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# Healthcare Utilization and Expenditures in Working-Age Adults with Atrial Fibrillation: The Effect of Switching from Warfarin to Non-Vitamin K Oral Anticoagulants

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## Abstract

**Objective—**Our objective was to evaluate the association between switching from warfarin to non-vitamin K oral anticoagulants (NOACs) and potential drug–drug interactions (DDIs), healthcare utilization, and expenditures in working-age adults with atrial fibrillation (AF).

**Methods—**We conducted a retrospective cohort study using data from 2010 to 2015 for patients who switched from warfarin to NOACs (switchers) and those who continued to receive warfarin (non-switchers). We identified medications known or suspected to have clinically significant interactions with NOACs or warfarin. We used multivariate logistic regression, negative binomial, and generalized linear models to evaluate the influence of switching to NOACs and of potential DDIs on inpatient visits, outpatient visits, number of outpatient visits, and non-drug medical expenditures. Inverse probability of treatment weighting was also applied in analyses.

**Results—**A total of 4126 patients with AF were included in the study. Switching to NOACs was significantly and negatively related to the number of outpatient, inpatient, and emergency room (ER) visits and non-drug medical expenditures. When potential DDIs were included in the models, switching remained significantly associated only with reduced inpatient and outpatient visits. Notably, having at least one potential DDI was associated with an increased likelihood of ER visits and the number of outpatient visits; it was also significantly and positively associated with non-drug medical expenditures.

**Conclusions—**Relative to persistent warfarin use, switching to NOACs was associated with fewer inpatient, ER, and outpatient visits and lower non-drug costs. Potential DDIs were also

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strongly and positively associated with healthcare utilization and expenditures. Both are critical to consider in the management of AF in working-age adults.

## 1 Introduction

In the USA, atrial fibrillation (AF) costs about $US6 million annually [1], with medical costs averaging $US3260 higher in working-age adults with vs. without AF [2]. Patients with AF are also at increased risk for severe stroke, which can, in turn, lead to additional healthcare expenses [3]. It is thus recommended that patients with AF at high risk for ischemic stroke and other thromboembolism events receive oral anticoagulants [4], including vitamin K antagonists (VKAs) (e.g., warfarin) and nonvitamin K oral anticoagulants (NOACs) (i.e., dabigatran, rivaroxaban, apixaban, and edoxaban).

Recent cost-effectiveness studies favored the use of apixaban and dabigatran 150 mg over warfarin. The incremental cost-effectiveness ratio was €12,227 per quality-adjusted life-year (QALY) for apixaban vs. warfarin [5] and $US20,797/QALY for dabigatran 150 mg vs. warfarin [6]. These studies used data from clinical trials and only included costs associated with drugs, international normalized ratio (INR) monitoring for warfarin, routine care for NOACs, or certain health conditions. However, in real-world settings, lower or comparable healthcare expenditure and/or healthcare utilization has been reported for NOAC users compared with warfarin users [7–10]. A 2017 study of elderly patients with AF in the USA found that apixaban users had fewer inpatient and outpatient visits and lower all-cause healthcare costs than warfarin users [10]. Similar findings were observed in another recent study of patients with AF in the USA between patients initiated on dabigatran and warfarin [11]. However, nonsignificant findings in a Medicare population were also reported between dabigatran and warfarin users regarding inpatient and outpatient visits and medical costs and total all-cause costs [7].

Previous studies comparing healthcare utilization and expenditure between warfarin and dabigatran users have been limited to elderly patients or patients naïve to oral anticoagulants. In addition, although, unlike warfarin, NOACs do not require routine coagulation monitoring, whether switching from warfarin to NOACs is associated with healthcare utilization, direct medical costs, and indirect costs such as productivity loss, particularly for working-age adults with AF, remains unknown. NOACs have also been associated with fewer drug–drug interactions (DDIs) and drug–food interactions than warfarin [12]. This reduction in DDIs when switching from warfarin to NOACs may lead to fewer adverse drug events and therefore lower healthcare utilization and expenditure. However, the influence of DDIs has rarely been incorporated into analyses comparing healthcare utilization and expenditure associated with NOACs vs. VKAs.

