

Title: Safety and effectiveness of direct oral anticoagulants versus low molecular weight heparin for cancer-associated thrombosis: a systematic review and meta-analysis

Running title: DOACs vs. LMWH in cancer-associated thrombosis: A Systematic Review and Meta-Analysis

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Supplementary Material

Table of Contents

Title Page	1
Table of Contents	3
Detailed literature search strategy.....	4
Table S1 Quality of included RCTs by Revised Cochrane risk-of-bias tool [1]	5
Table S2 Quality of the included cohort studies by New Castle Ottawa scale [9]	6
Fig. S1 Funnel plot of RRs of DOACs vs. LMWH for recurrent VTE in cohort studies	8
Fig. S2 Funnel plot of RRs of DOACs vs. LMWH for major bleeding in cohort studies.....	9
Fig. S3 Sensitivity analysis: Forest plot of Risk Ratios of DOACs vs. LMWH in cohort studies restricted to ITT results only	10
References	12

Detailed literature search strategy

We conducted a systematic literature search from the inception of relevant databases up to 30 June 2025, to identify studies that assessed the safety and effectiveness of DOACs compared to LMWH in patients with CAT. The literature search was performed using PubMed (MEDLINE database), Excerpta Medical Database (Embase), and Cochrane Library. The keywords and search strategies were as follows: ('new oral anticoagulant' OR 'NOAC' OR 'direct oral anticoagulants' OR 'DOAC' OR 'factor Xa inhibitor' OR 'thrombin inhibitor' OR 'apixaban' OR 'rivaroxaban' OR 'edoxaban' OR 'dabigatran') AND ('LMWH' OR 'low molecular weight heparin' OR 'dalteparin' OR 'enoxaparin' OR 'tinzaparin' OR 'bemiparin' OR 'nadroparin' OR 'reviparin' OR 'parnaparin' OR 'certoparin') AND ('cancer' OR 'tumor' OR 'malignancy' OR 'neoplasm' OR 'carcinoma' OR 'adenoma' OR 'adenocarcinoma' OR 'lymphoma' OR 'leukemia' OR 'CAT' OR 'cancer-associated thrombosis' OR 'cancer-associated venous thrombosis') AND ('DVT' OR 'venous thrombosis' OR 'venous thromboembolism' OR 'VTE' OR 'venous thrombosis' OR 'venous thromboses' OR 'deep venous thrombosis' OR 'deep venous thromboses' OR 'thrombosis' OR 'thromboembolism' OR 'PE' OR 'pulmonary embolism'). We further examined the reference lists of review articles to identify any additional relevant studies.

Table S1 Quality of included RCTs by Revised Cochrane risk-of-bias tool [1]

	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Study	Raskob et al. (2018)[2]					
	Young et al. (2018)[3]					
	Agnelli et al. (2020)[4]					
	McBane et al. (2020)[5]					
	Planquette et al. (2022)[6]					
	Schrag et al. (2023)[7]					
	Sinn et al. (2025)[8]					
Domains: D1: Bias arising from the randomization process. D2: Bias due to deviations from intended intervention. D3: Bias due to missing outcome data. D4: Bias in measurement of the outcome. D5: Bias in selection of the reported result.						
Judgement  High  Some concerns  Low						

Table S2 Quality of the included cohort studies by New Castle Ottawa scale [2]

First author, publication year	Selection				Comparability [†]		Outcome [§]			Total Scores
Agno et al. (2017)[3]	*	*	*	*	*		*	*	*	8
Ross et al. (2017)[4]	*	*	*	*	*		*	*		7
Alzghari et al. (2018)[5]	*	*	*	*	*		*	*	*	8
Chaudhury et al. (2018)[6]	*	*	*	*			*	*		6
Simmons et al. (2018)[7]	*	*	*	*	*	*	*	*	*	9
Streiff et al. (2018)[8]	*	*	*	*	*	*	*	*	*	9
Lee et al. (2019)-gastrointestinal and pancreatobiliary cancer[9]	*	*	*	*	*	*	*	*	*	9
Lee et al. (2019)-lung cancer[10]	*	*	*	*	*	*	*			7
Lee et al. (2019)-urologic cancer[11]	*	*	*	*	*	*	*			7
Phelps et al. (2019)[12]	*	*	*	*	*	*	*	*	*	9
Signorelli et al. (2019)[13]	*	*	*	*	*	*	*	*		8
Wysokinski et al. (2019)[14]	*	*	*	*	*	*	*	*	*	9
Faqah et al. (2020)[15]	*	*	*	*	*		*	*		7
Kim et al. (2020)[16]	*	*	*	*	*	*	*	*		8
Lee et al. (2020)-gynecologic cancers[17]	*	*	*	*	*	*	*			7
Chen et al. (2021)[18]	*	*	*	*	*	*	*	*	*	9
Cohen et al. (2021)[19]	*	*	*	*	*	*	*	*	*	9
Douros et al. (2021)[20]	*	*	*	*	*	*	*	*	*	9
Fovel et al. (2021)[21]	*	*	*	*	*		*			6
Cohen et al. (2023)[22]	*	*	*	*	*	*	*	*	*	9
Coleman et al. (2023)[23]	*	*		*	*	*	*	*	*	8
Guan et al. (2023)[24]	*	*	*	*	*	*	*	*		8
Riaz et al. (2023)[25]	*	*	*	*	*	*	*	*	*	9

