





# National Physician Survey for Nonvalvular Atrial Fibrillation (NVAF) Anticoagulation Comparing Knowledge, Attitudes and Practice of Cardiologist to PCPs

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## Abstract

**Introduction:** NVAF is estimated to affect between 6.4 and 7.4 million Americans in 2018, and increases the risk of stroke 5-fold. To mitigate this risk, guidelines recommend anticoagulating AF patients unless their stroke risk is very low. Despite these recommendations, 30.0-60.0% of NVAF patients do not receive indicated anticoagulation. To better understand why this may be, we surveyed PCPs and cardiologists nationwide on their attitudes, knowledge and practices toward managing NVAF with warfarin and direct-acting oral anticoagulants (DOACs). **Methods:** We surveyed 1,000 PCPs and 500 cardiologists selected randomly from a master list of the American Medical Association, using a paper based, anonymous, self-administered, mailed scannable survey. The survey contained questions on key demographics and data concerning attitudes, knowledge and practices related to prescribing DOACs. The surveys went out in the fall/winter of 2017-8 with a \$10 incentive gift card. Survey responses were scanned into an Excel database and analyzed using SAS 9.3 (Cary, NC) for descriptive and inferential statistics. **Results:** Two hundred and forty-nine providers (167 PCPs, 82 cardiologists) participated in the study with a response rate of 18.8% (249/1320). Respondent mean years  $\pm$  SD of experience since completing residency was  $23.2 \pm 13.8$ . Relative to cardiologists, less PCPs use CHADsVASC (36.8% vs. 74.4%) ( $p < 0.0001$ ); more have never used HAS-BLED, HEMORR2HAGES, or ATRIA (38.5% vs. 9.8%) ( $p < .0001$ ); more felt that their lack of knowledge/experience with DOACs was a barrier to prescribing the agents ( $p = 0.005$ ); and more reported that they could use additional education on DOACs (87.0% vs. 47.0%) ( $p < 0.0001$ ). Overall, cardiologists were more concerned about ischemic stroke outcomes, while PCPs were more concerned with GI bleeding. Cardiologists also felt that clinical trial data were most helpful in choosing the most appropriate DOAC for their patients, while PCPs felt that Real World Data was most useful. **Conclusions:** Cardiologists were more concerned with ischemic stroke while anticoagulating patients and utilized screening instruments like CHADsVASC in a majority of their patients. PCPs were concerned with GI bleeds when anticoagulating but nearly 40.0% utilized no screening tools to assess bleeding risk. Our findings show that future education about DOACs would be warranted especially with PCPs.

## Keywords

anticoagulants, atrial fibrillation, cardiology

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## Introduction

In 2010, atrial fibrillation (AF) affected an estimated 2.7 million to 6.1 million persons in the United States, and for the year 2030 this figure is projected to reach 21.1 million.<sup>1-3</sup> As demonstrated by the American Heart Association's 2017 Heart

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Disease and Stroke Statistics, AF is a major risk factor for stroke, increasing the risk by almost 5-fold across all ages.<sup>1,4</sup> Reasons for the projected increase in atrial fibrillation rates may be multifactorial involving increasing advanced age, BMI, cardiac disease history and tobacco use.<sup>1</sup> Stroke risk can be reduced by approximately 60.0% with dose-adjusted warfarin.<sup>3</sup> Guidelines from several medical societies recommend anticoagulating AF patients unless they are at very low risk for stroke.<sup>5,6,7</sup> Furthermore, the rate of anticoagulation for AF patients is a National Quality Forum-endorsed quality measure.<sup>8</sup>

Among the most prevalent subtypes of AF is Nonvalvular Atrial Fibrillation (NVAF), defined as cases in which the supraventricular tachyarrhythmia occurs in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or a mitral valve repair.<sup>6</sup> For cases of NVAF, direct oral anticoagulants (DOACs) have overall demonstrated noninferiority to, or in certain cases even superiority over, vitamin K inhibitors such as warfarin for reducing the risk of stroke and systemic thromboembolism<sup>9-12</sup> all while lowering the bleeding risk. Compared to warfarin, DOACs have also been demonstrated to be more effective with preventing stroke.<sup>13</sup>