To our knowledge, no published population-based studies have investigated the healthcare utilization and expenditure of working-age patients with AF who switch from warfarin to NOACs compared with those of patients who continue to receive warfarin. Moreover, research on the economic burden of potential DDIs with oral anticoagulants has been limited. Therefore, the purpose of this study was to evaluate the influence of switching from

warfarin to NOACs on healthcare utilization and expenditure in working age adults with AF, while considering exposure to potential DDIs and other factors.

# 2 Methods

## 2.1 Study Design

We conducted a retrospective cohort study using data from an adjudicated claims database of commercially insured individuals from 2010 to 2015. We used Andersen's behavioral model for health service use to guide our study design and select the variables [13]. The index date was defined as the date of first observed warfarin or NOAC prescription between 2011 and 2014, the baseline period was defined as 6 months before the index date, and the follow-up period was defined as 1 year after the index date.

## 2.2 Data Source

The database includes medical, pharmacy, and enrollment data. The population is similar in age and sex to the US commercially insured census population for individuals aged < 65 years. These data are made available through a license to IQVIA's Real World Data: Adjudicated Claims—US (also known as PharMetrics Plus), 10% sample January 2006–December 2015.

## 2.3 Inclusion and Exclusion Criteria

We included patients who (1) had a first observed oral anticoagulant prescription between January 2010 and December 2014; (2) had an International Classification of Diseases and Related Health Problems, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code of AF (427.31); (3) were continuously enrolled in health plans 6 months before and 1 year after the index date; and (4) were aged 18–63 years at the index date (or 18–64 during the study period). We excluded patients who had switched more than once. Figure 1 details the steps taken to obtain the final cohort.

## 2.4 Measures

### 2.4.1 Dependent Variables

**2.4.1.1 Healthcare Utilization and Expenditures:** We calculated the number of inpatient, outpatient, and emergency room (ER) visits during the 1-year follow-up period. Non-drug medical expenditures were assessed by summing the expenditure from inpatient and outpatient services, surgery, and ER visits for each eligible patient with AF during the 1-year follow-up period.

### 2.4.2 Independent Variables

**2.4.2.1 Switching to Non-Vitamin K Oral Anticoagulants:** We classified patients who switched from warfarin to NOACs as 'switchers'. We required the switcher to have at least one warfarin prescription at baseline but no prescription of warfarin during follow-up. Patients who received only warfarin and no NOAC prescription during the entire study period were referred to as 'non-switchers'. We identified medications using generic names and national drug codes in the pharmacy claims.

**2.4.2.2 Exposure to Potential Drug–Drug Interactions:** All DDI variables were measured during the 1-year follow-up period. We assessed whether patients encountered any potential DDI with oral anticoagulants (yes/no). We identified medications that may interact with NOACs for switchers or with warfarin for non-switchers, according to the list provided by IBM Micromedex® Drug Interaction Checking [14]. We included contraindications and major DDIs for warfarin (e.g., simvastatin, tamoxifen, clarithromycin) and for NOACs (e.g., itraconazole for dabigatran, clarithromycin for rivaroxaban, and vortioxetine for apixaban). We required the DDI to have at least a 1-day overlap between the drugs. Additionally, for the secondary analyses, we calculated the number of DDIs by using the highest observed number of potential DDIs in a single day based on prescription claims. We also calculated the duration of exposure to DDIs by dividing the number of days with potential DDIs by the number of days of follow-up period. We assumed that patients finished all the prescribed medications before the date of refill.

**2.4.2.3 Other Independent Variables:** Other independent variables included sex, age, region (east, mid-west, south, and west), type of healthcare insurance (health maintenance organization, preferred provider organization, other), baseline stroke/transient ischemic attack (TIA), cardioembolic complications (ischemic stroke, TIA, systemic embolism, and myocardial infarction), major bleeding events, renal failure, liver diseases, and $CHA_2DS_2$-VASc scores, as well as the number of chronic conditions (arthritis, asthma, cancer, chronic obstructive pulmonary disease, dementia, depression, hyperlipidemia, hepatitis, HIV, osteoporosis, schizophrenia, and substance abuse disorders) in the baseline and follow-up periods [15]. All chronic conditions were identified using ICD-9-CM diagnosis codes.

