Supplementary materials

eTable1. PRISMA checklist

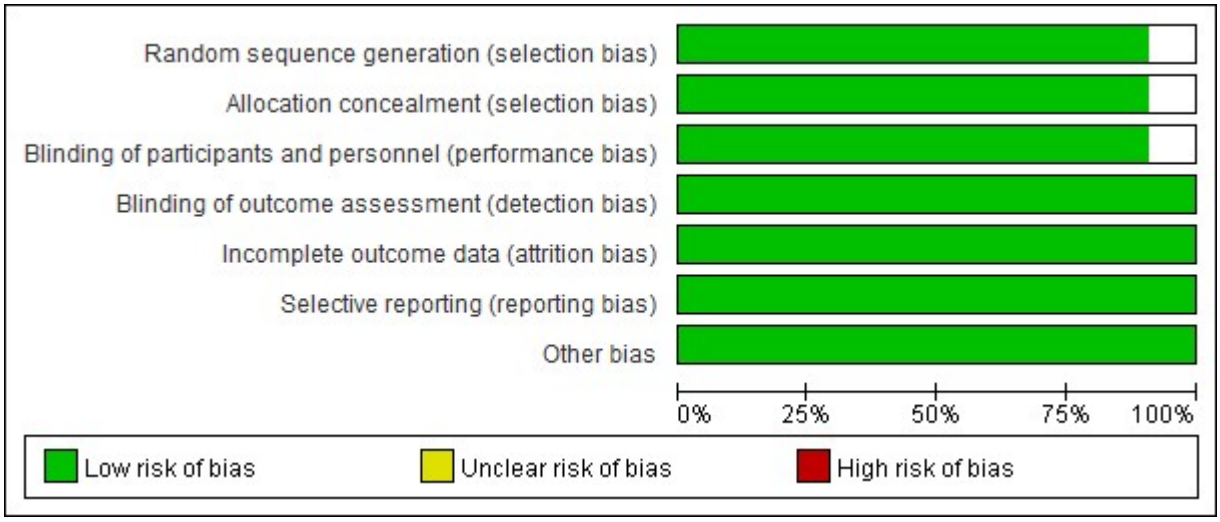
Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	3

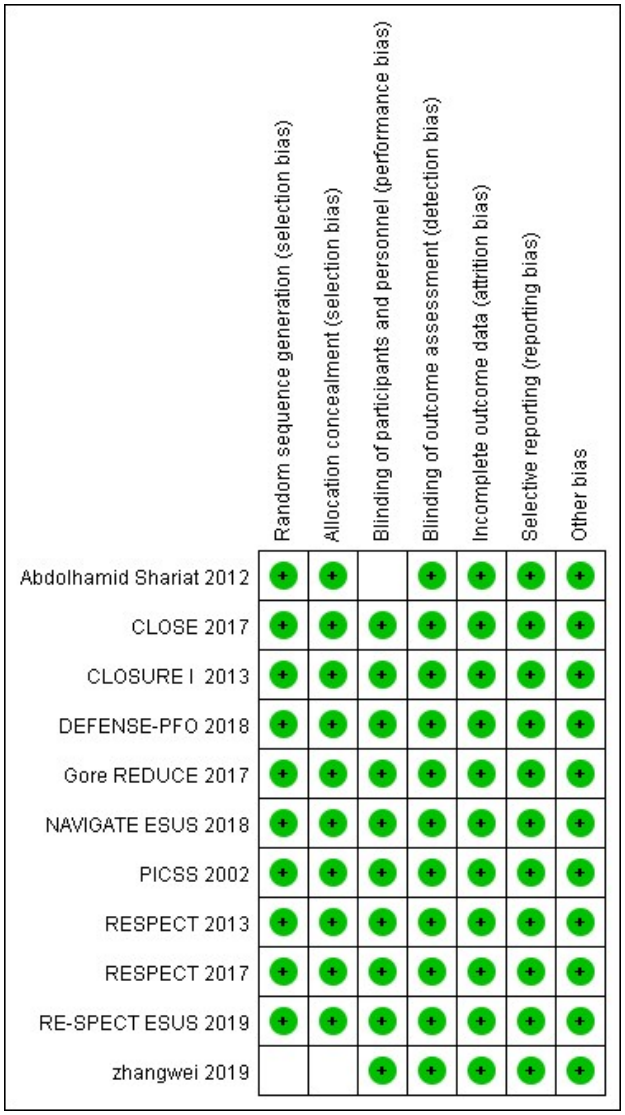
Section and Topic	Item #	Checklist item	Location where item is reported
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	4
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	4
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	5
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	5
Study characteristics	17	Cite each included study and present its characteristics.	5

Section and Topic	Item #	Checklist item	Location where item is reported
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	5
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	5
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	5
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supplementary
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	6
	23b	Discuss any limitations of the evidence included in the review.	6
	23c	Discuss any limitations of the review processes used.	6
	23d	Discuss implications of the results for practice, policy, and future research.	6
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	3

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	3
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	8
Competing interests	26	Declare any competing interests of review authors.	8
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplementary

eFigure1. Risk of Bias





eFigure2. Summary estimates for efficacy outcomes from network meta-analysis

Odds ratio (95% credible intervals) between column and row treatment regimens are reported. Statistically significant results, where the 95% credible interval does not include 1, are in bold. NOAC indicates non–vitamin K antagonist oral anticoagulant.

Antiplatelet	0.81 (0.41, 1.6)	**0.38 (0.16, 0.68)**	0.79 (0.27, 2.27)
1.24 (0.63, 2.44)	Warfarin	**0.46 (0.18, 0.94)**	0.98 (0.28, 3.37)
2.66 (1.48, 6.44)	**2.16 (1.06, 5.68)**	Surgical closure	2.14 (0.72, 8.26)
1.26 (0.44, 3.68)	1.03 (0.3, 3.55)	0.47 (0.12, 1.39)	NOAC

eFigure3. Summary estimates for safety outcomes from network meta-analysis

Odds ratio (95% credible intervals) between column and row treatment regimens are reported. Statistically significant results, where the 95% credible interval does not include 1, are in bold. NOAC indicates non–vitamin K antagonist oral anticoagulant.

Antiplatelet	1.7 (0.65, 4.76)	1.66 (0.68, 3.82)	2.17 (0.67, 7.63)
0.59 (0.21, 1.53)	Warfarin	0.97 (0.31, 2.81)	1.27 (0.28, 5.8)
0.6 (0.26, 1.46)	1.03 (0.36, 3.24)	Surgical closure	1.31 (0.38, 5.01)
0.46 (0.13, 1.49)	0.79 (0.17, 3.63)	0.76 (0.2, 2.61)	NOAC

eTable2. Rank probabilities for efficacy outcomes

Rank probabilities for each treatment at every ranking position are presented. It reads as probability of being the best treatment, second best, and so on. NOAC indicates non–vitamin K antagonist oral anticoagulant.

