Supplements

18/4/2023

Efficacy and Safety of Therapeutic Interventions in acute pulmonary embolism: Systematic review and network meta-analysis

Syntaxes Used in Database Searches: EMBASE

No.	Query	Results
#18	((((('pulmonary thromboembolism':ti,ab,kw OR 'pulmonary artery thromboembolism':ti,ab,kw OR 'massive pulmonary embolism':ti,ab,kw OR 'submassive pulmonary embolism':ti,ab,kw OR 'acute pulmonary embolism':ti,ab,kw OR 'pulmonary embolism':ti,ab,kw OR 'bronchial vascular hypertrophy':ti,ab,kw OR 'intrapulmonary shunt':ti,ab,kw OR 'pulmonary artery filling defect':ti,ab,kw OR 'lung embolism':ti,ab,kw OR 'lung embolization':ti,ab,kw OR 'lung embolus':ti,ab,kw OR 'lung emboly':ti,ab,kw OR 'lung microembolism':ti,ab,kw OR 'lung microembolization':ti,ab,kw OR 'lung microembolus':ti,ab,kw OR 'lung thromboembolism':ti,ab,kw OR 'pulmonary embolization':ti,ab,kw OR 'pulmonary embolus':ti,ab,kw OR 'pulmonary microembolism':ti,ab,kw OR 'pulmonary thromboembolic disease':ti,ab,kw) OR ('lung embolism'/exp OR 'massive pulmonary embolism'/exp OR 'submassive pulmonary embolism'/exp OR 'acute pulmonary embolism'/exp OR 'pulmonary shunt'/exp)) AND (((embolectomy:ti,ab,kw OR 'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw) OR ('embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp)) OR (('antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw) OR ('fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp)))) AND (('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti) OR ('cohort analysis'/exp OR 'analysis, cohort':ti,ab OR 'cohort analysis':ti,ab OR 'cohort fertility':ti,ab OR 'cohort life cycle':ti,ab OR 'cohort studies':ti,ab OR 'cohort study':ti,ab OR 'fertility, cohort':ti,ab OR cohort:ti,ab) OR ('case control study'/exp OR 'case control study':ti,ab OR 'case-control	2005

	studies':ti,ab OR 'case-control study':ti,ab OR 'control study, case':ti,ab OR 'matched case control':ti,ab OR 'matched case control studies':ti,ab OR 'matched case control study':ti,ab OR 'case control':ti,ab))) NOT 'review'/exp	
#17	'review'/exp	2645279
#16	((('pulmonary thromboembolism':ti,ab,kw OR 'pulmonary artery thromboembolism':ti,ab,kw OR 'massive pulmonary embolism':ti,ab,kw OR 'submassive pulmonary embolism':ti,ab,kw OR 'acute pulmonary embolism':ti,ab,kw OR 'pulmonary embolism':ti,ab,kw OR 'bronchial vascular hypertrophy':ti,ab,kw OR 'intrapulmonary shunt':ti,ab,kw OR 'pulmonary artery filling defect':ti,ab,kw OR 'lung embolism':ti,ab,kw OR 'lung embolization':ti,ab,kw OR 'lung embolus':ti,ab,kw OR 'lung emboly':ti,ab,kw OR 'lung microembolism':ti,ab,kw OR 'lung microembolization':ti,ab,kw OR 'lung microembolus':ti,ab,kw OR 'lung thromboembolism':ti,ab,kw OR 'pulmonary embolization':ti,ab,kw OR 'pulmonary embolus':ti,ab,kw OR 'pulmonary microembolism':ti,ab,kw OR 'pulmonary thromboembolic disease':ti,ab,kw) OR ('lung embolism'/exp OR 'massive pulmonary embolism'/exp OR 'submassive pulmonary embolism'/exp OR 'acute pulmonary embolism'/exp OR 'pulmonary shunt'/exp)) AND (((embolectomy:ti,ab,kw OR 'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw) OR ('embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp)) OR (('antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw) OR ('fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp)))) AND (('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti) OR ('cohort analysis'/exp OR 'analysis, cohort':ti,ab OR 'cohort analysis':ti,ab OR 'cohort fertility':ti,ab OR 'cohort life cycle':ti,ab OR 'cohort studies':ti,ab OR 'cohort study':ti,ab OR 'fertility, cohort':ti,ab OR cohort:ti,ab) OR ('case control study'/exp OR 'case control study':ti,ab OR 'case-control	2641

	studies':ti,ab OR 'case-control study':ti,ab OR 'control study, case':ti,ab OR 'matched case control':ti,ab OR 'matched case control studies':ti,ab OR 'matched case control study':ti,ab OR 'case control':ti,ab))	
#15	('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti) OR ('cohort analysis'/exp OR 'analysis, cohort':ti,ab OR 'cohort analysis':ti,ab OR 'cohort fertility':ti,ab OR 'cohort life cycle':ti,ab OR 'cohort studies':ti,ab OR 'cohort study':ti,ab OR 'fertility, cohort':ti,ab OR cohort:ti,ab) OR ('case control study'/exp OR 'case control study':ti,ab OR 'case-control studies':ti,ab OR 'case-control study':ti,ab OR 'control study, case':ti,ab OR 'matched case control':ti,ab OR 'matched case control studies':ti,ab OR 'matched case control study':ti,ab OR 'case control':ti,ab)	3602004
#14	'case control study'/exp OR 'case control study':ti,ab OR 'case-control studies':ti,ab OR 'case-control study':ti,ab OR 'control study, case':ti,ab OR 'matched case control':ti,ab OR 'matched case control studies':ti,ab OR 'matched case control study':ti,ab OR 'case control':ti,ab	225545
#13	'cohort analysis'/exp OR 'analysis, cohort':ti,ab OR 'cohort analysis':ti,ab OR 'cohort fertility':ti,ab OR 'cohort life cycle':ti,ab OR 'cohort studies':ti,ab OR 'cohort study':ti,ab OR 'fertility, cohort':ti,ab OR cohort:ti,ab	1015303
#12	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	2543752
#11	(('pulmonary thromboembolism':ti,ab,kw OR 'pulmonary artery thromboembolism':ti,ab,kw OR 'massive pulmonary embolism':ti,ab,kw OR 'submassive pulmonary embolism':ti,ab,kw OR 'acute pulmonary embolism':ti,ab,kw OR 'pulmonary embolism':ti,ab,kw OR 'bronchial vascular hypertrophy':ti,ab,kw OR 'intrapulmonary shunt':ti,ab,kw OR 'pulmonary artery filling defect':ti,ab,kw OR 'lung embolism':ti,ab,kw OR 'lung embolization':ti,ab,kw OR 'lung embolus':ti,ab,kw OR 'lung emboly':ti,ab,kw OR 'lung microembolism':ti,ab,kw OR 'lung microembolization':ti,ab,kw OR 'lung microembolus':ti,ab,kw OR 'lung thromboembolism':ti,ab,kw OR 'pulmonary embolization':ti,ab,kw OR 'pulmonary embolus':ti,ab,kw OR 'pulmonary microembolism':ti,ab,kw OR 'pulmonary thromboembolic disease':ti,ab,kw) OR ('lung embolism'/exp OR 'massive pulmonary embolism'/exp OR 'submassive pulmonary embolism'/exp OR 'acute pulmonary embolism'/exp OR 'pulmonary shunt'/exp)) AND (((embolectomy:ti,ab,kw OR	17694

	'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw) OR ('embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp)) OR (('antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw) OR ('fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp)))	
#10	((embolectomy:ti,ab,kw OR 'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw) OR ('embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp)) OR (('antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw) OR ('fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp))	328959
#9	('antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw) OR ('fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp)	189777
#8	'fibrinolytic therapy'/exp OR 'fibrinolytic agent'/exp	145903
#7	'antithrombogenic agent':ti,ab,kw OR 'antithrombic drug':ti,ab,kw OR 'fibrinoly*':ti,ab,kw OR 'thromboly*':ti,ab,kw	99473
#6	(embolectomy:ti,ab,kw OR 'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic	162146

Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

	therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw) OR ('embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp)	
#5	'embolectomy'/exp OR 'interventional cardiovascular procedure'/de OR 'atherectomy'/exp OR 'percutaneous coronary intervention'/exp OR 'percutaneous transluminal angioplasty'/exp OR 'catheter directed thrombolysis'/exp OR 'percutaneous thrombectomy'/exp	146994
#4	embolectomy:ti,ab,kw OR 'percutaneous thrombectomy':ti,ab,kw OR 'percutaneous coronary intervention':ti,ab,kw OR 'catheter directed thrombolysis':ti,ab,kw OR 'catheter directed thrombolytic therapy':ti,ab,kw OR cdt:ti,ab,kw OR 'catheter based thrombectomy':ti,ab,kw OR 'catheter directed thrombectomy':ti,ab,kw OR 'endovascular embolectomy':ti,ab,kw OR 'endovascular thrombectomy':ti,ab,kw OR 'mechanical thrombolysis':ti,ab,kw OR 'mechanical clot disruption':ti,ab,kw OR atherectomy:ti,ab,kw OR 'atheroma resection':ti,ab,kw OR 'percutaneous transluminal angioplasty':ti,ab,kw OR 'percutaneous transluminal':ti,ab,kw OR 'transluminal artery dilatation':ti,ab,kw OR 'transluminal angioplasty':ti,ab,kw	87886
#3	('pulmonary thromboembolism':ti,ab,kw OR 'pulmonary artery thromboembolism':ti,ab,kw OR 'massive pulmonary embolism':ti,ab,kw OR 'submassive pulmonary embolism':ti,ab,kw OR 'acute pulmonary embolism':ti,ab,kw OR 'pulmonary embolism':ti,ab,kw OR 'bronchial vascular hypertrophy':ti,ab,kw OR 'intrapulmonary shunt':ti,ab,kw OR 'pulmonary artery filling defect':ti,ab,kw OR 'lung embolism':ti,ab,kw OR 'lung embolization':ti,ab,kw OR 'lung embolus':ti,ab,kw OR 'lung emboly':ti,ab,kw OR 'lung microembolism':ti,ab,kw OR 'lung microembolization':ti,ab,kw OR 'lung microembolus':ti,ab,kw OR 'lung thromboembolism':ti,ab,kw OR 'pulmonary embolization':ti,ab,kw OR 'pulmonary embolus':ti,ab,kw OR 'pulmonary microembolism':ti,ab,kw OR 'pulmonary thromboembolic disease':ti,ab,kw) OR ('lung embolism'/exp OR 'massive pulmonary embolism'/exp OR 'submassive pulmonary embolism'/exp OR 'acute pulmonary embolism'/exp OR 'pulmonary shunt'/exp)	107805

Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

#2	'lung embolism'/exp OR 'massive pulmonary embolism'/exp OR 'submassive pulmonary embolism'/exp OR 'acute pulmonary embolism'/exp OR 'pulmonary shunt'/exp	98045
#1	'pulmonary thromboembolism':ti,ab,kw OR 'pulmonary artery thromboembolism':ti,ab,kw OR 'massive pulmonary embolism':ti,ab,kw OR 'submassive pulmonary embolism':ti,ab,kw OR 'acute pulmonary embolism':ti,ab,kw OR 'pulmonary embolism':ti,ab,kw OR 'bronchial vascular hypertrophy':ti,ab,kw OR 'intrapulmonary shunt':ti,ab,kw OR 'pulmonary artery filling defect':ti,ab,kw OR 'lung embolism':ti,ab,kw OR 'lung embolization':ti,ab,kw OR 'lung embolus':ti,ab,kw OR 'lung emboly':ti,ab,kw OR 'lung microembolism':ti,ab,kw OR 'lung microembolization':ti,ab,kw OR 'lung microembolus':ti,ab,kw OR 'lung thromboembolism':ti,ab,kw OR 'pulmonary embolization':ti,ab,kw OR 'pulmonary embolus':ti,ab,kw OR 'pulmonary microembolism':ti,ab,kw OR 'pulmonary thromboembolic disease':ti,ab,kw	62420

Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

Syntaxes Used in Database Searches: PUBMED

Search number	Query	Search Details	Results
20	#18 NOT #19	((((((((((((((((((((("Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract]) OR "Massive Pulmonary Embolism"[Title/Abstract]) OR "Submassive Pulmonary Embolism"[Title/Abstract]) OR "Acute pulmonary embolism"[Title/Abstract]) OR "Pulmonary Embolism"[Title/Abstract])) OR "intrapulmonary shunt"[Title/Abstract]) OR "pulmonary artery filling defect"[Title/Abstract]) OR "lung embolism"[Title/Abstract]) OR "lung embolization"[Title/Abstract]) OR "lung embolus"[Title/Abstract])) OR "lung microembolism"[Title/Abstract]) OR "lung microembolization"[Title/Abstract])) OR "lung thromboembolism"[Title/Abstract]) OR "pulmonary embolization"[Title/Abstract]) OR "pulmonary embolus"[Title/Abstract]) OR "pulmonary microembolism"[Title/Abstract]) OR "Pulmonary thromboembolic disease"[Title/Abstract]) AND "Pulmonary Embolism"[MeSH Terms]) AND ((((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "Percutaneous Coronary Intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "Mechanical Thrombolysis"[Title/Abstract]) OR	1,359

		"mechanical clot disruption"[Title/Abstract]) OR "Atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR "percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]) OR (((((("Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp]) OR "Angioplasty"[MeSH Terms:noexp]) OR "Atherectomy"[MeSH Terms]) OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp]) OR "atherectomy, coronary"[MeSH Terms])) OR ((((("antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract]) OR "fibrinoly*"[Title/Abstract]) OR "thromboly*"[Title/Abstract]) OR ("Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action]))))) AND ((((((((((("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type]) OR "randomized"[Title/Abstract]) OR "placebo"[Title/Abstract]) OR "clinical trials as topic"[MeSH Terms:noexp]) OR "randomly"[Title/Abstract]) OR "trial"[Title]) NOT ("animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms]))) OR "Cohort Studies"[MeSH Terms]) OR "cohort"[Title/Abstract]) OR "case-control studies"[MeSH Terms]) OR "case control"[Title/Abstract])) NOT "Review"[Publication Type]	
19	"Review" [Publication Type]	"Review"[Publication Type]	2,641,047

18	#11 AND #17	((((((((((((((((((("Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract]) OR "Massive Pulmonary Embolism"[Title/Abstract]) OR "Submassive Pulmonary Embolism"[Title/Abstract]) OR "Acute pulmonary embolism"[Title/Abstract]) OR "Pulmonary Embolism"[Title/Abstract])) OR "intrapulmonary shunt"[Title/Abstract]) OR "pulmonary artery filling defect"[Title/Abstract]) OR "lung embolism"[Title/Abstract]) OR "lung embolization"[Title/Abstract]) OR "lung embolus"[Title/Abstract])) OR "lung microembolism"[Title/Abstract]) OR "lung microembolization"[Title/Abstract])) OR "lung thromboembolism"[Title/Abstract]) OR "pulmonary embolization"[Title/Abstract]) OR "pulmonary embolus"[Title/Abstract]) OR "pulmonary microembolism"[Title/Abstract]) OR "Pulmonary thromboembolic disease"[Title/Abstract]) AND "Pulmonary Embolism"[MeSH Terms]) AND ((((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "Percutaneous Coronary Intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "Mechanical Thrombolysis"[Title/Abstract]) OR "mechanical clot disruption"[Title/Abstract]) OR "Atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH	1,545

		Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR "percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]) OR (((((("Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp]) OR "Angioplasty"[MeSH Terms:noexp]) OR "Atherectomy"[MeSH Terms]) OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp]) OR "atherectomy, coronary"[MeSH Terms])) OR ((((("antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract]) OR "fibrinoly*"[Title/Abstract]) OR "thromboly*"[Title/Abstract]) OR ("Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action])))) AND ((((((((((("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type]) OR "randomized"[Title/Abstract]) OR "placebo"[Title/Abstract]) OR "clinical trials as topic"[MeSH Terms:noexp]) OR "randomly"[Title/Abstract]) OR "trial"[Title]) NOT ("animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms]))) OR "Cohort Studies"[MeSH Terms]) OR "cohort"[Title/Abstract]) OR "case-control studies"[MeSH Terms]) OR "case control"[Title/Abstract])	
17	#12 OR #13 OR #14 OR #15 OR #16	((((((((("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type]) OR "randomized"[Title/Abstract]) OR "placebo"[Title/Abstract]) OR "clinical trials as topic"[MeSH Terms:noexp])	3,393,722

		OR "randomly"[Title/Abstract]) OR "trial"[Title]) NOT ("animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms])))) OR "Cohort Studies"[MeSH Terms]) OR "cohort"[Title/Abstract]) OR "case-control studies"[MeSH Terms]) OR "case control"[Title/Abstract]	
16	"case control"[Title/Abstract]	"case control"[Title/Abstract]	124,307
15	"Case-Control Studies"[Mesh]	"case-control studies"[MeSH Terms]	1,073,197
14	cohort[Title/Abstract]	"cohort"[Title/Abstract]	524,138
13	"Cohort Studies"[Mesh]	"Cohort Studies"[MeSH Terms]	1,983,481
12	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals [mh] NOT (humans [mh] AND animals[mh]))	((((((("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type]) OR "randomized"[Title/Abstract]) OR "placebo"[Title/Abstract]) OR "clinical trials as topic"[MeSH Terms:noexp]) OR "randomly"[Title/Abstract]) OR "trial"[Title]) NOT ("animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms]))	1,188,338
11	#3 AND #10	((((((((((((((((((("Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract]) OR "Massive Pulmonary Embolism"[Title/Abstract]) OR "Submassive Pulmonary Embolism"[Title/Abstract]) OR "Acute pulmonary embolism"[Title/Abstract]) OR "Pulmonary Embolism"[Title/Abstract])) OR "intrapulmonary shunt"[Title/Abstract]) OR "pulmonary artery filling defect"[Title/Abstract]) OR "lung embolism"[Title/Abstract]) OR "lung embolization"[Title/Abstract]) OR "lung embolus"[Title/Abstract])) OR "lung microembolism"[Title/Abstract]) OR "lung microembolization"[Title/Abstract])) OR "lung thromboembolism"[Title/Abstract]) OR "pulmonary embolization"[Title/Abstract]) OR "pulmonary embolus"[Title/Abstract]) OR "pulmonary	5,386

		microembolism"[Title/Abstract]) OR "Pulmonary thromboembolic disease"[Title/Abstract]) AND "Pulmonary Embolism"[MeSH Terms]) AND ((((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "Percutaneous Coronary Intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "Mechanical Thrombolysis"[Title/Abstract]) OR "mechanical clot disruption"[Title/Abstract]) OR "Atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR "percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]) OR (((((("Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp]) OR "Angioplasty"[MeSH Terms:noexp]) OR "Atherectomy"[MeSH Terms]) OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp]) OR "atherectomy, coronary"[MeSH Terms])) OR ((((("antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract])	

