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**Barriers to Integrating Direct Oral Anticoagulants into Anticoagulation Clinic Care: A Mixed-
Methods Study**

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Background:

Outpatient anticoagulation clinics were initially developed to care for patients taking vitamin K antagonists, such as warfarin. There has not been a systematic evaluation of the barriers and facilitators to integrating direct oral anticoagulant (DOAC) care into outpatient anticoagulation clinics.

Methods:

We performed a mixed methods study, consisting of an online survey of anticoagulation clinic providers and semi-structured interviews with anticoagulation clinic leaders and managers between March and May of 2017. Interviews were transcribed and coded, exploring for themes around barriers and facilitators to DOAC care within anticoagulation clinics. Survey questions pertaining to the specific themes identified in the interviews were analyzed using summary statistics.

Results:

Survey responses were collected from 159 unique anticoagulation clinics and 20 semi-structured interviews were conducted. Three primary barriers to DOAC care in the anticoagulation clinic were described by the interviewees: (1) a lack of provider awareness for ongoing monitoring and services provided by the anticoagulation clinic; (2) financial challenges to providing care to DOAC-patients in an anticoagulation clinic model; and (3) clinical knowledge versus scope of care by the anticoagulation staff. These themes linked to three key areas of variation, including (1) the size and hospital affiliation of the anticoagulation clinic; (2) the use of face-to-face versus telephone-based care; and (3) the use of nurses or pharmacists in the anticoagulation clinic.

Conclusions:

Anticoagulation clinics in the United States experience important barriers to integrating DOAC care. These barriers vary based on the clinic size, model for warfarin care, and staff credentials (nursing or pharmacy).

Introduction

Outpatient anticoagulation clinics were initially developed to optimize care for patients taking vitamin K antagonists, primarily warfarin.[1] Expert nurses and pharmacists within these clinics provide high-level care leading to improved patient satisfaction and high-quality warfarin management. In recent years, the use of direct oral anticoagulants (DOAC) for patients who traditionally would have received warfarin therapy has grown rapidly.[2] While these DOAC-treated patients face many of the same challenges as warfarin-treated patients, they do not require frequent dose changes or blood work. Despite calls for an evolution in anticoagulation clinics services, including care of DOAC-treated patients, anticoagulation clinics have largely been underutilized for these DOAC patients.[3]

To better understand how anticoagulation clinics have responded to the growth in DOAC use, we conducted a mixed-methods study of anticoagulation clinic providers in the United States. By combining both survey data and themes from qualitative interviews, we aimed to better understand and describe the barriers and facilitators that anticoagulation clinics experience when adopting care pathways for DOAC-treated patients.

Methods

Study Design and Subject Recruitment

Our mixed-methods study involved two methods of data collection. The quantitative data was collected via an online survey of anticoagulation clinic providers (Online Appendix). Details have been published previously.[4] Briefly, we invited all active members of the Anticoagulation Forum (a large peer organization of anticoagulation service providers in North America) to

participate in an online survey. We excluded responses from anticoagulation clinics located outside the United States, clinics who serviced only inpatients, or duplicate responses.

The qualitative data was collected through semi-structured interviews with anticoagulation clinic leaders (Online Appendix). During the survey, if participants responded affirmatively to a survey question that they possessed detailed knowledge about their clinic's staff model, structure, and policies, they were subsequently invited to participate in a semi-structured interview. Most of the interviews occurred during the Anticoagulation Forum meeting held in Los Angeles in April 2017. Four of the interviews occurred by phone in the four weeks following the Anticoagulation Forum meeting. All interviews were conducted in April or May of 2017.

Qualitative Interview Setting

A total of 20 qualitative interviews were conducted by two research assistants, one nurse practitioner, and one physician from the research team. Interviews were conducted in-person with anticoagulation clinic leaders at the Anticoagulation Forum Meeting. Interviews lasted an average of thirty-five minutes. We developed a semi-structured interview guide created to assess the structure, function, staffing, and payment models in contemporary anticoagulation clinics (online appendix). The semi-structured interview guide attempted to understand the details of clinic staffing models and patient management at each clinic. Interviews were audio recorded and transcribed verbatim.