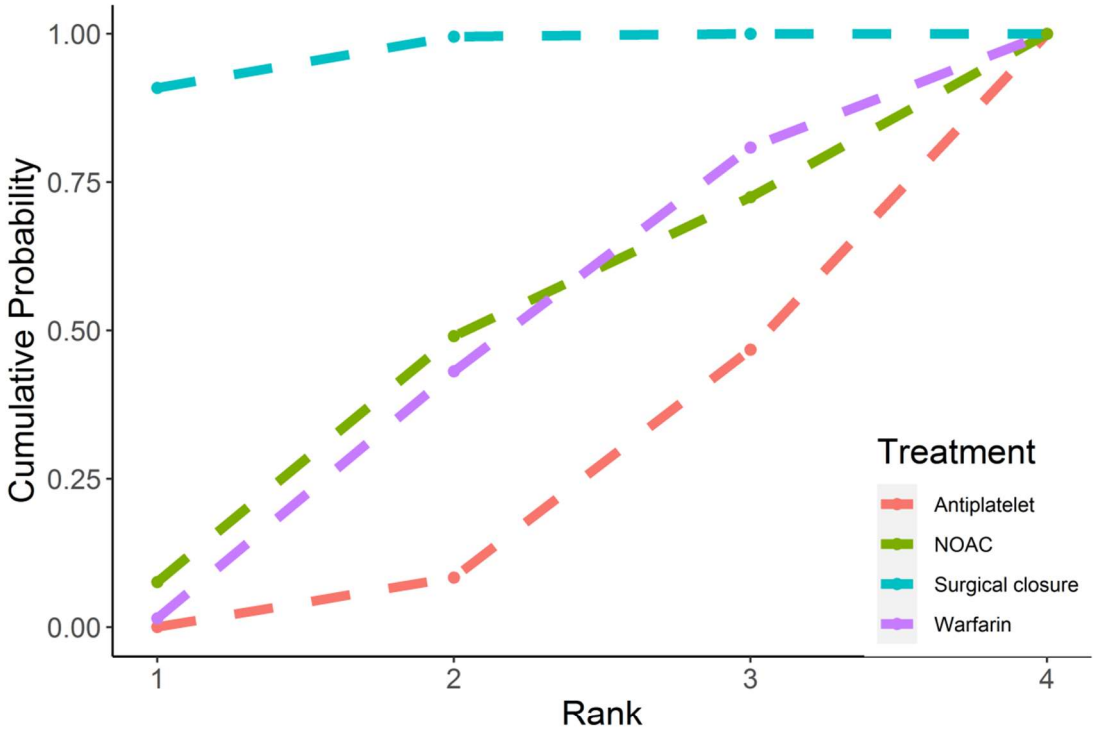
	First	Second	Third	Fourth
Antiplatelet	0.00065	0.08275	0.3844	0.5322
Warfarin	0.01485	0.41615	0.37705	0.19195
Surgical closure	0.9086	0.08655	0.0044	0.00045
NOAC	0.0759	0.41455	0.23415	0.2754

eTable3. Rank probabilities for safety outcomes

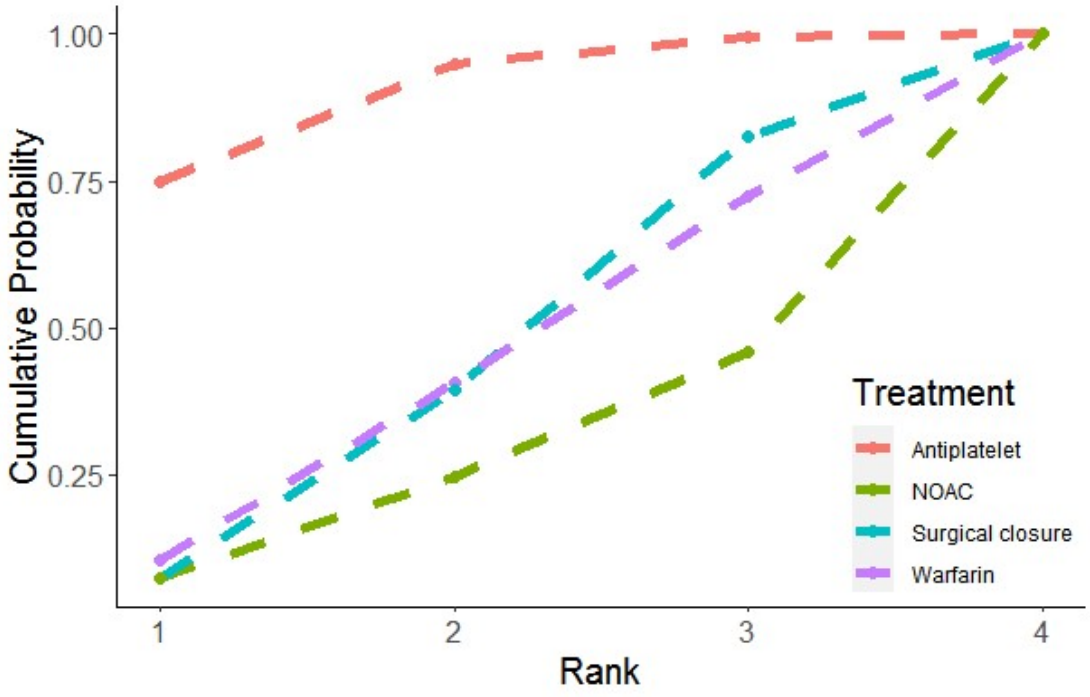
Rank probabilities for each treatment at every ranking position are presented. It reads as probability of being the best treatment, second best, and so on. NOAC indicates non–vitamin K antagonist oral anticoagulant.

	First	Second	Third	Fourth
Antiplatelet	0.74735	0.2022	0.0441	0.00635
Warfarin	0.1047	0.30355	0.3143	0.27745
Surgical closure	0.07305	0.32105	0.431	0.1749
NOAC	0.0749	0.1732	0.2106	0.5413

eFigure4. Cumulative rank probability plot for efficacy outcomes



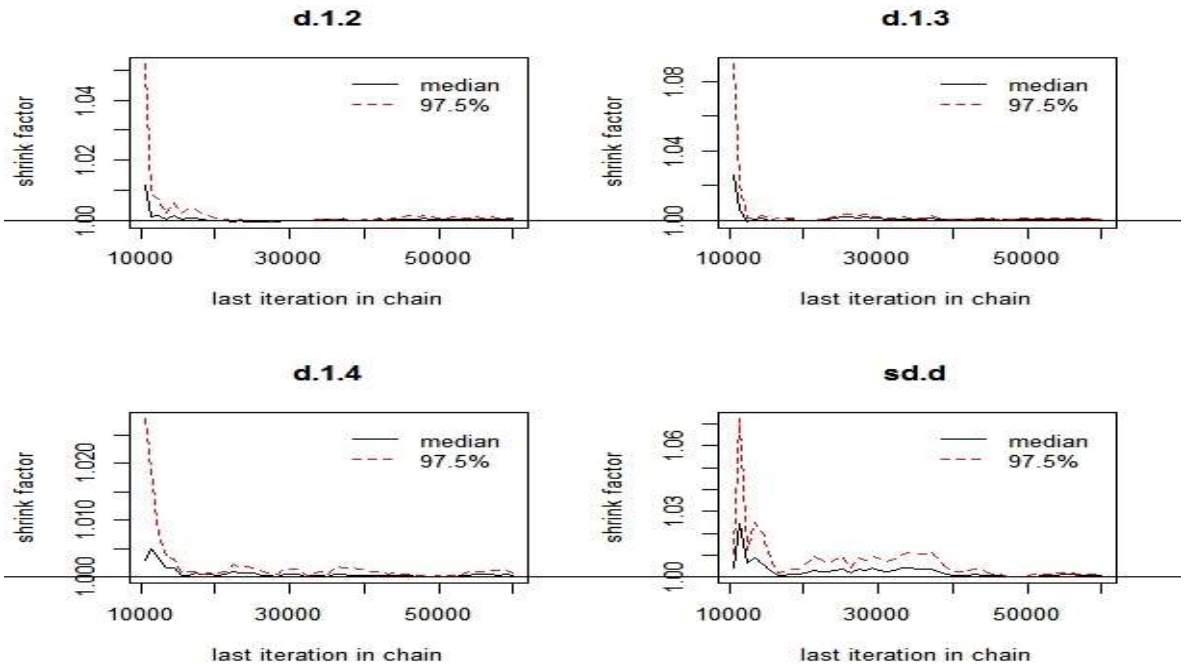
eFigure5. Cumulative rank probability plot for safety outcomes



