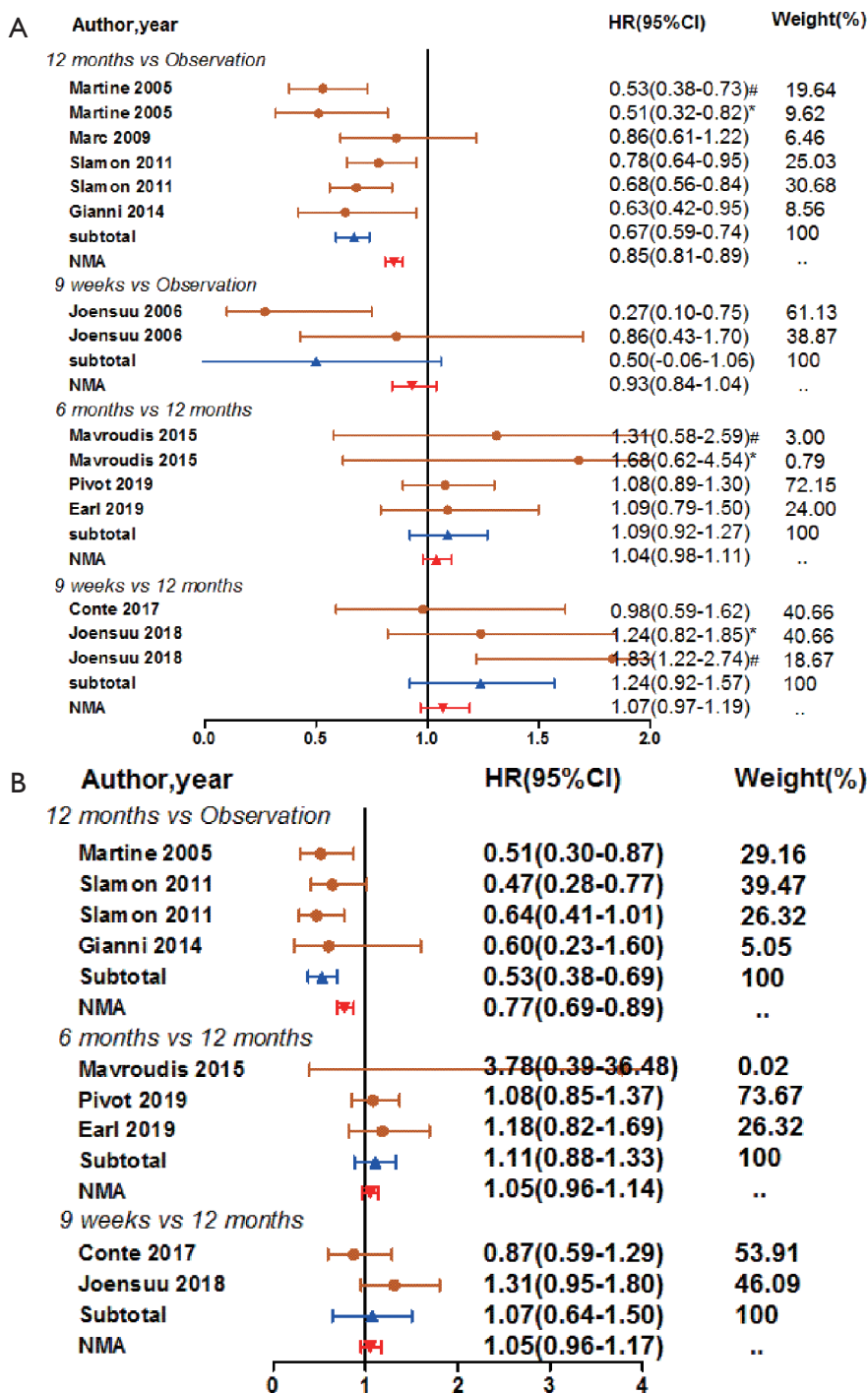
