Prospective evaluation of an extended interval of INR follow-up in a VA anticoagulation service

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Purpose:

The purpose of this study is to determine the feasibility, safety, and acceptability of implementing an extended interval of INR follow-up in Veterans on a stable dose of warfarin.

Summary:

Patients will be prescreened for study eligibility. Patients must have an INR goal of 2-3, be on indefinite warfarin therapy, and be on a stable warfarin dose for at least 6 months, except for a single, one-time adjustment. Planned procedures with INR(s) out of range would not exclude a patient. All participants will be provided usual care from the anticoagulation clinic, including a thorough INR assessment and plan for warfarin. The exception to usual care is the duration of follow-up. If the participant continues to be on a stable dose of warfarin and the INRs are within the goal range of 2-3 (including lab variation), follow-up visits will be scheduled following the extended interval protocol, which includes visits at 5-6 weeks, then 7-8 weeks, and then 11-12 weeks. If a situation arises where the extended interval is no longer appropriate (e.g. single INR outside of goal range and lab variation, a participant has a procedure requiring interruption of warfarin, drug interaction, hospitalization, etc.), the issue will be managed per usual care. If there was a permanent weekly dose adjustment or if the temporary dose change was more than 1 month, the participant would return to usual clinic care. They could requalify for the extended interval protocol when they have been on the same warfarin dose for at least 6 months, except for a single, one-time adjustment. Planned procedures with INR(s) out of range would not exclude a patient. If there was not a permanent weekly dose adjustment or if the temporary dose change was less than or equal to one month, two therapeutic INRs 4 weeks apart will be needed prior to starting the participant on the extended interval. Patient satisfaction will be evaluated at baseline, 6, 12, and 24 months. Additionally provider satisfaction, confidence, and knowledge of the extended interval protocol will be evaluated at baseline and at the end of the study. A chart review will be conducted to evaluate adherence to the extended interval protocol by study staff, including inadvertent protocol violations. Bleeding and thromboembolic events will be evaluated to ensure the safety of an extended follow-up interval.

Specific Aims:

1. To determine the feasibility of implementing an extended interval of INR follow-up in Veterans on a stable dose of warfarin.

   Goal: We aim to enroll 75 patients within 3 months.

   Goal: The anticoagulation pharmacy staff will be able to accurately follow the extended interval protocol.

2. To assess the safety of extending the interval of INR follow-up in patients.

   Hypothesis: We hypothesize that there will not be a difference between the bleeding and thromboembolic events from baseline (12 months prior to study enrollment) to events/year at 6, 12, and 24 months.

   Hypothesis: We hypothesize that there will not be a difference in the patient's time in therapeutic range (TTR) from baseline (12 months prior to study enrollment) compared to the TTR at 12 and 24 months.

3. To examine patients' and providers' acceptance of the intervention (to extend the follow-up interval of INR monitoring).

   Hypothesis: We hypothesize that both patients and providers will favorably view the intervention.

Background:

Anticoagulation treatment with vitamin K antagonists, such as warfarin, can be complicated by many variables, such as drug interactions, diet, health status, other medications, and adherence. Frequent INR monitoring is required to keep patients' INR values within their target therapeutic range to lower the risk of hemorrhagic or thrombotic adverse events. However, some patients remain on the same warfarin dose with INRs within their goal range for extended periods of time. Predictors of very stable INR control for patients on long-term anticoagulation with warfarin include age greater than 70 years, male gender, INR target less than 3.0, and absence of heart failure, diabetes, or other chronic diseases.[1, 2]

The most recent American College of Chest Physicians 2012 guidelines recommend an INR testing frequency of up to 12 weeks over 4 weeks in patients on warfarin with consistently stable INRs (Grade 2B; weak recommendation, moderate-quality evidence).[3] The guidelines define stable INRs as at least 3 months of INRs that are within therapeutic range, thus not requiring changes in warfarin dose. These guidelines are now more comparable to those from the United Kingdom, where the practice of a 12-week INR monitoring interval has been usual practice.[4] Despite the guideline recommendations, many United States anticoagulation providers are hesitant to extend the duration of INR follow-up to 12 weeks, as historically, the recommended interval and standard clinical practice for INR follow-up was a maximum of 4-6 weeks.

