Proportion of Patients on Warfarin Therapy Who Are Eligible for Conversion to a Direct Oral Anticoagulant in the Setting of COVID-19

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Abstract

Background: Warfarin, a commonly prescribed anticoagulant, requires frequent lab monitoring. Lab monitoring puts patients at risk of COVID-19 exposure and diverts medical resources away from health care systems. Direct oral anticoagulants (DOACs) do not require routine therapeutic monitoring and are indicated first line for nonvalvular atrial fibrillation (NVAF) stroke prevention and venous thromboembolism (VTE) prevention/treatment. Objective: The purpose of the study was to determine the proportion of patients who qualify for DOACs and assess for predictors of qualification. Methods: This cross-sectional study investigated patients on warfarin managed by Michigan Medicine Anticoagulation Service. Direct oral anticoagulant eligibility criteria were established using apixaban, dabigatran, and rivaroxaban package inserts. Patient eligibility was determined through chart review. The primary outcome was the proportion of patients who qualify for DOACs based on clinical factors. Predictors of DOAC qualification were assessed. Results: This study included 3205 patients and found 51.8% (n = 1661) of patients qualified for DOACs. Qualifying patients were older (71.9 vs 59.4 years, P < 0.0001) with a higher CHA2DS2-VASc (3.7 vs 3.4, P < 0.0007). The primary disqualifying factor was extreme weight, high and low. Accounting for a patient’s sex and referral source, age > 65 (odds ratio [OR] = 1.9, P < 0.0001) and NVAF indication (OR = 5.6, P < 0.0001) were significant predictors for DOAC qualification. Conclusion and Relevance: Approximately 52% of patients on warfarin were eligible for DOACs. This presents an opportunity to reduce patient exposure to health care settings and health care utilization in the setting of COVID-19. Increased costs of DOACs need to be assessed.

Keywords
direct oral anticoagulants, novel oral anticoagulants, COVID-19, warfarin, anticoagulation, atrial fibrillation, venous thromboembolism

Introduction

Direct oral anticoagulants (DOACs) are recommended as first-line treatment in deep vein thrombosis (DVT) and pulmonary embolism (PE) and in nonvalvular atrial fibrillation (NVAF) for stroke prevention.1 Despite the efficacy and safety outcomes driving these recommendations, warfarin remains commonly prescribed.2 3 4 Patients on long-term warfarin therapy may be unwilling to switch medication therapy, their providers may not have evaluated whether they qualify for a DOAC, or they may not be able to afford a DOAC. Warfarin has a long, proven history of use and a lower drug cost.5

The COVID-19 pandemic has introduced unique challenges to the management of patients on warfarin. Patients may be fearful of COVID-19 exposure in the health care setting when they present for international normalized ratio (INR) testing, which is commonly done weekly to monthly,
Patients may be in quarantine, which will prevent them from presenting to clinic. A survey study found higher INR values and lower compliance with INR testing during COVID-19 compared with before COVID-19 and that the major cause (94% of respondents) of noncompliance with INR testing was the COVID-19 pandemic. Approximately 40% of Americans have delayed seeking medical treatment throughout the pandemic. Limited access to grocery stores and foods containing vitamin K makes it challenging for patients to maintain a consistent diet, which may make INR values fluctuate. In addition to these concerns, COVID-19 itself has a known association with coagulopathy. Studies have seen disseminated intravascular coagulation (DIC) and venous thromboembolism (VTE) develop in COVID-19 patients, especially in those with severe forms of the disease, defined as requiring intensive care unit (ICU) management. This may put hypercoagulable patients at further risk of thrombotic events if exposed to COVID-19. There have also been increases in fibrinogen degradation products and increases in prothrombin time (PT), a lab value used to calculate INR. COVID-19 may interfere with anticoagulation therapy and monitoring. COVID-19 has also been associated with bleeding complications, for example, in extracorporeal membranous oxygenation (ECMO) patients with appropriate levels of heparin therapy. Given that bleeding did not appear to be due to inappropriate levels of anticoagulation, researchers suspected the bleeding complication to be due to enhanced-fibrinolytic type DIC, a known association of COVID-19 infection; vascular endotheliitis, which COVID-19 is considered to cause; or acquired von Willebrand syndrome, a known phenomenon in ECMO due to endothelial shearing. These further considerations of COVID-19 pathology provide another benefit to limiting health care exposure to patients that are coagulopathic at baseline.

