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Cost-effectiveness of rivaroxaban versus warfarin for treatment of nonvalvular atrial fibrillation in patients with worsening renal function

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ABSTRACT

Background: Nonvalvular atrial fibrillation (NVAF) is highly prevalent and increases the risks of cardiovascular events. In a recent subgroup analysis, treatment response was shown to vary for patients exhibiting worsening renal function (WRF) on-treatment. It is important to understand the cost-effectiveness of novel oral anticoagulant (NOAC) use in this population.
Methods: A cost-effectiveness analysis (CEA) was conducted using a Markov model to determine whether NOAC rivaroxaban treatment is cost-effective relative to warfarin in NVAF patients with on-treatment WRF. Input parameters were sourced from clinical literature including a multicenter clinical trial and subgroup analysis. We studied elderly US male patients at increased risk for stroke ($CHADS_2$ score ≥ 2) undergoing treatment for NVAF and exhibiting WRF. Main outcome measures included total healthcare costs in 2017 US dollars (societal perspective), total quality-adjusted life years (QALYs), incremental cost-effectiveness ratio (ICER), and incremental net monetary benefits (INMB) per-patient.
Results: The remaining lifetime use of rivaroxaban is associated with 5.69 QALYs at a cost of $66,075 per patient, while warfarin produced 5.22 QALYs with costs of $78,504 per patient. At a willingness-to-pay (WTP) of $150,000 per QALY, incremental net monetary benefits (INMB) per patient are $83,590. In our population, treatment with warfarin was dominated by rivaroxaban in 99.4% of 10,000 simulations.
Conclusions: Rivaroxaban is likely a dominant treatment over warfarin in elderly US male NVAF patients exhibiting WRF, providing increased QALYs at a decreased overall cost. Application of these findings may require healthcare providers to predict which patients are likely to exhibit WRF.

1. Introduction

1.1. Background

Atrial fibrillation (AF) is a common form of heart arrhythmia. It is caused by irregular beating and blood flow in the atria, resulting in an irregular flow to the ventricles. Left untreated, the disease increases the risk of severe cardiovascular events including stroke to four or five times that of a person without AF [1]. A variation of this heart condition where the irregular beating is not caused by a heart valve issue is nonvalvular atrial fibrillation (NVAF). Precisely, this form of atrial fibrillation exists in the "absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair" as defined by the ACC/AHA/HRS 2014 Guidelines for the Management of Patients with Atrial Fibrillation [2]. An estimated 2.7 to 6.1 million people in the United States suffered from atrial fibrillation in 2014 [2]. NVAF is estimated to account for up to 30% of these cases [3].

Warfarin was first approved by the U.S. Food and Drug Administration (FDA) in 1954 and has been used since as part of standard care for cerebrovascular event prevention caused by atrial fibrillation and for the treatment of venous thromboembolism [4–6]. Despite low acquisition cost due to generic status, warfarin requires patients to maintain a specific diet, a narrow therapeutic range, and limit use of other drugs which may interact adversely with warfarin [7]. Rivaroxaban was approved by the FDA in 2011 for treatment of NVAF after completion of the head-to-head randomized controlled trial (RCT): Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET-AF) [8]. The RCT showed statistically significant non-inferiority of rivaroxaban for prevention of stroke and systemic thromboembolism when compared to warfarin, with similar rates of bleeding [9]. Despite greater drug acquisition costs when compared to warfarin, rivaroxaban offers a wider

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therapeutic range eliminating the need for close monitoring of patients. The resulting ease of self-treatment decreases indirect costs faced by the patient and increases general health-related quality of life (HRQoL) [10,11].