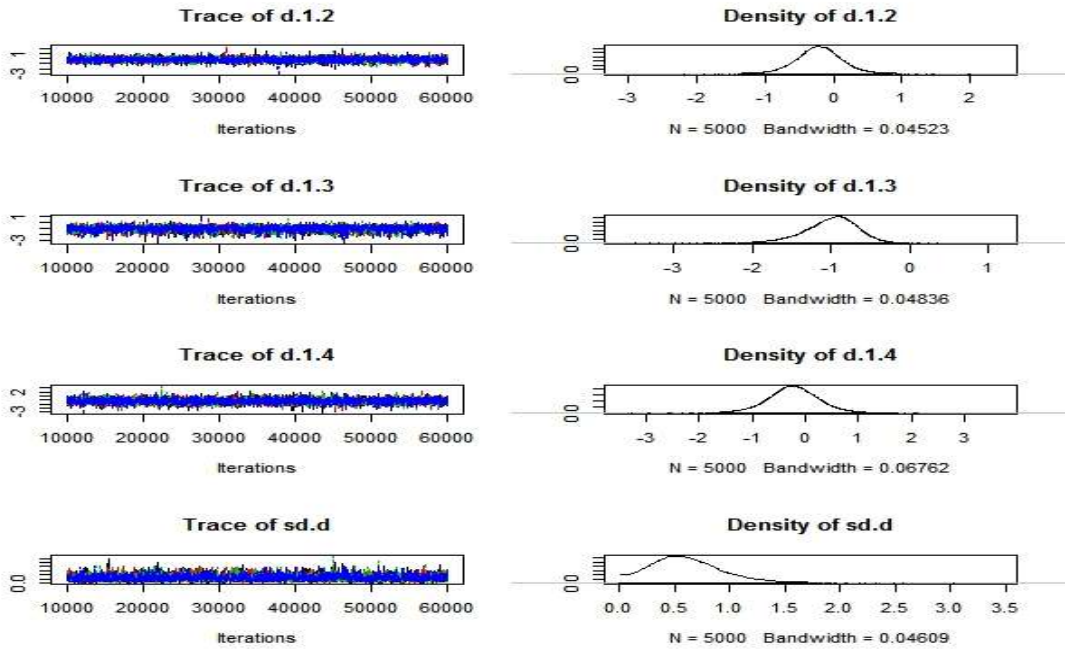
eFigure6. Model diagnostics of the NMA under the assumption of evidence consistency

We checked model convergence using the Gelman-Rubin diagnostics statistics(eFigure6.1 (a) and eFigure6.2 (a)) and trace plots(eFigure6.1 (b) and eFigure6.2 (b)) for all model parameters. We reported diagnostics for the NMA models under the assumption of evidence consistency for the two primary outcomes. All the other outcomes provided similar results. We found that Gelman-Rubin statistics got close to 1 fast, showing that the four Markov chain Monte Carlo (MCMC) chains mixed well regardless of their different initial starting points. Similarly, trace plots showed that every MCMC chains converged well.

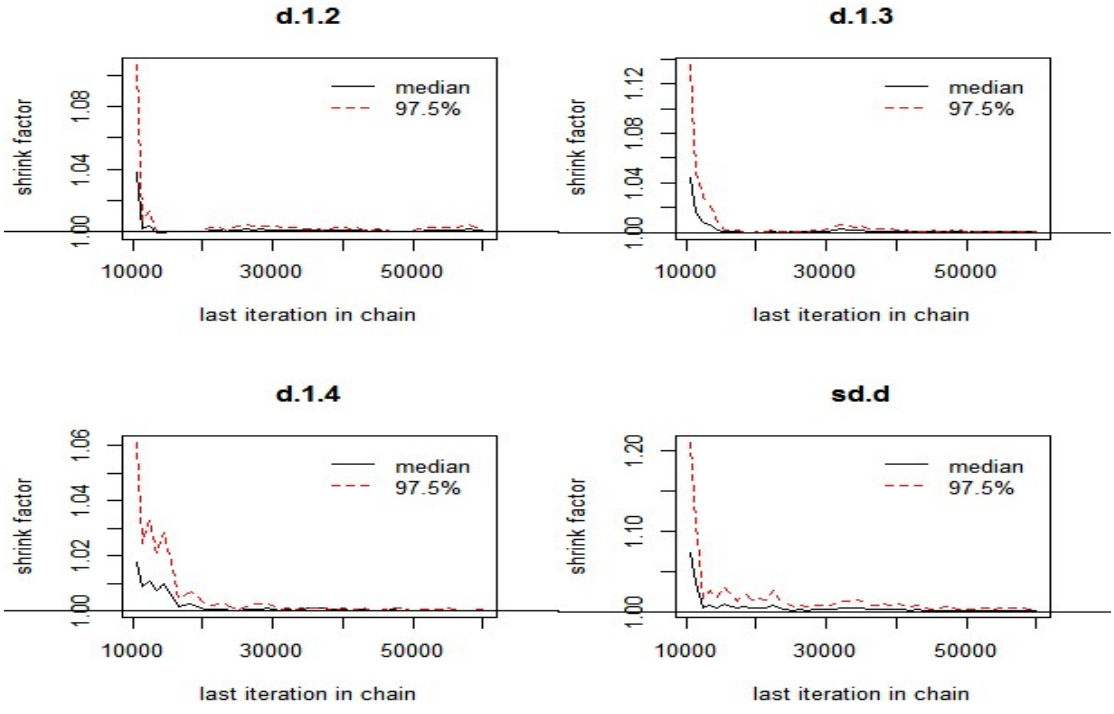
eFigure6.1 (a) efficacy outcomes



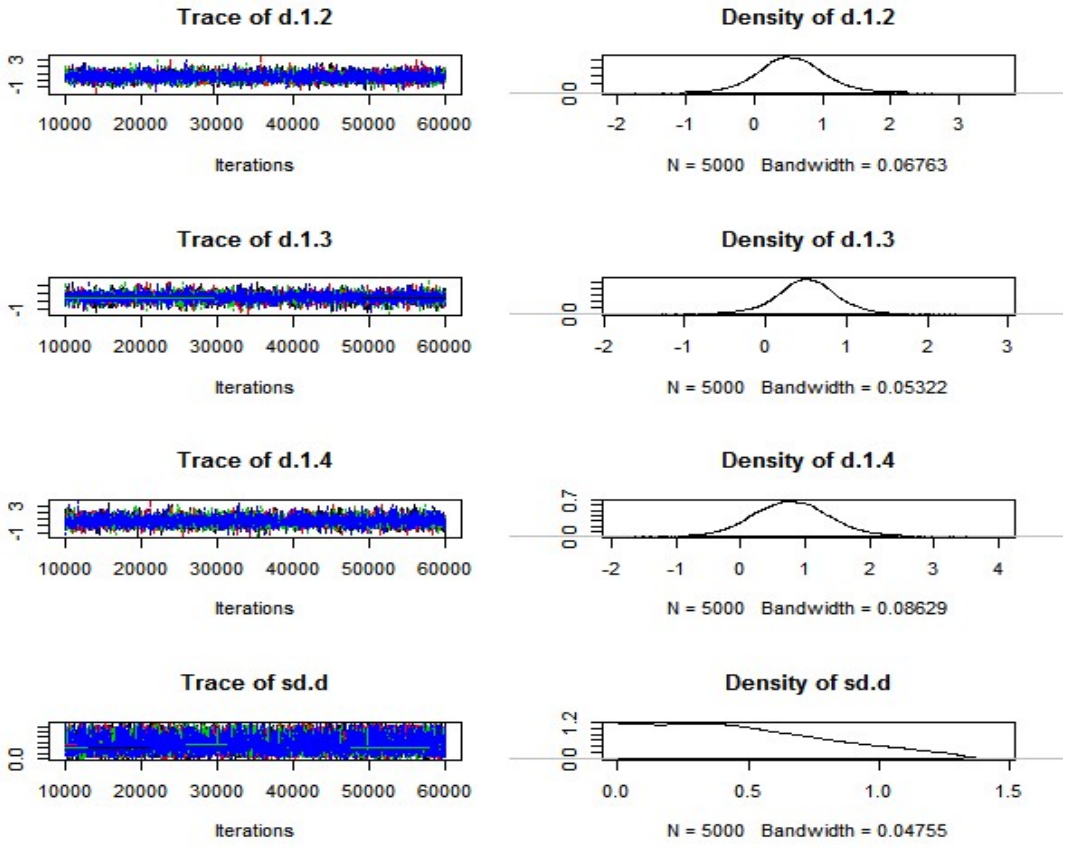
eFigure6.1 (b)



