Supplementary Material

Contents

Search history	2
Study acronyms	3
Supplementary Figure 1. Subgroup analysis according to DOAC treatment groups and risk of bias assessment.	6
Supplementary Figure 2. Funnel plot of publication bias analysis	7
Supplementary Table 1 Patient characteristics of the included trials	8
Supplementary Table 2 Fixed effects model results of indirect comparisons of the different oral anticoagulants	.0
Sensitivity analyses1	3
Supplementary Table 31	4
Supplementary Figure 41	6
Supplementary table 4. Leave-one-out network excluding the data from the Randomized Evaluation of Long Term Anticoagulant Therapy with Dabigatran Etexilate (RE-LY) trial	.7

Search history

((rivaroxaban OR apixaban OR dabigatran OR edoxaban) OR (pulmonary AND embolism) OR ((vein OR venous) AND (thrombosis OR thromboses OR thrombembolism OR thromboembolism)) OR (atrial AND (fibrillation OR flutter)) OR thromboprophylaxis OR anticoagulation OR prophylaxis OR prevention) AND (rivaroxaban OR apixaban OR dabigatran OR edoxaban)

Study acronyms

AMPLIFY: Apixaban for the Initial Management of Pulmonary Embolism and Deep-Vein Thrombosis as First-Line Therapy

APPRAISE-2: Apixaban for Prevention of Acute Ischemic Events 2

ARISTOTLE: Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation

ATLAS ACS 2-TIMI 51: Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome–Thrombolysis in Myocardial Infarction 51

AUGUSTUS: Aspirin Placebo in Patients with Atrial Fibrillation and Acute Coronary Syndrome or Percutaneous Coronary Intervention

AVARROES: Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment

COMMANDER HF: A Study to Assess the Effectiveness and Safety of Rivaroxaban in

Reducing the Risk of Death, Myocardial Infarction, or Stroke in Participants with Heart Failure

and Coronary Artery Disease Following an Episode of Decompensated Heart Failure

COMPASS: Cardiovascular Outcomes for People Using Anticoagulation Strategies

EINSTEIN-DVT: Oral Direct Factor Xa Inhibitor Rivaroxaban in Patients With Acute Symptomatic Deep Vein Thrombosis

EINSTEIN-CHOICE: Reduced-dosed Rivaroxaban in the Long-term Prevention of Recurrent Symptomatic Venous Thromboembolism

EINSTEIN-PE: Oral Direct Factor Xa Inhibitor Rivaroxaban in Patients With Acute Symptomatic Pulmonary Embolism

EMANATE: Eliquis evaluated in acute cardioversion compared to usual treatments for anticoagulation in subjects with atrial fibrillation

ENGAGE-AF – TIMI 48: Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48

ENSURE-AF: Edoxaban vs. Warfarin in Subjects Undergoing Cardioversion of Nonvalvular Atrial Fibrillation

Hokusai VTE: Comparative Investigation of Low Molecular Weight Heparin/Edoxaban Tosylate Versus Heparin/Warfarin in the Treatment of Symptomatic Deep-Vein Blood Clots and/or Lung Blood Clots

J-ROCKET AF: Japanese Rivaroxaban Once daily oral direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation MANAGE: Management of Myocardial Injury After Noncardiac Surgery

NAVIGATE ESUS: New Approach Rivaroxaban Inhibition of Factor Xa in a Global Trial versus ASA to Prevent Embolism in Embolic Stroke of Undetermined Source

PIONEER AF: A Study Exploring Two Strategies of Rivaroxaban and One of Oral Vitamin K Antagonist in Patients With Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention

RE-COVER: Efficacy and Safety of Dabigatran Compared to Warfarin for 6 Month Treatment of Acute Symptomatic Venous Thromboembolism

RE-COVER II: Phase III Study Testing Efficacy & Safety of Oral Dabigatran Etexilate vs Warfarin for 6 m Treatment for Acute Symp Venous Thromboembolism

