

Economic impact of switching versus rivaroxaban or apixaban after a bleeding event in the United States: a cost-consequence analysis evaluating clinical event-related costs in patients with non-valvular atrial fibrillation

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Background

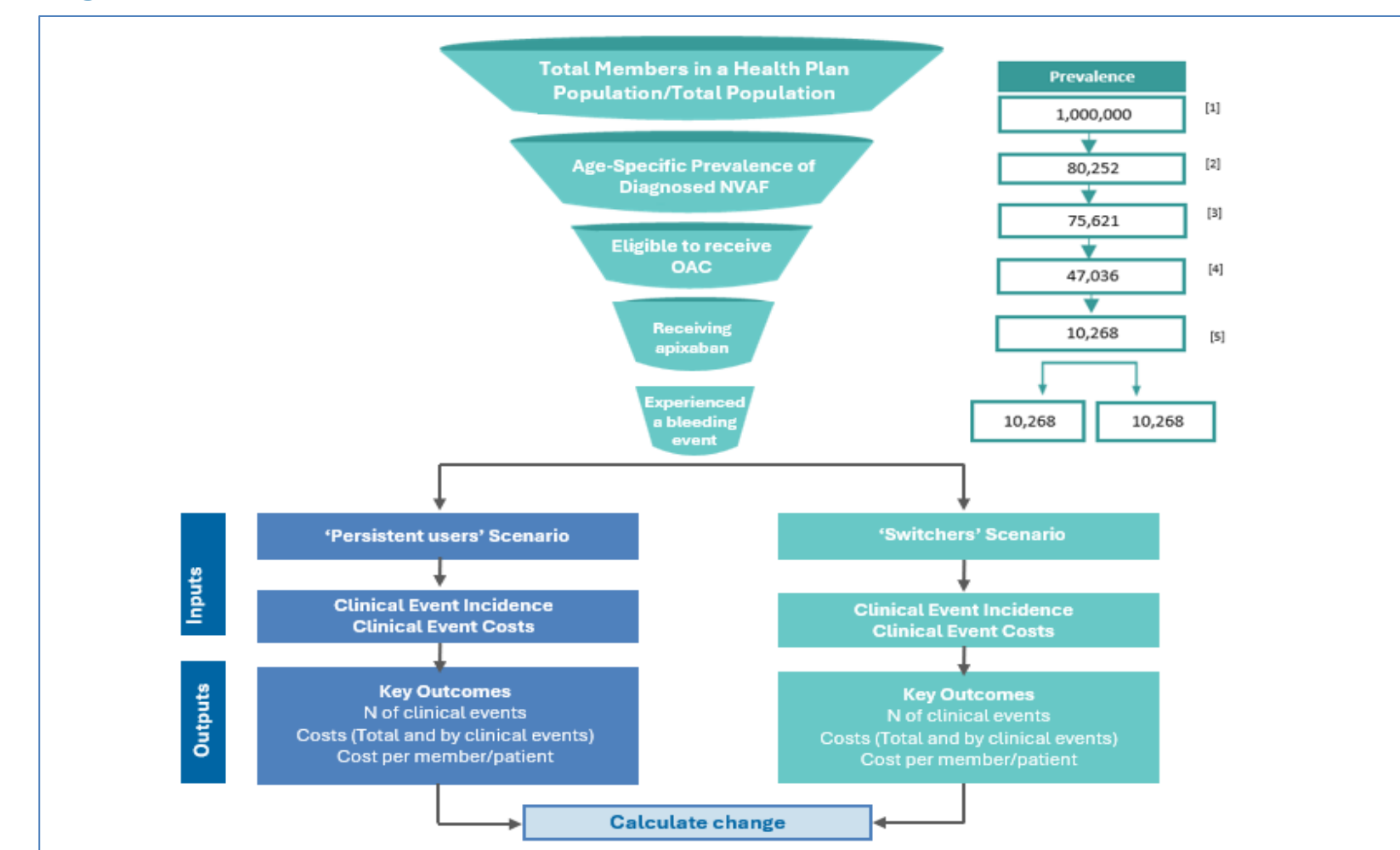
- Direct oral anticoagulants (DOACs) are widely used to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF). However, bleeding is an unintended consequence of DOAC exposure, often prompting treatment interruption, discontinuation, or switching.
- A recent real-world analysis found that, among patients with NVAF who experienced a bleeding event after initiating apixaban, switching to rivaroxaban increased the risk of major bleeding (MB), while stroke/systemic embolism (SE) risks remained similar.¹
 - The risk of major bleeding was higher in patients who switched from apixaban to rivaroxaban (9.59 per 100 patient-years) compared with those who persisted on apixaban (5.43 per 100 patient-years) [HR: 1.69, 95% CI 1.13–2.53].¹
 - The risk of stroke/SE was similar between patients who switched from apixaban to rivaroxaban (2.07 per 100 patient-years) and those who persisted on apixaban (1.15 per 100 patient-years) [HR: 1.79, 95% CI 0.77–4.20].¹
 - Real-world clinical outcomes of treatment switching in patients with NVAF were reported in the study; however, evidence on the economic implications of switching from apixaban to rivaroxaban following a bleed remains limited.
- The aim of this analysis was to compare clinical event-related costs between: (1) patients who initiated and persisted on apixaban ('persistent users') following a bleed and (2) patients receiving apixaban who switched to rivaroxaban ('switchers') following a bleed.