Qualitative Analytic Approach

Our research team employed a three-step group coding process when analyzing the transcripts from the Anticoagulation Forum Conference. The investigators and research assistants first read several transcripts together and came to a consensus on coding as well as what major themes could be pulled from the transcripts. The research assistants and a research coordinator came together to develop a codebook using open coding with code names, meanings, and examples from the transcripts. The coding team coded two interviews separately, and then reviewed and discussed edits that needed to be made to the final codebook as a group. This

codebook and the initial two interviews were reviewed and modified in conjunction with the lead investigator. With the final codebook in place, the two research assistants completed coding the remainder of the transcripts. All transcripts were coded using MAXQDA 12 software.

Once all the transcripts were coded, the analytic team came back together to identify relationships between codes and additional common themes throughout the transcripts. Relationships between different themes and categories were analyzed using original quotes and by retrieving thematic segments from the transcripts. Once the common codes and themes were identified throughout the transcripts, the team developed a conceptual model displaying the clinic variation represented, the clinic challenges discussed, and what outcomes came as a result of the clinic variation and challenges.

Quantitative Analytic Approach

Survey respondents were limited to those residing and working within the United States. Duplicate responses were eliminated to ensure only a single response (first submitted) from each anticoagulation clinic that provided outpatient anticoagulation care. The survey design employed a logic mechanism intended to minimize the number of questions any single respondent had to complete. Therefore, results are reported only for the survey respondents who were shown each individual question. Missing values were excluded from the denominator when calculating percentages.

Statistical analysis was performed using Stata version 14.2 (StataCorp, College Station, TX). Summary statistics (mean \pm standard deviation [SD] or median and interquartile range [IQR]) are presented for all analyses.

Regulatory Oversight and Project Sponsorship

This project was reviewed and deemed exempt from regulation by the University of Michigan institutional review board (HUM00126169). Funding for this survey and analysis was provided by Pfizer. Pfizer Medical Affairs authors provided input to study question development and

design, but University of Michigan investigators made all final decisions regarding survey design, data analysis, and results reporting.

Results

Three primary themes emerged from the qualitative interviews as key barriers to incorporating DOAC patients into anticoagulation clinic care (Figure). These were (1) a lack of provider awareness about the need for ongoing monitoring and the services provided by the anticoagulation clinic for DOAC patients; (2) financial challenges to providing care to DOAC-patients and maintaining the anticoagulation clinic budget; and (3) clinical knowledge versus scope of care by the anticoagulation clinic staff. In addition to these themes, three important characteristics of anticoagulation clinics highlight the variability of clinic structures and function that impact those barriers. These areas of variation were (1) the size and health system affiliation of the anticoagulation clinic; (2) the use of face-to-face versus telephone-based patient interactions; and (3) the use of nurses versus pharmacists to provide the majority of anticoagulation care.

Clinic Variation

The 159 surveyed anticoagulation clinics represent a wide variety of models for care. The median number of patients managed was 925, ranging from 35 to 9000. These clinics were staffed with a median of 6 full-time-equivalent (FTE) staff, ranging from less than 1 FTE to 30 FTE staff members. Academic affiliation was reported by 31/159 (19.5%) of the survey respondents. Among the twenty interviewees, 6 (30%) self-described as large clinics while 3 (15%) self-reported as medium size and 11 (55%) self-reported as small sized clinics.

Of the surveyed anticoagulation clinics, 54/158 (34.2%) use only a face-to-face model, 29/158 (18.4%) exclusively use a telephone-based model, and 75/158 (47.5%) use a combination of these approaches. One respondent did not indicate their model of patient interaction. Among the twenty interviewees, 4 (20%) use a face-to-face model exclusively, 8 (40%) primarily use a telephone-based model, and 8 (40%) use both face-to-face and telephone-based care. From the

semi-structured interviews, clinic leaders acknowledged that the size of their patient population often dictated how their anticoagulation clinic was structured. Smaller clinics serving fewer patients often developed as an extension of a smaller physician practice and, therefore, used a face-to-face model with point-of-care INR testing. Larger clinics serving more outpatients frequently had to employ a phone-based model without point-of-care INR testing to accommodate their large patient population.

