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: 3
Date: 2 February 2016

Reviewer: Marie P Schneider

Reviewer’s report:

Dear Authors,

Thank you for your review, which increased the study methodology. This represents a huge study (>700 patients), and a very complex design; Figure 1 helps understanding it. There are still weaknesses in the methodology (e.g. how is persistence measured in GP summary care records; this is not obvious to the readers; describe which novel anticoagulant patients will be switched to; study III is missing in the abstract).

The reference list needs to be checked again, as example references 10 and 11 are missing. Reference 21 is old and refers to an abstract only; this reference is weak for this very important aspect in methodology. There are other updated references of the 8-item Morisky adherence scale. Line 76: authors referred 9 publications, all from the same authors and no original cost-effectiveness papers. The literature search has to be refined.

There are still typo errors in the text, for example ‘Additionally, there are currently no antidotes currently’ (line80). Text needs to be checked carefully.

Line 67: ‘relatively fewer drug-drug interactions’; this statement is misleading as NOAC are substrates of the P-glycoprotein and P450 CYP3A4, and are therefore both vulnerable of inducers and inhibitors of these enzymes, leading to many interactions. This has been reflected in the exclusion criteria: ‘taking concurrent interacting drugs which are contra-indicated’ (Line 229) but not in the background section.

Line 143: ‘Anticoagulated patients who meet the inclusion criteria, defined by their TTR’. Please specify the inclusion/eligibility criteria more clearly.

Lines 170-190: specify more clearly that included patients in study 1 do not switch to NOACs (pre-switch study).

Lines 215-216: ‘The findings from group 2 patients will then be compared to the findings of group 3 patients. Authors should specify how they will match the patients of groups 2 and 3 as they are not randomized, with a risk of bias. I do not think that the design is controlled as stated in the manuscript. It is rather a case-control study. It will be difficult to test the effectiveness of the intervention. Why not doing a RCT or using alternative designs like the stepped-wedge
design?

Line 211: please give a definition of ‘Treatment pathway’. Is this the intervention on adherence that will be tested? By reading the manuscript, I got the feeling that you are using the psychometric outcomes of the studies to build up the intervention. Please clarify the intervention and the way you intend to proceed to build it up.

Lines 281-282: I think there is an important, ethical problem here as all patients should be offered the standard of care or local guidance, i.e. switch to NOACs if eligible, and then they should be introduced to the research study, and not reverse as described in the manuscript.

Lines 327-330: it is not clear which outcome authors use to calculate the sample size of the intervention?

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.