**Spotlight**

**Novel Anticoagulants Achieve Rapid Market Penetration despite Higher Costs**

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**Background**

Stroke is a leading cause of disability in the United States—and the fifth leading cause of death.¹ Patients with atrial fibrillation are five times more likely to suffer a stroke and may be prescribed anticoagulants to reduce this elevated risk. These medications prevent blood clots from forming when irregular heart rhythms caused by atrial fibrillation allow blood to pool in the heart.²

Warfarin, an oral anticoagulant that was originally approved in 1954 and is widely available in generic form, was previously the standard treatment for stroke prevention in patients with atrial fibrillation.³,⁴ Warfarin requires frequent monitoring and dose adjustments to address risks of uncontrolled bleeding events; it also carries multiple drug and diet interactions that may increase risk of side effects or decrease therapeutic effectiveness for some users.⁵

In October 2010, novel oral anticoagulants (NOACs) began entering the market as an alternative to warfarin for patients with nonvalvular atrial fibrillation. NOACs have a different mechanism of action and do not require frequent monitoring or dose adjustments. Notably, the products were also priced substantially higher than existing therapies.⁶

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¹ Catherine Gillespie is now with IHME Client Services.

**Trends in Utilization of Warfarin and NOACs by Privately Insured Patients with Atrial Fibrillation**

Our study included commercially insured adults ages 50 to 64 and Medicare Advantage enrollees ages 65 and older with atrial fibrillation who filled a new prescription for an oral anticoagulant between 2010 and 2014, a period that includes the final nine months before NOACs began entering the market. Three NOACs entered the market during the study period: dabigatran (10/19/2010; sold as Pradaxa),⁶
rivaroxaban (11/04/2011; sold as Xarelto), and apixaban (12/28/2012; sold as Eliquis).

During the first three quarters in our study period (i.e., before NOACs began to enter the market), all index fills were for warfarin. Over the study period, NOACs became more popular than warfarin, particularly among younger adults in our study cohort (figure 1). By the end of 2014, NOACs accounted for 79 percent of index fills for adults ages 50 to 64 on commercial plans and 47 percent of index fills for Medicare Advantage enrollees ages 65 and older.

**Trends in Total Annual per Capita Spending on Oral Anticoagulants Following the Introduction of NOACs**

Following the introduction of NOACs to the marketplace, total annual per capita spending (i.e., out-of-pocket and plan paid amounts) on oral anticoagulants among newly treated atrial fibrillation patients increased dramatically—growing from a couple hundred dollars per year to several thousand dollars per year for some patients.

These observed increases in total annual per capita spending (figure 2) were greater for adults ages 50 to 64 on commercial plans (increasing from $157 to $2,237 per year, a 14-fold increase) than for Medicare Advantage enrollees ages 65 and older (increasing from $133 to $1,593 per year, a 12-fold increase).

**Trends in Annual per Capita Spending on NOACs and Warfarin among Privately Insured Patients with Atrial Fibrillation**

Total annual per capita spending on NOACs was considerably higher than total annual per capita spending on warfarin. This difference also increased over time: per capita spending on NOACs was more than 17 times greater than per capita spending on warfarin when NOACs first entered the market—and grew to more than 25 times greater than spending on warfarin by the end of the study period.

![FIGURE 1](image.png)

**NOAC Utilization Increased Rapidly among Atrial Fibrillation Patients between 2010 and 2014**

Note: MA = Medicare Advantage; COM = commercial insurance.
These findings were partially driven by reductions in total annual spending per patient for warfarin, which fell over the study period from $209 to $162 among enrollees ages 50 to 64 on commercial plans and from $188 to $145 among Medicare Advantage enrollees ages 65 and older.

Meanwhile, total annual spending per patient for NOACs increased considerably between 2010 and 2014: from $3,103 to $4,142 for commercial enrollees and from $3,048 to $3,894 for Medicare Advantage enrollees (figure 3).

**Trends in Enrollee and Health Plan Spending on Oral Anticoagulants Following the Introduction of NOACs**

Over the study period, annual out-of-pocket spending on oral anticoagulants approximately tripled for commercial enrollees ages 50 to 64 and quintupled for Medicare Advantage enrollees ages 65 and older. This increase translated into an added out-of-pocket burden of approximately $300 to $400 per year for patients who were adherent to their anticoagulant treatment.

These out-of-pocket spending increases, while substantial, were dwarfed by the increases in annual plan spending on oral anticoagulants. Among adherent adults ages 50 to 64 on commercial plans, plan spending grew from $106 per patient per year to $2,784 per patient per year (figure 4). This represents a jump from 43 percent of the total cost of treatment to 86 percent of the total cost.

Among adherent Medicare Advantage enrollees ages 65 and older, plan spending grew from $104 per patient per year to $1,572 per patient per year—a jump from 53 percent of the total cost to 75 percent of the total cost.