## 2.5 Statistical Analyses

We conducted descriptive analyses for patient characteristics, clinical profiles, health utilization, and economic outcomes. We performed chi-square tests, two sample *t* tests, or Wilcoxon rank-sum tests, and Pearson's correlation coefficients to assess bivariate relationships between outcome variables and independent variables. Multivariate logistic regression models were used to examine how switching and exposure to potential DDIs were associated with the likelihood of inpatient visits and ER visits. Negative binomial models were utilized to evaluate the impact on the number of outpatient visits. Because of the skewed distribution of the costs data, we used generalized linear models (GLMs) with the log-link function and gamma distribution to analyze the associations between potential DDIs, switching to NOACs, and non-drug medical expenditures in the follow-up period. We also applied recycled predictions to estimate the absolute expenditure differences between switchers and non-switchers and differences between patients with AF with and without potential DDIs. To reduce the observed selection bias between switchers and non-switchers (see Table 1 in the Electronic Supplementary Material [ESM] for the differences in baseline characteristics between switchers and non-switchers), we derived inverse probability of treatment weights (IPTW) by conducting a logistic regression on switcher vs. non-switcher with baseline characteristics, including region, insurance type, having renal disease, having liver disease, having prior major bleeding, $CHA_2DS_2$-VASc scores, and number of chronic conditions. The IPTWs were used as weights in all multivariate analyses. We used SAS 9.4

(SAS Institute Inc., Cary, NC, USA), Stata 14 (Stata Corp, College Station, TX, USA), and R programming language (version 3.3.3; R Foundation, Vienna, Austria) for the analyses.

## 3 Results

A total of 4126 patients with AF were included in this cohort. Over 70% of the patients were male, and 67.4% lived in south or mid-west USA (Table 1). The median age was 58 years [interquartile range (IQR) 52–61]. The majority of patients (88.3%) were non-switchers during our study period. For the 1-year follow-up period, the prevalence of DDIs for all patients were 74.2% (43.0 and 78.3% for switchers and non-switchers, respectively). The average 1-year proportion of days with potential DDIs was 26% (Table 1). In the 1-year follow-up, 34.4% of patients with AF had at least one inpatient visit, and 34.5% had at least one ER visit. The average (± standard deviation) number of outpatient visits was 31.8 ± 26.2. The average non-drug medical expenditure was $US25,401.57 ± 61,499.09.

### 3.1 Healthcare Utilization

In the bivariate associations during the 1-year follow-up period, both not switching to NOACs and potential DDIs were positively associated with inpatient and ER visits and the number of outpatient visits: inpatient visits 22.7% vs. 35.9% ($p < 0.0001$), ER visits 29.3% vs. 35.2% ($p = 0.01$), number of outpatient visits 20.5 ± 17.9 vs. 33.3 ± 26.7 ($p < 0.0001$) for switchers vs. non-switchers. Results for patients with and without potential DDIs were as follows: inpatient visits 39.2% vs. 20.5% ($p < 0.0001$), ER visits 38.5% vs. 23.1% ($p < 0.0001$), number of outpatient visits 35.3 ± 27.5 vs. 21.9 ± 18.5 ($p < 0.0001$).

In the multivariate analyses after adjustments (IPTW), switching to NOACs remained significantly and negatively associated with number of outpatient visits [incidence rate ratio (IRR) 0.61, 95% confidence interval (CI) 0.55–0.65], and with a decreased likelihood of one or more inpatient visits [adjusted odds ratio (AOR) 0.45; 95% CI 0.35–0.57] and ER visits [AOR 0.79; 95% CI 0.63–0.99] during the follow-up period. Inclusion of potential DDIs in the model substantially attenuated the association between switching and ER visits (AOR 0.90; 95% CI 0.71–1.15) but did not appreciably affect the association with inpatient and outpatient visits. In model 2, patients who encountered potential DDIs were more likely to make one or more ER visits (AOR 1.47; 95% CI 1.11–1.95) and more outpatient visits (IRR 1.25; 95% CI 1.15–1.35) but DDIs were not related to inpatient visits (AOR 1.29; 95% CI 0.98–1.69) (Table 2). In addition, both number and duration of potential DDIs were significantly and positively associated with all measures of healthcare utilization in the follow-up period (except for proportion of days with potential DDIs and ER visits, data not presented).

