Author’s response to reviews

Title: Ulcer Metastasis? Anatomical Locations of Recurrence for Patients in Diabetic Foot Remission

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Author’s response to reviews:

We have revised the manuscript in accordance with the feedback provided by the reviewers. We believe the manuscript is significantly improved as a result of the peer review process and thank the editors for the opportunity to revise it and the reviewers for their time and constructive feedback.

Reviewer #1

The discussion is a little limited and reads more like advice to carers rather than a discussion of key findings.

We thank the reviewer for these comments. We have expanded the Discussion to make clearer that the implications presented are based on the findings of the research. However, because we believe our results are underappreciated, and because we believe better appreciation of these results may improve patient outcomes, highlighting the implications of our research is an important objective and appropriate for the Discussion.

Reviewer #2

I would like to commend the authors for this research which makes a very important contribution to the evidence base. By stratifying granularly all documented diabetic foot ulcer (DFU) sites in the participant's history, they provide readers with illuminating insights on - (1) how vastly distinct the majority of DFU recurrence sites are; (2) only in a minority of cases (17%) have a DFU recurred back to the same anatomical location. This is a glaringly under-reported aspect in the majority of publications tackling the topic of DFU recurrence.
Thank you, we are delighted to note the awareness we have raised of these two key points. We agree, it is under-reported, and it is our hope to raise awareness of this in the clinical community.

Major

Background, line 119-121 and 123 - I question the presumption made in the statement: 'It is now commonplace to talk about a DFU as a "malignancy" of the foot, and sometimes "wound hospice" is a viable alternative to conventional treatment'. The reason being this may not be universally reflective of settings outwith the authors' institutions and/or the United States. This presumption and subjective view is also similarly made in line 123, 'The cancer analogy is apt'.

We agree that this may not be as common as originally presented. We have edited the manuscript accordingly.

Results, Figure 1a - This information is excellent and highly valuable.

Thank you, we are glad you find it as such.

Results, Figure 1b - I am not sure if I am seeing the value of Figure 1b. Could the authors please explain their intention in presenting this graph?

Figure 1b shows the percentage of participants who had documented wounds to less than or equal to N locations, where N is the value on the x-axis. Presenting this figure helps the reader quickly ascertain, for example, that slightly more than 80% of patients had wounds documented to three or fewer anatomical locations. This saves the reader the trouble of adding the percentages in Figure 1a (~40% had wounds to one location, ~30% had wounds to two locations, and ~10% had wounds to three locations). Because the data in Figure 1b are potential redundant to Figure 1a, and because some readers may not be familiar with the terminology “cumulative distribution,” we have expanded the caption of Figure 1b as well as changed the word “proportion” to “percentage” on the figure to help address this issue.

Results, Table 1 and Figure 2 - Could the authors please explain the differences in percentage values for each anatomical locations as stated between Table 1 and Figure 2? The titles for both identified DFUs as stratified by anatomical locations occurring prior to and during the study. However, as an example, in relation to the percentage values for DFU occurring prior to, it is stated as 56% in Table 1 and 27.0% in Figure 2 for the hallux.

We are grateful that the reviewer highlighted this needed clarification. Table 1 shows data on a per-participant basis, whereas Figure 2 shows data on a per anatomical location basis. For example, in Table 1, 56% of participants had a wound to the hallux documented prior to the study. However, because each participant can have wounds to multiple locations documented prior to the study, only 27% of all wounds documented were to the hallux. We have added a brief clarification in the manuscript to address this important distinction.

Minor

Abstract, line 43 - DFU is a widely utilised abbreviation, however authors still ought to make this clear after their first use of diabetic foot ulceration in the abstract. I appreciate this may be an oversight as
the authors were mindful to do so in their introduction.

Duly noted, and modified accordingly.

Abstract, line 43 - I wonder if there is a better way to paraphrase 'considering multiple wounds uncensored during follow up' as the intended meaning behind this phrase is ambiguous.

We have removed the use of the word uncensored, which in retrospect was redundant given the context.

Background, line 116 - Please remove the number (1) after breast and prostate.
Background, line 123 - Please restart numbering at (1).

We have moved the citation nearer to the research being cited. We do believe it is important to cite the fact that previous researchers have compared foot ulcerations to common cancers in terms of morbidity and mortality, but we agree that the placement of the citation was inappropriate in the previous revision.

Background, line 133-135 - This sentence may benefit from being rephrased. Perhaps as 'In fact, … reported that 38% of plantar forefoot DFU (excluding minor digits) recurred to the contralateral limb in patients in diabetic foot remission.'

We have edited this sentence to summarize the finding more clearly.

Background, line 146-147 - Rather than '… in order to better characterise the anatomical locations to which DFU are likely to recur', it would be more accurate to state that, '… the anatomical locations at which DFU have recurred in study participants.'

We have edited this sentence as suggested and agree that it is a more accurate description of the effort than the previous phrasing.

Methods, line 162 - It would be helpful to specify what types of 'lesions' warranted an alert.

We have added in a clarification of the word “lesion.”

Methods, line 175-176 - This would be better placed within the first paragraph of the results section.

Agreed, and moved to the Results section.

Results, line 216-219 - The two percentages (52% and 49%) referred to in this statement are not vastly different. May I suggest for both to be conveyed similarly as 'nearly half', instead of one as a 'majority' and the other as 'nearly half'.

Agreed, and modified accordingly.

Discussion, line 246 - Is there a missing word? '…other pre-ulcerative (signs?) and findings.'

We apologize for the lack of clarity and have modified it.

Discussion, line 248 - Could the authors please explain what they mean by 'sound foot'?
We have modified the verbiage to “foot without a wound”.

Discussion, line 248-252 - This very long sentence would benefit from truncation.

Agreed, and modified as per recommendation.

Discussion, line 267-269 - Rather than likelihood, this would be better conveyed as a limitation.

We have eliminated the use of the word likelihood.

Overall - Please ensure consistency in the positioning of titles. I note that the title is positioned before Table 1, whereas the title is positioned after all three figures.

We have moved all titles below figures and tables.

Discretionary

May I suggest that the authors remove their widespread use of the oxford comma throughout their manuscript - e.g. 'resulting in reduced morbidity, mortality, and cost' - and/or truncate long sentences. I have been equally guilty of committing the same crime in my writing and have stood corrected on multiple occasions.

We thank the reviewer for this feedback but respectfully decline to address this discretionary recommendation.

The title encapsulates the content of this paper concisely, however may I suggest that the authors consider remove the phrase 'Ulcer metastasis?' from their title for directness.

We thank the reviewer for this feedback but respectfully decline to address this discretionary recommendation.

Discussion, line 243-244 - May I suggest that the authors substitute the word 'focus' in this statement. The word focus implies a narrowing or zeroing in, whereas the authors are rightfully advocating for a broadening or wider consideration of areas to encompass both of the patients' feet.

Agree, and have modified the manuscript accordingly.

Discussion, line 253-257; Conclusion, line 281-284 - May I suggest that the authors remove the promotion for once-daily temperature monitoring due to their conflict of interest.

We have removed the reference to foot temperature monitoring given our conflict.