Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Impact of pharmacist intervention on anticoagulation management and risk for potential COVID-19 exposure during the COVID-19 pandemic

Lindsey C. Lee, Phillip Farwig, Lauren Kirk, Virginia D. Mitchell, Jennifer A. Sabatino, Kelli D. Barnes

The Ohio State University General Internal Medicine Clinics, 2050 Kenny Road Suite 2335, Columbus, OH 43221, United States of America
The Ohio State University College of Pharmacy, 500 W. 12th Avenue, Columbus, OH 43210, United States of America

ARTICLE INFO

Keywords:
Pharmacist
COVID-19
Warfarin
Anticoagulation
Direct oral anticoagulant (DOAC)
Population health

INTRODUCTION

Patients taking warfarin require frequent international normalized ratio (INR) monitoring in healthcare settings, putting them at increased risk of Coronavirus disease 2019 (COVID-19) exposure during the pandemic. Thus, strategies to limit in-person visits to healthcare facilities were recommended by the Anticoagulation Forum. The objective of this study was to describe the number and types of changes made to anticoagulation therapy as a result of pharmacist intervention during the COVID-19 pandemic.

MATERIALS AND METHODS

A retrospective chart review of patients included in a primary care COVID-19 anticoagulation intervention was conducted. During this intervention, pharmacists provided individualized recommendations for anticoagulation changes in patients taking warfarin to limit their healthcare facility exposure while also maintaining safe anticoagulation management practices.

RESULTS

As a result of pharmacist intervention, 83 (55.7%) of the 149 patients included in the intervention had changes in anticoagulation including: switching to a direct oral anticoagulant (n = 12), extending the INR monitoring interval (n = 48), switching to home INR monitoring (n = 21), or stopping anticoagulation (n = 2). For those patients who were taking warfarin for the entire 6 months pre- and post-intervention, the total number of healthcare facility and laboratory visits with an INR completed decreased from 8.8 to 6.4 (p < 0.001) per patient without a statistically significant decrease in time in therapeutic range (p = 0.76).

CONCLUSIONS

This study depicts rapid implementation of a population health-based approach to assess all patients taking warfarin for options to minimize healthcare visits and decrease risk for COVID-19 exposure. Methods to reduce healthcare visit burden while maintaining patient safety should be considered as a regular component of anticoagulation management post-pandemic.

1. Introduction

At the beginning of the coronavirus disease 2019 (COVID-19) pandemic, many communities and states within the United States enacted stay-at-home orders and the Centers for Disease Control and Prevention (CDC) recommended healthcare providers utilize telehealth strategies when possible to reduce risk of COVID-19 transmission in healthcare settings [1–3]. As a result, healthcare delivery in the United States transitioned from a model composed of predominantly face-to-face visits to one with high utilization of telehealth visits [4]. Patients taking warfarin required special considerations for care during the pandemic, as they require frequent international normalized ratio (INR) monitoring to ensure medication safety and efficacy, with the majority of this monitoring occurring in medical offices and laboratories. Thus, it is imperative to minimize risk for COVID-19 exposure while simultaneously ensuring appropriate and safe warfarin monitoring [5].

As a result of the COVID-19 pandemic, healthcare providers had to adapt to provide care in different ways. This included utilization of telehealth services, operation of drive-up point of care testing, and implementation of protocols to reduce COVID-19 exposure for both patients and providers [6,7]. The Anticoagulation Forum provided recommendations for safely managing anticoagulation during the COVID-19 pandemic including converting patients to direct oral anticoagulants (DOACs), extending the INR monitoring interval, utilizing home...
INR monitoring, visiting laboratories at non-peak times, using drive-through INR monitoring, and using telehealth visits [5].

A robust collection of literature illustrates the positive impact of pharmacist management of warfarin, resulting in higher time in therapeutic range (TTR) and fewer bleeding events [8–14]. Multiple studies have also demonstrated the impact of pharmacists on appropriate and safe use of DOACs [15,16].