Supplementary Material: DOACs vs. LMWH in cancer-associated thrombosis: A Systematic Review and Meta-Analysis

Cohen et al. (2024)[26]	*	*	*	*	*	*	*	*	*	9
Kengkla et al. (2024)[27]	*	*	*	*	*	*	*	*	*	9
Linder et al. (2024)[28]	*	*	*	*	*	*	*	*	*	9
Chung et al. (2025)[29]	*	*	*	*			*	*		6
Cohen et al. (2025)[30]	*	*	*	*	*	*	*	*		8

† Balanced age was assigned the first star.

§ A cohort study with a follow-up time of three months or more was assigned the second star. A cohort study with a clear follow-up rate exceeding 80% was assigned the third star.

Fig. S1 Funnel plot of RRs of DOACs vs. LMWH for recurrent VTE in cohort studies

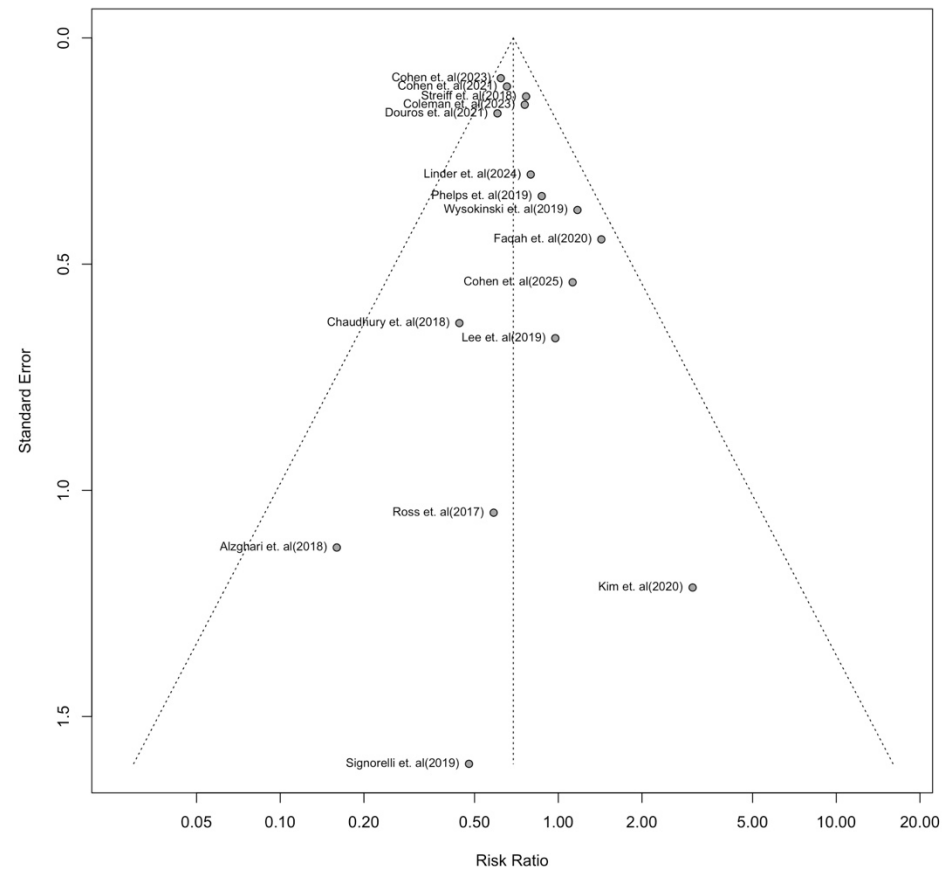


Fig. S2 Funnel plot of RRs of DOACs vs. LMWH for major bleeding in cohort studies