The interval of INR follow-up has not been extensively studied in the literature. Several retrospective studies have evaluated the use of an extended interval between INRs.[5-7] Two of these studies concluded that the time-in-therapeutic range (TTR) improved as the time between INR tests was extended[5, 6], whereas one study showed a decrease in TTR.[7] Three randomized controlled trials have evaluated INR intervals longer than 4 weeks.[8-10] Fihn et al. utilized computer-generated recommendations for follow-up, with intervals of up to 12 weeks.[9] The computer program determined a follow-up interval based on lab values and goals, number of previous visits, lab value variability, and cost of the visits and possible complications. Pengo et al. compared 4-week to 6-week follow-up intervals in patients with a prosthetic heart valve.[8] They found that extending the follow-up interval to 6 weeks did not increase the risk of bleeding or thromboembolic events. Most recently, Schulman et al. compared an INR assessment every 4 weeks to every 12 weeks in a noninferiority trial.[10] This study defined warfarin stability as patients being on the same warfarin dose for at least 6 months or longer, and permitted one time dose changes for an INR out of range. The patients who were randomized to the every 12 week follow-up continued to have contact with the anticoagulation clinic staff every 4 weeks. The authors concluded that extended follow-up intervals of 12 weeks were noninferior and safe to follow-up intervals of every 4 weeks. They also recommended further research without patient contact every 4 weeks before implementing the extended 12-week follow-up interval in routine practice.

A concern with extending the interval of INR follow-up is bleeding or thromboembolic events. Two retrospective, longitudinal cohort studies compared stable patients, defined as all INRs

within goal INR range for 6 or 12 months, to other patients, defined as one or more INRs outside of goal range during a 6 or 12 month period.[1, 2] Both studies found that bleeding and thromboembolic events were significantly lower with stable patients compared to the other patients on warfarin. Schulman et al. found no difference between the 4-week and 12-week groups in regards to major bleeding events, objectively verified thromboembolic events, and death.[10] Schulman defined bleeding events per previously published criteria.[11] Although the Schulman et al study demonstrated favorable results, it is unknown if the patient contact every 4 weeks contributed to the positive outcomes. Additionally, the anticoagulation population in a VA Anticoagulation Clinic may be different (increased age, more comorbidities). Thus, we propose to examine an extended interval of INR follow-up in eligible patients at the William S. Middleton Memorial Veterans Hospital.

The Anticoagulation Clinic at the William S. Middleton Memorial Veterans Hospital and its associated community-based outpatient clinics is a pharmacist-managed service. The clinic currently follows approximately 1800 unique patients. The clinic manages the initiation of antithrombotic therapy, follows patients on short-term and long-term antithrombotic therapy, manages the transition from inpatient to outpatient care, and coordinates warfarin interruptions for procedures using low-molecular weight heparin if warranted. During an initial visit to the clinic, patients are oriented to warfarin as well as clinic procedures. A patient and provider responsibilities document is reviewed with all patients. For subsequent visits and INR assessments, patients are either seen in clinic or receive follow-up by telephone. The maximum interval between INRs is currently 5-6 weeks. Pharmacists have prescriptive authority under a scope of practice. This type of clinic is similar to other anticoagulation clinics in the Veteran Affairs system nationally and is considered high-quality anticoagulation management.[12]

Methods and Procedures

Design:
A prospective cohort study is proposed to assess the feasibility, safety, and acceptability of extending the interval of INR follow-up to 12 weeks in stable warfarin patients. All participants consenting to study participation will have their INR follow-up interval extended according to the study protocol. If a participant's warfarin dose and INRs continue to be stable, the follow-up interval will be extended from 5-6 weeks, to 7-8 weeks, and then to 11-12 weeks. Participants will be surveyed to explore their opinions and satisfaction with the changes to their follow-up interval at various points in the study (baseline, 6 months, 12 months, 24 months). At the end of the study, a focus group will be held for a random subset of participants to obtain further information related to acceptability of this type of follow-up.