This study describes a pharmacist-run population health intervention to manage anticoagulation in a primary care setting during the COVID-19 pandemic. The primary objective of this study was to describe the number and types of changes made to anticoagulation therapy as a result of pharmacist intervention during the COVID-19 pandemic. Secondary objectives included: (1) defining barriers to switching warfarin to a DOAC, (2) tracking the number of major bleeding and thrombosis events after changes in anticoagulation therapy, (3) describing the impact of an extended INR monitoring interval on patient TTR, and (4) comparing the number of in-person healthcare and laboratory visits for each patient in the 6 months before and after pharmacist intervention.

2. Materials and methods

2.1. Setting

This intervention was completed at six National Committee for Quality Assurance tier-3 patient centered medical homes (PCMHs) associated with a large academic medical center between March 18, 2020 and April 13, 2020. Clinical pharmacists are embedded in these clinics and provide patient care with a team of attending physicians, medical residents, nurse practitioners, nurses, medical assistants (MAs), social workers, and dietitians. The healthcare teams in these clinics care for >50,000 patients each year. An electronic health record (EHR) that includes patient vitals, office visit encounter notes, hospital and emergency department visit notes, and laboratory results from the entire health system, as well as outside records from other participating health systems, was used to provide and document care.

2.2. Intervention

An EHR report was generated to identify all patients with a general internal medicine (GIM) primary care provider (PCP) that had an anticoagulation management encounter in the previous 3 months. Patients who were taking warfarin and had their INR monitoring managed by a GIM PCP were included in the intervention. Patients were excluded from the intervention if they were already enrolled in home INR monitoring, had already received recommendations for anticoagulation management during the pandemic prior to the intervention, or were deceased. Pharmacists reviewed the EHR for each patient to determine the best recommendation for anticoagulation management during the COVID-19 pandemic. Recommendations made by the pharmacist included (1) switching to a DOAC, (2) extending the INR monitoring interval, (3) transitioning to home INR monitoring, (4) stopping anticoagulation, (5) no change in anticoagulation plan, and (6) unknown. For some patients, the pharmacist would list multiple acceptable recommendations for anticoagulation management in order to provide options if the primary plan was not accepted by the physician or the patient or if there were other barriers identified, such as cost. If multiple recommendations were made by the pharmacist, the first recommendation listed was documented as the pharmacist recommendation. If the recommendation made was to discuss further with the PCP and no further documentation was made, the recommendation was categorized as unknown.

The percentage of pharmacist recommendations accepted by the PCP and the patient were tracked. Recommendations were considered accepted by the PCP if the physician documented that they agreed with the pharmacist recommendation or if outreach was later started to communicate the recommendation to the patient. Recommendations made to patients were considered accepted or declined based upon reviewing the EHR for (1) the presence or absence of a new DOAC order, (2) documentation indicating a delay in the next INR monitoring date, (3) the initiation of the process to obtain a home INR monitor, or (4) the notification to the physician that the patient declined changes.

Barriers to switching a patient from warfarin to a DOAC, including cost, patient preference, provider preference, or other, were quantified. Additionally, the number and type of bleeding or thromboembolic events, which were defined as (1) any hospitalization or emergency department visit for bleeding or thromboembolism or (2) imaging showing VTE, in the 6 months after pharmacist intervention were collected.

The TTR, calculated using the Rosendaal method, was compared for 6 months before and after the intervention for all patients remaining on warfarin who had at least one INR collected in the 6 months before and after the intervention date [27]. Patients were excluded from this measure if they were not taking warfarin for the full 6 months before and after the intervention, were not managed by a GIM PCP for 6 months before and after the intervention, had no INR completed in the 6 months before or after the intervention, or were deceased within 6 months of the intervention. Additionally, for all patients taking an oral anticoagulant managed by a GIM PCP for the entire 6 months before and after the intervention, the number of healthcare visits during that time, including both outpatient office visits and laboratory visits, with an INR completed were compared. Patients were excluded from this measure if they were not taking anticoagulation for the full 6 months before and after intervention, were switched to a DOAC after the intervention by a different provider, were not managed by a GIM PCP for a full 6 months before and after the intervention, or were deceased within 6 months of the intervention. If a point-of-care INR was completed during an office visit and confirmed on the same day by a venipuncture INR, this was classified as one healthcare visit. Both measures were compared using a two-sided paired Student’s t-test, and p-values <0.05 were considered statistically significant. This study was reviewed and approved by the institutional review board for human subject research at the academic health center.

