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Research paper

Identifying prescribing differences of direct oral anticoagulants for atrial fibrillation within the Military Health System☆

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ABSTRACT

Background: Direct oral anticoagulants (DOACs) are a first-line anticoagulant therapy for eligible patients with atrial fibrillation. Prescribing differences in the Military Health System have not yet been assessed.

Methods: We conducted a retrospective cross-sectional study using administrative claims data from the Military Health System Data Repository from fiscal years 2018–2019. We identified TRICARE Prime and Prime Plus patients between the ages of 18 and 64 with a diagnosis of atrial fibrillation and a CHA_2DS_2-VASc score of ≥2. Descriptive statistics and odds of receiving DOACs by gender, age, race, and socioeconomic status were calculated.

Results: A total of 5289 TRICARE Prime and Prime Plus patients within the Military Health System who carried a diagnosis of atrial fibrillation and a CHA_2DS_2-VASc ≥2 were identified. Of all patients, 2373 (40.71 %) were prescribed a DOAC whereas 287 (4.92 %) were prescribed warfarin within 90 days of diagnosis of atrial fibrillation. Black patients were significantly less likely to be prescribed a DOAC compared to White patients (adjusted odds ratio [aOR], 0.82; 95 % CI 0.68–0.99), as were females compared to males (aOR, 0.64; 95 % CI 0.52–0.79). Senior officers were significantly more likely to be prescribed a DOAC compared to senior enlisted service members (aOR, 0.64; 95 % CI 0.52–0.79).

Conclusions: Our study shows that differences exist within the Military Health System in the prescription of DOACs for atrial fibrillation by race, gender, and socio-economic status. These differences cannot be explained by differences in access to insurance or cost of medications.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the United States, with a growing estimated prevalence of 5.6 to 15.9 million individuals by 2050 [1]. This condition is particularly common in older individuals. For men and women without AF at age 40, the lifetime risk of developing AF is 26 % and 23 %, respectively [1]. This condition is clinically important because AF is associated with an increased risk of stroke as measured in patients deemed high risk per the CHA_2DS_2-VASc risk estimation algorithm. Oral anticoagulation therapy reduces stroke risk in high-risk AF patients with atrial fibrillation. It has been well-established that direct oral anticoagulants (DOAC) have a decreased risk of bleeding compared to warfarin and are equally efficacious for prevention of stroke in patients with non-valvular AF [2]. For that reason, recent clinical practice guidelines have endorsed DOACs as first-line anticoagulant therapy for eligible patients with AF [3].

Studies from the private sector [4] and the Veterans Administration (VA) [5] demonstrate that disparities by race and ethnicity exist regarding the initiation of oral anticoagulation as well as the use of DOACs over warfarin. Disparities may be due to mechanisms at the patient level, healthcare professional level, and system level in a framework previously described by Essien et al. [5]. Disparities by race and ethnicity in the private sector may be attributed to insurance access and the pricing of medications. However, in the VA, which is another large federal healthcare system, access to medications through a uniform national drug formulary is the same for all enrollees. Disparities in

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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the VA system have been attributed to different racial and ethnic group patients being less willing to accept novel therapeutics, or having decreased patient activation at the patient level.

Prior research conducted in the US Military Health System (MHS), which provides care to 9.6 million Americans, has shown elimination of racial disparities for certain conditions and includes active duty service members, retirees, and dependent beneficiaries [6]. Disparities in prescription of DOACs in AF patients have not yet been assessed in the MHS which provides care to a nationally representative population with access to prescription medications at low or no cost [7–10]. This retrospective cross-sectional study aims to identify prescribing disparities within the MHS by age, race, gender, beneficiary status, and socioeconomic status since all patients have access to medications through an insurance system in which cost is not a barrier.

