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Supplementary Figure S5 Direct comparison of forest plots for each outcome

Supplementary Figure S6 Sensitivity analysis

Supplementary Methods S1. PRISMA Main Checklist

Supplementary Methods S2. PRISMA Abstract Checklist

References

Table S6 Included studies

The network meta-analysis included 2 randomized controlled trials and 14 observational studies.

First Author,Year[Reference]	Study design
Floris H B M Schreuder,2021[1]	RCT
Rustam Al-Shahi Salman,2021[2]	RCT
Satoshi Suda,2023[3]	Retrospective cohort
Wu, Victor Chien-Chia,2021[4]	Retrospective cohort
Alireza Sadighi,2020[5]	Prospective cohort
Peter Brønnum Nielsen,2019[6]	Retrospective cohort
Mohammed K. Badi,2019[7]	Retrospective cohort
Loris Poli,2018[8]	Prospective cohort
Peter Brønnum Nielsen,2017[9]	Prospective cohort
Gye Young Park,2016[10]	Retrospective cohort
Chuan-Tsai Tsai,2020[11]	Retrospective cohort
So-Ryoung Lee,2020[12]	Retrospective cohort
Sylvie Perreault,2019[13]	Retrospective cohort
Tze-Fan Chao,2016[14]	Retrospective cohort
Kuramatsu JB,2015[15]	Retrospective cohort
Jens Erik Nielsen-Kudsk1,2017[16]	Retrospective cohort

Table S7 Definitions of thromboembolism and recurrent intracranial hemorrhage

Study	Thromboembolism	Recurrent intracranial hemorrhage
Satoshi Suda,2023	Ischemic stroke,deep venous thrombosis	Imaging aids in the diagnosis of new intracranial haemorrhage
Wu, Victor Chien-Chia,2021	Ischemic stroke & systemic embolism	It was defined according to the principal diagnosis at admission or an emergency visit during which IS was previously validated
Floris H B M Schreuder,2021	Ischemic stroke	Clinical evidence of the sudden onset of a new neurological deficit, or an increase in an existing deficit, persisting for more than 24 hours,with a corresponding intracerebral haemorrhage on a CT or MR scan or at post-mortem investigation
Rustam Al-Shahi Salman,2021	Ischemic stroke	Recurrent symptomatic spontaneous intracranial haemorrhage
Alireza Sadighi,2020	Ischemic stroke & systemic embolism	Definition missing
Peter Brønnum Nielsen,2019	Ischemic stroke	The 10th revision of ICD codes was used to identify outcomes:ICD: I61
Mohammed K. Badi,2019	Ischemic stroke	It wasdefined as nontraumatic intracerebral hemorrhage identified on brain imaging)
Loris Poli,2018	ischemic stroke/systemic embolism	NA
Peter Brønnum Nielsen,2017	Ischemic stroke & systemic embolism	Definition missing
Gye Young Park,2016	Ischemic strokes, pulmonary thromboembolism, deep vein thrombosis, or other systemic embolisms	Recurrent CNS bleeding
Chuan-Tsai Tsai,2020	Ischemic stroke	Definition missing
So-Ryoung Lee,2020	Ischemic stroke	NA
Sylvie Perreault,2019	Ischemic stroke,fatal ischemic stroke	intracranial hemorrhage,fatal intracranial hemorrhage
Tze-Fan Chao,2016	Ischemic stroke	Definition missing
Kuramatsu JB,2015	New cerebral Infarction	Definition missing
Jens Erik Nielsen-Kudsk1,2017	Ischemic stroke	Definition missing

Table S8 Direct comparison of the number of outcome events

Thromboembolism

Study	Intervention	Events	Total
Satoshi Suda,2023	OAC	5	108
Satoshi Suda,2023	No therapy	2	52
Wu, Victor Chien-Chia,2021	OAC	5	186
Wu, Victor Chien-Chia,2021	No therapy	15	186
Floris H B M Schreuder,2021	NOAC	6	50
Floris H B M Schreuder,2021	Antiplatelet	6	51
Rustam Al-Shahi Salman,2021	OAC	3	101
Rustam Al-Shahi Salman,2021	No therapy	21	102
Alireza Sadighi,2020	OAC	7	38
Alireza Sadighi,2020	No therapy	10	55
Peter Brønnum Nielsen,2019	NOAC	29	348
Peter Brønnum Nielsen,2019	Warfarin	32	274
Mohammed K. Badi,2019	NOAC	16	88
Mohammed K. Badi,2019	Warfarin	18	128
Mohammed K. Badi,2019	No therapy	17	92
Loris Poli,2018	OAC	2	55
Loris Poli,2018	Antiplatelet	8	29
Loris Poli,2018	No therapy	13	62
Gye Young Park,2016	Warfarin	9	254
Gye Young Park,2016	No therapy	17	174
Chuan-Tsai Tsai,2020	NOAC	72	973
Chuan-Tsai Tsai,2020	Warfarin	76	973
Sylvie Perreault,2019	OAC	6	260
Sylvie Perreault,2019	No therapy	11	423
Tze-Fan Chao,2016	Warfarin	130	1154
Tze-Fan Chao,2016	Antiplatelet	581	3552
Tze-Fan Chao,2016	No therapy	964	8211
Kuramatsu JB,2015	OAC	4	108
Kuramatsu JB,2015	No therapy	16	153
Jens Erik Nielsen-Kudsk1,2017	OAC	6	103
Jens Erik Nielsen-Kudsk1,2017	LAAO	2	103

