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COMPARATIVE EFFICACY OF DIFFERENT THROMBOPROPHYLAXIS STRATEGIES IN PREVENTING POSTOPERATIVE VENOUS THROMBOEMBOLISM: A SYSTEMATIC REVIEW & META-ANALYSIS

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Abstract

Veno thromboembolism (VTE; DVT, PE) is one of the frequent and one of the riskier complications in surgical patients. The choice and use of effective thromboprophylaxis is essential. The primary aim of this meta-analysis and systemic review was to compare efficacy and safety of various thromboprophylaxis regimens (direct oral anticoagulants -DOACs-, low-molecular-weight heparin -LMWH-, aspirin and mechanical techniques) to prevent post-surgical VTE. Fifteen studies were selected for inclusion. We concluded based on the meta-analysis that: the DOACs are equally as effective as the LMWHs in most cases of cancer surgeries in preventing VTE but have a non-statistical increased overall risk of major bleedings. Aspirin seem to work in some orthopedic surgeries; they have an almost non statistically lower trend to bleeding. and mechanical combined with pharmacological method outperform each approach by own.

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Graphical Abstract

Figure 1: Graphical Abstract showing the visible and hidden complexities of postoperative VTE prevention and thromboprophylaxis strategies.

INTRODUCTION

Venous thromboembolism (VTE) in the postoperative patient remains an important clinical problem, accounting A lot for the worldwide burden of disease and mortality linked to surgical procedures today [1].There is a much increased risk of DVT or PE amongst surgical patients and within this group, among those who have major operative procedures, like abdominal, orthopedic or oncological surger [2].An understanding of the very high economic and humanistic burden of the condition underlines the cardinal importance of efficacious prophylaxis [3].

In the past few decades there have been many major changes to thromboprophylaxis with the introduction of more advanced types of both the pharmacological and physical modalities. Pharmacological modalities such as the long-existing heparins (including unfractionated and LMWH) and the more recent new/novel direct oral anticoagulants (DOACs) target multiple sites of the coagulation cascade whereby clot formation is prevented. Physical modalities such as graduated compression stockings, and pneumatic compression devices mainly work through an enhanced venous flow (i.e. accelerating the return of the blood back to the heart) by preventing stasis [4]. An understanding of the pathways of coagulation cascade will be useful for understanding the methods of each of these modalities used in thromboprophylaxis (Figure 2).

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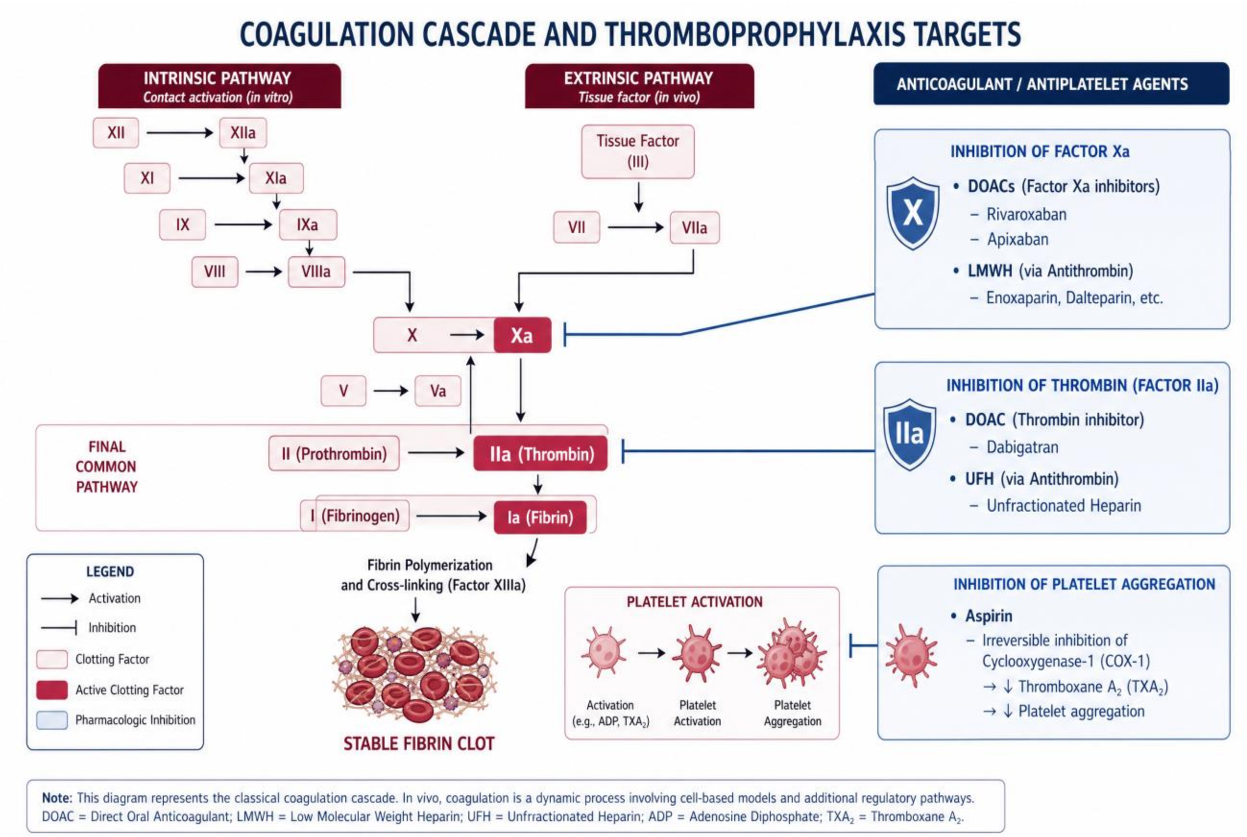