Despite anticoagulation recommendations, the availability of DOACs, and the fact that undertreating AF results in thousands of preventable ischemic strokes in the U.S. each year, roughly 30.0-60.0% of AF patients do not receive indicated anticoagulation.<sup>14-17</sup> A recent qualitative study<sup>18</sup> of physician attitudes toward DOACs identified 4 themes that may help explain why under-treatment is so prevalent. First, the likelihood of physicians prescribing DOACs depends upon their willingness to try new medications and their successful experience with them. Second, while physicians typically balance the benefits and risks of anticoagulation in AF patients, they do not always do so accurately. Third, when considering anticoagulation, patient convenience and preference as well as physician convenience are important decision-making variables. Finally, higher out-of-pocket cost for DOACs deter many physicians from prescribing them.<sup>18</sup>

In follow up to the aforementioned qualitative study, Bauer et al surveyed<sup>19</sup> primary care physicians (PCPs) and cardiologists at a community-based integrated health system and identified among PCPs several barriers to prescribing DOACs. The primary findings were that compared to cardiologists, PCPs cared for fewer patients with AF, were less likely to initiate DOACs for patients with newly diagnosed AF, and were more likely to report lacking knowledge about this class of pharmacotherapy (manuscript pending).<sup>19</sup> To determine whether these findings could be reproduced in a larger, more representative sample, we surveyed PCPs and cardiologists nationwide on their attitudes, knowledge, and practices with respect to their use of DOACs for the management of AF.

## Methods

### Study Design

We conducted a cross-sectional survey of PCPs and cardiologists by mailing a paper based, self-administered scannable

survey to obtain data on key demographics and on attitudes, knowledge and practices related to DOAC prescription practices for NVAF.

Participants were enrolled under an IRB approval waiver of HIPAA and consent.

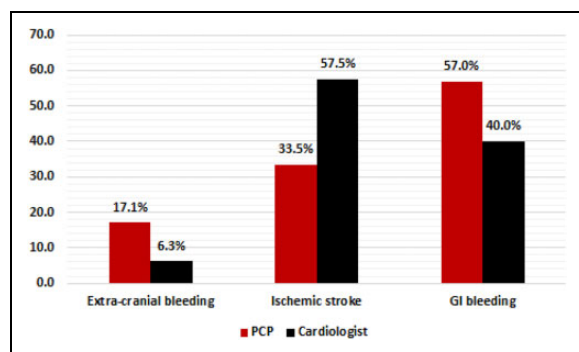
### Setting, Survey and Data Collection

We obtained a list of names and addresses for 1400 PCPs and 700 cardiologists from the American Medical Association (AMA) Physician Masterfile. The providers listed in the Masterfile came from diverse backgrounds, durations in practice and US geographies. We randomly sampled from the file 500 cardiologists (including subspecialists) and 1000 primary care physicians to whom we mailed a survey with anticipated response rate of 30.0-40.0%. Of the 1,500 surveys sent out, with a cover letter explaining the survey and a self-addressed stamped return envelope 80 were returned unopened due to wrong address and 100 surveys that were unreturned/lost to follow-up.

In the fall/winter of 2017-8, we mailed surveys to 1,000 PCPs and 500 cardiologists selected randomly, along with a \$10 incentive gift card. The survey contained questions on key demographics and physician attitudes, knowledge and practices related to prescribing DOACs.

The survey data collection period included 3 waves of mailings. The envelope had a code number on it to determine which physician responded. For physicians who didn't respond to the prior wave of mail, we sent a second and—as necessary—third follow up wave of mailings. Wave 1 surveys included a ten-dollar (\$10) Amazon Gift Card as an incentive to complete the survey. If mailings were returned unopened or undeliverable, then within the affected specialty, the next random name of either a PCP or a cardiologist was selected to be the addressee of the next mailed survey. All survey responses were forwarded by the NorthShore University HealthSystem (NSUHS) research team to the study sponsor (Pfizer), and were scanned by administrative personnel using the Teleforms© version 10.7. This generated an Excel database containing survey responses that was transferred to NSUHS via secure File Transfer Protocol electronic means for analysis.

