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RESEARCH ARTICLE

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Guideline-concordant initiation of oral anticoagulant therapy for stroke prevention in older veterans with atrial fibrillation eligible for Medicare Part D

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Objective: To characterize the rate of guideline-concordant initiation of oral anticoagulation (OAC) among elderly Veterans with atrial fibrillation (AF) and high stroke risk.

Data Sources/Study Setting: Veterans Health Administration (VHA) Corporate Data Warehouse (CDW) linked with Medicare claims 2011-2015.

Study Design: We identified 6619 elderly, high stroke-risk patients with a new episode of AF initially diagnosed in the VHA during fiscal years 2012-2015. We used logistic regression to estimate marginal effects of associations between patient characteristics and OAC initiation within 90 days of the first AF episode.

Data Extraction Methods: We identified OACs using generic drug names. We calculated comorbidities and risk scores using diagnosis codes from 1 year of baseline data.

Principal Findings: Overall, 66.5% of Medicare-eligible Veterans with AF at high risk of stroke initiated an OAC within 90 days. We found lower initiation rates for patients enrolled in Medicare Part D and those ineligible for drug co-payment subsidies. OAC initiation rates increased during the study among VHA-reliant patients but not among dual VHA-Part D enrollees.

Conclusions: One-third of elderly Veterans at risk of stroke are not receiving recommended therapy. Increased coordination between Medicare and VHA providers may lead to improvements in anticoagulation quality and stroke prevention.

KEYWORDS
chronic disease, medical decision-making, pharmaceuticals: prescribing/use/costs, VA Health Care System

1 | BACKGROUND

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, estimated to affect 33.5 million globally.[1] Its prevalence in the United States is projected to increase from an estimated 5.2 million patients in 2010 to 12.1 million cases in 2030.[2] Patients with AF are five times more likely than the general population to suffer an ischemic stroke due to thromboembolism.[3] Moreover, the stroke risk is highly age-dependent, increasing from 4.6% per year in individuals aged 50-59 years to more than 20% in those aged 80-89 years.[4]

Oral anticoagulant (OAC) therapy decreases stroke incidence by nearly half in AF patients and is associated with reducing stroke severity and inpatient mortality after stroke.[3-5] However, despite the proven benefits of this therapy and clear clinical guidelines

recommending it, prior research consistently shows that OACs are underused in patients with AF.[6,7] In particular, in the US Veterans Health Administration (VHA), only 43.1% of patients diagnosed with AF and considered to be at high risk of stroke were prescribed OACs in 2011, a decrease from 51.3% in 2001.[8] This finding, however, does not account for two important recent developments.

First, the approval of direct oral anticoagulants (DOACs) expanded the options for AF therapy. Warfarin, the only OAC previously available, is a vitamin-K antagonist that requires regular therapeutic drug monitoring and dose adjustment at specialized VHA anticoagulation clinics. Dabigatran was the first DOAC added to the VHA formulary in October 2011, followed by three additional DOACs over the next 5 years—rivaroxaban, apixaban, and edoxaban.[9] All DOACs have demonstrated similar or superior efficacy in reducing stroke risk in comparison with warfarin, as well as similar or superior rates of major bleeding.[10-15] Importantly, DOACs do not require regular drug monitoring, thus decreasing patient care burden. Since the VHA requires monitoring of patients anticoagulated with warfarin in its own clinics, DOAC adoption may also decrease involvement with VHA care, although prior success in keeping patients in the recommended therapeutic range, cost, and clinical reluctance to change prescribing habits may lead physicians to prefer warfarin over DOACs.

Second, Medicare began covering outpatient medications through part D in 2006, creating an alternative and potentially more convenient channel for older Veterans to acquire their medications compared to the VHA prescription drug benefit. Coupled with the availability of DOACs, Part D drug coverage may be an increasing source of oral anticoagulation therapy among elderly Veterans initially diagnosed with AF in the VHA, as more than 80% of patients living with AF are 65 or older and qualify for Medicare coverage.[16] At the same time, Veterans receiving care simultaneously from both the VHA and community networks could undermine coordination and follow-up and lead to suboptimal guideline adherence.

In this study, we combine VHA and Medicare data to account for the potential effects of these recent developments on guideline-concordant OAC treatment initiation among Veterans with AF. Our study is the first to evaluate overall guideline-concordant prescription rates for OACs among Veterans initially diagnosed with AF in the VHA after the approval of direct anticoagulants, which have increased the therapeutic options for stroke prevention. An earlier paper by Rose et al[17] examined DOAC prescriptions only and focused on potentially inappropriate prescribing in patients with contraindications for DOACs. Moreover, by including Medicare Part D prescriptions, we capture a more complete picture of OAC prescribing in these patients. We are thus able to assess whether these data partially account for the low rates of initiation found previously.[8] Our study also identifies patient-level characteristics associated with lower rates of guideline-concordant initiation. Finally, we present some important challenges and lessons learned from working with linked VHA-Medicare data relevant for other studies examining quality of care for dual VHA-Medicare populations.

