An Economic Model Exploring the Impact of Formulary Restrictions on the Incidence and Cost of Clinical Events in Patients with Non-Valvular Atrial Fibrillation Receiving Direct Oral Anticoagulants in the United States

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Introduction

- To control healthcare expenditure and minimize unnecessary drug use, health plans often regulate prescriptions using utilization management strategies, such as prior authorization (PA; approval for a treatment prior to prescribing) or step therapy (ST; patients must fail cheaper alternatives first).
- However, these strategies can delay access to treatment, reduce patient compliance, and incentivize use of cheaper treatments regardless of safety and efficacy profiles.[1-3]
- Direct-acting oral anticoagulants (DOACs) are recommended to reduce risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF) and are among the most widely used medications by Medicare patients,[4] however, patient access is often subject to formulary restrictions including PA or ST.
- Furthermore, analyses by Zhou et al.[2] indicate that Medicare patients with AF on restricted plans (PA or ST required for all DOACs) had reduced DOAC usage (30.2% versus 32.2%), lower medication adherence (32.1% versus 34.3%) and an increased risk of adverse clinical outcomes compared with unrestricted access plans (≥ 1 DOACs available without PA or ST).

Objective

- This study aimed to evaluate the potential impact of restricted (PA or ST required for all DOACs) versus unrestricted (≥ 1 DOACs available without PA or ST) access to DOACs on the incidence and cost of clinical events in patients with NVAF from the US Medicare perspective, based on data from Zhou et al.[2]

Methods

Model structure

- A decision analytic model was developed to assess the incidence and cost of stroke, major bleeding (MB), transient ischemic attack (TIA) and all-cause mortality (ACM) in adult patients with NVAF with and without formulary restrictions for DOACs over a one-year time horizon.
- The model compared two cohorts: 1) patients who initiated on treatment with "unrestricted access", where ≥ 1 DOACs were available without PA or ST; and 2) patients who initiated on treatment with "restricted access", where all DOACs required PA or ST, based on Zhou et al.[2]

Model inputs

- The target population was derived based on a hypothetical cohort of 1,000,000 US Medicare Fee-For-Service plan members; epidemiology inputs and market share estimates were applied to determine the treatment-eligible population.[5-7] The treatment-eligible population comprised the starting population for both the "unrestricted access" and "restricted access" cohorts.
- Incidence rates and hazard ratios (HRs) for clinical events were derived from a published longitudinal cohort study (**Table 1**),[2] and were used to calculate clinical event probabilities and the number of expected clinical events for each cohort.
- Costs for clinical events were sourced from a published cost-consequence analysis[8] based on Medicare-specific databases in the US (CMS.gov[9] and AHRQ[10]) and a published analysis of Medicare end of life costs.[11] Costs were inflated to 2024 US dollars using the consumer price index.[12]
- For individuals experiencing a clinical event, a one-off event-specific acute management cost was applied at the time of event occurrence. For stroke and MB events, an additional monthly event-specific long-term management cost was applied from the time of event occurrence until the end of the model time horizon (**Table 1**).
- The potential impact of formulary restrictions was quantified using the difference in events and costs between the "unrestricted access" and "restricted access" cohorts.

Table 1. Summary of model inputs

Parameter	UNRESTRICTED ACCESS Incidence rate* per 100 PYs	RESTRICTED ACCESS HR (95% CI)	ACUTE COST US$ per event	LONG-TERM MONTHLY COST US$ per event
Ischemic stroke	0.67	1.082 (1.026–1.142)	$15,215.56	$509.03
Hemorrhagic stroke	0.27	1.109 (1.020–1.206)	$8,723.37	$509.03
Transient ischemic attack	0.78	1.081 (1.028–1.136)	$5,285.34	$0.00
Gastrointestinal bleeding	1.99	1.030 (0.994–1.068)	$8,969.29	$370.64
Intracranial hemorrhage	0.29	1.103 (1.011–1.203)	$9,617.96	$509.03
All-cause mortality	5.81	1.115 (1.095–1.137)	$13,556.57	$0.00

Abbreviations: CI, confidence interval; HR, hazard ratio; PY, person-years
*Incidence rates were calculated based on the percentage of patients experiencing each clinical event during the observation time (5.92 years) in Zhou et al.[2]

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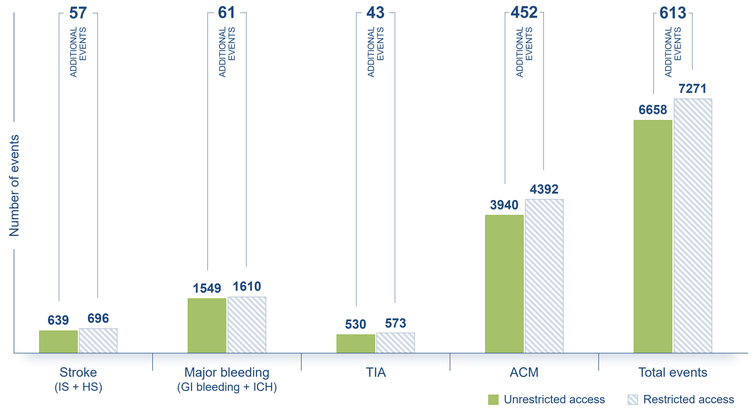
Results

- Of 1,000,000 Medicare members, 67,984 patients were estimated to have prevalent NVAF and receiving DOAC treatment.
- Over the one-year time horizon, the "restricted access" cohort accrued an additional 613 clinical events (including 57 strokes, 61 MBs, 43 TIAs, and 452 ACM [**Figure 1**]) resulting in associated annual incremental clinical costs of $8,008,860 ($9.82 per NVAF patient/month; $0.67 per member/month) versus the "unrestricted access" cohort (**Table 2**), where the higher incidence of ACM in patients with restricted access was a key driver of these costs.