Recurrent intracranial hemorrhage

Study	Intervention	Events	Total
Satoshi Suda,2023	OAC	0	108
Satoshi Suda,2023	No therapy	0	52
Wu, Victor Chien-Chia,2021	OAC	3	186
Wu, Victor Chien-Chia,2021	No therapy	7	186
Floris H B M Schreuder,2021	NOAC	4	50
Floris H B M Schreuder,2021	Antiplatelet	1	51
Rustam Al-Shahi Salman,2021	OAC	8	101
Rustam Al-Shahi Salman,2021	No therapy	4	102
Alireza Sadighi,2020	OAC	5	38
Alireza Sadighi,2020	No therapy	3	55
Peter Brønnum Nielsen,2019	NOAC	27	348
Peter Brønnum Nielsen,2019	Warfarin	22	274
Mohammed K. Badi,2019	NOAC	1	88
Mohammed K. Badi,2019	Warfarin	6	128
Mohammed K. Badi,2019	No therapy	6	92
Gye Young Park,2016	Warfarin	13	254
Gye Young Park,2016	No therapy	0	174
Chuan-Tsai Tsai,2020	NOAC	26	973
Chuan-Tsai Tsai,2020	Warfarin	46	973
Sylvie Perreault,2019	OAC	4	260
Sylvie Perreault,2019	No therapy	23	423
Tze-Fan Chao,2016	Warfarin	241	1154
Tze-Fan Chao,2016	Antiplatelet	628	3552
Tze-Fan Chao,2016	No therapy	730	8211
Kuramatsu JB,2015	OAC	4	108
Kuramatsu JB,2015	No therapy	5	153
Jens Erik Nielsen-Kudsk1,2017	OAC	2	103
Jens Erik Nielsen-Kudsk1,2017	LAAO	1	103

All-cause death

Study	Intervention	Events	Total
Wu, Victor Chien-Chia,2021	OAC	21	186
Wu, Victor Chien-Chia,2021	No therapy	37	186
Floris H B M Schreuder,2021	NOAC	9	50
Floris H B M Schreuder,2021	Antiplatelet	11	51
Rustam Al-Shahi Salman,2021	OAC	15	101
Rustam Al-Shahi Salman,2021	No therapy	11	102
Alireza Sadighi,2020	OAC	10	38
Alireza Sadighi,2020	No therapy	20	55
Mohammed K. Badi,2019	NOAC	14	88
Mohammed K. Badi,2019	Warfarin	40	128
Mohammed K. Badi,2019	No therapy	33	92
Loris Poli,2018	OAC	5	55
Loris Poli,2018	Antiplatelet	7	29
Loris Poli,2018	No therapy	12	62
Gye Young Park,2016	Warfarin	13	254
Gye Young Park,2016	No therapy	22	174
Chuan-Tsai Tsai,2020	NOAC	187	973
Chuan-Tsai Tsai,2020	Warfarin	389	973
Sylvie Perreault,2019	OAC	20	260
Sylvie Perreault,2019	No therapy	80	423
Kuramatsu JB,2015	OAC	9	108
Kuramatsu JB,2015	No therapy	47	153
Jens Erik Nielsen-Kudsk1,2017	OAC	7	103
Jens Erik Nielsen-Kudsk1,2017	LAAO	2	103

Table S9 Consistency tests for direct and indirect comparisons

Thromboembolism

P＞0.05

Intervention	P-Value
Antiplatelet , NOAC	0.41
Antiplatelet , No therapy	0.88
Antiplatelet , OAC	0.14
Antiplatelet , Warfarin	0.64
NOAC, No therapy	0.83
NOAC, Warfarin	0.46
No therapy, Warfarin	0.26

Recurrent intracranial hemorrhage

P＞0.05

Intervention	P-Value
Antiplatelet , NOAC	0.23
Antiplatelet , No therapy	0.69
Antiplatelet , Warfarin	0.59
NOAC, No therapy	0.06
NOAC, Warfarin	0.46

All-cause death

P＞0.05

Intervention	P-Value
Antiplatelet , NOAC	0.19
Antiplatelet , No therapy	0.65
Antiplatelet , OAC	0.55
NOAC, No therapy	0.84
NOAC, Warfarin	0.21
No therapy , Warfarin	0.4

Table S10 Meta-regression analysis of different factors for each outcome

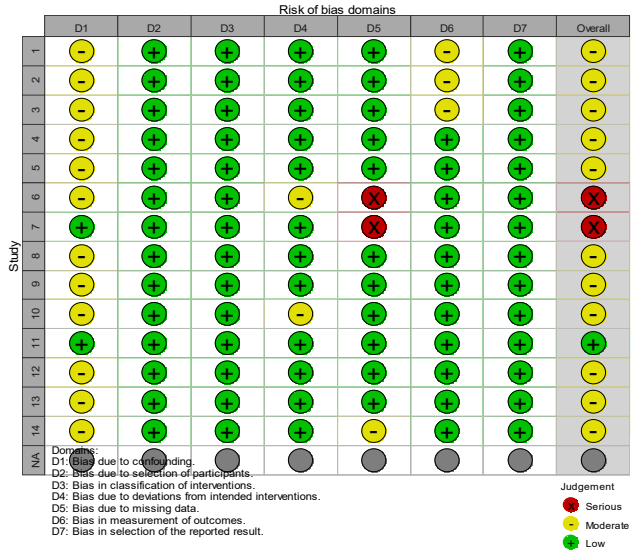
Factors	Outcome	Effect size	p-value
	Thrombosis		
Follow-up		-0.8	0.439
Prosperity		1	0.331
Sex		-0.65	0.524
	Recurrent intracranial hemorrhage		
Follow-up		1.35	0.203
Prosperity		-0.07	0.942
Sex		1.1	0.293
	All-cause death		
Follow-up		0.78	0.458
Prosperity		-0.42	0.686
Sex		-0.94	0.37

Table S11 GRADE assessment of the quality of evidence from network meta-analysis results

Comparison	Nature of the evidence	Confidence	Reason for downgrading	Reason for upgrading
OAC vs NOAC	Indirect	Low		
OAC vs Warfarin	Indirect	Low		
OAC vs Antiplatelet	Mixed	Low		
OAC vs LAAO	Mixed	Moderate	Imprecision	
OAC vs No therapy	Mixed	Moderate	Study limitations	
NOAC vs Warfarin	Mixed	Low		
NOAC vs Antiplatelet	Mixed	Moderate	Imprecision	
NOAC vs LAAO	Indirect	Moderate		Large magnitude of effect
NOAC vs No therapy	Mixed	Moderate	Imprecision	
Warfarin vs Antiplatelet	Mixed	Moderate	imprecision	
Warfarin vs LAAO	Indirect	Moderate		Large magnitude of effect
Warfarin vs No therapy	Mixed	Moderate	Study limitations	
Antiplatelet vs LAAO	Indirect	Moderate		Large magnitude of effect
Antiplatelet vs No therapy	Mixed	Low		
LAAO vs No therapy	Indirect	Low		
Total ranking of treatments		Low	Study limitations	