eFigure6.2(a) safety outcomes



eFigure6.2 (b)

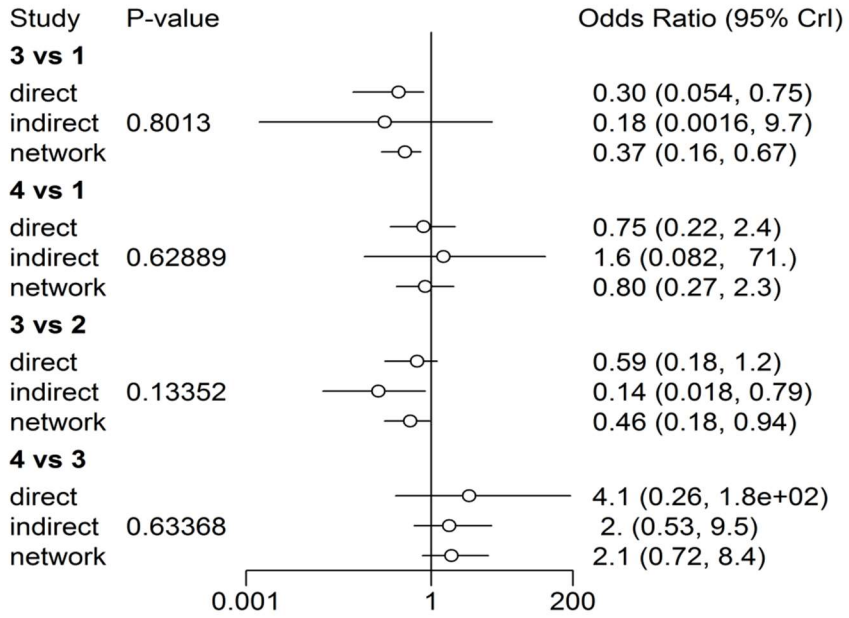

Trace of d.1.2
Density of d.1.2
Iterations
N = 5000 Bandwidth = 0.06763
Trace of d.1.3
Density of d.1.3
Iterations
N = 5000 Bandwidth = 0.05322
Trace of d.1.4
Density of d.1.4
Iterations
N = 5000 Bandwidth = 0.08629
Trace of sd.d
Density of sd.d
Iterations
N = 5000 Bandwidth = 0.04755

eAppendix1

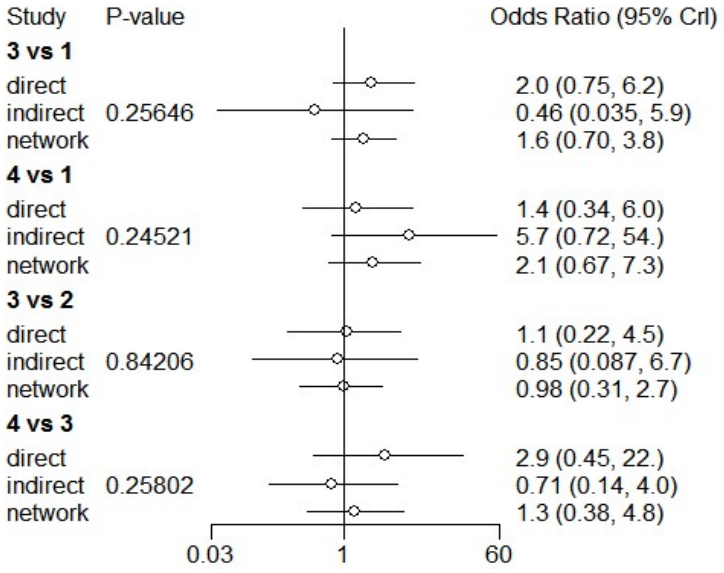
NMA with the assumption of evidence inconsistency

We assessed statistical evidence inconsistency in our NMA. Evidence inconsistency is defined as discrepancy between direct and indirect comparisons of treatment effects. We conducted this investigation for the two primary outcomes under the main network structure. Note that the outputs below used a treatment code as follows: 1=Antiplatelet; 2=Warfarin; 3=Surgical closure; and 4=NOAC.