2 | METHODS

2.1 | Data

We combined administrative utilization claims data from the VHA Corporate Data Warehouse (CDW)[18,19] and Medicare between fiscal years 2011 and 2015. We extracted relevant patient characteristics from the Medicare Beneficiary Summary File and from the CDW. Patient information was linked using each Veteran's Medicare beneficiary identifier (*beneid*) and Social Security Number (SSN) in the Medicare data with the scrambled Social Security Number (ScrSSN) as a unique identifier present in the VHA data. The match was performed by the VA Information Resource Center (VIReC), resulting in a finder file that matches SSN to *beneid*, and using date of birth and gender as additional variables in case of multiple *beneid* matches per SSN. Once this match was completed, VIReC matched the SSN to a ScrSSN so Medicare data could be linked to the VHA data. Combining patient characteristics from both sources resulted in a relatively low proportion of patients with missing information, such as race, marital status, or ZIP code of residence. We extracted *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* (ICD-9-CM) diagnosis codes from the CDW inpatient and outpatient encounter tables and from Medicare fee-for-service (FFS) Outpatient, Inpatient, MEDPAR, and Carrier (Physician/Supplier) Research Identifiable Files.[20] Medicare data were provided by VIReC's VA/CMS Data for Research Project.[21] We identified drug prescriptions for OACs from both the CDW and from Medicare Part D claims from October 1, 2011 to December 31, 2015. Prescription data obtained from CMS included Medicare Part D stand-alone plans and Medicare Advantage Part D plans.

2.2 | Sample selection

2.2.1 | Main sample

We identified a cohort of Veterans with at least one AF episode initially diagnosed in the VHA CDW data between October 1, 2011, and September 30, 2015 (Fiscal Years, FY 2012-2015). An AF episode was defined as the presence of a diagnosis of AF (identified by the ICD-9-CM code 427.31) in at least two outpatient encounters between 7 and 120 days apart. We required that the first encounter with an AF diagnosis be in the VHA, but the second encounter could be either in the VHA or in a Medicare claim. This selection procedure requiring at least two AF diagnoses mirrors the most recent previous study in the VHA[8] and ensures that our results were not an artifact of selecting patients with transient AF which does not require OAC therapy. By definition, this cohort excludes patients with only one diagnosis of AF present in the data. Even though the clinical guidelines recommend that OACs should be prescribed according to the thromboembolic risk of the patient regardless of the AF pattern (ie, paroxysmal, persistent, or chronic),[22] in this sample, we sought to exclude patients in which

AF may have occurred transiently without any lasting adverse clinical manifestations, for which providers may justifiably decide OAC therapy is not necessary.

The year prior to each patient's first AF episode was defined as the baseline year. We also ensured that patients had no AF diagnosis during a lookback period of 24 months prior to the initial diagnosis. (October 1, 2009-September 30, 2013) We only included patients aged 66 and above at the time of diagnosis in order to ensure that all patients were eligible for Medicare for at least 1 year prior to diagnosis. We excluded patients enrolled in Medicare Advantage plans during the study period to ensure completeness of both baseline and outcome data. We excluded patients who qualified to receive retiree drug subsidies, as these patients may receive prescriptions through private employer-sponsored supplementary insurance plans. We excluded patients who died within 90 days of their first VHA AF diagnosis since their outcome period is censored, but we did not exclude patients with hospitalizations within this period. This would leave out the sickest part of the population without a strong justification, as patients with a hospitalization may still fill an OAC prescription after discharge. To minimize the number of Veterans who might have had unsubsidized employer-sponsored drug coverage, we also excluded patients not enrolled in Medicare Part D and without a prescription from a VHA pharmacy in the year prior to their diagnosis (see Figure 1 for the detailed steps in the sample selection procedure).

Finally, we excluded patients at high bleeding or falling risk. We estimated patients' bleeding risk using three separate scores, for which we provide exact definitions in the Supporting Information: ATRIA,[23] HAS-BLED,[24] and HEMORR$_2$HAGES.[25] We used a modified version of HAS-BLED because labile INR values were unavailable for newly diagnosed patients. Evidence suggests that HAS-BED can identify patients at high bleeding risk despite omitting this variable.[26] Patients with excessive fall risk were identified as having dementia, gait abnormalities, lack of coordination, or a personal history of a fall. We also used a modified version of HEMORR$_2$HAGES excluding genetic factors since this was not available in the data, as in previous research.[27]

2.2.2 | Extended sample

We also identified an extended cohort of patients in which we required that patients only have one AF diagnosis based on VHA data coded during an outpatient encounter. This definition was consistent with other previous studies which assumed one AF diagnosis was sufficient to determine persistent AF.[28,29] We then applied the same exclusions detailed above for the main sample.