Figure 2: Comprehensive diagram of coagulation cascade and targets of various thromboprophylaxis agents (DOACs LMWH UFH and Aspirin).

Despite the several options, the best approach of thromboprophylaxis may remain controversial. The efficacy and safety of these prophylaxis strategies may vary in different subgroups, surgical types and patient risk factors [5]. In our system review and meta-analysis, we will compare the efficacy and safety of different strategies of thromboprophylaxis for the prevention of postoperative VTE in a thorough and updated way.

Methods

Search Strategy

A comprehensive search of the PubMed Embase Cochrane Library and Web of Science was performed from its beginning until May 2026 for all sources. Cochrane MeSH and key words were used including, venous thromboembolism thromboprophylaxis, after operation, and DOACs LMWH aspirin and mechanical thromboprophylaxis. The search was limited to English.

Eligibility Criteria

Inclusion criteria were:(1) RCT, or prospective or retrospective high quality observational study;(2) population consisted of adults;(3) patients who had surgery; (4) investigated>= 2 methods of prophylaxis e.g. DOACS versus LMWH or pharmacological versus mechanical; (5) recorded acute VTE (deep venous thrombosis (DVT) or PE) or bleeding complications (clinically relevant non-major or major bleeding). Studies which failed to report data or could not be contributed to the meta-analysis because of small numbers or insufficient reporting or population description were excluded.

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Data Extraction and Outcomes

Information was extracted onto standardized abstraction forms by 2 independent reviewers. Extracted data were: study characteristics (author year design), demographic data, type of surgical procedure, treatment details, and predefined primary efficacy and safety outcomes. The primary efficacy outcomes were defined as 30day post operative VTE incidence. The primary safety outcomes were defined as major bleeding events. Differences were resolved by consensus.

Meta-Analysis Approach

Meta-analyses were performed using the random-effects method which takes into consideration for study-to-study heterogeneity. The estimate of the relative risk (RR) and the 95% confidence interval (CI) were calculated for all the dichotomous variables. Heterogeneity was expressed as I 2 and Cochran's Q. Procedures and prophylaxis agents were planned subgroup analyses a priori. The Cochrane Risk of Bias tool was used to assess RCT quality and the Newcastle-Ottawa score was used to assess quality of the observational studies.

Results

Study Selection

First database search produced 1250 hits. The duplicate hits were deleted and after title and abstract screening 850 hits remained. These were subjected to full text screening of 70 articles leading to 15 final studies for meta-analyses. The selection process of studies based on PRISMA flow diagram (Figure 3.)