Additionally, we plan to assess anticoagulation clinic provider study staff's knowledge of the study protocol prior to the enrollment of participants for quality improvement and programmatic evaluation. At the end of the study, we also plan to hold a focus group for all anticoagulation clinic provider study staff to obtain further information related to the extended INR interval follow-up process.

Participants: We propose to enroll 75 eligible patients on warfarin from the William S. Middleton Memorial VA Hospital in Madison, WI and the Madison VA's associated community-based outreach clinics. Patients must also meet the following criteria to be invited to participate:

- 18 years of age or older
- requirement for indefinite warfarin therapy
- target INR of 2-3

- stable weekly warfarin dose for the past 6 months
    - not more than a single, one-time adjustment (boost/omission) in the past 6 months
    - planned interruption for a procedure or surgery with INR(s) out of range in the past 6 months would not exclude a patient
- a patient of the Madison VA anticoagulation clinic for the previous 12 months

Patients will not be eligible to participate in the study if they meet any of the following criteria:

- consistently drink ≥4 alcoholic beverages/day or a documented episode of alcohol binging in the past 6 months
- diagnosis of cancer and on active chemotherapy/radiotherapy in the past 3 months
- life expectancy of < 1 year
- enrolled in other investigational drug protocols
- only receiving anticoagulation care at the Madison VA for part of the year (e.g. snowbirds)
- receiving visiting nurse services for INR monitoring
- thrombocytopenia (<100K) within past 12 months
- history of bleeding or thromboembolism requiring medical intervention within past 6 months
- treatment for active liver disease (e.g. hepatitis)
- diagnosis or documentation in EMR suggesting cognitive impairment
- activated power of attorney
- inability to provide informed consent
- non-English speaking
- unstable mental health disorder that impairs judgment
- history of non-adherence to anticoagulation clinic policies and procedures (i.e. missed appointments, self-adjustment of warfarin dose, nonadherence, etc.).

Procedures:

Patient identification: A study staff member will review anticoagulation clinic patients' electronic medical records (EMR) for eligibility criteria prior to each appointment day until 75 patients are enrolled in the study or 3 months has elapsed. A list of eligible patients will be provided to study staff so they are aware that a patient is eligible prior to interacting with the patient during a routine clinic visit. After the initial group of patients has completed 6 months in the study and after a safety review, additional patients may be enrolled if 75 patients were not initially enrolled.

Patients who are eligible will be invited to participated in a research study, either face-to-face or over the phone, depending on the type of anticoagulation clinic visit. If they are interested, they will be provided information on the study requirements during that anticoagulation clinic visit. Potential participants will have the opportunity to ask questions they have regarding the study and the consent process initiated. Participants will not be paid for participation in the study. Subjects who receive phone calls and utilize secure messaging as part of their anticoagulation clinic visits will first receive an invitation letter by mail. At the subsequent anticoagulation clinic visit, they will be introduced to the study during a phone call. A separate recruitment call will not be made.

<u>Face-to-face visit:</u> For a face-to-face clinic follow-up visit, the informed consent, participant responsibilities agreement, and HIPAA authorization form will be reviewed and the patient will be provided with two copies of these documents. One copy of these documents will be collected during the visit and the patient will keep one copy. Once the documents are reviewed and signed, the patient will be considered enrolled in the study. The extended interval protocol

could be started during the same anticoagulation visit and the follow-up interval extended. During this visit, the participant will also complete the baseline survey.