### 3.2 Healthcare Expenditures

The univariate analyses indicated that switchers had significantly lower non-drug medical expenditures than non-switchers ($US18,865.6 ± 36,397.5 vs. 26,264.1 ± 64,035.0; $p = 0.01$). Likewise, patients with potential DDIs also had higher non-drug medical expenditure than those without potential DDIs ($US29,574.4 ± 67,859.1 vs. 13,408.1 ± 35,007.8; $p < 0.0001$).

After adjustments with IPTW, switching to NOACs remained significantly and negatively associated with non-drug medical expenditures during the follow-up period (GLM model 1, Table 3). According to the results from recycled predictions, switchers averaged $US7851.8 lower non-drug medical expenditures (coefficient − 0.34; 95% CI − 0.52 to − 0.16; $p <$ 0.0001) than non-switchers (Table 3). Adding potential DDIs to the model (Table 3, model 2) substantially attenuated this association. Notably, concomitant use of medication with the potential for significant interactions with oral anticoagulants was associated with an average increase in non-drug costs of $US9044.8 (coefficient 0.39; 95% CI 0.17–0.61; $p < 0.0001$). Using the number of potential DDIs to assess potential DDI burden yielded comparable results (data not presented).

## 4 Discussion

To our knowledge, this is the first study to examine the impact of switching from warfarin to NOACs and of exposure to potential DDIs on healthcare utilization and economic outcomes in patients with AF. We developed novel methods to assess the intensity and duration of potential DDIs to evaluate the influence of DDI burden as a determinant factor in the relationships between switching to NOACs and healthcare utilization and expenditure. This study also used a database that offers healthcare information on a nationally representative, commercially insured, working-age (aged 18–64 years) US population. In this study, switching from warfarin to NOACs was associated with a reduced likelihood of inpatient and ER visits, fewer outpatient visits, and lower non-drug medical expenditures in the 1-year follow-up period. The significant associations remained for inpatient and outpatient visits but were substantially attenuated for ER visits and non-drug medical expenditures when the influence of exposure to DDIs was considered, suggesting that exposure to potential DDIs may mediate the association between switching and the latter outcomes. In addition, we found that having at least one potential DDI was significantly associated with more ER visits, number of outpatient visits, and higher non-drug medical expenditures. Furthermore, the number of potential DDIs was significantly and positively associated with all measures of healthcare utilization and with non-drug medical expenditure.

One of the major benefits of switching to NOACs for working-age adults is that routine blood monitoring is not required [16]. Accordingly, our findings indicated significantly fewer outpatient visits for switchers. Our results for this population of working-age adults with AF were consistent with those for patients with AF in the general or elderly population [7–11]. In addition, recently published studies reported fewer inpatient and ER visits with NOACs than with warfarin [7, 10], consistent with our results from the 1-year follow-up period. Furthermore, several studies have shown that medical or total all-cause costs for NOAC users were lower than or similar to those for patients remaining on warfarin [7–10]. In this investigation, switching to NOACs was significantly and negatively associated with non-drug medical expenditure in the 1-year follow-up period, an association largely explained by exposure to potential DDIs.

Of note, a large proportion (74.2%) of our sample were exposed to at least one potential DDI while receiving oral anticoagulants during the follow-up period, and the potential DDI exposure was significantly higher for non-switchers than for switchers (78 vs. 43%,

respectively). A higher DDI burden, as measured by the number of potential DDIs, were significantly associated with greater healthcare utilization and higher non-drug medical expenditure. These findings suggest that cumulative exposure to DDIs, especially the number of potential DDIs, is an important determinant of healthcare burden, whereas the duration of potential DDIs may mainly affect the inpatient and outpatient visits of working-age adults with AF. While the concomitant use of medications with the potential for DDIs may in part reflect comorbidity, disease severity, or other health events associated with high healthcare utilization and expenditures [17, 18], some of these factors may be unlikely to explain our findings. For example, adjustment for comorbid conditions in the model did not appreciably affect the relationship between exposure to potential DDIs and healthcare use and expenditure. Moreover, DDIs with oral anticoagulants can lead to a number of adverse events associated with increased healthcare utilization and costs. For example, initiating antimicrobial therapy in chronic warfarin users is associated with a twofold increase in bleeding events [18], leading to deterioration in patient health [12, 19] and possible increases in healthcare utilization and expenditures.

