



# A Cost-Effectiveness Analysis of Rivaroxaban Compared to Warfarin for the Management of Venous Thromboembolism in Western Kenya

Emily T. O'Neill<sup>1</sup> · Andrew W. Huang<sup>1</sup> · Marta Wilson-Barthes<sup>2</sup> · Imran Manji<sup>3</sup> · Gabriel Kigen<sup>4</sup> · Naftali Busakhala<sup>4</sup> · Samuel Nyanje<sup>5</sup> · Omar Galárraga<sup>1,2</sup> · Sonak D. Pastakia<sup>6</sup>

Accepted: 28 May 2025 / Published online: 28 June 2025

© The Author(s) 2025

## Abstract

**Background and Objective** Access to direct oral anticoagulants (DOACs) in sub-Saharan Africa is limited due to prohibitive upfront costs, making warfarin the standard of care for many patients, especially those relying on public-sector healthcare. This study evaluated the cost-effectiveness of using the DOAC, rivaroxaban, compared to warfarin for treating venous thromboembolism (VTE), a cardiovascular disorder caused by blood clots in the veins, in western Kenya.

**Methods** We developed a discrete-time individual state-transition Markov model to simulate a VTE patient's quality-adjusted life-years (QALYs) and annual treatment costs under a rivaroxaban or warfarin therapy strategy. Transition state probabilities were derived from real-world event-rate data observed in patients treated with rivaroxaban ( $n = 160$ ) or warfarin ( $n = 116$ ) for VTE at Moi Teaching and Referral Hospital in western Kenya. Base-case parameter values were obtained from cohort event rates, local costs, and literature-derived utility values. Cost-effectiveness was assessed over a 1-year time horizon using an incremental cost-effectiveness ratio (ICER) threshold of (US)\$6020.40 per QALY gained (equivalent to three times Kenya's 2021 per capita GDP). Deterministic and probabilistic sensitivity analyses were conducted to assess parameter and model uncertainty.

**Results** After 12 months, total mean treatment costs per patient were \$216.00 and \$173.00 using warfarin and rivaroxaban, respectively. In the base-case analysis, rivaroxaban therapy resulted in an additional 0.023 QALYs per patient compared to warfarin, with an ICER of \$–1862.00 per QALY gained. Based on probabilistic sensitivity analysis with Monte Carlo simulation, when costs, utility values, and event rates were varied, rivaroxaban was cost-effective compared to warfarin in 84.1% of all simulations at a willingness-to-pay threshold of \$6020.40 per QALY. One-way sensitivity analyses and scenario analyses were stable with rivaroxaban therapy, resulting in fewer costs and higher QALYs.

**Conclusions** In this study, rivaroxaban is a clinically and economically superior alternative to warfarin. This research may catalyze further discussions with policymakers and industry partners to scale up the appropriate use of rivaroxaban in resource-constrained settings.

## 1 Introduction

Venous thromboembolism (VTE), a cardiovascular disorder caused by blood clotting in veins, is associated with high morbidity and mortality as well as costly healthcare expenditures [1]. To this day, VTE remains a significant burden of disease across the globe, with 0.75–2.69 cases per 1000 individuals annually [2].

There are many inciting causes of VTE, including surgery, prolonged immobility, pregnancy, certain medications, and other comorbidities [3]. Acute (3–6 months) or chronic anticoagulation is prescribed for treatment following

incident VTE [4]. The choice of anticoagulation varies depending on patient and clinician preference, drug allergies, medication interactions, availability, and cost. The most common anticoagulants include injectable heparins, low-molecular-weight heparin, vitamin K antagonists, and direct oral anticoagulants (DOACs) [5].

Warfarin, a vitamin K antagonist, is one of the oldest and most widely used anticoagulants. Due to its long-expired patent protection and considerable time on the market, per-tablet costs are generally less expensive than those of other newer options [5, 6]. However, therapy requires specific dose adjustments based on interacting medications, drug metabolism, and diet. In addition to tailored regimens, patients receiving warfarin require frequent monitoring to ensure safe

### Key Points

Our analysis suggests that over 12 months, the direct oral anticoagulant rivaroxaban was clinically and economically superior to warfarin in western Kenya for venous thromboembolism.

Rivaroxaban use was associated with cost savings compared to warfarin and lower therapy-related adverse drug events.

Further work is needed to implement the scale-up of rivaroxaban in resource-constrained settings like western Kenya where warfarin therapy remains standard of care.

study from SSA, specifically Ethiopia, comparing the cost-effectiveness of rivaroxaban to warfarin. Rivaroxaban was found to be cost-effective compared to warfarin for the treatment of VTE; however, to our knowledge, no studies have focused on the public sector or on a setting in Kenya [14]. Conducting setting-specific investigations is essential for countries in SSA as prior observational studies have shown significantly higher bleeding risks in patients on warfarin in western Kenya compared to other regions [11]. These and many other setting-specific differences could alter assumptions from the multitude of cost-effectiveness assessments completed in different regions. More research is warranted into the effectiveness and costs of these medications within public sector settings. Here, we provide one of the first cost-effectiveness analyses (CEAs) of using rivaroxaban for VTE treatment in western Kenya.

