

## Reimagining Anticoagulation Clinics in the Era of Direct Oral Anticoagulants

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**Abstract**—Anticoagulation clinics were initially developed to provide safe and effective care for warfarin-treated patients with atrial fibrillation, venous thromboembolism, and mechanical valve replacement. Traditionally, these patients required ongoing laboratory monitoring and warfarin dose adjustment by expert providers. With the introduction of direct oral anticoagulants (dabigatran, rivaroxaban, apixaban, and edoxaban), many have questioned the need for anticoagulation clinic. However, we think that the growing number of oral anticoagulant choices creates an urgent need for expanding the traditional role of the anticoagulation clinic. We outline 3 key purposes that a reimagined anticoagulation clinic would serve: (1) to assist patients and clinicians with selecting the most appropriate drug and dose from a growing list of anticoagulant options (including warfarin), (2) to help patients minimize the risk of serious bleeding complications with careful long-term monitoring and peri-procedural management, and (3) to encourage ongoing adherence to these life-saving medications. We also describe how repurposing anticoagulation clinics as broader medication safety clinics would promote safe and effective care across a range of cardiovascular conditions for high-risk medications (eg, spironolactone, amiodarone). Finally, we highlight a few existing health systems that are overcoming key challenges to implementing a reimagined anticoagulation or medication safety clinic structure. (*Circ Cardiovasc Qual Outcomes*. 2016;9:182-185. DOI: 10.1161/CIRCOUTCOMES.115.002366.)

**Key Words:** anticoagulant ■ anticoagulation ■ nurse management ■ pharmacist management ■ warfarin

Millions of Americans take warfarin daily for atrial fibrillation or venous thromboembolism. Although highly effective for preventing thromboembolic complications, use of warfarin can also cause life-threatening bleeding. Individual variability around warfarin metabolism requires careful dose titration and patient education about diet–drug and drug–drug interactions to minimize such complications. To address these challenges, anticoagulation clinics were developed as a multidisciplinary means to mitigate the risk of bleeding while ensuring safe and effective care for patients taking warfarin. In the United States, over 3000 multidisciplinary anticoagulation clinics currently monitor INR laboratory tests for millions of Americans treated with warfarin, reducing emergency department visits, hospitalizations, and thromboembolic complications.<sup>1</sup> Their primary function is to provide a safety net for patients taking anticoagulant drugs with critical safety profiles.

Since 2009, 4 new direct oral anticoagulants (DOACs) have been introduced as potential replacements for warfarin, and the use of these agents is growing quickly.<sup>2,3</sup> Given that the metabolism of these medicines does not vary individually, and they therefore do not require INR laboratory testing or frequent dose adjustments, frequent monitoring is perceived to

be unnecessary. Much of the marketing around these drugs has emphasized this advantage. This can be equated with diminished need for specialized anticoagulation clinics. However, rather than diminish the importance of anticoagulation clinics, we think the growing number of DOACs creates an urgent need for expanding the traditional role of the anticoagulation clinic. A reimagined anticoagulation clinic would serve 3 key purposes for every patient on anticoagulant medications: (1) to assist patients and clinicians with selecting the most appropriate drug and dose from a growing list of anticoagulant options (including warfarin), (2) to help patients minimize the risk of serious bleeding complications with careful long-term monitoring and peri-procedural management, and (3) to encourage ongoing adherence to these life-saving medications.

When anticoagulants are first initiated, anticoagulation clinics should serve as an informational resource and decision support service. Specifically, patients and providers need detailed information about each available anticoagulant to determine which is most appropriate. Patients and providers will benefit from the expertise of the specialized pharmacists and nurses who assist with appropriate drug selection and dosing given comorbid renal or liver impairment and concurrent

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medication use. Although the DOACs have far fewer drug–drug interactions than warfarin, there are still some medicines that require DOAC dose reduction or avoidance. Leveraging an anticoagulation clinic pharmacist’s expertise will help patients and providers prevent and manage these important potential interactions. The anticoagulation clinic staff can also review the cost implications of various anticoagulants for patient out-of-pocket expenses given their prescription drug and insurance coverage.<sup>4</sup> These providers can also spend more time with patients than most primary care or specialty physicians. After the initial medication is selected, anticoagulation clinics will periodically evaluate and follow up, answering any patient questions or concerns. This ongoing relationship likely improves DOAC adherence, an essential component of safe and effective anticoagulant care.<sup>5</sup> Expanding the anticoagulation clinic’s ability to assist in medication selection, patient education, and encouraging adherence will benefit patients and providers alike.