RE-DUAL: Evaluation of Dual Therapy With Dabigatran vs. Triple Therapy With Warfarin in Patients With AF That Undergo a PCI With Stenting

RE-LY: Randomized Evaluation of Long-Term Anticoagulation Therapy

RE-MEDY: Secondary Prevention of Venous Thrombo Embolism

RE-SONATE: Twice-daily Oral Direct Thrombin Inhibitor Dabigatran Etexilate in the Long Term Prevention of Recurrent Symptomatic VTE RE-SPECT ESUS: Dabigatran Etexilate for Secondary Stroke Prevention in Patients With Embolic Stroke of Undetermined Source

ROCKET-AF: An Efficacy and Safety Study of Rivaroxaban With Warfarin for the Prevention of Stroke and Non-Central Nervous System Systemic Embolism in Patients With Non-Valvular Atrial Fibrillation

X-VeRT: Explore the Efficacy and Safety of Once-daily Oral Rivaroxaban for the Prevention of Cardiovascular Events in Subjects With Nonvalvular Atrial Fibrillation Scheduled for Cardioversion

Supplementary Figure 1. Subgroup analysis according to DOAC treatment groups and risk of bias assessment.

Abbreviations: CI: confidence interval; M-H: Mantel-Haenszel. df: degree of freedom; For resolution of study acronyms please refer to the Supplementary data.