2.3 | Variable construction

2.3.1 | Dependent variable

The outcome of interest was guideline-concordant prescribing rate for AF patients. This variable was defined as an indicator for receiving an outpatient prescription for apixaban, dabigatran, rivaroxaban, edoxaban, or warfarin from VHA or Medicare Part D within 90 days of the first AF diagnosis.

2.3.2 | Demographics

We extracted patients' age at their first AF episode, sex, race and ethnicity, and marital status at the time of diagnosis. We derived the patients' rural/urban status based on rural-urban commuting area (RUCA) codes from the ZIP code of residence.[30] We also calculated the haversine distance from the centroid of the patient's ZIP code of residence to the nearest VHA facility. We obtained ZIP code median household income for each of the years 2011-2015 from the Census Bureau and matched it to the sample by the ZIP code of residence in the year of the first AF diagnosis.

2.3.3 | Stroke risk

To calculate each patient's stroke and bleeding risk, additional ICD-9-CM codes were extracted from medical records during baseline (see Table S1). Stroke risk was calculated using the CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior transient ischemic attack (TIA) or stroke, vascular disease, age ≥65, female sex category) score, which is the scoring system utilized in the 2014 American College of Cardiology & American Heart Association clinical AF guidelines to determine OAC therapy recommendations. Specifically, these guidelines recommend OAC therapy initiation for all AF patients at high risk of stroke (CHA_2DS_2-VASc ≥ 2) and should be considered for patients at moderate risk (CHA_2DS_2-VASc = 1).[22] In clinical practice today, CHA_2DS_2-VASc is the gold standard for estimating stroke risk due to its superiority compared to the previous $CHADS_2$ tool in stratifying patients at low to intermediate risk of stroke.[31]

2.3.4 | Comorbidities

We also constructed indicators for relevant comorbidities using definitions of conditions present in the Elixhauser score,[32] a widely used measure of clinical risk that predicts patient mortality and hospital resource use,[33,34] as well as several conditions used in previous studies of anticoagulation in the VHA.[35]

2.3.5 | Drug financing options

We constructed indicators for whether patients were enrolled in Medicare Part D during the month of the first AF diagnosis and the three subsequent months. We also extracted indicators for whether the patients were eligible for cost-sharing subsidies for prescription drugs. On the Medicare Part D side, we constructed indicators for whether patients qualified for the program's low-income subsidy, which helps pay for beneficiaries cost-sharing expenses.

On the VHA side, we recorded whether Veterans were in Enrollment Priority Group 1 and were thus exempt from co-pays for all drugs, were in Groups 2 through 6, thus only facing co-pays for some prescription drugs, or in Group 8, co-paying for all drugs.