Figure 1. Total number of clinical events for "unrestricted access" and "restricted access" cohorts over a one-year time horizon



Abbreviations: ACM, all-cause mortality; GI, gastrointestinal; HS, hemorrhagic stroke; ICH, intracranial hemorrhage; IS, ischemic stroke; TIA, transient ischemic attack

Table 2. Cost outcomes for "unrestricted access" and "restricted access" cohorts over a one-year time horizon for the US Medicare perspective

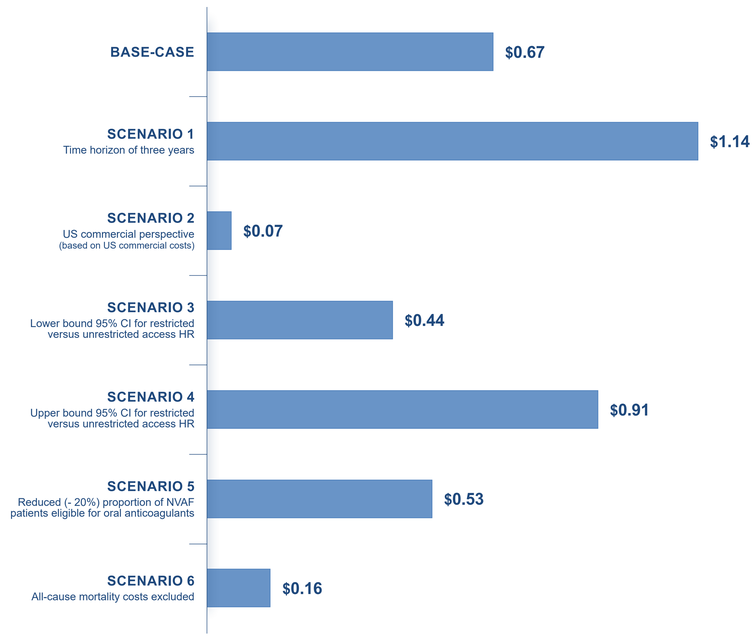
Parameter	UNRESTRICTED ACCESS	RESTRICTED ACCESS	INCREMENTAL†
Ischemic stroke	$8,435,250	$9,126,732	$691,482
Hemorrhagic stroke	$2,208,303	$2,448,978	$240,675
Transient ischemic attack	$2,801,754	$3,028,617	$226,862
Gastrointestinal bleeding	$15,380,831	$15,841,862	$461,031
Intracranial hemorrhage	$2,548,211	$2,810,641	$262,431
All-cause mortality	$53,416,901	$59,543,280	$6,126,379
TOTAL COSTS	**$84,791,251**	**$92,800,110**	**$8,008,860**
TOTAL INCREMENTAL COST per patient‡ per year			$117.81
TOTAL INCREMENTAL COST per patient‡ per month			$9.82
TOTAL INCREMENTAL COST per member* per year			$8.01
TOTAL INCREMENTAL COST per member* per month			$0.67

†Difference between restricted and unrestricted access cohorts.
‡Incremental costs divided by the number of patients (N = 67,984).
*Incremental costs divided by population size (N = 1,000,000).

Scenario analyses

- Scenario analyses were conducted to test the impact of alternative input values and assumptions on the model outcomes. The scenarios and results are demonstrated in **Figure 2**.
- In line with base case analysis, patients with NVAF with unrestricted access to DOACs had more favourable cost outcomes compared with the "restricted access" cohort across all scenarios tested.

Figure 2. Scenario analysis results (Incremental cost per member per month)



Limitations

- It was assumed that clinical event rates were consistent over the entirety of the time horizon.
- This cost-consequence analysis only considered clinical event-management costs and did not account for the wider economic benefits and implications of formulary restrictions.

Conclusions

PA and ST are commonly used by health plans to lower prescription drug spending and to reduce unnecessary drug use. However, in practice, enacting such restrictions (PA or ST) may have a negative impact on the incidence and cost of clinical events in some patient groups.

Results from the current study estimate that restricting access to DOACs in patients with NVAF may lead to an increased number of adverse clinical outcomes and higher associated costs for US Medicare payers. Results of scenario analyses were consistent with base case analysis, suggesting robustness of findings.

Clinically guided prescribing and ensuring that patients have **unfettered access** to their prescribed DOAC is **essential for optimizing clinical outcomes** and **improving healthcare efficiency**.

Disclosures

This study was sponsored by Pfizer and Bristol Myers Squibb.

RS, EV and SD are employees and shareholders of Pfizer. CD and ES are employees of Health Economics and Outcomes Research limited who received consulting fees from Pfizer in relation to the conduct of this study.

References

1. Happe LE, et al. J Manag Care Spec Pharm. 2014; 120(7): 677-84.
2. Zhou B, et al. Am J Manag Care. 2022; 28(10):521-528.
3. Park Y, et al. J Manag Care Spec Pharm. 2017; 23(8): 893-901.
4. Centers for Medicare and Medicaid Services. Medicare Drug Price Negotiation Program: Selected Drugs for Initial Price Applicability Year 2026.
5. Turakhia MP, et al. PLoS One. 2018; 13(4): e0195088.
6. Lip GY, et al. Stroke. 2010; 41(12): 2731-8.
7. IQVIA Pharmascope data.
8. Subash R, et al. J. Med. Econ. 2025;28(1), 224–234
9. Centers for Medicare and Medicaid Services. Acute Inpatient PPS.
10. Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey (MEPS) Household Component (HC)
11. Duncan I, et al. Am J Hosp Palliat Care. 2019;36(8):705-10.
12. Destatis Statistisches Bundesamt. Consumer price index and inflation rate.