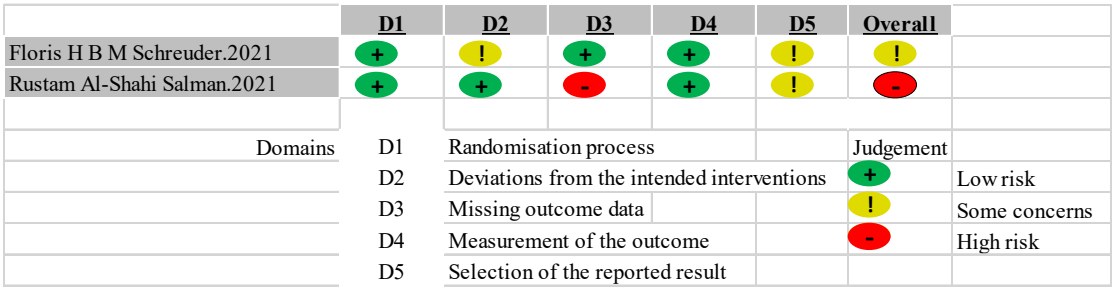
Supplementary Figure S1 Risk of bias assessment of included studies

Supplementary Figure S1A. Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I)



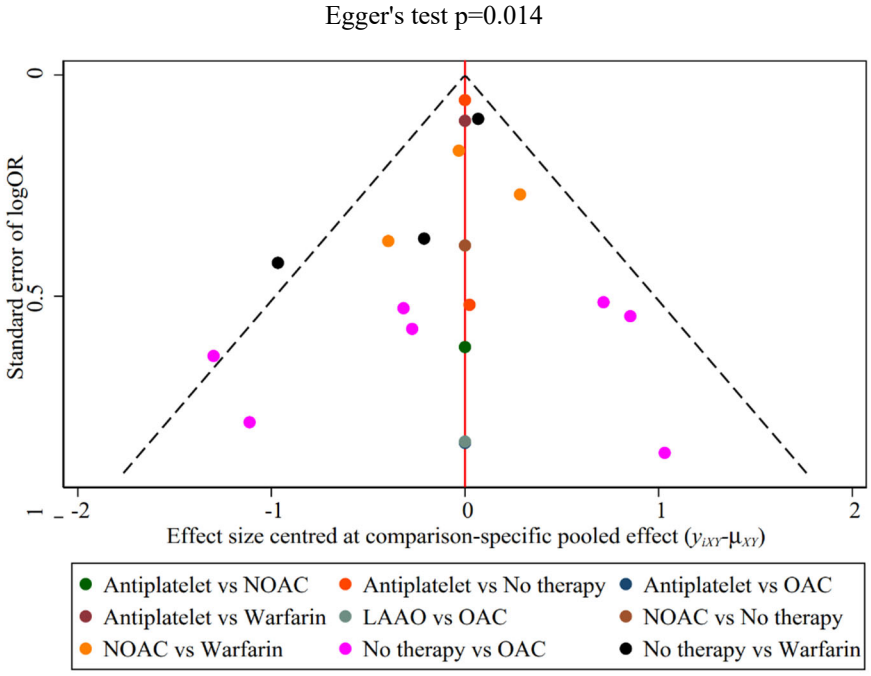
Study1:Satoshi Suda,2023,**2**:Wu,Victor Chien-Chia,2021,**3**:Alireza Sadighi,2020,**4**:Peter Brønnum Nielsen,2019,**5**: Mohammed K. Badi,2019,**6**: Loris Poli,2018,**7**: Peter Brønnum Nielsen,2017,**8**: Gye Young Park,2016,**9**: Chuan-Tsai Tsai,2020,**10**: So-Ryoung Lee,2020,**11**: Sylvie Perreault,2019,**12**: Tze-Fan Chao,2016,**13**: Kuramatsu JB,2015,**14**: Jens Erik Nielsen-Kudsk1,2017.

Supplementary Figure S1B. RoB 2 Cochrane tool for assessing the risk of bias in randomized clinical trials