2. Materials and methods

This retrospective cross-sectional study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

2.1. Data source and study population

Using administrative claims data from the MHS Data Repository (MDR) from fiscal years 2018–2019, we identified TRICARE Prime and Prime Plus patients between the ages of 18 and 64 with a diagnosis of atrial fibrillation (AF) and a CHA_2DS_2-VASc score of $\geq$2. The MDR houses all healthcare claims for MHS beneficiaries receiving care at military treatment facilities (also known as direct care) and at civilian treatment facilities (also known as private sector care) accessed through their TRICARE benefits. TRICARE is the Department of Defense (DoD) insurance benefit product providing coverage to 9.6 million beneficiaries, including active duty personnel, retirees, and their dependents [11].

Additionally, we identified all patients in the study population who were prescribed warfarin or a DOAC within 90 days of the non-valvular AF diagnosis. The DOACs included were apixaban, dabigatran, edoxaban, and rivaroxaban. Exclusion criteria included the following: individuals with a CHA_2DS_2-VASc score $<$2, not enrolled in TRICARE in the 2 years prior to the index diagnosis of AF, with any form of aortic or mitral valve disease, repair or replacement within 2 years of index AF diagnosis, who died or were discharged to hospice care within 90 days after their index AF diagnosis, and those who were on antiplatelets or a prescription for both warfarin and DOAC. Additional exclusions included patients ages 65 and older due to TRICARE becoming secondary payer to Medicare, and those associated with the National Guard and Reserves were also excluded due to their inconsistent access to the MHS.

2.2. Statistical analyses

We developed descriptive statistics on patient demographics and type of prescription received, and conducted univariate and multivariate logistic regressions for the odds of receiving DOACs. Due to the low receipt rate, we did not report the results of regression analysis assessing the receipt of warfarin only. Patient demographics were obtained at the time of non-valvular AF diagnosis, and included gender, age, race, beneficiary status, rank or sponsor's rank as a proxy for socio-economic status. Reporting of race is a mandatory requirement for active service members only, of whom only constitute 20 % of the MHS population, and as such there is a high rate missing race in the dependent population. Approximately 42 % of our study population had a missing race. Due to the rate of missing race, multiple imputations with 10 and 40 iterations were used in the multivariate logistic regression and validated by comparing imputed results. Results from 10 iterations are reported due the resulting parameter estimates being closer to parameter estimates from those found in the full multivariate regression model with missing values included. All analyses were conducted using SAS 9.4. This study was approved by the Institutional Review Board of the Uniformed Services University of the Health Sciences as part of the Comparative Effectiveness and Provider Induced Demand Study.

3. Results

3.1. Cohort demographics

A total of 5289 TRICARE Prime and Prime Plus patients within the MHS who carried a diagnosis of AF and a CHA_2DS_2-VASc $\geq$2 were identified between the years 2018–2019 and included in analyses. Table 1 shows the baseline demographic and clinical characteristics of our study population. The majority of the study population were female (58.62 %), White (37.06 %), between the ages of 55 and 64 (78.73 %), dependents, and associated with a senior enlisted rank (81.20 %). Of all patients, 2373 (40.71 %) were prescribed a DOAC whereas 287 (4.92 %) were prescribed warfarin within 90 days of diagnosis of AF. Race data were missing for 41.93 % of the study population.

3.2. Predictors of DOAC treatment

Table 2 shows both the unadjusted and adjusted logistic regression

Table 1
Study population[a] demographic and clinical characteristics, FY 2018–2019.

	Total population with AF diagnosis (N = 5829)
	N (%)
Gender	
Female	3417 (58.62)
Male	2412 (41.38)
Age group	
18–24	18 (0.31)
25–34	60 (1.03)
35–44	182(3.12)
45–54	1162 (16.81)
55–64	4589 (78.73)
Race	
White	2160 (37.06)
Black	805 (13.81)
Asian/Pacific Islander	173 (2.97)
American Indian/Alaska Native	22 (0.38)
Other	225 (3.86)
Unknown/missing	2444 (41.93)
Beneficiary status	
Active duty	70 (1.20)
Dependent of active duty	188 (3.23)
Dependent of other	3109 (53.34)
Retiree	2434 (41.76)
Other	13 (0.22)
Missing	15 (0.26)
Rank	
Junior enlisted	137 (2.35)
Senior enlisted	4733 (81.20)
Junior officer	354 (6.07)
Senior officer	441 (7.57)
Warrant officer	158(2.71)
Others and missing	<11
Drug treatment within 90 days of diagnosis	
Direct oral anticoagulants	2373 (40.71)
Warfarin	287 (4.92)