A second key purpose of the reimagined anticoagulation clinic is to reduce harm from bleeding related to an inappropriate dose. For warfarin-treated patients, this is done through INR laboratory draws and warfarin dose adjustments. In DOAC-treated patients, dosing is directly linked to a patient’s renal function, as well as the indication. Although most providers know to check renal function when initially prescribing DOAC therapy, ongoing monitoring of renal function is often overlooked. Over 20% of atrial fibrillation patients develop renal dysfunction, with DOAC dosing implications.<sup>6</sup> This can lead to life-threatening bleeding complications when the DOAC dose is not adjusted for declining renal function. The anticoagulation clinic is a resource already in place to monitor these patients and make necessary dosing adjustments.

A reimagined anticoagulation clinic would also reduce harm from bleeding in the peri-procedural period. Each year, over 500 000 atrial fibrillation patients undergo procedures that require interruption of their anticoagulation therapy.<sup>7,8</sup> Anticoagulation clinic providers have specialized expertise that should be leveraged to help all anticoagulated patients avoid complications when procedures are indicated. The time needed to stop an anticoagulant before and after a procedure varies greatly depending on the medication, a patient’s renal function, and the bleeding risk of the proposed procedure. A centralized model where all peri-procedural anticoagulation decisions are managed by the anticoagulation clinic nurses and pharmacists will allow for standardized, evidence-based care that can rapidly incorporate and implement new clinical evidence. It also gives patients and providers a clear go-to team for answers and coordination, instead of relying on the patient to coordinate opinions from multiple providers, potentially from different health systems. Importantly, it will remove that burden from primary care providers, cardiologists, proceduralists, and surgeons.

A third key purpose of the reimagined anticoagulation clinic is to encourage long-term medication adherence. A medicine is of no benefit (and potential harm) when not taken regularly. This is especially important for DOAC-treated patients, for whom skipping 1 to 2 doses may leave them unprotected from a deadly stroke or pulmonary embolism. Clinic visits were scheduled at least every 3 months in the

major trials comparing warfarin to DOACs and have been recommended every 3 to 6 months by the European Heart Rhythm Association.<sup>9</sup> Continual contact with the health system is an important reminder to take medications and an opportunity to address any challenges patients might be facing. A recent Veterans Affairs study demonstrated that long-term monitoring of dabigatran treatment (one of the DOAC medications) by an anticoagulation clinic with support from pharmacists was associated with the highest likelihood for medication adherence.<sup>5</sup> The Veterans Affairs model has inspired other models, including the University of Michigan Anticoagulation Clinic, to perform several roles related to consultation for drug and dose selection, monitoring for changes in renal function and medication adherence, and identification of lowest-risk patients for whom anticoagulant therapy is not indicated. Anticoagulation clinic support and consultation should be used to ensure safe, high-quality anticoagulation care.

Despite these examples and opportunities, barriers exist to widespread adoption of a reimagined anticoagulation clinic. The greatest challenge is financing. With increasing utilization of DOACs, health systems and insurers may be tempted to discourage use of anticoagulation clinics and avoid paying for these services. This is especially true because existing studies of cost-effectiveness for DOAC medications did not include the costs of anticoagulation clinic support. Additionally, it may require a change in culture and habitual practice patterns, to encourage providers to consult the anticoagulation clinic early for assistance with drug selection and dosing, and throughout the patient’s care, to standardize peri-procedural anticoagulation, and to establish and oversee a renal function monitoring plan in DOAC-treated patients. Finally, institutional policies may need to be updated to empower specialist nurses and pharmacists to manage these specific clinical scenarios. Expanding both the role and the availability of anticoagulation clinics, which may not be universally available for all patients, should be a top priority for patient-centered care.