## 2 Methods

This pharmacoeconomic evaluation included a cost-utility analysis with cost-effectiveness assessed by the incremental cost-effectiveness ratio (ICER). A treatment strategy of 15 mg of oral rivaroxaban administered twice daily for 3 weeks, followed by 20 mg daily for 3–6 months, was compared to a treatment strategy of orally administered warfarin by point of care (POC) INR-guided therapy for 3–6 months. POC INR-guided therapy includes multiple clinic visits in which blood draws are done on the patient to measure the INR and ensure it is within the typical target range of 2–3. A discrete-time individual state-transition Markov model was developed to simulate a VTE patient's monthly costs and health states under a rivaroxaban or warfarin treatment strategy. The target population includes post-incident VTE (index event) patients treated at the MTRH anticoagulation clinic who were eligible for warfarin or a DOAC. Additional details on the methodology and results from this clinical investigation have been published previously [11]. The time horizon for the model was 1 year, with a cycle length of 1 month. A 1-year time horizon was chosen based on published literature indicating that the hazard rate for VTE recurrence is highest within the first 6–12 months following the initial event, despite never falling to zero, and was further informed by clinical input from anticoagulation specialists at MTRH [15]. Patients in our model were drawn from real-world data, with treatment durations typically ranging from 3 to 6 months and follow-up limited to the same period. No discount rate was included as the time horizon was for 1 year. Analyses were conducted in R (version 4.2.1, R Project for Statistical Computing) and used publicly available R code adapted from Alarid-Escudero et al. (2022) [16].

and effective anticoagulation, as measured by the international normalized ratio (INR). Given warfarin's many drug and diet interactions, research indicates that only two-thirds of patients achieve a therapeutic INR, and only 10% of those patients attain a stable INR within the therapeutic range for 1 year [7, 8].

DOACs have consistently been shown to be non-inferior to warfarin for managing VTE [9]. They are associated with lower bleeding risks, less patient monitoring, fewer clinic visits, and a lower incidence of food and drug interactions [9, 10]. In Kenya, DOAC use is limited due to high upfront tablet costs and lack of insurance coverage in the public sector for outpatient medications; a single tablet of the DOAC rivaroxaban can cost up to 20 times that of warfarin [11]. Despite these cost differences, data from western Kenya indicate that the frequency of bleeds amongst warfarin users is significantly higher (30.3%; 95% confidence interval (CI) 22.0–38.5) than rivaroxaban (14.4%; 95% CI 9.3–20.8) [11]. These data align with other international studies indicating lower rates of fatal bleeding with rivaroxaban compared to warfarin [10, 12, 13]. These observations have triggered a paradigm shift toward DOACs as the standard of care (SOC) in many high-income countries (HICs) for VTE treatment.

While DOACs have become SOC in HICs, most patients in sub-Saharan African (SSA) countries struggle to access these more expensive medications. In response to the lack of DOAC access, the anticoagulation clinic based at Moi Teaching and Referral Hospital (MTRH), a tertiary academic medical center in Eldoret, Kenya, partnered with Bayer® East Africa Limited to provide rivaroxaban at a subsidized price. This partnership expanded access to rivaroxaban in a public sector patient population that did not previously have access to this treatment. Based on a review of the existing literature, there has been one published

## 2.1 Model Structure

Figure 1 shows the structure and transition states of the Markov chain model. Health states included Recurrence, Major Bleed, Clinically Relevant Non-Major Bleed (CRNMB), Off Treatment, and No Event. We classified Major Bleed and CRNMB per the International Society of Thrombosis and Hemostasis (ISTH) definitions [17]. In the base-case analysis, we assume that 20% of patients who experience a Major Bleed or CRNMB on either treatment strategy are likely to go off treatment based on the clinical experience of experts practicing in the MTRH anticoagulation clinic. In our base-case analysis, patients in the Off Treatment or Recurrence state do not transition to another state. We identify Off Treatment and Recurrence as absorbing health states that the patient remains in until the end of the 1-year simulation.

## 2.2 Model Inputs

Table 1 shows the parameters used to model the base-case scenario and sensitivity analyses. Monthly transition state probabilities were derived from event rates using data from the MTRH anticoagulation clinic. Patients treated for 3–6 months with rivaroxaban ( $n = 160$ ) or warfarin ( $n = 116$ ) for VTE were followed up at the MTRH anticoagulation clinic. Clinical events and patient costs were documented monthly. The methods for the observational study assessing warfarin and rivaroxaban for VTE treatment at the MTRH anticoagulation clinic are described elsewhere [11].

Using the World Bank exchange rate, we converted Kenyan Shillings (KSH) costs to 2022 US Dollars (\$) [18]. In our a priori model, we established that rivaroxaban would be a more cost-effective option at a willingness-to-pay (WTP) threshold of  $\leq \$6020.40$  per QALY gained (3x Kenya's 2021 per capita GDP) based on the World Health Organization's recommended threshold for low- and middle-income countries [19].

We obtained utility values associated with VTE and the identified clinical outcomes from the literature (Table 1). The baseline utility value for someone with no adverse event was 0.825 [14, 20–23]. The utility value associated with being Off Treatment was estimated to be 0.68, reflecting an increased risk of VTE recurrence among patients in this health state [23–25]. Drug, event, and all associated clinical and non-clinical costs (e.g., laboratory costs, transportation costs to the clinic, bed costs) were obtained from MTRH, the MTRH anticoagulation clinic, and local transportation costs in Eldoret, Kenya. Component costs are presented in the Online Supplemental Material (OSM), Table 1a. Since drug- and clinic-related costs incurred from the study populations

were not normally distributed and highly skewed, median costs were used in the base-case analysis.

## 2.3 Primary Analysis

The base-case scenario evaluated rivaroxaban's costs and clinical outcomes compared to warfarin for primary VTE treatment among patients who required anticoagulation therapy for 3–6 months.