Increases in the percentage of supratherapeutic INRs during COVID-19 have been observed and may increase the risks of bleeding. Maintaining a therapeutic INR level can be difficult to control even in the absence of pandemic-related concerns. One meta-analysis saw a time spent in therapeutic range of 55% to 68% in NVAF treatment. Another meta-analysis saw a time spent in therapeutic range of only 48% (range = 37%-55%) in long-term care management for all indications of warfarin. This puts the patient at risk of bleeds if the INR is too high and at risk of thrombosis if the INR is too low. Treatment of warfarin complications such as bleeding further increases health care resource utilization and patient exposure to the health care system.

Direct oral anticoagulant therapy benefits include fewer drug interactions, no routine therapeutic monitoring, no dietary restrictions, fixed dosing, and decreased risk of intracranial bleeds. Direct oral anticoagulants demonstrated comparable efficacy to warfarin in prevention of VTE recurrence and have lower risk of intracranial hemorrhage. When dosed at 150 mg, apixaban and dabigatran had decreased risk of ischemic stroke in NVAF in comparison with warfarin. In addition, apixaban showed lower risk of major bleeding in NVAF and had a lower risk of overall mortality when compared with warfarin. Switching patients from warfarin to DOAC is feasible and patients showed increased satisfaction with their anticoagulant therapy. In addition, there is now a Food and Drug Administration–approved DOAC reversal agent, which could have been a prior hesitation to starting a patient on a DOAC.

Following the suggestion to develop standard screening to determine eligibility for DOAC therapy during the COVID-19 pandemic, this study will determine the proportion of patients in an outpatient anticoagulation clinic on warfarin who would be eligible for treatment with a DOAC. This will help determine the impact of implementing such screening at anticoagulation clinics. Other studies have addressed patient satisfaction following conversion to DOAC therapy and found decreased patient sense of burden, improved sense of benefit, and improved patient satisfaction. This will be the first study to analyze the proportion of warfarin patients qualifying for DOAC substitution.

### Methods

#### Study Design

A cross-sectional study of patients on warfarin therapy managed by Michigan Medicine Anticoagulation Service was performed to determine the proportion of patients who qualified for DOAC therapy. Patient demographic and medical data were extracted by reviewing patients’ charts within Michigan Medicine’s electronic medical records. This study was approved by the Michigan Medicine Institutional Review Board.

#### Patient Selection

Patient data were collected throughout June and July 2020. Patients included were at least 18 years old and on warfarin therapy (n = 3,205) managed by Michigan Medicine Anticoagulation Service. Patients with a left ventricular assist device (LVAD) were excluded.

#### Outcomes

The primary outcome was the proportion of patients who qualified for anticoagulation therapy with a DOAC. Secondary outcomes were clinical predictors for patients who qualify for a DOAC, the proportion of patients on warfarin therapy who met the Center for Disease Control and Prevention’s criteria for high risk of COVID-19, and changes in time within therapeutic range (TTR) during...
High-risk patients were defined as those with chronic lung disease (asthma, chronic obstructive pulmonary disease, emphysema), diabetes mellitus type 1 or 2, heart conditions (coronary artery disease, hypertension, heart failure), liver cirrhosis, patients over 65 years of age, current or former smokers, and obese or overweight patients.