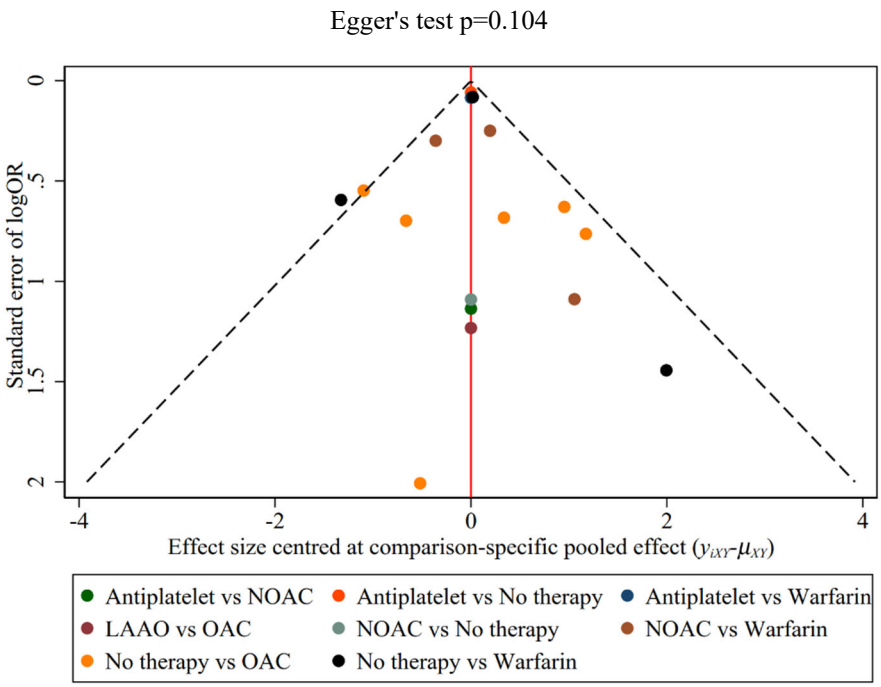


Supplementary Figure S2. Publication Bias Assessment

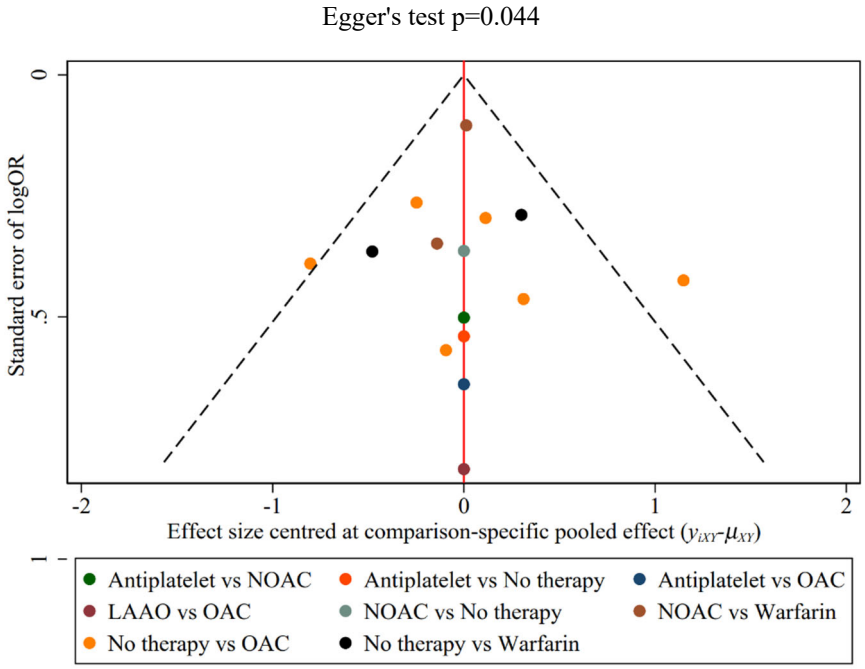
Supplementary Figure S2A Thromboembolism



Supplementary Figure S2B Recurrent intracranial hemorrhage



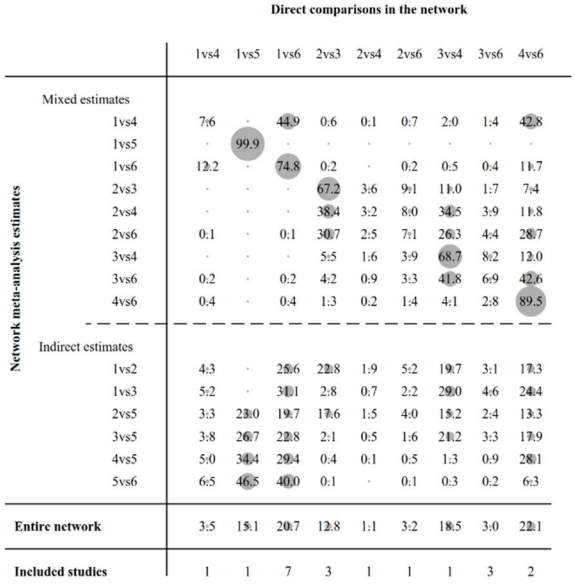
Supplementary Figure S2C All-cause death



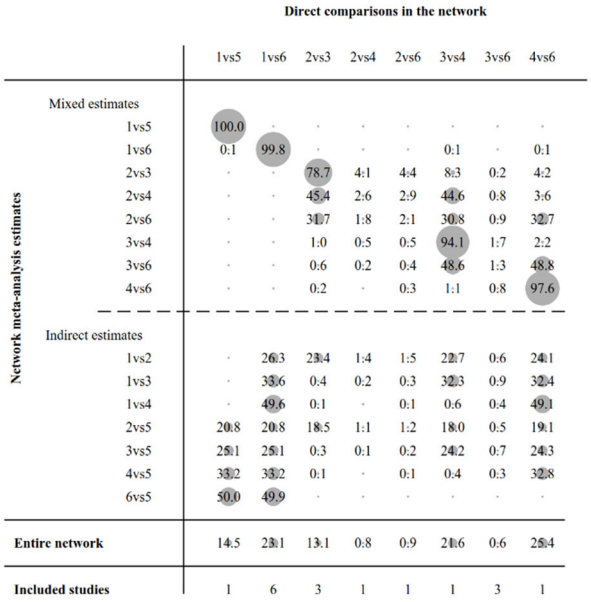
The horizontal axis displays the study's effect quantity. The standard error of the logOR is represented on the vertical. The red line indicates the amount of combined effect. The oblique dotted lines on both sides represent 95% confidence intervals.