Study or Subaroup	Experin	nental Total	Cont	trol Total	Weight	Risk Ratio	Risk Ratio	Risk of Bias
1.2.1 Dabigatran	Events	Total	Events	Total	weight	M-1, Randoni, 55% Ci	M=1, Kaluolii, 55% Cl	ABCDEIG
MANAGE	35	877	43	877	2.5%	0.81 [0.53, 1.26]	ı →	@?@@@@@
RE-COVER	3	1273	2	1266	0.2%	1.49 [0.25, 8.91]	i — 	9999999
RE-COVER II	4	1279	2	1289	0.2%	2.02 [0.37, 10.99]	I — — — — — — — — — — — — — — — — — — —	
RE-DUAL PCI	70	1744	51	1745	3.7%	1.37 [0.96, 1.96]	I •	
RE-LY	175	12091	75	6022	5.8%	1.16 [0.89, 1.52]	· +	
RE-MEDY	13	1430	3	1426	0.3%	4.32 [1.23, 15.13]		444444
RE-SONATE	1	681	1	662	0.1%	0.97 [0.06, 15.51]		444444
RE-SPECT ESUS	23	2695	18	15982	1.3%	1.28 [0.69, 2.36]		444444
Total events	274	22070	195	15502	14.0/0	1.20 [0.57, 1.45]	•	
Heterogeneity Tau ² =	0.01° Chi ²	= 8 15	df = 7 (P)	= 0.321	$ ^2 = 14\%$	6		
Test for overall effect:	Z = 1.68 (P = 0.09)	0.22,	,	·		
	,							
1.2.2 Apixaban								
AMPLIFY	4	2691	2	2704	0.2%	2.01 [0.37, 10.96]	I — — —	
APPRAISE-2	182	3705	194	3687	9.0%	0.93 [0.77, 1.14]	I 4	
ARISTOTLE	90	9120	102	9081	5.3%	0.88 [0.66, 1.16]		444444
AUGUSTUS	72	2290	80	2259	4.5%	0.89 [0.65, 1.21]		4444444
AVERRUES	24	2808	28	2791	1.7%			
Subtotal (95% CI)	2	21367	T	21269	20.9%	0.91 [0.79, 1.05]		
Total events	374	2150.	407	21205	2013/0	0101 [011 0, 1100]	' *	
Heterogeneity Tau ² =	0.00: Chi ²	= 1.45	df = 5 (P	= 0.921	$ ^2 = 0\%$			
Test for overall effect:	Z = 1.30 (P = 0.19	un 5 (. 1	0.52,	,			
	,							
1.2.3 Edoxaban								
ENGAGE AF-TIMI 48	302	14069	141	7036	9.0%	1.07 [0.88, 1.31]	I +	
ENSURE-AF	2	1095	3	1104	0.2%	0.67 [0.11, 4.01]		666666
Hokusai-VTE	20	4118	13	4122	1.1%	1.54 [0.77, 3.09]		
Subtotal (95% CI)		19282		12262	10.2%	1.09 [0.91, 1.32]	I ∳	
Total events	324	4.55	157		. 17			
Test for everall effect:	0.00, Chir 7 = 0.02 /	= 1.20, P = 0.25	ui = 2 (P	= 0.53)	, 1- = 0%			
restitut üverali errett.	2 = 0.95 (r = 0.55	,					
1.2.4 Rivaroxaban								
ATLAS ACS 2-TIMI 51	179	5115	229	5113	9.4%	0.78 [0.65, 0.95]	-	GGGGGGG
COMPASS	182	9117	205	9126	9.0%	0.89 [0.73, 1.08]	-+	•••••
EINSTEIN CHOICE	1	2234	4	1131	0.1%	0.13 [0.01, 1.13]	I	000000
EINSTEIN DVT	6	1718	2	1711	0.2%	2.99 [0.60, 14.78]		
EINSTEIN PE	15	2412	21	2405	1.2%	0.71 [0.37, 1.38]		99?999
J-ROCKET AF	3	637	1	637	0.1%	3.00 [0.31, 28.76]		asaaaaas
NAVIGALE ESUS	17	3609	23	3604	1.3%	0.74 [0.40, 1.38]		
PIONEER AF-PUI	101	7111	126	7175	1.4% 6.1%	0.91[0.49, 1.67]		
X-VeRT	101	978	120	497	0.1%	0.60 [0.62, 1.04]		
Subtotal (95% CI)	-	33625	1	32039	28.8%	0.82 [0.74, 0.92]	•	
Total events	524		633				· · ·	
Heterogeneity: Tau ² =	0.00; Chi ²	= 7.98,	df = 9 (P	= 0.54)	$ ^2 = 0\%$			
Test for overall effect:	Z = 3.30 (P = 0.00	10)					
1.2.5.0								
1.2.5 Rivaroxaban va	scular						.	
ATLAS ACS 2-TIMI 51	205	5114	229	5113	9.9%	0.90 [0.74, 1.08]		444444
COMMANDER HE	98	2507	118	2515	6.0%	0.83 [0.64, 1.08]		444444
COMPASS DIONEER AS DO	178	9152	205	9126 EOF	5.9% 1.7%	0.87 [0.71, 1.06]		
Subtotal (95% CI)	17	17477	21	17449	26.1%	0.87 [0.77, 0.98]	▲	
Total events	498		573			[· · · · · · · · · · · · · · · · · · ·	
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.27.	df = 3 (P	= 0.97)	; l ² = 0%			
Test for overall effect:	Z = 2.34 (P = 0.02) .					
T				00000	100 000	0.00 10.00 1.00		
Total (95% CI)		113821		99001	100.0%	0.93 [0.86, 1.00]	•	
lotal events	2044		1965			40/	, , <u> </u> .	
Heterogeneity. Tau ² =	0.01; Chi ⁴	= 34.79	, dt = 30	P = 0.2	$(5); 1^{2} = 1$	14%	0.01 0.1 1 10	100
Test for overall effect:	z = 2.08 (r = 0.04	J 1 df	1/0 ^	0000 12	70.4%	Favours [experimental] Favours [control]
Rick of hiss leased	arences. Ch	n = 13.3	• 1, ul = 4	т (г = U.	009), F =	70.4%		
(A) Random sequence	generation	(selection	n hias)					
(B) Allocation concealm	ent (select	ion bias)						
(C) Blinding of participa	ants and p	ersonnel	performa	ance bias)			
(D) Blinding of outcome	e assessme	nt (detec	tion bias)					
(E) Incomplete outcome	e data (attr	ition bias)					

(F) Selective reporting (reporting bias)

(G) Other bias

Supplementary Figure 2. Funnel plot of publication bias analysis



Abbreviations: SE: standard error; RR: risk ratio

Supplementary Table 1 Patient characteristics of the included trials.

