Author's response to reviews

Title: Predictors of Warfarin Use in Atrial Fibrillation in the United States: A Systematic review and Meta-Analysis

Authors:

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Version: 2 Date: 28 November 2011

Reviewer's report

Title: Predictors of Warfarin Use in Atrial Fibrillation
Version: 1 Date: 21 October 2011
Reviewer: William L Baker
Reviewer's report:

Major Compulsory Revisions:

1) The authors do not make it clear how this project, both in the introduction as well as the discussion, is relevant to a Family Medicine audience. How should this population of reader use the information provided by this project in their practice?

The last sentence of the INTRODUCTION and the CONCLUSION now addresses how this meta-analysis can be used by family practice decision-makers (e.g., to target interventions or methods to improve utilization of warfarin when it is indicated for stroke prevention).

Minor Essential Revisions:

1) The Objective of the study as well as the method contains a few contradictions in tense (past vs. future). These should be addressed & corrected.

Addressed.

2) I would suggest stating in the title that this data is representative of a United States population only.

Done.

3) I would suggest including a few search terms in the 1st paragraph of the Methods section to give readers an idea of those used in the search. They can be referred to the appendix for a more detailed description.
Added.

4) Page 10, "Results of Meta-Analysis", 1st paragraph, Line 9: The sentence beginning "While age per 10-year increase..." is a fragment.
Corrected.

5) Page 13, 2nd paragraph: What data, either from the current study or the medical literature, supports the text regarding age and stroke risk?
References (3 and 44) added to support the text regarding age and stroke risk.

6) Page 14, 2nd paragraph, 3rd line: The author of reference #55 should be "Fang and colleagues" rather than "Wang and colleagues".
Corrected.

7) I would recommend adding 2 additional limitations to the paper: A) Did you look at differences in predictors between valvular & non-valvular atrial fibrillation?
Added to discussion.

B) I would recommend mentioning the fact that this information is representative of practice in the US and may not be applicable to other countries.
Added to discussion.

8) Reference #49 is missing the names of the authors of this paper.
Authors added.

9) Figure 1: Provide reference numbers for both Hylek 1996 and the 2001 Guideline Update that are provided in the footnote.
Added.

Discretionary Revisions:

1) Somewhere in the methods section, I would recommend defining the term "ideal candidate".

We have added text to the methods section to clarify what is meant by an “ideal candidate for warfarin” = patient populations without warfarin contraindications.

Level of interest: An article of outstanding merit and interest in its field

Thank you!

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"
Reviewer: Olivia J Phung
Reviewer’s report:
Minor Essential Revisions
1. General Comments:
a. This is a thorough and well-conducted systematic review on the factors (either patient or prescriber) which may be associated with warfarin usage. This is an important topic to evaluate because we will then be able to target interventions or methods to improve utilization of warfarin when it is indicated for stroke prevention. This systematic review also adds to the current understanding of prescribing patterns and factors which influence prescribing.

Thank you kindly!
b. Ensure that all methods are presented in past tense.
Corrected per reviewer #1.
c. Please be consistent in the usage of “p-value” or “P value”
Corrected.
d. Minor grammatical corrections are needed throughout the manuscript.
The manuscript has been revised to address grammatical errors.

2. Abstract
a. Would recommend changing the word “time” to “year of study”. “Time” could mean many different things, whereas an actual calendar year was what was analysed.
Done.
b. For advancing age as a dichotomous variable, would add statement that cutoffs varied per study. As it stands, the reader is unsure what age cutoff was evaluated.
Recommended text has been added to the abstract.

3. Results
a. Authors stated that there was a moderately strong correlation between warfarin use and progressing time. Please provide criteria for determining “moderately strong” in the Methods section.

This was based upon Cohen’s Rule of Thumb for interpreting correlations. This fact has been added to the Methods section.
b. Strength of evidence grading
i. Third sentence has an extra period at the end. Please remove.
ii. Last sentence: Should there be a closing parenthesis at the end of “n=370”? Added.

4. Tables and Figures
   a. Table 3: Please separate I2 and Cochrane Q p-value into two separate columns. This would improve readability of the table.
      Done.
   b. Table 3: SOE is not used in the table and does not need to be defined in the legend.
      Removed from Legend.

Level of interest: An article of outstanding merit and interest in its field

Thanks much!

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

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

Declaration of competing interests:
I declare that I have no competing interests

EDITOR'S COMMENTS:

"The reviewers have now made some suggestions to improve your manuscript to which you should respond point by point. However I have some additional concerns and suggestion which should be addressed.

Title: The title should include the study design, as stipulated in Instructions for BMC Family Practice authors.

Done.

Abstract: The conclusion is a summary of the main findings but does not mention implications for practice or research.

A statement has been added to the conclusion to communicate the implications of this research on practice/research (e.g., to target interventions or methods to improve utilization of warfarin when it is indicated for stroke prevention).

Introduction: You claim that warfarin is underused in patients with AF. Reference 6 does not support this claim. The objective of the cited meta-analysis was to evaluate the effect of specialty clinic versus usual care by community physicians on anticoagulation control, measured as the proportion of time spent in therapeutic INR range."
Reference 6 has been deleted.