## 2.4 Sensitivity Analysis

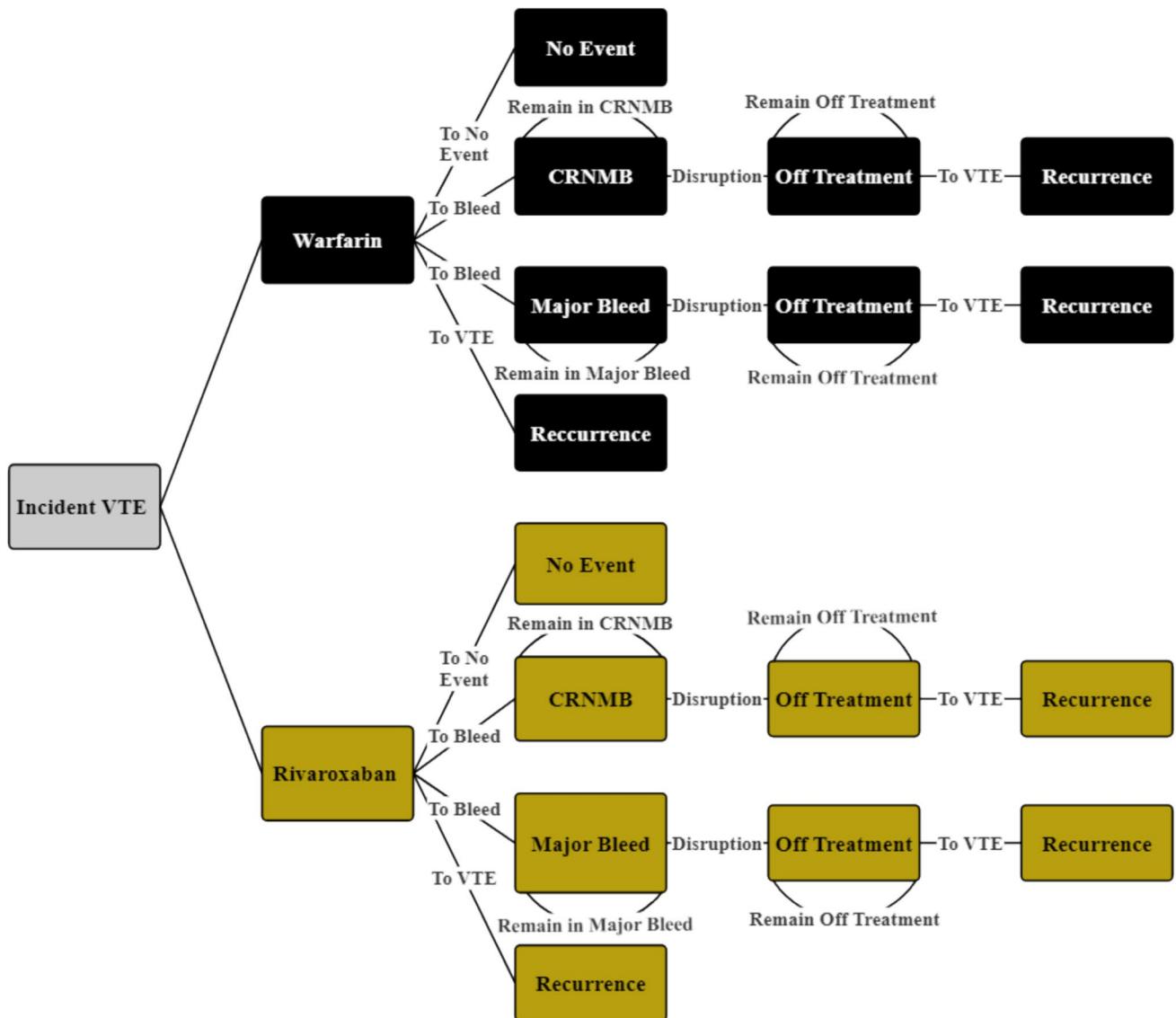
We conducted several sensitivity analyses to evaluate the robustness of the ICER results. First, we use minimum and maximum cost and utility values (Table 1) to conduct a one-way deterministic sensitivity analysis to account for parameter uncertainty and identify key drivers influencing the results. Second, we conducted two probabilistic sensitivity analyses (PSA) using 1000 iterations of the model in a Monte Carlo simulation to (1) draw event-rate parameter values from a prior distribution suggested from the empirical data and (2) draw cost and utility parameter values from prior distributions suggested from the literature. In the first PSA, bootstrapping generated 1000 iterations of event rate data to determine 95% CIs derived from observational cohort data. Confidence intervals were then fit to characterize transition state probability uncertainty. In the second PSA, we include variation for costs and utilities, using gamma and logit distributions, respectively, and event-rate variation introduced in the first PSA. Variation in cost and utility values, represented as minimum and maximum ranges, were derived from the literature as well as local costs data (Table 1).

Finally, we conducted a separate scenario analysis to reflect real-world clinical scenarios. In this scenario analysis, we varied the transition state probability of VTE recurrence from Off Treatment to a literature-derived 7.4% to illustrate the increased risk of having this clinical outcome following early anticoagulation discontinuation [15].

## 3 Results

### 3.1 Base-Case Analysis

In the base-case analysis, warfarin (mean cost = \$216.00) was more costly than rivaroxaban (mean cost = \$173.00). The total number of QALYs gained by administering rivaroxaban was 0.848 over 1 year, compared to 0.824 QALYs gained with warfarin. Rivaroxaban was found to be the dominant treatment strategy in the base-case analysis, with an ICER of  $-\$1862.00$  per QALY gained (Table 2).



**Fig. 1** Markov Decision Model illustrating transition states in patients using either warfarin or rivaroxaban treatment strategies for VTE treatment. CRNMB clinically relevant non-major bleed, VTE venous thromboembolism

### 3.2 Sensitivity Analyses

Figure 2 shows the results of the one-way deterministic sensitivity analyses. The ICER was most sensitive to the cost of treating CRNMB and major bleeding under the rivaroxaban treatment. Under a warfarin treatment strategy, the ICER was most sensitive to changes in the costs and utilities for the No Event health state (Fig. 2).