Telephone visit: All patients will receive an initial invitation letter after being pre-screened for eligibility. For a telephone clinic follow-up visit, and after verbally stating their interest in the study, two copies of the informed consent, participant responsibilities agreement, and HIPAA form, and one copy of the baseline survey will be mailed to the patient. For the documents with two copies, one copy will be for the participant to keep for their records and one copy is for the study team's records. About 7-10 days from the anticoagulation clinic visit, the potential participant will be contacted by a study team member by phone to ask if the participant if they have any questions about the study and/or the forms and if would like to enroll in the study. If the potential participant is agreeable to enrolling in the study, the study team member will conduct the informed consent process over the telephone. After signing the forms, the patient will mail the informed consent, participant responsibilities agreement, HIPAA form, and satisfaction survey to the study staff at the Madison VA using a pre-addressed stamped envelope. If the patient cannot be reached or the documents are not received after three phone calls/phone messages, the patient will be considered not interested in study participation. Once the signed informed consent, HIPAA form, and participant responsibilities agreement are received, the participant will be enrolled in the study. The extended interval protocol will be started at the next anticoagulation visit with the patient and the follow-up interval extended.

Secure messaging: All patients will receive an initial invitation letter after being pre-screened for eligibility. If a patient usually receives communication from the anticoagulation clinic staff by secure messaging, the patient will be contacted by phone instead of by secure message for their next anticoagulation visit. This is usual practice for these patients if their INR is out of range or additional information is needed from the patient. Additionally, secure messaging is somewhat new to the clinic and previously, these patients were contacted by phone. During their anticoagulation visit on the phone, patient interest in the study will be determined. . If they are interested, the same steps detailed above for the telephone visit will apply to these patients.

Intervention: Participants will be provided usual care from the anticoagulation clinic. After having an INR drawn, the participant will be assessed either face-to-face, over the phone, or through secure messaging about health changes and other aspects that are pertinent to their anticoagulation. The participant will be provided with a plan for their warfarin dose and a follow-up date. The exceptions to usual care include the duration of follow-up.

Follow-up visits will be scheduled following the extended interval protocol, which includes visits at 5-6 weeks (if not already), then 7-8 weeks follow up, and then follow up at 11-12 weeks, if the participant continues to be on a stable dose of warfarin and the INRs are within the goal range of 2-3 (including lab variation) (figure 1). If the participant is already at a 5-6 week follow-up, which is usual care, their next follow-up interval will be 7-8 weeks. Follow-up visits will continue to be scheduled at 11-12 weeks if those criteria are met. If a situation arises where the extended interval is no longer appropriate (e.g. single INR outside of goal range and lab variation, a participant has a procedure requiring interruption of warfarin, drug interaction, hospitalization, etc.), the clinical situation will be managed per usual care (figure 2). If there was a permanent weekly dose adjustment or if the temporary dose change was more than 1 month, the participant would return to usual clinic care. They could requalify for the extended interval protocol when they have been on the same warfarin dose for at least 6 months, except for a single, one-time adjustment. Planned procedures with INR(s) out of range would not exclude a patient. If there was not a permanent weekly dose adjustment or if the temporary

dose change was less than or equal to one month, two therapeutic INRs 4 weeks apart will be needed prior to starting the participant on the extended interval.

If an unexpected INR is drawn, the pharmacist provider will assess the reason why the INR was drawn (figure 3). If it was due to a change in health status, the participant would most likely require shorter follow-up which would meet the criteria for the situation described previously. If it was truly a random INR, the next follow-up should be scheduled for the originally intended interval (e.g. Scheduled for 8 week follow-up and INR was drawn at 6 weeks. Next follow-up scheduled for 8 weeks).