3. Results

A total of 832 patients with a PCP in the network of PCMHs that had an anticoagulation management encounter for INR monitoring in the previous three months were identified. Of these, 789 patients were actively taking warfarin and 149 of these patients were included in the intervention. Of the 683 patients excluded, 489 (71.6 %) were receiving anticoagulation management from an outside provider, 79 (11.5 %) were already enrolled in home INR monitoring, 62 (9.1 %) were no longer active patients of a GIM PCP, 43 (6.3 %) were no longer actively prescribed warfarin, 8 (1.2 %) were deceased, and for 2 (0.3 %) the PCP had already received recommendation for anticoagulation management during COVID-19 pandemic prior to the intervention. Baseline
characteristics of the patients included in the intervention are shown in Table 1.

Pharmacist recommendations and acceptance rates by the PCP and the patient are shown in Tables 2 and 3. Anticoagulation type after the intervention is shown in Fig. 1. The reasons for an unsuccessful switch to a DOAC (n = 31) were patient preference (14, 45.2%), cost (8, 25.8%), provider preference (7, 22.6%), and unable to reach the patient to discuss (2, 6.5%).

The mean number of healthcare facility and lab visits with an INR completed and mean TTR in the 6 months before and after pharmacist intervention are shown in Table 4.

There were a total of 3 bleeding events and 1 thromboembolic event in the 6 months following the intervention. One bleeding event occurred in each group of patients including those with no change in their anticoagulation, patients with an extended INR monitoring interval, and patients switched to a DOAC. One thromboembolic event occurred in the group of patients with no change in anticoagulation.

4. Discussion

The COVID-19 pandemic was an unprecedented time in healthcare that required immediate action to safely manage patients taking warfarin while also minimizing risk for COVID-19 exposure. This study depicts rapid implementation of a population health-based approach to assess all patients taking warfarin to determine if a feasible and appropriate option to minimize healthcare visits and decrease risk for COVID-19 exposure existed.

DOACs differ from warfarin in several ways, including a rapid onset of action, shorter duration of action, and less frequent monitoring requirements [17]. DOACs are preferred over warfarin for patients with nonvalvular atrial fibrillation and for patients with venous thromboembolism (VTE) requiring acute management or long-term therapy without contraindications to DOACs. The use of DOACs also decreases the need for laboratory monitoring and healthcare visits [18–20]. Pharmacist knowledge of appropriate DOAC indications and dosing, ways to transition from warfarin to a DOAC, and ways to overcome barriers to DOAC use were imperative to this intervention, however even with pharmacist support only 26% of patients actually switched to a DOAC when recommended. This is actually higher than a previous study based in the United Kingdom where only 186 of 3800 patients (5%) taking warfarin were switched to a DOAC [21]. Barriers prevent patients from switching to DOACs, including a lack of provider comfort with DOAC prescribing, a lack of provider awareness of DOAC benefits, higher medication cost to the patient, patient preference, and provider preference [22,23]. Given the difficulty of overcoming these barriers, utilization of alternate methods to safely monitor INR were required for many patients.

In this intervention, 62 of the pharmacist recommendations for changes in anticoagulation were accepted by the PCP and subsequently by the patient, and a total of 83 patients had changes in their

| Table 1 |
| --- |
| **Baseline demographic information (N = 149).** |
| Mean age in years (±SD) | 69.9 ± 13.3 |
| Sex, n (%) |  |
| Female | 66 (44.3) |
| Male | 83 (55.7) |
| BMI, n (%) |  |
| BMI <18.5 | 1 (0.7) |
| BMI 18.5 to <25 | 24 (16.1) |
| BMI 25.0 to <30 | 47 (31.5) |
| BMI 30 to <40 | 59 (39.6) |
| BMI ≥40 | 18 (12.1) |
| Insurance, n (%) |  |
| Medicare | 98 (65.8) |
| Medicaid | 13 (8.7) |
| Combo Medicare/Medicaid | 5 (3.4) |
| Private | 30 (20.1) |
| None | 3 (2.0) |
| Creatinine clearance (mL/min), n (%) |  |
| <30 | 10 (6.7) |
| ≥30 | 139 (93.3) |
| Indication for anticoagulation, n (%) |  |
| Non-valvular atrial fibrillation | 54 (36.2) |
| Multiple indications | 40 (26.8) |
| Venous thromboembolism | 35 (23.5) |
| Mechanical heart valve | 12 (8.1) |
| Other* | 8 (5.4) |