Supplementary Figure S3 Direct and indirect evidence proportion for each network estimate

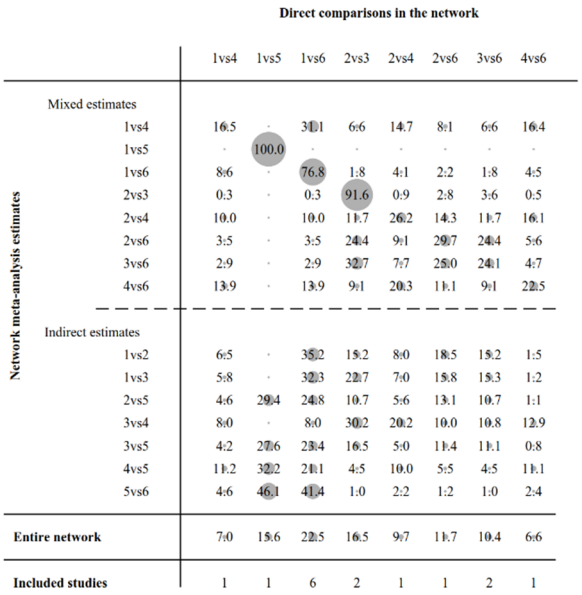
Supplementary Figure S3A Thromboembolism



Supplementary Figure S3B Recurrent intracranial hemorrhage



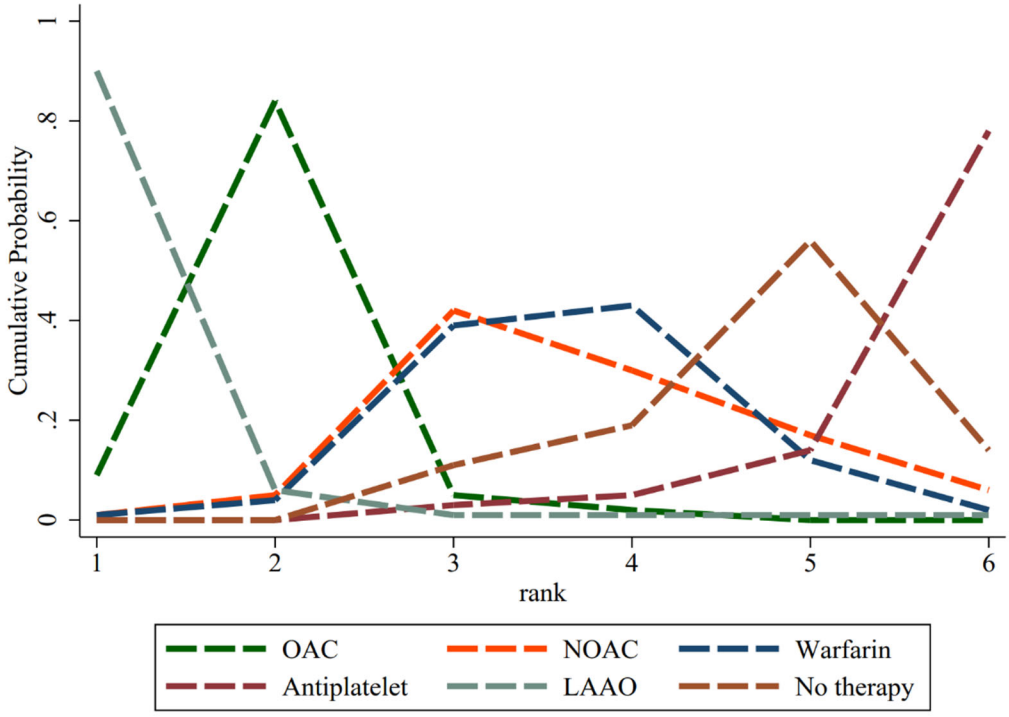
Supplementary Figure S3C All-cause death



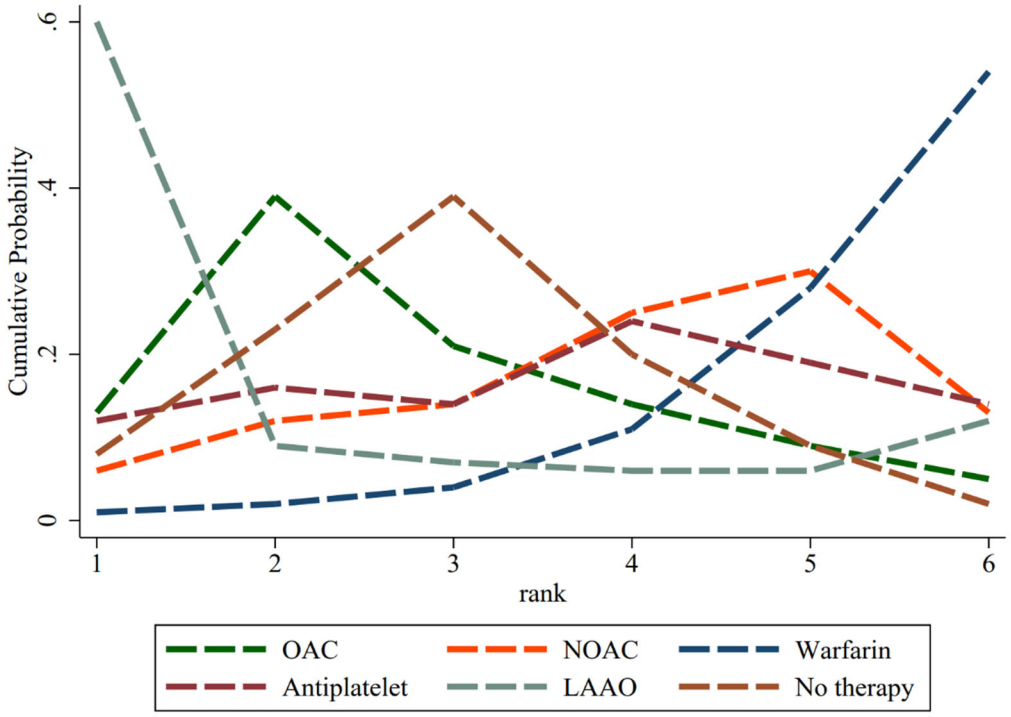
1vs4:OAC vs Antiplatelet,1vs5:OAC vs LAAO ,1vs6:OAC vs No therapy ,2vs3NOACvsWarfarin 2vs4NOAC vs Antiplatelet ,2vs6NOAC vs No therapy ,3vs4:Warfarin vs Antiplatelet,3vs6:Warfarin vs No therapy,4vs6:Antiplatelet vs No therapy.

