Author’s response to reviews

Title: Critical Appraisal of International Guidelines for the Screening and Treatment of Asymptomatic Peripheral Artery Disease : A Systematic Review

Authors:

Qinchang Chen (chenqch6@mail2.sysu.edu.cn)
Lingling Li (lill9@mail2.sysu.edu.cn)
Qingui Chen (chqgui@mail2.sysu.edu.cn)
Xixia Lin (linxia183@126.com)
Yonghui Li (feifeifei13579@163.com)
Kai Huang (huangk37@mail.sysu.edu.cn)
Chen Yao (yaochen@mail.sysu.edu.cn)

Version: 1 Date: 12 Nov 2018

Author’s response to reviews:

Dear Prof. Moxon,

Thank you very much for your letter and advice. We have carefully revised the manuscript and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in the revised manuscript. Point-by-point responses to the reviewers’ comments are listed below this letter. In addition, the editorial corrections required have been done. We would like to express our sincere thanks to the reviewers and the editorial team for the constructive and positive comments. We hope that the revised version of the manuscript is now acceptable for publication in the journal.

I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Chen Yao
Replies to Tejas P Singh (Reviewer 1)

Comment 1: Thanks for this interesting systematic review on the guidelines for screening and treatment of asymptomatic PAD. Interesting to see the authors views on current guidelines; although I think a major takeaway from this review is that there is a need for high quality evidence that directly evaluates the value of screening for asymptomatic PAD patients.

Answer: Thanks for the positive comment. We have emphasized the need for high quality evidence in the discussion section (line 232-253).

Comment 2: It would be good to clearly define in the introduction/selection criteria what treatments are specifically being looked at; i.e pharmacological treatment, exercise, endovascular/open surgical etc. This becomes more apparent when looking at the tables, but please define this early on.

Answer: Thanks for the advice. We have added more details about treatments into the selection criteria. (line 109-111).

Comment 3: In the background the authors define PAD as 'periphery artery disease' where as in the introduction of the manuscript this is defined as 'peripheral artery disease' - please be consistent. 'guidance documents'? guidelines

Answer: All the term ‘periphery artery disease’ has been replaced by the term ‘peripheral artery disease’. And the term ‘guidance documents’ has been changed as the term ‘guidelines’.

Comment 4: Line 76-78: Is this true ? It has previously been reported that despite BMT PAD pts are a high risk of major cardiovascular events. The use of 'cardiovascular disease' appears misleading here - do we mean events?


Answer: We are sorry for the unclear and misleading statement. The term ‘cardiovascular events’ rather than ‘cardiovascular disease’ is exactly what we want to express. (Line 76-78)

Comment 5: Would be worth acknowledging some of the current multi-component vascular RCT’s which are assessing the screening for PAD:


Answer: Thanks for the constructive advice. We have cited these researches in the introduction section (line 80-81).

Comment 6: Line 171: Some guidelines 'did' not

Answer: We have corrected it. (line 176-177).

Comment 7: Line 222: PAD is 'a' condition with significant morbidity and mortality

Answer: We have corrected it. (Line 228)

Comment 8: Discussion/Conclusion: Please specify what high quality evidence is needed? The paucity of data here is likely the key problem, and the authors should explore this further. How many this explain heterogeneity in current guidelines?

Answer: Thanks for the advice. We have discussed what further study were needed to provide high quality in future in the discussion section. In terms of heterogeneity, we think evidences available now did not focus on asymptomatic PAD only and usually contained patients with different risks, which might explain the heterogeneity in current guidelines. Meanwhile, since there is no clear-cut evidence for treatment, the recommendation for medication might be more sensitive to conflicts of interest with pharmaceutical industry and biased toward a more aggressive treatment policy. We have added these into the discussion section.(Line 285-288)

Comment 9: Line 258-259: Please provide references to support 'AGREE II instrument has been recognized and widely used in the guideline appraisal.'

Answer: We have added the related references (Reference 14, 35,36).

Comment 10: Line 261-263: 'suggestion on how to improve in the future' - can the authors be more specific on the suggestion please; is this simply the requirement for high quality evidence or are there any other suggestions that should be considered in the development of guidelines.

Answer: See the answer to Comment 1.

Comment 11: Do the guidelines included in this systematic review intend to be global or restricted to a particular area (e.g. Australasia)? Probably important to state as this would likely
influence guidelines if based on data restricted to a specific region (i.e. specific regions may have a greater/lesser burden of disease).