Figure 3 illustrates the results of the two PSAs performed. In the first PSA, where transition state probabilities are varied, utility values and costs reflect base-case assumptions, mean costs incurred from rivaroxaban (\$184.00) were lower than those incurred from warfarin (\$227.00). QALYs gained remained slightly higher for rivaroxaban (0.840) than warfarin (0.824), with an ICER of \$-2644.00 per QALY gained. We selected our model's worst-performing Monte Carlo

**Table 1** Parameter values for the base case

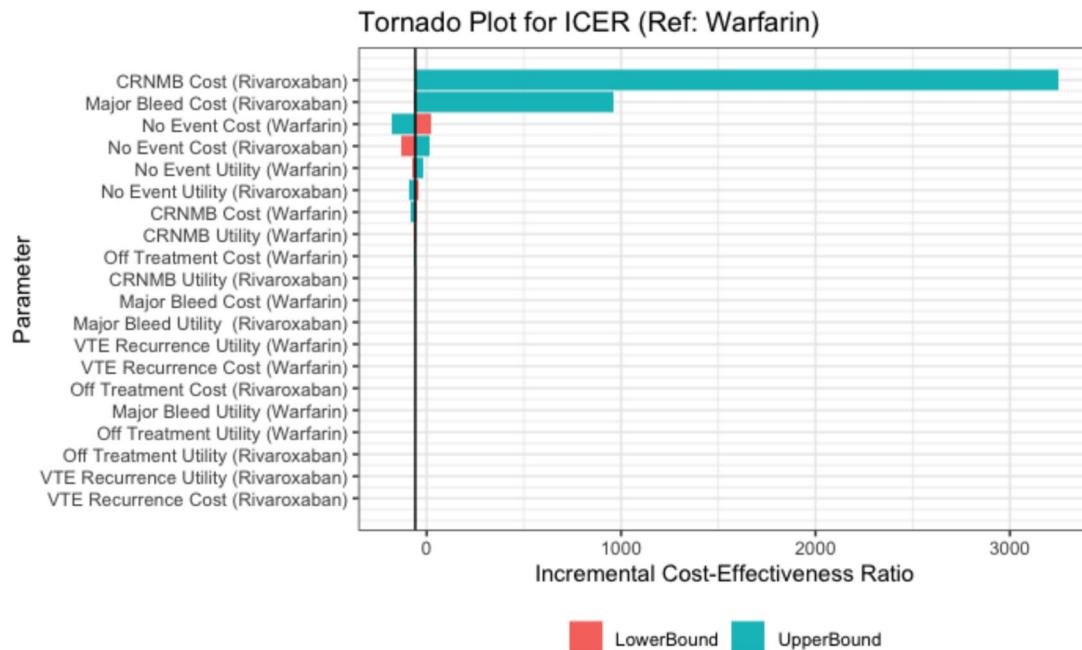
Parameter	Base case	Uncertainty parameter	Distribution	Sources
Rivaroxaban event rates (per 6 months)	(95% CI)			
No event to recurrence	0	(0, 0)	Uniform	Study population
No event to major bleed	0.017	(0, 0.031)	Uniform	Study population
Major bleed to off treatment	0.002	(0, 0.005)	Uniform	Study population
No event to CRNMB	0.112	(0.088, 0.187)	Uniform	Study population
CRNMB to off treatment	0.013	(0, 0.019)	Uniform	Study population
No event to no event	0.856	(0.800, 0.906)	Uniform	Study population
Warfarin event rates (per 6 months)	(95% CI)			
No event to recurrence	0.026	(0, 0.060)	Uniform	Study population
No event to major bleed	0.008	(0, 0.034)	Uniform	Study population
Major bleed to off treatment	0.001	(0, 0.003)	Uniform	Study population
No event to CRNMB	0.279	(0.224, 0.397)	Uniform	Study population
CRNMB to off treatment	0.031	(0.019, 0.0413)	Uniform	Study population
No event to no event	0.655	(0.569, 0.741)	Uniform	Study population
Total rivaroxaban costs (annually)	Min–Max			
Recurrence	\$215	\$207–\$305	Gamma	MTRH
Major bleed	\$490	\$283–\$50807	Gamma	MTRH
CRNMB	\$304	\$283–\$25326	Gamma	MTRH
Off treatment	\$0	\$0–\$215	Gamma	MTRH
No event	\$142	\$76–\$208	Gamma	MTRH
Total warfarin costs (annually)	Min–Max			
Recurrence	\$267	\$254–\$343	Gamma	MTRH
Major bleed	\$435	\$401–\$795	Gamma	MTRH
CRNMB	\$332	\$310–\$401	Gamma	MTRH
Off treatment	\$0	\$0–\$267	Gamma	MTRH
No event	\$165	\$74–\$295	Gamma	MTRH
Warfarin and Rivaroxaban Utility Values (Annually)	Min–Max			
Recurrence	0.76	0.57–0.95	Logit	Ryan et al., Locadia et al., Sun et al. [23–25]
Major bleed	0.61	0.15–0.86	Logit	Hogg et al., Santos et al., Ryan et al., Sun et al. [20, 21, 23, 25]
CRNMB	0.65	0.51–0.68	Logit	Sun et al. [25]
Off treatment	0.68	0.57–0.83	Logit	Ryan et al., Locadia et al., Sun et al. [23–25]
No event	0.825	0.75–1.00	Logit	Dersch et al., Hogg et al., Santos et al., Bamber et al., Ryan et al. [14, 20–23]

CRNMB clinically relevant non-major bleed, MTRH Moi Teaching and Referral Hospital

**Table 2** Results from the base-case analysis (US\$)

Strategy	Costs	Effective QALYs	Incremental costs	QALYs gained	ICER
Rivaroxaban	\$173.00	0.848	– \$43.00	0.023	\$–1862.00
Warfarin	\$216.00	0.824	–	–	–