A potentially significant driver for reimagining anticoagulant care is the changing healthcare payment landscape. New payment models encourage healthcare organizations to focus on holistic strategies that improve care and reduce expenses. For instance, accountable care organizations are responsible for total costs of care, not just fee-for-service costs. Therefore, embracing strategies to reduce adverse drug events are likely to be financially beneficial and act as a key facilitator for such system redesign.

To that end, instead of reimagining the anticoagulation clinic to serve a broader need for anticoagulated patients, a more logical approach may be for current anticoagulation clinics to evolve into medication safety clinics. These repurposed clinics would play a valuable role promoting safe and effective care across a broader range of cardiovascular conditions for high-risk medications. Specific to anticoagulation care, the clinics might ensure that patients with acute deep venous thrombosis have rapid follow-up after an emergency department (or primary care) visit to review and assess anticoagulant therapy compliance. Avoiding costly emergency department visits and hospital admissions likely also improves patient

satisfaction.<sup>10</sup> They would also play a more central role in the management of perioperative anticoagulation management, determining when bridging anticoagulation is necessary and educating patients on safe bridging anticoagulant administration. Given that bridging anticoagulants are frequently overused, reductions in the use of outpatient low molecular weight heparin or inpatient unfractionated heparin should lead to significant savings.<sup>7,11</sup>

Beyond the care of patients taking anticoagulants, a medication safety clinic could also provide valuable support in many settings: for patients taking mineralocorticoid receptor antagonists (e.g. spironolactone) for hypertension or heart failure; for patients taking amiodarone for arrhythmia control; and for patients taking other cardiovascular medications that require long-term monitoring and dose adjustment. Recent studies have shown that only 7.2% of patients initiated on a mineralocorticoid receptor antagonist receive appropriate potassium and renal function monitoring in the initial 90 days.<sup>12</sup> Widespread use of spironolactone after publication of the Randomized Aldactone Evaluation Study (RALES) trial was associated with marked increases in hospital admissions and in-hospital death from hyperkalemia.<sup>13</sup> Similarly, only half of patients prescribed amiodarone receive the recommended liver and thyroid function screening that is advised.<sup>14</sup> In at least one case, a pharmacist-led medication clinic was able to significantly improve the rate of liver, thyroid, and pulmonary function screening for amiodarone patients in a cost-saving manner.<sup>15</sup> A medication safety clinic would leverage the existing anticoagulation clinic infrastructure of nurse and pharmacist experts designed for longitudinal medication monitoring to reduce complications from a variety of effective, yet potentially dangerous, cardiovascular medications. In this manner, the business justification supporting a medication safety clinic would be even greater than that of a more narrowly focused anticoagulation clinic.

Although these approaches make logical sense, robust data are lacking. In addition to the retrospective study reporting medication adherence from the Veterans Affairs system, prospective data (preferably randomized or cluster-randomized) assessing patient outcomes will be important.<sup>5</sup> Similarly, rigorous assessment of medication safety clinic function and the costs associated with avoided complications will be needed to strengthen the business case. In the meantime, experimenting with different clinic designs will lead to innovative new approaches focused on improving patient safety. Similarly, clinicians may find themselves relying on medication safety clinics to routinely manage and monitor their patients at highest risk for complications. This approach will ensure high-quality, patient-centered care for DOACs, warfarin, and other common cardiovascular medications. Already, Blue Cross–Blue Shield of Michigan has invested in a multicenter collaboration (the Michigan Anticoagulation Quality Improvement Initiative) to measure anticoagulant care delivery and implement new approaches aimed at safe and efficient management of high-risk therapy.