Pharmacists staffed 109/159 (68.6%) of surveyed anticoagulation clinics and registered nurses staffed 88/159 (55.4%) of clinics. A minority of clinics (41/159, 25.8%) used both pharmacists and registered nurses concurrently. Among the twenty interviewees, 11 (55%) used pharmacists and 16 (80%) used registered nurses. Similar to the survey results, 7 (35%) interviewees reported that their anticoagulation clinic used both pharmacists and registered nurses. From the semi-structured interviews, variation in the scope of practice by type of provider was confirmed. Pharmacists frequently acknowledged their role (or potential role) in assisting with initial decision making of specific anticoagulants while nurses expressed that this was out of scope for their practice.

Barriers to DOAC Care

The first theme to emerge from the interviews was that most providers were unaware of the services provided by the anticoagulation clinic for DOAC patients or the benefits of referral to the anticoagulation clinic (Table 1). From the survey data, 83/159 (52.2%) of respondents indicate that their anticoagulation clinic provides care for DOAC patients, but the median estimated percent of their clinic made up of DOAC patients was 10% (interquartile range [IQR] 5%-30%).^[4] There was no association between a clinic offering DOAC care and the clinic size (OR 1.013, 95% CI 0.993-1.034, $p=0.191$ for every 100 patients managed in the clinic). Similarly, the clinic size is not associated with the percent of patients within the clinic treated with DOACs (Spearman's rho -0.113 , $p=0.445$).

The second theme centered around the many financial challenges that anticoagulation clinics face (Table 1). The financial challenges included financial barriers for clinic patients (cost of medication) and financial difficulties experienced by clinics in regard to reimbursements. Depending on how the clinic is financed, providing management to patients who do not require point-of-care testing or billable face-to-face visits is a significant barrier to providing care for DOAC patients. From the survey, 88/128 (68.8%) of responding clinics report billing for clinic services. Details of specific services or populations (e.g. lab testing, DOAC versus warfarin patients) billed were not collected. Of these, 68/88 (77.3%) bill both patients and insurance companies while 18/88 (20.5%) only bill insurance companies and 2/88 (2.3%) only bill patients. Billing patients or insurance companies was more common among clinics that predominantly use point-of-care INR testing (80/103, 93.0%) as compared to clinics that rely on standard venipuncture lab INR results (6/23, 7.0%, $p<0.001$).

The third theme involved the challenges with clinical knowledge versus scope of care by anticoagulation staff (Table). While titrating warfarin dosing and scheduling INR lab draws is usually accomplished through provider-approved protocols, making recommendations around peri-procedural management of DOACs or assisting with drug selection is not as routinely covered by these same physician-approved protocols. Additionally, while many interviewees expressed that their nursing and pharmacist staff had clinical knowledge about how to manage DOACs (e.g. appropriate drug selection, peri-procedural management, dose adjustment for renal function), they frequently saw that physicians and other clinical providers were not always following the best available evidence. Some interviewees noted a difference between nursing and pharmacist staff in their roles for DOAC care. From the survey, assisting with anticoagulant drug selection was more common in clinics that used both nurses and pharmacists (27/41, 65.9%) and pharmacists only (37/68, 54.4%) than clinics that used nurses only (17/47, 36.2%; $p=0.018$). Similarly, assisting with perioperative management was more common in clinics that used both nurses and pharmacists (40/41, 97.6%) and pharmacist only clinics (62/68, 91.2%) than nurse only clinics (37/47, 78.7%; $p=0.014$).

Overcoming Barriers

The interviewees identified a number of potential strategies for overcoming barriers to providing DOAC care. The strategies focused on the lack of provider awareness about the need for ongoing DOAC care by the anticoagulation clinic. Interviewees highlighted both local and national efforts to increase awareness among the broader provider population. These efforts include informational meetings led by medical directors and anticoagulation clinic staff, as well as integrating anticoagulation clinic awareness to physician and staff orientation.