QALYs quality-adjusted life-years, ICER incremental cost-effectiveness ratio



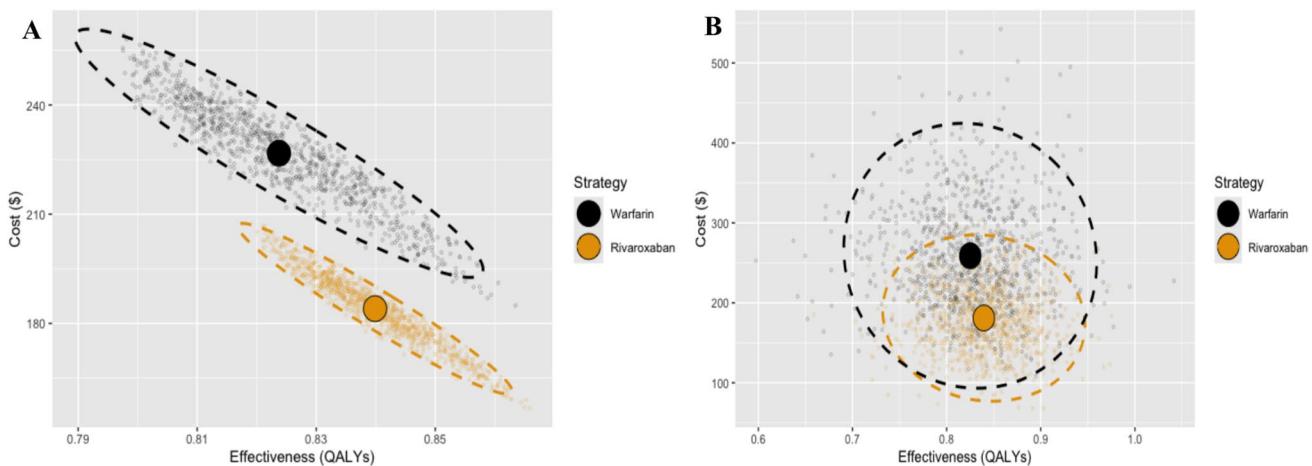
**Fig. 2** Tornado diagram that demonstrates the influence of each parameter on the ICER. The vertical black line indicates the ICER in the base case. Blue bars indicate the change in the ICER under the maximum parameter value and red bars indicate the change in ICER

under the minimum parameter value. *CRNMB* clinically relevant non-major bleed, *ICER* incremental cost-effectiveness ratio, *VTE* venous thromboembolism

simulation to evaluate the cost-effectiveness of a strategy that assumes the highest costs and lowest effectiveness. We observed that the cost of both treatments was below the accepted willingness-to-pay (WTP) threshold (rivaroxaban = \$206.84; warfarin = \$259.22), with rivaroxaban being the least costly (ICER \$-2322.46 per QALY). We found that

rivaroxaban was cost-effective in 98.4% of simulations compared warfarin in the first PSA where event rates are varied.

In the second PSA, where event rates, costs, and utility values were varied simultaneously, mean costs incurred from rivaroxaban (\$181.00) were less than warfarin (\$259.00). QALYs gained were 0.840 and 0.825 for rivaroxaban and



**Fig. 3** **A–B** Cost-effectiveness distributions for warfarin and rivaroxaban under Monte Carlo simulations. **A** Monte Carlo simulation with variation in event rates drawing from a uniform distribution. **B** Monte Carlo simulation with variation in event rates drawing from a uniform distribution, costs fitting a gamma distribution, and utilities

fitting a logit distribution. In both figures, each point represents a single simulation for a given strategy, gold for rivaroxaban and black for warfarin. The dashed ellipses lines represent 95% confidence intervals, visualizing clustering of each strategy on the cost effectiveness plane

warfarin, respectively, with a resulting ICER of \$-5390.00 per QALY gained. We again evaluated the treatment under the worst-case scenario; both medications fell below the accepted WTP threshold (rivaroxaban = \$350.62; warfarin \$542.48), with rivaroxaban dominating (ICER \$-3114.58 per QALY). We found that rivaroxaban was cost-effective in 84.1% of simulations compared warfarin in the final PSA where all model inputs are varied. In both PSAs, cost values for both treatments were higher than the base case, and QALYs were slightly lower for rivaroxaban. For warfarin, QALYs were identical to the base case in the first PSA and slightly higher in the second PSA. Despite these variations, rivaroxaban was still more cost-effective and clinically effective than warfarin.

In our scenario analysis, we varied the transition probability of VTE recurrence when a patient experiences the Off Treatment health state from 0 to 0.074. Here, we found that the mean total costs were the same as the base case. There was a slight decrease in total QALYs gained from warfarin (0.823) and rivaroxaban (0.847) compared to the base case. The ICER continued to favor rivaroxaban (\$-1807.00 per QALY) (OSM Fig. 1a).

## 4 Discussion

To our knowledge, we present the first cost-effectiveness evaluation comparing SOC warfarin to the DOAC rivaroxaban in western Kenya using event rates from a local public sector patient population receiving primary treatment for VTE. Our base-case analysis uses event rates (No Event, Recurrence, CRNMB, Major Bleed, and Off Treatment) from 276 patients treated with rivaroxaban or warfarin in western Kenya. All cost and event-rate data were obtained locally in Eldoret, Kenya. Despite higher upfront pill costs for rivaroxaban, our findings illustrate that rivaroxaban would be a cost-saving therapy compared to warfarin in this patient population with an ICER of \$-1,862.00 per QALY gained.