During follow-up visits, study staff will receive information from the participant in one of three ways: directly from the participant (either by phone or in person), from an individual the anticoagulation clinic has received permission to speak with and a release of information is on file, or by written assessment form (paper or by secure messaging), which is used by the anticoagulation clinic as part of usual care. For the latter two, if clarification is needed about the participant's health status or anticoagulation therapy, study staff will contact the participant by phone to discuss further. Study staff will attempt to call the participant 3 times. If the participant is unable to be reached, a voicemail will be left for the participant (if previously authorized by the participant), a standard clinic letter will be sent to the participant, and the participant will be rescheduled for follow-up at an interval no longer than 4 weeks (not the extended interval), but could be sooner as clinically appropriate. If the participant returns the call to the anticoagulation clinic and it is appropriate, the follow-up interval can be extended to the originally intended interval.

As with usual care, if an acute medical problem is identified, the participant will be forwarded to telephone triage, the emergency room, or 911. If a non-acute problem is identified, the participant's primary care provider, nurse case manager, or appropriate provider will be contacted.

If a participant has a question or a medical problem related to anticoagulation, the anticoagulation clinic is available for participants from 8am-4:30pm, Monday through Friday. If a participant requires medical assistance outside of those hours, there is a 24-hour telephone triage phone line available for participants.

Patient satisfaction: Study participants will receive a survey at baseline and at approximately 6, 12, and 24 months. The survey includes the Duke Anticoagulation Satisfaction Scale, a validated survey instrument assessing a participant's satisfaction with their anticoagulation therapy and management.[13] If the participant has a face-to-face visit, they will fill out a paper copy of this survey during a clinic visit. If the participant has a telephone visit, the survey will be mentioned during the phone call and the participant will be mailed a copy of the survey with a pre-addressed stamped envelope. If the participant has a secure messaging visit, the survey will be mentioned in the return secure message and the participant will be mailed a copy of the survey with a pre-addressed stamped envelope. If the survey is not received by study staff within 2 weeks of the visit, the participant will be called to remind them to mail in the survey. Participants will be called up to three times to remind them to mail in the survey. At the end of the study, 10 randomly chosen participants will be asked if they would be interested in attending a focus group to explore their opinions further.

Provider satisfaction, confidence, and knowledge: Pharmacist providers who are study team members will be surveyed prior to the enrollment of the first participant about their knowledge of and confidence with the extended interval protocol. At the end of the study, all pharmacist

providers who are study staff will be invited to attend a focus group to discuss the feasibility of incorporating extended INR intervals into the anticoagulation clinic as well as their satisfaction and attitudes.

Quality assurance: A member of the study staff not involved with the participant's direct warfarin management will conduct a chart review. The chart review will be conducted to evaluate inadvertent protocol violations by anticoagulation study staff in the management of the study participants. Deviations will be categorized and quantified by type and frequency of protocol violation.

Safety: If at any time a participant reports or clinic staff are alerted to a bleeding event, it will be documented in the participant chart, as per standard of care practice. The following criteria, which are currently used in the Anticoagulation Clinic at the Madison VA to collect bleeding and thromboembolic events, will be used to differentiate major and serious bleeding:

Major

- Fatal or symptomatic bleed into a critical area or organ
- Bleeding leading to hospitalization
- Transfusion of 2 units or more packed red blood cells

Serious

- Bleeding leading to ED or UC visit or additional testing

After a major bleed, the participant will be removed from the extended follow-up interval and will not be eligible to qualify for the extended follow-up interval for 6 months after the event. After a serious bleed, the patient will be managed with usual care. If they did not have a permanent weekly dose change or if the temporary dose change was less than or equal to one month in duration, they must have 2 therapeutic INRs 4 weeks apart to begin the extended INR interval protocol.

If at any time a participant reports or clinic staff are alerted to a thromboembolic event, it will be documented in the EMR. The participant will be removed from the extended follow-up interval and not be eligible to qualify for the extended follow-up interval for 6 months after the event.

If at any time, anticoagulation clinic study staff do not feel it is appropriate to continue a participant with an extended follow-up interval, the participant can return to usual care. If at any time, the participant does not want to continue with an extended follow-up interval, they can return to usual care.