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### References

- Rudd KM, Dier JG. Comparison of two different models of anticoagulation management services with usual medical care. *Pharmacotherapy*. 2010;30:330–338. doi: 10.1592/phco.30.4.330.
- Barnes GD, Lucas E, Alexander GC, Goldberger ZD. National trends in ambulatory oral anticoagulant use. *Am J Med*. 2015;128:1300–1305.e2. doi: 10.1016/j.amjmed.2015.05.044.
- Barnes GD, Ageno W, Ansell J, Kaatz S; Subcommittee on the Control of Anticoagulation. Recommendation on the nomenclature for oral anticoagulants: communication from the SSC of the ISTH. *J Thromb Haemost*. 2015;13:1154–1156. doi: 10.1111/jth.12969.
- Salata BM, Hutton DW, Levine DA, Froehlich JB, Barnes GD. Cost-Effectiveness of dabigatran (150 mg twice daily) and warfarin in patients  $\geq 65$  years with nonvalvular atrial fibrillation. *Am J Cardiol*. 2016;117:54–60. doi: 10.1016/j.amjcard.2015.09.048.
- Shore S, Ho PM, Lambert-Kerzner A, Glorioso TJ, Carey EP, Cunningham F, Longo L, Jackevicius C, Rose A, Turakhia MP. Site-level variation in and practices associated with dabigatran adherence. *JAMA*. 2015;313:1443–1450. doi: 10.1001/jama.2015.2761.
- Roldán V, Marín F, Fernández H, Manzano-Fernández S, Gallego P, Valdés M, Vicente V, Lip GY. Renal impairment in a “real-life” cohort of anticoagulated patients with atrial fibrillation (implications for thromboembolism and bleeding). *Am J Cardiol*. 2013;111:1159–1164. doi: 10.1016/j.amjcard.2012.12.045.
- Steinberg BA, Peterson ED, Kim S, Thomas L, Gersh BJ, Fonarow GC, Kowey PR, Mahaffey KW, Sherwood MW, Chang P, Piccini JP, Ansell J; Outcomes Registry for Better Informed Treatment of Atrial Fibrillation Investigators and Patients. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Circulation*. 2015;131:488–494. doi: 10.1161/CIRCULATIONAHA.114.011777.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Després JP, Fullerton HJ, Howard VJ, Huffman MD, Judd SE, Kissela BM, Lackland DT, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Matchar DB, McGuire DK, Mohler ER III, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Willey JZ, Woo D, Yeh RW, Turner MB; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29–322. doi: 10.1161/CIR.0000000000000152.
- Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, Sinnaeve P, Camm AJ, Kirchhof P. EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary. *Eur Heart J*. 2013;34:2094–2106. doi: 10.1093/eurheartj/eh134.
- Falconieri L, Thomson L, Oettinger G, Pugliese R, Palladino M, Galanis T, Merli G. Facilitating anticoagulation for safer transitions: preliminary outcomes from an emergency department deep vein thrombosis discharge program. *Hosp Pract (1995)*. 2014;42:16–45. doi: 10.3810/hp.2014.10.1140.
- Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, Garcia DA, Jacobson A, Jaffer AK, Kong DF, Schulman S, Turpie

- AG, Hasselblad V, Ortel TL; BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med*. 2015;373:823–833. doi: 10.1056/NEJMoa1501035.
12. Cooper LB, Hammill BG, Peterson ED, Pitt B, Maciejewski ML, Curtis LH, Hernandez AF. Consistency of laboratory monitoring during initiation of mineralocorticoid receptor antagonist therapy in patients with heart failure. *JAMA*. 2015;314:1973–1975. doi: 10.1001/jama.2015.11904.
  13. Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *N Engl J Med*. 2004;351:543–551. doi: 10.1056/NEJMoa040135.
  14. Raebel MA, Carroll NM, Simon SR, Andrade SE, Feldstein AC, Lafata JE, Nelson WW, Chan KA, Gunter MJ, Tolsma D, Platt R. Liver and thyroid monitoring in ambulatory patients prescribed amiodarone in 10 HMOs. *J Manag Care Pharm*. 2006;12:656–664.
  15. Spence MM, Polzin JK, Weisberger CL, Martin JP, Rho JP, Willick GH. Evaluation of a pharmacist-managed amiodarone monitoring program. *J Manag Care Pharm*. 2011;17:513–522.

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