		OR "fibrinoly*"[Title/Abstract]) OR "thromboly*"[Title/Abstract]) OR ("Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action]))))	
10	#6 OR #9	((((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "Percutaneous Coronary Intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "Mechanical Thrombolysis"[Title/Abstract]) OR "mechanical clot disruption"[Title/Abstract]) OR "Atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR "percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]) OR (((((("Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp]) OR "Angioplasty"[MeSH Terms:noexp]) OR "Atherectomy"[MeSH Terms]) OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp]) OR "atherectomy, coronary"[MeSH Terms])) OR ((((("antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract])	284,213

		OR "fibrinoly*"[Title/Abstract]) OR "thromboly*"[Title/Abstract]) OR ("Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action]))	
9	#7 OR #8	"antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract] OR "fibrinoly*"[Title/Abstract] OR "thromboly*"[Title/Abstract] OR "Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action]	211,598
8	("Fibrinolytic Agents"[Mesh]) OR "Fibrinolytic Agents" [Pharmacological Action]	"Fibrinolytic Agents"[MeSH Terms] OR "Fibrinolytic Agents"[Pharmacological Action]	170,314
7	"antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract] OR fibrinoly*[Title/Abstract] OR thromboly*[Title/Abstract]	"antithrombogenic agent"[Title/Abstract] OR "Antithrombic Drug"[Title/Abstract] OR "fibrinoly*"[Title/Abstract] OR "thromboly*"[Title/Abstract]	68,961
6	#4 OR #5	((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "Percutaneous Coronary Intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "Mechanical Thrombolysis"[Title/Abstract]) OR "mechanical clot disruption"[Title/Abstract]) OR "Atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR	85,716

		"percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]) OR (((((("Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp]) OR "Angioplasty"[MeSH Terms:noexp]) OR "Atherectomy"[MeSH Terms]) OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp]) OR "atherectomy, coronary"[MeSH Terms])	
5	(((((("Mechanical Thrombolysis"[Mesh]) OR "Endovascular Procedures"[Mesh:NoExp]) OR "Angioplasty"[Mesh:NoExp]) OR "Atherectomy"[Mesh]) OR "Percutaneous Coronary Intervention"[Mesh:NoExp]) OR "Atherectomy, Coronary"[Mesh]	"Mechanical Thrombolysis"[MeSH Terms] OR "Endovascular Procedures"[MeSH Terms:noexp] OR "Angioplasty"[MeSH Terms:noexp] OR "Atherectomy"[MeSH Terms] OR "Percutaneous Coronary Intervention"[MeSH Terms:noexp] OR "atherectomy, coronary"[MeSH Terms]	45,246
4	(Embolectomy[Title/Abstract] OR percutaneous thrombectomy[Title/Abstract] OR percutaneous coronary intervention[Title/Abstract] OR catheter directed thrombolysis[Title/Abstract] OR catheter directed thrombolytic therapy[Title/Abstract] OR CDT[Title/Abstract] OR catheter based thrombectomy[Title/Abstract] OR catheter directed thrombectomy[Title/Abstract] OR endovascular embolectomy[Title/Abstract] OR endovascular thrombectomy[Title/Abstract] OR Mechanical Thrombolysis[Title/Abstract] OR Mechanical Clot	((((((((((((((("Embolectomy"[Title/Abstract] OR "percutaneous thrombectomy"[Title/Abstract]) OR "percutaneous coronary intervention"[Title/Abstract]) OR "catheter directed thrombolysis"[Title/Abstract]) OR "catheter directed thrombolytic therapy"[Title/Abstract]) OR "CDT"[Title/Abstract]) OR "catheter based thrombectomy"[Title/Abstract]) OR "catheter directed thrombectomy"[Title/Abstract]) OR "endovascular embolectomy"[Title/Abstract]) OR "endovascular thrombectomy"[Title/Abstract]) OR "mechanical thrombolysis"[Title/Abstract]) OR "mechanical clot disruption"[Title/Abstract]) OR "atherectomy"[Title/Abstract]) OR (((((("plaque, atherosclerotic"[MeSH	54,993

	Disruption[Title/Abstract] OR atherectomy[Title/Abstract] OR atheroma resection[Title/Abstract] OR percutaneous transluminal angioplasty[Title/Abstract] OR percutaneous transluminal[Title/Abstract] OR transluminal artery dilatation[Title/Abstract] OR transluminal angioplasty[Title/Abstract])	Terms] OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields])) OR "atherosclerotic plaque"[All Fields]) OR "atheroma"[All Fields]) OR "atheromas"[All Fields]) AND "resection"[Title/Abstract])) OR "percutaneous transluminal angioplasty"[Title/Abstract]) OR "percutaneous transluminal"[Title/Abstract]) OR (("transluminal"[All Fields] OR "transluminally"[All Fields]) AND "artery dilatation"[Title/Abstract])) OR "transluminal angioplasty"[Title/Abstract]	
3	#1 AND #2	((((((((((((((((((("Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract]) OR "Massive Pulmonary Embolism"[Title/Abstract]) OR "Submassive Pulmonary Embolism"[Title/Abstract]) OR "Acute pulmonary embolism"[Title/Abstract]) OR "Pulmonary Embolism"[Title/Abstract])) OR "intrapulmonary shunt"[Title/Abstract]) OR "pulmonary artery filling defect"[Title/Abstract]) OR "lung embolism"[Title/Abstract]) OR "lung embolization"[Title/Abstract]) OR "lung embolus"[Title/Abstract])) OR "lung microembolism"[Title/Abstract]) OR "lung microembolization"[Title/Abstract])) OR "lung thromboembolism"[Title/Abstract]) OR "pulmonary embolization"[Title/Abstract]) OR "pulmonary embolus"[Title/Abstract]) OR "pulmonary microembolism"[Title/Abstract]) OR "Pulmonary thromboembolic disease"[Title/Abstract]) AND "Pulmonary Embolism"[MeSH Terms]	23,456
2	"Pulmonary Embolism"[Mesh]	"Pulmonary Embolism"[MeSH Terms]	38,498
1	("Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract] OR "Massive	"Pulmonary Thromboembolism"[Title/Abstract] OR "pulmonary artery thromboembolism"[Title/Abstract] OR "Massive Pulmonary Embolism"[Title/Abstract] OR	40,306

	Pulmonary Embolism"[Title/Abstract] OR "Submassive Pulmonary Embolism"[Title/Abstract] OR "Acute pulmonary embolism"[Title/Abstract] OR "pulmonary embolism"[Title/Abstract] OR "bronchial vascular hypertrophy"[Title/Abstract] OR "intrapulmonary shunt"[Title/Abstract] OR "pulmonary artery filling defect"[Title/Abstract] OR "lung embolism"[Title/Abstract] OR "lung embolization"[Title/Abstract] OR "lung embolus"[Title/Abstract] OR "lung emboly"[Title/Abstract] OR "lung microembolism"[Title/Abstract] OR "lung microembolization"[Title/Abstract] OR "lung microembolus"[Title/Abstract] OR "lung thromboembolism"[Title/Abstract] OR "pulmonary embolization"[Title/Abstract] OR "pulmonary embolus"[Title/Abstract] OR "pulmonary microembolism"[Title/Abstract] OR "Pulmonary thromboembolic disease"[Title/Abstract])	"Submassive Pulmonary Embolism"[Title/Abstract] OR "Acute pulmonary embolism"[Title/Abstract] OR "pulmonary embolism "[Title/Abstract] OR "intrapulmonary shunt"[Title/Abstract] OR "pulmonary artery filling defect"[Title/Abstract] OR "lung embolism"[Title/Abstract] OR "lung embolization"[Title/Abstract] OR "lung embolus "[Title/Abstract] OR "lung microembolism"[Title/Abstract] OR "lung microembolization "[Title/Abstract] OR "lung thromboembolism"[Title/Abstract] OR "pulmonary embolization"[Title/Abstract] OR "pulmonary embolus"[Title/Abstract] OR "pulmonary microembolism"[Title/Abstract] OR "Pulmonary thromboembolic disease"[Title/Abstract]	

Syntaxes Used in Database Searches: Cochrane

ID	Search	Hits
#1	(pulmonary thromboembolism OR pulmonary artery thromboembolism OR massive pulmonary embolism OR submassive pulmonary embolism OR acute pulmonary embolism OR pulmonary embolism OR bronchial vascular hypertrophy OR intrapulmonary shunt OR pulmonary artery filling defect OR lung embolism OR lung embolization OR lung embolus OR lung emboly OR lung microembolism OR lung microembolization OR lung microembolus OR lung thromboembolism OR pulmonary embolization OR pulmonary embolus OR pulmonary microembolism OR pulmonary thromboembolic disease):ti,ab,kw (Word variations have been searched)	5992
#2	MeSH descriptor: [Pulmonary Embolism] explode all trees	1005
#3	#1 OR #2	5992
#4	(Embolectomy OR percutaneous thrombectomy OR percutaneous coronary intervention OR catheter directed thrombolysis OR catheter directed thrombolytic therapy OR CDT OR catheter based thrombectomy OR catheter directed thrombectomy OR endovascular embolectomy OR endovascular thrombectomy OR Mechanical Thrombolysis OR Mechanical Clot Disruption OR atherectomy OR atheroma resection OR percutaneous transluminal angioplasty OR percutaneous transluminal OR transluminal artery dilatation OR transluminal angioplasty):ti,ab,kw (Word variations have been searched)	14838
#5	MeSH descriptor: [Mechanical Thrombolysis] explode all trees	31
#6	MeSH descriptor: [Endovascular Procedures] this term only	398
#7	MeSH descriptor: [Angioplasty] this term only	284
#8	MeSH descriptor: [Atherectomy] explode all trees	142
#9	MeSH descriptor: [Percutaneous Coronary Intervention] this term only	1910
#10	MeSH descriptor: [Atherectomy, Coronary] this term only	118
#11	#5 OR #6 OR #7 OR #8 OR #9 OR #10	2742
#12	#4 OR #11	15364
#13	(fibrinoly* OR thromboly* OR antithrombogenic agent OR Antithrombic Drug):ti,ab,kw (Word variations have been searched)	11078
#14	MeSH descriptor: [Fibrinolytic Agents] explode all trees	2160
#15	#13 OR #14	11078
#16	#12 OR #15	24205
#17	#3 AND #16	543

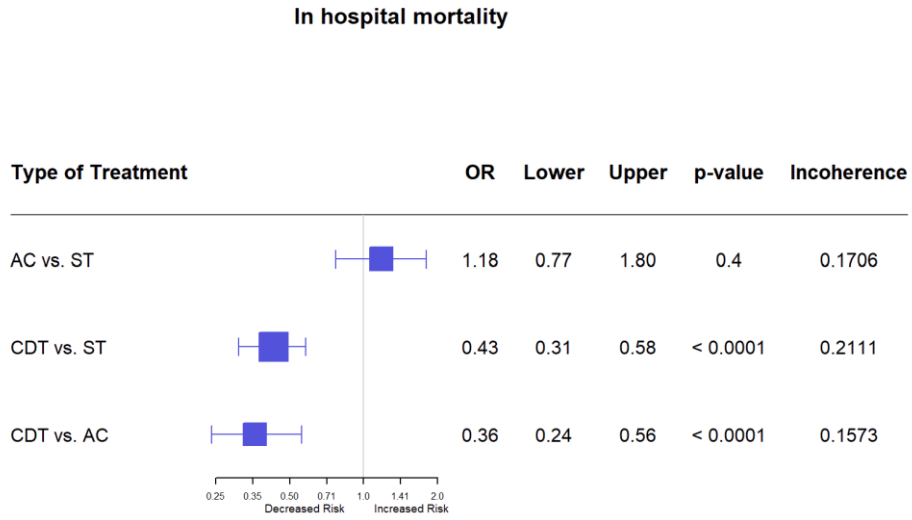
Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

Syntaxes Used in Database Searches: Clinical trials

Terms	Search Results*	Entire Database**
Synonyms		
Pulmonary Embolism	123 studies	520 studies
Pulmonary embolus	7 studies	20 studies
Blood Clots in the Lung	2 studies	3 studies
lung embolism	--	3 studies
Pulmonary artery embolism	--	2 studies
Embolism	123 studies	2,124 studies
Embolus	7 studies	59 studies
Pulmonary	123 studies	23,241 studies
Lungs	101 studies	21,489 studies
Pulmo	--	2 studies
Fibrinolytic	110 studies	2,197 studies
Thrombolytic Therapies	9 studies	54 studies
thrombolytic	120 studies	2,343 studies
Fibrinolytic Agents	107 studies	2,123 studies
thrombolysis	25 studies	280 studies
Antithrombotic Agent	1 studies	19 studies
Fibrinolytic Drugs	--	3 studies
Fibrinolysis	4 studies	115 studies
thrombolysis	34 studies	355 studies
thrombolytic	15 studies	123 studies

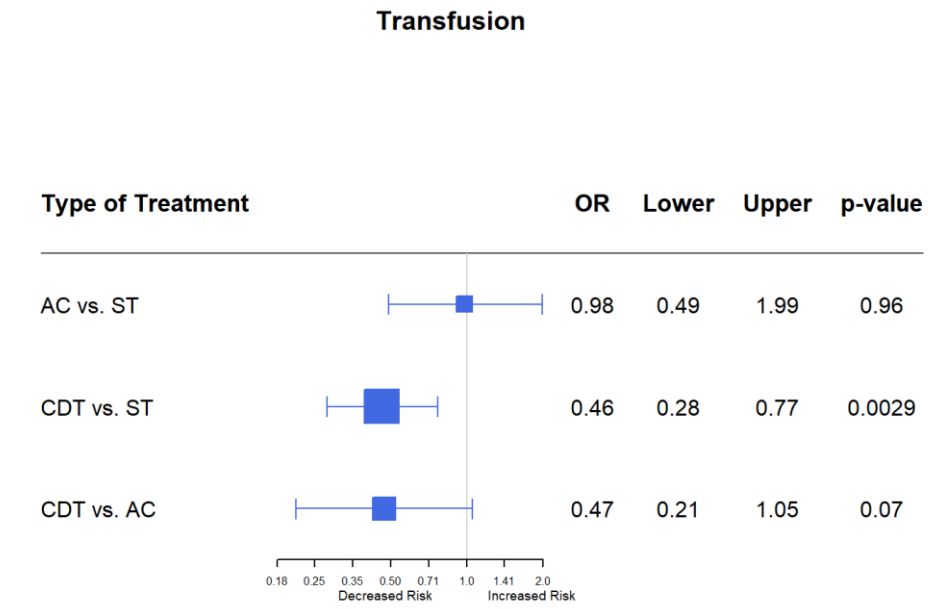
Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

Figure S1: In hospital mortality main graph



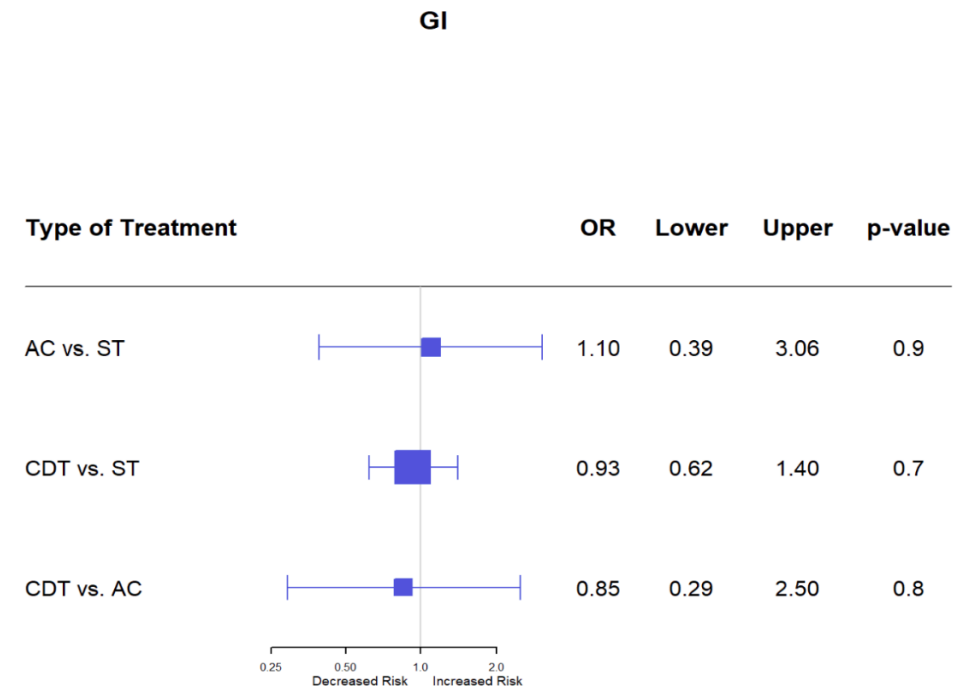

```
Quantifying heterogeneity / inconsistency:
tau^2 = 0.1328; tau = 0.3644; I^2 = 46.1% [17.8%; 64.7%]
```

Figure S2: Transfusion main graph




```
Quantifying heterogeneity / inconsistency:
tau^2 = 0.1647; tau = 0.4058; I^2 = 35.1% [0.0%; 65.0%]
```

Figure S3: GI main graph



Quantifying heterogeneity / inconsistency:
tau^2 = 0.2017; tau = 0.4491; I^2 = 71.7% [46.2%; 85.1%]

Table S1: results of primary and secondary outcomes:

OR (95%CI)	Mortality	ICH	Major bleeding	Minor bleeding	GI bleeding	Blood transfusion
AC vs ST	1.20 [0.83; 1.73]	**0.33 [0.17; 0.63]**	**0.49 [0.36; 0.67]**	**0.35 [0.24; 0.52]**	1.10 [0.39; 3.06]	0.98 [0.49; 1.99]
CDT vs ST	**0.42 [0.31; 0.57]**	**0.44 [0.29; 0.64]**	**0.61 [0.53; 0.70]**	1.11 [0.66; 1.86]	0.93 [0.62; 1.40]	**0.46 [0.28; 0.77]**
CDT vs AC	**0.35 [0.24; 0.51]**	1.33 [0.63; 2.79]	1.24 [0.88; 1.75]	3.14 [1.73; 5.68]	0.85 [0.29; 2.50]	0.47 [0.21; 1.05]

Appendix 1, as submitted by the authors. Appendix to: Planer D, Yanko S, Matok I, et al. Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis. *CMAJ* 2023. doi: 10.1503/cmaj.220960.