The survey sought information on provider demographics and knowledge via questions from the Pfizer "Assessment of Provider Knowledge and Therapeutic Approaches for Reducing Stroke Risk in Patients with Nonvalvular Atrial Fibrillation."<sup>20</sup> Additional questions covered the domains of attitudes, knowledge, and practice pertaining to anticoagulation management of patients with NVAF. Attitude questions explored the likelihood of using various pharmacologic therapies; knowledge questions explored the physician's knowledge of safety, efficacy, and side effects for each approved DOAC; and practice questions sought provider estimates for the number of NVAF patients receiving care, including the number of patients on pharmacotherapy with each of the 4 DOACs and warfarin. These items were based on questions from Bauer et al.'s recent survey of PCPs and cardiologists conducted across NSUHS.<sup>19</sup> Neither the survey nor the analytics database



**Figure 1.** Anticoagulation outcomes\* that worry physicians the most. (\*Intracranial bleeds were omitted).

contained physician identifier information. Instead, only the person responsible for study mailings had access to respondent names and code numbers.

### Data Analysis

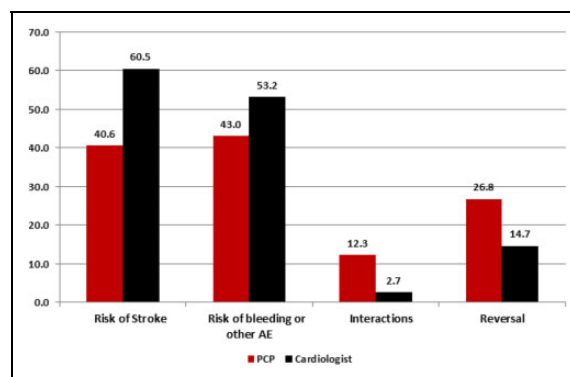
In collaboration with a biostatistician, the principal investigator generated descriptive statistics from survey responses in preparation for further analysis. Survey responses were analyzed using SAS 9.3 (Cary, NC). The descriptive statistics summarized physician responses to attitude, knowledge and practice items. For the statistical analysis, survey responses were tested for differences between PCPs and cardiologists. This between-group comparison was done using chi-square tests for categorical and ordinal variables. Ordinal variables were further analyzed with Wilcoxon Rank-Sum tests, while continuous variables were analyzed with independent samples t-tests. Statistical significance was defined as a p-value < .05. All analyses were conducted using SAS9.3 (SAS Institute, Cary, NC)

### Results

Two hundred forty-nine physicians (167 PCPs, 82 cardiologists) participated in the study, yielding a survey response rate of 18.8% (249 out of 1320 surveyed). Of the 167 PCPs, 58.1% were family medicine physicians and 31.7% were internal medicine physicians (the remaining 10.0% were geriatricians and other). Of the 82 cardiologists, 82.9% were general cardiologists. Among all physicians, the mean time elapsed since completing residency was  $23.2 \pm 13.8$  years (mean  $\pm$  SD). Stratified by specialty, these figures were  $24.1 \pm 14.5$  years for PCPs and  $21.6 \pm 12.2$  years for cardiologists.

The potential outcome that PCPs weighed and worried about the most when considering whether to anticoagulate NVAf patients was GI bleeding (57.0%), followed by ischemic stroke (33.5%) and extra-cranial bleeding (17.1%). For cardiologists, by contrast, these figures were ischemic stroke (57.5%) (p-value 0.0005), followed by GI bleeding (40.0%) (p-value 0.0141) and extra-cranial bleeding (6.3%) (p-value 0.0258) (Figure 1).

The 4 most common factors influencing specialist choice of anticoagulation for NVAf were as follows: the risk of ischemic



