Reviewer's report

Title: Standardized Warfarin Monitoring Decreases Adverse Drug Reactions

Version: 1 Date: 02 Aug 2019

Reviewer: Reviewer 3

Reviewer's report:

"PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)

Yes - there is a clear objective

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

No - there are minor issues

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

Yes - experiments and analyses were performed appropriately

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?

Yes - the author's interpretation is reasonable
OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?

Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The authors have satisfactorily addressed the comments raised by two reviewers and have also clearly indicated the modifications in red color in the manuscript. However, there are still other few comments to improve the manuscript.

The authors have analyzed the trends of warfarin prescription and ADR to warfarin over the 5-year period, starting from 2013. They have clearly presented their findings in tabular way with statistical significance levels as well.

Taking into consideration the study design, chi square test would not be a better statistical test. Rather, repeated measure ANOVA (if data were normally distributed) or Friedman's test (if data were non-normally distributed) or multilevel modeling would be relevant and appropriate statistical test. Other comments have been given in separate section.

ADDITIONAL REQUESTS/SUGGESTIONS:

Abstract (Lines 37-38): Rewrite the statement 'number and total cost change of severe warfarin ADRs' clearly.

Background (Line 69): Specify whether 'protime' is generic term or brand version of the procedure. If it is brand version, mention protime®.

Methods:

* Specify the study design very clearly. Table 3 shows that you followed trend analysis or time series study design. Clarify this.
Elaborate upon the basis of sample size calculation for each year and sampling technique employed for each year. These are very crucial for the external validity of your findings.

Statistical analysis:

Lines 142-145: Table 3 shows that you performed follow up for 4 years, even adding new patients. This shows you repeatedly measured the INR from the patients taking warfarin and interpreted these for your study purpose. In such scenario of repeated design, chi square test is not better suited; it seems that you tried to compute Bayes factor with the Poisson model as your sampling plan. If this was the condition, row sum or column sum multinomial model would be better. Above all, repeated measure ANOVA (if data were normally distributed) or Friedman's test (if data were non-normally distributed) or multilevel modeling would be relevant and appropriate statistical test.

Table 4: You've only mentioned the numbers of warfarin ADRs. It would be better to show the ADRs exactly in appendix as well."

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.

Yes

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

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

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