* Other includes antiphospholipid syndrome, portal vein and hepatic artery thrombosis, valvular atrial fibrillation, atrial flutter, repair of dissecting aneurysm of ascending thoracic aorta, stroke, cerebral embolism.

| Table 2 |
| --- |
| **Physician acceptance of pharmacist recommendation (N = 149).** |
| Change in anticoagulation | Pharmacist recommendation (N) | Recommendations accepted by PCP (N) (%) |
| Switch to DOAC | 42 | 35 (83.3) |
| Extend INR interval | 44 | 34 (77.3) |
| Home INR monitoring | 33 | 29 (87.9) |
| No change | 22 | 21 (95.5) |
| Unknown | 5 | – |
| Stop anticoagulation | 3 | 2 (66.7) |
| Total | 149 | 121 |

| Table 3 |
| --- |
| **Patient acceptance of pharmacist recommendation (n = 100*.** |
| Change in anticoagulation | Recommendation discussed with patient, n | Recommendations accepted by patient, n (%) |
| DOAC | 35 | 11 (31.4) |
| Extend INR interval | 34 | 32 (94.1) |
| Home INR monitoring | 29 | 17 (58.6) |
| Stop anticoagulation | 2 | 2 (100) |
| Total | 100 | 62 (62) |

* Pharmacists did not discuss recommendations with patients who had no changes made to their anticoagulation regimens or patients for which the pharmacist recommendation was not accepted by the PCP. Thus, the 21 patients for which no change to anticoagulation was recommended by the pharmacist and accepted by the PCP, and the 28 patients for which the pharmacist recommendation were not accepted by the PCP were not contacted to discuss recommendations.

![Fig. 1. Anticoagulation after pharmacist intervention (N = 149).](image-url)
anticoagulation management. When the primary recommendation was not accepted by either the PCP or the patient, or was not feasible due to cost or other barriers, pharmacists provided alternate recommendations that could be utilized to reduce healthcare visit burden. For this reason, 21 patients did not accept the primary pharmacist recommendation, but still had changes made to their anticoagulation, such as an extended INR monitoring interval or home INR monitoring.

As a result of this intervention, the number of healthcare facility visits decreased without significant changes in TTR for patients remaining on warfarin. These findings are consistent with a study of a pharmacist-run anticoagulation clinic that compared anticoagulation care in the 3 months before and after the start of the COVID-19 pandemic [24]. Patients in this previous study had a mean of 3.9 visits and a TTR of 60.6% in the 3 months prior to the start of the COVID-19 pandemic and 2.3 visits (p < 0.001) and a TTR of 65.8% (p = 0.21) during the first three months of the COVID-19 pandemic [24].

Interestingly, 94.1% of pharmacist recommendations to extend the INR monitoring interval were accepted by the patient. The American College of Chest Physicians recommends to consider extending the INR interval up to 12 weeks for patients with consistently therapeutic INRs rather than the traditional maximum INR monitoring interval of 4 weeks [25], and thus pharmacists were able to limit exposures to healthcare settings through recommending extended monitoring intervals. The desire to continue with warfarin therapy due to patient and provider comfort levels and their own past stability with warfarin may have contributed to this low acceptance rate of DOACs and the very high acceptance rate to extend INR interval.