The quality of anticoagulation management and the indication for warfarin are two different topics.

Please not that: Weisbord SD, Whittle J, Brooks RC.Is warfarin really underused in patients with atrial fibrillation? J Gen Intern Med. 2001; 16: 743-9 have shown in one study that warfarin is not underused. You state the objective of your meta-analysis is to review factors associated evaluating the association between prescriber and/or patient characteristics and subsequent prescription of warfarin for stroke prevention in patients with atrial fibrillation (AF).

Detection of underuse or evaluation of validity of reasons to forgo prescription of warfarin despite AF is not mentioned as objective. You do not describe in the method section how you assessed underuse. The wording concerning non-prescription of warfarin in your manuscript should therefore be less accusatory.

We have softened the language in our manuscript in multiple places, including the conclusion sections of the abstract and main text.

Discussion: You cite again reference 6 as evidence for suboptimal utilization of warfarin. This is misleading since it does not differentiate between suboptimal management and underuse. This should be clarified.

Reference 6 has been deleted per above suggestion.

Conclusion: Your conclusion should relate to factors associated with warfarin prescription for stroke prevention in AF you have explored. You did not do a review of appropriateness of non-prescription or underuse of warfarin for AF. Therefore your conclusion should not be Warfarin use appears suboptimal. The observed increased proportion of patients receiving Warfarin could be due to many other factors not assessed in this review.

We have revised the conclusion statement in the abstract and main text to remove this statement.

EDITORIAL REQUIREMENTS:

Please make the following formatting changes during revision of your manuscript. Ensuring that the manuscript meets the journal’s manuscript structure will help to speed the production process if your manuscript is accepted for publication

1. Requesting ethics statement: Please document ethical approval of your study in the Methods Section of the manuscript. Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm). A statement to this effect must appear in the Methods section of the manuscript, including the
name of the body which gave approval, with a reference number where appropriate.

This paper does not report the results of "experimental research", thus no ethics statement is needed.

2. Requesting consent statement:

Please state in the Methods section whether written informed consent for participation in the study was obtained from participants or, where participants are children, a parent or guardian.

This paper does not report the results of "experimental research", thus no ethics statement is needed.

3. Title page: Please restructure the title page in the manuscript file. The Title Page should contain, IN THE MINIMUM: Title, Author list, Affiliations (department names, institution name, street name, city, zip code, country), email addresses of all authors. The author list and email addresses must be IDENTICAL in the manuscript file and on the submission system, and it must be clear which affiliation pertains to each author.

Added.

*** Please remove the keywords, word count, funding, etc. from your title page.
Removed.

4. Abstract: Please correctly format the abstract of your manuscript and ensure that the abstract is identical in the manuscript file and on the submission system.

5. Competing interests: Please include a 'Competing interests' section after the Conclusions. If there are none to declare, please write 'The authors declare that they have no competing interests'. Please check the instructions for authors on the journal website for a full list of questions to consider when writing your competing interests statement.

Added.

6. Please include an AUTHOR'S CONTRIBUTION section before the Acknowledgements and Reference list.

For the Authors' contributions we suggest the following format: AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination. All authors read and approved the final manuscript.

Added.
The abstract of the manuscript must be structured into separate sections: Background, the context and purpose of the study; Methods, how the study was performed and statistical tests used; Results, the main findings; Conclusions, brief summary and potential implications. Please minimize the use of abbreviations and do not cite references in the abstract.

The abstract has been restructured.

7. Tables: Please ensure that the order in which your tables are cited is the same as the order in which they are provided. Every table must be cited in the text, using Arabic numerals. Please do not use ranges when listing tables.

Done.

Tables must not be subdivided, or contain tables within tables. Please note that we are unable to display vertical lines or text within tables, no display merged cells: please re-layout your table without these elements.

Vertical lines removed.

Tables should be formatted using the Table tool in your word processor. Please ensure the table title is above the table and the legend is below the table. For more information, see the instructions for authors on the journal website.

Done.

8. Additional files: All additional files must be mentioned in the text in numerical order, or removed from the system. Please ensure all files are referred to as additional files (not, for example, supplementary data). Please add a section titled "Additional files" at the end of the manuscript (after the tables) listing the following for each file: the title of the data, and a short description of the data.

Done. There are now 9 additional files.

9. Structure: Please check the instructions for authors on the journal website to ensure that your manuscript follows the correct structure for this journal and article type.

Done.

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We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.

We look forward to receiving your revised manuscript by 2 December 2011. If
you imagine that it will take longer to prepare please give us some estimate of when we can expect it.

You should upload your cover letter and revised manuscript through http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=man&txt_man_id=257717056. You will find more detailed instructions at the base of this email.

Please don't hesitate to contact me if you have any problems or questions regarding your manuscript.

With best wishes,

Miss Eden Bobier on behalf of Prof Jean-Francois Chenot

e-mail: editorial@biomedcentral.com