Figure S4: Combined network meta-analysis primary and secondary outcomes.

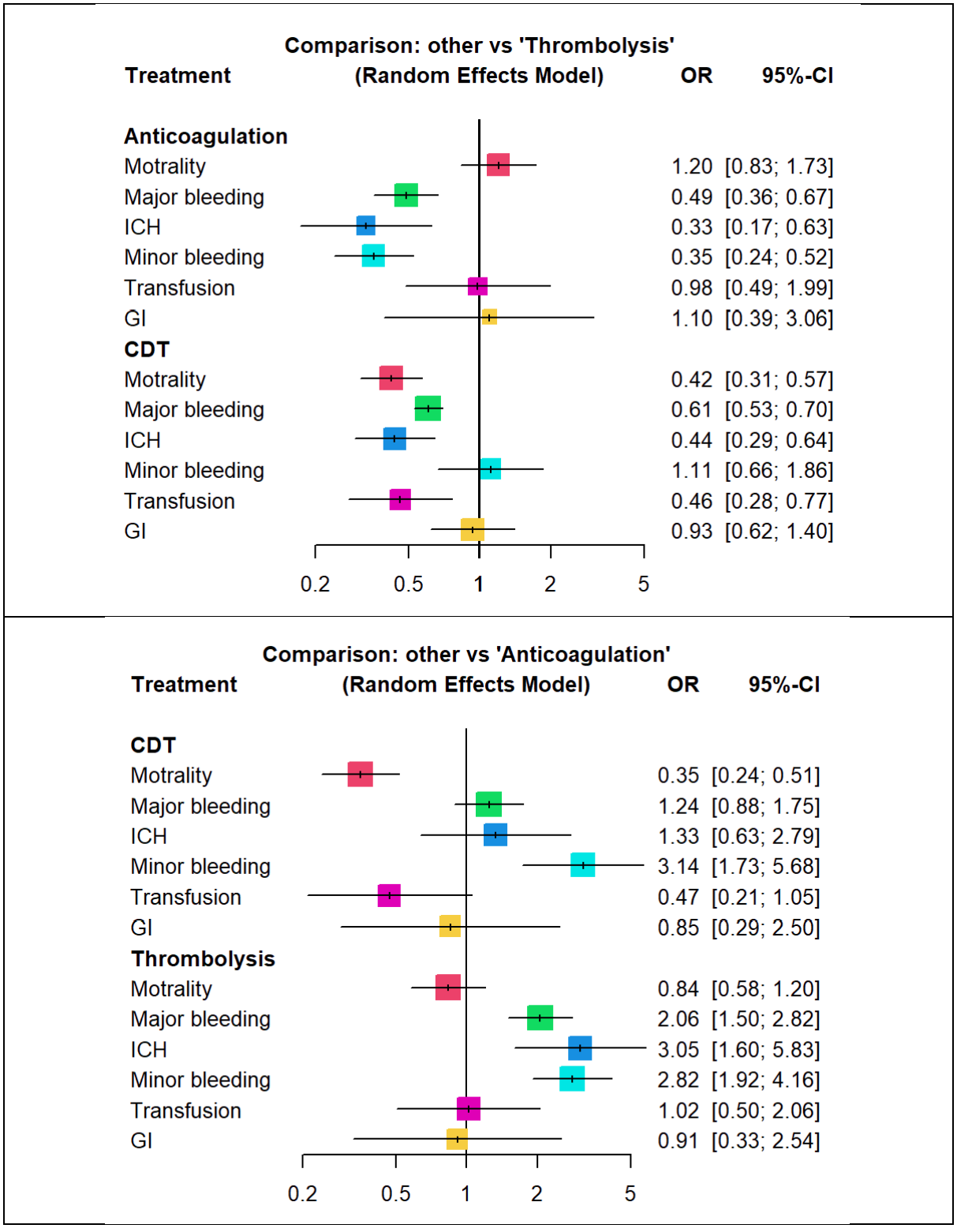


Figure S5: All-cause mortality vs RCT vs NON RCT sensitivity analysis presented in forest plots.

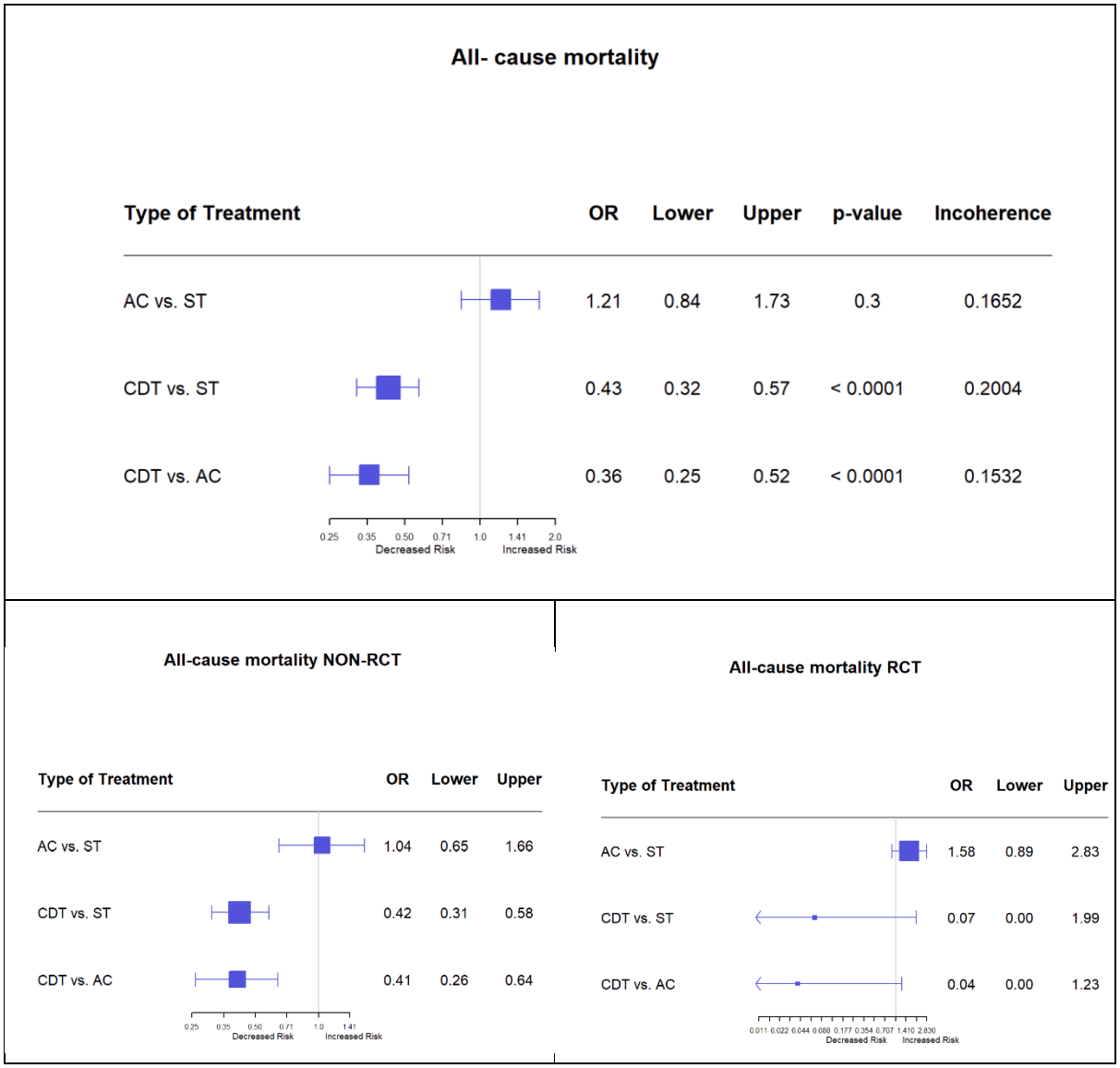


Figure S6: Major bleeding vs RCT vs NON RCT sensitivity analysis presented in forest plots.

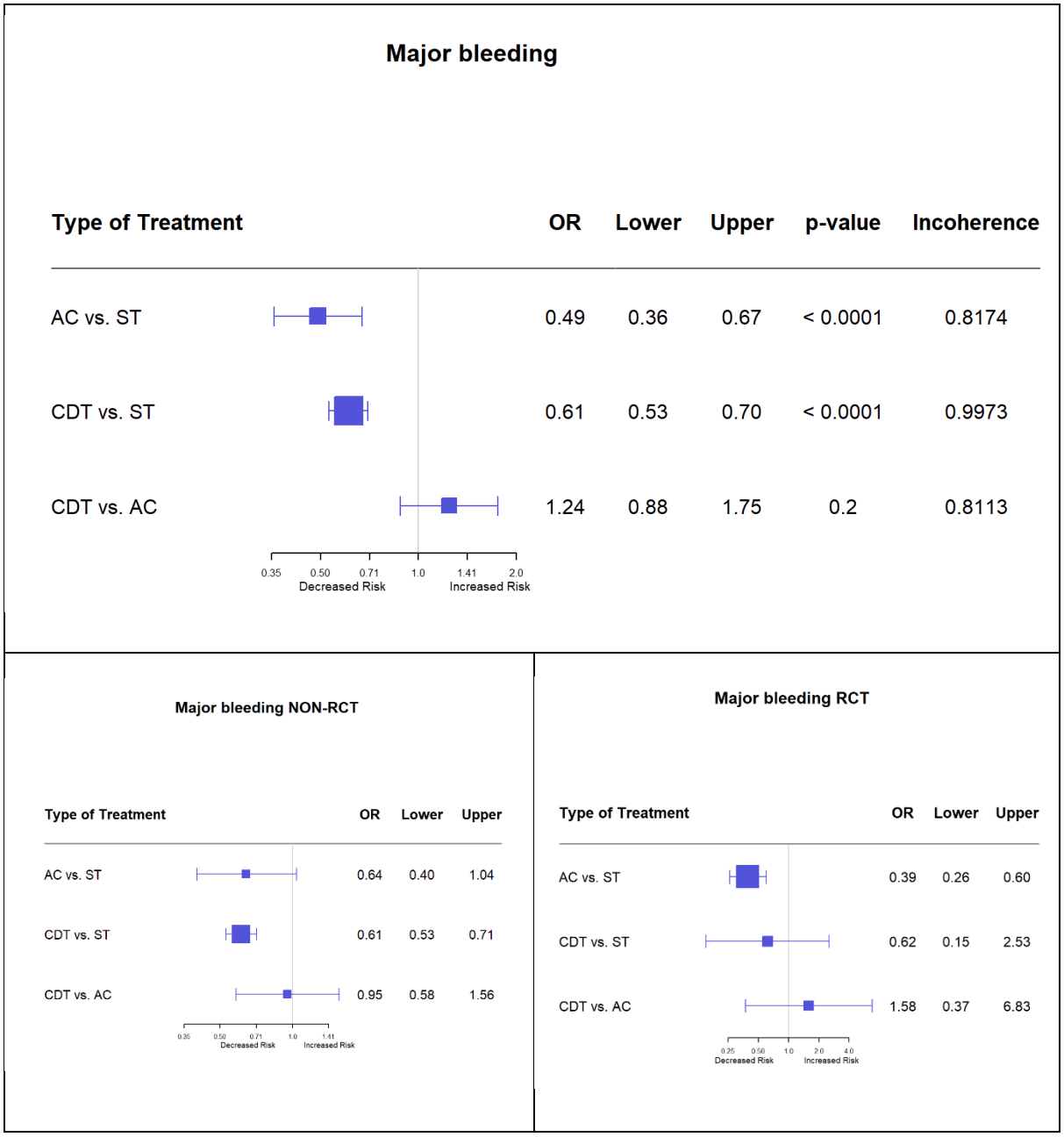


Figure S7: ICH vs RCT vs NON RCT sensitivity analysis presented in forest plots.