“We’ve presented at some meetings and, you know, grand rounds and so forth to kind of let them know we can offer that service.”

“Each new provider that comes into the facility is trained on how to refer and they are required in their training process to do a training session on anticoagulation.”

Interviewees also discussed innovative uses of automatic electronic medical record search functions to identify patients in need of anticoagulation clinic services.

“We also, through Epic, through Healthy Planet, have reports that will let us know the patients that are scheduled for procedures, uh, as well as the major drug-drug interactions as long as it's prescribed within our system.”

Finally, they identified the potential role that published literature and national organizations (such as the Anticoagulation Forum) can have on raising awareness for DOAC care within an anticoagulation clinic setting.

“I guess the biggest ways these forums can help is any kind of literature that can show that they should be tracked on a regular basis.”

“But I do see where [Anticoagulation] Forum could play a role in that if they can provide national experts who are saying, ‘Yes there is value to DOAC management,’ we have something to go back on, instead of it's just us. We're not just trying to keep our job, we see this as a value to patients.”

Discussion

In this mixed-methods study of anticoagulation clinic providers, key barriers to integrating care of DOAC patients included lack of referring provider awareness, fiscal challenges, and clinic staff knowledge versus their scope of care. These barriers were largely influenced by the size and type of anticoagulation clinic, the method by which patients interacted with the clinic and had INR labs collected, and the staff who comprised the anticoagulation clinic (nursing versus pharmacist). These findings were reflected in both the broad survey responses as well as the semi-structured interviews conducted with anticoagulation clinic leaders.

Although many clinicians focused on the lack of routine laboratory monitoring for DOAC patients, there has not been as robust a consideration for the other services anticoagulation clinics provide patients and how DOAC-treated patients might benefit. Our study highlights that most anticoagulation clinic providers and leaders recognize an important role in helping to care for these patients; however they experience important barriers to implementing protocols and clinical pathways for DOAC care. We have previously highlighted the role that anticoagulation clinics should have in assisting with DOAC management. These include providing assistance with drug and dose selection, ongoing laboratory monitoring (especially of renal function), and assistance with peri-procedural management. Each of these is a key patient safety support process that may help to reduce the frequent emergency department visits for adverse drug events and other medication-related complications.

Understanding the barriers is an important step to implementing new protocols or clinical pathways to care for DOAC patients. Many other determinants of successful program

implementation are also important to consider. For example, it is crucial to justify the reason for DOAC management pathways within anticoagulation clinics. Therefore, more robust evidence to define the frequency and consequence of inappropriate prescribing would better solidify the “problem gap to be closed.” Next, evidence showing that referral to an anticoagulation clinic can reduce this gap in care would help anticoagulation clinic managers justify their care delivery program. Similarly, outlining the frequency with which DOAC medications are mismanaged before a surgical procedure, leading to cancelations, poor patient satisfaction, or adverse clinical events must be measured and reported. Then, evidence supporting improved care through an anticoagulation clinic model would improve the likelihood of broad practice adoption.

Our study has a number of important strengths. The use of mixed-methods allows for us to combine the richness of a qualitative analysis with the generalizability of a quantitative study. In this way, we have been able to identify key themes that emerged from the 20 interviewees and explore their generalizability across the broader survey respondents. Second, we believe that this is the first in depth report on barriers and facilitators to DOAC care within the anticoagulation clinic. A few limitations are important to mention as well. First, as with all survey and qualitative work, we are only able to comment on data from willing survey respondents and interviewees. Additionally, while the AC Forum is the largest organization of anticoagulation providers in North America, its membership is not compulsory or inclusive of all anticoagulation clinics. These features may limit the generalizability of our findings. Second, due to the heterogeneity of anticoagulation clinic structures, each and every finding from this analysis may not be applicable to all anticoagulation clinics. While clinical knowledge versus scope of care was a significant barrier identified in the interviews, we do not have data on the frequency of physician-level support for the anticoagulation clinics from the survey data. Additionally, we did not interview anticoagulation clinic managers from clinics that did not manage DOAC-treated patients. Finally, as with all observational research, we are only able to comment on association and not causality. By pairing quantitative findings with qualitative findings, we are about to strengthen the likely association between our key findings.