Deterministic sensitivity analyses revealed that the model output was sensitive to the wide range of costs incurred from treating a bleeding event under rivaroxaban therapy. We acknowledge that the wide cost ranges for rivaroxaban are influenced by the newer reversal agents utilized in bleeding incidents with this medication (e.g., Andexanet alfa). These reversal agents are yet to be readily available in Kenya, leaving patients in this setting with a higher risk for irreversible major bleeding events [11]. Despite incorporating these ranges for robustness in our sensitivity analyses, we anticipate that the real-world costs associated with reversing this medication in Kenya would not reach the upper end of this range due to limited access. For warfarin treatment, cost-effectiveness was most influenced by the costs of remaining

in the No Event health state. The cost range for No Event under warfarin therapy includes the cost of the drug itself, the expenses related to regular monitoring (e.g., lab tests, clinic visits) required to ensure its safe and effective use, and indirect costs for transportation to the clinic. Variations in the frequency and intensity of warfarin management likely explain the model's sensitivity, as seen in other studies assessing warfarin-associated costs [26–28].

Our base-case analysis results were stable when evaluating parameter and model uncertainty using PSAs and scenario analyses. Using second-order Monte Carlo techniques to assess uncertainty within event rates, utilities, and costs, we observed marginally elevated costs for warfarin and rivaroxaban, along with slightly diminished QALYs for rivaroxaban, compared to the base-case analysis, potentially reflecting the introduction of parameter uncertainty in the models. However, rivaroxaban emerged as dominant, cheaper, and more effective than warfarin. We performed a scenario analysis to test model uncertainty. When the event rate of VTE recurrence is varied during anticoagulation disruption following a bleed, QALYs slightly diminish due to the increased VTE recurrence rate. Still, rivaroxaban continued to be more clinically effective and cost-effective. Given the increasing availability of generic formulations on the market today, we predict rivaroxaban tablet prices will continue to decrease, increasing the cost-effectiveness of this agent further.

Previous literature has found rivaroxaban to be more cost-effective than warfarin in both VTE patients and patients on long-term anticoagulation for atrial fibrillation [22, 29–31]. A similar study in Ethiopia found that rivaroxaban was cost-effective below the WTP threshold (ICER \$125.683 per QALY) compared to warfarin for VTE patients over a lifetime [14]. A UK study comparing rivaroxaban to warfarin for VTE treatment over 3, 6, and 12 months found that rivaroxaban dominated warfarin as the cheaper and more effective option (12-month ICER \$-56.00 per QALY), which aligns with our results [22]. Compared to warfarin, rivaroxaban may exert its cost-saving effects by reducing clinic visits and associated clinic costs [26, 29]. Reduced need for clinical oversight may be cost-saving for both the patient and the provider while reducing the clinical burden on the health system [32, 33]. The dynamics of these costs are essential, as medications like rivaroxaban require more up-front payments from patients to acquire them. This presents a significant barrier to lower-income patients who rely on the public sector for their care, which continues to contribute to the limited uptake of DOACs despite results highlighting their benefits. Despite global advancements in evaluating DOAC usage, limited literature exists in SSA. Further research is needed to understand the mechanisms behind the cost-saving effects of rivaroxaban in western Kenya and evaluate additional DOAC usage in SSA.

Our findings suggest several important policy implications. Given that rivaroxaban was both cost-saving and more clinically effective than warfarin in the analysis, rivaroxaban may alleviate clinician and health system strain due to its simplified dosing and lack of INR monitoring. Policymakers in western Kenya may consider strategies to improve its accessibility such as adding rivaroxaban to national essential medicines lists, expanding public sector subsidies, or negotiating reduced procurement costs.

#### 4.1 Limitations

The current study has limitations. First, though we use event-rate data from VTE patients in Eldoret, Kenya, these patients were identified from two studies. Baseline clinical comparisons among patients in the rivaroxaban arm and warfarin arm were not available; neither was the precise length of anticoagulation duration. VTE treatment can vary in duration due to the etiology, whether provoked or unprovoked, and underlying medical conditions [34]. Since we cannot compare baseline covariates, we acknowledge that there may be unobservable causes for the difference in event rates between the two treatments. Still, these data represent the real-world dynamics of this patient population more accurately than large clinical trials performed predominantly outside SSA. Second, we accounted for non-medical expenditures, such as transportation costs from the MTRH clinic. However, we did not account for the loss of productivity costs associated with treatment or clinical events since these data were not available for the patients in the warfarin arm. Third, utility values used in this study are predominantly outside SSA and may not represent the utility values of patients within SSA and, more specifically, Kenya. While this is a limitation, we relied on the best available published data and our results remained stable across multiple sensitivity analyses in which we varied these inputs. Fourth, our analysis did not include the impact of Kenya's national health insurance program due to the lack of coverage for outpatient therapies and most inpatient services associated with the clinical events identified in our study. Despite this, the costs in this model most accurately represent the costs patients pay for these therapies in western Kenya. Finally, our findings are specific to the healthcare context of western Kenya, including local cost data and clinical practices from MTRH, which may limit generalizability to other regions within SSA. Differences in healthcare infrastructure, access to anticoagulation monitoring, and population health profiles could influence the cost-effectiveness of rivaroxaban in other settings. Future studies using country-specific data would help validate these findings across diverse SSA contexts.

## 5 Conclusion

Our analysis provides critical insight into the cost-effectiveness of the DOAC rivaroxaban compared to warfarin amongst patients with VTE relying on public sector care delivery in western Kenya. In HICs, warfarin is no longer the SOC due to drug interactions, diet restrictions, and intensive clinical monitoring that can lead to higher rates of under- or over-anticoagulation. Given the high upfront pill costs associated with DOACs, patients in western Kenya are still using warfarin as SOC over more effective therapeutic alternatives. Our results indicate that rivaroxaban is cost-saving and clinically superior compared to warfarin for VTE treatment. Further work is warranted on implementing the scale-up of rivaroxaban in resource-constrained settings like western Kenya to sustain long-term use of these agents.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40261-025-01454-7>.