Answer: We intended to include global guidelines in our analysis. But we included guidelines in English only. So this might cause some limitation. We have discussed it in the discussion section.

(Line 295-301)

Replies to Vikram Iyer, MBBS (Hons) (Reviewer 2)

Comment 1: Congratulations on addressing a very interesting topic in this paper. There is a clear need for greater correlation and consensus among international guidelines for the investigation and management of asymptomatic PAD and this review illustrates this very well. However, there are a few issues with the review which will need to be addressed prior to making it fit for publication:

Answer: We thank the referee for the positive comment of this work.

Comment 2: Review of the manuscript by someone with native or near-native English fluency (particularly in scientific writing) is strongly recommended as there are innumerable grammatical and syntactical errors which make the manuscript difficult to comprehend at times. This is an essential recommendation.

Answer: Thanks for the advice. The manuscript has been revised to correct the grammatical and syntactical errors under the instruction of a near-native English speaker.

Comment 3: The creation of the data extraction template needs to be discussed in more detail. No references to previously published data extraction tools are listed in the methodology section. Did the authors create a new template themselves or is this an adapted version of a pre-existing, validated template?

Answer: Sorry for the unclear statement of the template. In fact, the data extraction template is adapted from the study of Nagler EV et al (BMC medicine, 2014, 12(1): 231.). We have cited the reference in the manuscript. (Line 137-138)

Comment 4: With respect to screening for asymptomatic PAD: the only guideline that put screening in the 'Harm' category was the ACC/AHA Guideline, which used invasive and non-invasive angiography as its investigation tool. This point merits significant discussion, as this is one of the guidelines meeting the threshold for an AGREE II score suggesting it is "recommended for use in clinical practice", and yet differs from the others by NOT recommending screening for asymptomatic PAD and using different (and invasive or potentially
harmful) tests. This should be included in the discussion section of the manuscript (essential recommendation).

Answer: Thanks for the advice. It is true that the ACC/AHA guideline is of high quality according to the AGREE II instrument and it is the only guideline which provides the opposed recommendations toward screening. So it is well worth discussing and we have added it in the discussion section. (Line 234-244)

Comment 5: - With respect to treatment of asymptomatic PAD, the authors mention lifestyle and medical therapies (including anti-platelet therapy, anti-hypertensive therapy, and lipid-lowering therapy, with targets where provided by the relevant guidelines) along with arterial reconstruction. It would be worth commenting on heterogeneity in the guidelines regarding individual classes of drugs, where this is available in the guidelines (suggestion to be incorporated at the authors' discretion).

Answer: Thanks for the advice. We have discussed the heterogeneity in the guidelines regarding therapies. (Line 254-267)

Comment 6: - The discussion in general is rather brief and superficial - the recommendations above may provide some additional discussion points, but additional discussion of any lifestyle modification recommendations from the guidelines, correlations with overall cardiovascular health recommendations may be of value. Furthermore, the methodology used in this review should also be discussed in further detail, given that this is the first attempt at a review of global asymptomatic PAD guidelines. This is an essential recommendation.

Answer: Thanks for the advice. We have added more discussion according to the comments. (Line 267-275)

Editorial corrections required

In accordance with BioMed Central editorial policies and formatting guidelines, all manuscript submissions to BMC Cardiovascular Disorders must contain a Declarations section which includes the mandatory sub-sections listed below. Please refer to the journal's Submission Guidelines web page for information regarding the criteria for each sub-section (https://bmccardiovascdisord.biomedcentral.com/)

Where a mandatory Declarations section is not relevant to your study design or article type, please write "Not applicable" in these sections.

For the 'Availability of data and materials' section, please provide information about where the data supporting your findings can be found. We encourage authors to deposit their datasets in publicly available repositories (where available and appropriate), or to be presented within the
manuscript and/or additional supporting files. Please note that identifying/confidential patient data should not be shared. Authors who do not wish to share their data must confirm this under this sub-heading and also provide their reasons. For further guidance on how to format this section, please refer to BioMed Central's editorial policies page (see links below).

- Declarations - Ethics approval and consent to participate
- Consent to publish - Availability of data and materials - Competing interests - Funding
- Authors' Contributions - Acknowledgements

Answer: We have added the Declarations section according to the instructions above.