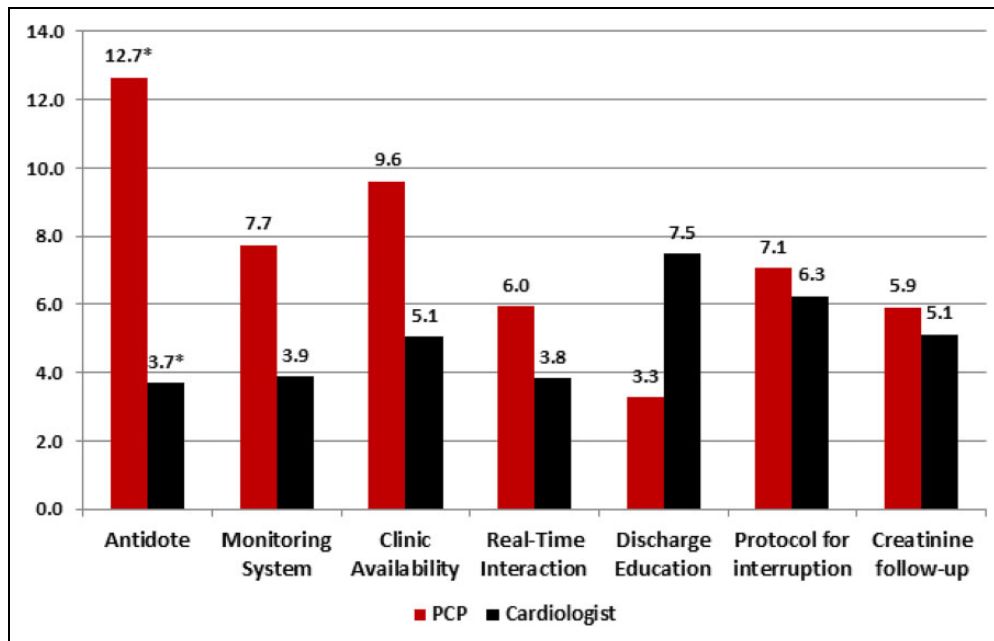
**Figure 2.** The 4 most common factors influencing physician choice of anticoagulation for NVAf. Risk of stroke is significantly different between PCPs and cardiologists (41.0% vs 60.0%, p-value 0.0041). And there was a difference between interactions with other medications—PCPs 12.0% vs cardiologists 3.0%, p-value 0.0403).

stroke (40.6% of PCPs, 60.5% of cardiologists, p-value 0.0041); the risk of bleeding or other medication-related adverse events (43.0% of PCPs, 53.2% of cardiologists, p-value 0.16) and the ability to reverse anticoagulation (26.8% of PCPs, 14.7% of cardiologists, p-value 0.0403) (Figure 2).

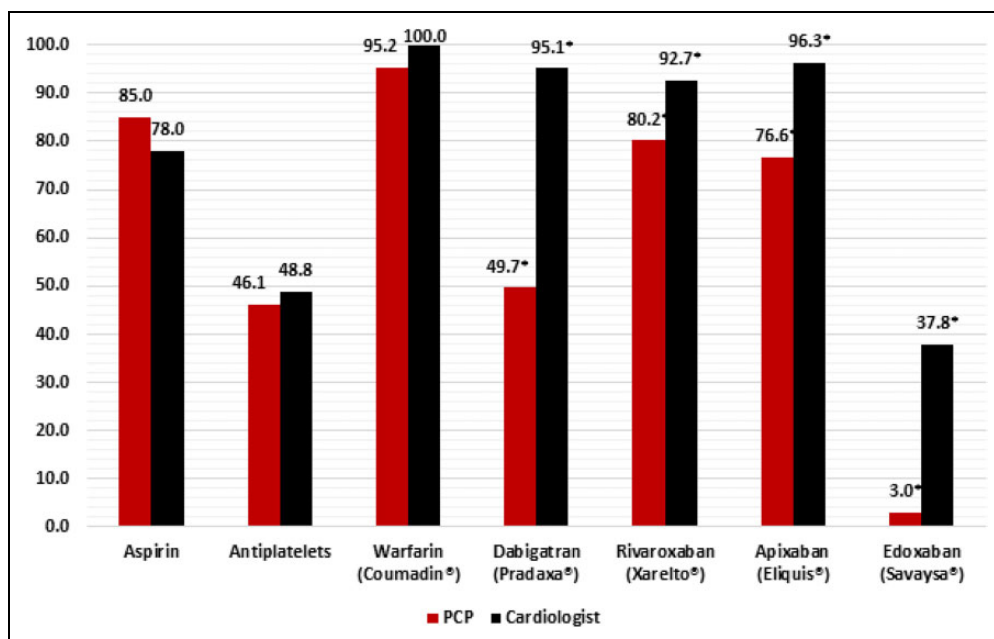
When considering DOAC management and prescriptions, 12.7% of PCPs prioritized the availability of an antidote, which was significantly more than the 3.7% percent of cardiologists prioritizing an antidote (p-value 0.0263). By contrast, 7.5% of cardiologists prioritized discharge education, which was less than the 3.3% of the PCPs prioritizing this item; while a potentially clinically significant difference, this was not a statistically significant difference. Figure 3 plots the frequency across these specialties for other, lower within-specialty priority categories.