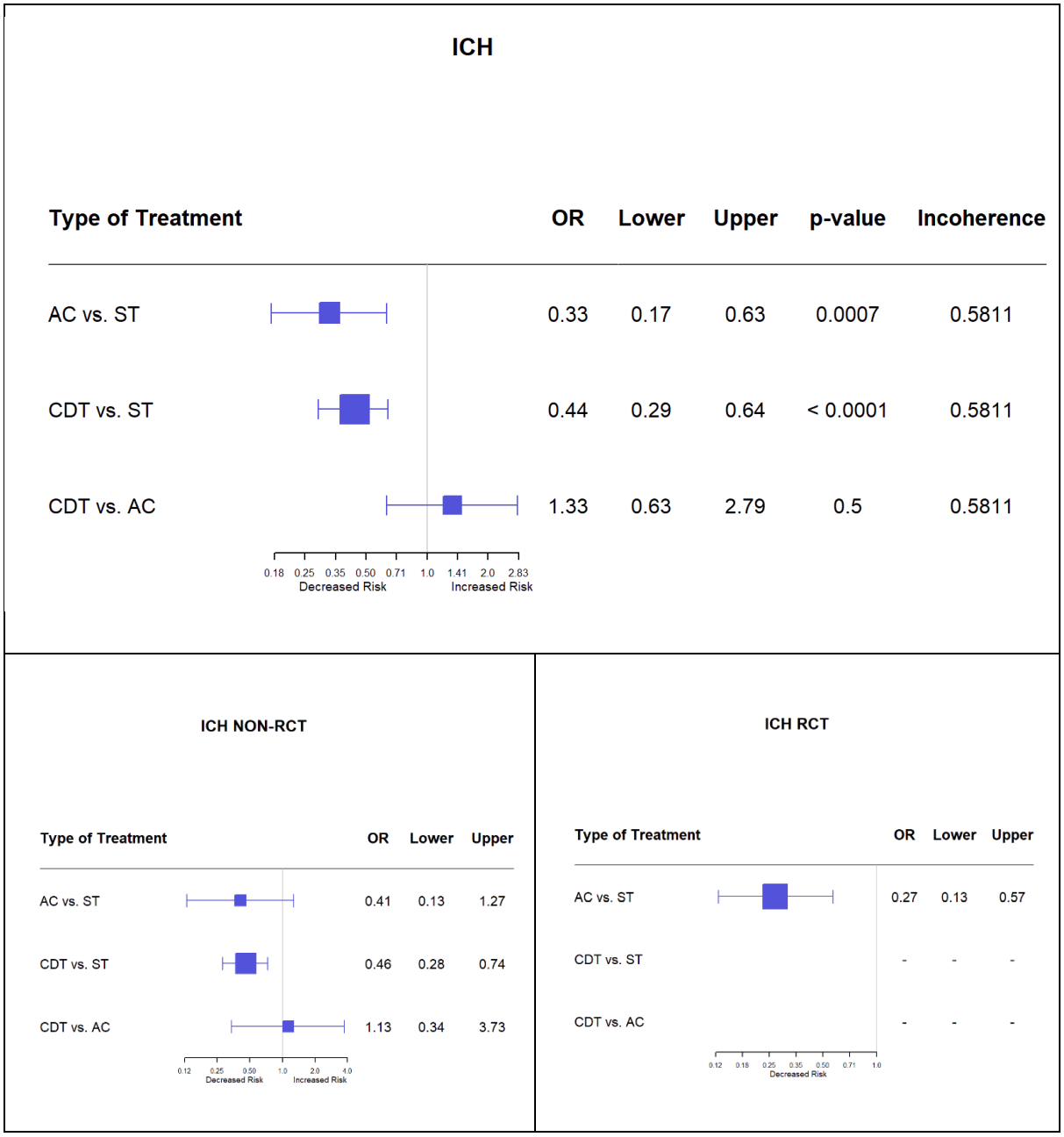


Figure S8: Minor bleeding main and sensitivity forest plots

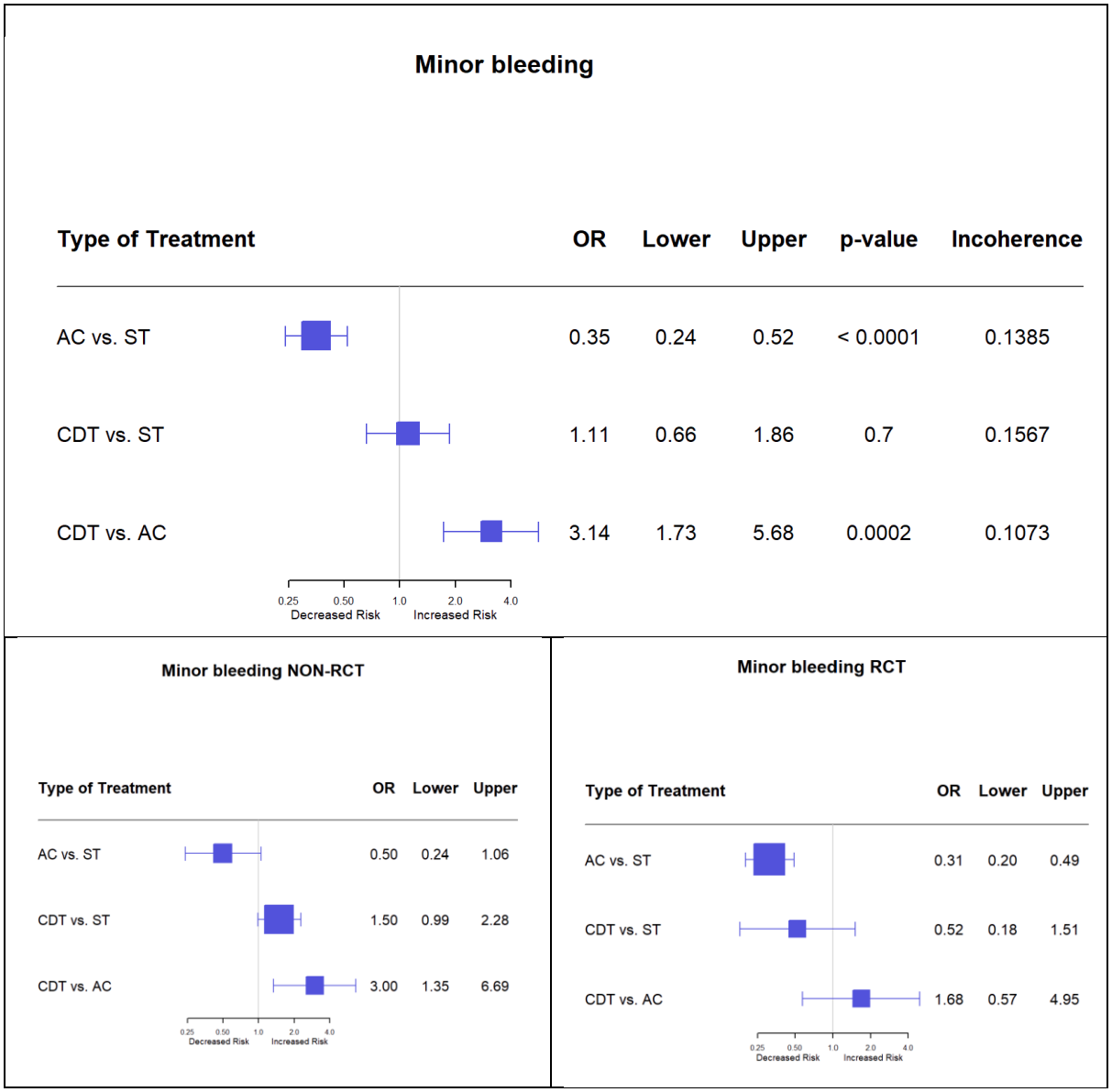


Figure S9: RCT and NON-RCT netgraphs

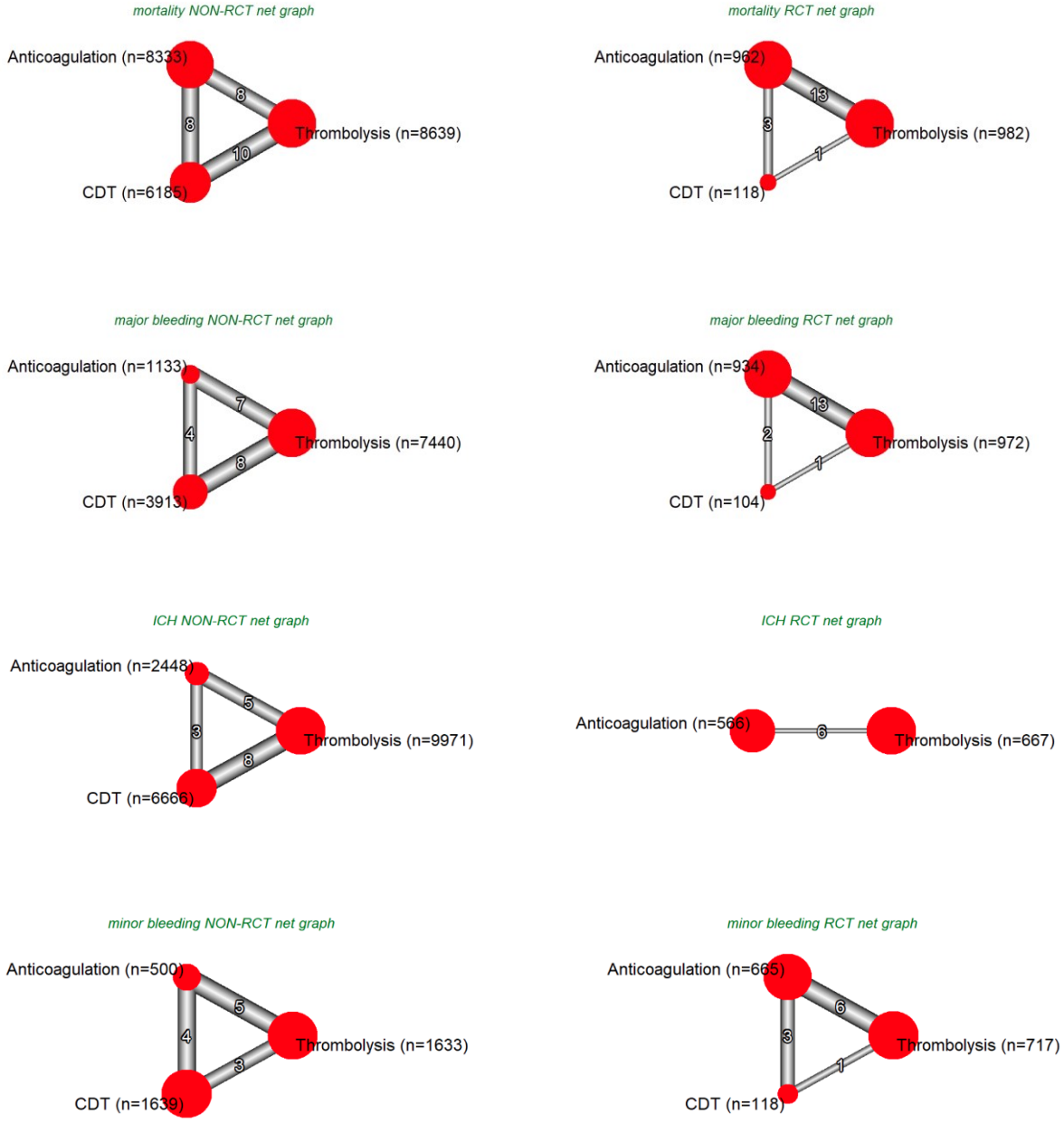
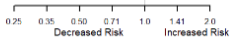


Figure S10: Sensitivity analysis without "unclear" studies:

All- cause mortality

Type of Treatment	OR	Lower	Upper	p-value	Incoherence
AC vs. ST	1.21	0.84	1.73	0.3	0.1652
CDT vs. ST	0.43	0.32	0.57	< 0.0001	0.2004
CDT vs. AC	0.36	0.25	0.52	< 0.0001	0.1532

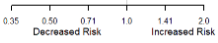


All- cause mortality without unclear studies

Type of Treatment	OR	Lower	Upper
AC vs. ST	1.23	0.93	1.63
CDT vs. ST	0.46	0.31	0.68
CDT vs. AC	0.37	0.27	0.50

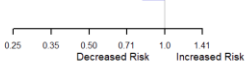
Major bleeding

Type of Treatment	OR	Lower	Upper	p-value	Incoherence
AC vs. ST	0.49	0.36	0.67	< 0.0001	0.8174
CDT vs. ST	0.61	0.53	0.70	< 0.0001	0.9973
CDT vs. AC	1.24	0.88	1.75	0.2	0.8113



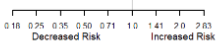
Major bleeding without unclear studies

Type of Treatment	OR	Lower	Upper
AC vs. ST	0.47	0.34	0.66
CDT vs. ST	0.43	0.25	0.74
CDT vs. AC	0.90	0.50	1.64



ICH

Type of Treatment	OR	Lower	Upper	p-value	Incoherence
AC vs. ST	0.33	0.17	0.63	0.0007	0.5811
CDT vs. ST	0.44	0.29	0.64	< 0.0001	0.5811
CDT vs. AC	1.33	0.63	2.79	0.5	0.5811



ICH without unclear studies

Type of Treatment	OR	Lower	Upper
AC vs. ST	0.28	0.15	0.52
CDT vs. ST	0.21	0.14	0.33
CDT vs. AC	0.76	0.36	1.63

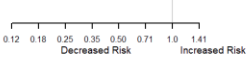


Figure S11: Sensitivity analysis with excluded studies:

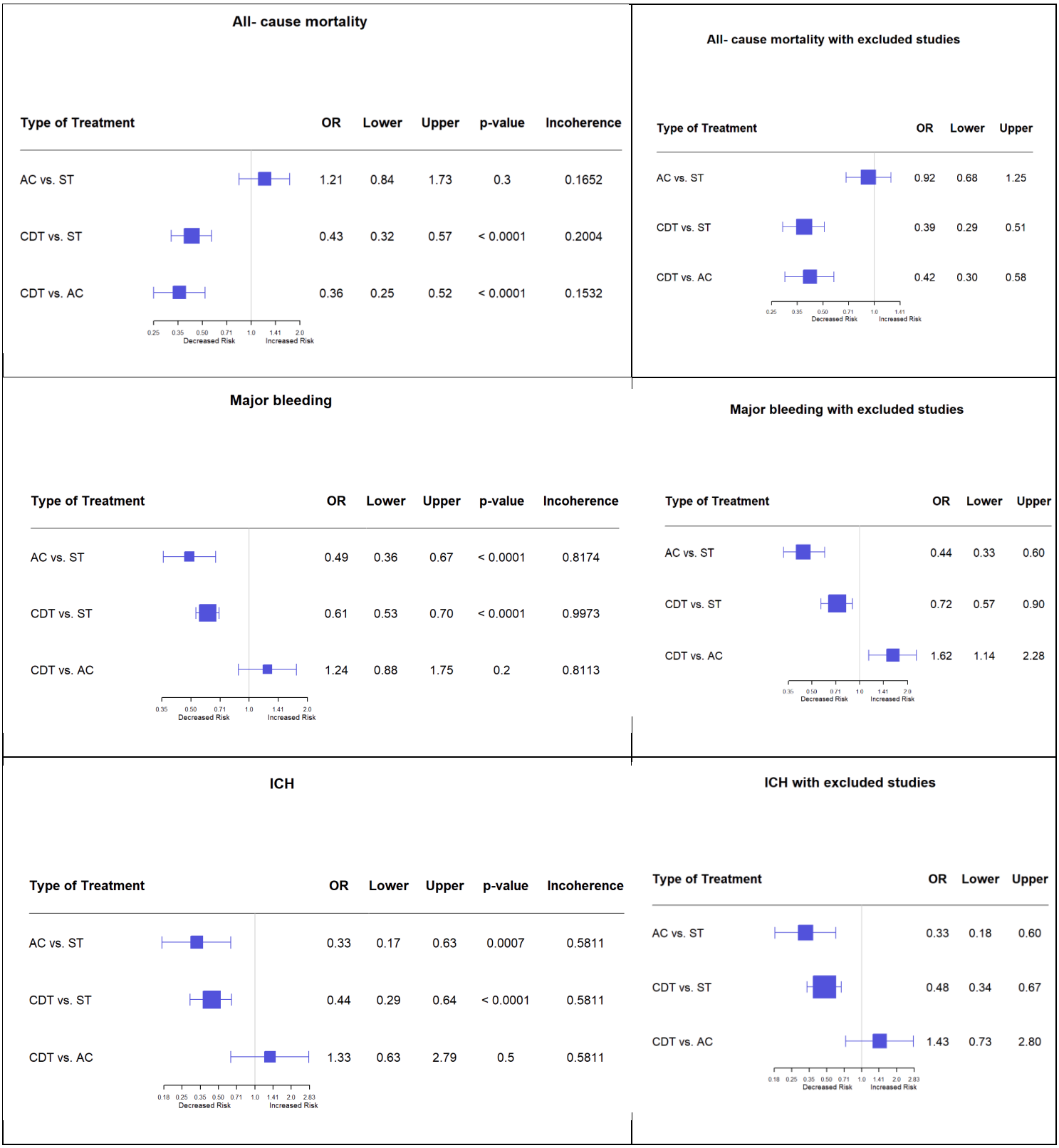


Figure S12: Combined primary outcomes for "intermediate-high" subgroup analysis and p-score.

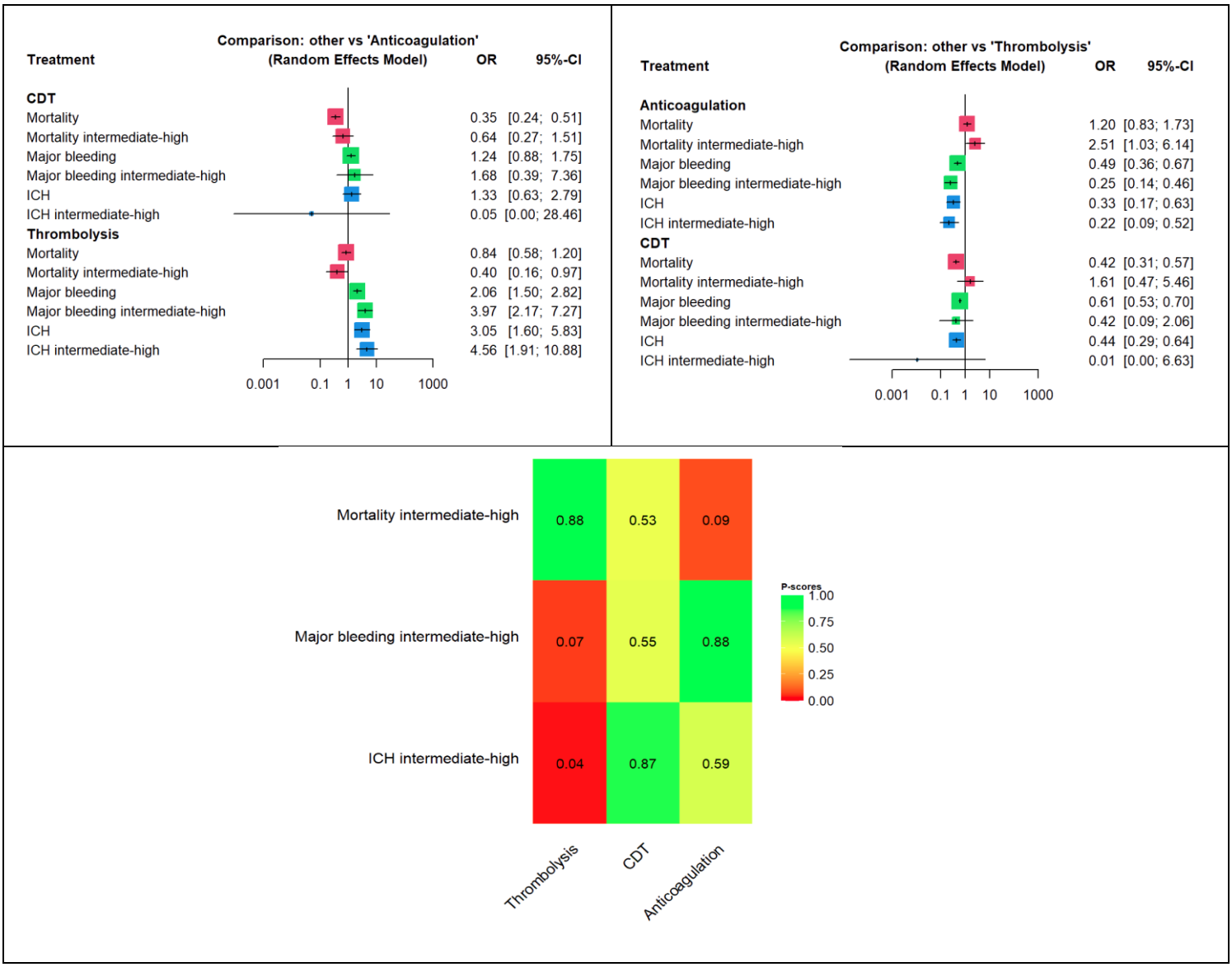
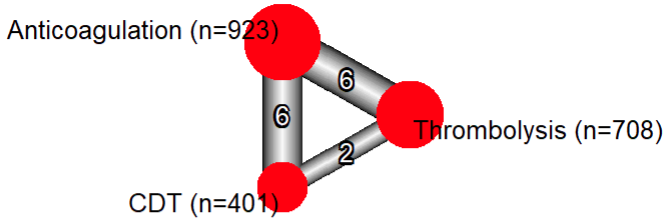
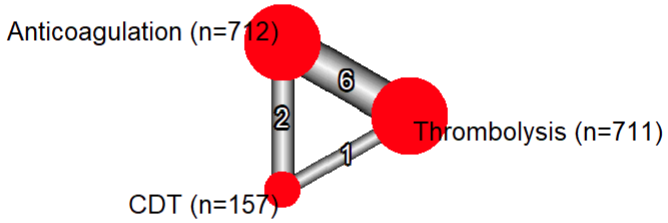