**Trends in Oral Anticoagulant Utilization and Spending Following the Introduction of NOACs**

By the end of 2014, just four years after the first NOAC received FDA approval to be marketed in the United States for the prevention of stroke among patients with nonvalvular atrial fibrillation, approximately 60 percent of patients taking daily oral anticoagulants for this purpose were using this new drug class. Spending on NOACs accounted for 91 percent of all spending on oral anticoagulants in our study cohort of older adults with atrial fibrillation (figure 5).
FIGURE 3.
Total Annual per Capita Spending on NOACs Was Considerably Higher than Spending on Warfarin throughout the Study Period

Note: MA = Medicare Advantage; COM = commercial insurance.

FIGURE 4.
The Share of Total Annual Spending on Anticoagulants Paid by Health Plans Increased Dramatically Following Introduction of NOACs to the Marketplace
Conclusion

Novel oral anticoagulants—a new therapeutic option for stroke prevention among patients with nonvalvular atrial fibrillation—rapidly penetrated the market following FDA approval and led to dramatic increases in spending on anticoagulant therapy. Our results found that health plans paid a disproportionately large share of the additional expense for NOACs during our study period, leading to dramatic increases in plan spending on anticoagulant therapy.9,10 By the end of our study period, health plans were spending 15 to 25 times more per patient per year on anticoagulants than they were before NOACs entered the market. Higher plan spending is typically passed on to consumers via higher premiums, higher deductibles, or higher out-of-pocket expenses for other products and services11; however, the extent to which this burden was passed on to consumers could not be discerned from these data. Notably, it was not until the most recent update to the atrial fibrillation treatment guidelines, published in July 2019, that sufficient evidence had accumulated to explicitly recommend use of NOACs as the preferred alternative to warfarin for reducing stroke risk for eligible patients with nonvalvular atrial fibrillation.12 Nevertheless, our analysis of real-world prescribing data indicates that NOACs became the most popular treatment choice for privately insured patients as early as 2011.

Meanwhile, the patents for Pradaxa, Eliquis, and Xarelto are expected to expire in the next several years. Assuming generic competitors enter the market, the widespread availability of generic NOACs will almost certainly lead to cost savings for both patients and health plans—and likely lead to the next notable shift in this evolving market.
Methodology

- Findings summarized in this Spotlight are based on a retrospective longitudinal analysis of de-identified insurance claims from the OptumLabs Data Warehouse.  

- The study population consisted of privately insured enrollees ages 50 and older with a minimum of three years of continuous enrollment with primary medical and prescription drug coverage. All enrollees had evidence of atrial fibrillation, identified using a claims-based algorithm developed by the Centers for Medicare and Medicaid Services, and initiated daily treatment with an oral anticoagulant (warfarin or NOACs) between January 1, 2010, and December 31, 2014.

- Approximately 19 percent of otherwise eligible study subjects were excluded from the analytic sample due to (a) a potential indication for short-term anticoagulation (i.e., presence of procedure or diagnosis codes for cardiac surgery, myocarditis, pericarditis, or pulmonary embolism) on any claims in the 3 months prior to index date (17.2 percent); (b) evidence of hyperthyroidism on any claims in the 12 months prior to the index date (2.2 percent); or (c) inability to determine index regimen due to fills for both warfarin and NOACs on the index date (0.03 percent).

- A total of 35,982 enrollees satisfied all eligibility requirements; enrollees ages 65 and older on commercial plans (N = 1,251) and enrollees ages 50 to 64 on Medicare Advantage plans (N = 1,259) were excluded from the primary analyses presented here. Of the remaining 33,472 enrollees, 22.2 percent were ages 50 to 64 on commercial plans (N = 7,420), and 77.8 percent were ages 65 and older on Medicare Advantage plans (N = 26,052).

- We used pharmacy claims to examine utilization of and spending on oral anticoagulants by atrial fibrillation patients (stratified into two categories: warfarin [4,327 unique NDCs] or NOACs [214 unique NDCs]) during the first 12 months after treatment initiation. The three FDA-approved NOACs that entered the market during the study period were dabigatran (10/19/2010; sold as Pradaxa), rivaroxaban (11/04/2011; sold as Xarelto), and apixaban (12/28/2012; sold as Eliquis). Although we did not distinguish between these products in our analysis, prior research has shown that rivaroxaban and apixaban eclipsed use of dabigatran and would have accounted for the overwhelming majority of all NOAC prescriptions by the end of our study period.

- To control for inflation and to minimize the impact of extreme outliers, all spending amounts were inflation-adjusted to 2016 dollars using the Medical Care component of the Consumer Price Index for All Urban Consumers, and the top 1 percent of spending amounts were winsorized.

- All analyses were stratified by age group and insurance type.