(A) efficacy outcomes



(B) safety outcomes

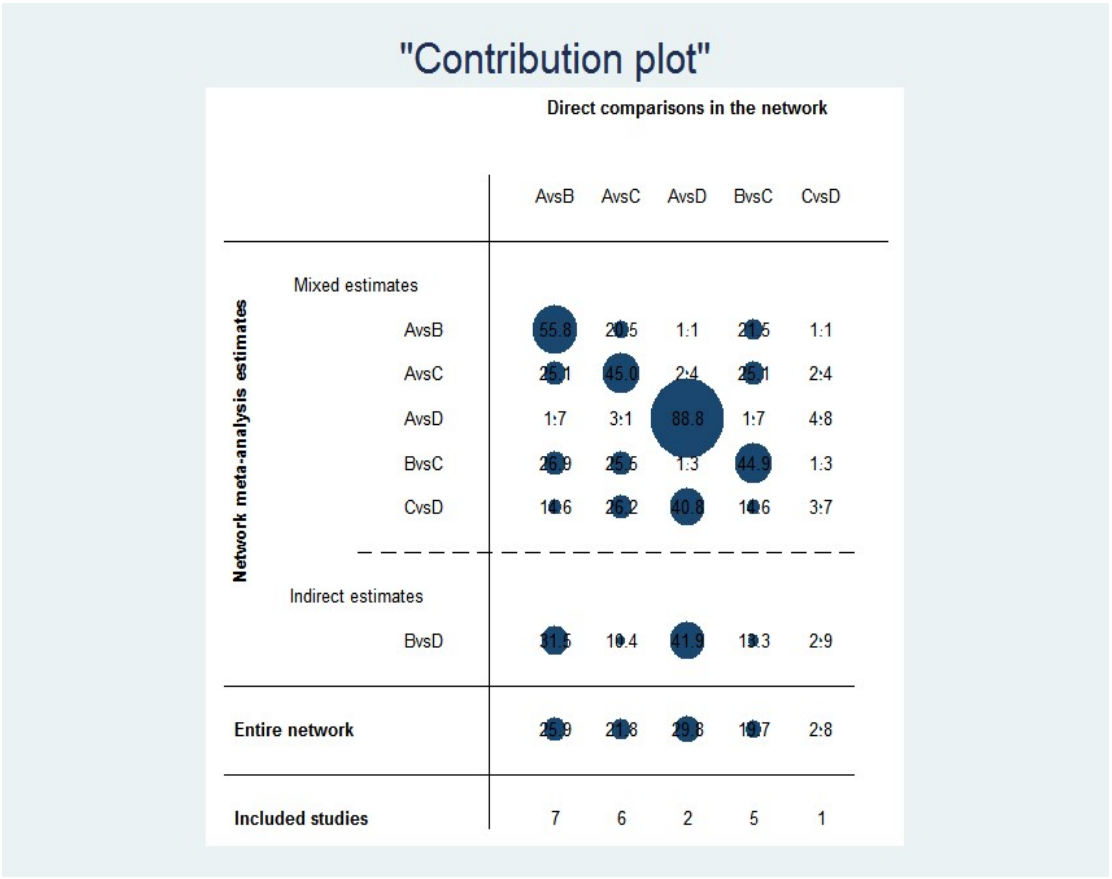


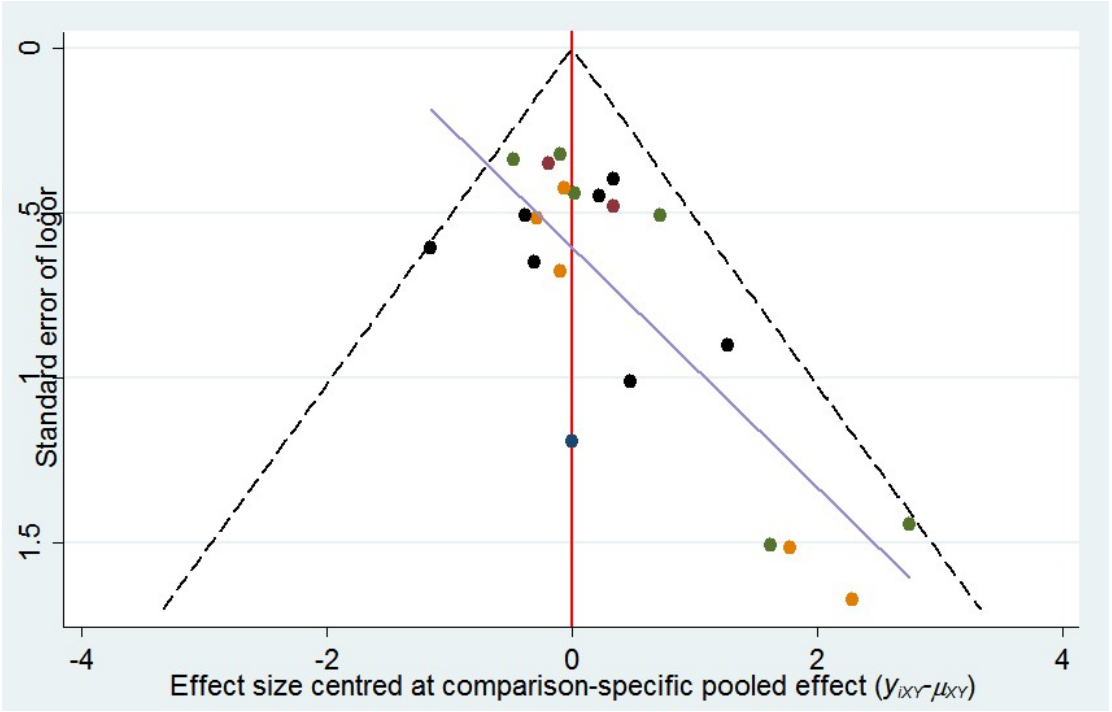
eAppendix2.

Evidence contribution graph and publication bias funnel graph

We used the evidence contribution graph to illustrate the contribution of each two interventions to the overall outcome. The size of the circle represents the degree of contribution. The larger the circle, the greater the contribution. The funnel chart shows the publication bias. According to the scatter plot, the closer the line is to 1, the smaller the publication bias.A=Antiplatelet; B=Warfarin; C=Surgical closure; D=NOAC.