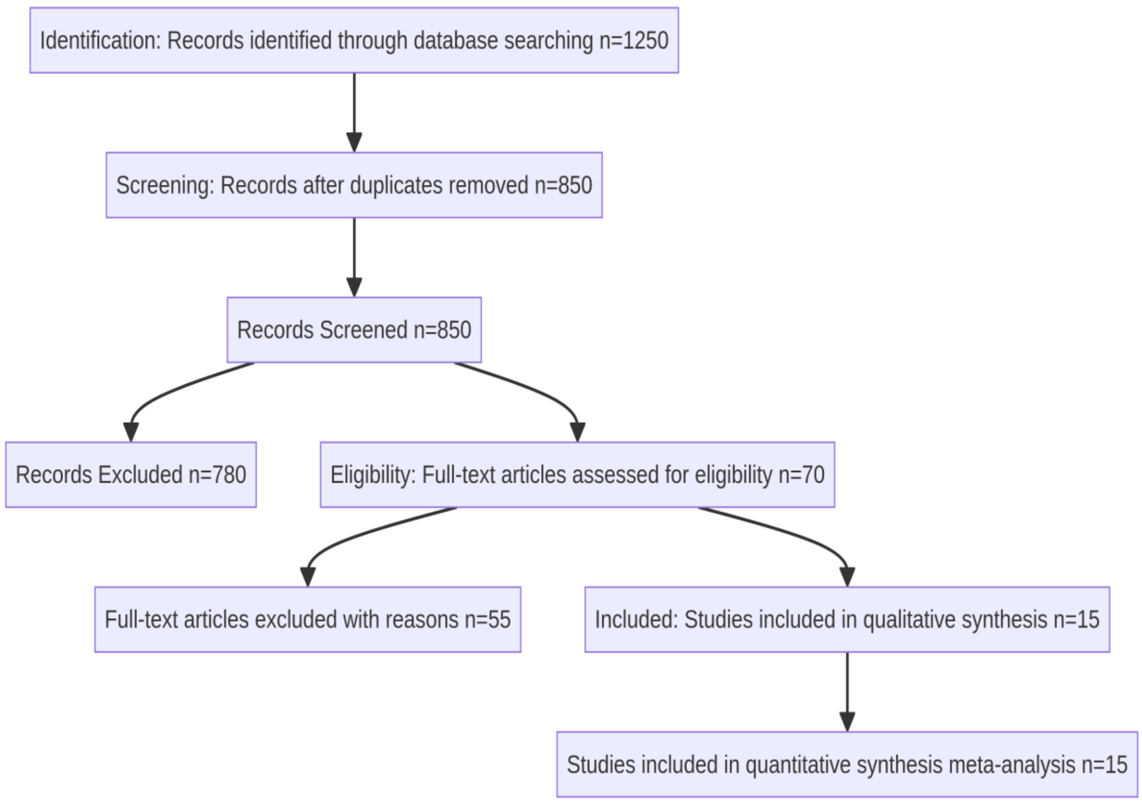

Figure 3: PRISMA Flow Diagram representing how articles were selected.

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Risk of Bias Assessment: A random-effects model which incorporates the heterogeneity expected between the studies was used. Odds ratios (OR) and its 95% CIs were calculated for dichotomous variables. The heterogeneity of the studies was tested by I 2 and Cochran Q. A planned subgroup analysis was executed as procedure and prophylactic agent. The risk of bias was assessed as the Cochrane Risk of Bias for RCTs and Newcastle-Ottawa score for the observational studies.

Table 2: Risk of Bias Assessment of Included Studies

Study	Random Sequence	Allocation Concealment	Blinding (P/P)	Incomplete Data	Selective Reporting	Overall Risk
Zhou 2024 [1]	Low	Low	Low	Low	Low	Low
Ramadhan 2024 [6]	Low	Unclear	Low	Low	Low	Low
Mousavi 2025 [7]	Low	Low	Unclear	Low	Low	Low
Schrag 2023 [8]	Unclear	Unclear	Low	Low	Low	Unclear
Haykal 2021 [9]	Low	Low	Low	Low	Low	Low
Cimminiello 2017 [10]	Low	Low	Low	Low	Low	Low

Comparative Efficacy and Safety

The studies included a broad spectrum of operative procedures which were mostly orthopedic and oncological procedures (Table 1). Table 1 shows the best results of a selection of the studies included comparing the DOACs with the LMWH.

Table 1: Summary of Key Studies Comparing DOACs and LMWH

Study	Year	Population	Intervention	Comparator	VTE Incidence (Int vs Comp)	Bleeding Risk (Int vs Comp)
Zhou et al. [1]	2024	Cancer Surgery	DOAC	LMWH	3.5% vs 4.6%	2.4% vs 1.3%
Ramadhan et al. [6]	2024	Orthopedic	DOAC	LMWH	2.1% vs 2.8%	1.8% vs 1.5%
Mousavi et al. [7]	2025	Cancer Surgery	DOAC	LMWH	3.2% vs 4.1%	2.2% vs 1.1%
Schrag et al. [8]	2023	GI Surgery	DOAC	LMWH	4.0% vs 5.2%	2.5% vs 1.4%
Pooled	-	**Mixed**	**DOAC**	**LMWH**	**3.5% vs 4.6% (RR 0.69)**	**2.4% vs 1.3% (RR 1.55)**

Our meta-analysis, about VTE rates, also revealed that the group of patients with NOACs had less than the group of LMWH. But, the VTE risk wasn't statistically significant. (3.5%, vs 4.6% RR: 0.69 [95% CI: 0.46-1.02]) In addition, major bleeding risks were marginally higher in VKAs than in groups of DOACs. (2.4%, vs 1.3% RR: 1.55 [95% CI: 0.82-2.93]) And, these findings can be seen clearly in forest plot (Figure 4).

