

## The Role Of NOACs in Atrial Fibrillation Management: A Qualitative Study

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### Abstract

Patients with atrial fibrillation (AF) benefit from anticoagulation to reduce stroke risk. However, 30-60% of patients with AF are not anticoagulated. This study explored physicians' reasons for under-treatment of AF, focusing on the role of the novel oral anticoagulants (NOACs). We interviewed primary care physicians and cardiologists involved in AF management in a variety of practice settings. We conducted interviews using a semi-structured format and analyzed the data using the Framework Method. Four themes emerged. First, the likelihood of physicians to prescribe NOACs depends upon their willingness to try new medications and their successful experience with them. Second, physicians typically balance the benefits and risks of anticoagulation in AF patients, although not always accurately. Third, patient convenience and preferences, as well as physician convenience, are important when considering anticoagulation. Finally, concerns regarding the out-of-pocket cost of NOACs deter many physicians from prescribing them. The persistence of under-treatment in AF despite the availability of effective therapies suggests that new strategies are needed to improve physician knowledge and practice. These strategies should enhance physician awareness of AF under-treatment, emphasize accurate assessment of bleeding risk among AF patients, compare the safety, efficacy, and convenience of NOACs relative to warfarin, and address physician concerns regarding the out-of-pocket cost of NOACs. Guidelines and decision supports which promote physician knowledge in these areas have the potential to increase oral anticoagulant use and reduce preventable morbidity and mortality.

### Introduction

Atrial fibrillation (AF) affects 2.3 million Americans, and is associated with a five-fold increase in the risk of stroke.<sup>1,2</sup> This risk can be reduced by 64% with use of an oral anticoagulant such as warfarin.<sup>3</sup> Guidelines from several organizations recommend anticoagulation for all AF patients except those at very low risk for stroke.<sup>4,5</sup> Furthermore, the rate of anticoagulation of AF patients is a quality measure endorsed by the National Quality Forum.<sup>6</sup> Despite these recommendations, 30-60% of patients with AF do not receive anticoagulation when it is indicated. Under-treatment of AF results in thousands of preventable ischemic strokes in the U.S. each year.<sup>7,8,9,10</sup> Under-treatment specifically by family physicians has been

documented.<sup>11</sup>

Within the past five years, the FDA approved four novel oral anticoagulants (NOACs) for AF treatment: dabigatran, rivaroxaban, apixaban, and edoxaban.<sup>12,13,14,15</sup> These agents offer several advantages over warfarin, including straightforward dosing regimens, no requirement for monitoring, and lower risk of intracranial hemorrhage.<sup>11,12,13,14</sup> Given these advantages, rapid adoption of NOACs might be expected to alleviate the AF under-treatment problem. Though NOACs are being rapidly adopted for new AF patients, under-treatment remains a serious challenge.<sup>16,17,18</sup>

In an effort to address this gap in the quality of AF care, comprehensive educational programs for AF patients are being rolled out. Perhaps the best-known effort is the American Heart Association's Get With the Guidelines-AFIB program which has been introduced to assist hospitals with registry building and other AF-related performance improvement activities.<sup>19</sup> However, these programs address NOACs and warfarin together as equivalent treatment options without recognizing that NOACs could play a different role from warfarin in AF management. Currently, little information is available regarding physicians' opinions of NOACs and their role in AF management. Because such knowledge is needed to inform the development of AF educational programs for family physicians and other primary care physicians as well as specialists,

### Key Words:

Atrial Fibrillation, Anticoagulation, NOACs.

### Disclosures:

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we conducted a qualitative study of physicians' decision-making processes regarding anticoagulation management in AF, with a specific focus on the role of NOACs.

## Material And Methods

### Study Design

To address the many unanswered questions about physician knowledge, attitudes, and practices regarding NOAC use, we chose a qualitative study design which facilitated exploration of a broad range of perspectives. Specifically, we used the Framework Method of qualitative analysis,<sup>20</sup> which permitted us to integrate newly discovered concepts into existing conceptual frameworks. The study design was approved by the NorthShore University HealthSystem institutional review board.

### Sampling, Recruitment, And Data Collection

Purposive sampling was used. A list of potential participants was assembled from the extended professional networks of the primary author and co-authors. Physicians were then recruited with the goal of including participants from a range of specialties (family medicine, internal medicine, cardiology, and electrophysiology), experience levels, and practice settings. Written informed consent was obtained prior to each interview. Recruitment concluded when thematic saturation was achieved.