Methods

Decision model framework

- The framework of the decision model is presented in **Figure 1**.
- The model assessed the incidence and cost of stroke/SE (composite of ischemic stroke, hemorrhagic stroke, and SE) and major bleeding (composite of gastrointestinal bleeding, intracranial hemorrhage, and other major bleeding).
- Outcomes were assessed under two scenarios: (1) 'Persistent users': patients who initiated and persisted on apixaban following a bleed, (2) 'Switchers': patients receiving apixaban who switched to rivaroxaban following a bleed.
- The model was developed over a one-year time horizon under the hypothetical one-million-member Medicare Fee For Service plan in the US.
- Incremental costs of clinical events were estimated by comparing the incidence and cost of stroke/SE and major bleeding between the two modelled scenarios. The difference between the 'switchers' and 'persistent users' scenarios represented the incremental cost.
- The target population for the 'persistent users' scenario was estimated using the US age distribution, age-specific NVAF prevalence, OAC eligibility, apixaban market share and proportion of patients with a bleeding event on therapy,¹⁻⁵ while the 'switchers' scenario assumed the entire cohort transitioned to rivaroxaban.

Figure 1. Decision model framework



Abbreviations: NVAF - Nonvalvular atrial fibrillation; OAC - Oral anticoagulant
 *Patients initiated apixaban based on market share [1] Assumption; [2] Calculated based on the US age distribution of people aged 65 years and above² and age-specific prevalence of diagnosed NVAF reported by Turakhia et al. 2018³; [3] 94.23% of diagnosed NVAF patients are estimated to receive OAC therapy reported by Lip et al. 2010⁴; [4] Of those, 62.2% of patients receive apixaban according to market share data⁵; [5] Of those, 21.83% experience a bleeding event reported by Lip et al. 2026.¹

Methods (continued)

Clinical Parameters

- Clinical event incidence for the 'persistent users' and 'switchers' scenarios was sourced from a retrospective observational study using Optum de-identified Clinformatics® Data Mart, a US claims database containing medical and pharmacy claims data for more than 80 million individuals with commercial employer-sponsored insurance or Medicare Advantage insurance.
- Monthly clinical event probabilities were estimated for each scenario, assumed constant over the time horizon, and applied to the monthly target population (**Table 1**).
- Data informing the distribution of severity of clinical events were derived from the pivotal apixaban and rivaroxaban clinical trials and were specific to each treatment.⁶⁻⁸
 - Fatal ischemic stroke and hemorrhagic stroke event rates were calculated by subtracting the sum of mild, moderate, and severe event rates from 1.
 - Intracranial hemorrhage and other major bleeding fatality was assumed equal for rivaroxaban and apixaban, with no fatality assumed for gastrointestinal bleeding and SE.

Cost Parameters

- The model includes costs for clinical events (acute and long-term) and fatal events, reported in US dollars for the 2023 cost year (**Table 1**).
- Clinical event costs were sourced from published US cost databases (CMS.gov,⁹ Medical Expenditure Panel Survey,¹⁰ and HCUPnet¹¹).
- Acute costs were applied as one-off imipant costs for events, with stroke costs weighted by severity; long-term management costs were applied monthly for affected patients over the remaining time horizon.
- Fatal event costs were applied as one-off costs for patients experiencing fatal clinical events; fatal stroke events were assigned the same costs as severe acute events, while fatal bleeding events were assumed to have zero cost.

