Reviewer's report

Title: Anticoagulated patient's perception of their illness, their beliefs about the anticoagulant therapy prescribed and the relationship with adherence: impact of novel oral anticoagulant therapy - The Switching Study

Version: 1 Date: 2 November 2014

Reviewer: Marie P Schneider

Reviewer's report:

Review of the article “Anticoagulated patient’s perception of their illness, their beliefs about anticoagulant therapy prescribed and the relationship with adherence: impact of novel oral anticoagulant therapy – The Switching Study” Auyeung et al., 2014

Dear Authors,

Thank you for your manuscript, which I read with interest. I made the following recommendations to improve in order to improve your manuscript.

Major Compulsory Revisions needed:

• Clarity and coherence of the paper need to be improved
• The question posed is original and important. Nevertheless the methodology is incomplete and needs major improvements.
• English needs to be improved

Details

1 Structure of the article

BMC recommendations and other information

• According to the BMC recommendations for the Study protocols submission (http://www.biomedcentral.com/bmchematol/authors/instructions/studyprotocol):
  - Page 1: please specify the trial identifier and registry name. If not yet registered, name of intended registry
  - Page 12: the list of abbreviations must appear before the competing interest

• Title

If possible specify the study design in the title

2 Background

• The article mentions the vitamin K antagonists (VKA) but not heparin. Please clarify.
• New oral anticoagulants can also be a source of drug-drug and drug-food interactions. The text leads to misunderstanding (l. 63-67)
• “Acknowledging that all patients will have differing beliefs about their medication is the first step in addressing the medication non-adherence problem” [19] (l.87). The reference tells that patients may have different beliefs about their medications but not that this understanding is the first step in addressing the medication non-adherence problem. Please add another reference or modify our text.

3 Is the question posed original, important and well defined?

Originality
• The question posed is original and important. Nevertheless, we recommend updating the references.

Clarity
• The research question is complex and difficult to understand.
• A lot of hypotheses and objectives are mentioned in the article; but many variables to collect are not specified (e.g. determination of symptomatic vs. asymptomatic patients). This point needs clarification.

4 Are the data sound and well controlled?

• Switch to NOAC

We need to understand better why the switch is proposed only to patients with TTR<50% (is this only an economic argument or are you following some therapeutic policies?). This switch might be clear in UK but it is not outside UK. We also refer to following UK excellence guidelines for AF (ref [23] in the article) saying:

“Trials of the non-VKA oral anticoagulants have shown that the degree of benefit of these agents compared with warfarin may depend on the time in therapeutic range (TTR) of the warfarin group. These trials assessed the degree of benefit in relation to the mean TTR for the warfarin group in that country. However, the inference of benefit is based on a number of assumptions. It is unclear that the population TTR can be extrapolated to decision-making in an individual. If, for example, an individual’s low TTR is a result of poor compliance, it is unlikely that compliance will improve with a non-VKA oral anticoagulant and uncertain whether a non-VKA oral anticoagulant will offer any benefit. Moreover, the threshold of TTR at which a non-VKA oral anticoagulant might offer benefit is unclear. The same question can be extended to include people before they start warfarin treatment, using criteria that prospectively identify those likely to have poor control on warfarin”

5 Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?

Participants:
• Please clarify the design for each sub-study (I, II and III)
• Specify if data will be analyzed according to the intention to treat guidelines.
• Specify which population will be included: AF and/or VTE, other?
• It is not clear if inclusion criteria are applied before dividing the population according to level of TTR or after.
• We do not understand why patients with a TTR between 50 and 75 are not considered; this will decrease the external validity of the results.
• TTR < 75% is not an exclusion criteria but rather a stratifying one.
• Pregnancy is a contra-indication to NOAC; why did you not include in the exclusion criteria?

Data collection

Socio-demographic data
• Please clarify how and when the socio-demographic data will be collected.

Medication adherence
• How adherence to NOAC was assessed? In the article you mention “by pill count and specific adherence screening questions at 1 year”
  - Please explain how the pill count will be done (mathematical formula?), when, where and by whom
  - Please clarify which kind of questions will be proposed. A validated questionnaire will be used? Please specify and provide a reference.
• Who administers the questionnaires to the patients (BMQ, IPQ-R, ACTS)? The researcher? The physician? Others?
• Time needed to fill in the questionnaires?

Study I
• Responses between the groups will be compared # specified in the figure and in the abstract but not in the text. Please clarify.

Study II
• Will the results of group 2a and results of group 2b (BMQ, IPQ-R, ACTS) be compared at baseline? Please clarify.
• Will Group 2b (warfarin) be followed during the whole study (from baseline to month 12)? If not, why?

Study III
“The results from studies I and II will be used to create a treatment pathway which will be used for group 3 ”
“The findings from the study will be used to inform a treatment pathway which aims to help support patients prescribed chronic NOAC therapy” (l. 116-117)
“The treatment pathway will be informed from the two-month follow-up data collected at visit 3 from patients in group 2 of study I. Group 3 patients will have the same follow-up in clinic as per the schedule outlined for group 2 patients” (l. 194-195)
• Please clarify what is a treatment pathway and what you intend to do?
• The pathway will inform the medical follow-up between months 0 and 2; why not extending this to month 12? How will this pathway support the prescription of chronic NOAC therapy? Please clarify.

Will the results of group 2a (study II - NOAC) and group 3 (study III - NOAC) be compared?

Limitations
Identify the possible limitations and bias that could influence the internal or external validity of the results.

6 What are the strengths and weaknesses of the methods?
The article presents an interesting design but the methodology is complex and needs to be improved. Readers need to know exactly which data will be collected, why, when, how and by whom. Please provide more details.

7 Is the interpretation (discussion) well balanced and supported by the data?
Discussion is interesting with comparisons with the literature. However, a reference is missing in the following sentence: “Current cost-analysis which states that these NOAC are cost-effective assumes full adherence to medication” (l. 291).

8 Can the writing, organization, tables and figures be improved?
• Writing: English needs to be improved
• Organization: the structure of the methods needs major improvements.
• Tables and figures: to understand the study design, the figure 2 is necessary; nevertheless, using a diagram with a timeline could increase clarity.

The legend of figure 1 should appear on the same page than the figure.
The list of abbreviations is not complete (the abbreviations used in the table 1 don’t appear in the list)

9 Are there any ethical or competing interests issues you would like to raise?
• Harms
Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct are not specified
• Confidentiality
How will personal information about potential and enrolled participants be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial?
• Data storage
How will the collected data be stored, where and how long?

10. Are the included additional files (supplementary materials) appropriate?
Yes, Ethics approval has been presented

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

- **Harms**
  Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct are not specified

- **Confidentiality**
  How will personal information about potential and enrolled participants be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial?

- **Data storage**
  How will the collected data be stored, where and how long?