**DOAC Qualification Criteria**

Patients were eligible for DOAC following “strict” criteria only if their primary indication for anticoagulation was NVAF, PE, or DVT. Nonvalvular atrial fibrillation indications included nonvalvular atrial fibrillation and atrial flutter. Patients were ineligible for DOAC therapy if any of the following criteria were met: body mass index (BMI) greater than 40 kg/m², weight greater than 120 kg, weight less than 50 kg, presence of a mechanical heart valve, moderate-severe mitral stenosis, triple-positive antiphospholipid syndrome (positive for lupus anticoagulant, anti-cardiolipin, and anti-β2glycoprotein I antibodies), severe liver cirrhosis defined as Child-Pugh class C, ongoing dialysis, history of bariatric surgery, concomitant use of combined p-glycoprotein and strong cytochrome P450 (CYP) inducers, or concomitant use of combined p-glycoprotein and strong CYP inhibitors if creatinine clearance was less than 30 mL/min as dabigatran can be used with these inhibitors given adequate kidney function. A second group with “flexible” eligibility criteria was included. “Flexible” criteria did not limit qualification to patients with NVAF and VTE and only required BMI to be less than 40 for weight criteria. All other qualification criteria and exclusionary factors were the same. Weight was used in the eligibility criteria due to the recommendation by the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis (ISTH) that DOACs not be used in patients with BMI greater than 40 kg/m² or weight greater than 120 kg. This is due to the very small percentage of patients at extreme weights included in the DOAC clinical trials. Although updated guidelines by ISTH in 2021 state rivaroxaban and apixaban can be used for VTE treatment in obese patients, further studies are needed as clinical data are still lacking. These guidelines also recommend not using dabigatran, edoxaban, and betrixaban in obese patients for VTE treatment and prevention.

**Data Collection**

Baseline demographics and characteristics (Table 1) were collected from the electronic medical records.

In patients with NVAF, we determined CHA₂DS₂-VASc to quantify stroke risk. Creatinine Clearance (CrCl) was determined using the Cockcroft-Gault formula and using the patient’s actual body weight.

**Table 1. Baseline Demographics and Characteristics.**

| Total patients | n = 3205 |
|----------------|----------|
| Age (years)    | 65.9 ± 16.2 |
| Male sex       | 1802 (56.2%) |
| CHA₂DS₂-VASc in patients with atrial fibrillation | 3.6 ± 1.6 |
| Serum creatinine (mg/dL) | 1.2 ± 1.0 |
| Creatinine clearance (mL/min) | 94.6 ± 52.7 |
| Weight (kg)    | 91.7 ± 26.2 |
| BMI (kg/m²)    | 31.3 ± 8.1 |
| Time within therapeutic range (TTR) (%) | 68.0 ± 16.3; 70.5 (0-100) |
| Primary indication category | |
| Atrial fibrillation/flutter | 1510 (47.1%) |
| VTE            | 824 (25.7%) |
| Valvular replacement | 334 (10.4%) |
| Other          | 537 (16.8%) |
| INR goals      | |
| 2-3            | 2790 (87.1%) |
| 2.5-3.5        | 281 (8.8%) |
| Other          | 134 (4.2%) |
| Managing provider by specialty | |
| Family medicine | 1137 (35.5%) |
| Cardiology     | 1240 (38.7%) |
| Electrophysiology | 186 (5.8%) |
| Vascular medicine | 292 (9.1%) |
| Other          | 350 (10.9%) |
| Racial group   | |
| White          | 2763 (86.2%) |
| Black          | 275 (8.6%) |
| Asian/Pacific Islander | 54 (1.7%) |
| Hispanic       | 47 (1.5%) |
| Other          | 66 (2.1%) |

Baseline characteristics of patients described as mean ± SD or by number (percentage of total study population) with n = 3205. Abbreviations: BMI, body mass index; INR, international normalized ratio; TTR, time in therapeutic range; VTE, venous thromboembolism and includes pulmonary embolus and deep vein thrombosis.

The severity of liver cirrhosis was calculated using the Child-Turcotte-Pugh classification. The severity of mitral stenosis was determined by reviewing problem list or echocardiogram results.