When assessing the risk of stroke and bleeding among NVAf patients, the CHA2DS2-VASc risk stratification system was reported as always being used by 36.8% of PCPs and by 74.4% of the cardiologists. It was reported as never used by 24.3% of PCPs and by only 1.2% of the cardiologists. When assessing bleeding risk, the frequency distributions for reportedly using the HAS-BLED classification system were as follows: always used by 23.6% of PCPs and by 21.8% of the cardiologists. Never used by 42.9% of PCPs and by 10.3% of cardiologists.

When reflecting on their historical use of oral anticoagulants for the management of NVAf, statistically significant within-DOAC differences existed between the 2 specialties for Dabigatran at 48.7% (n = 83) for PCPs and 95.1% (n = 78) for cardiologists (p value < 0.0001); for Rivaroxaban at 80.2% (n = 134) for PCPs and 92.7% (n = 76) for cardiologists (p-value 0.0149); for Apixaban at 76.6% (n = 128) for PCPs and 96.3% (n = 79) for cardiologists (p-value < 0.0001); and for Edoxaban at 3% (n = 5) for PCPs and 37.8% (n = 31) for cardiologists (p-value < 0.0001). These differences achieved near statistical significance for warfarin at 95.2% (n = 159) for PCPs and 100% (n = 82) for cardiologists (p-value 0.0556). No significant differences existed between specialties for



**Figure 3.** Importance of treatment parameters when considering DOAC use.



**Figure 4.** Medications prescribed for a patient with NVAf. More cardiologists prescribed Dabigatran, Rivaroxaban, Apixaban, and Edoxaban than PCPs.

treating with aspirin and other antiplatelet agents, being prescribed for NVAf by 85.0% ( $n = 42$ ) of PCPs and 78.0% ( $n = 64$ ) of cardiologists ( $p$ -value 0.2115). (Figure 4.)

When assessing the most appropriate type of information to guide their choice of DOAC, the majority of responses for both PCPs (65.1%) and cardiologists (44.2%) favored real world data ( $p$ -value 0.0042). Phase III clinical trial data were cited as another helpful criteria by 8.3% of PCPs and 32.5% of cardiologists ( $p$ -value  $< 0.0001$ ). For choosing the most

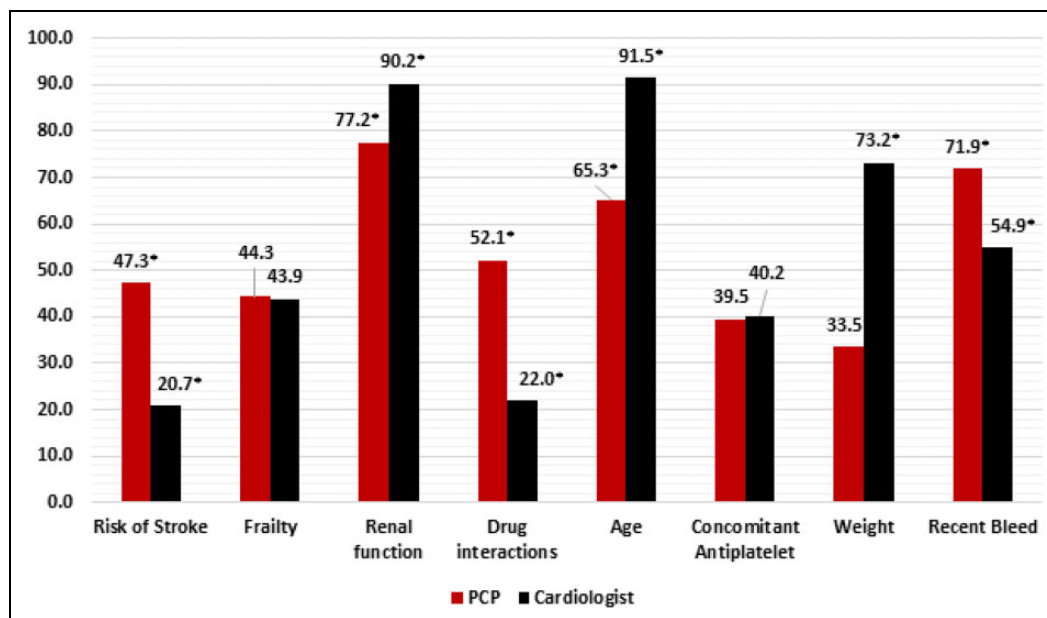
appropriate DOAC, information on patient adherence was ranked the least helpful factor by 27.3% of PCPs and 41.3% of cardiologists ( $p$ -value 0.0467) (Figure 5).