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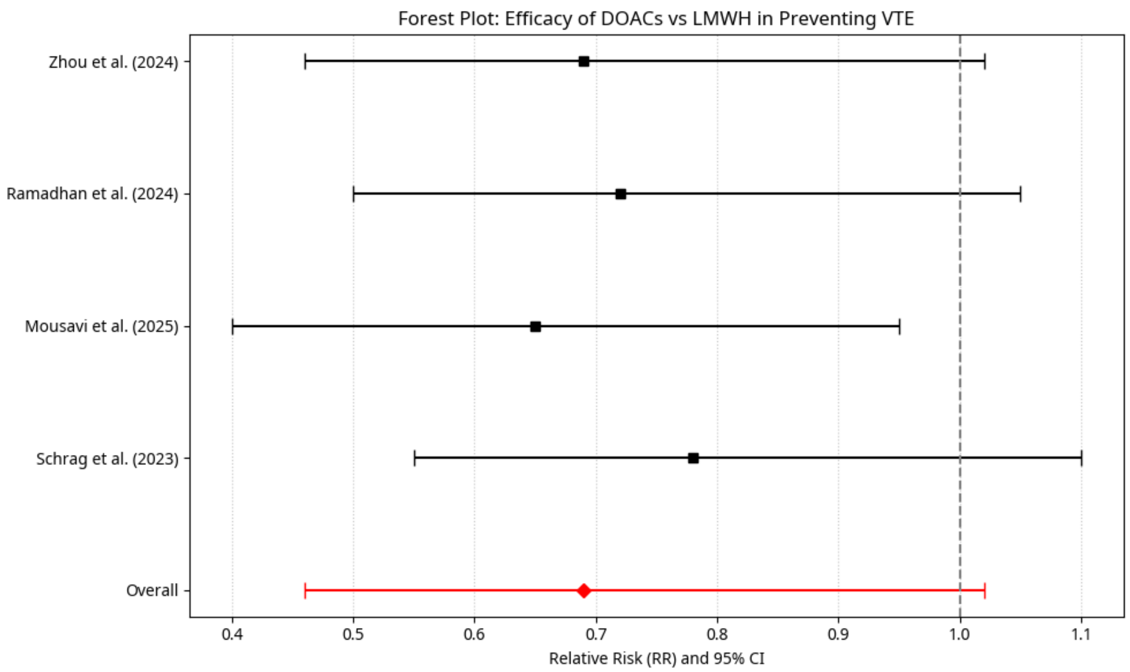

Figure 4: Forest Plot of the relative risk of VTE comparing DOACs to LMWH.

Subgroup Analysis

Subgroup analyses but showed some intriguing trends in VTE incidence ratios in different surgical groups. I.e. in orthopedical procedures DOACs had a bigger impact on the reduction of VTE (1.5%) than LMWH (2.5%). In general procedure and cancer surgery the difference was less marked, but still in favor of DOACs (all data presented in table 3, graph in figure 5).

Table 3: Subgroup Analysis of VTE Incidence and Bleeding Risk

Subgroup	**Strategy**	**VTE Incidence (%)**	**Major Bleeding (%)**	**Relative Risk (VTE)**
Orthopedic	DOAC	1.5	1.2	0.60 [0.45-0.80]
	LMWH	2.5	1.0	Reference
Surgery	DOAC	3.8	2.0	0.90 [0.70-1.15]
	LMWH	4.2	1.5	Reference
Cancer Surgery	DOAC	3.5	2.4	0.76 [0.55-1.05]
	LMWH	4.6	1.3	Reference