A subgroup analysis of the ROCKET-AF RCT was conducted by Fordyce et al. [12] in patients with on-treatment worsening renal function (WRF). WRF was defined as a decrease of >20% from screening creatinine clearance (CrCl) at any point during the study. After excluding patients in the original RCT without an additional CrCl measure, 12,612 patients were classified as having either stable renal function (SRF) (n = 9292) or WRF (n = 3320). Results for WRF patients taking rivaroxaban showed a reduction in stroke or systemic embolism compared with those taking warfarin (1.54 versus 3.25 events per 100 patient-years, $P = 0.05$). This difference was not observed for patients with SRF under rivaroxaban versus warfarin, suggesting that the benefits of the drug were largely concentrated among patients with WRF. In addition, there was no statistically significant difference in major or nonmajor clinically relevant bleeding among WRF patients on warfarin versus rivaroxaban but patients with WRF treated with rivaroxaban were found to have an increase in gastrointestinal bleeding not exhibited in SRF patients (3.21 versus 1.28 events per 100 patient-years, $P = 0.02$) [12]. It is unclear whether rivaroxaban is a cost-effective treatment alternative to warfarin in this population.

1.2. Objectives

Various studies have utilized results from ROCKET-AF to analyze the cost-effectiveness of rivaroxaban relative to warfarin in NVAF in the US. Lee et al. [13] utilized a Markov model to assess the cost-effectiveness of rivaroxaban compared to adjusted-dose warfarin for the prevention of stroke in patients with AF from a Medicare perspective. In 10,000 Monte Carlo simulations, rivaroxaban was shown to be cost-effective 80% and 91% of the time with willingness to pay thresholds of $50,000 and $100,000 per QALY, respectively [13]. Harrington et al. [14] used a Markov model from a societal perspective to study cost/QALY gains of NOACs including rivaroxaban over warfarin, finding that rivaroxaban would be highly cost-effective at any reasonable threshold with an incremental cost-effectiveness ratio (ICER) of $3190/QALY [14]. Canestaro et al. [15] took a societal perspective in analyzing NOACs including rivaroxaban vs. warfarin, finding an ICER of $111,465 [15]. While there are various results in the literature on the cost-effectiveness of rivaroxaban versus warfarin in the general NVAF patient population, this study is the first to utilize results in the subgroup analysis by Fordyce et al. to investigate cost-effectiveness in the group of patients exhibiting on-treatment WRF (decrease of >20% from screening CrCl). Improved knowledge on treatment cost-effectiveness in this patient population may help inform resource allocation by healthcare providers and medical decision makers.

2. Methods

2.1. Model overview

A literature-based Markov model (Fig. 1) was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA) from the United States societal perspective to analyze the cost-effectiveness of the following treatment strategies: (1) rivaroxaban 15 or 20 mg daily, or (2) warfarin with target international normalized ratio (INR) between 2.0 and 3.0. We evaluated these interventions for the treatment of NVAF, specifically in the male patient population susceptible to on-treatment WRF (patients experiencing a decrease of >20% from screening CrCl as measured by the Modification of Diet in Renal Disease (MDRD) equation) [16]. Consistent with the RCT, patients were assumed to be treated with 20 mg once daily unless baseline measures revealed moderate renal dysfunction (CrCl of 30 to 49 mL/min), in which we assumed a reduced dose of 15 mg once daily. The model horizon was 25 years to allow for a lifetime analysis, with 30-day cycles. Analysis of costs and quality-adjusted life years (QALYs) gained were calculated using a theoretical cohort of 1000 males of age 73 and similar characteristics to those in the ROCKET-AF trial subgroup analysis by Fordyce et al. [9,12] All costs were adjusted to 2017 US Dollars ($) using the medical component of the US consumer price index [17]. Following convention for US based studies, both costs and QALYs were discounted at the same rate of 3% per year [18].

2.2. Health states

Health states in the model for both treatment arms included well with NVAF and WRF, ischemic stroke (IS), intracranial hemorrhage (ICH), myocardial infarction (MI), major bleeding (MB), systemic embolism (SE), non-major clinically relevant bleeding (NMCRB), and death. Events were defined consistently with the ROCKET-AF RCT and subgroup analysis, except for ICH which we separated out from MB to allow for modeling of its individual impact on patients [9,12]. IS, ICH, and MI were modeled to occur with three levels of severity (minor, moderate, or severe) reflective of having no complications, complications, or major complications, respectively. Events with three levels of severities (IS, ICH, and MI) would occur as modeled in the bottom right of Fig. 1. Minor events were considered to not have lasting effects on the patients outside of 30 days, while moderate and severe events were assumed to result in permanent minor and major residual deficits for the patients, respectively. Moderate and severe events contained both acute states, where event costs and utility decrements would be incurred, and post-event states where patients would live out the rest of their lives at increased incremental healthcare costs and decreased utilities [19,20]. Patients were permitted to transition through the model for the entire 25 years or until death after which costs and QALYs would equal zero.