A lack of knowledge or experience with a medication was identified as a barrier to recommending or attempting to prescribe a DOAC for 11.7% of PCPs ( $n = 19$ ) and only 1.2% of cardiologists ( $n = 1$ ,  $p$ -value 0.0050)

While reflecting on the dosing of DOACs, the following were selected as key factors influencing their decision to use a reduced

	% Most Useful		% Least Useful	
	PCP	Cardiologist	PCP	Cardiologist
Phase III Trial	8.3	32.5	24.1	13.0
Subgroups from Trial	2.1	9.1	25.7	14.3
Real World Data	65.1	44.2	1.4	0.0
Safety/Efficacy for Dosages	18.5	20.3	1.4	8.1
Cost and Coverage	13.8	11.8	8.3	14.5
Patient Adherence	4.9	2.7	27.3	41.3

**Figure 5.** DOAC medication characteristics considered by providers. Cardiologists and PCPs ranked real world data as most useful, and patient adherence as least useful.

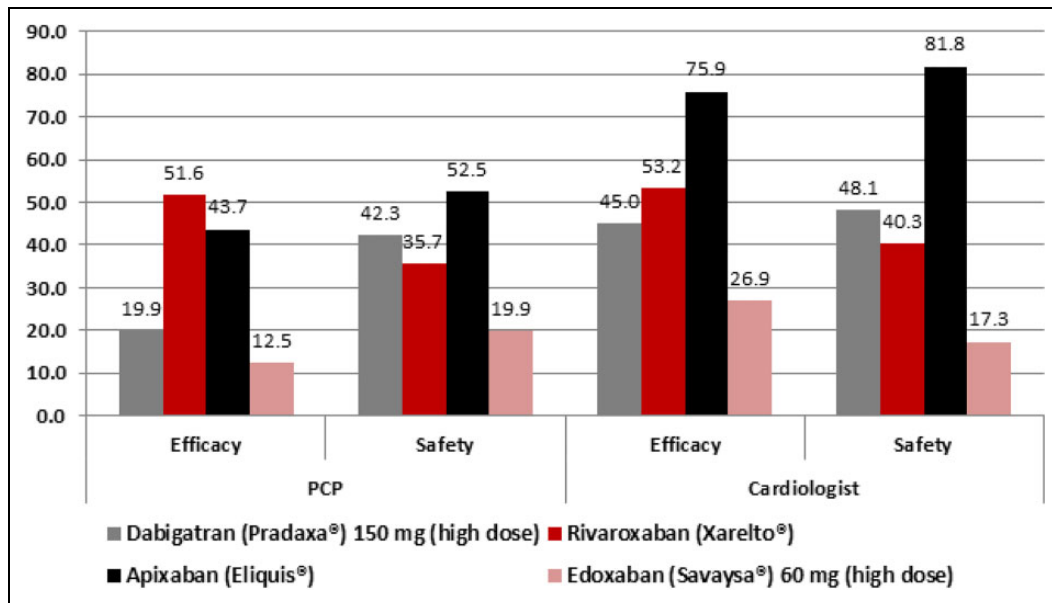


**Figure 6.** Patient factors considered when using a DOAC.

dose: A low risk of stroke, cited by 47.3% of PCPs ( $n = 79$ ) and 20.7% of cardiologists ( $n = 17$ ) ( $p$ -value  $< 0.0001$ ); reduced renal function, cited by 77.2% ( $n = 129$ ) of PCPs and 90.2% of cardiologists ( $n = 74$ ) ( $p$ -value 0.0146); The potential for drug-drug interactions, cited by 52.1% of PCPs ( $n = 87$ ) and by 22% of cardiologists ( $n = 18$ ) ( $p$ -value  $< 0.0001$ ); patient age, cited by 65.3% of PCPs ( $n = 109$ ) and 91.5% of cardiologists ( $n = 75$ ) ( $p$ -value  $< 0.0001$ ); patient weight, cited by 33.5% of PCPs ( $n = 56$ ) and 73.2% of cardiologists ( $n = 60$ ) ( $p$ -value  $< 0.0001$ ); and a history of recent bleed, cited by 71.9% of PCPs ( $n = 120$ ) and by 54.9% of cardiologists ( $n = 45$ ,  $p$ -value 0.0101) (Figure 6).