Finally, our findings highlight the importance of addressing potential DDIs in all patients with AF receiving oral anticoagulants. We recommend clinicians carefully consider potential DDIs when managing patients receiving warfarin or NOACs. Notably, it has been recommended that comprehensive information (e.g., prevalence and severity) on potentially serious DDIs be included in the development of clinical guidelines for the treatment of AF [20]. In support of this recommendation, a recent study showed a substantial reduction in bleeding events after comprehensive guidelines on managing significant DDIs with warfarin were incorporated [21]. Furthermore, given the high burden of chronic conditions and the elevated likelihood of concomitant medication use in many AF populations, collaborative disease management for patients with AF may be particularly important to optimize cost-effective treatment strategies. Unfortunately, few disease-specific guidelines currently consider likely comorbidity, drug–disease interactions, and DDIs [22–24]; clearly, more research is needed regarding the collaborative management of all these important issues.

This study has several limitations. First, potential DDIs were assessed using proxy measures based on prescription drug claims data, which may not accurately capture actual patient drug use. For example, because patients may have discontinued certain medications because of adverse effects or other factors, we may sometimes have overestimated the number of potential DDIs and proportion of days with potential DDIs. Moreover, our measures of DDI burden did not include moderate and minor DDIs that could increase the INR or risk of bleeding and, in turn, potentially lead to adverse effects and associated increases in healthcare utilization and expenditures. Second, our follow-up period was only 1 year, which limits conclusions regarding the possible effects of switching or potential DDIs on longer-term healthcare use and expenditures. Third, we only included direct medical expenditures covered by third-party payers, which likely influenced the overall costs associated with both switching and DDI burden. For example, as mentioned, switching to NOACs may result in significant reductions of indirect costs due to a decline in productivity losses. Clearly, additional population-based studies are needed to examine the longer-term effects of switching to each specific NOAC and of DDI burden on healthcare utilization and healthcare costs, including both direct and indirect costs. Fourth, we may have included many warfarin

users or non-switchers who newly initiated VKA therapy and were thus at higher risk of bleeding events [25]. This may lead to a potential increase in inpatient and ER visits among non-switchers compared with switchers, which may result in selection bias. Our results also did not capture information for patients who were multiple switchers during the 1-year follow-up period; this group of patients may differ from the switchers included in this study.

## 5 Conclusion

In working-age adults with AF, switching to NOACs was associated with significantly fewer outpatient, ER, and inpatient visits and with lower non-drug medical expenditures. Exposure to potential DDIs was common in this population and was associated with significantly greater healthcare utilization and higher healthcare expenditure. These findings suggest that the potential effects of both switching and DDI burden have important implications for healthcare use and expenditure and must be considered when managing AF in working-age adults.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

We used an adjudicated claims database of commercially insured individuals, which is made available through a license to IQVIA's Real World Data: Adjudicated Claims—US (also known as PharMetrics Plus), 10% sample. All rights reserved. The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IQVIA or any of its affiliated or subsidiary entities.

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## Key Points

Relative to persistent warfarin use, switching from warfarin to non-vitamin K oral anticoagulants (NOACs) was associated with fewer inpatient, emergency room, and outpatient visits and lower non-drug costs overall.

Exposure to potential drug–drug interactions (DDIs) was common in this population and was associated with significantly greater healthcare utilization and higher healthcare expenditures.

We recommend prescribers carefully consider known DDIs with oral anticoagulants and take the cumulative effect of potential DDIs into account when considering treatment options.