2.3. Transition probabilities

Monthly transition probabilities were derived from rivaroxaban and warfarin event rates provided in Fordyce et al. (Table 1) [12]. As the primary subgroup analysis of the ROCKET AF RCT studying renal function in our population of interest, it was identified as the best source of information for calibrating event probabilities in the model. Severity distributions for MI, IS, and ICH were derived from the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) 2014 data on US hospital discharges utilizing Medicare Severity-Diagnosis Related Group (MS-DRG) codes from previous NVAF literature [21,22]. Severities were stratified by event type as well as age, based on the closest available age category in HCUP data. Yearly US baseline mortality rates from the Centers for Disease Control and Prevention (CDC) were adjusted by a multiplier of 1.34 to account for increased general mortality in the NVAF population

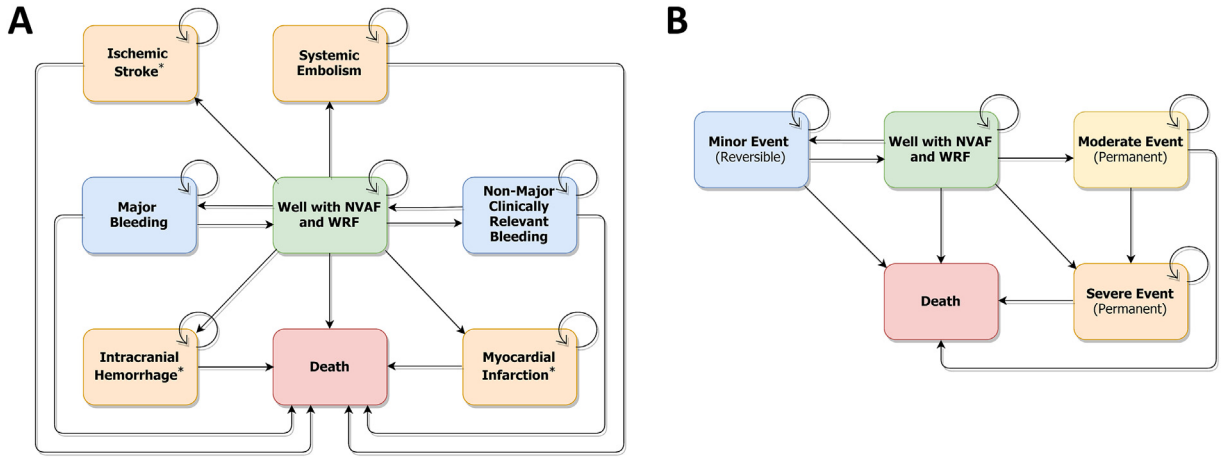

Fig. 1. A. General Markov model structure. B. Transitions for health states with three levels of severity (ischemic stroke, intracranial hemorrhage, myocardial infarction).

Table 1
Baseline transition probability baseline inputs and sensitivity analysis ranges.

