Format for ANSWERING REVIEWERS

July 23, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 20176-Review.doc).

Title: Adherence to cardiovascular medications in the South Asian population: A systematic review of current evidence and future directions

Author: Julia M Akeroyd, Winston J Chan, Ayeesha K Kamal, Latha Palaniappan, Salim S Virani

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 20176

The revision has greatly benefited from the scientific editor's and reviewers' thoughtful comments, and we thank the editor and reviewers for helping us improve the quality of our manuscript. Below, we provide a point-by-point response to the comments from the reviewers and the scientific editorial office.

Scientific Editors' Comments for the Author:

We addressed the scientific editor's comments provided in the text of the edited manuscript file:

Comment 1:
Please highlight the changes made to the manuscript according to the peer-reviewers' comments
Response:
We have highlighted the changes made to the manuscript according to peer reviewers' comments

Comment 2:
Please have the corresponding author drafts up the Biostatistics, Conflict-of-interest statement, Data sharing statement files, and signs them, respectively.
Response:
The corresponding author has signed and provided the conflict of interest and data sharing statements. Given that this is a review paper, and no pooled estimates or meta-analyses were conducted, the biostatistics statement file was not applicable.

Comment 3:
Please provide the audio core tip.
Response:
We have provided an audio core tip.

<u>Comment 4</u>:

Please revise the format of the references in Table 1

<u>Response:</u>

The references in Table 1 have been reformatted according to the scientific editors' specifications.

<u>Comment 5</u>:

Please write the comments. Writing requirement see the file named "Format of Original Articles"

<u>Response:</u>

We have included the following sections under the comments:

Background

Cardiovascular disease (CVD) is the leading cause of death worldwide, with an estimated 17.5 million people dying from CVD in 2012. Approximately one-fifth of the global population resides in South Asia, where patients suffer from a disproportionately high rate of CVD-related morbidity and mortality. Adherence to medication is critical to the effectiveness of CVD risk management. Therefore, the aim of this review is to examine current methods of assessing adherence and strategies to improve adherence to cardiovascular disease (CVD) medications, among South Asian CVD patients.

Research frontiers

Current research indicates a growing epidemic of premature CVD in South Asian populations. Establishing suitable strategies to assess adherence to CVD medications is of particular importance to South Asian countries for various reasons. First, low availability of electronic medical records in most health care settings precludes accurate assessment of medication adherence using electronic medication refill data by health care providers. Second, the overall health literacy and the opportunities to improve provider and patient awareness of the importance of medication adherence may be limited. Lastly, low availability of pharmacy records and medication refill data also limit the use of traditional measures used to assess medication adherence.

Innovations and breakthroughs

Understanding adherence to CVD medications in South Asian populations is an important research question. This study focuses on the specific challenges and complexities related to CVD medication adherence in native South Asians.

Applications

This review demonstrates the need to identify a gold standard for assessment of adherence related to CVD medications in South Asians. Additionally, there is a need to employ intervention strategies directed towards provider-patient communication and to tie these interventions to intermediate outcome measures in order to determine their effects on CVD outcomes.

Terminology

Adherence in this review is defined as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider." The Morisky Medication Adherence Scale (MMAS) is a 4 or 8-item self-report questionnaire that results in a score ranging from 0 (non-adherent) to 4 or 8 (fully adherent).

Peer-review

In this manuscript, Virani et al. reviewed mainly adherence to antihypertensives in South Asian populations and the methodology of studies conducted in this field. It is an interesting topic and the presentation of data is impressive.

We have also addressed the steps listed in the scientific editor's email:

Step 1

Please revise your manuscript according to the reviewers' comments

Response:

We have revised the manuscript according to the reviewer's comments, and highlighted the corresponding changes.

Step 2

Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Systematic Reviews.

Response:

The manuscript has been updated according to the Guidelines and Requirements for Manuscript Revision-Systematic Reviews

Step 3

Please provide an Audio Core Tip

Response:

We have provided an audio file describing the final core tip of the manuscript.

Step 4

Please subject the manuscript to CrossCheck analysis and the final title to Google Scholar search, and store screenshot images of the results

Response:

We have subjected this manuscript to a manual check in order to prevent scholarly and professional plagiarism. Given that we do not have access to iThenticate software, we believe this is sufficient. We have subjected the final title to a Google Scholar Search and provided a screenshot image of the results.

Step 5

Please provide the files related to academic rules and norms. The files related to academic rules and norms include the biostatistics statement, conflict-of-interest statement, and data sharing statement.