A participant will no longer be eligible for an extended INR interval if they meet any of the exclusion criteria at any time during the study, except for a bleeding or thromboembolic event. If a major bleeding or thromboembolic event occurs, they will be eligible to requalify after being on a stable warfarin dose for 6 months. A patient will also no longer be eligible for the extended INR interval if their INR goal changes and is no longer 2-3. A participant will be withdrawn from the study and no more data collected from the participant if they withdrawal their consent for the study or if death occurs.

A data monitoring committee will review the data collected, including bleeding and thromboembolic events for safety, protocol violations, and feasibility data at six months after the last patient is enrolled (at 3 months or when the 75th patient is enrolled), and then annually. If the data monitoring committee feels that the study is safe to continue, the study will continue until patients have been enrolled in the study for 2 years.

The events rates for 2013 clinic data are listed below, including a 95%CI. Additionally, ranges for event rates over the past 4 years are included.

- Major bleed: 1.88% (95%CI 1.3-2.62%); range of 1.8-2%
- Serious bleed: 0.5% (95%CI 0.23-0.94%); range of 0-0.5%
- Thromboembolism: 0.22% (95%CI 0.06-0.6%); range of 0.2-0.44%

Stoppage rules for the study:

1. Stoppage rules for the study (based on event rates from the Schulman, et al. article) are included below. If the study is stopped early, all subjects will be scheduled for an INR within 6 weeks of their last INR, which is usual practice for the clinic.

Data from Schluman study				Madison VA	
Event	**# from Schulman study**	**Rate per 1 year**	**95%CI of the 1 year rate from Schulman**	**Approx Count Based on 50 patients enrolled using upper end of 95% CI**	**Stoppage of Study**
TE (includes TE-related death)	4	1.6%	0.4-4	2	3
Composite of TE, TIA, and major bleeding, TE-related death	12	4.8%	2.5-8.2	4.1	5

2. If an event occurs:
   a. The PI or one of the Co-PIs will thoroughly evaluate the event to determine if it was related to study participation. . The following chart will be used to determine if the event was related to study participation.

Bleeding or TE event¥	**On Extended Interval at Time of Event or within 6 Weeks of Event**	**INR Measure at visit following extended interval and/OR at Time of Event**	**Relationship to Hemostasis (as relates to INR direction/ magnitude)**	**Level of Attribution**
Yes	Yes	Within target range	-	Possible
Yes	Yes	Outside target range	No relationship or uncertainty	Possible
Yes	Yes	Outside target range	Possible relationship	Probable
Yes	Yes	Outside target range	Definite relationship	Definite*

*Stopping rules apply to the events with a definite attribution. (Additional events may apply based on the discretion of the DMC and IRB.)

¥ If the event was due to accident, injury, or other clear cause, attribution may not follow table.

b. If a patient has a major bleeding or thromboembolic event, our protocol states that the patient will return to usual care and must be on the same dose for 6 months until they are able to requalify for the extended INR interval.

Adverse events (AEs) collected for this study only include bleeding and thromboembolic events. Serious adverse events (SAEs) will be documented per VA and IRB definitions. AEs will be entered into OnCore after the retrospective review of the medical record at 6, 12, and 24 months after participant enrollment in the study. SAEs are entered into the SAE documentation area in OnCore as they occur, which may not align with the time period for the chart review. The SAEs that include bleeding or thromboembolism will be entered in real-time to the AE table in OnCore.