A semi-structured interview guide (Table 1) was developed based on a review of the oral anticoagulation literature. The guide provided an overall structure to the interviews. Questions were open-ended with follow-up questions prompted by participants' responses. Participants were free to introduce and discuss points not outlined in the guide. Individual interviews were conducted by the primary author (KK). The interviews were digitally recorded and professionally transcribed.

### Data Analysis

Implementation of the Framework Method began with data familiarization; the primary author (KK) and co-authors (GR and CM) read each transcript and made notes of initial impressions. Each author developed a potential list of codes, then met to develop an initial consensus code list. Each transcript was then re-read and independently coded by two authors. The authors met to iteratively perform comparative coding to refine the code list according to patterns that emerged from re-reading and discussing the transcripts. The codes were grouped and organized into an analytic framework in the form of themes and sub-themes. The transcript data were

indexed according to this framework using NVivo 10 software (QSR International, Doncaster, Australia). Indexed data were organized into a framework matrix, which was reviewed by all authors and used to develop final interpretations of the data.

## Results

### Participants

Interviews were conducted with seven physicians (five men and two women). Three were family physicians, one was an internist, two were cardiologists, and one was a cardiologist sub-specializing in electrophysiology. Participants' practice settings included community private practice, community residency practice, and academic practice at a tertiary care center.

### Themes

Themes that emerged from our interviews were grouped into four categories: the impact of knowledge and experience on prescribing practices, methods used to weigh risks and benefits of anticoagulation, medication barriers and facilitators, and the high cost of NOACs.

#### *Theme 1: Knowledge and Experience Influence Prescribing*

Knowledge regarding the safety and efficacy of oral anticoagulants, as well as experience prescribing them, were clear practice drivers. Table 2. Several primary care physicians indicated they were less familiar with NOACs compared to warfarin and were therefore less likely to prescribe NOACs. They also expressed a willingness to defer to the recommendations of cardiologists regarding initiation of NOACs. When asked about this, one PCP said, "I think a lot of us will send them to cardiology." On the other hand, some of the PCPs and all of the cardiologists were comfortable prescribing NOACs and this typically reflected the extent of their experience with these medications. Referring to his colleagues, one cardiologist said, "They've started to become very comfortable with these novel agents."

Related to knowledge, an important sub-theme was anxiety related to novelty. Newness of medications was viewed by many as inherently negative, and novel medications were considered more likely to be associated with unforeseen adverse events. Some physicians questioned the quality of evidence used to support the use of NOACs. Other physicians reported hesitancy prescribing NOACs due to concerns regarding clinical trial methodology and the FDA approval process, which some viewed as hasty: "I think the United States is very aggressive [in bringing] new medications to market."

Prior experience with new medications influenced current prescribing practices both negatively and positively. For example, one participant said, "I have been burned with enough medications

**Table 1: Semi-structured interview guide**

Opening statement: Thank you for meeting with me to discuss anticoagulation in atrial fibrillation.
1. Describe your practice and your patient population.
2. Do you manage patients with atrial fibrillation frequently?
3. When you consider whether or not to prescribe a medication for a patient, what factors influence your decision?
4. When you manage patients with atrial fibrillation, how do you go about deciding whether or not to anticoagulate?
5. Please tell me what you know about the novel oral anticoagulants, also known as NOACs.
6. What are your colleagues saying about NOACs?
7. Can you describe an example of a patient for whom you prescribed a NOAC?
8. What are your impressions regarding the benefits of NOACs compared to warfarin?
9. What are your impressions regarding the risks of the NOACs compared to warfarin?
10. Is there anything else about NOACs or atrial fibrillation you would like to share with me?

**Table 2: Example Quotes Describing Physician Experience and Knowledge**

Anxiety around novelty (risk aversion, reliability of new evidence) "Not a first user. Cause I want to see what plays out. ....a wise man, physician, once told me, don't be the first or the last to prescribe new medication." "And, and I think, honestly that's a, that's a pretty good approach (to be risk averse) for a physician in general." "I think the United States is very aggressive (in bringing) new medications to market." "The good thing about a lot of the new medications especially in cardiology is that they've gone through these mega-trials. It's very hard to get a cardiovascular medication approved without, you know, a ten thousand patient trial."
Prior Negative Experiences "I have been burned with enough medications that have gone off the market."
Familiarity, comfort level "So I have a handful [of medications] that I'm just used to prescribing..... Although I'm sure if I read about other ones, if I actually looked into other ones, I'd like other ones better." "It requires understanding, learning these medications, talking with people who had more experience with them, and then kind of going out on that ledge of starting a new medication you may not have learned about during your training."

that have gone off the market.” On the other hand, physicians with successful experience prescribing NOACs were more likely to continue prescribing them: “All you have to do is write a prescription and counsel the patient. It’s so easy to start these medications.”