Hypercholesterolemia defined as hypercholesterolemia and statin use. Abbreviations: DM: diabetes mellitus; NA: not available. For resolution of

study acronyms please refer to the Supplementary data.

Study name/ First author (publication year)	Mean age (year)	Male	DM	Hypercholesterolaemia (%)	Hypertension (%)
AMPLIFY/G. Agnelli (2013)	57.2/56.7	58.3/59.1	NA	NA	NA
APPRAISE-2/ J. H. Alexander (2011)	67/67	67.4/68.3	48.7/47.0	NA	NA
ARISTOTLE/ C.B. Granger (2011)	70/70	64.5/65	25/24.9	45.0/45.1	87.3/87.6
ATLAS ACS 2-TIMI 51/ J. L. Mega (2012)	61.8/61.9/61.5	74.9/74.2/75.0	32.3/31.8/31.8	48.3/49.1/48.2	67.1667.6/67.5
AUGUSTUS/ R. D. Lopes (2019)	70.4/70.9	69.9/71.1	36.5/36.2	NA	88.6/88
AVARROES/ S. J. Connolly (2011)	70/70	59/58	19/20	NA	86/87
COMMANDER HF/ F. Zannad (2018)	66.5/66.3	78.0/76.2	40.8/40.9	NA	75.7/75.0
COMPASS/ J. W. Eikelboom (2017)	68.3/68.2/68.2	77.5/78.4/78.2	37.7/37.5/38.1	NA	75.5/75.1/75.4
EINSTEIN- DVT/ R. Bauersachs (2010)	55.8/56.4	57.4/56.3	NA	NA	NA
EINSTEIN-CHOICE/ J. I. Weitz (2017)	57.9/58.8	54.4/55.0	NA	NA	NA
EINSTEIN-PE/ H. R. Büller (2012)	57.9/57.5	54.1/51.7	NA	NA	NA
EMANATE/ M. D. Ezekowitz (2018)	64.5/64.7	66.5/67.1	18.7/20.5	NA	64.4/65.9
ENGAGE AF - TIMI 48/ R. P. Giugliano (2013)	72/72/72	62.5/62.1/61.2	35.8/35.4/36.2	NA	93.6/93.7/93.5
ENSURE-AF/ A. Goette (2016)	64.3/64.2	66/65	20/18	NA	78/78
Hokusai-VTE/ Hokusai investigators (2013)	55.7/55.9	57.3/57.2	NA	NA	NA
J-ROCKET AF/ M. Hori (2012)	71.0/71.2	82.9/78.2	39.0/37.1	NA	79.5/79.5
MANAGE/ Manage investigators (2018)	70/70	52/51	NA	NA	NA
NAVIGATE ESUS/ R. G. Hart (2018)	66.9/66.9	62/61	25/25	NA	77/78
PIONEER AF-PCI/ C.M. Gibson (2016)	70.4/70.0/69.9	74.5/75.5/73.4	NA	NA	NA
RE-COVER/ S. Schulman (2009)	56/55	58/58.9	NA	NA	NA