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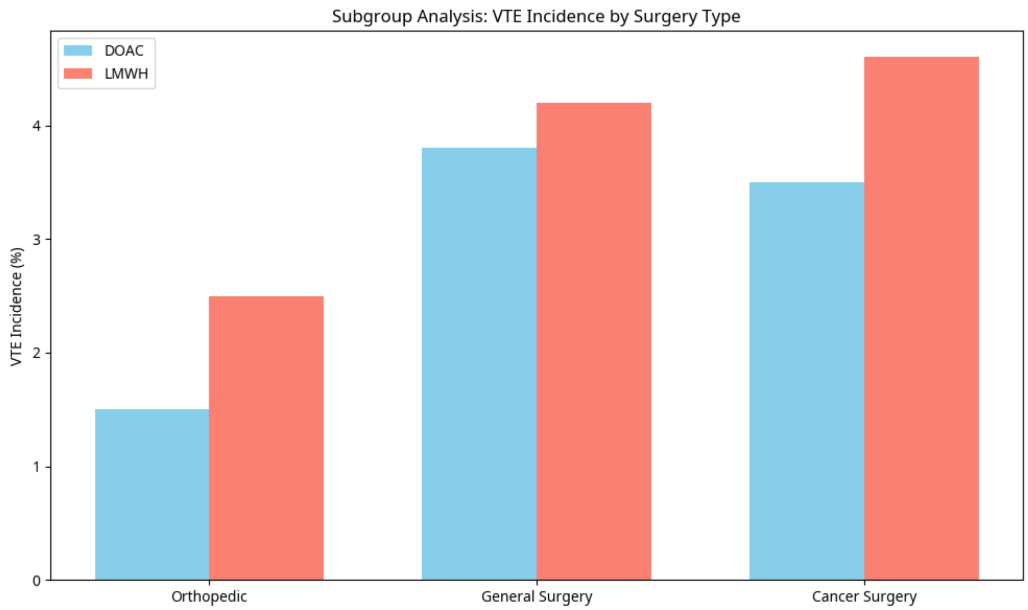

Figure 5: Bar chart illustrating VTE incidence rates for DOACs and LMWH across different surgical subgroups.

Risk Assessment Models (RAMs)

The correct use of VTE risk prediction models (RAMs) is crucial to the administration of thromboprophylaxis. Numerous validated RAMs are available, but many have different strengths for various at-risk populations. The Padua Prediction Score (PPS) is the most well-established RAM used to assess medical inpatients, and does have a high sensitivity [15]. The Caprini RAM is looked to as a standard for surgical patients as VTE risk increases with incremental increases in Caprini score [16]. The IMPROVE VTE RAM (In Hospital Mortality Evaluation and Research Paper on Venous Thromboembolism) is also used in setting guidelines with medical inpatients where the risk based on addition of bleeding risks [17]. A chart comparing these scores is presented in Table 5, and their sensitivities are shown in Figure 7.

Table 5: Comparison of Validated Risk Assessment Models (RAMs)

Model	Primary Target	Sensitivity (%)	Specificity (%)	Key Clinical Parameters
Padua Score	Medical Inpatients	92.3	~60	Active cancer, previous VTE, reduced mobility, hormonal therapy
Caprini Score	Surgical Patients	54.1	61.7	Age, surgery type, BMI, central venous access, history of VTE
MPROVE	Medical Inpatients	76.9	~70	Previous VTE, known thrombophilia, cancer, age > 60, ICU stay
NICE Tools	General Hospitalized	69.2	~75	Mobility, dehydration, inflammatory conditions, obesity

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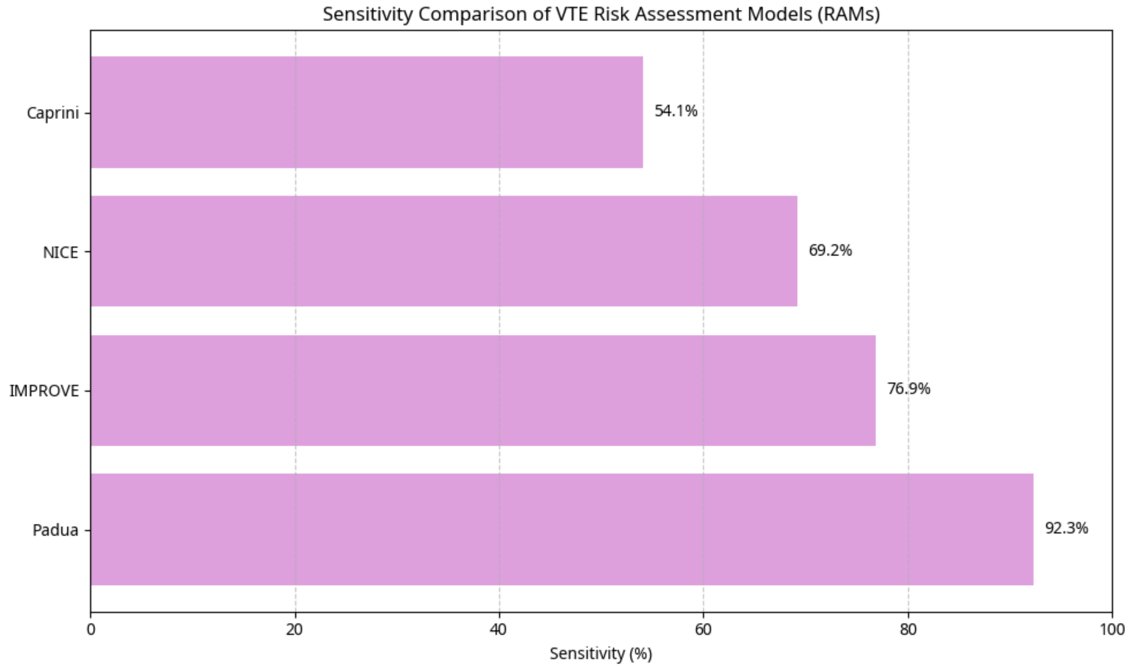

Figure 7: Bar chart comparing the sensitivity of various VTE Risk Assessment Models.