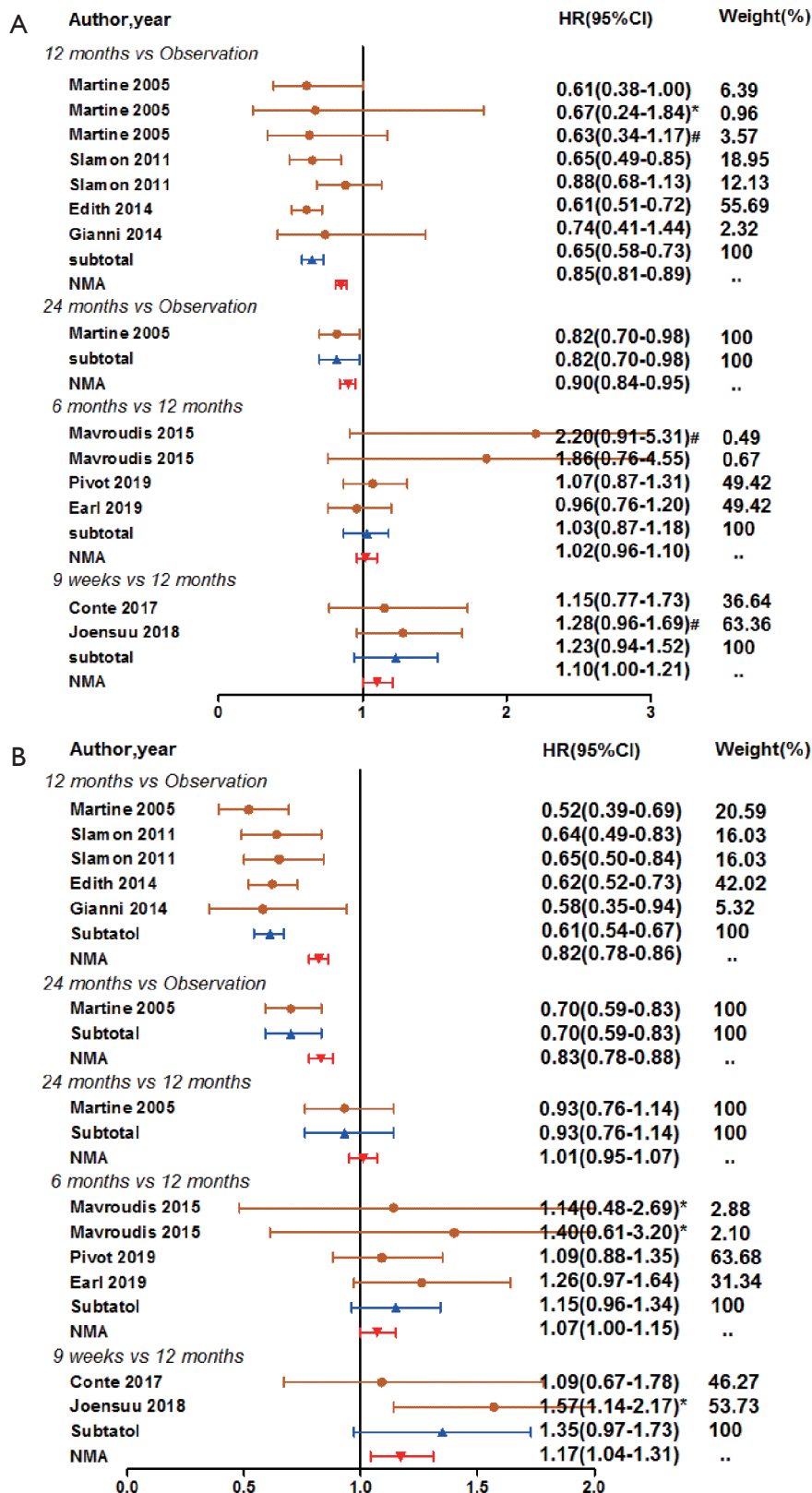