**Statistical Methods**

Statistical analysis was conducted using STATA 13.0 software. To determine differences in the baseline characteristics of patients, the patients who qualified for DOAC were compared with those who did not based on criteria previously described. Student t tests were used to compare average age, CHA₂DS₂-VASc score, serum creatinine, creatinine clearance, and INR goal.
clearance, weight, BMI, and TTR. χ² tests were used to compare categorical variables including percentage male sex, primary anticoagulation indication, INR treatment goal, specialty of the managing provider, and race. Univariate and multivariate logistical regression was used to determine whether there were any predictors of DOAC qualifiers within the demographic data collected. Finally, a t test was used to compare average TTR before the COVID-19 pandemic with average TTR during the COVID-19 pandemic. The TTR was determined from a value reported in the electronic medical record.

### Results

The demographic and clinical characteristics of our warfarin patient population are described in Table 1.

Following strict criteria for DOAC qualification, 51.8% of warfarin patients were eligible for DOAC. Using a more flexible set of criteria, this percentage increases to 77%. Among the group of patients considered high-risk of COVID-19, 49.8% could be switched from warfarin to DOAC (Table 2).

Weight extremes and presence of a mechanical valve were the most common reason for not qualifying for a DOAC. Using extreme weight defined as BMI greater than 40 or weight less than 50 kg or weight greater than 120 kg, 17.5% of patients did not qualify. This is compared with using extreme weight defined as BMI greater than 40, with 12.4% of patients not qualifying. Patients excluded due to the presence of a mechanical heart valve made up 11.6% of patients. Use of a strong CYP inhibitor resulted in 4.3% of patients not qualifying for DOAC treatment. Other less frequent reasons for exclusion included dialysis, concomitant CYP inducer, moderate-severe mitral stenosis, triple-positive antiphospholipid syndrome, bariatric surgery, and severe liver cirrhosis as detailed in Table 3.

Patients who were eligible for DOAC were older (P < 0.0001), more commonly male (P < 0.0001), and had higher CHA2DS2VASc scores (3.7 vs 3.4, P = 0.0007). The DOAC-eligible patients also have a lower serum creatinine (P < 0.0001) and lower creatinine clearance (P < 0.0001) than those who did not qualify. Patients who qualified weighed significantly less and had significantly lower BMIs than patients who did not qualify (P < 0.0001, P < 0.0001). The TTR was found to be higher in patients who qualified for a DOAC compared with those that did not qualify (P < 0.0001). A statistically significant difference was found in the indications of patients who qualify for a DOAC and the indications in those that do not qualify (P = 0.0001). Among patients with NVAF, 75.4% qualified. Among patients with VTE, 63.8% qualified.

Analyzing INR goals, 94.7% of patients qualifying had a goal of 2 to 3, 2.9% had a goal of 2.5 to 3.5, and 2.4% had some other INR goal, whereas 78.8% of those who did not qualify had an INR goal of 2 to 3, 15.1% had an INR goal of 2.5 to 3.5, and 6.1% had some other INR goal. A difference was found in the specialty of the managing provider among those who qualified versus those who did not qualify (P < 0.0001). Significantly more patients were found to be white among those that qualified compared with those that did not qualify (P < 0.0001). Further details on characteristics of patients that qualified versus did not qualify are described in Table 4.

In the univariate analysis, male sex (odds ratio[OR] = 1.3, P < 0.001, 95% CI [1.15-1.53]), age greater than 65 (OR = 3.9, P < 0.001, 95% CI [3.39-4.57]), NVAF indication (OR = 6.5, P < 0.001, 95% CI [5.60-7.64]), and referral (OR = 1.7, P < 0.001, 95% CI [1.49-2.00]) were all found to be statistically significant predictors for DOAC qualification. After accounting for referral and male sex, age greater than 65 (OR = 1.92, P < 0.0001, 95% CI [1.62-2.28]) and NVAF indication (OR = 5.6, P < 0.0001, 95% CI [4.68-6.63]) were found