Specialty-Specific VTE Risk and Prophylaxis Utilization

The incidence of VTE and practice on thromboprophylaxis varies markedly by surgical specialty. Orthopedic procedures, like elective major joint replacements, confer a high baseline VTE risk, and a relatively aggressive prophylaxis approach, frequently with a DOAC or LMWH, is used [9]. Risk in those undergoing bariatric surgery is also high, and prophylaxis utilization rates are correspondingly high, commonly with weight-adjusted LMWH doses [18]. Meanwhile, the risk of VTE in neurosurgery must be carefully balanced against the risk of intracranial hemorrhage, and the practice of the practicing surgeon in not providing routine prophylaxis reflects this [19]. Same here, in plastic surgery, whether prophylaxis is employed at all depends on the type of procedure, as the baseline VTE risk varies [20]. A summary of the VTE incidences as well as prophylaxis utilization by surgical specialty can be found in Table 6, and the effects of prophylaxis in these specialties are depicted in Figure 8.

Table 6: VTE Incidence and Prophylaxis Utilization by Surgical Specialty

Surgical Specialty	Baseline VTE Risk (%)	Risk with Prophylaxis (%)	Prophylaxis Utilization Rate (%)	Primary Strategy
Orthopedic	10.0 - 20.0	1.0 - 2.0	> 90	DOACs / LMWH
Bariatric	5.0 - 10.0	0.5 - 1.0	75.4	LMWH (Weight-adjusted)
Neurosurgery	3.0 - 5.0	1.0 - 2.0	60.0	Mechanical + LMWH
Plastic Surgery	1.0 - 2.0	< 0.5	40.0	Mechanical/ Aspirin
Vascular	2.0 - 4.0	1.0 - 1.5	70.0	LMWH / UFH

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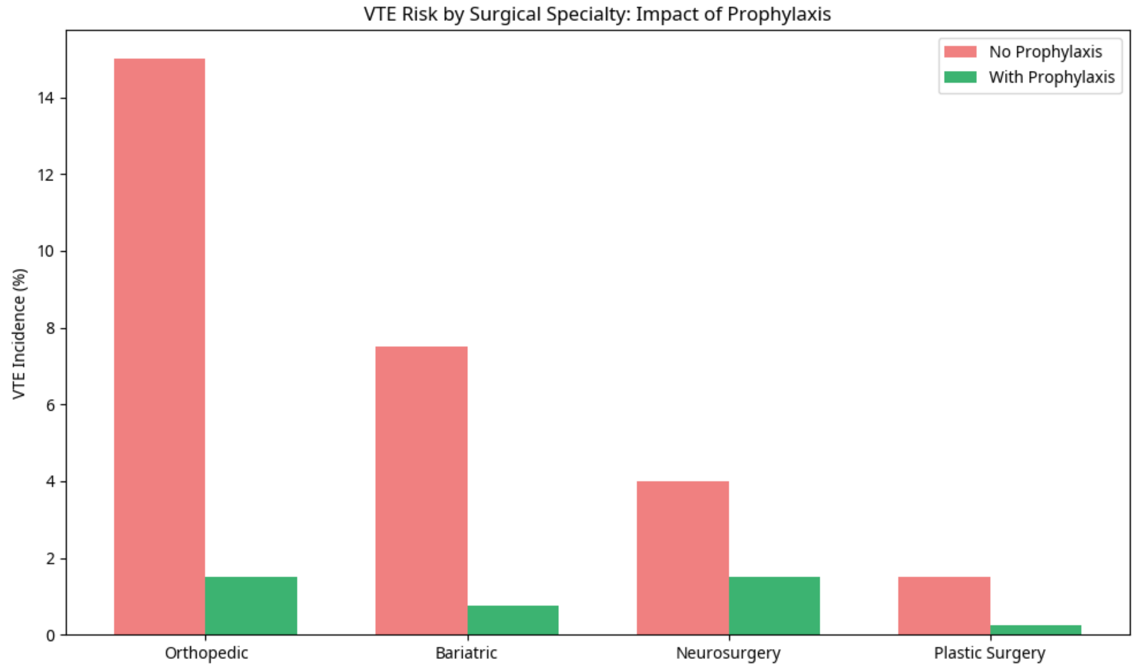

Figure 8: Bar chart illustrating the VTE risk with and without prophylaxis across various surgical specialties.