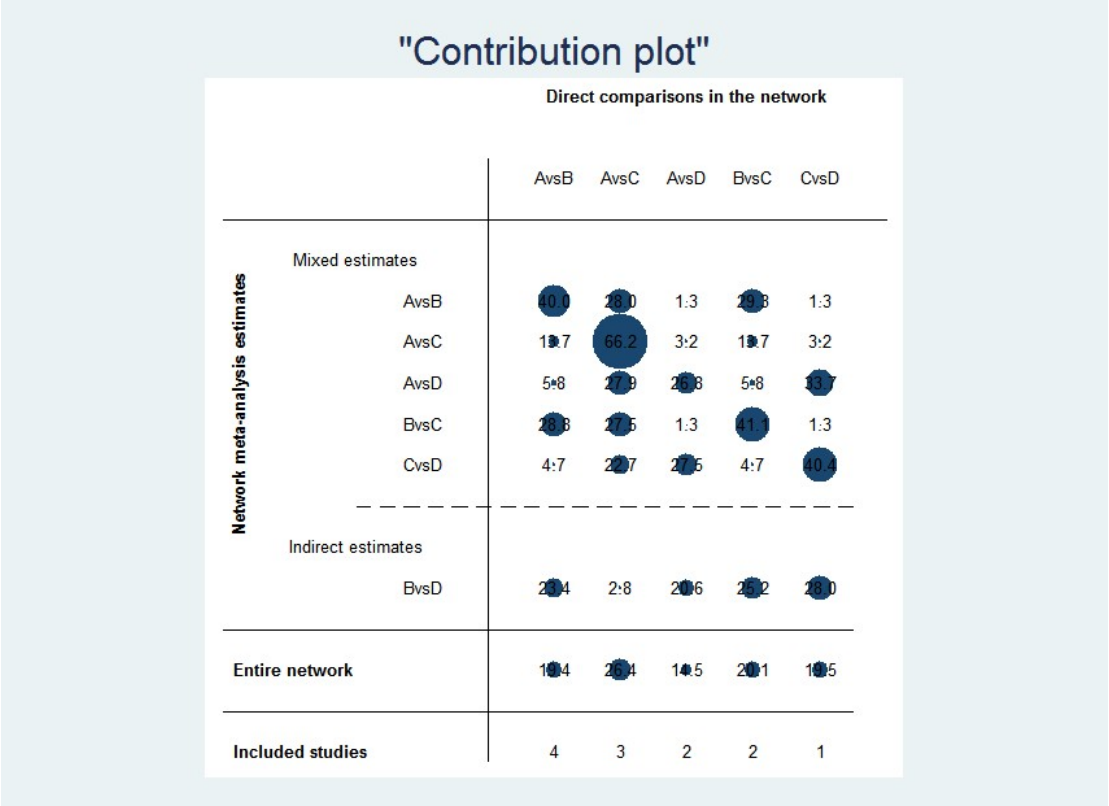
(A) efficacy outcomes

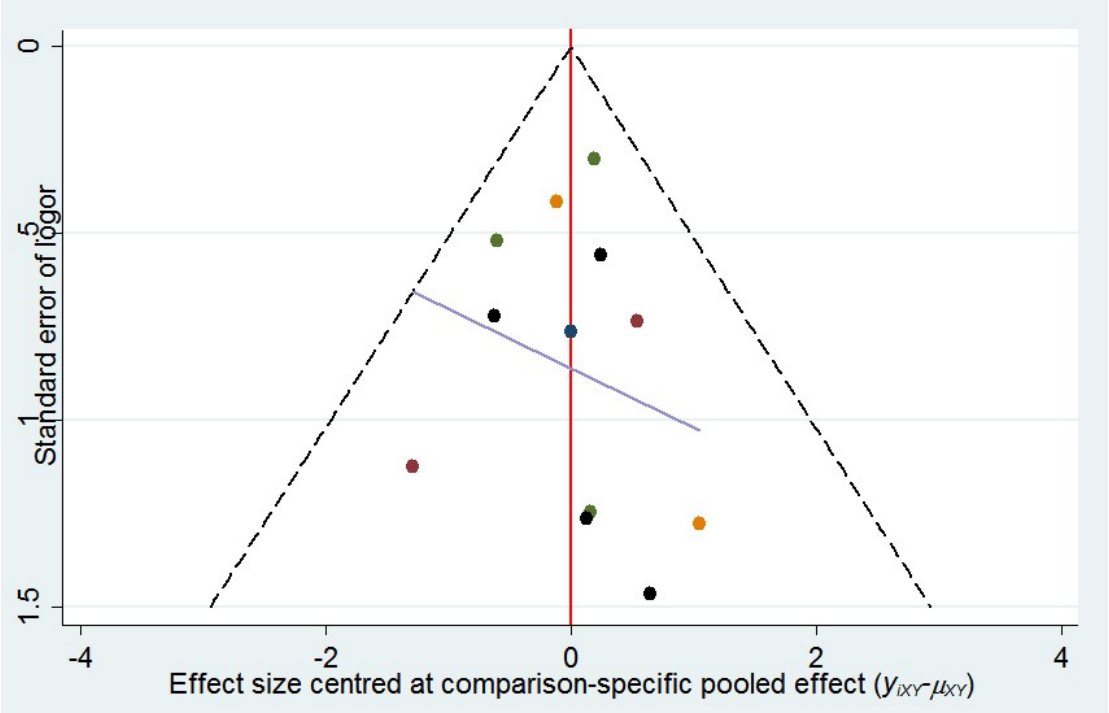




(A) safety outcomes

A=Antiplatelet; B=Warfarin; C=Surgical closure; D=NOAC.





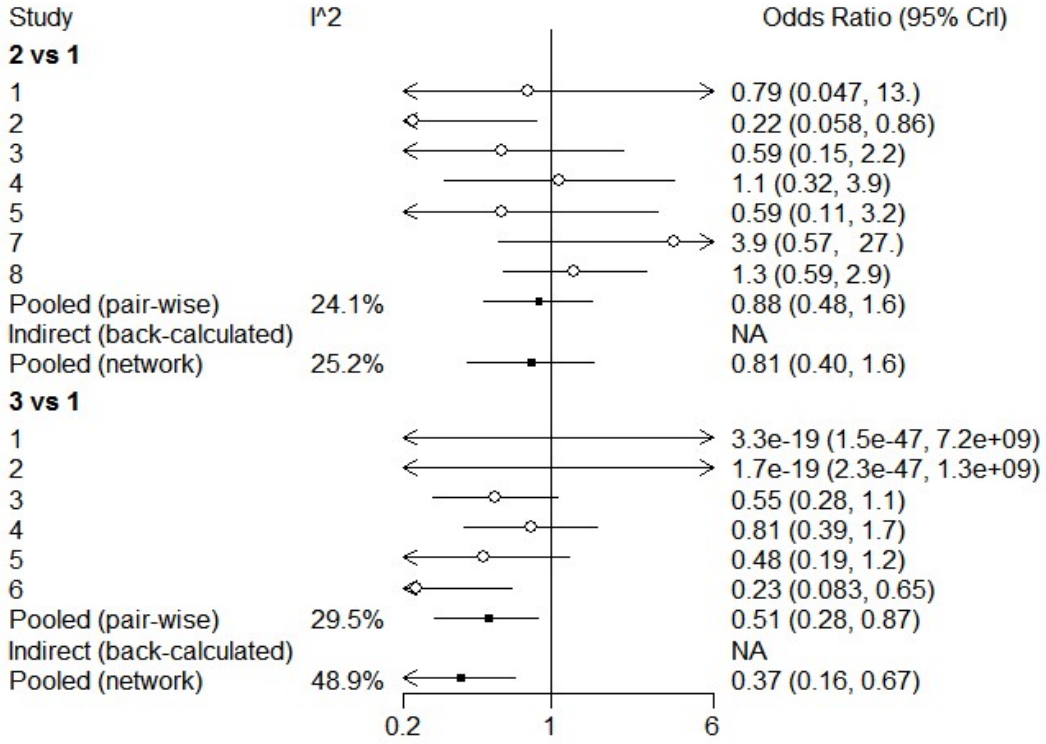
eAppendix3.

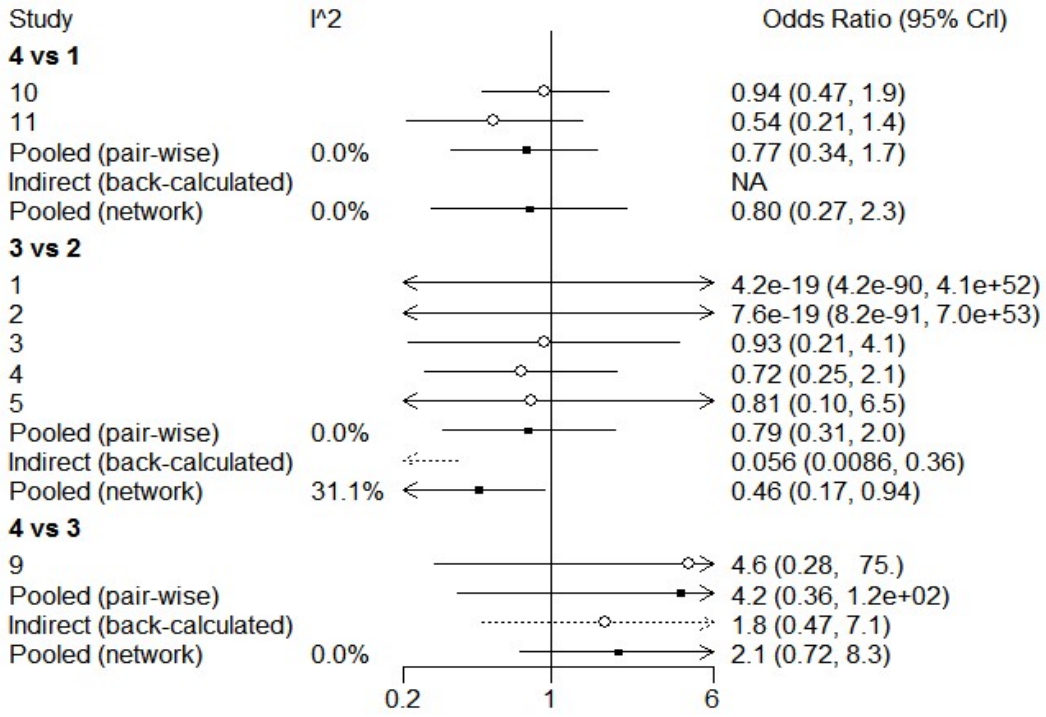
Comparative Analysis of Pairwise Intervention

Each intervention will be compared in pairs. The figure shows the results of direct comparisons in the literature and the results of indirect comparisons in the network model.

