Reviewer’s report

Title: Standardized Warfarin Monitoring Decreases Adverse Drug Reactions

Version: 0 Date: 21 Dec 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

No - there are major issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are major issues

Statistics - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues
OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This paper reports the time trends of warfarin prescription at discharge from hospital and ADR to warfarin. The authors also had the objective to evaluate time in therapeutic range and the rate of use of an electronic health module to monitor warfarin treatment. Although not explicitly stated, from the analysis and discussion it appears that one of the objectives was to evaluate whether the establishment of an anticoagulation task force had a positive effect on TTR and adverse drug reactions. This study has several major issues:

REQUESTED REVISIONS:

1. The objectives should be restated clearly explaining if they also include the effect of the establishment of the anticoagulation task force.

2. The appropriateness of the study design depends on its objective, so at the moment I am unsure about this issue.

3. The current description of the methods do not allow to express a judgement about the conduction of the study, with special regard to evaluation of ADRs;

4. I am unsure about the use of a Poisson model to analyse TTR, the authors should provide the rationale for this choice;

5. The interpretation of these data should take into account information from other sources. The lack of a control group, if relevant (see above), should be acknowledged.

6. If the objective is just to describe changes in warfarin prescription, ADR, and TTR, then this should be made clear, and confusion about the effect of the adoption of a software and education strategy should be avoided; furthermore, comparison with statistics from other sources should be provide. If the objective is to describe the changes observed in relation to the implementation of
the above-mentioned measures, then the lack of a control group is a major issue that should be acknowledged in the limitation;

7. The methods do not allow a complete understanding of the data. More information is needed about the software and the education program. More importantly, more information is needed about ADR: how were they established? What was the likelihood that a patient with a warfarin-related ADR was referred to another hospital and thus missed from this study?

8. The statement that warfarin is the most commonly used anticoagulant for thrombosis and pulmonary embolism is probably true, but the references supporting it are a bit dated and many of them are about indication, not prevalence of use. Of note, the most recent reference is from 2012, that is just after the approval of DOAC. The authors should acknowledge that the epidemiology of anticoagulants prescription is rapidly changing. Indeed, the results of this paper show that in 2017 warfarin accounted for less than 50% of prescriptions.

9 Poisson regression was used to analyze TTR. This variable is supposed to be numerical, while Poisson distribution is used for count data. The authors should report the rationale for this choice.

10. Some statements in the discussion are confusing. For example, at page 10 the authors state that "... the proportion of warfarin prescriptions [...] decreased over the 5 years". Soon after, however, they state that "the number of patients treated with warfarin in our study remained constant". Please explain.

Note: This reviewer report can be downloaded - see attached pdf file.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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