Parameter input	Point estimate (95% CI)			Source(s)
*Baseline yearly event rates under warfarin, * denotes computation or numerical approximation*				
Systemic embolism	0.009 (0.004, 0.015)*			[12]
Myocardial infarction	0.014 (0.008, 0.021)*			[12]
Ischemic stroke	0.019 (0.012, 0.027)*			[12]
Major bleed	0.024 (0.015, 0.033)*			[12]
Intracranial hemorrhage	0.009 (0.004, 0.015)*			[12]
Non-major clinically relevant bleeding	0.095 (0.071, 0.104)*			[12]
*Baseline yearly event rates under rivaroxaban, * denotes computation or numerical approximation*				
Systemic embolism	0.005 (0.002, 0.010)*			[12]
Myocardial infarction	0.006 (0.002, 0.011)*			[12]
Ischemic stroke	0.010 (0.005, 0.017)*			[12]
Major bleed	0.039 (0.027, 0.049)*			[12]
Intracranial hemorrhage	0.007 (0.003, 0.012)*			[12]
Non-major clinically relevant bleeding	0.074 (0.056, 0.084)*			[12]
Clinical events	Severity			Source(s)
Severity distributions by decade of age	Minor (%)	Moderate (%)	Severe (%)	[21]
Myocardial infarction – 70–79	21.6	33.1	45.2	[21]
Myocardial infarction – 80+	16.9	32.8	50.3	[21]
Ischemic stroke – 70–79	19.7	49.7	30.5	[21]
Ischemic stroke – 80+	10.7	49.9	39.4	[21]
Intracranial hemorrhage – 70–79	25.8	44.5	29.7	[21]
Intracranial hemorrhage – 80+	20.9	44.8	34.3	[21]
Clinical events	Parameter (range)			Source(s)
Yearly risk multiplier of clinical events by decade of age compared to 70–79 year-olds	80–89 year-olds	90–99 year-olds		
Myocardial infarction	1.30 (1.04, 1.56)	1.69 (1.08, 2.43)		[26]
Ischemic stroke	1.40 (1.12, 1.68)	1.96 (1.25, 2.82)		[26]
Bleeding events (ICH, MB, NMCRB)	1.97 (1.58, 2.36)	3.88 (2.48, 5.59)		[26]
Yearly risk multiplier of other events				
Death rate multiplier for NVAF	1.34 (1.07, 1.61)			[24–26]
Death after minor or major residual deficit	1.80 (1.44, 2.16)			[15]

[23–26]. Patients who experienced a clinical event resulting in minor or major residual deficit were assumed to be at an additional 1.80 multiplicatively increased yearly risk of death [15]. Consistent with previous CEA literature on NVAF, yearly risks of clinical events were assumed to increase multiplicatively with each decade increase in age [26]. All transition probabilities are assumed to be generated from exponential survival functions and hence could be computed and adjusted in manners consistent with the declining exponential approximation of life expectancy (DEALE) method [27,28].

2.4. Costs

All costs in the model were separated into direct and indirect costs and reported in 2017 US dollars ($), adjusted with the US medical CPI when necessary [17]. Direct costs included costs of pharmaceutical acquisition, INR monitoring for warfarin treatment, hospitalization from clinical events, physician fees from clinical events, regular physician visit costs, and general incremental healthcare costs post-minor and major residual deficit (Table 2). Hospitalization costs were derived from HCUP discharge data and physician costs were derived from hospitalization costs using commercial professional fee ratios (PFRs) for US hospital discharges from the literature by respective MS-DRGs [21,29]. Rivaroxaban drug costs were acquired from the U.S. Department of Veterans Affairs (VA) Pharmaceutical Pricing list and warfarin costs inclusive of requisite international normalized ratio (INR) monitoring were obtained from the literature [22,30]. Incremental healthcare costs post-events resulting in minor and major residual deficits were calculated from hospitalization costs using ratios from a long-term NVAF cost analysis [19]. Indirect costs were computed as the time spent on necessary treatment-related activities multiplied by the current US average compensation rate from the US Bureau of Labor Statistics [11,31,32]. These calculations included time spent: per visit to clinic (travel, waiting, and consultation time), communicating with providers, per visit to the pharmacy, and preparing special diets required by the treatment regimen [11].

2.5. Utilities

Baseline utilities in the model accounted for general quality of life of living with atrial fibrillation as well as decrements for discomfort of the treatment regimens (Table 3). Event and post-event utility decrements were acquired from a nationally representative catalog of preference-based scores for chronic conditions in the United States and included temporary event disutilities as well as permanent decrements for living post-moderate or post-severe clinical events [20]. This catalog of utilities has been used in various US perspective CEA studies on atrial fibrillation [10,14,15,26]. Patients experiencing mild events in the model were assumed to return to baseline after one cycle (30 days) without permanent disutility. Other than through disutility directly associated with treatment, state event utilities were assumed to be the same across both treatment regimens. All additional disutilities experienced by patients in the model were assumed to compound additively with the baseline utility.

