Author's response to reviews

Title: Title: Incidence and determinants of diabetes-related lower limb amputations in Ghana, 2010-2015- a retrospective cohort study

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Version: 2 Date: 21 Sep 2018

Author's response to reviews:

Editor-In-Chief,

BMC Endocrine Disorders

Dear Editor,


Thanks very much for your response concerning the article sent to you. We wish to thank the reviewers and yourself for the constructive and useful comments.

We strongly believe the paper has vastly improved, taking advantage of your generous comments. We have attached a memo addressing your concerns. We look forward to your evaluations.

Sincerely,

Dr Osei Sarfo-Kantanka
Reviewer #2:

Abstract

1. The improvement in amputation rates in developed countries is very variable and is rarely dramatic. Please change the wording

   Ans: We thank the reviewer for the comment, we have addressed it.

2. The results describing a rate of 2.4 per 1000 is NOT 2.4% - the % signs should be removed

   Ans: We thank the reviewer for this. We have done as requested.

Background

3. One of the references in 8-10 is from Cameroon - not necessarily resource rich. Is this reference relevant? There are other developed countries who report lower amputation rates with National data

   Ans: We have replaced the reference with one from the United States.

Methods

4. Line 91 - is "estimated GFR" that was used?

   Ans: We have made the change that it was estimated GFR that was used.
5. P6 the last sentence in the first paragraph needs to be written with greater clarity as to what is meant.

Ans: The sentence has been re-written to provide clarity.

6. Analyses - was PVD used as a risk factor to see if it was a strong predictor

Ans: Peripheral Vascular disease was used in the analysis and indeed was the strongest predictor of lower limb amputations although inadvertently not added initially.

7. p9 line 2 - typo error

Ans: Error has been corrected.

Results

8. Table 1: Data on duration of diabetes does not seem to fit with difference in age of diagnosis and current age - I wonder if the age at diagnosis has been swapped between the two subgroups?

Ans: It was and this has been corrected.

9. Why are the endpoints of eGFR and PVD not included in Table 1

Ans: The endpoints has been added
10. Is it possible that the cohort selected has self-selected and has more "severe diabetes"? That may be why they are attending a tertiary clinic

Ans: Yes indeed the cohort referred to the tertiary clinic are deemed to include a severe form of the disease and this has been pointed out.

11. It would be good if the authors could discuss why they think the amputation rate is increasing - The high rate of amputation is discussed but not why it is increasing. Could this be due patients living longer? What was the mean age of death in the group in 2010 and 2015?

Ans: The reason why diabetes related amputation has been described as requested. The mean age of death is however not part of the analysis.

12. p11 para 2 line 2 - typo error

Ans: the error has been corrected.

Reviewer 3

The study procedure needs to be expanded to provide more information on how cases (LLA) were identified and what constituted "consistency" in follow-up.

Ans: We have described how cases of LLA were identified and what was meant by consistency in follow up to mean those patients who completed one full year of follow up after enrolling in the clinic.

There is an inconsistency in the interpretation of the results (line 129) -- not all antihypertensives were lower in people with LLA. The sentence in Line 175 appears to be redundant.
Ans: We have clarified the interpretation of the results in line 129 to give meaning to it. The sentence in Line 175 has also been eliminated.

Reviewer 4:
Ideally, lower limb amputations should be divided into major and minor and analysed separately.

Ans: Comment well noted. It will be addressed in that manner in subsequent manuscripts. Practical terms we concentrated on only lower limb amputations although we distinguished using Table 2.

"Peripheral artery disease (PAD) was diagnosed based on symptoms such as intermittent claudication allied to ankle-brachial index measurements (less than 0.9), doppler ultrasonography and magnetic resonance imaging angiography"

Are the results of these investigations available?

The results were not recorded as part of this study. We just took a careful indication as to the main investigative modalities available for patients with PVD in our setting.

"Variables included in the model were: age (years) at presentation, gender, type of diabetes, lipid status, renal function, and symptoms of peripheral neuropathy."

No vascular parameters were included. Please comment.

Ans: Peripheral Vascular Disease was included as part of the analysis.

"We excluded 127 of them because they presented to the clinic with foot disorders"

This is not clear.

Ans: We as part of the study wanted to include only patients who developed diabetes foot disorders necessitating amputation after enrolling in the study.
The main causes of amputation included PVD i.e. 63% of LLA, PSN; 24% and 13% were due to a combination of the two. "

What is the evidence for these statements? Were any of these amputated feet infected?

Ans: We restricted our self to finding the main risk factors associated with diabetes – related amputations in this study and relied on description from the clinical notes.

Please provide full names, academic titles, degrees and corresponding author names and full addresses

Ans: We thank the reviewer for the suggestion, we have fully complied with this directive

Line 153 "Predictors of lower limb amputations Independent factors associated with LLA in our diabetes cohort are shown in Table 3” Were vascular factors investigated?

Ans: Yes, dyslipidaemia, hypertension, Body Mass Index, Nephropathy and PVD were investigated.

Line 165
"We identified gangrene/PVD as the leading cause of diabetes-related LLA in the cohort." PVD are not directly interchangeable. Gangrene may occur in a neuropathic non-ischemic foot secondary to infection.

Ans: We have clarified the statement to relieve the confusion.
Figure 2. This is not clear. The colors are difficult to distinguish. Is the gangrene wet gangrene (indicating predominantly infection) or dry gangrene (indicating ischemia)?

Ans: It is our respectful opinion that the colors are distinguishable.