Supplementary Figure S4 Cumulative probability ranking plots of different intervention strategies for each outcome

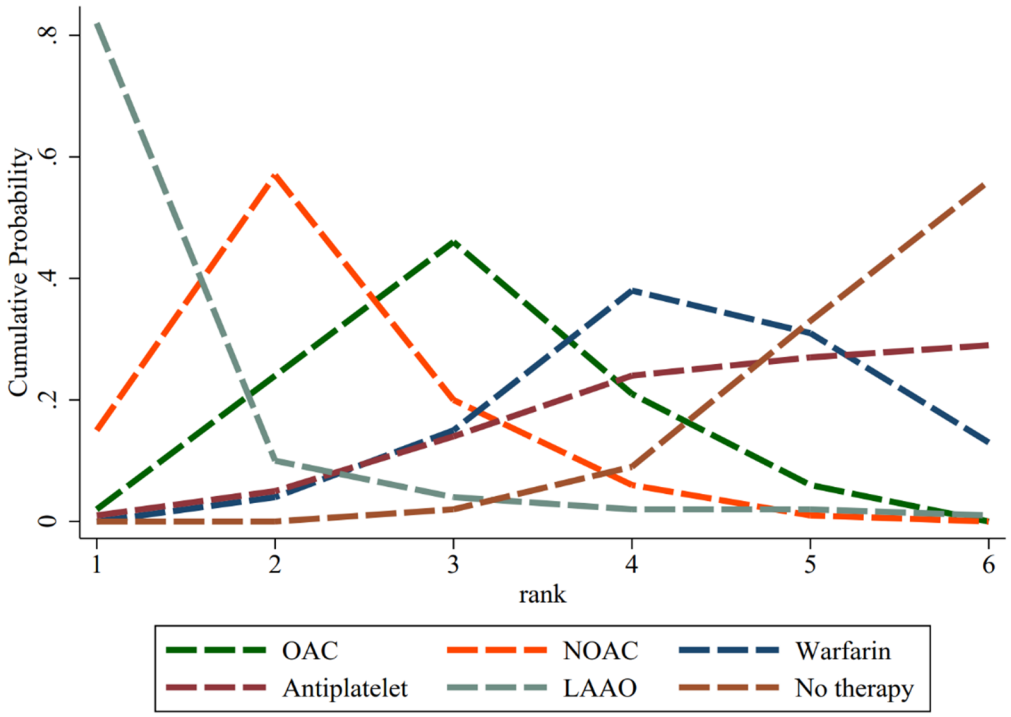
Supplementary Figure S4A Cumulative probability ranking plots of Thromboembolism



Supplementary Figure S4B Cumulative probability ranking plots of recurrent intracranial hemorrhage

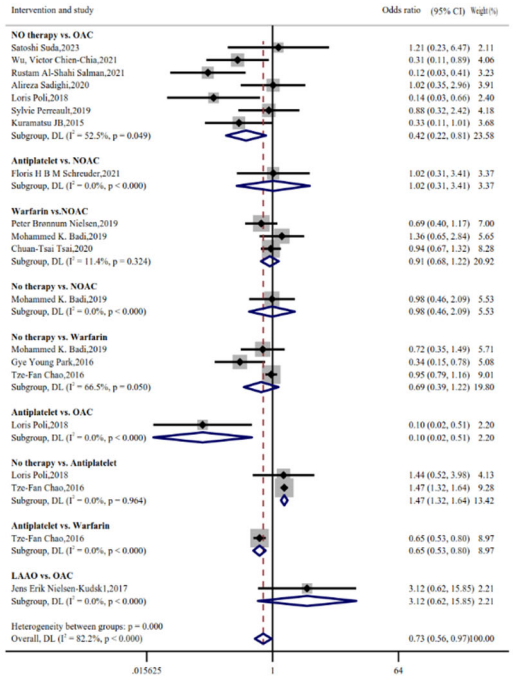


Supplementary Figure S4C Cumulative probability ranking plots of all-cause death

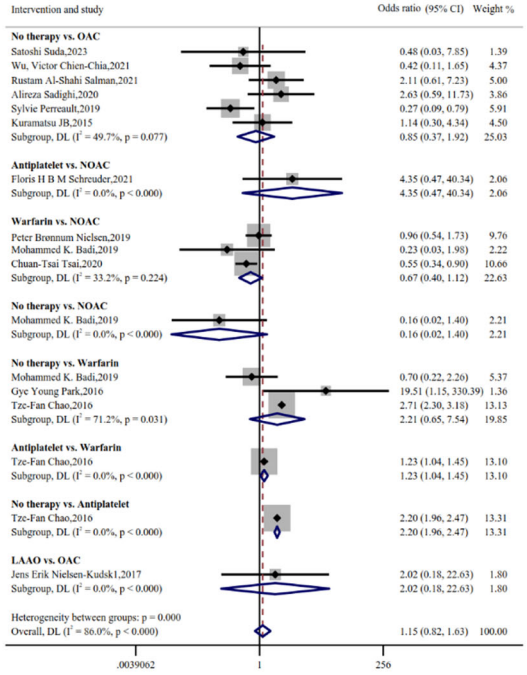


Supplementary Figure S5 Direct comparison of forest plots for each outcome

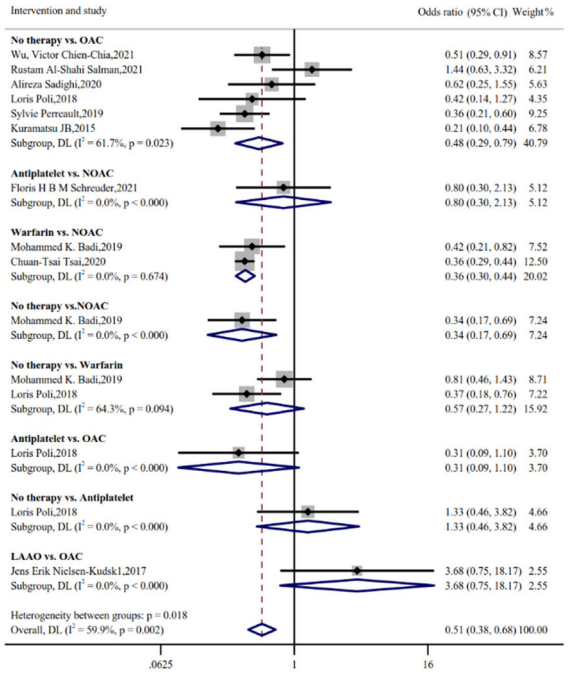
Supplementary Figure S5A Forest plot for direct comparison of thromboembolism