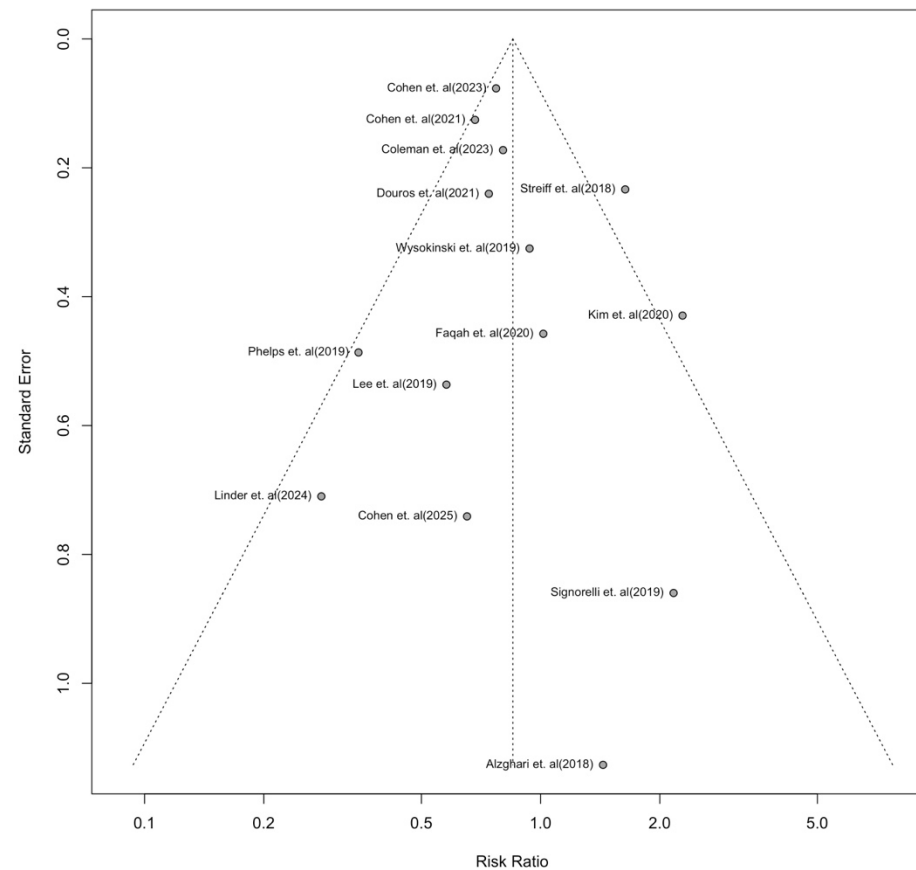
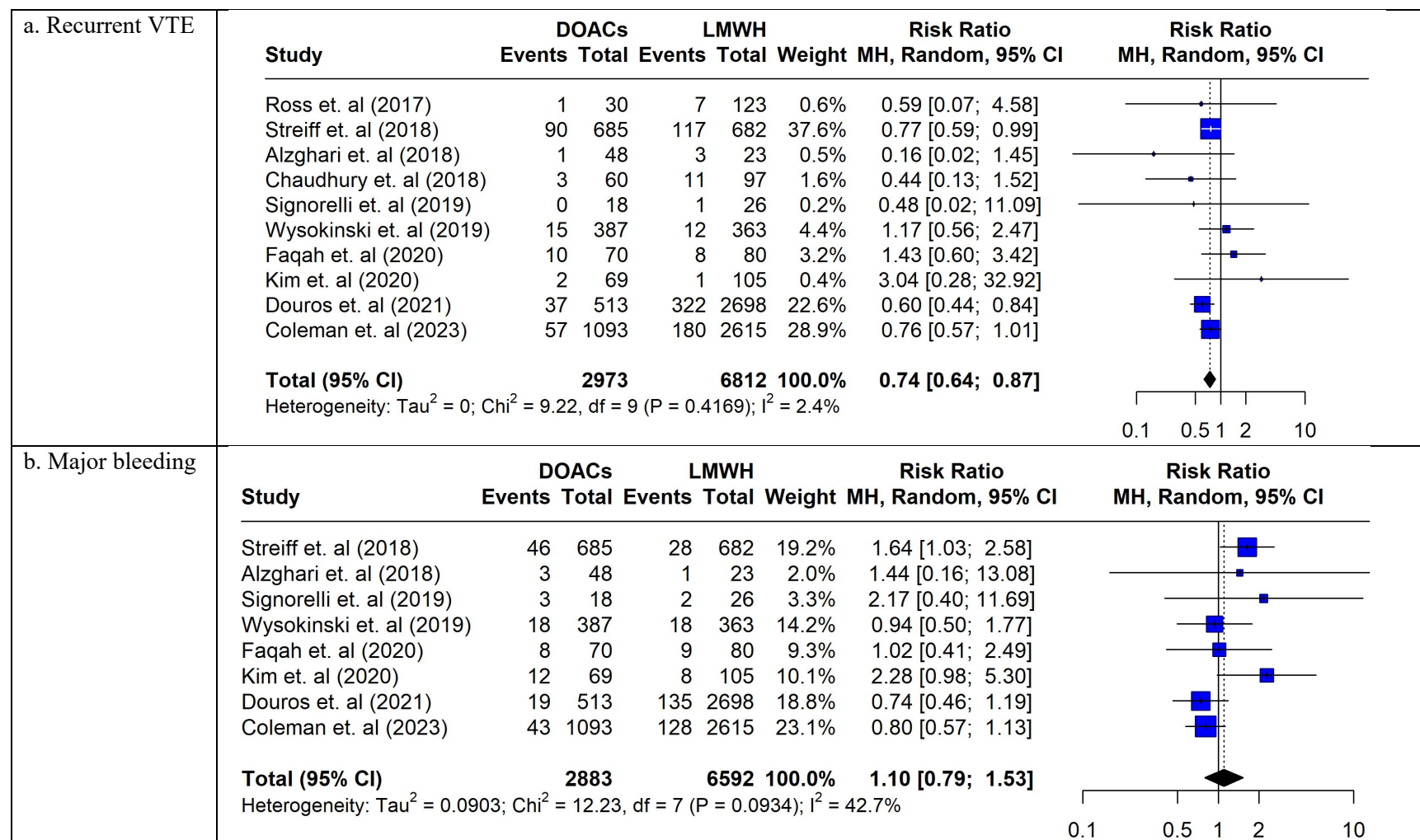
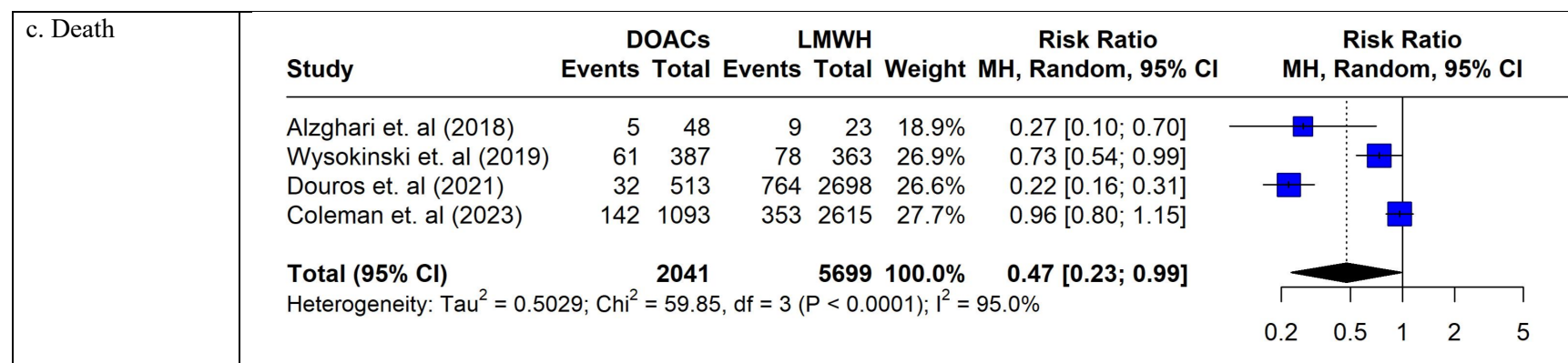


Fig. S3 Sensitivity analysis: Forest plot of Risk Ratios of DOACs vs. LMWH in cohort studies restricted to ITT results only



DOACs: Direct oral anticoagulants; LMWH: Low molecular weight heparin; MH: Mantel-Haenszel; CI: confidence interval.

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