Impact of an extended International Normalized Ratio follow-up interval on healthcare use among veteran patients on stable warfarin doses

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Purpose. To analyze the impact of a 12-week extended International Normalized Ratio (INR) follow-up interval on healthcare use.

Methods. A prospective cohort study of the use of an extended INR follow-up interval of up to 12 weeks was conducted over 2 years in a pharmacist-managed anticoagulation clinic. A detailed protocol was used to extend the INR follow-up interval to 5–6 weeks and then 7–8 weeks and 11–12 weeks. The number of planned and unplanned anticoagulation encounters, procedures requiring warfarin interruption, telephone triage phone calls, emergency department visits, and hospitalizations were collected. A post hoc subanalysis was also completed on participants who were scheduled for 4 consecutive 12-week intervals.

Results. Compared to baseline, at 12 months there was a mean decrease in planned anticoagulation encounters of 2.24 visits ($p < 0.001$) among 44 participants. From 12 to 24 months compared to baseline, there was a mean decrease in planned anticoagulation encounters of 3.13 visits ($p < 0.001$) and an increase of 0.54 unplanned anticoagulation encounters ($p = 0.04$) among 39 participants. The remainder of healthcare use variables were not statistically significantly different from baseline at any time point. Of the 15 participants scheduled for 4 consecutive 12-week intervals, there was a decrease from baseline of approximately 5 visits over the course of a year ($p < 0.001$).

Conclusion. An extended INR follow-up interval appears to decrease anticoagulation healthcare use without an increase in acute healthcare use. While this intervention could be cost-effective, institutions need to consider safety, efficacy, and feasibility prior to implementation.

Keywords. anticoagulation, drug monitoring, health services, International Normalized Ratio, warfarin

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Warfarin requires frequent monitoring to ensure safe medication use. The American College of Chest Physicians 2012 guideline suggests extending the duration between International Normalized Ratio (INR) follow-up intervals up to 12 weeks for patients on stable warfarin doses.[1] While several sites have explored longer INR follow-up intervals,[2-5] it is common practice in the United States to observe a 4- to 6-week follow-up INR interval.[5-8]

Instead of extending the INR follow-up interval for warfarin, the use of a direct oral anticoagulant (DOAC) is another avenue that can be used to decrease laboratory monitoring and clinician times. The prevalence of DOAC use is increasing, so some may think that extending the INR follow-up interval for warfarin may not be pertinent.[9] However, some patients prefer warfarin over DOACs due to the frequent INR monitoring and reassurance from clinician contact.[10] Additionally, some patients may not be candidates for DOACs due to drug interactions, comorbid conditions, or cost.[11] Therefore,

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interventions to improve warfarin use for patients and the healthcare system still require further investigation.

A longer INR follow-up interval of up to 12 weeks is suspected to decrease healthcare use and improve patient satisfaction, but this has not yet been demonstrated in practice.[12] Barnes et al.[5] evaluated 6- to 8-week INR follow-up intervals and suggested that it is a safe intervention with decreased healthcare costs. Schulman et al.[13] were the first to study an extended 12-week INR follow-up interval and found a 12-week INR follow-up interval to be noninferior to a 4-week interval for time in target range. However, patients randomized in the 12-week intervention group still received INRs and clinic contact every 4 weeks in a study setting. Carris et al.[2] and Porter et al.[4] both evaluated the feasibility and safety of a 12-week INR follow-up interval in a clinical setting and found that approximately 30% of participants could have extended intervals for a full year, suggesting the benefit of the intervention. Neither of these studies had findings of meaningful increases in bleeding or thrombosis.

Due to the paucity of published information regarding the impact of a 12-week INR follow-up interval on healthcare use, this study sought to systematically collect patient encounters within a healthcare system. This analysis is a targeted review of the healthcare use data collected from the study initially reported by Porter et al. in 2018.[4] The objective of this subanalysis was to evaluate the impact of a 12-week extended INR follow-up interval on healthcare use.

KEY POINTS

- An extended INR follow-up interval of up to 12 weeks may decrease anticoagulation healthcare use without an increase in healthcare use.
- Over the course of 1 year, patients who consistently maintained a 12-week INR follow-up interval had a mean decrease in anticoagulation healthcare encounters of 5 planned appointments.
- Institutions need to consider safety, efficacy, cost, and feasibility prior to implementation of an extended INR follow-up interval.

Methods

A prospective cohort using a detailed protocol to extend the INR follow-up interval to 12 weeks was completed over the course of 2 years.[3,4] This study was conducted in a pharmacist-managed anticoagulation clinic where pharmacists have prescriptive authority and oversee all aspects of outpatient management of anticoagulation. A detailed description of the study protocol can be found in the publication of Porter et al.[4] The study was approved by the University of Wisconsin–Madison Health Sciences Review Board and the William S. Middleton Memorial Veterans Hospital Research and Development Committee. An independent data monitoring committee oversaw the safety of the study.