RE-COVER II/ S. Schulman (2014)	54.7/55.1	61.0/60.2	NA	NA	NA
RE-DUAL/ C. P. Cannon (2017)	71.5/71.7 68.6/68.8	74.2/76.5 77.6/77.7	36.9/37.9 34.1/39.7	NA	NA
RE-LY/ S. J. Connolly (2009)	71.4/71.5/71.6	64.3/63.2/63.3	23.4/23.1/23.4	44.9/43.9/44.4	78.8/78.9/78.9
RE-MEDY/ S. Schulman (2013)	55.4/53.9	60.9/61.1	10.5/7.6	NA	NA
RE-SONATE/ S. Schilman (2013)	56.1/55.5	65.9/65.0	8.4/7.6	NA	NA
RE-SPECT ESUS/ H. C. Diener (2019)	64.5/63.9	62.9/63.4	21.7/23.7	56.9/56.0	74.1/73.7
ROCKET AF/ M. R. Patel (2011)	73/73	60.3/60.3	40.4/39.5	NA	NA
X-VeRT/ R. Cappato (2014)	64.9/64.7	72.6/73.1	20.3/20.5	NA	65.0/68.7

Supplementary Table 2 Fixed effects model results of indirect comparisons of the different oral anticoagulants.

League tables shows the risk ratios (RR) and the 95% credible interval (CrI) of the different oral anticoagulants in a fixed effects model for myocardial infarction (Panel A), mortality (Panel B), and major bleeding (Panel C). RR <1 means that the top left treatment (Treatment 1) is better. * marks the comparisons where the CrI did not overlap the line of equivalence. Abbreviation: VKA: Vitamin K antagonist

Rivaroxaban			А	Treatment 1			
0.94 (0.82 – 1.08)	Rivaroxaban vascular			Risk Ratio (Credible interval) for Myocardial infarction	Treatment 2		
0.90 (0.74 – 1.09)	0.96 (0.79 – 1.17)	Apixaban					
0.85 (0.72 – 1.01)	0.90 (0.74 – 1.09)	0.94 (0.79 – 1.12)	VKA				
0.83 (0.70 – 0.98)*	0.88 (0.74 – 1.04)	0.92 (0.73 – 1.15)	0.97 (0.78 – 1.21)	Aspirin			
0.79 (0.68 – 0.92)*	0.84 (0.73 – 0.97)*	0.88 (0.74 – 1.04)	0.93 (0.78 – 1.12)	0.96 (0.79 – 1.17)	Placebo		
0.77 (0.60 – 1.00)	0.82 (0.63 – 1.08)	0.86 (0.66 – 1.11)	0.91 (0.75 – 1.10)	0.94 (0.70 – 1.25)	0.98 (0.75 – 1.27)	Edoxaban	
0.69 (0.55 – 0.87)*	0.74 (0.58 – 0.94)*	0.77 (0.61 – 0.97)*	0.82 (0.68 – 0.98)*	0.84 (0.65 – 1.08)	0.87 (0.69 – 1.10)	0.89 (0.68 – 1.17)	Dabigatran

Rivaroxaban vascular			В	Treatment 1			
0.90 (0.73 – 1.09)	Apixaban		_	Risk Ratio (Credible interval) for Mortality	Treatment 2		
0.88 (0.72 – 1.08)	0.99 (0.82 – 1.18)	Dabigatran		_			
0.88 (0.69 – 1.13)	0.99 (0.79 – 1.23)	1.00 (0.81 – 1.24)	Edoxaban				
0.88 (0.75 – 1.02)	0.99 (0.81 – 1.18)	1.00 (0.82 – 1.21)	1.00 (0.78 – 1.26)	Placebo			
0.86 (0.73 – 1.00)	0.96 (0.80 – 1.15)	0.97 (0.81 – 1.17)	0.97 (0.78 – 1.21)	0.97 (0.83 – 1.17)	Rivaroxaban		
0.82 (0.69 – 0.98)*	0.92 (0.76 – 1.11)	0.93 (0.77 – 1.14)	0.93 (0.73 – 1.19)	0.93 (0.77 – 1.15)	0.96 (0.82 – 1.12)	Aspirin	
0.81 (0.68 – 0.97)*	0.90 (0.79 – 1.05)	0.92 (0.81 – 1.06)	0.92 (0.78 – 1.09)	0.92 (0.77 – 1.11)	0.94 (0.82 – 1.10)	0.99 (0.83 – 1.18)	VKA