Abbreviations: AF = atrial fibrillation.
Note: Race is categorized in the MDR as White, Black, Asian or Pacific Islander, American Indian or Alaska Native, Other.
[a] MHS beneficiaries 18–64 with a diagnosis of atrial fibrillation and a CHA_2DS_2-VASc score $\geq$2. Removing anyone on antiplatelets and anyone on both warfarin and direct oral anticoagulants. Excluding national guard/reserves and their dependents.

Table 2
Logistic regression results for predictors of direct oral anticoagulants treatment in study population.[a]

	Unadjusted univariate results		Imputed and adjusted multivariate results	
	OR	95 % confidence limits	aOR	95 % confidence limits
Gender				
Male (reference group)	1	1	1	1
Female	0.69*	0.62–0.77	0.64*	0.52–0.79
Age group				
18–24	0.16*	0.04–0.70	0.16*	0.04–0.68
25–34	0.23*	0.11–0.46	0.23*	0.11–0.49
35–44	0.34*	0.23–0.49	0.33*	0.22–0.51
45–54	0.60*	0.52–0.69	0.62*	0.53–0.72
55–64 (reference group)	1	1	1	1
Race				
White (reference group)	1	1	1	1
Black	0.73*	0.62–0.86	0.84*	0.71–0.99
Asian/Pacific Islander	0.89	0.65–1.22	0.86	0.62–1.19
American Indian/ Alaska Native	1.17	0.50–2.71	1.02	0.47–2.19
Others	1.22	0.93–1.61	1.13	0.87–1.47
Beneficiary status				
Dependent of active duty (reference group)	1	1	1	1
Active duty	0.68	0.37–1.28	0.59	0.31–1.14
Dependent of other	1.31	0.96–1.80	0.73	0.50–1.07
Other	1.33	0.42–4.25	0.68	0.19–2.43
Retiree	1.76*	1.28–2.42	0.65*	0.43–0.99
Rank				
Junior enlisted	0.65*	0.45–0.94	0.83	0.56–1.22
Senior enlisted (reference group)	1	1	1	1
Junior officer	0.86	0.69–1.08	0.89	0.71–1.11
Senior officer	1.30*	1.07–1.58	1.26*	1.03–1.54
Warrant officer	1.23	0.89–1.69	1.33	0.96–1.85

Abbreviations: AF = atrial fibrillation; OR = odds ratio; aOR = adjusted odds ratio.
Note: Race is categorized in the MDR as White, Black, Asian or Pacific Islander, American Indian or Alaska Native, Other.
[a] MHS beneficiaries 18–64 with a diagnosis of atrial fibrillation and a CHA_2DS_2-VASc score $\geq$2. Removing anyone on antiplatelets and anyone on both warfarin and direct oral anticoagulants. Excluding national guard/reserves and their dependents. Total N = 5829.
* Statistically significant with p-value < 0.05.

results for predictors of DOAC treatment. Compared to White patients, the odds of initiating DOAC therapy were significantly lower for Black patients (adjusted odds ratio [aOR], 0.82; 95 % CI 0.68–0.99). Compared to male patients, women were significantly less likely to be prescribed a DOAC (aOR, 0.64; 95 % CI 0.52–0.79). Finally, compared to senior enlisted service members, senior officers were significantly more likely to be prescribed a DOAC (aOR, 1.26; 95 % CI 1.03–1.54). Fig. 1 shows a forest plot of these differences.

4. Discussion

We identified 5289 patients with AF, of whom 2373 received DOACs. Our results demonstrated that, for patients in the MHS with non-valvular AF, differences exist in the prescription of DOACs based on differences in race, gender, and rank. Each of these factors was independently associated with differences in the prescription of DOACs. Specifically, Black, female, and lower rank beneficiaries were less likely to be prescribed DOACs than beneficiaries who were White, male, and higher ranking.