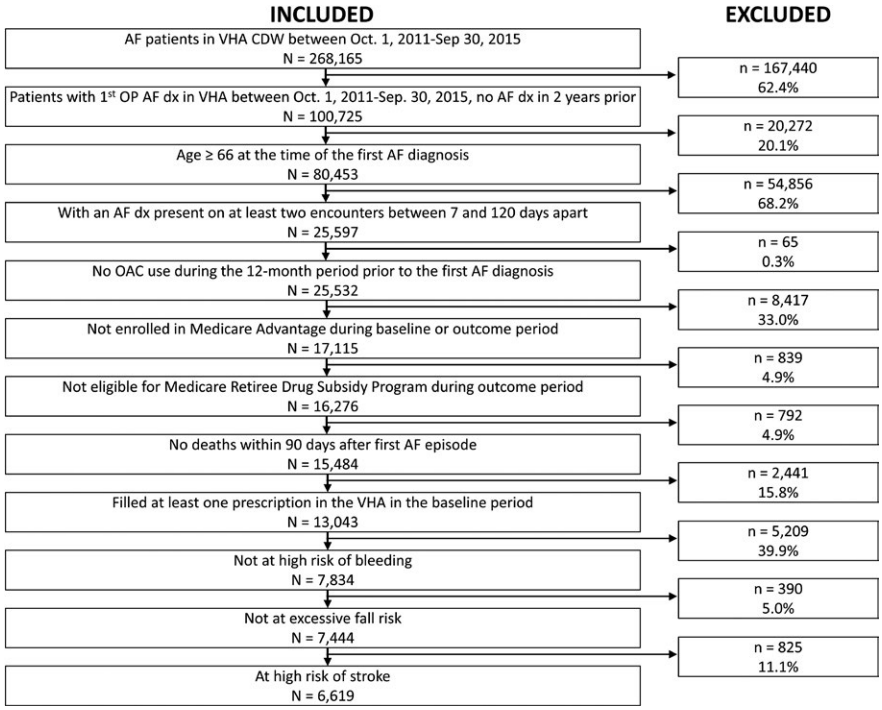

FIGURE 1 Sample selection procedure for main study sample

2.4 | Statistical analysis

We used multivariate logistic regression models with year fixed effects to estimate the association between patient characteristics and the probability of initiating OAC treatment for the patients with a CHA_2DS_2-VASc score above 1, for whom guidelines recommend OAC therapy. Because these characteristics may have different associations for Veterans with access to VHA while also enrolled in Medicare Part D versus patients relying only on VHA prescriptions, we estimate the models separately for these two groups. The first group has access to prescriptions financed by Part D plans, but may or may not use them for OAC treatment. Conversely, the second group likely relies only on VHA for their prescriptions. This sample is Medicare-eligible, not enrolled in Part D and had at least one prescription filled in the VHA during the baseline period. Moreover, Medicare low-income subsidies are only relevant for Part D enrollees. We report marginal effects for all models, representing percentage changes in the probability of OAC initiation compared to the reference group. All analyses were performed using Stata software version 14.0 (College Station, TX, USA)[36] and resources and facilities in the VA Informatics and Computing Infrastructure (VINCI). The Institutional Review Board (IRB) at VHA Boston reviewed and approved this study.

3 | RESULTS

3.1 | Sample characteristics

We identified 6619 Veterans with a new outpatient episode of AF in the VHA system from FY 2012-2015. The average patient age was 75.6 (SD = 7.5) and the majority of the patients were white (91.3%) and male (98.2%), reflecting the demographic profile of the elderly VHA population (Table 1). The average patient lived in a ZIP code with a USD 51 712 median household income and located about 13.8 miles away from the nearest VHA facility.

3.2 | Drug financing

Overall, 19.5% of the sample was enrolled in Medicare Part D for at least 1 month in the 90 days following their first VHA AF diagnosis. Many of the patients in our sample also benefitted from cost-sharing subsidies for prescription drugs. More than one-fifth of patients paid no co-pays for drugs dispensed by the VHA (Priority Group 1), about half only paid co-pays for some drugs (Groups 2-6), and one-quarter pays co-pays for all prescriptions (Groups 7-8). Of patients with some Medicare Part D enrollment, about 33.7% also qualified for subsidies covering cost-sharing expenses.

3.3 | Patient factors associated with OAC initiation

Overall, 66.5% of the Veterans in our main sample initiated OAC therapy within 90 days of their first VHA AF diagnosis. Patients with Part D coverage were less likely to initiate guideline-concordant OAC therapy than patients without coverage (53.8% vs 69.6%, $P < 0.01$) (Table 1).

OAC initiation rates were similar across Veterans with CHA_2DS_2-VASc scores of 2-6, indicating moderate risk of stroke (Figure 2). Our main sample had no patients with a CHA_2DS_2-VASc score of 7 or higher, likely because these patients also had other risks that led to their exclusion.

Average marginal effects for the association between patient characteristics and guideline-concordant OAC initiation for the main sample, stratified by Part D coverage status, are shown in Table 2.

Age had a strong association with OAC initiation rates. VHA-only patients aged 76-85 were about 7.3% points less likely to receive an OAC, and patients above 86 were about 20.5% points less likely to initiate therapy within 90 days of the first AF episode. These associations were also consistent for those with Part D. Table S6 shows the full results, including the coefficients for all the relevant comorbidities.

We found no association between OAC treatment initiation and household income in the patient's ZIP code of residence. Residence in a rural area and the distance from the patient's ZIP code to the nearest VHA facility also were not significantly associated with OAC initiation rates, suggesting no rural/urban disparity and that physical distance to a VHA facility does not affect guideline adherence for anticoagulation.

Our results indicate that VHA cost-sharing subsidies were associated with only slightly higher rates of OAC initiation, suggesting no major cost-based disparities in access. For patients relying on VHA prescriptions only, facing co-pays for all drugs was associated with a 3.7% point lower OAC prescription rate compared to those exempt from co-pays. For Veterans enrolled in Part D, the association was much larger, but not statistically significant—patients co-paying for all drugs were about 9.5% points less likely to fill a guideline-concordant OAC prescription, respectively. Part D beneficiaries qualifying for Medicare low-income subsidies had OAC initiation rates 14.7% points higher on average compared to non-eligible beneficiaries, suggesting the higher Part D co-pays may provide a stronger barrier for filling prescriptions compared to the VHA co-pays.

The adjusted proportion of patients initiating OAC treatment within 90 days increased over time, as shown by the fiscal year fixed effects coefficients in Table 2. On average, guideline-concordant rates of initiation for VHA-only patients were higher by approximately 7.4 points in 2014 and 9.2% points in 2015, compared to 2012. For patients with Medicare Part D, rates in 2013-2015 were comparable to those in 2012, suggesting little improvement for these patients. Unadjusted trends in OAC initiation rates, shown in Figure S2 (Figure S3 for the extended sample), are also consistent with the multivariate analyses. For VHA-only patients, rates increased from 64.3% in FY2012 to 75.5% in FY2015, while for VHA-Part D dual users the trend was almost flat, with rates increasing slightly from 51.3% to 55.3% over the study period.

