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: 4
Date: 19 April 2016
Reviewer: Marie P Schneider

Reviewer's report:

Dear authors,

Thank you very much for your answers. Most of my questions have been answered appropriately but some are still pending. I acknowledge the clinical importance of the subject you are addressing. However, I am still concerned about the methodological weaknesses of the scientific design.

The background of the manuscript is very clear, however it became very long. For example, Lines 121-122 are a repetition of lines 114-115 and could be dropped. My main concern here, which I already addressed in my former review, is that I do not think all readers will understand the definition of ‘treatment pathway’. Please define in your manuscript what a treatment pathway is, give references and describe its objectives. I feel this is important as it is the heart of your series of studies.

At this point, my main concerns in the method section are as follows:
1. I do not agree with your answer (Feb 15th) on the design of the study III. I agree that RCT are not always appropriate. However, there are alternate designs. I would recommend you to ensure that both groups (studies II and III) will be comparable by using the right design in order to be able to determine the effectiveness of the therapeutic pathway. This is a main concern to address in your method.

2. It is clear now that you are recruiting patients with TTR<50% and TTR>75% in order to increase the statistical power of the study. I still think that the exclusion of patients with a TTR between 50-75% is a clinical bias of your study unless you better explain clinically why you intend to develop a treatment pathway for patients with a TTR<50% exclusively and not for patients between 50 and 75%. These clinical and/or economic arguments should be based on the clinical experience at King’s College Hospital and based on the literature.

3. Study I, groups 1 and 2: your outcomes here is the comparison of the questionnaires between both groups. Methodologically, an outcome can be compared between groups only if it is measured at the same time. It does not seem to be the case here (‘once through the post’ for group 1 and visit 1 for group 2). This issue has to be addressed.
4. ‘The treatment pathway will be informed from (...) data collected at visit 3’ (L. 212-213). However, if I understand it well, the research data collected at this visit are limited to pill count (L.201-202). Pill count represents a limited amount of data for informing a pathway.

5. The findings from group 2 will be compared to the findings of group 3 (L. 215-216): variables to compare have to be described.

6. Questionnaires are sometimes administered by the clinical pharmacists (L. 254-256) and sometimes be the research team (L.277-278) if I understood it well. Why not keeping the same procedure along the different parts of the study? If administered by the pharmacists, I am afraid there will be an important risk of desirability bias in the patients’ answers. This has to be addressed in the manuscript.

7. ‘Specific adherence screening questions will be asked to assess adherence in the preceding months’ (L. 267-268). Timing has to be precisely specified.

8. It is hard to follow the methodology around adherence measurement: pill count at months 1 and 2, and Morisky at 1 year (Table1), which means that there is no common adherence measure all along the study. In your response (February 15th), you mentioned the proportion of days covered, which I do not find in the manuscript. I am afraid that this split methodology represents a huge limitation for the reach of your results.

9. Sociodemographic information (Table 1): all measured variables have to be listed, for example in the footnote of the table (L.602).

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.