2.6. Sensitivity analyses

Deterministic (one-way) and probabilistic sensitivity analyses were conducted to test robustness of baseline model results. For deterministic analysis, parameters were individually varied within their 95% confidence intervals when available, or ±20% when confidence intervals were not available. In the scenario of a dominated result, the outcome of interest in sensitivity analyses was changed from the ICER between rivaroxaban and warfarin to the INMB assuming a willingness to pay (WTP) of US $150,000 per QALY [33]. Probabilistic sensitivity analysis involved simulating 10,000 iterations of the model in Monte Carlo fashion [34,35]. Following health economic modeling conventions realistic probabilistic distributions were fit to characterize uncertainty in the parameters [36]. Baseline utility and baseline event probabilities were fit to beta distributions, clinical event utility decrements and hospitalization costs were fit to gamma distributions, clinical event severities were fit to Dirichlet distributions, and professional fee ratios were fit to uniform distributions.

3. Results

3.1. Incremental net monetary benefits

Results from the Markov model for discounted total costs and QALYs accumulated by each treatment arm are reported on a per-patient basis. Use of rivaroxaban is associated with a gain of 5.69 QALYs at a cost of $66,075 per-patient (PP), while use of warfarin produced 5.22 QALYs at costs of $78,504 PP. Incremental costs and QALYs for rivaroxaban treatment versus warfarin are -$12,429 and 0.47 QALYs, respectively. In the US male WRF population, treatment of NVAF with rivaroxaban dominates treatment with warfarin. Given a dominant base-case result, the outcome measure of interest is changed from ICER to INMB. At a WTP of $150,000 per QALY, INMB per patient are $83,590 under rivaroxaban treatment.

Table 2
Baseline input costs and sensitivity analysis ranges.