Supplementary Figure S5B Forest plot for direct comparison of recurrent intracranial hemorrhage

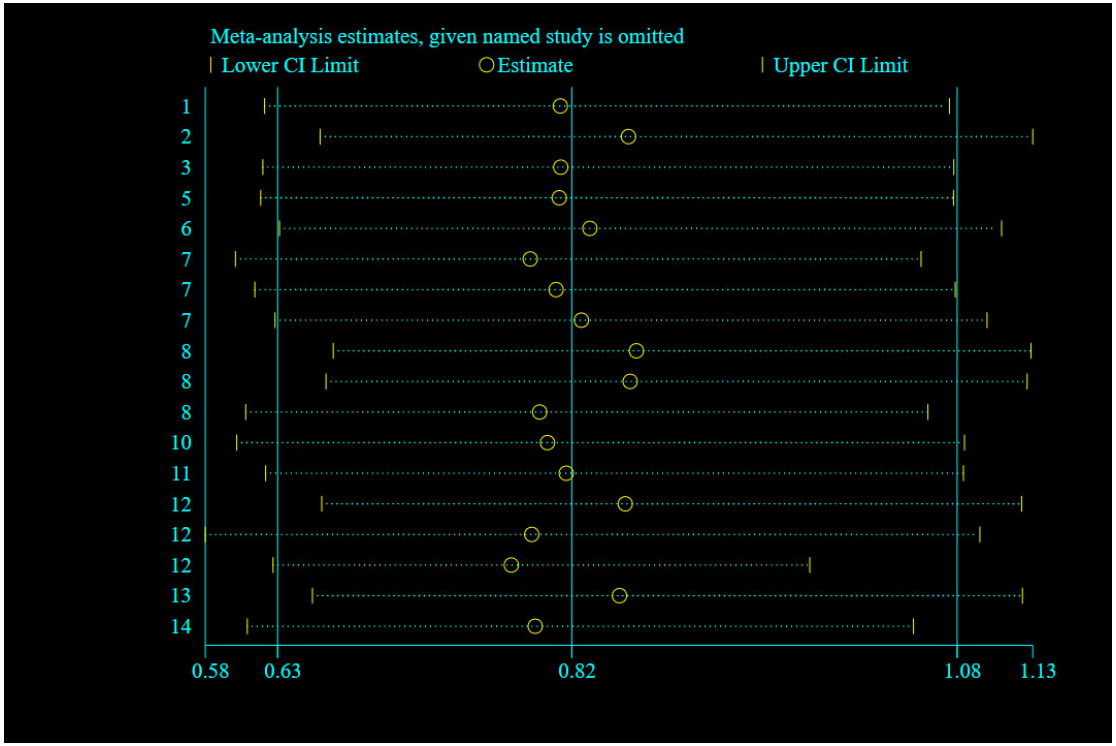


Supplementary Figure S5C Forest plot for direct comparison of all-cause death



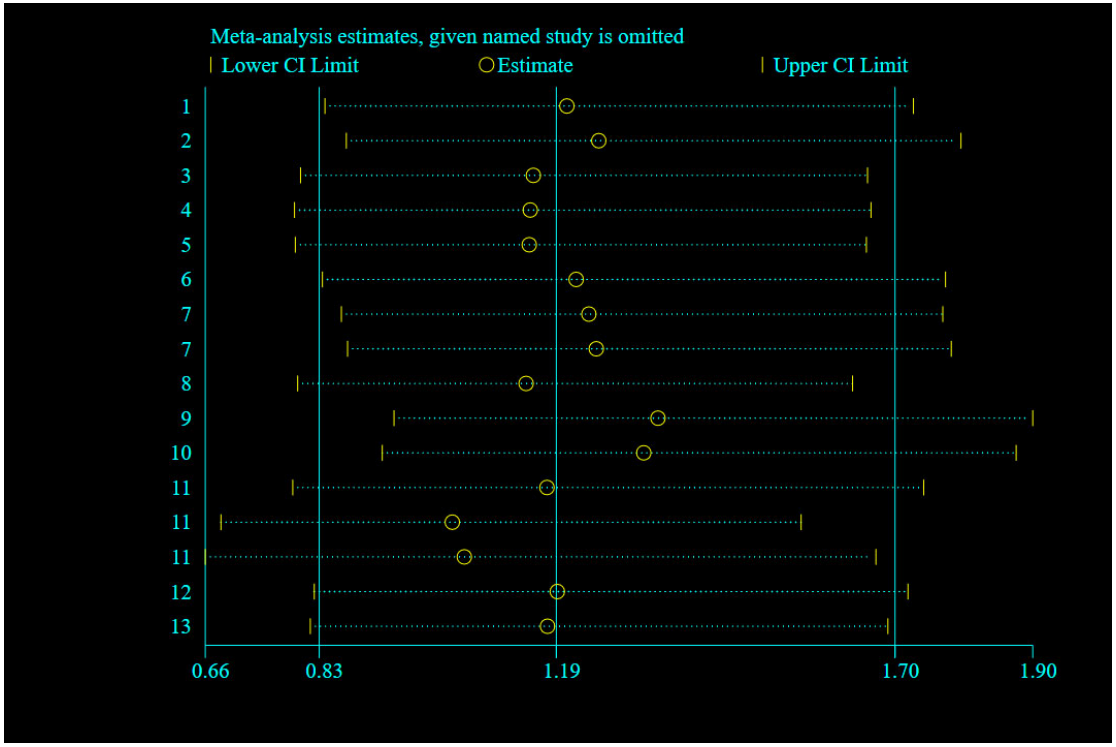
Supplementary Figure S6 Sensitivity analysis