Several comorbidities had significant associations with OAC initiation rates. In particular, congestive heart failure, hypertension, and diabetes were associated with higher rates of therapy initiation, as expected from their contribution to higher stroke risk. Patients with a prior stroke or TIA, whom the guidelines identify as obligatory patients for OAC therapy, were also significantly more likely to initiate it compared to patients without stroke or TIA, by 17.7% points on average, controlling for other patient characteristics. Among mental health conditions, only anxiety has a significant negative association with therapy initiation. Moreover, pulmonary circulatory disorders and obesity were positively associated with OAC initiation rates, while pericarditis and pericardial effusion and weight loss were negatively associated with these rates.

The patients in our sample who initiated OAC therapy overwhelmingly did so in the VHA, which is expected considering that we selected patients who present their first AF diagnosis in the VHA. Warfarin was still the preferred drug dispensed at treatment initiation (Table 3). Of prescriptions filled within 90 days of the first VHA AF diagnosis, 87.3% of prescriptions were for warfarin. Although the majority of prescriptions financed by Medicare Part D were for DOACs, most of these were subsequent prescriptions, that is, were filled after the patient had initiated OAC therapy within the VHA.

The results from the extended sample analysis are largely consistent with those from the main sample, although the overall rates of OAC initiation within 90 days of an AF diagnosis were even lower, at 51.4% of patients (see Table S8). These rates suggest that studies which identify AF patients by the presence of only one diagnosis may significantly underestimate the rate of guideline-concordant prescriptions by including patients that do not have persistent AF and may not require treatment.

4 | DISCUSSION

We find that 66.5% of Medicare-eligible Veterans with persistent AF at high risk of stroke in FY 2012-2015 were prescribed an OAC within 90 days, as recommended by clinical guidelines. Even after accounting for Medicare Part D, almost one-third of these Veterans did not initiate OAC therapy. Lack of guideline adherence is correlated with higher mortality[6] and with increased stroke incidence and severity.[5] Therefore, OAC prescribing among Veterans with AF and no contraindications to OAC therapy is a potential avenue for improvement to reduce morbidity and mortality associated with stroke.

A review by Ogilvie et al[7] covering US and international papers published between 1997 and 2008 identified suboptimal treatment initiation rates (defined as levels below 70% in patients with a $CHADS_2 \geq 2$) in 7 of 9 included studies. Among these, two studies of Veterans in single VHA facilities showed highly divergent results. One study showed initiation of warfarin above 90% in ideal patients in the Connecticut Healthcare System,[37] while another found initiation rates of less than 40% among patients treated at the Boston Healthcare System.[38]

More recently, at least two nationwide studies examined OAC prescription rates in VHA patients with AF. Turakhia et al[39] found overall warfarin prescription rates of 54.0% with lower rates for primary care only patients with $CHADS_2 \geq 2$ and ATRIA < 4 (48.5%), but significantly higher rate of warfarin use for similar patients treated in cardiology (70.2%). Moreover, they found declining overall rates of OAC initiation over time, driven by patients treated in primary care only. Buck et al[8] similarly found OAC initiation rates of 43.1% in 2011, down from 51.3% in 2002. In contrast, we find overall higher rates nearing 70% among patients with persistent AF and with no clear contraindications, in addition to an overall upward trend for VHA-only patients, which make up the majority of our sample.

TABLE 1 Characteristics of Medicare-eligible Veterans with a new AF episode during FY 2012-2015