**Acknowledgements** We want to express our deepest gratitude to the late Dr. Dennis Njuguna, whose unwavering dedication and passion to be a leader for clinical pharmacy in Kenya served as the cornerstone of this project. Before his passing, he led this project as part of his Masters in Clinical Pharmacy Thesis at Moi University in Eldoret, Kenya. Though he is no longer with us, his influence and contributions continue to resonate within this work. His memory will forever inspire and guide us, and we are grateful for the indelible mark he left on this project.

## Declarations

**Funding** Our study was not supported by any grants or external funding.

**Conflicts of Interest** S.P. reports receiving professional fees from Becton Dickinson for consulting work on philanthropic activities outside the submitted work. E.O. no conflict. A.H. no conflict. M.B. no conflict. I.M. no conflict. G.K. no conflict. N.B. no conflict. S.N. no conflict. O.G. no conflict. The Anticoagulation Clinic obtained rivaroxaban (Xarelto®) from Bayer East Africa Limited as part of a Rivaroxaban Access Program. There was no contribution (financial or otherwise) from the company in terms of data collection, manuscript writing and submission.

**Ethics Approval** This study did not require ethics approval, as it involved secondary analysis of de-identified, aggregate data and did not involve human subjects. Clinical data used in the analysis were drawn from a previously approved observational study conducted by our research group, which received ethics approval from Moi Teaching and Referral Hospital's Internal Review Board. No new data were collected, and all analyses complied with national research ethics guidelines in Kenya.

**Consent to Participate** Not applicable.

**Consent for Publication** Not applicable.

**Code Availability** The data and code that support the findings of this study are available in a public data repository on GitHub [<https://>

github.com/Eoneill29/CEA-anticoag], DOI reference: <https://doi.org/10.5281/zenodo.1458562>.

**Availability of Data and Material** Clinical data used to determine event rates and ultimately transition state probabilities are available upon request.

**Authors' Contributions** E.O. participated in conceiving the study, literature search, data analysis, interpretation of the data, writing and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. S.P. participated in conceiving the study, interpretation of the data, critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. A.H. and M.B. participated in data analysis, interpretation of the data, critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. I.M., G.K., N.B., S.N., and O.G. participated in interpreting results, providing critical revisions, and final approval of the manuscript. All authors read and approved the final version of manuscript and are accountable for the work.

**Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

## References

1. Lyman GH, Culakova E, Poniewierski MS, Kuderer NM. Morbidity, mortality and costs associated with venous thromboembolism in hospitalized patients with cancer. *Thromb Res.* 2018;164(Suppl 1):S112–8.
2. Raskob GE, Angchaisuksiri P, Blanco AN, et al. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol.* 2014;34(11):2363–71.
3. Nicholson M, Chan N, Bhagirath V, Ginsberg J. Prevention of venous thromboembolism in 2020 and beyond. *J Clin Med.* 2020;9(8):2467.
4. Blondon M, Bounameaux H. Secondary prevention of venous thromboembolism: one regimen may not fit all. *Circulation.* 2015;132(20):1856–9.
5. Hirsh J. Oral anticoagulant drugs. *N Engl J Med.* 1991;324(26):1865–75.
6. Kamath CC, Giblon R, Kunneman M, et al. Cost conversations about anticoagulation between patients with atrial fibrillation and their clinicians: a secondary analysis of a randomized clinical trial. *JAMA Netw Open.* 2021;4(7): e2116009-e.
7. Pokorney SD, Simon DN, Thomas L, et al. Patients' time in therapeutic range on warfarin among US patients with atrial fibrillation: Results from ORBIT-AF registry. *Am Heart J.* 2015;170(1):141–8 (8.e1).
8. García-Sempere A, Hurtado I, Bejarano D, et al. Group-based trajectory models to assess quality of INR control and its association with clinical outcomes. *Med Care.* 2020;58(4):e23–30.
9. Fang MC, Reynolds K, Fan D, et al. Clinical outcomes of direct oral anticoagulants vs warfarin for extended treatment of venous thromboembolism. *JAMA Netw Open.* 2023;6(8): e2328033-e.
10. Cohen AT, Bauersachs R. Rivaroxaban and the EINSTEIN clinical trial programme. *Blood Coagul Fibrinolysis.* 2019;30(3):85–95.
11. Njuguna D, Nwaneri F, Prichard AC, et al. Risk of bleeding associated with outpatient use of rivaroxaban in VTE management at a National Referral Hospital in Western Kenya. *Clin Appl Thromb Hemost.* 2023;29:10760296231184216.
12. Kohn CG, Bunz TJ, Beyer-Westendorf J, Coleman CI. Comparative risk of major bleeding with rivaroxaban and warfarin: Population-based cohort study of unprovoked venous thromboembolism. *Eur J Haematol.* 2019;102(2):143–9.
13. Obayo A, Ngunga M, Shah J, Sokwala A, Barasa A. Bleeding complications in patients on new oral anticoagulants for venous thromboembolism in Kenya. *Cardiovasc J Afr.* 2022;33(4):186–92.
14. Derseh MT, Solomon K, Tamene W, Yayebrad AT, Ambaye AS. A cost effectiveness analysis of rivaroxaban compared to warfarin for deep vein thrombosis (DVT) treatment in Ethiopia. *Clinicoecon Outcomes Res.* 2021;13:821–34.
15. Iorio A, Kearon C, Filippucci E, et al. Risk of recurrence after a first episode of symptomatic venous thromboembolism provoked by a transient risk factor: a systematic review. *Arch Intern Med.* 2010;170(19):1710–6.
16. Alarid-Escudero F, Krijkamp E, Enns EA, et al., editors. A tutorial on time-dependent cohort state-transition models in r using a cost-effectiveness analysis example. 20220916 ed; 2023.
17. Kikkert WJ, Geloven NV, Laan MHVD, et al. The Prognostic value of Bleeding Academic Research Consortium (BARC)-defined bleeding complications in st-segment elevation myocardial infarction. *J Am Coll Cardiol.* 2014;63(18):1866–75.
18. The World Bank. Official exchange rate (LCU per US\$, period average)-Kenya. 2022. <https://data.worldbank.org/indicator/PA.NUS.FCRF?locations=KE>. Accessed 1 Nov 2022.
19. World Health O, Baltussen RMPM, Adam T, et al editors. Making choices in health: WHO guide to cost-effectiveness analysis/ edited by T. Tan-Torres Edejer ... [et al]. Geneva: World Health Organization; 2003.
20. Hogg K, Kimpton M, Carrier M, Coyle D, Forgie M, Wells P. Estimating quality of life in acute venous thrombosis. *JAMA Intern Med.* 2013;173(12):1067–72.
21. Santos IF, Pereira S, McLeod E, Guillermín AL, Chatzitheofilou I. Economic analysis of rivaroxaban for the treatment and long-term prevention of venous thromboembolism in Portugal. *Acta Med Port.* 2014;27(5):615–24.
22. Bamber L, Muston D, McLeod E, Guillermín A, Lowin J, Patel R. Cost-effectiveness analysis of treatment of venous thromboembolism with rivaroxaban compared with combined low molecular weight heparin/vitamin K antagonist. *Thromb J.* 2015;13:20.
23. Ryan ES, Havrilesky LJ, Salinaro JR, Davidson BA. Cost-effectiveness of venous thromboembolism prophylaxis during neoadjuvant chemotherapy for ovarian cancer. *JCO Oncol Pract.* 2021;17(8):e1075–84.
24. Locadia M, Bossuyt PM, Stalmeier PF, et al. Treatment of venous thromboembolism with vitamin K antagonists: patients' health state valuations and treatment preferences. *Thromb Haemost.* 2004;92(6):1336–41.
25. Sun KX, Cui B, Cao SS, et al. Cost-effectiveness analysis of direct oral anticoagulants versus vitamin K antagonists for venous thromboembolism in China. *Front Pharmacol.* 2021;12: 716224.
26. Bobade RA, Helmers RA, Jaeger TM, Odell LJ, Haas DA, Kaplan RS. Time-driven activity-based cost analysis for outpatient anticoagulation therapy: direct costs in a primary care setting with optimal performance. *J Med Econ.* 2019;22(5):471–7.
27. Jaberi N, Kavosi Z, Hooshmandi E, Moradi N, Keshavarz K, Borhani-Haghghi A. The Study of cost-effectiveness of