Table 1. Summary of Key Model Inputs and Sources

Input			
Target population, n*	10,268		
Clinical Event Incidence and HR**			
	Incidence Rate (per 100 person years) in 'Persistent users'	Incidence Rate (per 100 person years) in 'Switchers'	HR for 'Switchers' vs. 'Persistent users' (95% CI)
Strokes			
Ischemic Stroke	0.94	1.18	1.26 (0.43-3.74)
Hemorrhagic Stroke	0.21	0.89	4.10 (0.92-18.35)
SE	0.00	0.00	0.00 (0.00-0.00)
Major Bleeding			
Gastrointestinal Bleeding	3.09	3.71	1.17 (0.63-2.18)
Intracranial Hemorrhage	0.75	1.24	1.56 (0.51-4.74)
Other Major Bleeding	1.86	4.95	2.48 (1.37-4.49)
Clinical Event Costs (2023 USD)			
	Acute [†] (one-off)	Long-term [‡] (per month)	Fatal event costs
Ischemic stroke			
Mild	\$10,845		
Moderate	\$13,151	\$492	\$20,116*
Severe	\$20,116		
Hemorrhagic Stroke			
Mild	\$4,791		
Moderate	\$6,972	\$492	\$13,527*
Severe	\$13,527		
Systemic Embolism			
	\$8,155	\$390	--
Gastrointestinal Bleeding			
	\$8,668	\$358	\$0
Intracranial Hemorrhage			
	\$9,295	\$492	\$0
Other Major Bleeding			
	\$11,687	\$390	\$0

Abbreviations: CI - confidence interval; HR - hazard ratio; USD - United States dollar
 *Calculated using Lip et al. 2026,¹ Tarazi et al. 2022,² Turakhia et al. 2018,³ Lip et al. 2010,⁴ Symphony Health 2023⁵; **Sources: Lip et al. 2026¹; [†]Sources: CMS.gov⁹; [‡]Sources: AHRQ MEPS¹⁰; ±Assumption: Assumed the same as severe acute costs.

Results

Base case

- After applying the eligibility criteria, 10,268 patients with prevalent NVAF who experienced a bleeding event while on apixaban therapy were identified.
- Over a one-year time horizon, switching these patients from apixaban to rivaroxaban was associated with an additional 127 stroke [25 ischemic strokes, 70 hemorrhagic strokes and 32 associated deaths], 443 MB [63 gastrointestinal bleeding, 50 intracranial hemorrhage, 316 major bleeding events and 13 associated deaths] events (**Table 2**).
- The additional clinical events associated with switching from apixaban to rivaroxaban resulted in a total incremental cost of \$6,929,447 (**Table 3**). At a per-member/patient level, the incremental clinical event costs translate to:
 - \$0.58 per member per month and \$56.24 per patient per month (**Table 3**).

Scenario analysis

- Impact of alternative inputs/assumptions were tested via scenario analyses (**Figure 2**).
- Across majority of scenarios, except for scenario 5, persistent use of apixaban was more favorable over switching patients to rivaroxaban.
- Scenario 5 in **Figure 2** presents the monthly events rates for the 'switchers' using a hazard ratio lower bound (95% CI) instead of the incidence rate used in the base-case analysis. Scenario results did not favor persistent apixaban use and indicated that switching to rivaroxaban resulted in cost savings associated with clinical events.
 - Scenario 5 and 6 should be interpreted with caution due to the wide confidence intervals observed for stroke/SE and MB component outcomes in Lip *et al.* (2026) resulting from a low sample size.¹
- Scenario 7 in **Figure 2** presents the comparison between patients who persisted on rivaroxaban versus patients who were switched to apixaban from rivaroxaban, using the same clinical data source as the base-case analysis. Results indicated that switching to apixaban resulted in cost savings associated with clinical events.

Table 2. Model results: clinical events over 1 year timeframe[†]