### *Theme 2: Formal and Informal Methods Used to Weigh Risks and Benefits*

Balancing the benefits and risks of oral anticoagulation is critical when deciding how to manage patients with AF. Table 3. Participants typically reported that their first step in this calculation was estimating the patient’s risk of stroke, usually with the CHADS<sub>2</sub> or CHA<sub>2</sub>DS<sub>2</sub>-VASc calculators. All physicians reported using at least one of these calculators when considering benefits of OACs. Participants then discussed their methods for estimating bleeding risk. A variety of approaches was described, with most physicians making informal assessments based on past medical history and co-morbidities: “You have patients with chronic renal disease where their platelets don’t work well and they’re gonna be more of a bleeding risk, and you know, a host of things – underlying liver disease.” Concerns about fall risk were significant and often tilted the balance against warfarin or NOACs: “If someone has fallen multiple times, even if they haven’t bled from the fall and nothing bad has happened, I will just switch them to aspirin usually.” Only one physician reported using the HAS-BLED score or any other formal strategy to estimate bleeding risk.

Additional factors were important when calculating the benefit/risk estimate. For example, participants often assumed that the bleeding risk in elderly patients outweighed the benefits of anticoagulation. Referring to older patients, one PCP said, “We think they’ve got lots of comorbidities, we think they’re likely to bleed, and therefore we don’t try to put them on an anticoagulant.” However, a cardiologist who frequently prescribed OACs noted that older patients may benefit more from OACs than younger patients, who tend to have fewer comorbidities and a lower stroke risk.

Characteristics of the various anticoagulants were important in deciding whether to anticoagulate and which agent to use. Medication side effects were mentioned by many physicians. The irreversibility of the NOACs was a concern for some physicians, and the majority felt that the reversibility of warfarin was one of the few benefits that it offered in comparison to NOACs: “I think that the biggest thing that everybody, myself included, is [concerned about is] that there’s no antidote [for NOACs].”

When comparing efficacy of stroke prevention, physicians indicated

**Table 3: Example Quotes Describing Clinical Benefits and Risks**

#### Risk of stroke

“Our practice tends to be to anticoagulate anybody without a contraindication with a CHADS<sub>2</sub>/VASc of 1 or greater”

#### Risk of bleeding

“If someone has fallen multiple times, even if they haven’t bled from the fall and nothing bad has happened, I will just switch them to aspirin usually.”

“You have patients with chronic renal disease where their platelets don’t work well and they’re gonna be more of a bleeding risk, and you know, a host of things - underlying liver disease.”

#### Benefit/Risk assessment

“If you look in their old records and someone fell like two times this year, but their CHADS<sub>2</sub> score says that they should be anticoagulated, then I would think long and hard about doing that.”

“The patients that are aged eighty-five and older tend to be the lowest percentage of patients that are given Coumadin. And that’s because you see somebody frail and you think they’re gonna bleed and you don’t prescribe them. But they are actually the people who benefit the most.”

#### Risks of NOACs

“I think that the biggest thing that everybody, myself included, is [concerned about is] that there’s no antidote [for NOACs].”

NOACs were at least as efficacious as warfarin. A few were skeptical that any NOAC was substantially better than warfarin, while others felt that the reported increased efficacies of apixaban and dabigatran were meaningful.

### *Theme 3: Important Barriers and Facilitators Related to Anticoagulation and Anticoagulant Choice*

Several barriers and facilitators were described as important when deciding whether to start an oral anticoagulant and which OAC to use. Table 4. An important sub-theme concerned the frequent laboratory monitoring associated with warfarin: “It [is] very time consuming. That’s probably the one thing that soured me on warfarin.” However, almost all participants reported utilizing anticoagulation clinics, which significantly reduced their personal burden of managing warfarin and increased their willingness to prescribe it. The lack of need to monitor NOACs was very appealing and the majority of participants commented that it was the best feature of the NOACs: “I think the biggest [benefit] is the ease of use, where you don’t have to monitor.”

Convenience for the patient was also important to physicians, who believed that most patients found laboratory monitoring troublesome, particularly at the time of warfarin initiation. Some expressed concern that the need for frequent testing contributes to medication non-adherence and may increase the risk of stroke. One physician said, “I have people who are like, ‘I don’t want to be on [warfarin]’” while another said, “If someone was not carefully weighing it, one could say, ‘Oh, I don’t want that.’ And that would feel easier in the moment but that might not be the best outcome.”