Description		Costs ($, 2017)		Source(s)
Acute costs, by event type		Hospital costs (95% CI)	Physician costs (range)	
Aged 70–79 minor	MI	$7943 ($7783–$8104)	$1160 ($1097–$1216)	[21,22,29]
	IS	$15,917 ($15,383–$16,460)	$1815 ($1446–$2206)	[21,22,29]
	ICH	$7878 ($7758–$7999)	$1198 ($1125–$1264)	[21,22,29]
Aged 70–79 moderate	MI	$9883 ($9706–$10,062)	$1443 ($1359–$1529)	[21,22,29]
	IS	$19,022 ($18,465–$19,587)	$2492 ($2105–$2899)	[21,22,29]
	ICH	$10,123 ($9947–$10,299)	$1549 ($1502–$1607)	[21,22,29]
Aged 70–79 severe	MI	$15,091 ($14,779–$15,406)	$2264 ($2113–$2419)	[21,22,29]
	IS	$26,922 ($25,600–$28,278)	$3715 ($3174–$4298)	[21,22,29]
	ICH	$15,846 ($15,451–$16,245)	$2615 ($2472–$2745)	[21,22,29]
Aged 70–79	SE	$13,570 ($12,130–$15,088)	$2551 ($1977–$3214)	[21,22,29]
All	MB	$15,149 ($14,810–$15,493)	$2651 ($2488–$2820)	[21,22,29]
	NMCRB	$5993 ($5882–$6106)	$1163 ($1106–$1221)	[21,22,29]
Aged 80+ minor	MI	$6932 ($6725–$7142)	$1012 ($948–$1071)	[21,22,29]
	IS	$16,590 ($15,527–$17,685)	$1891 ($1460–$2370)	[21,22,29]
	ICH	$7394 ($7243–$7547)	$1124 ($1050–$1192)	[21,22,29]
Aged 80+ moderate	MI	$8692 ($8483–$8904)	$1269 ($1188–$1353)	[21,22,29]
	IS	$17,999 ($17,335–$18,674)	$2358 ($1976–$2764)	[21,22,29]
	ICH	$9427 ($9254–$9603)	$1442 ($1397–$1498)	[21,22,29]
Aged 80+ severe	MI	$12,127 ($11,835–$12,422)	$1819 ($1692–$1950)	[21,22,29]
	IS	$22,601 ($21,375–$23,861)	$3119 ($2650–$3627)	[21,22,29]
	ICH	$12,787 ($12,453–$13,127)	$2110 ($1992–$2218)	[21,22,29]
Aged 80+	SE	$10,891 ($8968–$12,999)	$2047 ($1462–$2769)	[21,22,29]
all	MB	$13,382 ($13,013–$13,755)	$2342 ($2186–$2503)	[21,22,29]
	NMCRB	$5871 ($5721–$6024)	$1139 ($1076–$1205)	[21,22,29]
Description		Costs ($, 2017)		Source(s)
Post-event costs, monthly		Calculated incremental costs, monthly $, 2017 (95% CI)		
Aged 70–79 moderate	MI	$1272 ($1249–1295)		[19,21]
	IS	$2448 ($2377–$2521)		[19,21]
	ICH	$1208 ($1187–$1229)		[19,21]
Aged 70–79 severe	MI	$1942 ($1902–$1983)		[19,21]
	IS	$3465 ($3295–$3640)		[19,21]
	ICH	$1892 ($1844–$1939)		[19,21]
	SE	$1747 ($1561–$1942)		[19,21]
Aged 80+ moderate	MI	$1119 ($1092–$1146)		[19,21]
	IS	$2317 ($2231–$2404)		[19,21]
	ICH	$1125 ($1105–$1146)		[19,21]
Aged 80+ severe	MI	$1561 ($1523–$1599)		[19,21]
	IS	$2909 ($2751–$3071)		[19,21]
	ICH	$1526 ($1486–$1567)		[19,21]
	SE	$1402 ($1154–$1673)		[19,21]
Other costs		Rivaroxaban costs (range)	Warfarin costs (range)	
Drug costs, including INR monitoring for warfarin (monthly)		$221.85 ($177.48–$266.22)	$23.61 ($18.89–$28.33)	[22,30]
Indirect time costs (monthly)		$104.39 ($83.51–$125.27)	$265.90 ($212.72–$319.09)	[11,31,32]
Physician office visit (CPT code 99212)		$67.42 ($53.94–$80.91)	$67.42 ($53.94–$80.91)	[11,38]

3.2. Sensitivity analysis results

In one-way sensitivity analysis, inputs showing greatest impact on INMB included the warfarin SE rate (33.7%), rivaroxaban SE rate (30.9%), warfarin IS rate (29.2%), warfarin treatment disutility (28.1%), rivaroxaban IS rate (26.6%), warfarin MI rate (23.2%), rivaroxaban ICH rate (20.1%), rivaroxaban MI rate (18.9%), warfarin ICH rate (18.8%), and the NVAF death rate multiplier (14.9%). Varying any other parameters led to changes of <7% in INMB. The greatest change in INMB, caused by variation in warfarin SE rate, resulted in a range for INMB of $55,381 to $109,886 per-patient, suggesting that the results of the model are highly robust to univariate changes. In probabilistic sensitivity analysis (Appendix Additional Figure), rivaroxaban was the dominant treatment in 99.4% of 10,000 iterations. In a simple scenario analysis where time costs were omitted, the percent of iterations with rivaroxaban dominant fell to 20.6%; however, rivaroxaban was still cost-effective in 91.2%, 96.7%, and 98.2% of these iterations at WTP thresholds of $50,000, $100,000, and $150,000 per QALY, respectively.

Table 3
Baseline utilities and sensitivity analysis ranges.