The Anticoagulation Forum did recommend additional alternative strategies that could be utilized to limit health care visits, including visiting laboratories at non-peak times, using drive-through INR monitoring, and using telehealth visits [5]. While some patients in this intervention did use laboratory monitoring and telehealth visits for INR monitoring, pharmacists did not include these specific recommendations in their intervention because they still required patients to come into the lab and instead pharmacists tried to utilize DOACs and home INR monitoring when appropriate. Additionally, drive through INR monitoring was available for some patients who chose to transition to outside anticoagulation clinics, but was not deemed a feasible option for the patient-centered medical homes described in this study.

Of the four patients with a bleeding or thromboembolic event, two patients had their anticoagulation altered during the intervention and 2 patients continued the same anticoagulation management plan as prior to the intervention. This study was not designed to determine causality for these events as patient specific factors and confounders may have contributed to these outcomes in both groups.

There are important limitations to this study. Due to the retrospective nature of the chart review, not all information discussed with providers was documented in the EHR, thus the specific recommendation made by the pharmacist for 5 patients was unknown. Additionally, if a patient had a bleeding or thromboembolic event at a health system that was not integrated with the health system EHR, this event would not have been identified during the chart review, however all major neighboring health systems do share their information in a health information exchange program.

5. Conclusion

This study describes the successful use of a pharmacist-driven population health intervention to manage anticoagulation during the COVID-19 pandemic. The number of healthcare facility visits was reduced without significantly decreasing the patients’ TTR. Methods to reduce healthcare visit burden, without minimizing safety, for patients taking warfarin should be considered as a regular component of anticoagulation management post-pandemic.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] A. Moreland, Timing of state and territorial COVID-19 stay-at-home orders and changes in population movement — United States, March 1-May 31, 2020, MMWR Mortal Mortal Wky Rep. 69 (2020), https://doi.org/10.15585/mmwr.mm6935e2.
[2] Centers for Disease Control and Prevention, Steps healthcare facilities can take to stay prepared for COVID-19. https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth-steps-to-prepare.html, 2020. (Accessed 15 June 2021).
[3] Centers for Disease Control and Prevention, Using telehealth to expand access to essential health services during the COVID-19 pandemic. https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth.html, 2020. (Accessed 15 June 2021).
[4] J. Gallagher, S. Mc Carthy, N. Woods, F. Ryan, S. Byrne, S. O’Shea, Economic evaluation of a randomized controlled trial of pharmacist-supervised patient self-testing of warfarin therapy, J. Clin. Pharm. Ther. 40 (1) (2015) 14–19, https://doi.org/10.1111/jcpt.12761.
[5] D.G. Barnes, J. Acosta, C. Graves, et al., Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum, J. Thromb. Thrombolysis 50 (1) (2021), https://doi.org/10.1007/s11239-020-02138-2.
[6] T. Do, S. Luon, K. Boothe, M. Stutsky, M. Renauer, Advancing ambulatory pharmacy practice through a crisis: Objectives and strategies used in an ambulatory care action team’s response to the COVID-19 pandemic, Am. J. Health Syst. Pharm. (2021), https://doi.org/10.1002/jhp4.xba014.
[7] I. Mohammad, H.D. Berrie, M. Lipari, et al., Ambulatory care practice in the COVID-19 era: Redesigning clinical services and experiential learning. J. Am. Coll. Clin. Pharm. (2020), https://doi.org/10.1093/jac/csz1276.
[8] A. Downing, M. Mortimer, J. Hiers, Impact of a pharmacist-driven warfarin management protocol on achieving therapeutic international normalized ratios, Am. J. Health Syst. Pharm. 73 (5 Suppl 1) (2016) S69–S73, https://doi.org/10.2146/ajhp150039.
[9] J. Gallacher, S. McCarth, N. Woods, F. Ryan, S. Byrne, S. O’Shea, Economic evaluation of a randomized controlled trial of pharmacist-supervised patient self-testing of warfarin therapy, J. Clin. Pharm. Ther. 40 (1) (2015) 14–19, https://doi.org/10.1111/jcpt.12761.
[10] V. Gupta, S.J. Kogut, S. Thompson, Evaluation of differences in percentage of international normalized ratios in range between pharmacist-led and physician-led anticoagulation management services, J. Pharm. Pract. 28 (3) (2015) 249–255, https://doi.org/10.1177/0897190015516368.
[11] B.S. Manzoor, W.H. Cheng, J.C. Lee, E.M. Uppuluri, E.A. Nutescu, Quality of pharmacist-managed anticoagulation therapy in long-term ambulatory settings: a systematic review, Ann. Pharmacother. 51 (12) (2017) 1122–1137, https://doi.org/10.1177/1060028017721241.
[12] L. Verret, J. Couturier, A. Rozon, et al., Impact of a pharmacist-led warfarin self-management program on quality of life and anticoagulation control: a randomized trial, Pharmacotherapy 32 (10) (2012) 871–879, https://doi.org/10.1002/j.1875-9114.2012.01116.
[13] S. Young, L. Bishop, L. Twells, C. Dillon, J. Hawboldt, P. O’Shea, Comparison of pharmacist managed anticoagulation with usual medical care in a family medicine clinic, BMC Fam. Pract. 12 (2011) 88, https://doi.org/10.1186/1471-2296-12-88.
[14] T. Enzetari-Maleki, S. Dousti, H. Hamishehkar, K. Gholami, A systematic review on comparing 2 common models for management of warfarin therapy; pharmacist-led service versus usual medical care, J. Clin. Pharmacol. 56 (1) (2016), https://doi.org/10.1002/jcph.576.