Figure S13: Netgraphs for "intermediate-high" subgroup

All- cause mortality for "intermediate-high" net graph



Major bleeding for "intermediate-high" net graph



ICH for "intermediate-high" net graph

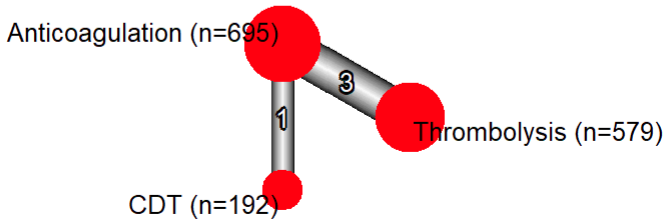
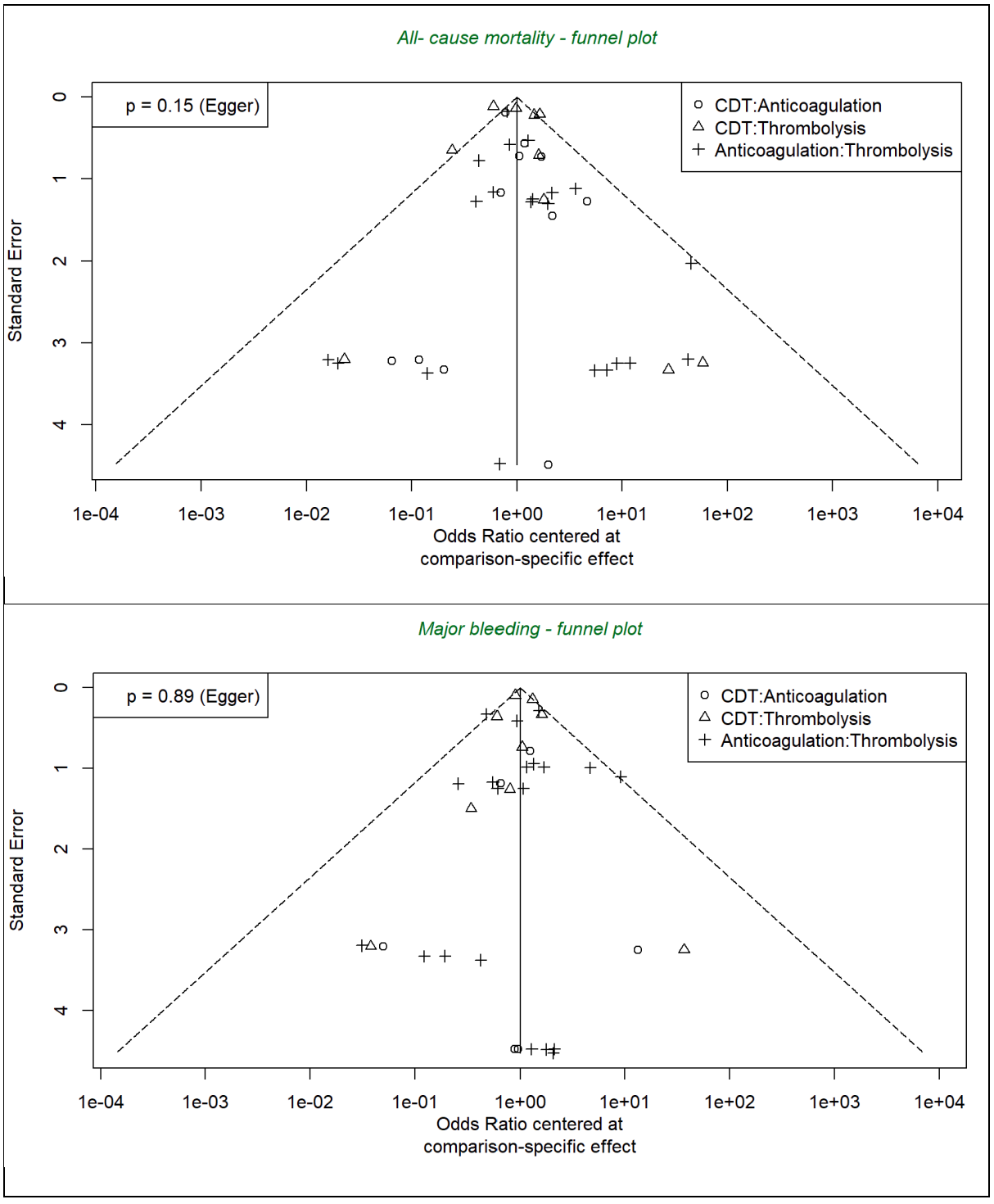
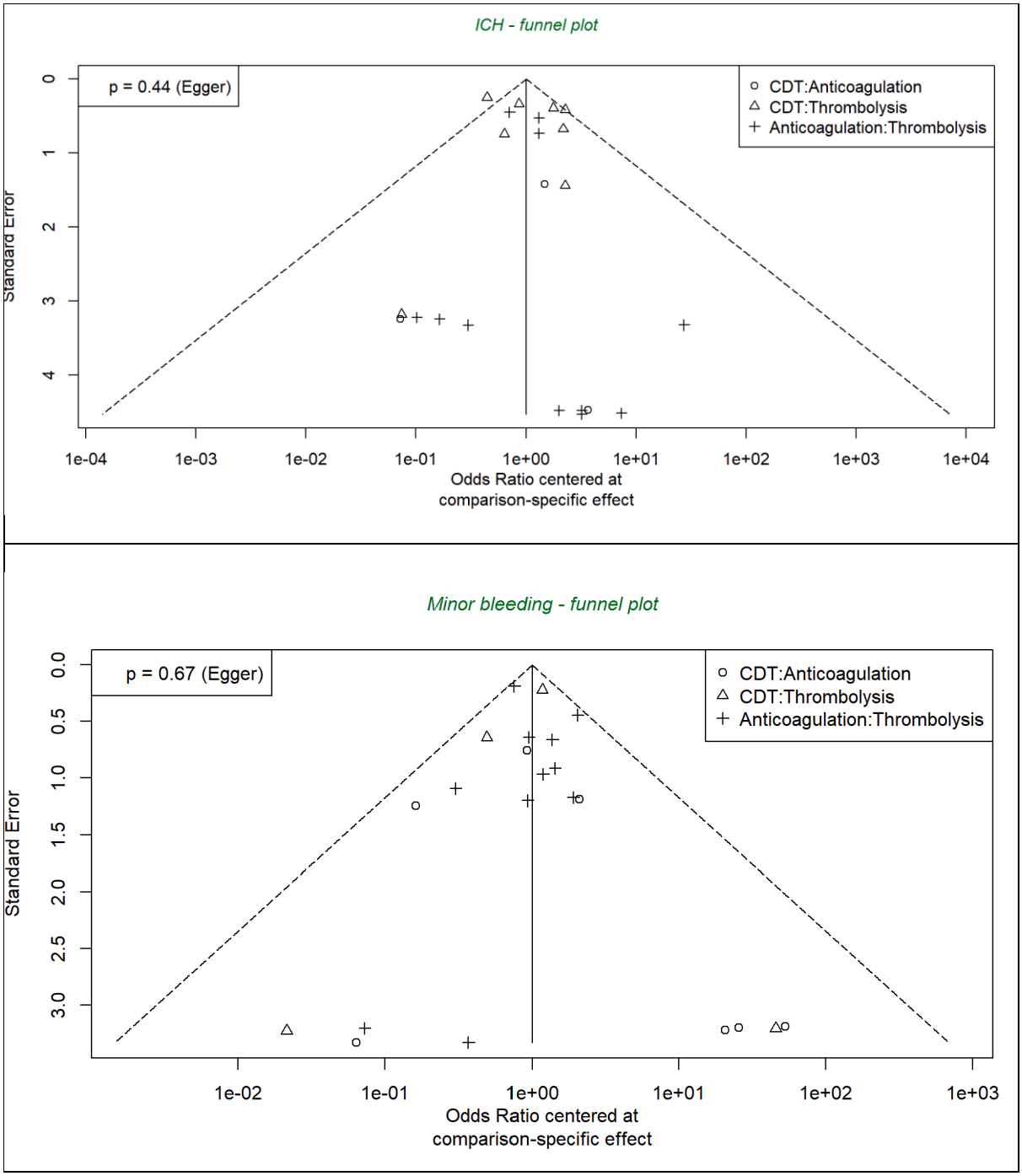
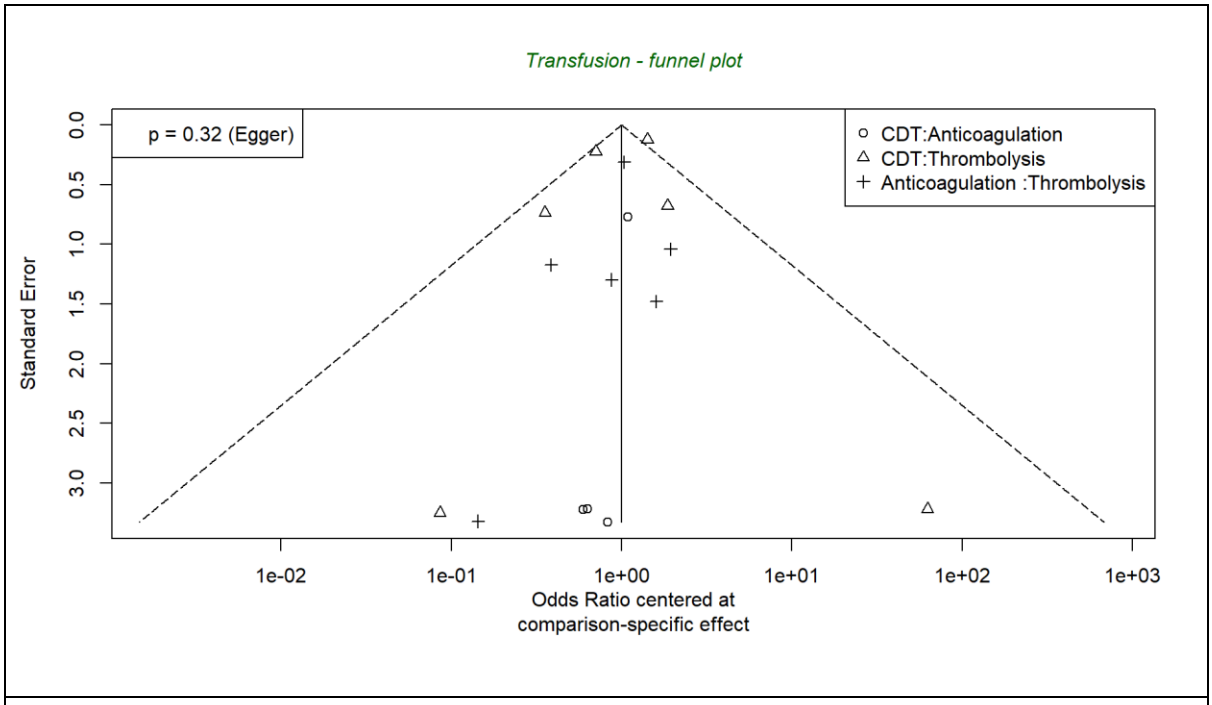


Figure S14: Funnel plots







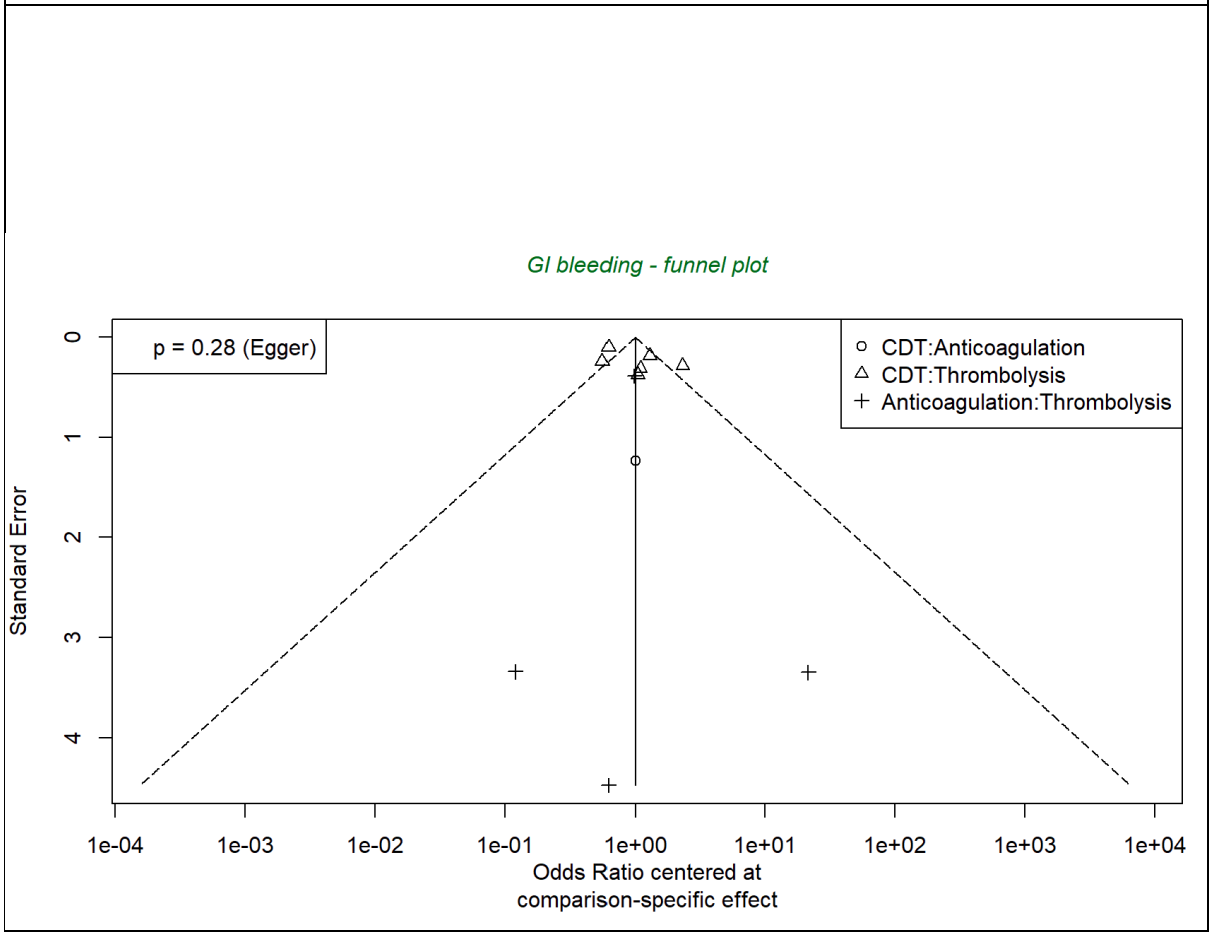


Figure S15: Mortality node splitting - direct and indirect evidence in network meta-analysis

```
Random effects model:

                    comparison  k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation 11 0.54 0.3563 0.4590 0.2655 1.7284  1.43  0.1532
 Thrombolysis:Anticoagulation 21 0.65 0.8267 0.6851 1.1685 0.5863 -1.39  0.1652
             CDT:Thrombolysis 11 0.84 0.4310 0.3974 0.6554 0.6064 -1.28  0.2004

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

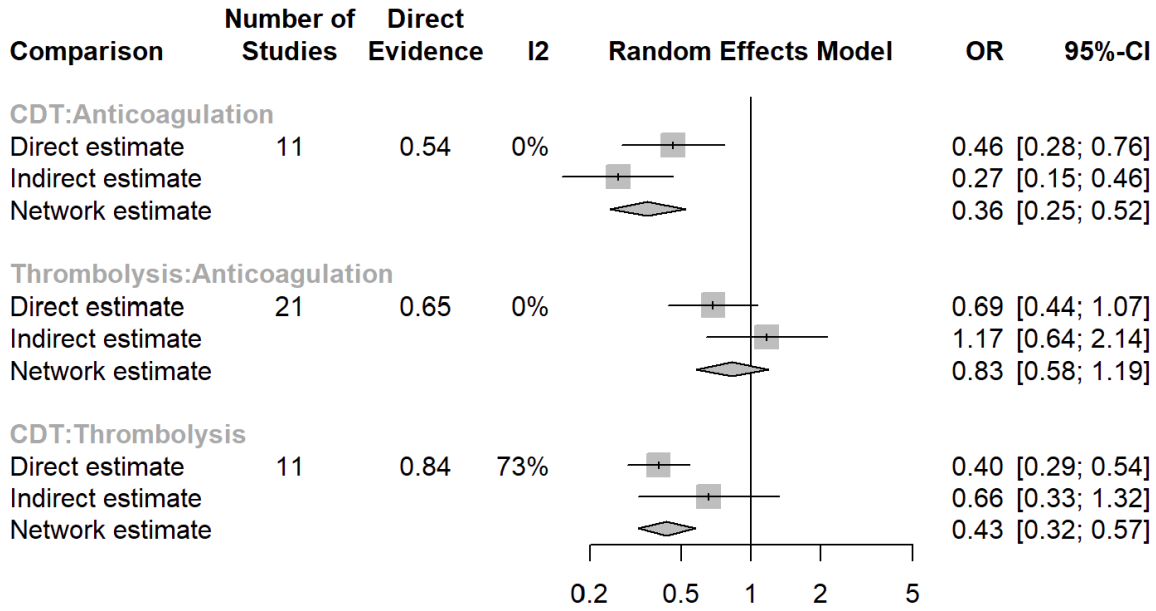


Figure S16: Major bleeding node splitting - direct and indirect evidence in network meta-analysis

```
Random effects model:

                    comparison  k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation  6 0.08 1.2442 1.0855 1.2590 0.8621 -0.23  0.8174
 Thrombolysis:Anticoagulation 20 0.94 2.0559 2.0759 1.7670 1.1748  0.24  0.8113
             CDT:Thrombolysis  9 0.99 0.6052 0.6052 0.6066 0.9976 -0.00  0.9973

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

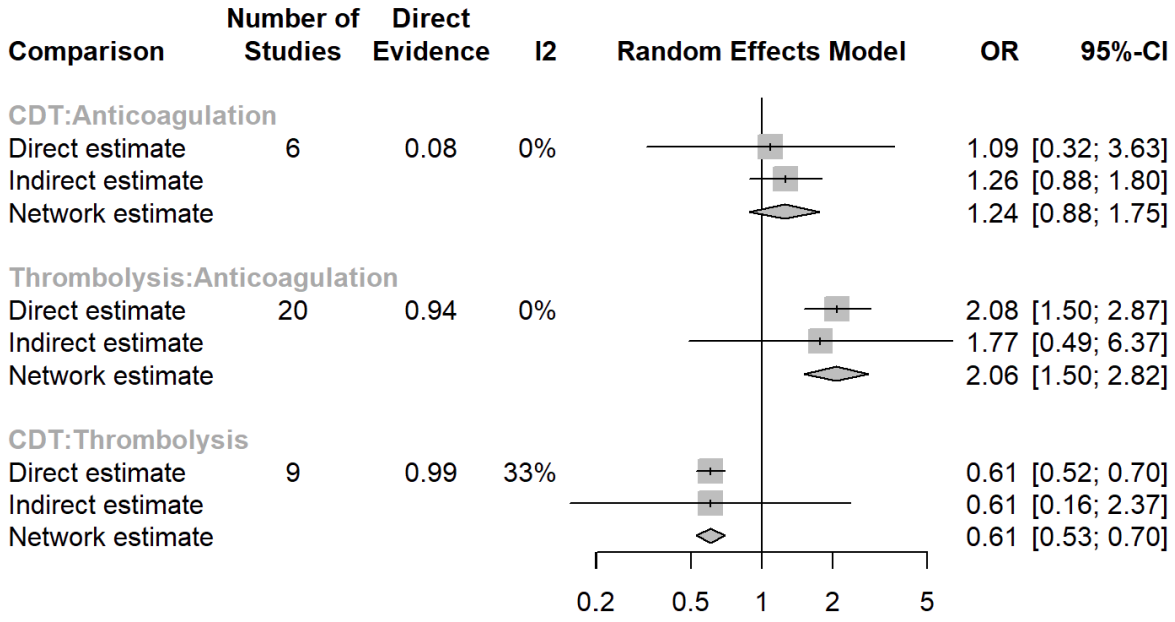


Figure S17: ICH node splitting - direct and indirect evidence in network meta-analysis

```
Random effects model:

                    comparison  k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation  3 0.09 1.3289 0.6809 1.4184 0.4801 -0.55  0.5811
 Thrombolysis:Anticoagulation 11 0.93 3.0527 3.2039 1.5382 2.0829  0.55  0.5811
             CDT:Thrombolysis  8 0.98 0.4353 0.4427 0.2125 2.0829  0.55  0.5811

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

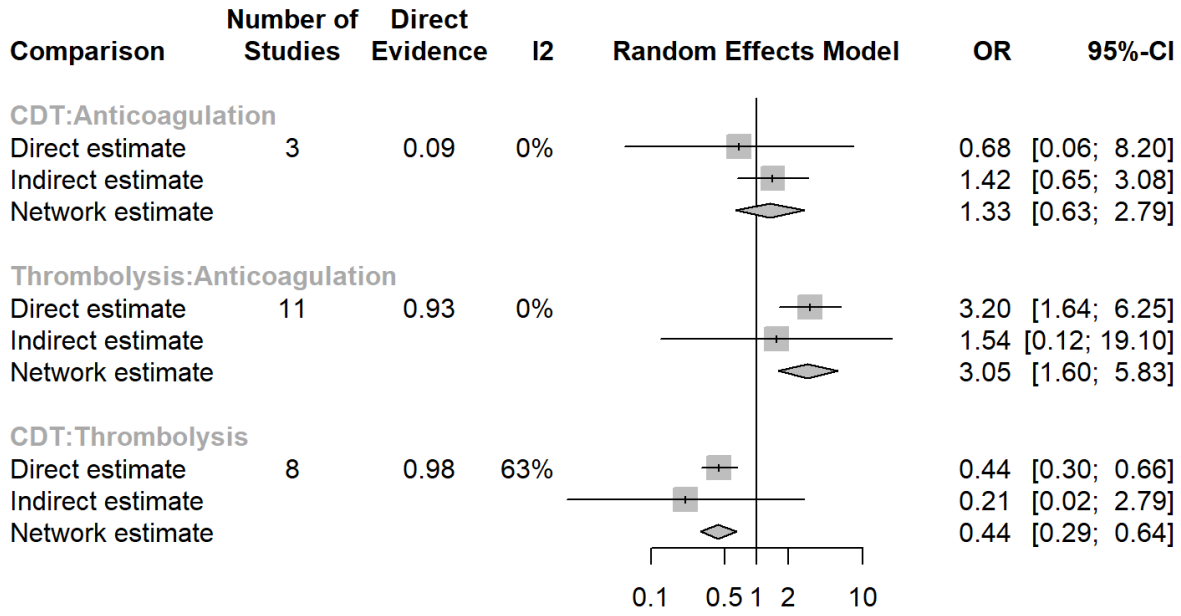


Figure S18: Minor bleeding node splitting - direct and indirect evidence in network meta-analysis