The racial differences seen in this cohort align with the results of previous work in other populations that demonstrated similar findings. For example, the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II (ORBIT-AF II) was a cohort study consisting of 12,417 patients. This study showed that, after controlling for clinical and socioeconomic factors, Black individuals were less likely than White individuals to receive DOACs for AF (aOR, 0.73 [95 % CI, 0.55–0.95]) [4]. Our study results are also consistent with the findings from a national study of VA patients published in 2021 [5]. That study, which consisted of 111,666 patients treated in the VA system from 2014 to 2018, demonstrated that Black patients were significantly less likely than White patients to initiate any DOAC when adjusting for clinical, sociodemographic, physician, and facility factors.

While racial differences exist for Black patients, there was no difference in prescription of DOACs for Asian patients compared to White patients which corresponds with prior literature [4]. When it comes to ethnicity, past research shows differing outcomes. Some studies found a disparity between Hispanic and White patients dependent upon the CHA_2DS_2-VASc score [4], while others show large disparities for Puerto Rican Hispanics and no difference for Black Hispanics [12]. We were unable to assess ethnic differences in our study due to missing-ness of data for military dependents.

When looking at gender, we found females were less likely to be prescribed DOACs compared to males which corresponds with results from the FLiPER-AF Stroke Study [12] but differs from research in Spain showing women having higher odds of DOAC prescription and use among individuals treated for AF [13]. Rank is used as a proxy for socioeconomic status when analyzing MHS data. Our results showing differences in prescription of DOACs by rank correspond with research is Spain showing that patients in socioeconomic deprived areas had lower odds of receiving DOAC therapy [13].

Racial disparities in healthcare are well documented in the United States [14]. Universal insurance has been a suggested means of mitigating disparities through equal access to care [15]; however, multiple studies show persistence of disparities even in publicly funded systems including Medicare, Medicaid, and the VA [16–18]. In the MHS many disparities are mitigated, but some persist specifically in private-sector care [6]. We did not assess setting of care in this analysis. Even so, this study suggests that factors beyond cost and access drive racial differences in prescription of DOACs.

Essein et al. [5] describes causes of disparities through the framework of the patient level, healthcare professional level, and system level. Our results cannot be explained by differences in access to insurance or cost of medications which are attributed to the system level. All patients included in our study had access to healthcare and medications at little or no cost. Therefore, there must be other reasons besides access to healthcare that contribute to the differences observed here.

At the patient level, racial and ethnic group patients may be hesitant or less willing to accept novel treatments as described in a study examining differences in attitudes toward medical innovation on the part of Black and White patients [19]. This study showed that, in general, Black patients had lower medical technology innovativeness and were correspondingly more likely to be hesitant about adopting particular new technologies [19]. This hesitancy could also extend to relatively new prescription drugs, such as DOACs. Similarly, a legacy of medical experimentation in racial and ethnic groups may also contribute to hesitancy about adopting new medical treatments due to a lack of trust in the healthcare system [20]. Patient choice is an understudied yet important phenomenon in the MHS. Prior research shows racial and ethnic group patients were more likely to transfer care from a military to a civilian setting for prostate cancer management despite the advantages of seeking care at a military facility [21]. Future research is warranted to determine if DOAC prescribing patterns are being driven by patient preference.

At the provider level, implicit bias on the part of healthcare professionals may contribute to differences in DOAC prescriptions [22]. For example, bias may lead to differential rates of referral to cardiologists, and hence differences in initiation of DOACs or transition from warfarin to DOACs [5]. As far as medication prescribing goes, provider bias has