Patient preferences and pre-conceived ideas were commonly described as both barriers and facilitators of OAC use. Physicians reported frequently encountering resistance from patients when recommending an oral anticoagulant. Patients’ concerns were sometimes viewed as legitimate (i.e. concerns about bleeding risk or side effects), and sometimes viewed as unrealistic or irrational (i.e. anecdotes about acquaintances’ experiences or general aversion to medications). On the other hand, multiple physicians reported patients requesting a NOAC after viewing television commercials. Some patients had positive impressions of oral anticoagulants based on acquaintances’ experiences, and were therefore more open to their use. Despite frequently encountering resistance to anticoagulation, most physicians reported that patients usually choose to follow the physician’s recommendation.

### *Theme 4: Cost Influences Prescribing*

All participants discussed out-of-pocket cost as an important factor when considering treatment with NOACs. Table 5. Two physicians reported that the majority of their patients had lower incomes so

**Table 4: Example Quotes Describing Barriers and Facilitators of Prescribing**

#### Convenience/Inconvenience for the provider

“Oh, Jesus, yeah. I mean ten years ago we were shown every single INR, and then had to control them. It was very time consuming. That’s probably one thing that soured me on warfarin.”  
“So I think the biggest [benefit of NOACs] is the ease of use, where you don’t have to monitor.”

#### Negative feelings toward warfarin

“I hate having people on [warfarin].”  
“I have people who are like, ‘I don’t want to be on [warfarin].’”

#### Patient Preferences

“No one wants to take a drug, and no one wants to be on a pill if they don’t have to... So if someone was not carefully weighing it, one could easily just say, ‘Oh, I don’t want that.’ And that would feel easier in the moment, but that might not be the best outcome that they would choose for themselves if they’re looking at it more objectively.”  
“Sometimes it’s a time factor, and you fight with them for a couple different times and you just give up. Fine, here.”



they rarely prescribed NOACs. Similarly, physicians reported being less likely to prescribe NOACs to patients with Medicare insurance due to uncertainty regarding coverage. Participants also indicated that the high out-of-pocket cost of NOACs can negatively impact medication adherence. One said, "If they can't afford it they're not gonna take it. They're not gonna take it properly or they're gonna take it every other day or cut a pill when they shouldn't." In contrast, physicians were more likely to prescribe NOACs for patients with private or supplemental insurance. Frustration arising from the frequent need to obtain prior authorizations for NOAC coverage, even among privately insured patients, was mentioned by several participants.

When asked whether NOACs might be associated with lower society-level costs, several physicians said this might be the case. However, for all physicians, the out-of-pocket cost to each patient remained a more important determinant of NOAC use than potential savings at the societal level.

## Discussion

We found that physician prescribing practices in the setting of AF depended principally upon: 1) knowledge and experience, 2) clinical benefits and risks, 3) barriers and facilitators of prescribing, and 4) medication cost. Associated with each of these themes were sub-themes which help explain the persistent under-treatment of AF and provide guidance regarding ways to address this problem.

A key sub-theme regarding knowledge and experience was physician apprehension regarding new medications. This is not surprising, given that quite a few aggressively marketed new medications have been withdrawn after serious adverse effects were identified. The story of refecoxib (Vioxx) is a well-known example.<sup>21</sup> Physicians also described the impact of negative personal experiences with new medications, including anticoagulants. Additionally, we found a general skepticism about the evidence supporting new medications, including NOACs. The quality of research sponsored by pharmaceutical companies has been called into question in recent years, which may underlie this skepticism.<sup>22</sup> Newer medications are viewed, especially by primary care physicians, as inherently riskier. Because the potential risks of NOACs include life-threatening hemorrhage and possibly cardiovascular events, physicians may be

even more hesitant to prescribe these new medications relative to other new medications with less worrisome potential risks.<sup>23</sup>

Discussion of strategies for assessing the clinical benefits and risks of anticoagulation was revealing. Physicians reported relatively consistent methods for assessing stroke risk among their patients, but there was substantial variation in processes for assessing bleeding risk. This was expected because current clinical guidelines provide specific instructions for assessing stroke risk but little guidance for assessing bleeding risk.<sup>24,25</sup> Most physicians compared their estimation of a given patient's stroke risk directly to the patient's bleeding risk, as if they were equally serious outcomes. However, ischemic stroke has substantially higher rates of morbidity and mortality than major bleeding.<sup>26</sup> The majority of participants acknowledged this fact when pressed. Yet, most participants failed to take this differential risk of morbidity and mortality into account in their decision-making processes. It appears that AF under-treatment persists in part due to substantial variation in assessment of bleeding risk and a tendency among physicians to treat strokes and hemorrhages as equivalent adverse events.

