Impact of a Pharmacist-Led Warfarin to Direct Oral Anticoagulant Conversion Initiative during the COVID-19 Pandemic
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Abstract
Purpose: To assess the impact of a pharmacist-led warfarin to DOAC conversion initiative during the COVID-19 pandemic.
Methods: Patients who were prescribed warfarin and followed with the anticoagulation clinic for INR monitoring were assessed by outpatient clinical pharmacists as potential candidates for transition to DOACs from March-August 2020.
Results: 530 patients were assessed for transition to DOACs, of which 373 (70.4%) were deemed by clinical pharmacists to be candidates for DOACs. Of the patients who were candidates for DOACs, 66 (17.7%) were transitioned from warfarin to a DOAC. Of the patients who transitioned to a DOAC, 59 (89.4%) remained on a DOAC after one year.
Conclusion: Outpatient clinical pharmacists are an effective resource to help identify patients who are candidates for DOACs and assist with transition from warfarin. Further, high persistence rates with DOAC therapy after one year demonstrate the positive impact of the clinical pharmacist on medication adherence.

Keywords: DOAC, COVID-19, anticoagulation

Background
Novel coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization (WHO) on March 11th, 2020.1 Given the need to halt the rapid spread of COVID-19, clinics had to adapt from traditional face-to-face to virtual models of care. However, this was challenging for patients taking warfarin who needed to physically come to the clinic for routine international normalized ratio (INR) monitoring via fingerstick or venous lab draw. One option identified to help limit patient exposure to COVID-19 was to transition from warfarin to a direct oral anticoagulant (DOAC) given no need for INR monitoring. Based on less bleeding with DOACs and greater convenience for patients and health-care providers (less monitoring, drug-drug, and drug-food interactions), guidelines on antithrombotic therapy for VTE (venous thromboembolism) disease suggest that a DOAC is used in preference to warfarin for the initial and long-term treatment of VTE in patients without cancer.2 In addition, DOACs have superiority to warfarin in some trials for preventing stroke and systemic embolism and were associated with lower risks of serious bleeding in patients with atrial fibrillation.3 The Anticoagulation Forum, an organization representing anticoagulant service providers, suggested clinics interested in transitioning patients from warfarin to a DOAC develop a standardized screening protocol to identify eligible patients, including careful assessment of weight, renal function, liver function, drug interactions, indication for anticoagulation, and in-depth review of the year-round cost implications.4

At the time of the COVID-19 pandemic, our health system utilized a nurse-run anticoagulation clinic, wherein out-of-protocol INR results were managed by advance practice providers (APPs), including nurse practitioners and physician assistants. There was very little clinical pharmacist involvement in outpatient anticoagulation management. However, our health system had seven clinical pharmacists embedded in seven primary care clinics throughout our region who provided comprehensive medication management services through direct patient care, including face-to-face, phone, and video visits. Outpatient clinical pharmacists utilized a collaborative practice agreement (CPA) to make medication changes, which included the ability to prescribe DOACs under the patient’s primary care provider. Outpatient clinical pharmacists were identified by the anticoagulation clinic as a resource to review patient charts to identify potential candidates for conversion from warfarin to a DOAC, as well as assist with the transition to a DOAC, and monitor adherence.

One study described implementation of a warfarin to DOAC conversion initiative in pharmacist-run anticoagulation clinics during the COVID-19 pandemic, but unfortunately did not report percentages of patients who were deemed to be candidates for DOACs or how many were switched to DOACs.5 Therefore, our study aimed to describe not only the process used to assess for potential conversion from warfarin to DOACs, but also the number of patients who were transitioned during the COVID-19 pandemic and remained on a DOAC after one year.

Methods
Reports were generated through the electronic health record (EHR) to identify patients who were enrolled in the anticoagulation clinic for warfarin monitoring with an INR goal of 2.0-3.0 as potential candidates for conversion to DOACs from March through August 2020. Anticoagulation nurses also

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were not candidates for DOACs included: no recent serum creatinine within the last six months to assess renal function, renal impairment (creatinine clearance less than 30 ml/min), body weight greater than 120 kg, BMI greater than 40 kg/m², history of gastric bypass, off-label indication, or other factors. Of the 373 patients who were deemed to be candidates for DOACs, 66 (17.7%) were transitioned from warfarin to a DOAC, whereas 307 patients (82.3%) were not transitioned to a DOAC and remained on warfarin. Reasons why patients were not transitioned to DOACs are outlined in Figure 2. 240 patients (78.2%) did not switch to a DOAC due to out-of-pocket cost, 23 patients (7.5%) were not interested in switching, 20 patients (6.5%) were unable to be reached by the pharmacist after three attempts, 15 patients (4.9%) were hesitant about switching, 5 patients (1.6%) were not switched due to residing in a nursing home, 3 patients (1%) did not switch due to experiencing side effects with a DOAC in the past, and 1 patient (0.3%) was not switched due to pharmacist concerns regarding cognition and understanding of the conversation.

Of the 66 patients transitioned to DOACs, 47 patients (71.2%) were transitioned from warfarin to apixaban, 18 (27.3%) to rivaroxaban, and 1 (1.5%) to edoxaban. No patients were transitioned to dabigatran.