[15] E. Ashjian, B. Kurtz, E. Renner, R. Yeshe, G.D. Barnes, Evaluation of a pharmacist-led outpatient direct oral anticoagulant service, Am. J. Health Syst. Pharm. 74 (7) (2017) 483–489, https://doi.org/10.2146/ajhp151026.

[16] C. Miele, M. Taylor, A. Shah, Assessment of direct Oral anticoagulant prescribing and monitoring pre- and post-implementation of a pharmacy protocol at a community teaching hospital, Hosp. Pharm. 52 (3) (2017) 207–213, https://doi.org/10.1310/hpj5203-207.

[17] A.E. Burnett, C.E. Mahan, S.R. Vazquez, L.B. Oertel, D.A. Garcia, J. Ansell, Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment, J. Thromb. Thromb. 41 (1) (2016) 206–232, https://doi.org/10.1007/s11239-015-1310-7.

[18] G.Y.H. Lip, A. Banerjee, G. Boriani, et al., Antithrombotic therapy for atrial fibrillation, Chest 154 (5) (2018) 1121–1201, https://doi.org/10.1016/j.chest.2018.07.040.

[19] C.T. January, L.S. Wann, H. Calkins, 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, Circulation 140 (2) (2019), https://doi.org/10.1161/CIR.0000000000006665.

[20] C. Kearon, E.A. Akl, J. Ornelas, et al., Antithrombotic therapy for VTE disease, Chest 149 (2) (2016) 315–352, https://doi.org/10.1016/j.chest.2015.11.026.

[21] R. Patel, J. Czuprynska, L.N. Roberts, et al., Switching warfarin patients to a direct oral anticoagulant during the coronavirus disease-19 pandemic, Thromb. Res. 197 (2021) 192–194, https://doi.org/10.1016/j.thromres.2020.11.004.

[22] G.D. Barnes, J. Acosta, C. Graves, et al., Barriers to integrating direct oral anticoagulants into anticoagulation clinic care: a mixed-methods study, Res. Pract. Thromb. Haemost. 3 (1) (2019) 79–84, https://doi.org/10.1002/rth2.12157.

[23] C.F. Sciria, T.M. Maddox, L. Marzec, et al., Switching warfarin to direct oral anticoagulants in atrial fibrillation: insights from the NCDR PINNACLE registry, Clin. Cardiol. 43 (7) (2020) 743–751, https://doi.org/10.1002/clc.23376.

[24] R. Cope, B. Fischer, N. Eladghm, M. Elakandary, N. Karam, Outpatient management of chronic warfarin therapy at a pharmacist-run anticoagulation clinic during the COVID-19 pandemic, J. Thromb. Thromb. (2021), https://doi.org/10.1007/s11239-021-02410-w.

[25] Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines - PubMed. Accessed April 28, 2021. https://pubmed.ncbi.nlm.nih.gov/22315259/.