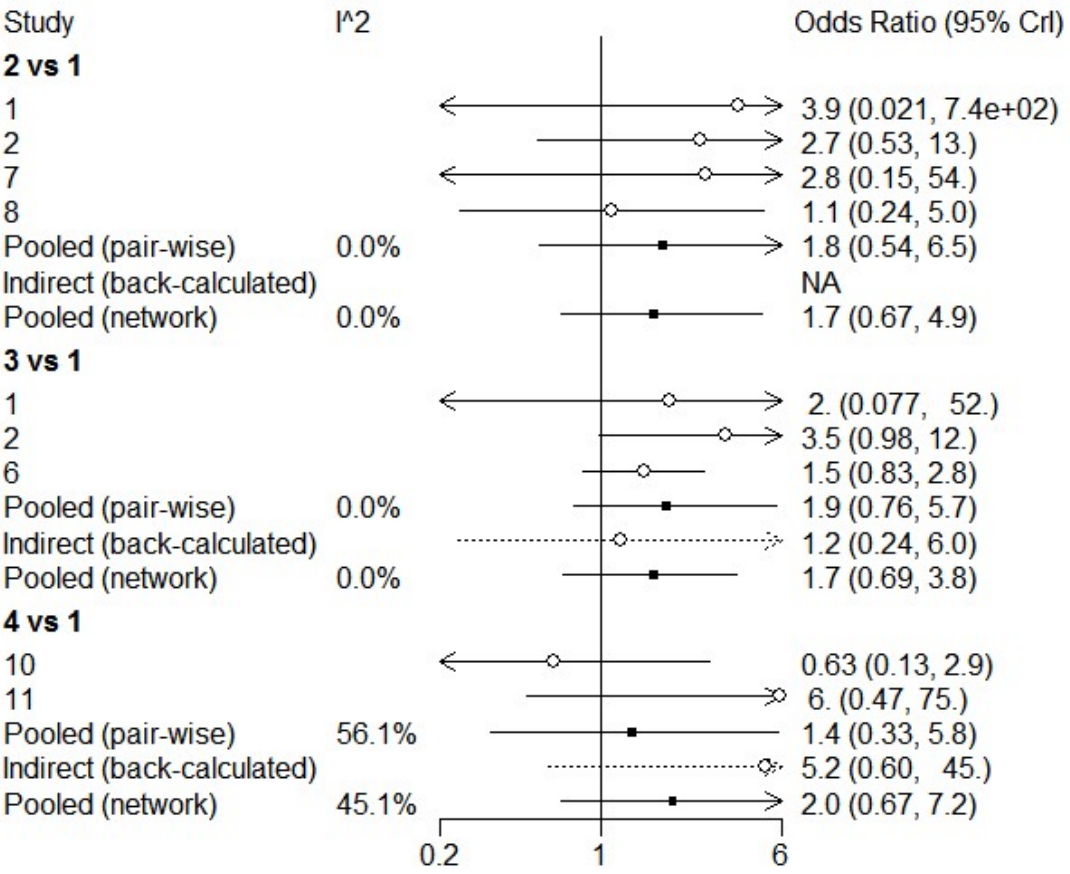
Please note: 1234 in bold represents:1=Antiplatelet; 2=Warfarin; 3=Surgical closure; and 4=NOAC. Normal bodies 1-11 represent the included literature numbers.

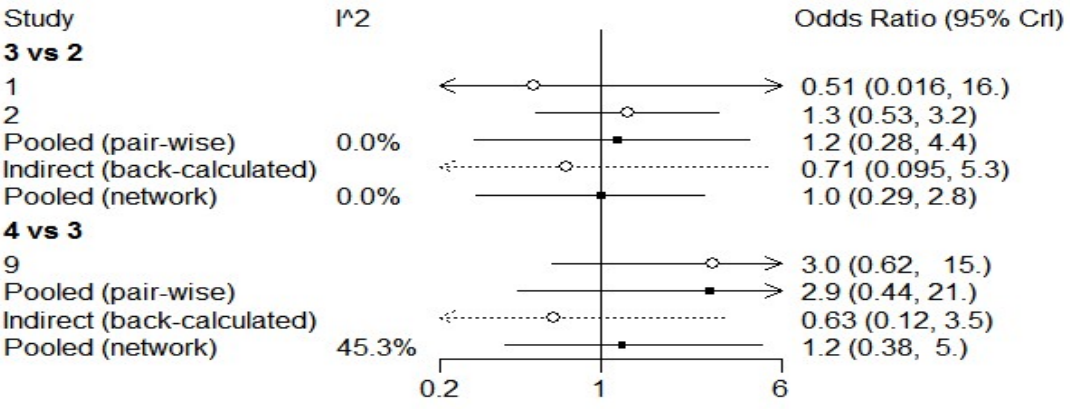
(A) efficacy outcomes





（B） safety outcomes

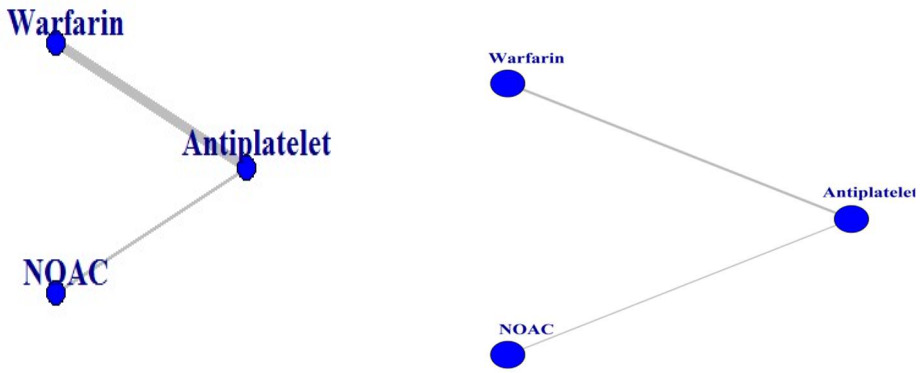

Study
I^2
Odds Ratio (95% CrI)
2 vs 1
1
3.9 (0.021, 7.4e+02)
2
2.7 (0.53, 13.)
7
2.8 (0.15, 54.)
8
1.1 (0.24, 5.0)
Pooled (pair-wise)
0.0%
1.8 (0.54, 6.5)
Indirect (back-calculated)
NA
Pooled (network)
0.0%
1.7 (0.67, 4.9)
3 vs 1
1
2. (0.077, 52.)
2
3.5 (0.98, 12.)
6
1.5 (0.83, 2.8)
Pooled (pair-wise)
0.0%
1.9 (0.76, 5.7)
Indirect (back-calculated)
1.2 (0.24, 6.0)
Pooled (network)
0.0%
1.7 (0.69, 3.8)
4 vs 1
10
0.63 (0.13, 2.9)
11
6. (0.47, 75.)
Pooled (pair-wise)
56.1%
1.4 (0.33, 5.8)
Indirect (back-calculated)
5.2 (0.60, 45.)
Pooled (network)
45.1%
2.0 (0.67, 7.2)
0.2
1
6


Study
I^2
Odds Ratio (95% CrI)
3 vs 2
1
0.51 (0.016, 16.)
2
1.3 (0.53, 3.2)
Pooled (pair-wise)
0.0%
1.2 (0.28, 4.4)
Indirect (back-calculated)
0.71 (0.095, 5.3)
Pooled (network)
0.0%
1.0 (0.29, 2.8)
4 vs 3
9
3.0 (0.62, 15.)
Pooled (pair-wise)
2.9 (0.44, 21.)
Indirect (back-calculated)
0.63 (0.12, 3.5)
Pooled (network)
45.3%
1.2 (0.38, 5.)
0.2
1
6

eAppendix4.