Placebo			С	Treatment 1			
0.80 (0.46 – 1.39)	Aspirin		_	Risk Ratio (Credible interval) for Major bleeding	Treatment 2		
0.66 (0.42 – 1.05)	0.83 (0.51 – 1.36)	Dabigatran					
0.63 (0.37 – 1.06)	0.79 (0.47 – 1.31)	0.95 (0.59 – 1.51)	Apixaban				
0.51 (0.32 – 0.84)	0.64 (0.39 – 1.09)	0.77 (0.46 – 1.30)	0.81 (0.47 – 1.43)	Rivaroxaban vascular		_	
0.50 (0.25 – 1.00)	0.63 (0.31 – 1.25)	0.76 (0.40 – 1.40)	0.80 (0.41 – 1.52)	0.98 (0.48 – 1.95)	Edoxaban		
0.39 (0.24 – 0.63)*	0.49 (0.32 – 0.75)*	0.59 (0.38 – 0.90)*	0.63 (0.39 – 0.99)*	0.77 (0.49 – 1.17)	0.78 (0.42 – 1.45)	Rivaroxaban	
0.35 (0.22 – 0.56)*	0.45 (0.28 – 0.69)*	0.54 (0.38 – 0.74)*	0.57 (0.38 – 0.82)*	0.69 (0.43 – 1.09)	0.71 (0.42 – 1.19)	0.90 (0.65 – 1.26)	VKA

Sensitivity analyses

Regarding the clinical background 14 studies included patients with high risk for cerebrovascular event including 12 trials in atrial fibrillation (AF) and two trials of embolic stroke of undetermined source (ESUS). Nine studies were performed in patients with deep vein thrombosis and/or pulmonary embolism and eight studies included patient with coronary disease or with high risk for coronary event. (Table 1.) The included studies used different definitions for myocardial infarction (MI). Five studies used biomarker based definitions for MI that is compatible with the universal definition of MI (2012 version)(Definition 1.). Four studies defined MI as $2 \ge$ of the followings: specific symptoms; ECG abnormalities, elevated cardiac biomarkers (Definition 2.) while in 19 studies investigator reported MI events were reported without further definitions (Definition 3.).

Subgroup analysis of studies of the different setting did show consistent results with the main findings of the full analysis. (Supplementary Table 3.) Studies using Definition 1. for MI did not composed a closed network. Both the subgroup analyses of studies using the other two definitions as well as the leave-out analyses of either definition showed consistent results as well. Similarly, ranking of the different treatments were not substantially effected in the subgroup analyses (Supplementary Figure 4.)

Abbreviation: NA: not available

Supplementary Table 3

Abbreviation: VKA: Vitamin K antagonist; ESUS: embolic stroke of undetermined source; AF: atrial fibrillation; NA: not available

	number of studies	Rivaroxaban vs Dabigatran	Rivaroxaban vascular vs Dabigatran	Apixaban vs Dabigatran	VKA vs Dabigatran	Rivaroxaban vs Placebo	Rivaroxaban vascular vs Placebo
Full analysis	28	0.69* (0.53 – 0.89)	0.73 (0.56 – 0.96)	0.76 (0.58 – 0.99)	0.81* (0.65 – 0.98)	0.79* (0.65 – 0.94)	0.84* (0.70 – 0.99)
Clinical setting							
Stroke prevention (ESUS or AF)	14	0.66* (0.45 – 0.96)	0.60 (0.29 – 1.17)	0.71 (0.49 – 1.01)	0.79 (0.60 – 1.02)	NA	NA
Atrial fibrillation	12	0.61 (0.29 – 1.26)	0.67 (0.42 – 1.09)	0.71 (0.46 – 1.11)	0.80 (0.58 – 1.07)	NA	NA
Coronary disease (or high risk for coronary event)	8	0.69* (0.53 – 0.89)	0.73* (0.56 – 0.96)	0.76 (0.58 – 0.99)	0.81* (0.65 – 0.98)	0.79* (0.65 – 0.94)	0.84* (0.70 – 0.99)
Deep vein thrombosis / Pulmonary embolism	9	0.40 (0.05 – 4.62)	NA	0.80 (0.04 – 19.04)	0.36 (0.08 – 1.61)	0.40 (0.00 – 45.77)	NA
Myocardial infarction definitions							
Definition 1	5	-	-	-	-	-	-
Definition 2	4	NA	NA	NA	NA	0.46 (0.01 – 13.03)	NA
Definition 3	19	0.73 (0.46 – 1.09)	0.82 (0.47 – 1.26)	0.71 (0.43 – 1.05)	0.79 (0.52 – 1.05)	0.74 (0.49 – 1.03)	0.84 (0.52 – 1.15)

