Author’s response to reviews

Title: Predictors of intra-hospital mortality in patients with diabetic foot ulcers in Nigeria: data from the MEDFUN Study.

Authors:
OLUFUNMILAYO OLUBUSOLA ADELEYE (funmiadeleye2004@yahoo.com)
Ejiofor T Ugwu (ofornet@yahoo.com)
Ibrahim D Gezawa (gezawa01@yahoo.com)
Innocent Okpe (innokpe@yahoo.com)
Ignatius Ezeani (ignatiusez@yahoo.com)
Marcelina Enamino (marcelina.enamino@yahoo.com)

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Dear Editor
BMC Endocrine Disorders,

Response letter in respect of Manuscript BEND-D-19-00404R1

With respect to sample size, this study was a prospective observational study with predetermined duration between March 2016 and April 2017. The inclusion criteria was consecutive patients admitted for DFU in all the participating centers who gave verbal consent during the pre-specified period. Therefore we could not predetermine or calculate a sample size.

The type 1 cases have been expunged due to small number and data has been reanalysed. The results section has been rewritten and discussion now reflects the current results section.

The previous answers to reviewers questions.

Reviewer 1 Praveen Pradeep PA, B.D.S, MPH., Ph.D.,
1.No separate analysis was conducted because of the small and negligible number of type 1 diabetic patients among the study participants. The sample size was 336, 96.1% were type 2 diabetics.
2. Total sample size is indicated in line 1 of the Results section, and table 1 under the variable section.
3. All study subjects were managed based on multidisciplinary care available in all participating centers, and those who survived were followed up for three months after discharge from the hospital.
4. Results have been rewritten in two paragraphs.
5. The Nigerian cohort of 40.5% mortality mentioned in the introduction has been included in lines 12 and 13 under discussion.
6. The frequency bars in figure 2 indicate the proportion of each ulcer grade and the corresponding mortality.
7. The sample size has been provided for each variable in figure 2.
8. The DAMA patients were demographically similar. Line 8 under the results section.
9. The impact of result on present practice is included in discussion section lines 5 and 6, conclusion section lines 5 to 10.

Reviewer 2  Kanakamani Jeyaraman
1. The observation that Nigerian patients are very young has been included in the discussion section. lines 41 – 45.
2. Although there may be some minor variations in care administered to the patients at the various study sites, the protocol was developed and standardized and was implemented by each author at the various study sites. There was no appreciable difference in the treatment received at the various centers. All the patients were managed in a multidisciplinary setting.
3. Amputation did not have a significant impact on mortality as shown in table 2.
4. The decision to amputate or not was the exclusive prerogative of the multidisciplinary foot care team at each study center.

Reviewer 3  Amanda Killeen, DPM
1. The number of patients screened and enrolled has been included in Line 1 of the results section and Table 1 variable section.
2. Operational definitions for shock, sepsis and loss of vibration perception have been included in line 2 of the 3rd paragraph methods section, lines 8 and nine of the 3rd paragraph of methods section and line 3 of 5th paragraph in the methods section.
3. All patients received Doppler for PAD. The operational definition for PAD is included in the last line of paragraph 3 in the Methods section.
4. Results have been presented in prose under 2 paragraphs.
5. Under Discussion section reference has been provided for lines 34-35 which state "…sepsis, as evidenced by positive blood culture…"
6. The second page lines 44-45 state "…subjects with PAD had eight times higher probability of death…" Table 2 shows the odds ratio for PAD to be 2.462 and the odds ratio for gangrene to be 8.211. This has been corrected.
7. Lines 46-50 discuss the severity of PAD in imaging but this was not defined in the methods section. This has been rectified in the last line of paragraph 3 under the methods section.

Limitations.
Non-uniformity of laboratory has been mentioned in lines 5 and 6 of paragraph 5 under the methods section.
CHARTS/TABLES
Colors have been adjusted in Figures 1 and 2.
Low frequency and higher mortality of subjects with Wagner grade 1 ulcer have been addressed in Discussion section lines 14,15,16,17 of paragraph 5.
Table 2 amputations have been clarified as done during hospitalization.

Reviewer 4 Tadesse Tolossa
1. Abstract write up has been revised.
2. The odds ratio has been rewritten the last line of the results section of Abstract.
3. Univariate has been expunged from the conclusion section. The recommendation has been added at the end of the conclusion.

Methods:
1. The sentence "The Multi-centre Evaluation of Diabetic Foot Ulcer in Nigeria (MEDFUN) was a one-year observational study conducted in six tertiary healthcare institutions across Nigeria, from March 2016 to April 2017. Has been corrected.
2. The sample size and sampling procedure can be found in lines 1,2,3,8 and 9 of the methods section.
3. Also corrected in lines 8 and 9 of the Methods section.
4. The inclusion criteria for the study are any diabetic patient admitted for diabetic foot ulcers during the study period in all the centers. Patients admitted for other reasons other than DFU were not enrolled. And this is clearly stated in lines 8 and 9 of the Methods section.
5. All the terms “We” have been expunged.

Results
1. We did not compute a response rate because it was not a questionnaire-based study.
2. The mortality rate has been deleted and Mortality is indicated in lines 8,9 and 10 of Results section highlighted in yellow.
3. Variables independently associated with mortality were sepsis and nephropathy and both have been included in the discussion section lines 22,23 and 24 of the last paragraph of the Discussion section.
4. Recommendations have been included in the conclusion section.