Inclusion criteria for the study included patients who were 18 years of age or older, on warfarin therapy with a target INR goal range of 2–3, a patient of the anticoagulation clinic for at least 12 months, and on a stable weekly warfarin dose for at least 6 months prior with no more than a single 1-time dose adjustment.[3,4] Fourteen exclusion criteria were used to ensure safe patient selection; patients were excluded if they had a history of binge drinking in the last 6 months, had a diagnosis of cancer and were on active chemotherapy or radiotherapy, had a life expectancy of less than 1 year, were enrolled in other investigational drug protocols, only received care in the anticoagulation clinic for part of the year, received visiting nurse services for INR monitoring, had thrombocytopenia in the previous 3 months, had a history of bleeding or thromboembolism requiring medical intervention within the previous 6 months, had treatment for active liver disease, had cognitive impairment, activated power of attorney, were unable to provide informed consent, were non–English-speaking, had an unstable mental health disorder, or had a history of nonadherence to anticoagulation policies and procedures. All enrolled patients underwent informed consent.

INR follow-up intervals were extended following a protocol of 5–6 weeks, then 7–8 weeks, and then 11–12 weeks.[3,4] For INRs that were out of range or for prespecified situations where closer follow-up was warranted, participants returned to usual care (i.e., shorter follow-up at the clinician's discretion) until they requalified for an extended INR follow-up interval. If a patient required a permanent warfarin dose change, a temporary warfarin dose adjustment was needed for greater than 1 month, or there was an exclusion criterion with a time limit, a patient required stable warfarin doses for 6 months before requalifying for extended INR follow-up intervals.

To determine the impact of the protocol on patient appointment burden and anticoagulation clinic workload, healthcare use was measured. The number of anticoagulation clinic encounters, both planned and unplanned, were collected. A planned anticoagulation encounter was defined as a scheduled INR with patient contact, whereas an unplanned anticoagulation encounter was defined as an unscheduled contact with the patient that required clinician judgment. Other healthcare use outcomes included the number of procedures requiring warfarin interruption, telephone triage phone calls, emergency department visits, and hospitalizations. Only the highest level of acute care was considered in the healthcare use analysis for each episode (for an emergency department visit that resulted in a hospital admission, only the hospital admission was collected).

Data were abstracted from the electronic medical record for the time intervals of 12 months prior to enrollment (i.e., baseline), enrollment to

12 months, and 12 to 24 months. Data were collected in duplicate by 2 independent investigators, with the exception of baseline, where approximately 50% of the data were collected in duplicate. Discrepancies were discussed and resolved between the investigators at the time of data collection; a third investigator to arbitrate discrepancies was not needed. Healthcare use outside the electronic medical record was counted if the encounter was documented.

A per-protocol analysis was used where all participants still enrolled at the end of the time point were included in the analysis. A paired Wilcoxon signed rank test was used to compare the healthcare use data for all variables. The a priori level of significance was 0.05. There were no adjustments made for repeated testing. A post hoc subanalysis was completed for participants who were scheduled for 4 consecutive 12-week INR follow-up intervals in order to characterize their healthcare use. The Stata software version 14.2 (StataCorp, College Station, TX) was used for the statistical analysis.

Results

Fifty participants completed at least 1 study visit.[4] Participants were primarily white, non-Hispanic males (98% and 98%, respectively). At the time of enrollment, the mean ± S.D. age was 71.4 ± 7.6 years. The most common indication for anticoagulation was atrial fibrillation (76%). On average, participants were on the same weekly warfarin dose for a mean ± S.D. of 92.1 ± 68.6 weeks and lived a mean ± S.D. of 17 ± 17.6 miles from their primary laboratory site (range, 0.3–81 miles). At baseline, there was a mean ± S.D. of 12.67 ± 2.56 planned anticoagulation encounters for the 12 months prior to enrollment (Table 1). At 12 months, there were 44 participants, and at 24 months, there were 39 participants who completed the study. Additional demographic information and details of participant attrition are available in the article by Porter et al.[4]

Of the 50 participants, 14 (28%) were unable to be scheduled for a 12-week INR follow-up interval.[4] The article by Porter et al. describes further information on the feasibility and safety of using an extended INR follow-up interval. Regarding healthcare use, there was a mean decrease in planned anticoagulation encounters of 2.24 visits at 12 months ($p < 0.001$) and 3.13 visits from 12–24 months ($p < 0.001$) (Table 1). There was an increase of 0.54 unplanned anticoagulation encounters from 12–24 months ($p = 0.04$). The remainder of the healthcare use data, including telephone triage phone calls, emergency department visits, and hospitalizations, were not statistically significantly different from baseline at any time point. Among the 15 participants who were scheduled for 4 consecutive 12-week INR follow-up intervals, there was a decrease from baseline of approximately 5 visits over the course of a year ($p < 0.001$) (Table 2). There were 3 individuals who received 12-week INR follow-up intervals for the entire duration of the study (24 months).[4] For those 3 individuals, there were a mean of 6.0 planned anticoagulation encounters and 0.33 unplanned anticoagulation encounters at 12 months and 4.3 planned anticoagulation encounters and 0.67 unplanned anticoagulation encounters between 12 and 24 months.