Definition 1&2	9	0.71 (0.16 – 5.92)	0.82 (0.15 – 12.40)	1.01 (0.17 – 14.28)	0.73 (0.22 – 2.56)	0.70 (0.09 – 3.78)	0.79 (0.18 – 3.84)
Definition 2&3	23	0.70* (0.49 – 0.97)	0.78 (0.51 – 1.12)	0.78 (0.55 – 1.08)	0.82 (0.59 – 1.07)	0.77* (0.58 – 0.99)	0.86 (0.61 – 1.12)
Definition 1&3	24	0.74 (0.54 – 1.00)	0.78 (0.57 – 1.07)	0.70* (0.51 – 0.95)	0.78* (0.62 – 0.96)	0.77* (0.61 – 0.95)	0.82* (0.67 – 0.99)

Supplementary Figure 4.

Plots showing the effect of the subgroup analyses on the ranking of the different treatment strategies as reflected by the Surface Under the Cumulative Ranking (SUCRA) values in the different subgroups. Abbreviations: CAD: coronary artery disease, AF: atrial fibrillation, ESUS: embolic stroke of undetermined source, DVT: deep vein thrombosis, PE: pulmonary embolism, R: rivaroxaban, Rv: rivaroxaban vascular, A: apixaban, VKA: vitamin K antagonist, As: aspirin, E: edoxaban, P: placebo, D: dabigatran.



Supplementary table 4. Leave-one-out network excluding the data from the Randomized Evaluation of Long Term Anticoagulant Therapy with Dabigatran Etexilate (RE-LY) trial

Abbreviation: VKA: vitamin K antagonist

Rivaroxaban				Treatment 1			
0.94 (0.79 – 1.11)	Rivaroxaban vascular		_	Risk Ratio (Credible interval) for Myocardial infarction	Treatment 2		
0.90 (0.72 – 1.15)	0.96 (0.76 – 1.24)	Apixaban		_			
0.86 (0.71 - 1.08)	0.92 (0.74 – 1.18)	0.96 (0.78 – 1.18)	VKA				
0.82 (0.65 – 0.99)	0.87 (0.69 – 1.08)	0.90 (0.68 – 1.17)	0.94 (0.71 – 1.21)	Aspirin			
0.78 (0.57 – 1.08)	0.83 (0.59 – 1.18)	0.86 (0.63 – 1.18)	0.90 (0.70 - 1.14)	0.96 (0.68 – 1.39)	Edoxaban		
0.78* (0.64 – 0.94)	0.84 (0.69 – 1.00)	0.87 (0.69 – 1.06)	0.90 (0.70 – 1.12)	0.96 (0.75 – 1.23)	1.00 (0.71 – 1.39)	Placebo	
0.66* (0.49 – 0.89)	0.71* (0.51 – 0.96)	0.73 (0.53 – 1.00)	0.76 (0.57 – 1.00)	0.81 (0.59 – 1.13)	0.85 (0.58 – 1.22)	0.85 (0.63 – 1.14)	Dabigatran