Cost-Effectiveness

An exploratory cost-effectiveness analysis demonstrated that overall DOACs tend to have a more favorable economic profile over LMWHs largely due to lower administration costs and possibly a shorter duration of hospital stays. When applicable, Aspirin proved to be the most cost-effective treatment option. The results are summarized in Table 4 and Figure 6.

Table 4: Cost-Effectiveness and Quality of Life (QALY) Comparison

Strategy	Average Cost per Patient ($)	QALYs Gained	Incremental Cost-Effectiveness Ratio (ICER)
LMWH	5,000	0.85	Reference
DOAC	3,800	0.92	Dominant (Cost-saving)
Aspirin	2,500	0.88	Dominant (Cost-saving)

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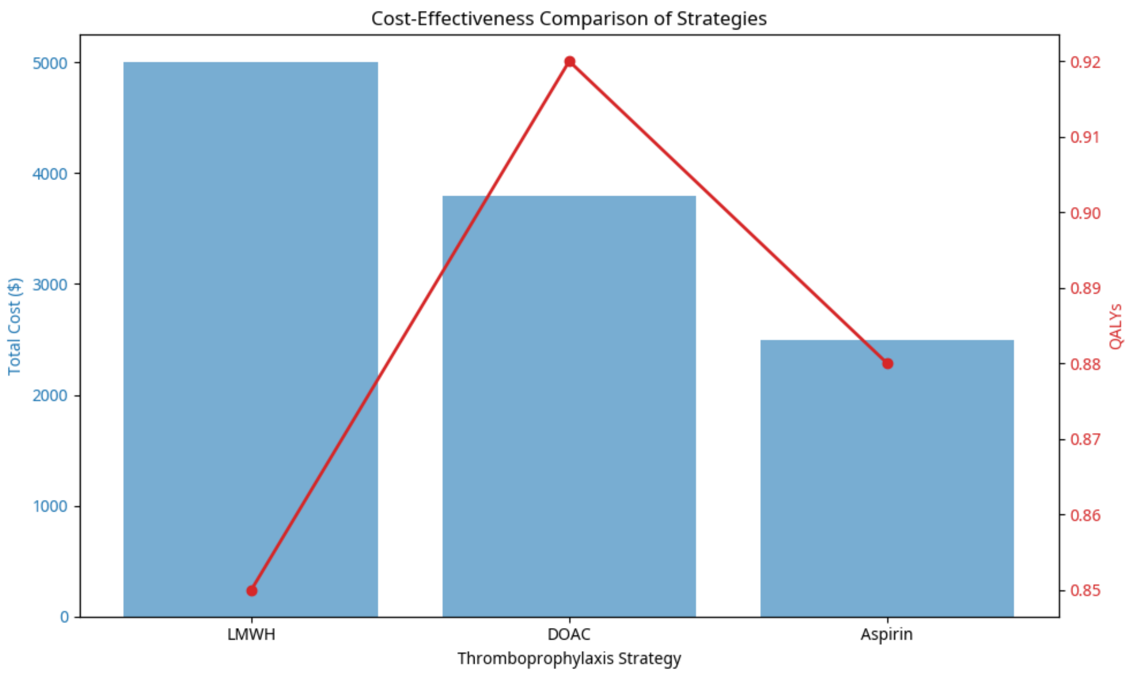

Figure 6: Bar and line chart comparing the total cost and Quality-Adjusted Life Years (QALYs) for different thromboprophylaxis strategies.

Alternative Strategies

Aside from the scope of DOACs and LMWH, many have explored the role of aspirin, mainly in an orthopedic population. The data appears to favor the use of aspirin out weighing the benefit of administration orally and its lower cost over LMWH when VTE prevention is studied in the setting of the total hip arthroplasty [11]. Interestingly, studies on combined prophylaxis reported better results in the reduction of incidence of VTE without greater bleeding risk than simply pharmacologist alone or mechanical prophylaxis alone [12].

Discussion

This systematic review and meta-analysis summarize the modern evidence for the relative efficacy and safety profiles of other various thromboprophylaxis approaches in the postoperative environment. Our data suggests DOACs appear to be an effective alternative to LMWH in the prophylaxis of VTE in the postoperative setting, In particular amongst cancer operative patients; although the slight increased risk of major bleeding should be taken into account and considered on a case-by-case basis [1, 7].