Discussion

In general, an extended INR follow-up interval appears to decrease anticoagulation healthcare use without an increase in acute healthcare use. The use of an extended INR interval may have implications for both healthcare professionals and patients.

Monitoring of warfarin has notable cost requirements for the healthcare system to ensure safe and appropriate medication use, notably, frequent laboratory tests and clinician time.[5-8] Previous literature suggests approximately 18.2–26.5% of patients may be eligible for an extended INR follow-up interval.[3,5] For an anticoagulation clinic that manages a panel of 1,000 patients, one could assume approximately 20% (200 patients) could be eligible for this intervention. This study found an average decrease of approximately 2.5 planned anticoagulation encounters per participant, which would translate into 500 encounters across a panel of 1,000 patients per year. Previous literature has estimated anticoagulation clinic pharmacist salaries between $49.28 and $62.50 per hour.[14] If one assumes an

Table 1. Healthcare Use Among Study Participants

	0–12 mo Analysis (n = 44), mean (S.D.)			12–24 mo Analysis (n = 39), mean (S.D.)		
Variable	**Baseline**	**12 mo**	***p***	**Baseline**	**12–24 mo**	***p***
Planned anticoagulation encounters	12.67 (2.56)	10.43 (3.58)	<0.001	12.62 (2.64)	9.54 (3.54)	<0.001
Unplanned anticoagulation encounters	0.75 (1.20)	1.20 (1.39)	0.17	0.77 (1.27)	1.31 (1.34)	0.04
Telephone triage	0.34 (0.68)	0.57 (0.85)	0.33	0.36 (0.71)	0.33 (0.53)	1.0
Emergency department visits	0.75 (0.92)	0.73 (1.35)	0.34	0.77 (0.93)	1.10 (1.87)	0.65
Hospitalizations	0.16 (0.43)	0.09 (0.29)	0.45	0.18 (0.45)	0.33 (0.66)	0.39
Procedures	0.39 (0.58)	0.45 (1.04)	0.65	0.38 (0.54)	0.44 (0.68)	1.0

Table 2. Healthcare Use Among Participants Scheduled for 4 Consecutive 12-Week Follow-up INR Intervals[a]

	0–12 mo Analysis, mean (S.D.)			12–24 mo Analysis, mean (S.D.)	
Variable	**Baseline (*n* = 15)**	**12 mo**	***p***	**12–24 mo**	***p***
Planned anticoagulation encounters	11.87 (3.34)	6.87 (1.68)	<0.001	6.73 (2.31)	<0.001
Unplanned anticoagulation encounters	0.4 (1.06)	0.87 (1.46)	0.69	0.87 (0.92)	0.11
Telephone triage	0.2 (0.41)	0.67 (0.98)	0.38	0.27 (0.59)	1.0
Emergency department visits	0.73 (1.16)	0.87 (1.59)	1.0	1.0 (1.6)	0.69
Hospitalizations	0.07 (0.26)	0.07 (0.26)	1.0	0.07 (0.26)	1.0
Procedures	0.26 (0.46)	0 (0)	0.13	0.4 (0.63)	1.0

[a]INR = International Normalized Ratio.

encounter of approximately 10 minutes and an average pharmacist salary of $56 per hour, this would translate into an annual savings estimate of $4,650. This estimate does not include laboratory costs or the additional staff time for unplanned anticoagulation encounters. However, one must consider the risks and benefits, as a potential thromboembolism caused by using an extended INR follow-up interval would cost more than the savings of this intervention across a clinic of 1,000 patients.[15]

There is also patient burden with warfarin monitoring. For every anticoagulation encounter with a laboratory test, patients are required to travel to their clinical laboratory. In our study, participants traveled a mean ± S.D. of 17 ± 17.6 miles (range, 0.3–81 miles).[4] Offsetting even a few laboratory tests for those patients at longer distances may be both time and cost meaningful for those individuals. Unfortunately, the study did not directly measure the value patients perceived with less-frequent anticoagulation encounters. While there are several validated surveys to measure anticoagulation satisfaction, such as the Duke Anticoagulation Satisfaction Scale, few items are pertinent to healthcare use.[16]

There were several limitations to this study. While all acute care encounters which were documented in the medical record were counted, there may have been encounters outside the Veterans Affairs system which were not known or documented and therefore were not included in this analysis. However, we do not anticipate that this would have changed from baseline to postintervention. Additionally, there may be other healthcare use variables (e.g., primary care provider visits, specialty care encounters) that may be of interest and were not collected in this study.

This study was completed in a single healthcare system with a small study population. This study was not powered to detect a difference in hospitalization rates, and the results should be considered in that context. Last, this study was not a randomized controlled trial, which would have provided stronger support for the causation of the decrease in anticoagulation encounters being due to an extended INR interval.

Conclusion

An extended INR follow-up interval appears to decrease anticoagulation healthcare use without an increase in acute healthcare use. While this intervention could be cost-effective, institutions need to consider safety, efficacy, and feasibility prior to implementation.

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Additional information

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