### Table 2. Percentage of Patients that Qualify for a DOAC.

| Criteria | Patients | Percentage |
|----------|----------|------------|
| **Strict criteria** | | |
| Approved indication only: Atrial fibrillation and VTE | 1661 | (51.8%) |
| Exclude: Weight > 120 kg or < 50 kg, BMI > 40, dialysis, mechanical heart valve, moderate-severe mitral stenosis, triple-positive APLS, cirrhosis with Child-Pugh class C, CYP inducer, strong CYP inhibitor, bariatric surgery | | |
| **Flexible criteria** | | |
| Exclude: BMI > 40, dialysis, mechanical heart valve, moderate-severe mitral stenosis, triple-positive APLS, cirrhosis with Child-Pugh class C, CYP inducer, strong CYP inhibitor, bariatric surgery | 2255 | (70.4%) |
| **At high risk of COVID-19** | | |
| | 1595 | (49.8%) |

Values in number of patients and percentage of total patients.

Abbreviations: APLS, antiphospholipid syndrome; BMI, body mass index (kg/m²); CYP, cytochrome P450 enzymes; DOAC, direct oral anticoagulant; VTE, venous thromboembolism.

### Table 3. Disqualification for DOAC Therapy by Factor.

| Factor | Patients | Percentage |
|--------|----------|------------|
| **Weight** | | |
| BMI > 40, weight < 50 kg or > 120 kg | 562 | (17.5%) |
| BMI > 40 | 398 | (12.4%) |
| **Mechanical heart valve** | | |
| Concomitant strong CYP inhibitor | 137 | (4.3%) |
| Dialysis | 85 | (2.7%) |
| Concomitant CYP inducer | 68 | (2.1%) |
| Moderate-severe mitral stenosis | 57 | (1.8%) |
| Triple-positive antiphospholipid syndrome | 39 | (1.2%) |
| **Bariatric surgery** | | |
| Cirrhosis with Child-Pugh class C | 18 | (0.6%) |

Abbreviations: BMI, body mass index; CYP, cytochrome P450 enzyme; DOAC, direct oral anticoagulant.
to be statistically significant predictors of qualification for a DOAC. As demonstrated in Table 5, multivariate analysis did not find male sex or referral from Family Medicine or Cardiology providers to be statistically significant.

No difference was found in TTR with TTR pre-COVID-19 found to be 68.6% ± 25.9% and TTR during the COVID-19 pandemic to be 67.2% ± 27.1% (Table 6).
Discussion

Several new variants emerged in the first few years of the COVID-19 pandemic, leading to waves of increases in cases, hospitalizations, and deaths with unvaccinated people being particularly affected.20 As the COVID-19 pandemic continues, switching patients from warfarin to DOAC may help reduce patient interaction to the health care system, assuage fears about exposure to COVID-19, and conserve health care system resources. This also has the potential to reduce costs to health care systems with a decreased utilization of labs and fewer appointments required for anticoagulation monitoring. The results of this study demonstrate that over half of patients anticoagulated through an anticoagulation clinic may qualify for a drug that requires less monitoring and less time spent in a health care facility.

Previous studies have outlined risks of warfarin therapy during the COVID-19 pandemic, demonstrated lower rates of adherence to INR testing and increased frequency of supratherapeutic INR values, and improved patient satisfaction with DOACs. The authors of these studies advocated screening patients for DOAC eligibility.11,14 Guidelines published by the National Health Service in England, the Italian Federation of Anticoagulation Clinics, and a treatment algorithm set forth in the American Journal of Cardiovascular Drugs also encourage the use of DOACs over warfarin during the COVID-19 pandemic.21-23

Even in the absence of a pandemic, there are multiple benefits to switching to a DOAC. These include lack of dietary restrictions and eliminating the cost and time it takes to present to lab monitoring appointments regularly, and their first line indication in NVAF stroke prevention and VTE recurrence prevention. DOACs have lower risk of intracranial hemorrhage compared with warfarin.2,4,24 Apixaban and dabigatran at 150 mg showed reduced risk of ischemic stroke in NVAF compared with warfarin.2,3 Apixaban showed lower risk of major bleeding compared with warfarin in NVAF.2 Apixaban showed lower overall risk of mortality compared with warfarin.2 DOACs showed similar efficacy to warfarin in VTE recurrence prevention.24