```
Separate indirect from direct evidence (SIDE) using back-calculation method

Common effects model:

                    comparison  k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation  7 0.19 3.9660 1.4752 4.9901 0.2956 -2.05  0.0404
 Thrombolysis:Anticoagulation 11 0.94 3.1747 3.4202 1.0743 3.1835  1.93  0.0538
             CDT:Thrombolysis  4 0.88 1.2492 1.4286 0.4641 3.0784  1.87  0.0613

Random effects model:

                    comparison  k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation  7 0.30 3.1365 1.4880 4.3125 0.3450 -1.61  0.1073
 Thrombolysis:Anticoagulation 11 0.90 2.8229 3.1070 1.1571 2.6851  1.48  0.1385
             CDT:Thrombolysis  4 0.81 1.1111 1.3343 0.5189 2.5712  1.42  0.1567

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

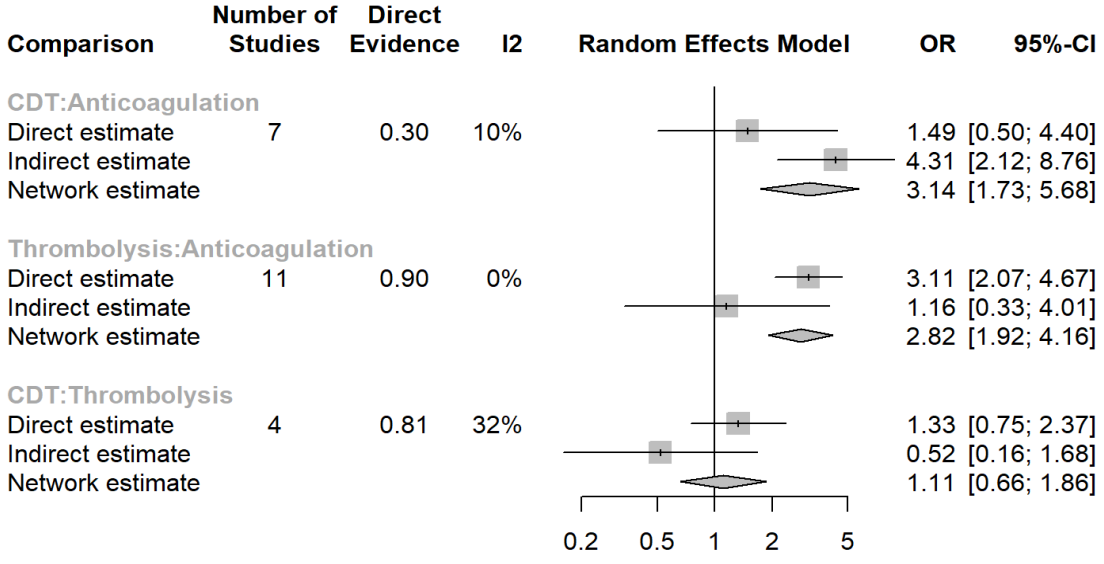


Figure S19: Transfusion node splitting - direct and indirect evidence in network meta-analysis

```
Separate indirect from direct evidence (SIDE) using back-calculation method

Common effects model:

                  comparison k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation 4 0.15 0.6808 0.1169 0.9229 0.1267 -2.68  0.0074
 Thrombolysis:Anticoagulation 6 0.87 1.0920 1.4251 0.1805 7.8957  2.68  0.0074
             CDT:Thrombolysis 6 0.98 0.6234 0.6476 0.0820 7.8957  2.68  0.0074

Random effects model:

                  comparison k prop    nma direct indir.    RoR     z p-value
          CDT:Anticoagulation 4 0.27 0.4684 0.1152 0.7891 0.1460 -2.08  0.0379
 Thrombolysis:Anticoagulation 6 0.82 1.0185 1.4522 0.2120 6.8500  2.08  0.0379
             CDT:Thrombolysis 6 0.91 0.4599 0.5433 0.0793 6.8500  2.08  0.0379

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

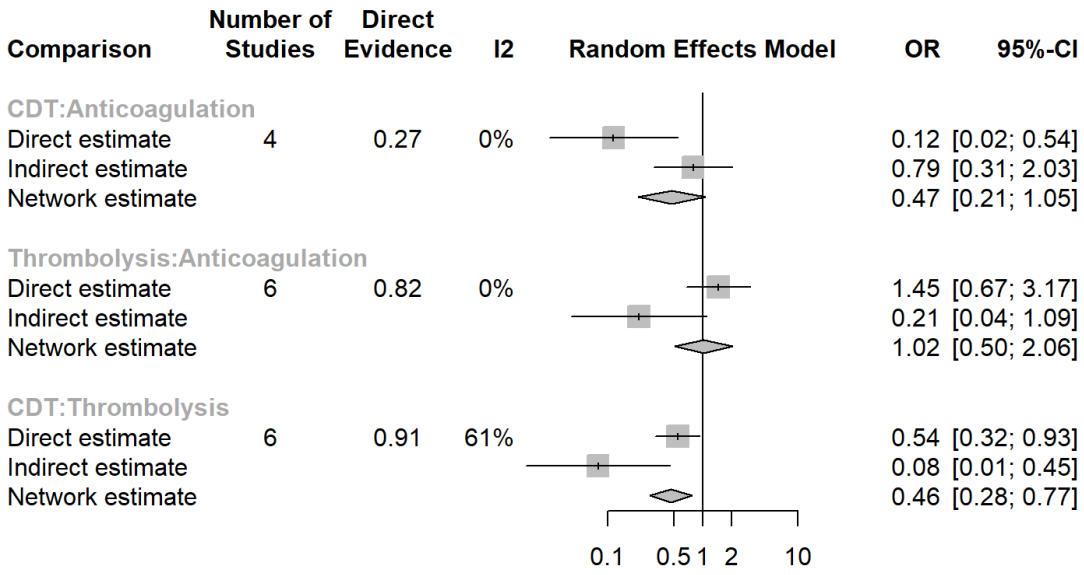


Figure S20: GI node splitting - direct and indirect evidence in network meta-analysis

```
Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

                  comparison k prop    nma direct indir.    RoR     z p-value
         CDT:Anticoagulation 1 0.18 0.8502 0.4949 0.9545 0.5185 -0.45  0.6496
 Thrombolysis:Anticoagulation 4 0.85 0.9114 1.0091 0.5232 1.9287  0.45  0.6496
            CDT:Thrombolysis 6 0.98 0.9329 0.9459 0.4904 1.9287  0.45  0.6496

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (OR) in network meta-analysis
 direct     - Estimated treatment effect (OR) derived from direct evidence
 indir.     - Estimated treatment effect (OR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