	VHA only (N = 5330)	VHA + enrolled in Part D (N = 1289)	*P*-value	Total (N = 6619)
Age (y)	75.4 (7.5)	76.6 (7.5)	<0.01	75.6 (7.5)
Male	98.1%	98.7%	0.15	98.2%
Race/Ethnicity				
White	91.9%	88.9%	<0.01	91.3%
Black	4.1%	6.8%	<0.01	4.6%
Hispanic	2.8%	2.9%	0.82	2.9%
Other	1.2%	1.3%	0.73	1.2%
Marital status				
Married	58.3%	50.7%	<0.01	56.9%
Single	37.6%	45.6%	<0.01	39.1%
Missing	4.1%	3.6%	<0.01	4.0%
Residence				
Urban	53.9%	54.6%	0.64	54.0%
Rural	46.1%	45.4%	0.64	46.0%
Distance to Nearest VHA Facility (Miles)	13.7 (12.8)	14.0 (13.2)	0.56	13.8 (12.9)
Missing	3.3%	3.3%	0.90	3.3%
ZIP Code Median Household Income (USD)	51 828 (18 936)	51 228 (19 496)	0.32	51 712 (19 046)
Missing	2.3%	2.7%	0.41	2.4%
CHA_2DS_2-VASc Stroke Risk Score	3.2 (0.9)	3.2 (1.0)	0.30	3.2 (0.9)
CHA_2DS_2-VASc^{3}2 (High Risk)	100.0%	100.0%	—	100.0%
ATRIA bleeding risk score	2.0 (1.1)	2.1 (1.0)	<0.01	2.0 (1.1)
HAS-BLED bleeding risk score	1.9 (0.3)	1.9 (0.3)	0.16	1.9 (0.3)
HEMORR2HAGES bleeding risk score	1.6 (0.7)	1.7 (0.8)	<0.01	1.6 (0.7)
Original reason for Medicare eligibility				
Age only	95.6%	96.7%	0.08	95.8%
Disability	4.1%	3.3%	0.14	4.0%
ESRD	0.3%	0.2%	0.68	0.3%
Medicare-Medicaid dual eligible	0.5%	26.8%	<0.01	5.6%
VHA priority status group				
Priority 1 (No Co-pays)	25.1%	10.2%	<0.01	22.2%
Priority 2-6 (Co-pays for Some Drugs)	45.0%	63.1%	<0.01	48.6%
Priority 7-8 (Co-pays for All Drugs)	26.2%	22.3%	<0.01	25.5%
Missing	3.6%	4.4%	0.18	3.8%
Part D Low-income Subsidy	0.0%	33.7%	<0.01	6.6%
OAC Rx within 90 Days of First AF Episode	69.6%	53.8%	<0.01	66.5%
Warfarin	60.7%	47.0%	<0.01	58.0%
DOAC	8.9%	6.7%	0.01	8.5%
Fiscal year of first AF episode				
2012	27.3%	29.2%	0.18	27.7%
2013	27.7%	27.7%	0.98	27.7%
2014	25.4%	24.7%	0.61	25.3%
2015	19.6%	18.4%	0.32	19.4%

Notes: P-values from two-sample *t* tests for the equality of means (for continuous variables) or asymptotic two-sample tests for the equality of proportions. The VHA-only group has had at least one prescription in the VHA but is not enrolled in Medicare Part D. The VHA + Part D group has both at least one VHA prescription during baseline and is also enrolled in a Part D plan.

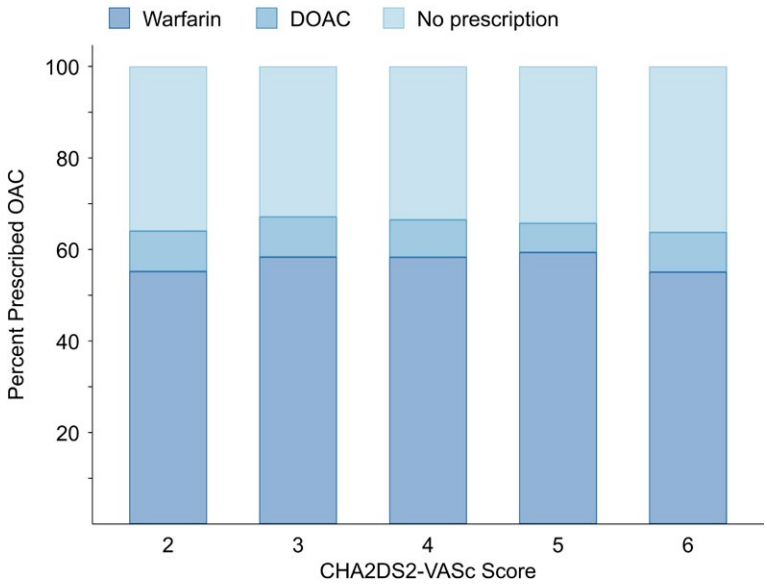

FIGURE 2 Percent of Medicare-eligible Veterans Initiating OAC Therapy within 90 days of a New AF Episode, by $CHAD_2DS_2$-VASc Score, FY 2012-2015

To our knowledge, this is the first study of OAC use in Veterans with AF to incorporate prescriptions filled through Medicare Part D, confirming the need for quality improvement initiatives to address these low prescription rates. Without considering Part D data, it was unknown whether Veterans diagnosed with AF were filling their prescriptions from non-VHA sources and following the guidelines or not receiving recommended treatment. To gain a complete picture for our sample, we restricted it to patients who were first diagnosed in the VHA and for whom we can be fairly confident that we have complete Medicare claims, as our sample is restricted to patients 66 years old and over and excludes enrollees in Medicare Advantage. This explains why our rates of Medicare Part D coverage are nearly 20%, as compared to 32% among VHA enrollees.[40] In contrast to the overall VHA enrollee population, our sample is heavily reliant on the VHA since they filled VHA prescriptions during baseline and their first AF diagnosis was recorded in the VHA.