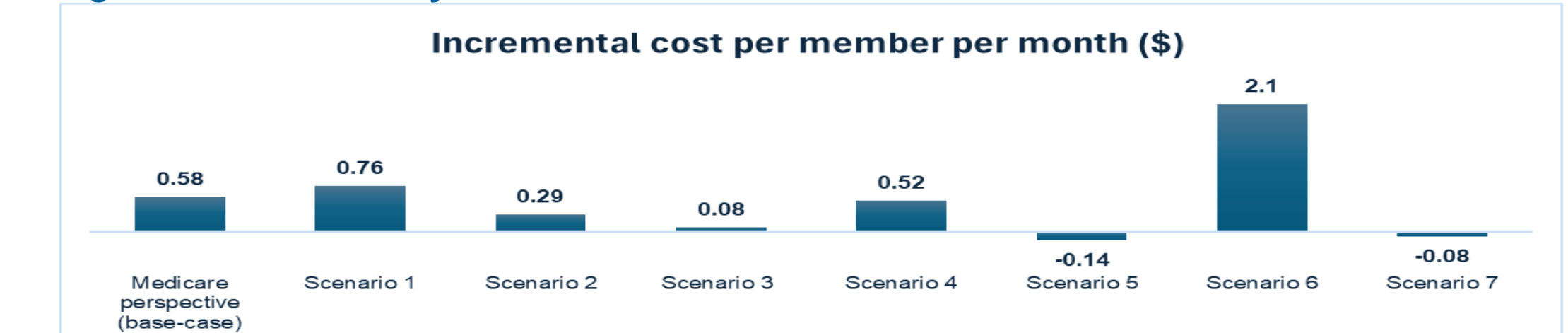
	'Persistent users' Scenario	'Switchers' Scenario	Difference‡ ('Switchers' minus 'Persistent users')
Number of eligible patients	10,268	10,268	-
Total number of clinical events	741	1,311	570
Stroke/Systemic embolism	118	212	94
Ischemic Stroke	96	121	25
Hemorrhagic Stroke	22	91	70
SE	0	0	0
Major Bleeding	585	1,015	430
Gastrointestinal Bleeding	317	380	63
Intracranial Hemorrhage	77	127	50
Other Major Bleeding	191	507	316
Deaths	39	84	45
Death from Ischemic Stroke	17	33	15
Death from Hemorrhagic Stroke	8	25	17
Death from Major Bleeding	14	27	13

Table 3. Model results: costs (\$) over 1 year timeframe

	8,945,197	15,874,645	6,929,447
Total Clinical Event Costs (\$)	8,945,197	15,874,645	6,929,447
Stroke/SE Cost	1,375,097	1,975,556	600,460
Major Bleeding Cost	7,118,667	12,907,685	5,789,018
Fatal Event Costs	451,433	991,403	539,970
Incremental Outcomes			
Total Cost per Patient per Month*		56.24	
Total Cost per Member per Month**		0.58	

Abbreviations: SE - Stroke/systemic embolism
 †Note: Cumulative totals may not equal the sum of components due to rounding. ‡Positive values favor the strategy of persistent apixaban use over switching these patients to rivaroxaban. *Calculated by dividing the total incremental clinical event costs per month by the number of NVAF patient eligible for treatment (10,268); **Calculated by dividing the total incremental clinical event costs per month by health plan members (1 million).

Figure 2. Scenario analysis results



Scenario 1: Time horizon 3 year (base case 1 year); Scenario 2: 50% switch to rivaroxaban (base case 100% switch); Scenario 3: Commercial perspective (base case Medicare perspective); Scenario 4: 'switcher' cohort event rates using hazard ratio (base case using incidence rate); Scenario 5: 'switcher' cohort event rates using hazard ratio lower bound (base case using incidence rate); Scenario 6: 'switcher' cohort event rates using hazard ratio upper bound (base case using incidence rate); Scenario 7: Rivaroxaban 'persistent user' vs 'switcher' to apixaban (base case apixaban 'persistent user' vs 'switcher' to rivaroxaban)

Conclusions

- The decision model suggested that switching from apixaban to rivaroxaban after a bleeding event in patients with NVAF was associated with an increase in clinical event-related costs compared with persisting on apixaban, driven primarily by the increased risk of MB.
- Across majority of scenarios comparing apixaban 'persistent users' and 'switchers', this conclusion was consistent.

Limitations

- The conclusions drawn from this model are subject to uncertainty, as over the time horizon, clinical event history was not tracked.
- The incidence rates and hazard ratios used in this analysis were not generated exclusively from a Medicare Fee for Service population, but instead from individuals insured through commercial employer-sponsored plans and Medicare Advantage.
 - The generalizability of the findings to patients with other types of insurance, no insurance, or those outside of the United States remains uncertain.

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Disclosures

This study was sponsored by the Bristol Myers Squibb/Pfizer Alliance. RS and TO are employees of Pfizer. RS is a shareholder of Pfizer. SCB and AM are employees of FIECON Ltd, who were paid consultants to BMS and Pfizer in connection with the conduct of this analysis.