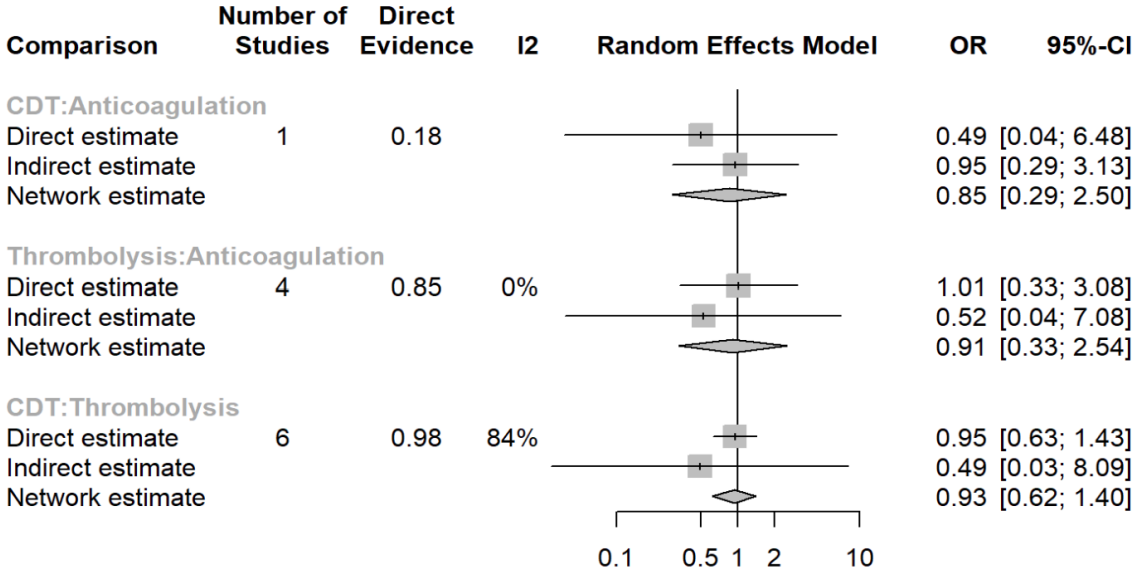


Figure S21: Mortality pairwise forest plot

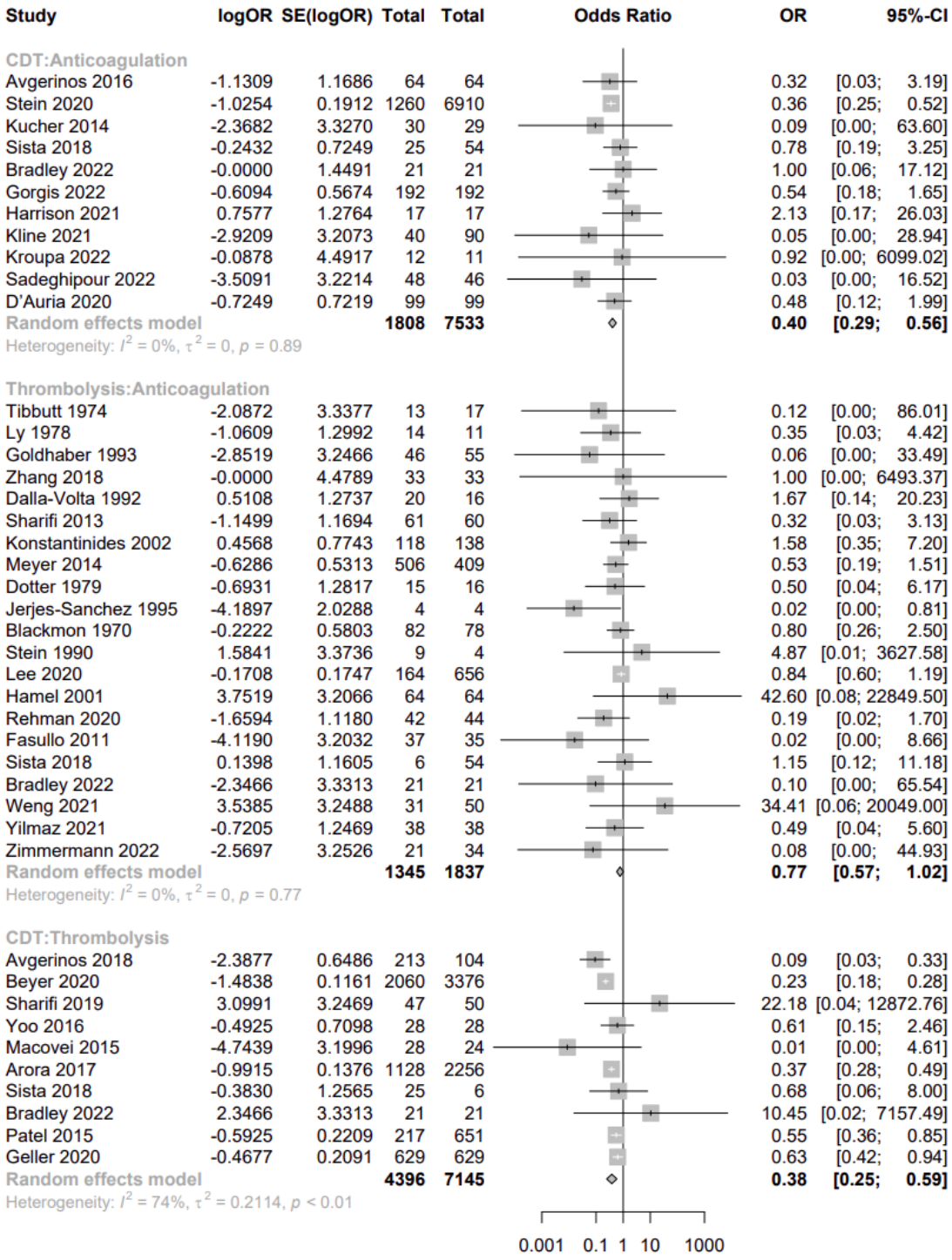


Figure S22: Major bleeding pairwise forest plot

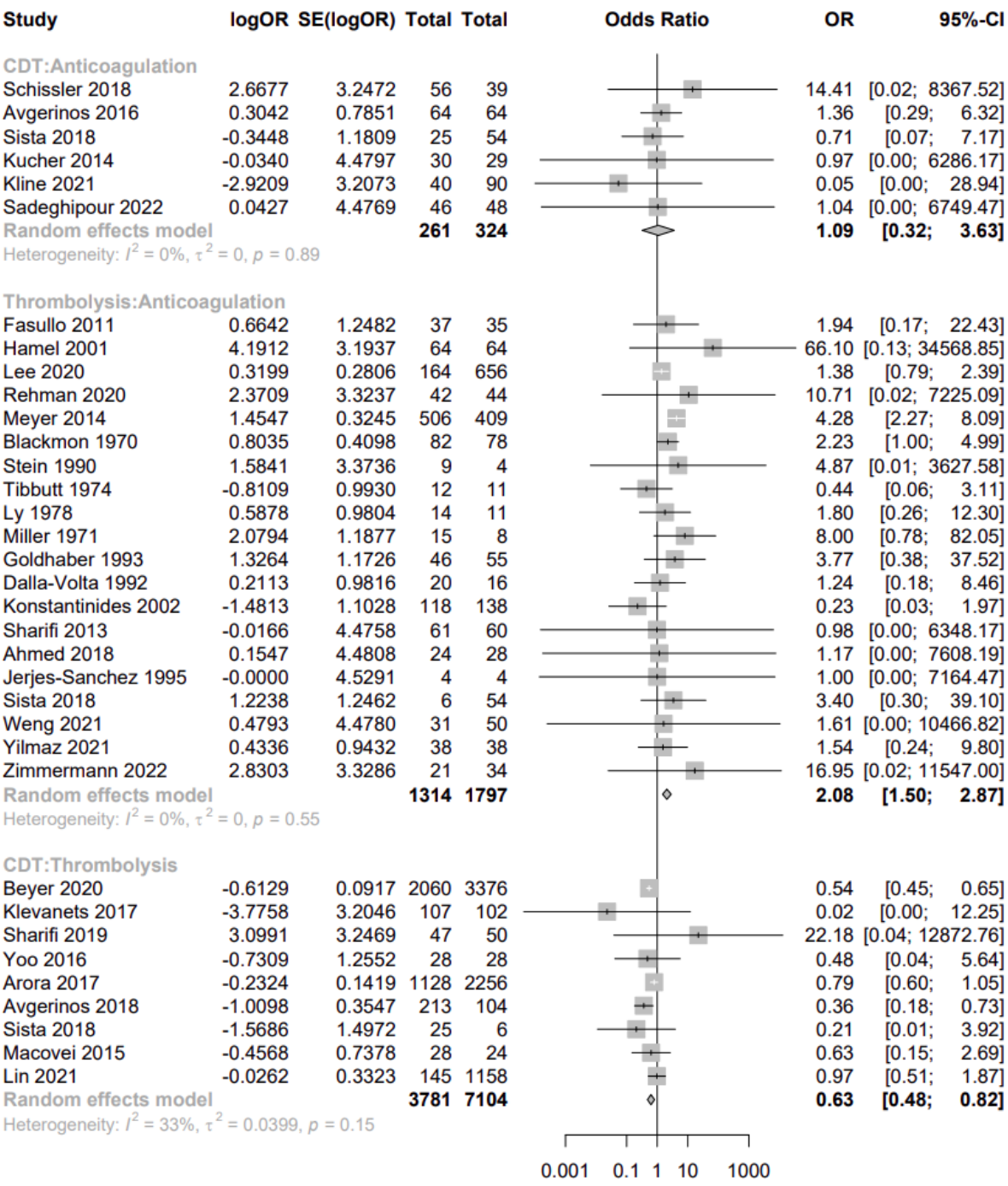


Figure S23: ICH pairwise forest plot

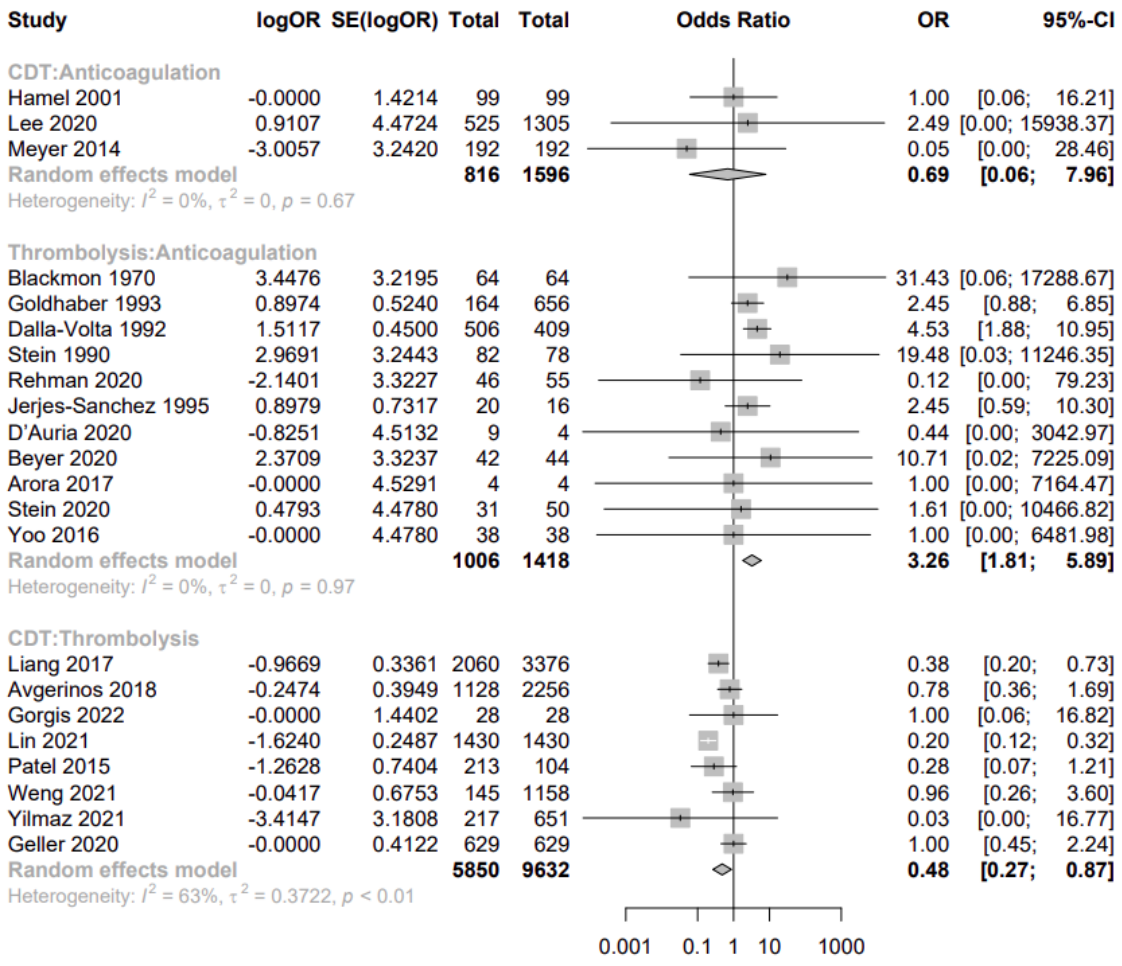


Figure S24: Minor bleeding pairwise forest plot

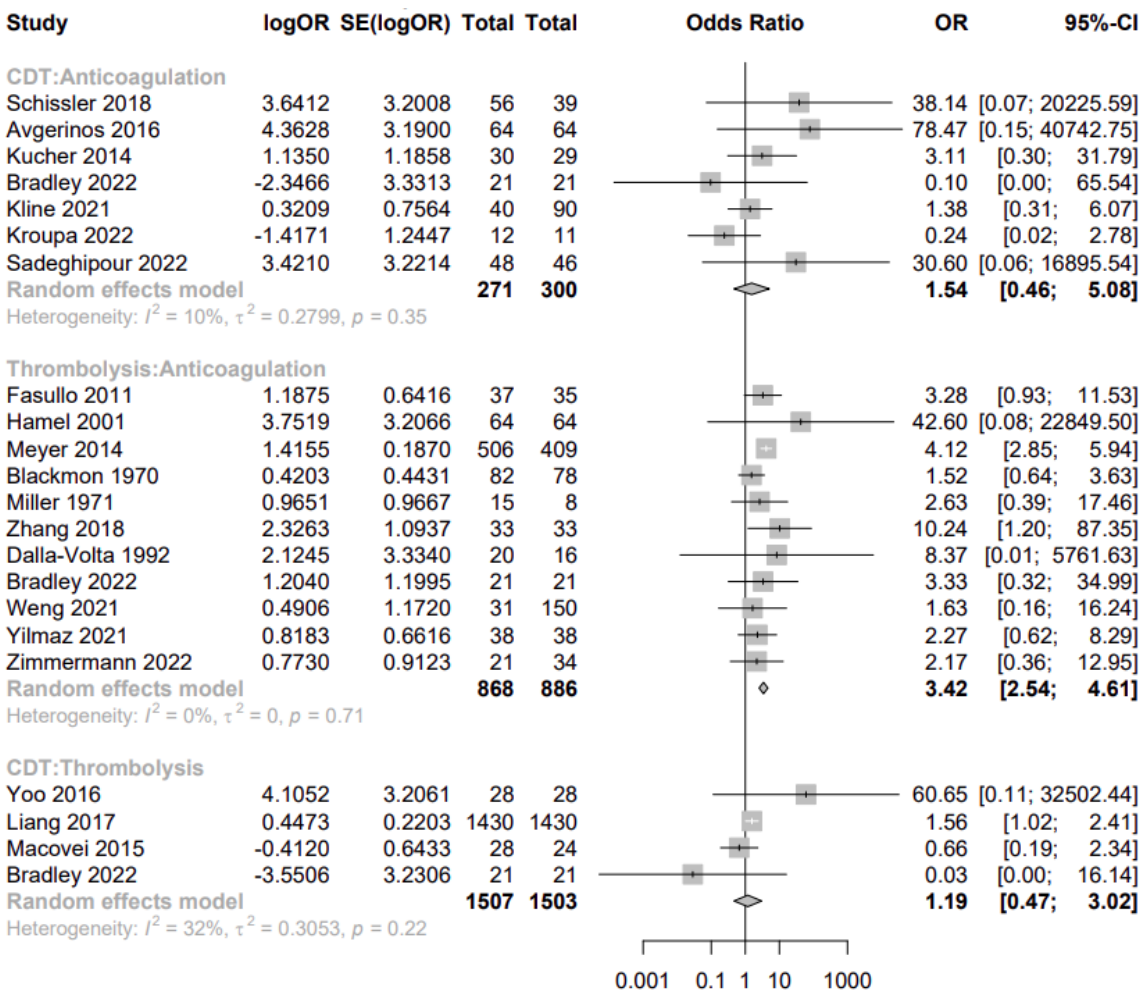


Figure S25: Transfusion pairwise forest plot

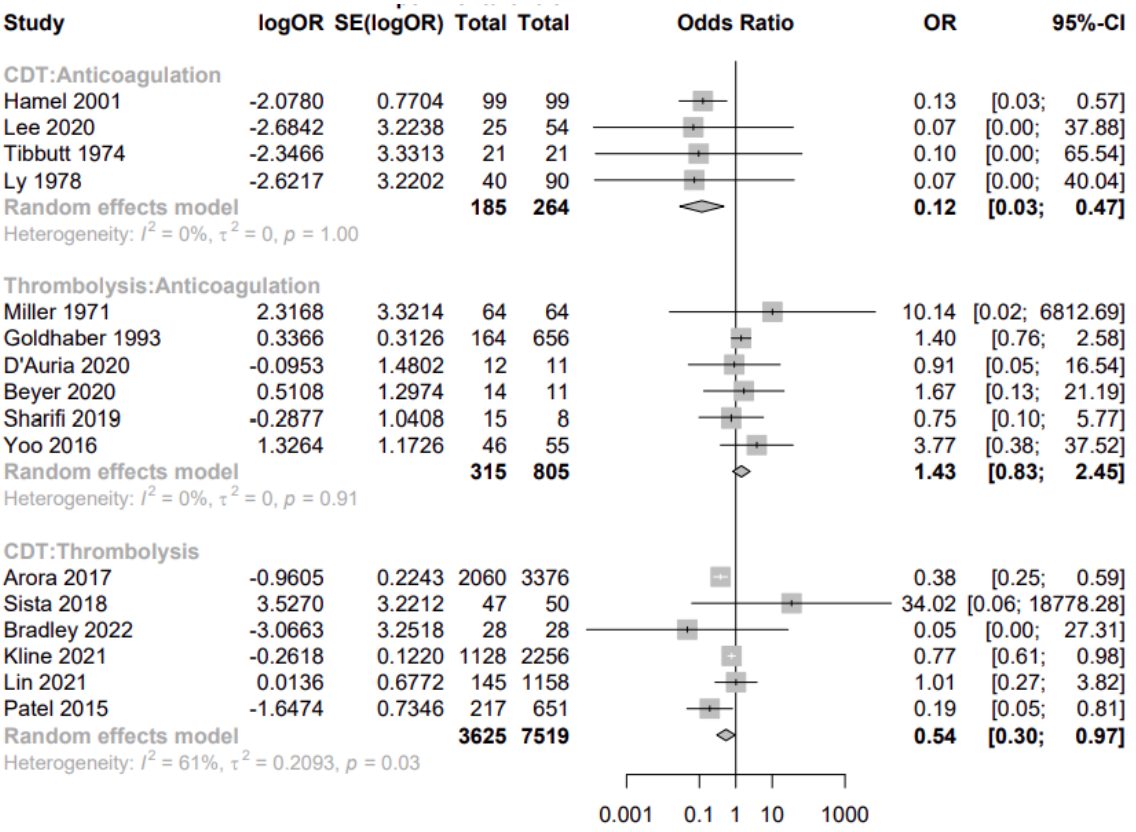


Figure S26: GI pairwise forest plot

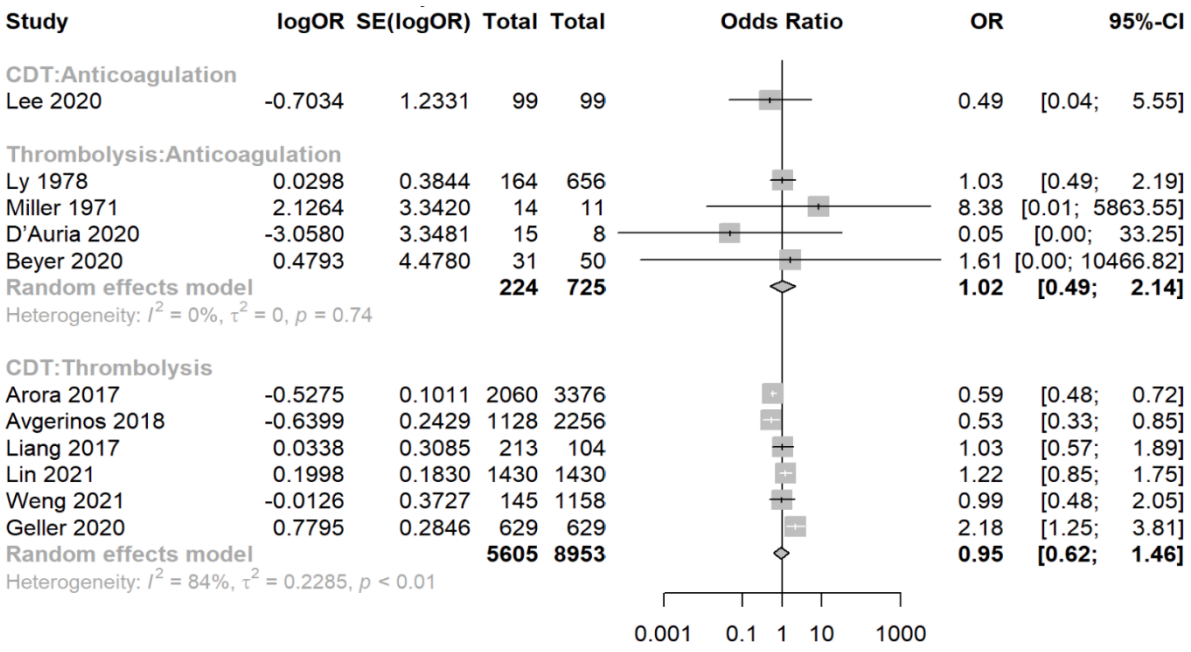


Table S2: summary key characteristics of treatment comparisons

Key characteristic	Thrombolysis vs Anticoagulation	CDT vs Anticoagulation	CDT vs Thrombolysis
All studies			
Number of studies[1]	23	12	13
n	3,347	3,105	15,929
Mean age	59.6	61.3	58.8
Mean male (%)	48.3	52.8	49.62
Mean O2 saturation (%)	89.3	94.7	90.03
Mean heart rate mean (beats per min)	101.7	99.8	100.3
Mean systolic blood pressure (mm Hg)	124.7	130.3	Data is insufficient
Cancer	16%	7%	8%
History of VTE\PE	18%	24%	20%
Immobilization	16%	22%	Data is
Hypercoagulable condition	13%	Data is insufficient	15%
Recent surgery	8%	10%	10%
RCTs			
Number of trails	15	3	1
n	1,999	176	52
Observational studies			
Number of studies	8	9	12
n	1,394	2,956	15,952
Intermediate-High			
Number of studies	7	6	2
Total n	1,414	726	160
Number of RCTs	3	2	0
RCT n	1,129	117	0
Number of cohorts	4	4	2
Cohort n	285	609	160

[1] There are two studies with three arms (Sista 2018 and Bradley 2022)

Figure S27: P-score ranking for main and secondary outcomes.

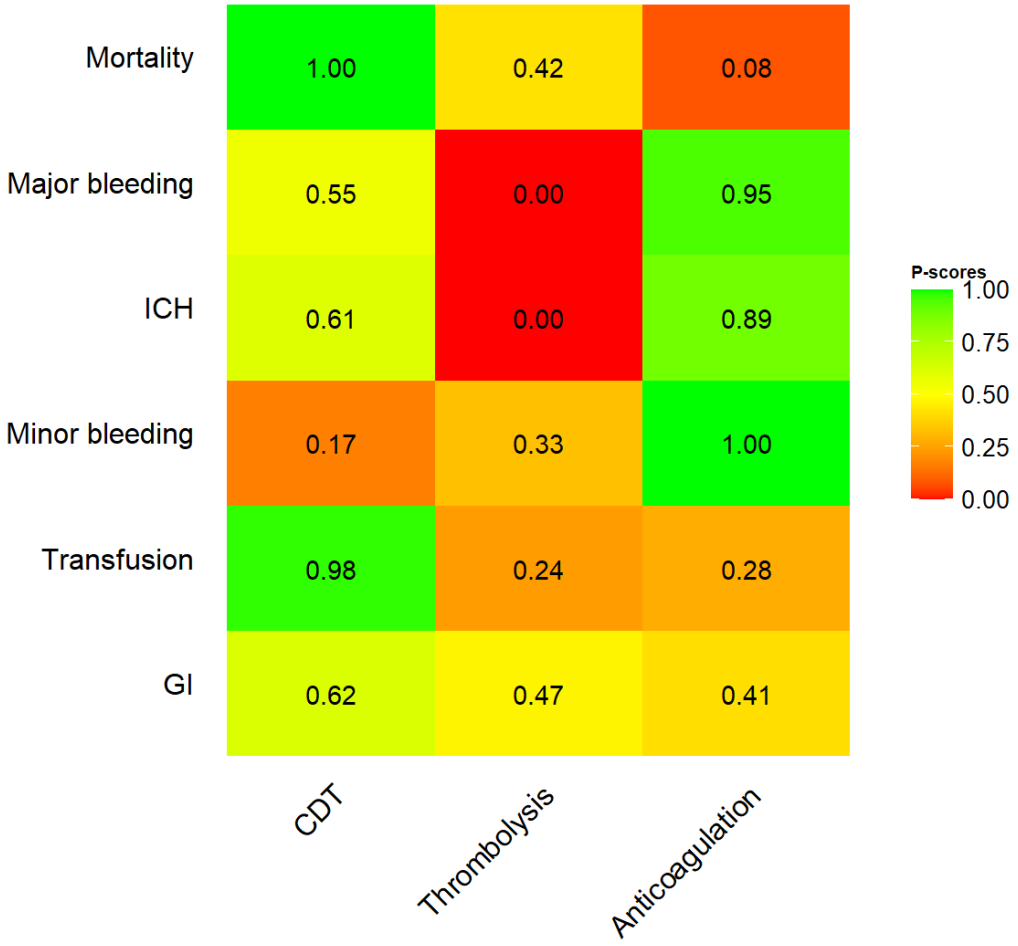
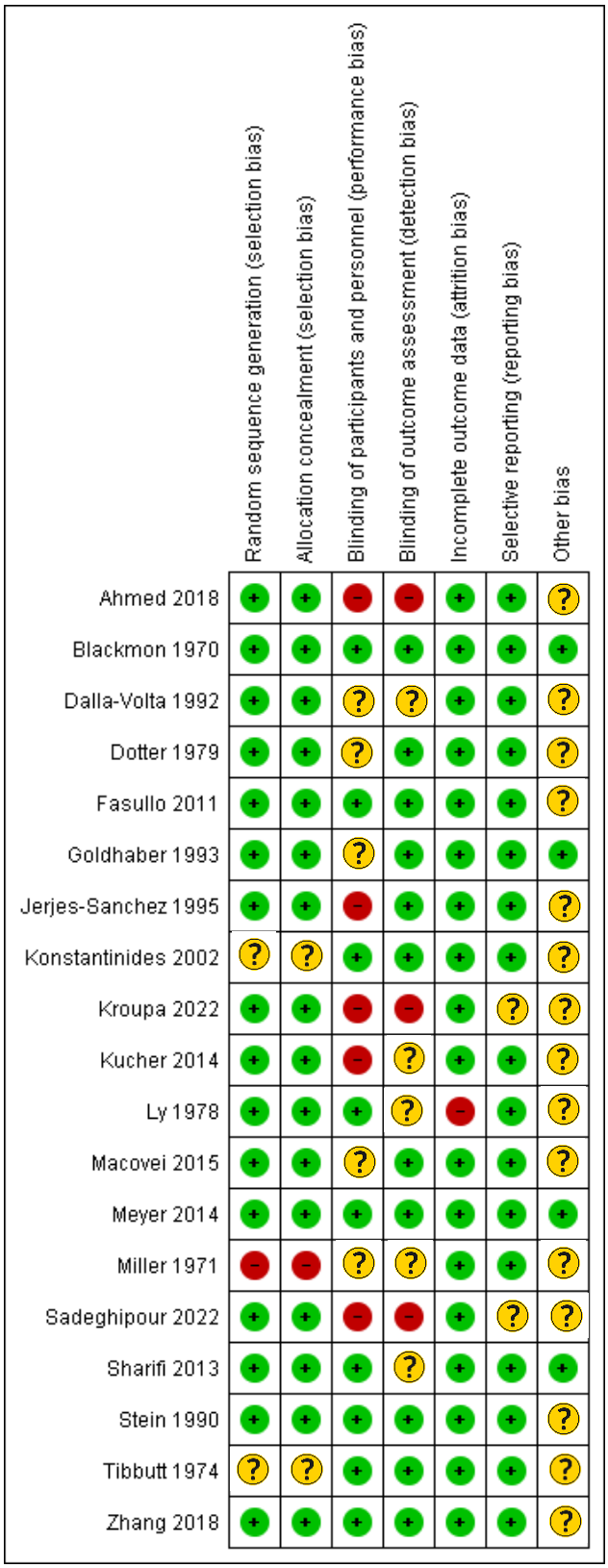