Response:

As mentioned previously, we have provided signed conflict of interest and data sharing statements. Given that this is a review paper, and no pooled estimates or meta-analyses were done, the biostatistics statement file was not applicable.

Step 6

Please revise the language of your manuscript. For manuscripts submitted by Non-Native Speakers of English, the authors are required to provide a language editing certificate, which will serve to verify that the language of the manuscript has reached Grade A.

Response:

This was not applicable to our manuscript.

<u>Step 7</u>
Please sign the Copyright Assignment form.
<u>Response:</u>
A signed Copyright Assignment Form has been submitted online.

<u>Step 8</u>
Submit the revised manuscript and all related documents.
<u>Response:</u>
The revised manuscript and all related documents have been submitted.

<u>Reviewer #1:</u>

<u>Comment 1</u>:
The authors performed an interesting a systematic review describing adherence to Cardiovascular Medications in the South Asian Population Despite the work strength, I recommend following the next issues: Authors should transfer the description of the study performed by Quareshi from the section " Strategy for improving adherence " to the section "Adherence assessment".
<u>Response:</u>
We thank the reviewer for the positive feedback and appreciate these important comments. As the reviewer noticed, the results section is divided into studies that simply assessed adherence to CVD medication as an outcome and studies that implemented interventions aimed at improving adherence to CVD medications. Given that Quareshi et al. examined the effectiveness of an educational intervention aimed at general practitioners to increase patient adherence to anti-hypertensive drugs, we feel that it is appropriate to keep this study described under "Strategies for Improving Adherence." If the reviewer or editors believe that this should be modified, we are happy to make the change.

<u>Comment 2:</u>
Authors should insert the chapter : " Definition" . This chapter should include definitions scattered in different sections of the article (i.e. Adherence; MEMS; ETC..)
<u>Response:</u>
Based on reviewer's feedback, we have included all relevant definitions under the "terminology" section at the end of the manuscript as required by the journal. Here we have provided clarification on definitions that are covered throughout the article including the definition of adherence and MEMS, and did not include an additional "definition" section in order to avoid redundancy. Below, we add text added to the terminology section which explains this in detail.

Text added to the manuscript:

"Terminology
Adherence in this review is defined as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider." The Morisky Medication Adherence Scale (MMAS) is a 4 or 8-item self-report questionnaire that results in a score ranging from 0 (non-adherent) to 4 or 8 (fully adherent)."

Comment 3:

I consider that the concept of "intentional and non- intentional adherence" is really interesting in this field. The authors explained that this classification was not applied to this study, but I think they should better contextualize this classification to the South Asia population

Response

Based on reviewer's feedback, we have added the following text to the discussion section to better contextualize this classification to the South Asia population:

"Unintentional and intentional non-adherence to medications are related to different patient characteristics. A review of medication adherence in native and immigrant South Asians noted that the primary factors related to non-adherence in the included studies were forgetfulness, side-effects and choosing not to take the medication[42]. This suggests that both unintentional and intentional nonadherence contribute to overall non-adherence in South Asian populations and successful interventions aimed at improving adherence in this population should address both mechanisms."

Reviewer #2:

Comment 1:

In this manuscript Virani et al. reviewed mainly adherence to antihypertensives in South Asian populations and the methodology of studies conducted in this field. It is an interesting topic an the presentation of data is impressive. 1-There are many absent spacing through the text. ? couldn't understand the reason for that. An example is "The reasons for exclusion of full text articles were that the papers were design/rationale or review papers (n=5), no adherence assessment was reported (n=2) and the study population was previously described in an included paper (n=2). Therefore, the final review included 17 articles. A summary of "

Response:

We thank the reviewer for the positive feedback and appreciate these comments. Based on reviewer's feedback, we have modified the text to ensure there is appropriate spacing throughout the document.

Comment 2:

In the results section first paragraph "A summary of the included studies is shown in the Table."is stated twice. I think once is enough.

Response:

Based on reviewer's feedback, we ensure that this is only stated once.

Comment 3:

The section "conclusions and future directions" is too long and repeating the data given previously. I advise it to be abridged.

Response:

Based on reviewer's feedback, we have modified the section "conclusions and future directions" to remove repetitive text and shorten the overall text.

We thank the reviewers and the editor for their time and consideration. The feedback that has been provided has certainly helped us improve the quality of our manuscript. We hope that our manuscript will now be acceptable for publication in *World Journal of Cardiology*.

Sincerely,

Julia M. Akeroyd, MPH

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