This is the first study to estimate the proportion of a warfarin-treated patient population that qualifies for a DOAC. More than half of this warfarin-treated population (51.8%) was found to be eligible for the use of DOAC treatment. Other anticoagulation clinics may be able to help their warfarin-treated patients switch to DOAC therapy. Use of predictive factors for DOAC eligibility—indication of NVAF and age over 65—may help other clinics screen patients more efficiently.

Study Limitations

The main limitation to the application of these findings is the cost of DOACs. As of the date of this publication, DOACs are not available generically and retail prices remain high. Out-of-pocket costs will depend on the patient’s medication insurance and as the average age of qualification is 71.9±13.8, many eligible patients are reliant on Medicare. These findings may have more significant impacts once a generic DOAC option is available.

These findings are examined within the scope of one anticoagulation clinic. The predictive factors for qualification may be less applicable to other anticoagulation services and providers.

Finally, this study looks at minimum requirements as listed on the DOAC package inserts in order to determine qualification criteria.25-27 This does not take into account other clinical reasons a patient may not qualify, such as gastrointestinal bleed risks, dose adjustment with decreased renal function, twice-a-day dosing with dabigatran and apixaban, or patient preferences.

Conclusion and Relevance

This study found 51.8% of patients receiving warfarin therapy to be eligible for DOACs. This demonstrates the potential utility of anticoagulation clinics screening patients for DOAC qualification. Screening should begin with patients over 65 years of age and with an indication of NVAF. Switching patients from warfarin to DOACs may limit COVID-19 exposure due to decreased exposure to the health care system for INR check and achieve greater numbers of patients receiving first-line therapy. Further study is needed to ascertain the number of patients willing to switch, cost being a major factor. Further study is also needed to determine patient satisfaction.

Declaration of Conflicting Interests

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Presentation of Work

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2. Poster presentation of preliminary data: Assessment of Qualification for Direct Oral Anticoagulant in Patients Currently on Warfarin Therapy Managed by Michigan Medicine Anticoagulation Service—American College of Cardiology’s 70th Annual Scientific Session.
3. Poster presentation of final data: Assessment of Qualification for Direct Oral Anticoagulant in Patients Currently on Warfarin Therapy Managed by Michigan Medicine Anticoagulation Service—Anticoagulation Forum 2021.

References

1. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in collaboration with the Society of Thoracic Surgeons [published correction appears in Circulation. 2019;140(6):e285]. Circulation. 2019;140(2):e125-e151. doi:10.1161/CIR.0000000000000665.

2. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981-992. doi:10.1056/NEJMoa1107039.

3. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation [published correction appears in N Engl J Med. 2010;363(19):1877]. N Engl J Med. 2009;361(12):1139-1151. doi:10.1056/NEJMoa0905561.

4. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365(10):883-891. doi:10.1056/NEJMoa1009638.

5. Agarwal S, Hachamovitch R, Menon V. Current trial-associated outcomes with warfarin in prevention of stroke in patients with nonvalvular atrial fibrillation: a meta-analysis. Arch Intern Med. 2012;172(8):623-633. doi:10.1001/archinternmed.2012.121.

6. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). Chest. 2008;133(suppl 6):160S-1985S. doi:10.1378/chest.08-0670.

7. Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombolysis. 2020;50(1):72-81. doi:10.1007/s11239-020-02138-z.

8. Tolga D, Fatih L. The short-term effect of the COVID-19 pandemic on the management of warfarin therapy. Kardiology. 2021;61(7):55-59. doi:10.18087/kardio.2021.n1593.