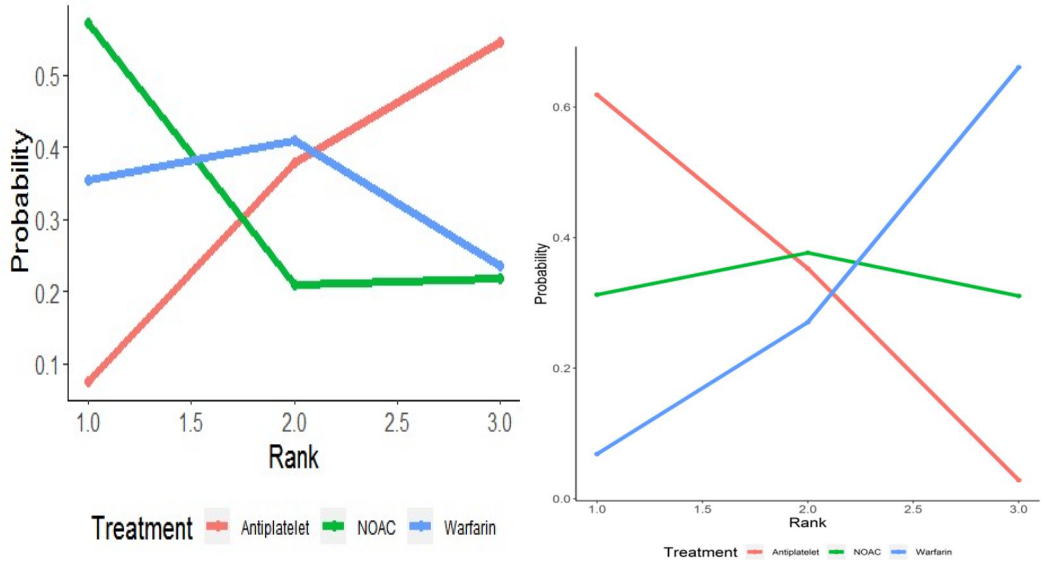
Sensitivity Analyses

This network did not Including surgical closure.



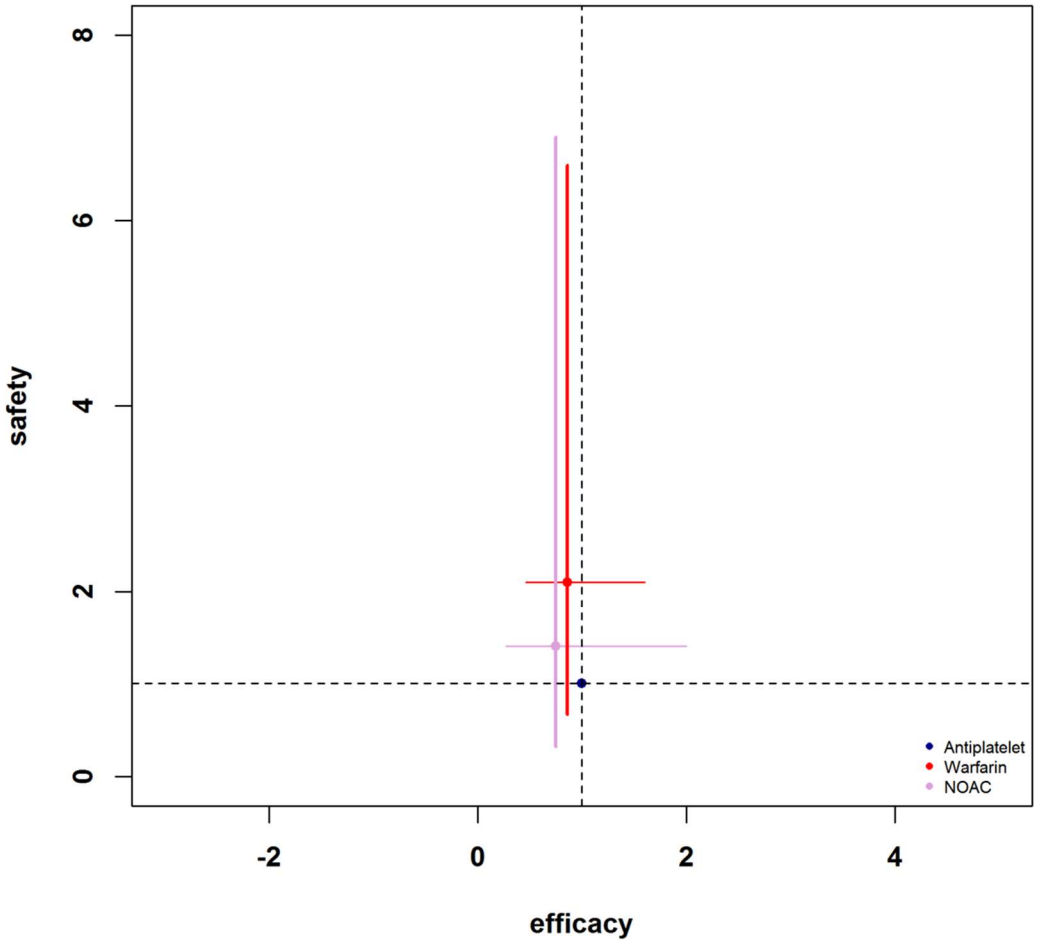
Network of 3 treatment strategies(Efficacy on the left, safety on the right)

Each node represents a certain intervention, the size of the node represents the size of the sample, and the thickness of the line represents the number of studies. NOAC indicates non–vitamin K antagonist oral anticoagulant.



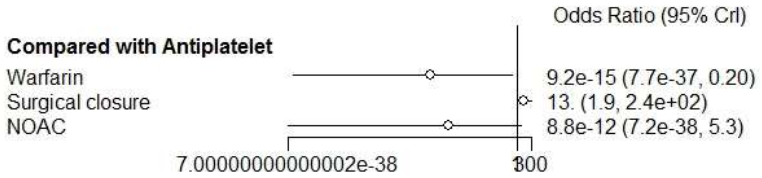
NOAC indicates non–vitamin K antagonist oral anticoagulant.

(Efficacy on the left, safety on the right)



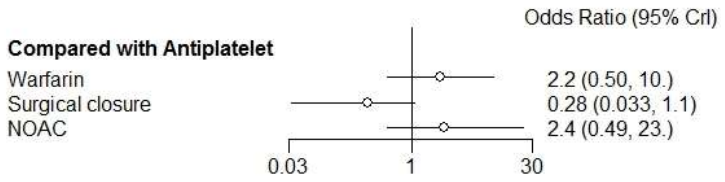
Odds Ratios for efficacy and safety

Odds ratios compared with antiplatelet drugs (reference) and associated 95% credible intervals are plotted: efficacy on the x-axis and safety on the y-axis. NOAC indicates non–vitamin K antagonist oral anticoagulant.



Forest Plots for Safety Outcomes（atrial fibrillation）

Odds ratios and 95% credible intervals (CI) comparted with antiplatelet drugs (reference) are plotted. A total of 2706 patients were contributed to network meta-analyses for Safety outcomes. The estimated between-trial effect heterogeneity and its 95% CI from NMA for each outcome is 9.2^{e-15} (95% CI, 7.7^{e-37}-0.2), 13 (95% CI, 1.9-240) , 8.8^{e-12} (95% CI, 7.2^{e-38}-5.3). NOAC indicates non–vitamin K antagonist oral anticoagulant.



Forest Plots for Safety Outcomes（major bleeding）

Odds ratios and 95% credible intervals (CI) comparted with antiplatelet drugs (reference) are plotted. A total of 2706 patients were contributed to network meta-analyses for Safety outcomes. The estimated between-trial effect heterogeneity and its 95% CI from NMA for each outcome is 2.2 (95% CI, 0.5-10), 0.28 (95% CI, 0.033-1.1) , 2.4 (95% CI, 0.49-23). NOAC indicates non–vitamin K antagonist oral anticoagulant.