Health state	Utility/decrement (95% CI)	Source(s)
Nonvalvular atrial fibrillation	0.810 (0.678, 0.914)	[10,20]
Renal impairment	−0.054 (−0.057, −0.052)	[20], Calculated
Warfarin treatment	−0.013 (−0.033, −0.002)	[20], Calculated
Rivaroxaban treatment	−0.002 (−0.007, 0.000)	[20], Calculated
Myocardial infarction	−0.125 (−0.106, −0.144)	[10,20]
Ischemic stroke	−0.139 (−0.118, −0.160)	[10,20]
Intracranial hemorrhage	−0.139 (−0.118, −0.160)	[10,20]
Systemic embolism	−0.120 (−0.102, −0.139)	[10,20]
Major bleed	−0.181 (−0.155, −0.209)	[10,20]
Non-major clinically relevant bleed	−0.013 (−0.049, 0.000)	[20], Calculated
Minor residual deficit	−0.250 (−0.923, −0.006)	[20], Calculated
Major residual deficit	−0.610 (−2.250, −0.015)	[20], Calculated

3.3. Limitations

We present a simplified representation of the true NVAF treatment and disease progression. Chronic diseases are complex conditions with many environmental, biological, and physiological processes at play. Our assessment assumes a discrete-time Markovian structure which may limit overall model precision. A cycle length of 30 days limits the number of clinical events that occur in any given month to one. The assumption of a 25-year time horizon does not consider possible advances in health technology and treatment for NVAF. The use of a 3%

discount rate may not be appropriate for the entire time horizon. In addition, this CEA relies heavily on values from the ROCKET-AF RCT and subsequent subgroup analysis by Fordyce et al. [9,12]. As the ROCKET-AF study focused on patients at generally higher risk of clinical events with a mean $CHADS_2$ score of 3.5, results may not be perfectly applicable to the entire NVAF population. Successful warfarin treatment has been shown to be strongly reliant on time in therapeutic range (TTR), which was 58% for the warfarin arm in ROCKET-AF, but may differ in the elderly US male population [9,37]. Acute costs were acquired by methods comparable to other NVAF CEAs, but post-event cost ratios are reliant on a retrospective database analysis in the US Medicare population [19]. Lastly, we find that US males with NVAF and on-treatment WRF may benefit significantly from use of rivaroxaban over warfarin, but useful application of these results may require healthcare providers to successfully predict which patients are likely to exhibit WRF prior to treatment initiation.

4. Discussion

This is the first CEA to investigate the cost-effectiveness of the NOAC rivaroxaban as compared to warfarin in treatment for nonvalvular atrial fibrillation for patients who exhibit on-treatment worsening renal function.

Earlier studies have found mixed results regarding the cost-effectiveness of the NOAC rivaroxaban relative to warfarin in different patient populations, suggesting that cost-effectiveness is highly dependent on patient characteristics. We find that rivaroxaban use in elderly (>73 years) male patients who experience a decrease of 20% or higher from initial creatinine clearance at any point during treatment results in additional QALYs at a decreased cost. These results are not surprising given that the subgroup analysis of ROCKET-AF by Fordyce et al. found that much of the reductions in stroke and systemic embolism risk of rivaroxaban treatment were concentrated in the WRF subset of the population, despite higher risk for gastrointestinal bleeds [12]. From an economic evaluation perspective, we find that the overall treatment benefits of rivaroxaban outweigh these increased bleeding rates relative to treatment under warfarin.

There are multiple implications from this line of research. These findings address a dearth in the literature on the cost-effectiveness in a patient population that experienced strongly decreased general frequency of clinical events on rivaroxaban despite greatly increased risk of bleeding events during the original ROCKET-AF trial. Our model allows us to quantify the economic impacts of these differential event and survival rates to reach a conclusion of supporting use of rivaroxaban over warfarin in this population. The dominant result in our base case model and subsequent sensitivity analyses support the robustness of this recommendation across various feasible scenarios. These results contribute to existing clinical findings and suggest that rivaroxaban use is also an economically prudent course of action over treatment with warfarin in this population. Further research on the cost-effectiveness of other NOACs in specialized patient populations may be necessary to justify increased utilization by healthcare providers and other medical decision makers.

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