9. Chen KL, Brozen M, Rollman JE, et al. How is the COVID-19 pandemic shaping transportation access to health care? Transp Res Interdiscip Perspect. 2021;10:100338. doi:10.1016/j.trip.2021.100338.

10. Iba T, Levy JH, Connors JM, Warkentin TE, Thachil J, Levi M. The unique characteristics of COVID-19 coagulopathy. Crit Care. 2020;24(1):360. doi:10.1186/s13054-020-03077-0.

11. Pearson LN, Johnson SA, Greene DN, et al. Side-effects of COVID-19 on patient care: an INR story. J Appl Lab Med. 2021;6(4):953-961. doi:10.1093/jalm/jfab025.

12. Neidecker M, Patel AA, Nelson WW, Reardon G. Use of warfarin in long-term care: a systematic review. BMC Geriatr. 2012;12:14. doi:10.1186/1471-2318-12-14.

13. de Jong LA, Koops M, Gout-Zwart JJ, et al. Trends in direct oral anticoagulant (DOAC) use: health benefits and patient preference. Neth J Med. 2018;76(10):426-430.

14. Patel R, Czuprynska J, Roberts LN, et al. Switching warfarin patients to a direct oral anticoagulant during the Coronavirus Disease-19 pandemic. Thromb Res. 2021;197:192-194. doi:10.1016/j.thromres.2020.11.004.

15. Wang KY, Syed N, Fanous M, et al. Transitioning eligible patients from warfarin to a direct oral anticoagulant: a prospective quality improvement study. Blood. 2021;138(suppl 1):2966. doi:10.1182/blood-2021-151830.

16. Hendriks T, McGregor S, Rakhes S, Robinson J, Ho KM, Baker R. Patient satisfaction after conversion from warfarin to direct oral anticoagulants for patients on extended duration of anticoagulation for venous thromboembolism—the SWAN Study. PLoS ONE. 2020;15(6):e0234048. doi:10.1371/journal.pone.0234048.

17. Centers for Disease Control and Prevention. Underlying medical conditions associated with high risk for severe COVID-19: information for healthcare professionals. Published February 2020. Accessed July 18, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html.

18. Martin K, Beyer-Westendorf J, Davidson BL, Huisman MV, Sandset PM, Moll S. Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. J Thromb Haemost. 2016;14(6):1308-1313. doi:10.1111/jth.13323.

19. Martin KA, Beyer-Westendorf J, Davidson BL, Huisman MV, Sandset PM, Moll S. Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation. J Thromb Haemost. 2021;19(8):1874-1882. doi:10.1111/jth.15358.

20. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19). Published April 2020. Accessed February 12, 2022. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html.

21. Williams H. Specialty guides for patient management during the coronavirus pandemic—clinical guide for the management of anticoagulant services during the coronavirus pandemic. National Health Service. Published 2020. Accessed October 21, 2022. https://www.nice.org.uk/media/default/about/covid-19/specialty-guides/specialty-guide-anticoagulant-services-and-coronavirus.pdf.

22. Kow CS, Sunter W, Bain A, Zaidi STR, Hasan SS. Management of outpatient warfarin therapy amid COVID-19 pandemic: a practical guide. Am J Cardiovasc Drugs. 2021;20(4):301-309. doi:10.1007/s11739-020-00415-z.

23. Poli D, Tosetto A, Palareti G, et al. Managing anticoagulation in the COVID-19 era between lockdown and reopening phases. Intern Emerg Med. 2020;15(5):783-786. doi:10.1007/s11739-020-02391-3.

24. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report [published correction appears in Chest. 2022;162(1):269]. Chest. 2021;160(6):e545-e608. doi:10.1016/j.chest.2021.07.055.

25. Eliquis (apixaban) [package insert]. Princeton, NJ: Bristol-Myers Squibb; 2012.

26. Pradaxa (dabigatran) [package insert]. Ridgefield, CT: Boehringer Ingelheim; 2013.

27. Xarelto (rivaroxaban) [package insert]. Titusville, NJ: Janssen; 2013.