In summary, anticoagulation clinics in the United States identify three key barriers to integrating care for DOAC patients into their work flow. These barriers are likely related to the diversity in anticoagulation clinic structure and function. While some clinics have developed innovative strategies to overcome some barriers, more work is needed to more broadly implement anticoagulation clinic care for DOAC-treated patients.

References

- 1 Ansell JE, Hughes R. Evolving models of warfarin management: anticoagulation clinics, patient self-monitoring, and patient self-management. *Am Heart J.* 1996; **132**: 1095-100.
- 2 Barnes GD, Lucas E, Alexander GC, Goldberger ZD. National Trends in Ambulatory Oral Anticoagulant Use. *Am J Med.* 2015; **128**: 1300-5 e2. 10.1016/j.amjmed.2015.05.044.
- 3 Barnes GD, Nallamothu BK, Sales AE, Froehlich JB. Reimagining Anticoagulation Clinics in the Era of Direct Oral Anticoagulants. *Circ Cardiovasc Qual Outcomes.* 2016; **9**: 182-5. 10.1161/CIRCOUTCOMES.115.002366.
- 4 Barnes GD, Kline-Rogers E, Graves C, Puroll E, Gu X, Townsend K, McMahon E, Craig T, Froehlich JB. Structure and function of anticoagulation clinics in the United States: an AC forum membership survey. *J Thromb Thrombolysis.* 2018; **46**: 7-11. 10.1007/s11239-018-1652-z.

Table – Quotes about Barriers to Direct Oral Anticoagulant Care in the Anticoagulation Clinic

<i>Code</i>	<i>Theme</i>	<i>Exemplar Quote</i>
<i>Provider unaware system exists</i>	<i>Referring Provider Awareness</i>	<i>“A lot of patients... they were a warfarin patient, they were switched to DOAC and cardiology never let us know, and at that point we were reaching them and saying, ‘Can you please place a referral so we can follow them.’ We were getting a lot of</i>