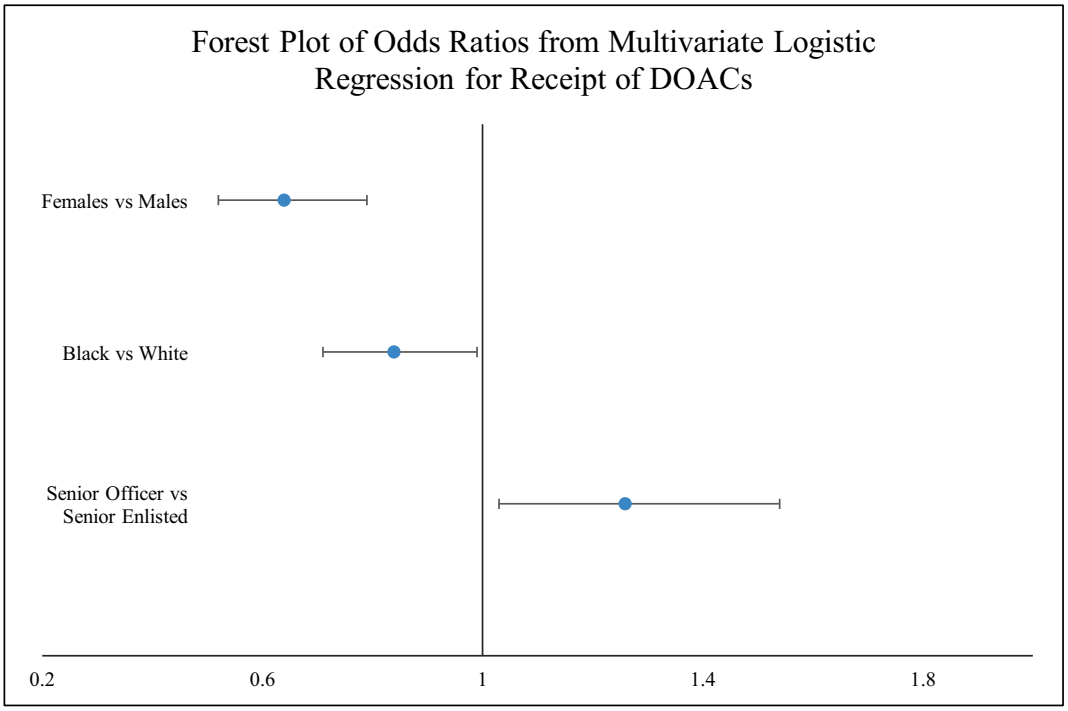

Fig. 1. Forest plot of select odds ratio results from multivariate logistic regression analysis for receipt of DOACs.
This figure shows odds ratios from multivariate logistic regression for receipt of DOAC by gender, race, and socioeconomic status.

been documented for certain conditions with a lower propensity to write prescriptions for atrial fibrillation patients [23]. This could potentially be mitigated by ensuring provider demographics match the demographics of the patient population being treated [22]. Lastly, at the system level, nonfinancial costs may play a role [24]. For example, costs such as child care, transportation, and time off work, may impact the ability of Black patients to utilize healthcare.

4.1. Limitations

This study had several limitations. As with any study using administration claims data, study data has the potential for coding errors. Additionally, our study only captured data on beneficiaries under 65 years of age due to TRICARE becoming a secondary payer at that time. The lack of data on older patients is worth noting, especially because AF is more common in older patients. While race data was missing, we were able to conduct multiple imputation for analysis. Ethnicity data was missing for too much of the population to include in analyses on the Hispanic population.

5. Conclusions

Despite offering universal coverage to a geographically diverse population, more research is needed to understand the underlying reasons for differences in DOAC prescription to ensure more equitable treatment and outcomes for patients in the MHS with non-valvular AF.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of data and material

The data that support the findings of this study are available from the United States Defense Health Agency. Restrictions apply to the availability of these data, which were used under federal Data User Agreements for the current study, and so are not publicly available.

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Ethics approval and consent to participate

Due the secondary analysis of existing, de-identified data, this study was deemed exempt from human subjects review by the Institutional Review Board of the Uniformed Services University of the Health Sciences. Because of these conditions, written consent to participate, including by parents or guardians for children under 18, is not applicable.

Consent for publication

Due to the use of de-identified data, consent for publication is not applicable.

Disclaimer

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