Reviewer’s report

Title: Predictors of lower extremity amputation in patients with diabetic foot ulcer: findings from MEDFUN, a multi-center observational study

Version: 1 Date: 29 Mar 2019

Reviewer: Shan Bergin

Reviewer's report:

The authors have done a good job of addressing most of the reviewers recommendations however I still feel they need to add clarity to some of the more significant parts of the manuscript before it is ready for publication.

Firstly, I would like to clarify two of the comments made in my original review that were unclear to the authors (because I failed to insert Line numbers - my apologies).

In Line 48-49 in the Background section the authors state "The International Diabetes Federation and World Health Organization jointly warn that these complications (the authors are referring to diabetes complications), if unchecked would threaten the viability of many African nations which are already grappling with many infectious diseases." This needs to be re-worded as it implies, as written, that diabetes is also an infectious disease.

In Line 54 in the Background section the authors state "One avoidable complication of diabetes that is associated with huge morbidity and mortality is diabetic foot ulcer (DFU)". As per my initial review, describing DFU as 'avoidable' understates the complexity of this as a complication - if it was truly 'avoidable' we would not see so many of them. My preference would be for the authors to describe these as 'potentially preventable' or similar. Further to this, the term 'huge' is not overly scientific and should be replaced wherever it appears in the manuscript.

The reviewers all identified issues with the same parts of the paper, namely:

- confusion around the second manuscript the authors have published (now listed as reference 18)
- the use of the Wagner classification system as opposed to others available
- the diagnosis of vascular disease within the study population
- the definition used for major and minor amputation
- the way in which the authors distinguished between Type 1 and Type 2 diabetes

Whilst the authors gave reasonable explanations regarding some of these in their responses to reviewer feedback, they also need to make corresponding changes to the manuscript in order to
add clarity to the paper. This then ensures a broader readership won't raise the same questions regarding the study methods and reliability of results.

Use of Wagner tool:

There are multiple classification tools available for grading wound severity, all of which I believe are flawed in some way. I don't have a particular issue with the use of Wagner in this study (except as per one of the reviewers it doesn't include wound area / size). The authors however need to make a statement about why they opted to use the Wagner tool so readers can be sure it was the right choice for this particular study. Shortfalls with the Wagner tool should also be discussed as a limitation.

Diagnosis of vascular disease:

I do have concern over how the diagnosis of PAD was made for the purposes of this study - some were made on the basis of pulse palpation and others on Doppler US - with US being a much more reliable method. So there is inconsistency in how the participants were diagnosed. The authors need to address this in the manuscript and justify why they used the methods they did. They refer to insufficient resources to allow them to US everyone and an inability to use ABI / TBI due to infected wounds. Both of these explanations need to be included in the manuscript. The inconsistent diagnostics used also needs to be raised as a potential limitation.

Definition of level of amputation:

I agree with the authors response that there is no agreed definition for level of amputation, however use of 'major' to describe anything above the ankle and 'minor' to describe anything below is fairly universally accepted. If the authors wish to use something different then I have no issue with that but I would suggest they state that this is their own definition 'for the purposes of this study' and perhaps explain the use of it.

Type 1 versus type 2 diabetes:

Similarly to the amputation definition, the way the authors have differentiated between type 1 and type 2 diabetes is outside of the internationally accepted clinical 'norm'. If there is variation in how this is done in Nigeria then again, the authors need to provide an explanation in the paper.
Confusion around the other MEDFUN study:

My issue with discussion about the original MEDFUN publication in this manuscript was about readers being able to discern between the two studies. I did not assume this paper was a duplicate or had been submitted elsewhere. This has been clarified somewhat following publication of the original study and the authors ability to now reference it. There are still a few sections where I think there is too much cross over but overall its not a major issue.

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