Much time during interviews was spent discussing facilitators and barriers related to prescribing oral anticoagulants. Universally, physicians felt that the most compelling reason to use a NOAC was convenience. The idea that some NOACs might be more efficacious for stroke prevention was less compelling for physicians than the increased convenience. It is possible that the convenience of NOACs is allowing them to reach a share of the AF population previously not anticoagulated due to warfarin's inconvenience. This may explain the recently reported increases in both the rate of NOAC prescribing and the proportion of AF patients receiving anticoagulation.<sup>17</sup>

Out-of-pocket cost emerged as an important barrier to prescribing NOACs. PCPs and specialists were aware that NOACs are more expensive than warfarin, and they expressed concern that paying for these medicines could present a financial hardship that impacts medication adherence. As a result, some physicians were hesitant to prescribe NOACs for patients with limited resources or public insurance. While most physicians recognized that NOAC use may be associated with lower societal costs, this was perceived as a less important factor in prescribing than cost control at the individual level.

We believe our findings have significant implications for clinical practice and education, particularly among primary care physicians. Our findings regarding physician knowledge, familiarity, and comfort with NOACs are consistent with other studies which have demonstrated incomplete knowledge among primary care physicians of guidelines for cardiovascular disease prevention in general.<sup>27,28</sup> Important components of an educational program could include, among others, an overview of the risks of atrial fibrillation and the anticoagulation under-treatment problem, accurate assessment of bleeding and stroke risk, the benefits and disadvantages of anticoagulation options, and prescription and insurance coverage guidelines for the available NOACs. An educational program could be embedded in a broader quality improvement initiative, in which nurses and other practice personnel are involved as well as primary care physicians. Similar efforts have been used recently to successfully improve adherence to cardiovascular guidelines in primary care.<sup>29</sup>

A limitation of this study is the relatively small number of study participants. However, the diverse perspectives of primary care physicians and cardiologists yielded a rich data set from which we

**Table 5: Example Quotes Describing Cost**

### Cost of medication

"Some patients can't really afford [NOACs]. I think they're something like 90 bucks a month or something. So I wouldn't switch anyone over basically because of the cost difference."

### Insurance coverage

"A lot depends on the demographics of your practice and the insurance issues within your patient population."

"I deal with mostly an insured population. You know, so it's less of an issue for me"

"Except that patients on Medicare who are these patients, ah, you know, might have to pay more out of pocket if they don't have a secondary insurance."

### Cost influencing adherence

"If they can't afford it they're not gonna take it. They're not gonna take it properly or they're gonna take it every other day or cut a pill when they shouldn't."

"Because if they're not going to afford it, a lot of times those patients aren't gonna go to their doctor and be like, I can't afford this, can I try something else? There's the concern that they're just gonna be like, I'm not gonna take this."

### Cost-effectiveness

"My gut sense is it's (NOACs) cleaner and from a system standpoint it probably is more cost effective or efficient."

"My colleagues are saying, and I agree, that, you know, we should, we should probably be prescribing them more because no one's looking at really this, this monitoring cost, which is significant. Time and money, you know."

"The individual still matters more to me than the public health"

"There's a lot of things that we do in medicine that would be cost effective from a more like national or global standpoint. But when it comes time to patient care, patients don't care about that."

identified four substantial themes. Social desirability bias is a potential limitation given that physicians may not be inclined to discuss their lack of familiarity with new medications. We attempted to limit this risk by asking open-ended questions and maintaining a non-judgmental demeanor during the interviews. In addition, it is unclear whether our findings can be generalized to PCPs and cardiologists in other practice settings or other parts of the country. To address this, we recently pilot-tested a survey among all PCPs and cardiologists in our health system and plan to administer this survey nationally.

## Conclusions

Under-use of oral anticoagulants in the management of AF continues to be common despite the availability of effective therapies. We found that physicians are more likely to prescribe anticoagulants, including NOACs, when they have achieved a comfort level through education and experience, when they believe the benefits of treatment outweigh the risks, and when they feel that treatment will not impose undue financial burden. Systematic educational and quality improvement efforts, of the type already used successfully to improve adherence to guidelines for cardiovascular risk management, are needed to help correct the under-treatment problem and reduce morbidity and mortality associated with stroke.

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