One year after the transition, 59 patients (89.4%) remained on a DOAC, one patient (1.5%) transitioned back to warfarin due to side effects from rivaroxaban, one patient (1.5%) was lost to follow-up, four patients (6.1%) were deceased, and one patient (1.5%) had anticoagulation discontinued by another provider.

Discussion
During the study period, many of the patients assessed for potential conversion to DOACs (70.4%) were deemed to be candidates by pharmacists. The main barrier for switching was cost, as 78.2% of the patients who were candidates for DOACs were not switched due to higher out-of-pocket cost for a DOAC compared to warfarin. Perhaps if this study was completed again in the future, once DOACs have transitioned to a more affordable option (loss of patent exclusivity, more competition, etc) for patients, the percentage of patients transitioned to DOACs would be higher. A promising finding of this study, however, is that of the 66 patients who were transitioned to DOACs from warfarin, a high percentage, 89.4%, remained on a DOAC one year after the transition. Excluding the four patients who were deceased during the follow-up period, this percentage is even higher, 95%. This may be because pharmacists tried to proactively assess patients’ insurance coverage and out-of-pocket costs for DOACs prior to transitioning from warfarin. As noted, zero patients switched from a DOAC back to warfarin because of cost when DOAC adherence/persistence was assessed after one year. Another study reported patients’ reluctance to transition to a DOAC was an unexpected challenge, which we also noted during our study as we had 23 patients (7.5%) who were either not interested or hesitant to switch.
One important change to note which happened in our health system after the initial study period was the transition from APPs (nurse practitioners or physician assistants) managing out-of-protocol INR results to a clinical pharmacist-led model. In September - October 2020, two full time outpatient clinical pharmacists were hired to oversee the nurse-run anticoagulation clinic and manage out-of-protocol INR results. One limitation of our study is the pharmacists who conducted the chart reviews to assess conversion from warfarin to a DOAC were generalists in primary care and did not specialize in anticoagulation. Perhaps if this study was completed by anticoagulation pharmacists instead of primary care pharmacists, our results would be different. We also acknowledge other healthcare systems may not have outpatient clinical pharmacists, which could also be a limitation for other institutions to utilize this model.

This study also did not evaluate clinical outcomes, such as stroke, VTE, bleeding, or hospitalizations, which could be an area of future study given DOACs are preferred for patients with atrial fibrillation, atrial flutter, or VTE rather than warfarin due to better outcomes.6,7 We also did not formally evaluate the impact on cost to our healthcare system for the estimated 530 hours of pharmacist time to complete these consultations; however, despite a higher acquisition cost, DOACs have shown in other studies to decrease overall healthcare costs compared to warfarin.6,7 As of May 2020, the national mean hourly wage for pharmacists was $60.32, according to the U.S. Bureau of Labor Statistics.8 In a study of VA patients with atrial fibrillation, use of DOACs reduced total medical expenditures by $25,688 over a 3-year period compared to warfarin (or about $8,562 per year per patient).6 Theoretically, given the 59 patients we converted (additional 132 pharmacist hours, theoretically $39,931.84 total), this is still less in terms of cost savings. We also did not assess if these interventions decreased rates of COVID-19 infections, as the goal of transitioning to a DOAC was to reduce exposure risk.

Another important aspect to note is patients were deemed not to be candidates for DOACs if their weight was above 120 kg and/or BMI above 40 kg/m². At the time of the initial study period, pharmacists referenced the ISTH 2016 guidelines, which recommended against the use of DOACs in patients with weight above 120 kg and/or BMI above 40 kg/m².3 Our institution now recommends that DOACs are safe and effective in patients with atrial fibrillation with body weight up to 140 kg and BMI up to 45 kg/m², and ISTH guidelines for VTE treatment were also updated in 2021 that DOACs can be used regardless of body weight or BMI.10 Perhaps if this study was completed again in the future, more patients would be deemed to be eligible for DOACs based on body weight and/or BMI.

Conclusion
Outpatient clinical pharmacists are an effective resource to help identify patients who are candidates for DOACs and assist with transition from warfarin. Further, high persistence rates with DOAC therapy after one year demonstrate the positive impact of the clinical pharmacist on medication adherence.

Key Points
1. Ambulatory care clinical pharmacists were called upon to review patients taking warfarin who followed with the anticoagulation clinic for potential transition to direct oral anticoagulants (DOACs) at the start of the COVID-19 pandemic.
2. Over 500 patient charts were reviewed, 70.4% of patients were candidates for DOACs, 17.7% were transitioned by pharmacists to DOACs.
3. At one year after conversion from warfarin to DOAC, 89.4% of patients converted remained on a DOAC.

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Figure 1.

INDICATION FOR ANTICOAGULATION

- Atrial fibrillation: 61.7%
- History of VTE: 23.4%
- Atrial fibrillation and history of VTE: 5.7%
- Other indication: 6.4%
- Atrial flutter: 2.8%

Figure 2.

Reasons patients who were candidates were not switched to a DOAC

- Out-of-pocket cost
- Patient not interested in switching
- Unable to reach patient
- Patient hesitant to switch
- Nursing home patient
- Previously experienced side effects on DOAC
- Pharmacist concerned about cognition/understanding