When asked to reflect on how efficacy and safety outcomes from phase III clinical trials comparing each DOAC to warfarin impacted their choice of anticoagulation, the survey

demonstrated the following: For Dabigatran, 19.9% of PCPs and 45.0% of cardiologists cited the DOAC as being more efficacious than warfarin for the composite outcome of stroke and systemic embolism ( $p$ -value 0.0001). For Rivaroxaban, 51.6% of PCPs and 53.2% of cardiologists reported equal efficacy to warfarin ( $p$ -value 0.81). For Apixaban, 43.7% of PCPs and 75.9% of cardiologists reported greater efficacy than warfarin ( $p$ -value  $< 0.0001$ ). For Edoxaban, 12.5% of PCPs and 26.9% of cardiologists reported greater efficacy than warfarin ( $p$ -value 0.0063). Finally, regarding DOAC safety in phase III clinical trials, 52.5% of PCPs and 81.8% of cardiologists believe that Apixaban is safer than warfarin, considering the rate of major bleeding ( $p$ -value  $< 0.0001$ ) (Figure 7).



**Figure 7.** Physician responses regarding DOAC knowledge compared to warfarin based on clinical trial data. Cardiologists are aware of the high efficacy and improved safety of DOACs when compared to warfarin.<sup>21-24</sup>

These responses were compared to the inferences drawn from each DOAC's landmark phase III trial. When respondent opinions and study inferences were concordant, we classified the response as correct. When the 2 were discordant, we classified these responses as incorrect. Figure 7 demonstrates the distributions of correct responses; as noted in the figure, the frequency of responses recorded for other DOACs were not statistically significant.

Finally, receiving more education on direct oral anticoagulants was reported as something that could be useful by 87.0% of PCPs (n = 140) and 46.8% of cardiologists (n = 37) (p-value < 0.0001).

## Discussion

Our study reveals key differences between PCPs' and cardiologists (82.9% general cardiologists)' knowledge, practices and attitudes on anticoagulation for NVAf, specifically when concerning 1) factors and outcomes influencing decision on type of anticoagulation, 2) the use of stroke risk and bleeding risk tools to calculate risk of concerning outcomes, 3) clinical attitudes when considering DOACs, 4) knowledge of DOACs efficacy and safety clinical trial data, and 5) educational needs to enhance DOACs knowledge.

AF is a major risk factor for stroke that can be mitigated with anticoagulation.<sup>1,4</sup> Given that a shocking 30.0-60.0% of patients with AF do not receive anticoagulation when indicated, it is critical to understand which factors influence a physician's decision to anticoagulate patients. It is also important to understand which factors influence a provider's choice of oral anticoagulant. To that end, our study shows that when selecting anticoagulation for NVAf, PCPs had greater concern with the anticoagulant's reversibility, while cardiologists

where more concerned with the risk of stroke. With regard to anti-coagulation outcomes—and after setting aside the possibility of intracranial bleeds—cardiologists remained greatly concerned with strokes (ischemic), while PCPs were more concerned with extra-cranial and GI bleeds. These findings are consistent with those of prior studies which cite bleeding risk as the most common reason for not anticoagulating AF patients.<sup>25</sup> This presents a complex dilemma as risk factors for stroke often accompany risk factors for bleeding.<sup>26</sup>

Current evidence based guidelines for stroke prophylaxis in NVAf patients suggest balancing the risk of bleeding with benefits of stroke prevention when considering anticoagulation therapy.<sup>27</sup> While numerous risk assessment tools exist, guidelines recommend using CHA2DS2-VASc for assessing stroke risk and HAS-BLED to assess bleeding risk. Per our study's data, cardiologists—but not PCPs—reported always assessing the risk of stroke with the CHA2DS2-VASc scoring system. An interesting finding our study is that while the majority of PCPs report concerns over bleeding, a significant portion of them reported never having used the HAS-BLED risk scoring system. Despite the predictive accuracy of bleeding risk assessment tools being limited,<sup>28</sup> the HAS-BLED score system is preferable since being validated in multiple cohorts.<sup>29</sup> Its important to note, however, that a HAS-BLED score has yet to be validated for populations using DOACs.<sup>30</sup> This validation would be particularly valuable in light of the increased adoption of DOACs that is attributed largely to a more favorable bleeding profile relative to warfarin.<sup>31</sup>