Figure S5 Subgroup analysis for disease-free survival based on the lymph node status. The pooled hazard ratios for lymph node-positive (A) and lymph node-negative patients (B) were produced by network meta-analysis and pairwise meta-analysis. \*, 1-3 lymph nodes positive; #,  $\geq 4$  lymph nodes positive. CI, confidence interval for pairwise meta-analysis and the credible interval for network meta-analysis; NMA, network meta-analysis.



**Figure S6** Subgroup analysis based on hormone receptor status. The pooled hazard ratios for hormone receptor-positive (A) and hormone receptor-negative patients (B) produced by network meta-analysis and pairwise meta-analysis. #, estrogen receptor positive; \*, progesterone or estrogen-receptor negative. CI, confidence interval for the pairwise meta-analysis and the credible interval for network meta-analysis; NMA, network meta-analysis.

A	Observation	0.85 (0.81–0.89)	0.88 (0.81–0.96)	0.93 (0.84–1.04)
	T-12 months		1.04 (0.98–1.11)	1.07 (0.97–1.19)
			T-6 months	1.06 (0.94–1.19)
				T-9 weeks
B	Observation	0.77 (0.69–0.87)	0.81 (0.70–0.93)	0.81 (0.69–0.95)
	T-12 months		1.05 (0.96–1.14)	1.05 (0.95–1.17)
			T-6 months	1.01 (0.88–1.15)
				T-9 weeks
C	Observation	0.87 (0.83–0.91)	0.90 (0.83–0.98)	0.83 (0.71–0.98)
	T-12 months		1.03 (0.97–1.11)	0.96 (0.81–1.12)
			T-6 months	0.92 (0.77–1.10)
				T-9 weeks

**Figure S7** Subgroup and sensitivity analyses in early breast cancer based on the lymph node status in the network meta-analysis. The columns were compared with the rows. Numbers in parentheses represent the 95% CI. HRs with P values <0.05 were considered statistically significant (red). Subgroup analysis was conducted in node-positive early breast cancer (A) and node-negative early breast cancer (B). (C) A sensitivity analysis was performed in lymph node-positive early breast cancer based on the number of positive lymph nodes ( $\geq 1$ , 1–3 and  $\geq 4$  lymph positive nodes). T, trastuzumab.

A	Observation	0.85 (0.81–0.89)	0.90 (0.84–0.95)	0.87 (0.80–0.95)	0.93 (0.84–1.04)
	T-12 months		0.95 (0.90–1.01)	1.02 (0.96–1.10)	1.10 (1.00–1.21)
			T-24 months	0.97 (0.88–1.07)	1.04 (0.93–1.18)
				T-6 months	1.08 (0.95–1.21)
				T-9 weeks	
B	Observation	0.82 (0.78–0.86)	0.83 (0.78–0.88)	0.88 (0.80–0.95)	0.95 (0.84–1.08)
	T-12 months		1.01 (0.95–1.07)	1.07 (1.00–1.15)	1.17 (1.04–1.31)
			T-24 months	1.06 (0.96–1.16)	1.15 (1.01–1.32)
				T-6 months	1.09 (0.95–1.25)
				T-9 weeks	
C	Observation	0.85 (0.81–0.89)	0.90 (0.84–0.96)	0.86 (0.79–0.94)	0.90 (0.75–1.08)
	T-12 months		1.05 (0.98–1.13)	1.01 (0.95–1.09)	1.06 (0.89–1.26)
			T-24 months	0.96 (0.87–1.06)	1.01 (0.84–1.22)
				T-6 months	1.05 (0.87–1.27)
				T-9 weeks	
D	Observation	0.82 (0.78–0.86)	0.83 (0.78–0.88)	0.87 (0.80–0.95)	0.85 (0.68–1.06)
	T-12 months		1.01 (0.95–1.07)	1.07 (0.99–1.15)	1.05 (0.84–1.23)
			T-24 months	1.06 (0.96–1.16)	1.03 (0.82–1.29)
				T-6 months	0.98 (0.78–1.23)
				T-9 weeks	

**Figure S8** Subgroup and sensitivity analyses for disease-free survival in early breast cancer based on the hormone receptor status in the network meta-analysis. The columns were compared with the rows. Numbers in parentheses represent the 95% CI. HRs with P values <0.05 were considered statistically significant (red). Subgroup analysis for disease-free survival was conducted in hormone receptor-positive early breast cancer (A) and hormone receptor-negative early breast cancer patients (B). A sensitivity analysis was performed in hormone receptor-positive (C) and hormone receptor-negative (D) early breast cancer after excluding the trials that reported estrogen receptor and progesterone receptor status. T, trastuzumab.

**Table S1** Summary of the confidence in each comparison and ranking

Comparison	Nature of the evidence	Confidence	Downgrading due to
T-12 months vs. observation	Mixed	High	
T-24 months vs. observation	Mixed	Moderate	Imprecision
T-9 weeks vs. observation	Mixed	Moderate	Imprecision
T-24 months vs. T-12 months	Mixed	Moderate	Imprecision
T-6 months vs. T-12 months	Mixed	Moderate	Imprecision
T-9 weeks vs. T-12 months	Mixed	Moderate	Inconsistency
T-12 weeks vs. T-12 months	Mixed	Moderate	Imprecision
T-6 months vs. observation	Indirect	Moderate	Imprecision
T-12 weeks vs. observation	Indirect	Moderate	Imprecision
T-24 months vs. T-12 months	Indirect	Moderate	Imprecision
T-24 months vs. T-12 weeks	Indirect	Moderate	Imprecision
T-24 months vs. T-9 weeks	Indirect	Moderate	Imprecision
T-6 months vs. T-12 weeks	Indirect	Moderate	Imprecision
T-6 months vs. T-9 weeks	Indirect	Moderate	Imprecision
T-12 weeks vs. T-9 weeks	Indirect	Moderate	Imprecision
Ranking of treatments	–	Moderate	Imprecision

T, trastuzumab.