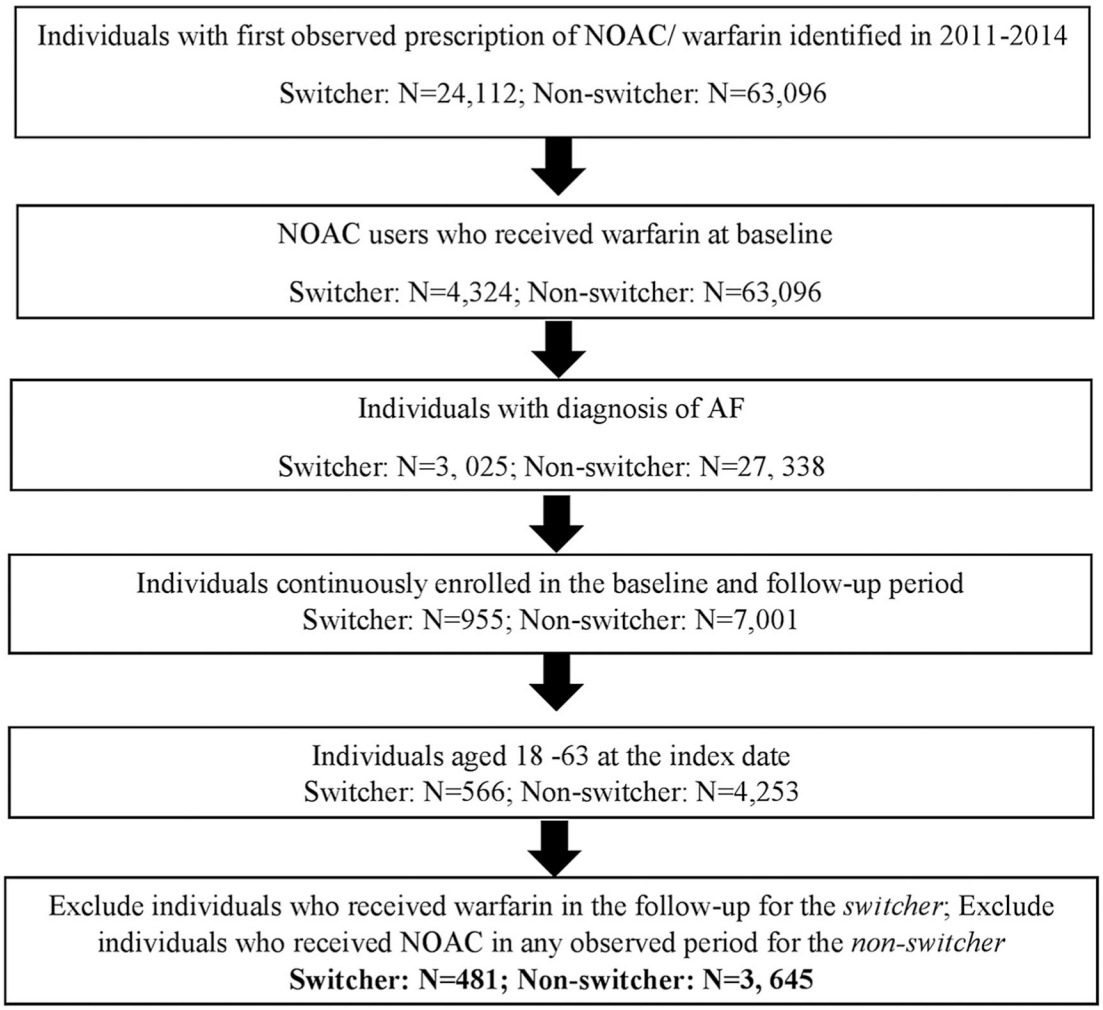


**Fig. 1.**
Flow chart to obtain the final study sample

## Table 1

Descriptive statistics of working-age adults with atrial fibrillation ($N = 4126$)

| | ***N*(%)/mean ± SD** |
|---|---|
| **Dependent variables** | |
| ***Healthcare utilization*** | |
| Having any inpatient visits (yes) | 1419 (34.4%) |
| Having any ER visits (yes) | 1425 (34.5%) |
| Number of outpatient visits | 31.79 ± 26.16 |
| ***Healthcare expenditures*** | |
| Non-drug medical expenditure ($) | 25,401.6 ± 61,499.1 |
| **Independent variables** | |
| ***Predisposing factor*** | |
| Sex | |
| Female | 1228 (29.8%) |
| Male | 2898 (70.2%) |
| Patient Region | |
| East | 1015 (24.6%) |
| Middle West | 1382 (33.5%) |
| South | 1398 (33.9%) |
| West | 331 (8.0%) |
| Age | 55.59 ± 7.15 |
| ***Enabling factors*** | |
| Type of health insurance | |
| HMO | 538 (13.0%) |
| PPO | 3073 (74.5%) |
| Other | 515 (12.5%) |
| ***Need factors*** | |
| Switching to NOACs | |
| No | 3645 (88.3%) |
| Yes | 481 (11.7%) |
| Exposure to potential DDIs | |
| *One year follow-up* | |
| Having any potential DDI (yes) | 3061 (74.2%) |
| Number of potential DDIs | 1.24 ± 1.04 |
| Proportion of days with potential DDIs | 0.26 ± 0.31 |
| Stroke/TIA | |
| Yes | 290 (7.0%) |
| No | 3836 (93.0%) |
| Cardioembolic complications event | |
| Yes | 502 (12.2%) |
| No | 3624 (87.8%) |
| Major bleeding event | |