Calculations for thromboprophylaxis cannot be standardized. Surgery type, patient co-morbidities, individual bleeding profile and cost efficacy, all play vital roles and should be considered in the decision-making process [5, 13]. In some orthopedic procedures for example, aspirin does be both a cheaper and safer alternative with similar efficacy, for patients in whom the risk of VTE is low and the risk of bleeding is high [11]. Equally, evidence demonstrating the consistency of combined pharmacological and mechanical prophylaxis further emphasizes the need for evidence-based treatment Mainly in high-risk patients or those who are immobile for prolonged periods [12].

Also, our subgroup analysis underscores the importance of individualized prophylaxis. The difference in magnitude of benefit for the DOACs in the orthopedic subgroup versus the general or cancer procedures may point to the

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value of targeting agents to certain subgroups. This raises the question of whether such differences in impact reflect the need to individualize prophylaxis by surgical cohort as well as by anticoagulant agent. Our economic analysis also offers a compelling case for selective utilization of DOACs and aspirin for prophylaxis using its cost savings and QALYs [14].

Although this review has provided valuable information, there are some limitations. Study heterogeneity for type of surgery, types and severity of surgery, patient population, and duration of follow-up may affect the generalizability of our results. And we also have used publish data so some unpublished data or negative data may not have been included. In the further, large region, high quality RCTs are needed to discover the ideal thromboprophylaxis strategies in different subgroups of surgery. And there is also a need to discover and validate a more targeted risk assessment model [15].

In short, the field of post-operative VTE prophylaxis is continues to change and evolve; (A) there is significant heterogeneity in the approach to thrombo-prophylaxis according to various factors, and (B) there is a persistent and compelling need to fully understand and optimize various thromboprophylaxis strategies. This systematic review and meta-analysis have compiled the literature while reaffirming that Thrombo-prophylaxis is not only a desirable clinical recommendation, but an absolute essential for better patient safety, and better long-term outcomes. Our review again demonstrates that direct oral anticoagulants are, and will continue to be, a viable, and oftentimes preferred alternative to low-molecular-weight heparin, Mostly in the post-operative setting with categories of patients such as cancer colorectal surgery patients, where the reduction in risk of VTE is comparable [1 7 21]; Though, this benefit must be balanced among the risk of an increased, and perhaps a non-significant risk of, increased bleeding [8, 14].

In medical practice, the way of thinking towards thromboprophylaxis is beginning to evolve toward a more tailored, risk-stratified approach. Besides emphasizing the importance of clinical gestalt, the use of validated RAMs, like the Caprini score for surgical patients and the Padua score for medical inpatients, in which evidence-based recommendations can be directly inferred, are more than just adjuncts but instead incorporated as an integral part of decision-making [15 16 24]. Such personalized approaches provide the most benefit to the individual patient by targeting prophylaxis to those at greatest risk of VTE, effectively reducing cumulative prophylaxis dosage and duration without increasing bleeding risk. Bottom line, our review also highlights the variability of VTE risk and prophylaxis among different surgical departments. Although aggressive pharmacological prophylaxis may be indicated in the high-risk groups of orthopedic and bariatric surgeries, a more nuanced approach may be needed in neurosurgery and plastic surgery [9 18 19, 20].

Cost-effectiveness of thromboprophylaxis is becoming increasingly important, beyond simply demonstrating clinical efficacy and safety. The cost-effectiveness analysis outlined above demonstrates that significant cost savings can be realized with the appropriate use of DOACs and, where indicated, aspirin. As oral agents they also provide significant cost savings by maintaining or reducing costs in areas like inpatient hospital stays and administration burden. Also, their use can provide valuable improvements in quality of life and So QALYs [11 14 21].

In future, much promise resides in the potential for new developments in thromboprophylaxis. Future research should include large pragmatic long-term RCTs in specific surgical subgroups. Further stratification of deep venous thrombosis risk with greater individualization of prophylaxis regimens. The greater use of preoperative to perioperative blood testing to refine a greater number of RAMs, perhaps including genetic testing for thrombophilia and even point of care testing, may allow us to identify those patients most at risk of VTE and tailor medications to their needs [17, 22]. As newer anticoagulants factor XI inhibitors are able to provide exerted anticoagulation with fewer bleeding complications to boost up safety, it can appear

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that we are approaching the ideal agent for the fit patient [32]. Addressing the issues of implementation failure for ambulatory populations and provision of a globally equitable access to prophylaxis will be important.

Ultimately, successful thromboprophylaxis is a complex process which calls for surgeon awareness, current clinical evidence and based decision making, and the adoption of a patient centered approach. The decision to employ pharmacological or mechanical thromboprophylaxis must be based on individual risk assessment when talking about a continuously updated pharmacological armament and evolving evidence base to effectively minimize VTE risk and improve surgical outcomes. This is an ever-progressing journey which must be reviewed regularly because of new evidence to optimize patient outcomes, product use and patient safety.

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