Several possible explanations for suboptimal levels of guideline-adherent treatment initiation have been previously proposed, and our analyses provide evidence for evaluating them. First, warfarin has a narrow therapeutic index and clinically significant interactions with hundreds of prescription medications, herbals, supplements, and foods, and requires continuous monitoring and dose adjustment in anticoagulation clinics. One hypothesis is that these unfavorable characteristics may deter providers from prescribing warfarin to patients without access to reliable transportation or with complicated medication regimens. We did not find support for this hypothesis. In our multivariate analyses, although several comorbidities were strongly associated with OAC initiation, neither Medicare disability status, nor the distance to the nearest VHA facility was independently associated with the probability of guideline-concordant treatment.

Another potential reason previously cited for poor OAC prescribing among high-risk patients is bleeding risk.[41] OACs may cause serious bleeding, including intracranial hemorrhage, which can be fatal. Consistent with this hypothesis, in our sample, patients with higher bleeding risk were less likely to initiate anticoagulation. Nevertheless, evidence shows that providers often overestimate the risk of intracranial hemorrhage among AF patients.[42] In one observational study among Medicare beneficiaries with AF at high risk of falls, ischemic stroke was nearly five times more common than intracranial hemorrhage.[43] Increasing provider education on incidence of intracranial hemorrhage during OAC therapy is therefore likely to increase initiation of these drugs in AF patients.

In other settings, the introduction of DOACs was associated with an increase in the OAC initiation rate by 25%-75%.[28,44] In our study, despite OAC initiation rates among Veterans without Medicare Part D coverage with AF increasing over time, the impact of DOACs has been lower for patients enrolled in Part D. This trend may be due to the providers' reluctance to provide DOACs with incomplete information about patients receiving care from multiple systems, given the DOACs' potential for overprescribing.[17] The overall lower rates of initiation among dual patients may be due to coordination of care issues in which providers in each system assume AF is being managed by providers in the other system. Previous research has highlighted that fragmented care between systems decreases medication adherence and leads to poorer health outcomes.[45,46] Correctly identifying Veterans who are at increased risk of falling through care coordination cracks will be increasingly important as the Veterans Choice Program expands, requiring comprehensive data on non-VHA services.[47,48]

Although Medicare prescriptions account for a small share of total prescriptions filled by our cohort, the drugs prescribed for this subgroup differ markedly from prescriptions filled in the VHA. DOAC prescriptions constituted a minority of total prescriptions, but encompassed nearly three-quarters of prescriptions filled through Medicare, possibly because of more aggressive marketing of new drugs outside the VHA or due to inertia caused by VHA's already existing infrastructure of anticoagulation clinics. However, we found that DOACs had a negligible effect on guideline-concordant rates of

TABLE 2 Marginal effects of associations between patient characteristics and initiation of OAC therapy within 90 days of a new AF diagnosis among patients at high risk of stroke (2012-2015)

	VHA only		VHA + enrolled in Part D	
	Average marginal effect × 100	Standard error	Average marginal effect × 100	Standard error
Age category (66-75 = ref.)				
76-85	−7.25***	1.51	−5.77	2.96
86+	−20.5***	1.94	−26.9***	4.57
Male (Female = ref.)	1.03	3.70	−1.92	12.2
Race/Ethnicity (White = ref.)				
Black	12.8***	3.40	3.16	6.01
Hispanic	8.42	4.57	7.39	7.72
Other	0.97	5.90	−1.59	11.6
Marital status (Married = ref.)				
Single	3.37*	1.32	5.11	2.90
Missing	0.88	3.22	−0.26	7.20
Rural Residence (Urban=ref.)	0.35	1.54	2.19	3.42
Quartile of distance to VHA (1 = ref.)				
2	−1.16	1.85	−0.016	4.93
3	−1.94	1.67	−2.51	4.36
4	0.21	1.91	3.35	4.60
Missing	−6.09	5.88	3.22	13.0
Quartile of ZIP Code Median Income (1 = ref.)				
2	3.14	1.80	1.34	3.39
3	2.72	1.89	4.03	3.91
4	1.15	2.09	−7.02	4.00
Missing	7.01	7.03	−2.69	13.8
Reason for Medicare Eligibility (Age only = ref.)				
Disability	1.41	3.59	6.55	10.3
Medicare-Medicaid Dual Eligible	−6.51	8.62	−10.1*	4.76
VHA Enrollment Priority Group (1 = ref.)				
Priority 2-6 (Co-pay for Some Rx)	0.84	1.80	1.46	4.44
Priority 7-8 (Co-pay for All Rx)	−3.67*	1.75	−9.45	4.99
Missing	4.52	3.79	−4.78	6.96
Part D Low-income Subsidy			14.7**	4.52
Fiscal Year of First AF Episode (2012 = ref.)				
2013	2.38	1.62	4.79	3.89
2014	7.36***	1.70	1.51	3.52
2015	9.18***	1.76	3.12	3.68
Selected comorbidities				
Congestive Heart Failure	5.96**	1.90	9.90*	3.93
Hypertension	4.34*	1.74	5.18	4.20
Diabetes	6.90***	1.28	4.67	2.86