Figure S28: Risk of bias assessment for randomized control studies, evaluated by the Cochrane Collaboration's Risk of Bias Tool



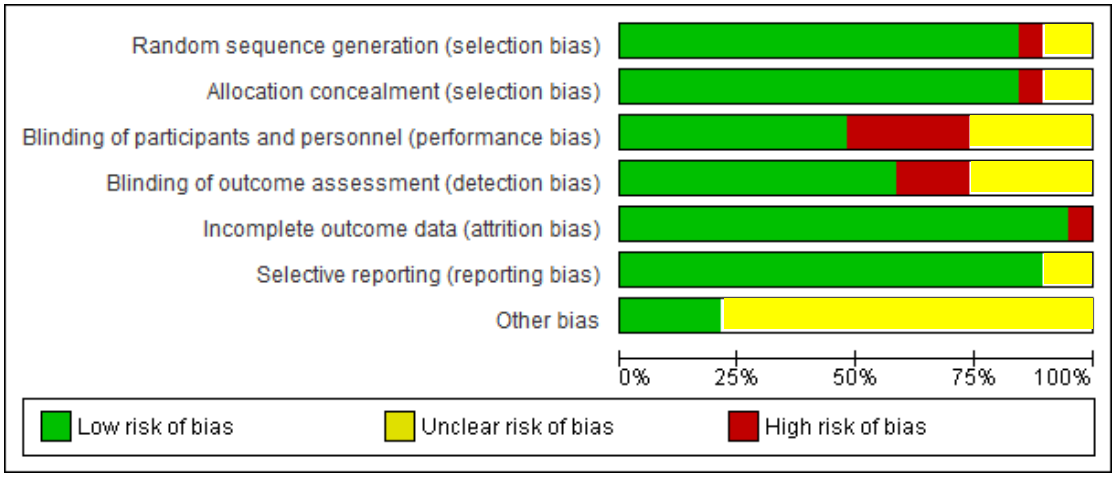


Table S3: Risk of bias and quality of nonrandomized studies, evaluated by the Newcastle-Ottawa Scale (NOS)

Cohort studies	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Study controls for severity of PE	Study controls for an additional factor	Assessment of outcome	Was follow-up long enough for outcomes to occur (≥30 days)	Adequacy of follow up of cohorts (loss-to-follow-up <20%)	Total score
S.D'Auria 2020	*	*	*	*	*	*	*	*	*	9
A.J.Schissler 2018	*	*	*	NA	*	*	*	*	*	8
S.E. Beyer 2020	*	*	*	*	NA	NA	*	*	*	7
J.W.Yoo 2016	*	*	*	*	*	*	*	NA	*	8
E.Hamel 2001	*	*	*	*	*	*	*	*	*	9
N.L.Liang 2017	*	*	*	*	*	NA	*	NA	*	7
S.Arora 2017	*	*	*	*	NA	*	*	*	*	8
E.D.Avgerinos 2016	*		*	*	*	NA	*	*	*	8
A.K.Sista 2018	*	*	*	*	*	*	*	NA	*	8
P.D.Stein 2020	*	*	*	NA	*	*	*	*	*	8
J.K.Lee 2020	*	*	*	*	*	*	*	*	*	9
Klevanets, J 2017	*	*	*	*	*	*	*	*	*	9
M.Sharifi 2019	*	NA	*	*	*	NA	*	*	*	7
E.D.Avgerinos 2016	*	*	*	*	*	NA	*	NA	*	7
E. Harrison 2021	NA	*	*	*	*	*	*	NA	*	7
M. Bradley 2022	*	*	*	*	NA	*	*	NA	*	7
S. Gorgis 2022	*	*	*	*	*	NA	*	*	*	8
T.M Kline 2021	*	*	*	*	*	NA	*	NA	*	7
N. Patel 2022	*	*	*	*	*	*	*	NA	*	8
D.S.H Lin 2021	*	*	*	*	*	*	*	*	*	9
E.S Yilmaz 2021	*	*	*	*	*	*	*	NA	*	8
C. Weng 2021	*	*	*	*	NA	*	*	*	*	8
L. Zimmermann 2021	*	*	*	*	*	*	*	*	*	9
Geller 2020	*	*	*	*	*	*	*	*	*	9
Case-control studies	Adequate case definition	Representativeness of the cases	Selection of Controls	Definition of Controls	Study controls for severity of PE	Study controls for an additional factor	Ascertainment of exposure	The same method of ascertainment for cases and controls	the same non-response rate for both groups	Total score
N.U. Rehman 2020	*	*	*	*	*	NA	*	*	*	8

Figure S28: GRADE assessment:

For the rating of the quality of the indirect evidence, Puhan (2019, BMJ) says this: The lower confidence rating of the two direct comparisons constitutes the confidence rating of the indirect comparison“ .

In the GRADE table in this NMA for all-cause mortality, direct estimates for ST vs AC and CDT vs AC are rated as low quality evidence. Any comparison including these should also be rated as low. In particular, the indirect comparison for CDT vs AC involves direct effects for CDT vs ST (moderate) and ST vs AC (low), so should be graded as low. There is no upgrading of indirect evidence in the GRADE framework (only single estimates from observational studies). The consequence is that the CDT vs AC NMA estimate should also be low quality, as both the indirect and direct evidence are low quality.

A) All-cause mortality

Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence
ST vs AC	0.69 (0.44-1.07)	MODERATE ⊕⊕⊕O	1.17(0.64-2.14)	LOW [1] ⊕⊕OO	0.83 (0.58-1.19)	MODERATE ⊕⊕⊕O
CDT vs ST	0.40 (0.29-0.54)	MODERATE[2,3] ⊕⊕⊕O	0.66 (0.33-1.32)	LOW [1] ⊕⊕OO	0.43 (0.32-0.57	MODERATE ⊕⊕⊕O
CDT vs AC	0.46 (0.28-0.76)	MODERATE ⊕⊕⊕O	0.27 (0.15-0.46)	MODERATE ⊕⊕⊕O	0.36 (0.25-0.52)	MODERATE ⊕⊕⊕O

For ICH, indirect evidence for ST vs AC has to be the lower of the quality ratings of the two involved direct comparisons (moderate and very low, so the result is “very low”). That results in the ST vs AC NMA rating being low (the rating of the direct estimate).

We grade the indirect comparison for ST vs AC as very low-quality evidence, the results in the ST vs AC NMA were also rate as low:

B) ICH

Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence
ST vs AC	3.20 (1.64-6.25)	LOW [2,3] ⊕⊕OO	1.54 (0.12-19.10)	VERY LOW [1,2] ⊕OOO	3.05 (1.60-5.83)	LOW ⊕⊕OO
CDT vs ST	0.44 (0.30-0.66)	MODERATE [2,3] ⊕⊕⊕O	0.21 (0.02-2.79)	LOW [1,2,3] ⊕⊕OO	0.44 (0.29-0.64)	MODERATE ⊕⊕⊕O
CDT vs AC	0.68 (0.06-8.20)	VERY LOW [1,2] ⊕OOO	1.42 (0.65-3.08)	LOW[1] ⊕⊕OO	1.33 (0.63-2.79)	LOW ⊕⊕OO

[1] Imprecision was downgraded by 1 level because the 95% of the relative risk (RR) was wide.
[2] <30% of the included studies are RCT evidence rated down by one level.
[3] Evidence rated up by one level because of very large magnitude of effect.

The quality of indirect evidence for major bleeding should be low for all three comparisons (as all there involve a low rating), so only AC vs ST has a high quality NMA estimate. The other two are low.

The quality of indirect evidence for major bleeding were changed to low for all three comparisons. The quality of NMA for CDT vs ST and CDT vs AC were also changed to low.

C) Major bleeding:

Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence	Odd ratio (95%CI)	Quality of evidence
ST vs AC	2.08 (1.50-2.87)	HIGH [3] ⊕⊕⊕⊕	1.77 (0.49-6.37)	LOW [2] ⊕⊕OO	2.06 (1.50-2.82)	HIGH ⊕⊕⊕⊕
CDT vs ST	0.61 (0.52-0.70)	LOW [2] ⊕⊕OO	0.61 (0.16-2.37)	LOW [2] ⊕⊕OO	0.61 (0.53-0.70)	LOW ⊕⊕OO
CDT vs AC	1.09 (0.32-3.63)	LOW [1] ⊕⊕OO	1.26 (0.88-1.80)	LOW [1] ⊕⊕OO	1.24 (0.88-1.75)	LOW ⊕⊕OO

[1] Imprecision was downgraded by 1 level because the 95% of the relative risk (RR) was wide.
[2] <30% of the included studies are RCT evidence rated down by one level.
[3] Evidence rated up by one level because of very large magnitude of effect.

These points are important, not only because they refer to proper application of GRADE, but because they highlight the uncertainty from NMA, especially when there are observational studies of potentially low quality involved in the comparisons of interest involving CDT.

Table S4: Reasons for studies exclusion

Study	Reasons for exclusion
Hobohm 2021 (5)	• High risk of bias due to Significant differences between Baseline characteristics (Hypoxia above 10% difference, RV dysfunction above 5% difference, shock above 5% difference, need for cardiac pulmonary resuscitation above 20%) • No adjusting was made to relevant outcomes.
Iskandar 2022 (6)	• There is no information available regarding the characteristics of the different groups that may affect the results. • No adjusting was made to rural relevant outcomes (in form of events).
Krishnan 2022 (7)	• High risk of bias due to Significant differences between Baseline characteristics (differences in age- above 4 years in patients over 60 years old). • No adjusting was made to rural relevant outcomes (in form of events). • No data on important covariance such as RV dysfunction, troponin, hemodynamic status, risk for bleeding.
Barrett 2010 (8)	• Eighteen patients received no definitive therapy from total of 51 patients. • High risk for selection bias due to Significant differences between Baseline characteristics (differences in age- above 7 years, differences in intracranial pathology- above 40%). • No adjusting was made to rural relevant outcomes (in form of events).
Konstantinides 1998 (9)	• Continuous variables outcomes - not suitable for NMA using Package 'netmeta' in R.
Nakamura 2005 (10)	• No data on important covariance such as RV dysfunction, troponin, hemodynamic status, risk for bleeding in the presentation. • Table 1 Significant differences between the groups such as differences in shock above 15% and RV afterload stress, and it is not clear whether this data is characteristics or outcomes.
A. Riera-Mestre 2012 (11)	• No standardization of the "no thrombolysis" group. • Mortality outcomes were presented in form of OR.
Sekulic 2020 (12)	• High risk of bias due to Significant differences between Baseline characteristics (differences in age- above 7 years, differences in PESI score, clinical differences in hypoxia and saturation (above 5%), differences in right ventricular systolic pressure (above 15%). • No adjusting was made to rural relevant outcomes (in form of events).
Zulty 2021 (13)	• High risk of bias due to Significant differences between Baseline characteristics (differences in

	Elevated troponin (above 25%), differences in RV strain on CT scan (above 25%). • No adjusting was made to rural relevant outcomes (in form of events). • The comparation to CDT was "standard treatment" (included both anticoagulation and possibly systemic thrombolysis).
Omaygenc 2021 (14)	• High risk of bias due to Significant differences between Baseline characteristics (differences in age- above 10 years, saturation (3%), Systolic pulmonary artery pressure (12%). • No adjusting was made to rural relevant outcomes (in form of events).

Table S5: Bleeding definitions

First author and year	Bleeding definitions
Fasullo 2011	Major: fatal, intracranial, required transfusions or intervention for hemodynamic deterioration. Minor bleeding: episodes not fulfilling major bleeding criteria
D'Auria 2020	ICD 9 and ICD 10 codes, internal billing codes
Schissler 2018	GUSTO criteria.(11)
Meyer 2014	Major bleeding: ICH, life threatening, fatal, need for transfusion Moderate bleeding: requiring blood transfusion(s), not life-threatening, not requiring emergency fluid replacement, inotropic support, or interventional treatment. Bleeding events were also reported using the criteria proposed by the International Society on Thrombosis and Haemostasias. (12)
Beyer 2020	Diagnostic and Procedure Billing Codes. (ICD-10 CM/PCS Code)
Dotter 1979	Not prespecified
Avgerinos 2016	Not prespecified
Klevanets 2017	Not prespecified
Macovei 2015	Major bleeding: brain bleeding or gastro- intestinal, massive hematoma on the puncture site or acute post-hemorrhagic anemia Minor bleeding: hematoma on the puncture site, transient ischemic attack
Sharifi 2019	GUSTO criteria.(11)
Jerjes-Sanchez 1995	Not prespecified
Blackmon 1970	Major bleeding: Hematocrit drop >10 points, 2 or more units packed RBC.
Stein 1990	Not prespecified
Yoo 2016	Major bleeding: fatal bleeding, hemorrhagic stroke, Hgb drop >2 g/dl, with or without the need for packed red cell transfusion.
Hamel 2001	Severe bleeding: intracranial hemorrhage, decrease in hemoglobin level (at least 4 g/100 ml), bleeding that required surgery or blood transfusion of 2 or more units.
Liang 2017	GUSTO criteria.(11)
Tibbutt 1974	Not prespecified
Ahmed 2018	Not prespecified
Ly 1978	Not prespecified
Miller 1971	Not prespecified
Kucher 2014	Major bleeding: overt bleeding with Hgb drop >2 g/dl, transfusion of ≥2 U of RBC, involvement of a critical site (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intra-muscular with compartment syndrome). Minor bleeding: Clinically overt bleeding not fulfilling the criteria of major bleeding.
Arora 2017	Identified using appropriate ICD-9 diagnosis and procedural code in secondary fields
Avgerinos 2018	GUSTO criteria.(11)
Goldhaber 1993	Major bleeding: required surgery (e.g., laparotomy for Retroperitoneal bleeding) or any intracranial bleeding.
Zhang 2018	Not prespecified

Sista 2018	Major bleeding: requiring transfusion, major hemoptysis requiring intubation, intracranial hemorrhage, or operation
Dalla-Volta 1992	Major bleeding was defined as an ICH or bleeding requiring transfusion of one or more units of blood
Sharifi 2013	Not prespecified
Konstantinides 2002	Major bleeding: fatal bleeding, hemorrhagic stroke, or a drop in the hemoglobin concentration by at least 4 g per deciliter, with or without the need for red-cell transfusion.
Lee 2020	ICD-9-CM codes
Stein 2020	Not prespecified
Rehman 2020	Not prespecified
Bradley 2022	GUSTO criteria.(11)
Gorgis 2022	GUSTO criteria.(11)
Sadeghipour 2022	Bleeding Academic Research Consortium (BARC). (13)
Kline 2021	TIMI bleeding (Thrombolysis in Myocardial Infarction) criteria for secondary analysis. (13)
Kroupa 2022	Bleeding Academic Research Consortium (BARC). (13)
Lin 2021	ICD-9 CM diagnostic codes. Major bleeding 3361, 3636, 37272, 37632, 37742, 37923, 4230, 430, 431, 4320, 4321, 4329, 531, 5312, 5314, 5316, 532, 5322, 5324, 5326, 5307, 533, 5332, 5334, 5336, 534, 5342, 5344, 5346, 5693, 53501, 53511, 53521, 53531, 53541, 53551, 53561, 53571, 53783, 53784, 56202, 56203, 56212, 56213, 56985, 578, 59381, 7191, 72992, 7725, 8520, 8522, 8524, 8530, 86601, 86602, 86611, 86612 Gastrointestinal bleeding 530.21, 530.7, 530.82, 531.xx-535.xx, 537.83, 537.84, 578.xx Intracranial hemorrhage 430.xx-432.xx
Patel 2015	ICD-9-CM codes
Weng 2021	Major bleeding was defined as fatal bleeding, hemorrhagic stroke, or a drop in the hemoglobin concentration by at least 4 g/dL
Yilmaz 2021	according to the International Society on Thrombosis and Haemostasis definition. (14)
Zimmermann 2022	Bleeding complications were defined according to The International Society on Thrombosis and Haemostasis criteria. (14)
Geller 2020	ICD-9-CM codes

Table S6: Mortality Outcomes in each study

Study	Mortality Outcome	Comments
Arora 2017	In-hospital mortality	
Avgerinos 2016	In-hospital mortality	
Avgerinos 2018	In-hospital mortality	
Beyer 2020	In-hospital mortality	
Blackmon 1970	14 days	
Bradley 2022	In-hospital mortality	
D'Auria 2020	30 days	
Dalla-Volta 1992	30 days	Alteplase group: day 6, day 19. Heparin group: day 2
Dotter 1979	In-hospital mortality	One patient treated with streptokinase died 4 days after the completion of therapy. Two heparin-treated patients died before the 72-hour therapy was completed
Fasullo 2011	In-hospital mortality	
Geller 2020	In-hospital mortality	
Goldhaber 1993	In-hospital mortality	
Gorgis 2022	In-hospital mortality	
Hamel 2001	In-hospital mortality	
Harrison 2021	In-hospital mortality	
Jerjes-Sanchez 1995	In-hospital mortality	
Kline 2021	In-hospital mortality	
Konstantinides 2002	In-hospital mortality	
Kroupa 2022	30 days	
Kucher 2014	30 days	1 death in the heparin group 20 days after randomization
Lee 2020	In-hospital mortality	
Lin 2021	In-hospital mortality	

Ly 1978	30 days	Heparin group: 15 hours, day 30. Streptokinase group: day 22
Macovei 2015	In-hospital mortality	
Meyer 2014	In-hospital mortality	
Patel 2015	In-hospital mortality	
Rehman 2020	In-hospital mortality	
Sadeghipour 2022	90 days	
Sharifi 2013	Unclear	Considering that there is no information regarding the four individuals who died, it is likely that they died not long after their hospitalization since PE is an acute cardiovascular disorder associated with a high mortality rate at an early stage.
Sharifi 2019	30 days	
Sista 2018	In-hospital mortality	
Stein 1990	In-hospital mortality	Died of an arrhythmia 19 days after treatment with rt-PA.
Stein 2020	In-hospital mortality	We combined data from non-saddle PE group and saddle PE group
Tibbutt 1974	In-hospital mortality	
Weng 2021	In-hospital mortality	
Yilmaz 2021	In-hospital mortality	
Yoo 2016	In-hospital mortality	
Zhang 2018	In-hospital mortality	No deaths in the 3-month follow up
Zimmermann 2022	In-hospital mortality	

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