Reviewer's report

Title: Trial of an educational intervention on patients' knowledge of atrial fibrillation and anticoagulant therapy, INR control, and outcome of Treatment with warfarin (TREAT)

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Reviewer: Eric Smith

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The authors describe a protocol for a randomized controlled trial of an educational intervention designed to improve adherence to warfarin therapy. The primary outcome is the amount of time with INR in the target therapeutic range (TTR). The authors are to be commended for the scientific rigor of this study using a randomized controlled design with a surrogate marker (TTR) of a useful clinical outcome (risk of thrombotic or bleeding events on warfarin). All too often, educational interventions are implemented based on face validity or before vs. after studies that could be confounded by secular trends.

My comments on the study are numerated below.

Major Compulsory Revisions

1. The protocol is sound overall, but I am concerned about the timing of INR checks post-discharge which are not pre-specified but will be determined by usual care. The authors note that clinic staff will be blinded to intervention arm, but the patients will not be. Patient complaints or comments could certainly influence the frequency and timing of INR checks. Because the timing of INR checks will be determined post-randomization there is a risk that bias could be introduced.

   Consider a scenario where dietary indiscretions (e.g. spinach binge!) are similar between groups but are more likely to be reported by the better educated group. This might result in more INR checks post-spinach in the better educated group, with more frequent documentation of sub-therapeutic INR. The less educated group would have had a similar time with sub-therapeutic INR, but this would not have been detected because information on dietary indiscretion was not reported to clinic staff. This would bias the study toward a negative result.

   I strongly encourage the authors to pre-specify INR checks to avoid the possibility of a biased result.

2. The project is funded by Bayer Healthcare. Can the authors be more explicit about their independence with regard to study design, analysis of the data, access to the data and right to publish the results?

3. Randomization will be stratified by age. Please explain the age categories that will be used.
4. Randomization will be stratified by specialist AF clinic vs. general cardiology clinic. Please explain how many of each type of clinic will be involved in the trial.

5. Results, description of usual care: "All patients will also receive the standard yellow book to identify that they are taking OAC therapy". Please omit the local term "yellow book" and simply explain the information provided in the booklet as part of usual care.

6. How long after initiation of warfarin therapy will patients be eligible for recruitment? It seems like the study will run entirely in the outpatient setting. Will patients started on OAC while admitted to hospital be eligible to join the study post-discharge?

7. Please be more specific about the assumptions used for your sample size calculation for the primary endpoint. What TTR is anticipated, and what is the standard deviation that is assumed?

8. For the secondary endpoint, please specify how "increase in knowledge" (page 12) will be measured. What number will be used to compare the groups and how is it derived?

9. A discussion of the limitations of the trial protocol is warranted. There is no "perfect" trial design, of course. To my way of thinking, limitations could include: a) patients are not blinded (a necessary limitation), b) trial is powered for a surrogate outcome marker, TTR, rather than clinical outcome (although I think this is a very justifiable choice of surrogate marker), c) the results may not be generalizable to patients with cognitive impairment or with limited English ability (who were not included for valid reasons), or patients from other cultures (because educational and lifestyle interventions may be relatively culturally specific).

Minor Essential Revisions
1. Last sentence of page 7: "as part standard care" should be "as part of standard care".

2. Page 9: "...be obtained by the researcher telephoning and an associate researcher..." should be "...be obtained by the researcher telephoning an associate researcher...".

Discretionary Revisions:
1. Inclusion criteria: Patients with valvular heart disease are excluded--why? For consideration: should the study be restricted to patients with the most common target INR of 2.0-3.0?

2. The study results, if positive, would have greater impact if the educational intervention can be applied at other sites. Do the authors have plans to disseminate knowledge of their intervention in the event of a positive result? For example, could the educational video be made available online for download?
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.