Measures: The outcomes of this study include feasibility, safety, and acceptability of extending the interval of INR follow-up to 12 weeks in stable warfarin patients. We propose to use the following measures:

1. Feasibility: We will examine the following:
    a. Rates of participant accrual (patient interest in participating and reasons for not participating). Number of withdrawals and reasons for withdrawal from protocol or study.
    b. Change in frequency of appointments from baseline
    c. Frequency and type of protocol deviations from both participants and study staff
    d. Frequency of time outside of extended INR interval protocol and why
    e. Knowledge assessment of study staff regarding study protocol
2. Safety: We will examine the following:
    a. Participant reported and EMR review of bleeding events. Study participant bleeding events for 12 months prior to enrollment and during the study will be compared to the clinic's bleeding event rate. The following definitions will be used to categorize bleeding:
        i. Major
            1. Fatal or symptomatic bleed into a critical area or organ
            2. Bleeding leading to hospitalization
            3. Transfusion of 2 units or more PRBCs
        ii. Serious
            1. Bleeding leading to ED or UC visit or additional testing
    b. Participant reported and EMR review of thromboembolic events that are objectively verified. Study participant thromboembolic events for 12 months prior to study enrollment and during the study will be compared to the clinic's thromboembolic event rate.
    c. Participant reported and EMR review of healthcare utilization: hospitalizations, ED visits, urgent office visits, telephone triage related to anticoagulation. Utilization for 12 months prior to study enrollment will be compared to utilization during study enrollment.
    d. Baseline TTR (12 months prior and 6 months prior) for each patient and during study[14]
    e. Number of extreme INRs (<1.5, ≥4.5)
3. Acceptability: We will examine the following:
    a. Participant satisfaction will be gathered at baseline and at 6, 12 and 24 months after study enrollment through use of a survey.
    b. Provider attitudes about the protocol will be gathered at baseline and at the end of the study.

c. At the end of the study, a participant focus group will be held to obtain further data on opinions. Participants will be randomly chosen to be invited to attend.
d. At the end of the study, a provider focus group will also be held to obtain further data on opinions. All providers will be invited to attend.

Data to be collected from the medical records (up to 12 months prior to study enrollment):

- Name
- Age
- Sex
- Race/ethnicity
- Medical conditions
- Warfarin dose and dosing history
- Medications
- International Normalized Ratios (INRs) and dates
- Complete blood count and kidney (serum creatinine, eGFR) and liver function
- Alcohol intake (for calculation of HAS-BLED score)
- Primary site for lab draws
- Home address
- Bleeding and clotting events
- Use of health care outside of the anticoagulation clinic (emergency room visits, hospitalizations, or non-routine primary care visits)
- Contact with the anticoagulation clinic

Charlson Comorbidity Index and HAS-BLED scores (for all patients) and $CHADS_2$ and CHA_2DS_2-VASc scores (for atrial fibrillation patients only) will be calculated at baseline.[15-18]

TTR will be calculated using the Rosendaal method.[14]

Data will only be shared with appropriate team members. Removal of access to research study data will be accomplished for study personnel when they are no longer part of the research team. The Information Security Officer and Privacy Officer will be notified within one hour of any actual or suspected data breach.

If a breach of confidentiality takes place, it will be immediately reported to the VA R&D department and the VA information security officer for further action. If there is any emotional upset by a participant, the will be asked if they would prefer to discontinue participation in the study and will have the opportunity to drop out. If warranted, participants can be referred to Integrated Care clinic regarding emotional upset. Integrated Care is a walk-in clinic at the Madison VA and is part of the Mental Health Department.

Sample Size: As this is a feasibility study, the primary concerns are whether or not this process could be incorporated into the normal anticoagulation clinic procedures and workflow. Results from this study can be utilized for calculating sample size and power statistical tests in future larger studies.

Analysis:

Accrual rate will be determined by average participants enrolled per week. Dropout rate will be determined by the number of participants lost to follow up out of the total number of participants

enrolled. Descriptive statistics (percentages, means, rates, and standard deviations) will be determined for all recorded baseline variables. Differences from baseline and at study completion will be compared utilizing McNemar Test for categorical data and paired t-test or Wilcoxon Signed-Rank Test for continuous and ordinal data (respectively). Thematic analysis will be utilized for to determine themes of satisfaction and/or concerns and barriers regarding the extended follow-up protocol from of the focus groups.

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