(Continues)

TABLE 2 (Continued)

	VHA only		VHA + enrolled in Part D	
	Average marginal effect × 100	Standard error	Average marginal effect × 100	Standard error
Stroke or TIA	17.7**	6.22	−11.9	15.1
Vascular disease	−2.77	1.50	−10.1**	3.73
Anxiety	−5.14*	2.37	−0.86	6.22
Pericarditis and Pericardial Effusion	−2.39	8.71	−56.0**	18.1
Pulmonary circulatory disorders	3.54	3.84	18.9*	7.38
Obesity	3.35*	1.57	−1.41	3.57
Weight loss	−8.06*	3.35	−8.75	6.81
Observations	5330		1289	

Notes: Models also control for the full set of comorbidity indicators. See Supporting Information for full regression results, including the full set of patient comorbidities. The VHA-only group has had at least one prescription in the VHA but is not enrolled in Medicare Part D. The VHA + Part D group has both at least one VHA prescription during baseline and is also enrolled in a Part D plan.
***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

TABLE 3 Payer and type of drug dispensed for OACs prescribed to patients in the main sample, FY 2012-2015

		First prescription		
Payer	Drug	Within 90 d of AF diagnosis	Beyond 90 d of AF diagnosis	Subsequent prescriptions[a]
VHA	Warfarin	3997 (87.3%)	250 (64.3%)	71 022 (85.6%)
	DOAC	580 (12.7%)	139 (35.7%)	11 911 (14.4%)
Medicare	Warfarin	0 (0%)	17 (10.6%)	195 (10.5%)
	DOAC	0 (0%)	144 (89.4%)	1670 (89.5%)

[a]Subsequent prescriptions are those filled after the first prescription for each patient initiating OAC therapy in our sample. Patients may initiate treatment in the VHA but may later pay for their prescriptions via Medicare Part D plans.

OAC initiation—instead, most DOACs were prescribed to patients who were already on warfarin, so Veterans were switching from a cheaper to more expensive medication regime. These findings demonstrate that as Veterans are referred more regularly outside the VHA through the Veterans Choice Program, the different prescribing and utilization patterns among community providers may have significant cost implications.[49] In January 2014, the Veterans Health Administration released a *Criteria for Use* document outlining specific indications for DOAC use in Veterans with AF,[50] though it is unclear what impact, if any, this document had on provider OAC choice.

Our study has several limitations. First, we excluded prescriptions filled through Medicaid; although we obtained Medicaid Analytical Extract (MAX) claims, the delay in research access to these files precluded their availability for the entire study period. However, exploratory analyses using 2012 data showed that Medicaid prescriptions make up a very small share of OAC prescriptions for this population (about 2% to 3%) and that most of these prescriptions are for continuation of therapy (as opposed to initiation), so we excluded them from the analysis for consistency through time. We also did not have access to data from supplemental Medicare and private insurance plans. However, by excluding patients eligible for retiree drug subsidies and restricting the sample to patients who had filled at least one prescription in the VHA during baseline, we likely mitigated the risk that patients in our sample received substantial prescriptions from sources not captured in our data.

Second, Veterans may be prescribed other drugs as an alternative to OACs, such as antiplatelet agents, which may partially explain poor guideline adherence in this population. Past research indicates that 9.7% of Veterans were initiated on clopidogrel shortly after AF diagnosis in FY2011.[6] However, antiplatelet agents are less effective than anticoagulants at reducing stroke risk and are not recommended by current AF guidelines for this indication.[22,51] Some patients may have also received inpatient parenteral anticoagulants (eg, heparin) during a hospitalization, which remains a limitation of our study.

Combining VHA and Medicare data was essential for this study. In the absence of Medicare data, it is possible that risk stratification of patients is incorrect, since many acute conditions (such as

previous strokes or hemorrhages) are reported in community hospitals and not in VHA. Moreover, we are better able to identify the first VHA AF diagnosis as well as prescriptions from non-VHA sources using Medicare claims.

In conclusion, about one-third of Veterans with AF at high stroke risk were not prescribed OACs despite evidence of their benefit in reducing morbidity and mortality. However, our results show that patients with a previous stroke/TIA are more likely to receive treatment and suggest overall improvement in the VHA over time. VHA providers have adopted newer DOACs to mixed degrees,[17] and our results suggest that the availability of these agents may have contributed to increased OAC initiation rates. This study illuminates several system-wide opportunities for targeted interventions to improve the quality of health care provided to Veterans with AF and suggests that patients receiving prescriptions through Medicare Part D may face lower quality compared to VHA-only patients. Future research should examine whether outcomes between similar patients receiving vs. not receiving anticoagulation therapy are significantly different in this population.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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