In recent years, there has been an increase in the adoption of DOACs,<sup>32,33</sup> a trend that is attributed not only to this drug class' favorable bleeding profile but also due to its simple dosing regimen and the lack of monitoring requirement, all while maintaining efficacy.<sup>9,10,11,12,13,14</sup> Our study demonstrates an overall trend



for increased adoption of DOACs, a trend that is more notable among cardiologists as supposed to PCPs. This could be driven in part by the fact that PCPs are more likely to be concerned about whether or not an antidote is available. While this has historically been considered to be the biggest drawback of DOACs,<sup>34</sup> a recently FDA-approved antidote should alleviate some of these concerns going forward.<sup>34,35</sup>

As previously described, a barrier to PCPs prescribing DOACs is a lack of knowledge about this class of pharmacotherapy.<sup>18</sup> That being said, among useful types of information when evaluating DOACs, most PCPs pointed to real world data while cardiologists reported that phase III clinical trial data are more useful. Relative to cardiologists, PCPs were less aware of the improved efficacy of Apixaban and Dabigatran when compared to warfarin for the composite of stroke (ischemic & hemorrhagic) and systemic embolism.<sup>9,11,12</sup>

Relative to PCPs, cardiologists had greater knowledge of safety outcomes, specifically as pertains to lower rates of major bleeding with Apixaban when compared to warfarin.<sup>11</sup> These differences may stem from the many barriers PCPs face toward adopting evidence based practice<sup>36,37</sup> and guidelines, particularly as pertains to the underutilization of DOACs for eligible patients.<sup>27,38,39</sup> The barriers can range from relevance of research to practice, lack of time, staying informed of rapidly evolving data and limited ability to search for critically appraised evidence-based information.

A recent study has shown that multilevel educational interventions can increase provider awareness of current guidelines and improve the adoption of oral anticoagulation for atrial fibrillation.<sup>39</sup> Our study supports the broader use of such interventions, specifically because of the considerable number of PCPs who reported that they could use more education on DOACs. While numerous online education resources and webinar teaching sessions exist, our survey suggests that a greater number of physicians prefer live, independent medication education and print material as a way to enhance their knowledge.

Overall, our study exposed critical differences between PCPs and cardiologists in terms of their evaluating NVAF patients for anticoagulation and their having appropriate knowledge and experience with DOACs. Such discrepancies could have emerged from a disparity in awareness rather than differences in outlook or preference. Our data suggest that future directives to resolve these differences with targeted educational programs and to improve adherence to evidence based guidelines among PCPs may be imperative.

## Limitation

The physician response rate for our study was 18.8%, which was lower than the anticipated rate of 30-40% based on our institutions prior experience and mean physician response rate of 54% from mail surveys published in medical journals.<sup>40</sup>

## Conclusion

Significant differences exist between PCPs and cardiologists in their knowledge, practices and attitudes concerning the anticoagulation of NVAF patients. We found that cardiologists are most concerned with ischemic stroke when choosing the most appropriate DOAC for patients with atrial fibrillation. They utilize stroke risk screening tools such as CHA2DS2-VASc in a majority of patients. Cardiologists believe phase III trial and real world data are useful for choosing DOACs, but rely on Phase III data more often than PCPs. When prescribing anticoagulants for patients with atrial fibrillation, PCPs are most concerned with GI bleeds, yet nearly 40.0% of PCPs have never used the HAS-BLED bleeding risk screening tool. PCPs feel their lack of experience with DOACs is a barrier for not prescribing these agents and that they are less knowledgeable about phase III clinical trial data on DOAC efficacy and safety relative to that of warfarin, thereby feeling that further education is necessary.

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## Declaration of Conflicting Interests


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## Research Ethics

Ethics approval was obtained from the Institutional Review Board (IRB) of NorthShore University HealthSystem (IRB # EH17-334) on November 28, 2017.

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