Supplementary Figure S6A Sensitivity analysis of thromboembolism



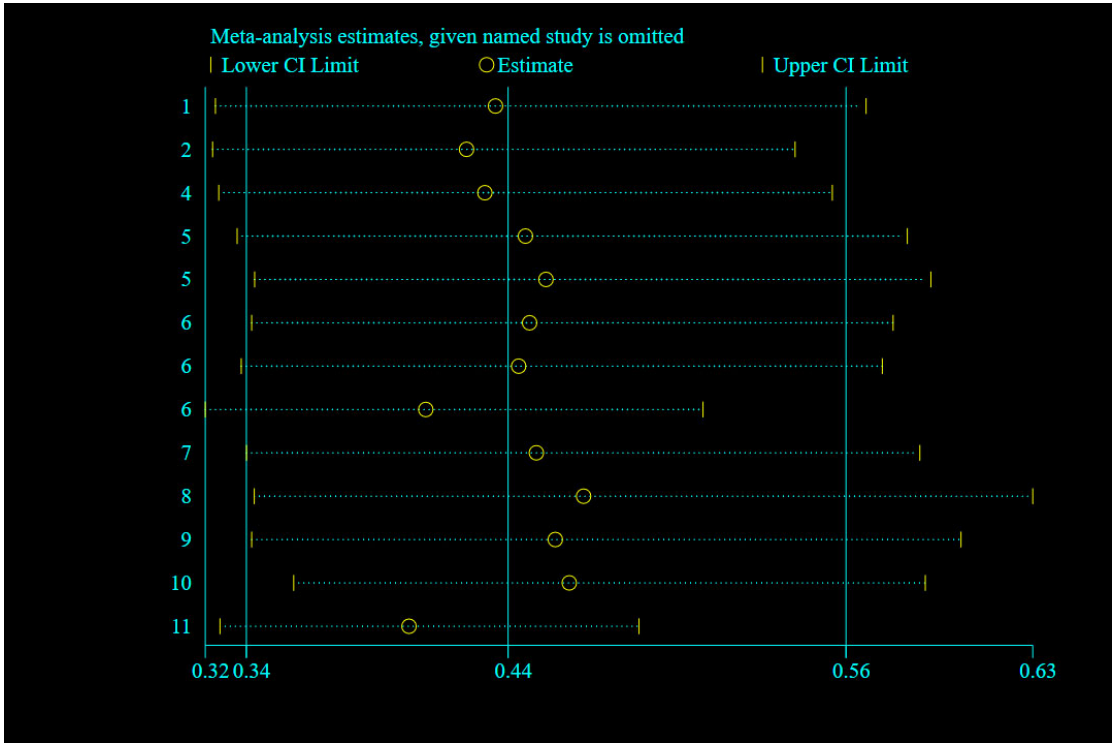
1:Satoshi Suda,2023,**2:**Wu,Victor Chien-Chia,2021,**3:**Floris H B M Schreuder,2021,**5:**Alireza Sadighi,2020,**6:**Peter Brønnum Nielsen,2019,**7:**Mohammed K. Badi,2019, **8:**Loris Poli,2018,**10:**Chuan-Tsai Tsai,2020,**11:**Sylvie Perreault,2019,**12:**Tze-Fan Chao,2016,**13:**Kuramatsu JB,2015,**14:**Jens Erik Nielsen-Kudsk1,2017

Supplementary Figure S6B Sensitivity analysis of recurrent intracranial hemorrhage



1:Satoshi Suda,2023,**2:**Wu,Victor Chien-Chia,2021,**3:**Floris H B M Schreuder,2021,**4:** Rustam Al-Shahi Salman,2021,**5:**Alireza Sadighi,2020,**6:**Peter Brønnum Nielsen, 2019,**7:**Mohammed K. Badi,2019,**8:**Gye Young Park,2016,**9:**Chuan-Tsai Tsai,2020,**10:**Sylvie Perreault,2019,**11:**Tze-Fan Chao,2016,**12:**Kuramatsu JB,2015,**13:**Jens Erik Nielsen-Kudsk1,2017

Supplementary Figure S6C Sensitivity analysis of all-cause death



1:Wu,Victor Chien-Chia,2021,**2:**Floris H B M Schreuder,2021,**4:**Alireza Sadighi,2020,**5:**Mohammed K. Badi,2019,**6:**Loris Poli,2018,**7:**Gye Young Park,2016,**8:**Chuan-Tsai Tsai,2020,**9:**Sylvie Perreault,2019,**10:**Kuramatsu JB,2015,**11:**Jens Erik Nielsen-Kudsk1,2017.

Supplementary Methods S1. PRISMA Main Checklist

Topic	No.	Item	The location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Pag.1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	Pag.2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pag.3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pag.3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pag.3-4
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pag.4, Supplementary References
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary material 1 and Figure 1
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.	Pag.4
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.	Pag.4
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.	Pag.4

Topic	No.	Item	The location where item is reported
	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.	Pag.4, Table1
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.	Pag.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.	Pag. 4-5
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)).	Pag.4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pag. 4-5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pag. 4-5
	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.	Pag. 4-5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pag. 4-5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Pag. 4-5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page. 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.	Pag.5, Fig.1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	NA
Study characteristics	17	Cite each included study and present its characteristics.	Table 1, Supplementary Reference
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary Figure 1

Topic	No.	Item	The location where item is reported
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimates and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Pag.5-6, Figure2-Figure5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pag.5-6
	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.	Pag. 5-6
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pag. 6
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Supplementary Figure 6
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Pag. 6
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pag. 7-8
	23b	Discuss any limitations of the evidence included in the review.	Pag. 7-8
	23c	Discuss any limitations of the review processes used.	Pag.8
	23d	Discuss implications of the results for practice, policy, and future research.	Pag.8-9
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.	Pag. 3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pag. 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Pag.3

Topic	No.	Item	The location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pag.9
Competing interests	26	Declare any competing interests of review authors.	Pag.9
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.	Pag.9

Supplementary Methods S2. PRISMA Abstract Checklist

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

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