| | ***N*(%)/mean ± SD** |
|---|---|
| Yes | 518 (12.5%) |
| No | 3608 (87.5%) |
| Renal disease | |
| Yes | 346 (8.4%) |
| No | 3780 (91.6%) |
| Liver disease | |
| Yes | 288 (7.0%) |
| No | 3838 (93.0%) |
| $CHA_2DS_2$-VASc score | 1.58 ± 1.19 |
| Number of chronic conditions | 1.03 ± 1.01 |

*DDI* drug–drug interactions, *ER* emergent room, *HMO* Health Maintenance Organization, *NOAC* non-vitamin K oral anticoagulant, *PPO* preferred provider organization, *SD* standard deviation, *TIA* transient ischemic attack

**Table 2**

Healthcare utilization among working-age adults with atrial fibrillation ($N = 4126$)

| | **Unadjusted Model** | | **Model 1** | | **Model 2** | | | |
|---|---|---|---|---|---|---|---|---|
| | **Switcher vs. non-switcher** | | **Switcher vs. non-switcher** | | **Switcher vs. non-switcher** | | **Having potential DDIs Yes vs. no** | |
| | **OR** | ***p* value** | **OR** | ***p* value** | **OR** | ***p* value** | **OR** | ***p* value** |
| Inpatient visits | 0.52 (0.42, 0.65) | < 0.0001 | 0.45 (0.35,0.57) | < 0.0001 | 0.49 (0.38,0.63) | < 0.0001 | 1.29 (0.98, 1.69) | 0.07 |
| ER visits | 0.53 (0.49, 0.56) | < 0.0001 | 0.79 (0.63,0.99) | 0.04 | 0.90 (0.71,1.15) | 0.39 | 1.47 (1.11, 1.95) | 0.01 |
| | IRR | | IRR | | IRR | | IRR | |
| Outpatient visits | 0.62 (0.58, 0.66) | < 0.0001 | 0.61 (0.55,0.65) | < 0.0001 | 0.66 (0.61,0.70) | < 0.0001 | 1.25 (1.15, 1.35) | < 0.0001 |

Model 1 included the following variables: switching to NOACs, insurance type, age, region, renal disease, liver disease, prior major bleeding, $CHA_2DS_2$-VASc, and number of chronic conditions. Model 2 also included potential DDIs. Having potential DDIs was significantly associated with having inpatient visits when switching to NOACs was excluded from the model 2

*DDI* drug-drug interaction, *ER* emergent room, *IRR* incidence rate ratio, *OR* odds ratio

**Table 3**

Healthcare expenditures among working-age adults with atrial fibrillation – generalized linear models ($N = 4126$)

| | Switcher vs. non-switcher | | | | Having potential DDIs yes vs. no | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean-recycled prediction | | GLM | | Mean-recycled prediction | | GLM | |
| | Switcher | Non-switcher | Coefficient (95% CI) | *p* value | Yes | No | Coefficient (95% CI) | *p* value |
| *One-year follow-up* | | | | | | | | |
| Non-drug medical expenditures | | | | | | | | |
| Model 1 | $ 19265.5 | $27117.3 | −0.34 (−0.52,−0.16) | < 0.0001 | - | - | - | - |
| Model 2 | $ 21996.4 | $26477.1 | −0.19 (−0.39,−0.02) | 0.08 | $27782.1 | $ 18737.3 | 0.39 (0.17,0.61) | < 0.0001 |

Model 1 included switching to NOACs, insurance type, age, region, renal disease, liver disease, prior major bleeding, $CHA_2DS_2$-VASc score, and number of chronic conditions; Model 2 also included having potential DDIs

*DDIs* drug–drug interaction, *GLM* generalized linear model