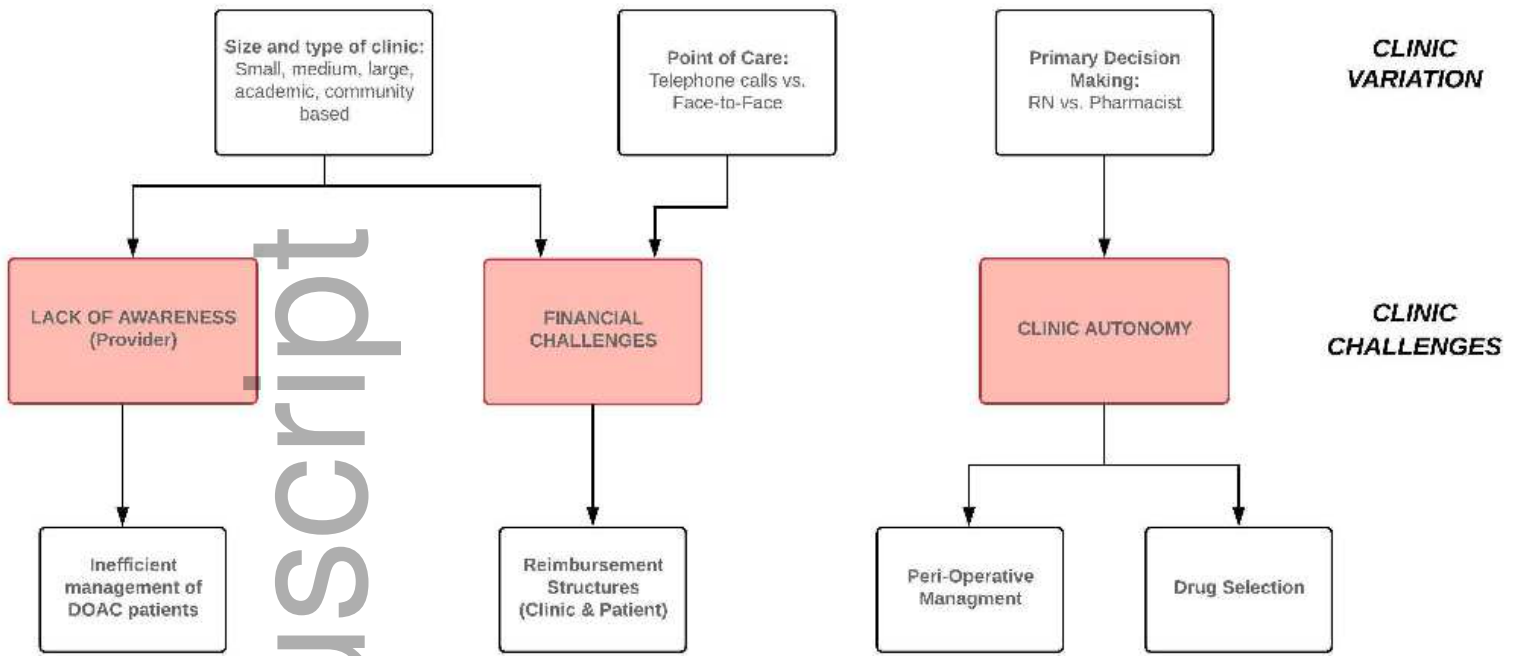
		<i>responses, 'Oh, you follow them?'"</i>
Provider aware system exists	Referring Provider Awareness	<i>"I think that they all are aware that we will manage and dose warfarin... Some providers are aware that we also follow DOAC patients. Although I think it's fair to say that the majority of them don't consider that as a reason to refer."</i>
Financial Structure (institutional funding)	Financial Challenges	<i>"There have been discussions. We've been down, I've been down different avenues and come to dead ends quite a few times, so, we're always looking for ways to potentially support our revenue. It's just it's difficult because of the way we operate, we don't see patients face-to-face. We used to do the point of care but then that became a kind of a negative in regards of revenue. "</i>
Concerns about understaffing	Financial Challenges	<i>"We need the admin pharmacists plus we're also using a little bit more of sort of our other pharmacists taking them away from face-to-face time to really manage those phone lists. That's a challenge and that, none of that work, you know, can be billed."</i>
Financial Structure (bill patients)	Financial Challenges	<i>"Obviously there is always going to be difficulty when it comes in terms of reimbursement purposes...because as pharmacists in our state we are not considered to be providers yet so we can't bill at the level that we provide services for... and so that has been a challenge."</i>
Staff Structure	Clinical Knowledge versus Scope of Care	<i>"Duration of therapy - we push back to the PCM all the time or to hematology or something like that. However, I will say that I do a lot of counseling of PCMs of what that duration of therapy should be. So, I don't make the determination myself because I'm just trying to cover myself and make the physician be involved." (interviewee is a Registered Nurse)</i>
Staff Structure	Clinical Knowledge versus Scope of Care	<i>"Our patient list on the DOACs is over 100 at this point. Mainly right now managed by the [pharmacists]; although, RN's like myself and the other RN's that we have they do DOAC education, but they don't do any recommendations for DOAC changes, conversions from warfarin to DOAC or vice versa the case that is necessary. That is left up to the pharmacist for their expertise"</i>

Challenges	Clinical Knowledge versus Scope of Care	<i>“We have some providers that want to hold DOACs for five or seven days, and they refuse to let us do what is medically necessary and safe for that patient and so we always document the reason why and that that is their responsibility not ours”</i>
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DOAC – direct oral anticoagulant; PCM – primary care manager; RN – registered nurse

Figure. Variation in Anticoagulation Clinic Structure and Associated Barriers to Integrating Direct Oral Anticoagulant Care

RN – registered nurse; DOAC – direct oral anticoagulant



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