riloxaban versus warfarin in patients with atrial fibrillation who developed ischemic stroke. *Stroke Res Treat*. 2021;2021:5534873.

28. Leminen A, Pyykönen M, Tynkkynen J, Tykkyläinen M, Laatikainen T. Modeling patients' time, travel, and monitoring costs in anticoagulation management: societal savings achievable with the shift from warfarin to direct oral anticoagulants. *BMC Health Serv Res*. 2019;19(1):901.
29. Pereira MP, Lima EG, Pitta FG, et al. Rivaroxaban versus warfarin in postoperative atrial fibrillation: Cost-effectiveness analysis in a single-center, randomized, and prospective trial. *JTCVS Open*. 2023;15:199–210.
30. Seaman CD, Smith KJ, Ragni MV. Cost-effectiveness of rivaroxaban versus warfarin anticoagulation for the prevention of recurrent venous thromboembolism: a U.S. perspective. *Thromb Res*. 2013;132(6):647–51.
31. Yang L, Wu J. Cost-effectiveness of rivaroxaban compared with enoxaparin plus warfarin for the treatment of hospitalised acute deep vein thrombosis in China. *BMJ Open*. 2020;10(7): e038433.
32. Berger JS, Ashton V, Laliberté F, et al. Healthcare Resource Utilization and Costs of Rivaroxaban Versus Warfarin Among Non-valvular Atrial Fibrillation (NVAF) Patients with Diabetes in a US Population. *Adv Ther*. 2023;40(3):1224–41.
33. Margolis JM, Deitelzweig S, Kline J, et al. Shorter hospital stays and lower costs for rivaroxaban compared with warfarin for venous thrombosis admissions. *J Am Heart Assoc*. 2016; 5(10).
34. Kearon C, Akl EA. Duration of anticoagulant therapy for deep vein thrombosis and pulmonary embolism. *Blood*. 2014;123(12):1794–801.

## Authors and Affiliations

Emily T. O'Neill<sup>1</sup>  · Andrew W. Huang<sup>1</sup> · Marta Wilson-Barthes<sup>2</sup> · Imran Manji<sup>3</sup> · Gabriel Kigen<sup>4</sup> · Naftali Busakhala<sup>4</sup> · Samuel Nyanje<sup>5</sup> · Omar Galárraga<sup>1,2</sup> · Sonak D. Pastakia<sup>6</sup>

✉ Sonak D. Pastakia  
spastaki@purdue.edu

Emily T. O'Neill  
Emily\_oneill@alumni.brown.edu

<sup>1</sup> Department of Health Services Policy and Practice, Brown University School of Public Health, 121 S. Main Street, Providence, RI 02903, USA

<sup>2</sup> Center for Global Public Health, Brown University School of Public Health, 121 S. Main Street, Providence, RI 02903, USA

<sup>3</sup> Directorate of Pharmacy and Nutrition, Moi Teaching and Referral Hospital, Eldoret, Kenya

<sup>4</sup> Department of Pharmacology and Toxicology, Moi University School of Medicine, Eldoret, Kenya

<sup>5</sup> Academic Model Providing Access to Healthcare (AMPATH), PO Box 4606-30100, Eldoret, Kenya

<sup>6</sup> Department of Pharmacy Practice, Purdue University College of Pharmacy, 640 Eskenazi Ave., Indianapolis, IN 46202, USA