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Peer review history for:

Turner MJ, Van Vuuren S, Leigh-de Rapper S. Analysing patient factors and treatment impact on diabetic foot ulcers in South Africa. *S Afr J Sci.* 2024;120(3/4), Art. #16301.

<https://doi.org/10.17159/sajs.2024/16301>

HOW TO CITE:

Analysing patient factors and treatment impact on diabetic foot ulcers in South Africa [peer review history]. *S Afr J Sci.* 2024;120(3/4), Art. #16301.

<https://doi.org/10.17159/sajs.2024/16301/peerreview>

Reviewer A: Round 1

Date completed: 10 October 2023

Recommendation: Resubmit for review

Conflicts of interest: None

Does the manuscript fall within the scope of SAJS?

Yes/No

Is the manuscript written in a style suitable for a non-specialist and is it of wider interest than to specialists alone?

Yes/No

Does the manuscript contain sufficient novel and significant information to justify publication?

Yes/No

Do the Title and Abstract clearly and accurately reflect the content of the manuscript?

Yes/No

Is the research problem significant and concisely stated?

Yes/No

Are the methods described comprehensively?

Yes/No

Is the statistical treatment appropriate?

Yes/No/**Not applicable**/Not qualified to judge

Do you believe somebody with more methodological expertise (in the area of this study) than yourself needs to review this?

Yes/No

If yes, can you suggest the type of expertise needed

Not applicable

Are the interpretations and conclusions justified by the research results?

Yes/Partly/**No**

Please rate the manuscript on overall contribution to the field

Excellent/Good/**Average**/Below average/Poor

Please rate the manuscript on language, grammar and tone

Excellent/Good/**Average**/Below average/Poor

Is the manuscript succinct and free of repetition and redundancies?

Yes/No

Are the results and discussion confined to relevance to the objective(s)?

Yes/**No**

The number of tables in the manuscript is

Too few/**Adequate**/Too many/Not applicable

The number of figures in the manuscript is

Too few/**Adequate**/Too many/Not applicable

Is the supplementary material relevant and separated appropriately from the main document?

Yes/No/**Not applicable**

Please rate the manuscript on overall quality

Excellent/**Good**/Average/Below average/Poor

Is appropriate and adequate reference made to other work in the field?

Yes/No

Is it stated that ethical approval was granted by an institutional ethics committee for studies involving human subjects and non-human vertebrates?

Yes/No/Not applicable

If accepted, would you recommend that the article receives priority publication?

Yes/**No**

Are you willing to review a revision of this manuscript?

Yes/No

Select a recommendation:

Accept / Revisions required / **Resubmit for review** / Decline

With regard to our policy on '[Publishing peer review reports](#)', do you give us permission to publish your anonymised peer review report alongside the authors' response, as a supplementary file to the published article? Publication is voluntary and only with permission from both yourself and the author.

Yes/No

Did you mentor someone during this peer review?

Yes/**No**

Comments to the Author:

General

The title of the manuscript would do with a revision, the way it seems it, the audience would not think this was a cross sectional study but a review of the literature

The objectives of the study could be stated succinctly in the objectives, I do not see why the co-morbidities were assessed in this study because we can not directly link them to the treatment of the DFUs or at least it is not clear from your findings if we can call them risk factors to the development of DFUs.

It would be very prudent to explicitly state the study design in the methods, this would also guide you in the conclusions thereof

The topic is very relevant

You spoke about review of treatment plans of DFUs but you did not talk about the antibiotics used in the management, you dwelt on the diagnosis but not the treatment itself. How are the DFUs being treated, with what antibiotics, are they oral or topical or injectables

The goals do not seem to agree with the title, you were reviewing treatment plans, but your major objectives were to look at the risk factors

"This study determined that the South African treatment guidelines and DFU classification system were in need of updating in order to align to international standards." Do you have internal and external validity to come up with a conclusion of this magnitude.

Comments to the Author:

Detailed

A Review of Diabetic Foot Ulcer Treatment Plans in the South African Public Healthcare Sector (*i do not think this can be called a review, I would suggest The gaps in diabetes foot ulcer diagnosis and management ...*)

Abstract

The aim does not seem to speak to the title and you
What does to attain 50% attrition rate mean

Significance of main findings

Furthermore, the use of preventative measure (s) among DFU patients was poor and that polypharmacy

~~Ethics~~-(Ethical clearance) was obtained from the Human Research Ethics Committee

As the goal of this research is to understand foot ulceration as a consequence of diabetes *Was this the goal of this research?*

Patient record review.....

A short, structured questionnaire was used in order to determine the use of preventative aids that had not been prescribed. *How do you determine the use of something that has not been prescribed?*

Next, a section on concurrent conditions and chronic medication use was included in order to establish the effect of these factors on ulcer severity. *Causation is difficult to determine from a cross sectional study*

Validating the retrospective review tool

The two patients who participated in the pilot study are of an acceptable sample size as the 121 established sample size for the study is (*was*) limited

Patient demographics

The results from this study demonstrated a higher prevalence of DFU among male participants (60%) in comparison to female participants (40%). *What is the gender distribution of the area which is serviced by the hospitals that were included in the study?*

The presence of diabetes related..... (*were all these diabetes related as the heading suggests*)

The largest proportion of ulcers were classified as grade one and grade two in severity and these patients (*patients*) presented with an average number

Medication use and the incidence of polypharmacy

Thereafter, the use of hydrochlorothiazide (a diuretic used in the treatment of hypertension) and paracetamol (an analgesic and antipyretic) was most frequently noted (33.3%). (*you cant define this as most frequent since the drugs in the preceding sentence had a frequency of 40%, can you?*)

Non-pharmacological management of DFUs....

In this study, 48.9% of patients did not make use of any preventive measures. The frequency and type of preventative measures used by patients in the... *can you please be consistent is it preventive or preventative*

Pharmacological management and treatment practices of DFUs

By evaluating the past treatment plan of patients in this cohort, gaps and missed opportunities in past treatment practices can be identified. This allows for the improvement of future DFU treatment plans. *Is this not supposed to be past tense*

Discussion

The findings in this study are consistent with previous studies where 58.3-69.9% of patients presented with hypertension. *How is 84% similar to 58.3 – 69.9%?*

Author response to Reviewer A: Round 1

The title of the manuscript would do with a revision, the way it seems it, the audience would not think this was a cross sectional study but a review of the literature

AUTHOR: Title change: "Evaluating the Influence of Patient Specific Factors and Treatment Plans on Diabetic Foot Ulcers in the South African Public Healthcare Sector"

The objectives of the study could be stated succinctly in the objectives, I do not see why the co-morbidities were assessed in this study because we cannot directly link them to the treatment of the DFUs or at least it is not clear from your findings if we can call them risk factors to the development of DFUs

AUTHOR: Co-morbidities were assessed to establish whether or not there was a link between number of co-morbidities present and ulcer severity. This was addressed under the heading "The presence of co-morbidities and complications" (Page 6)

It has been shown that a high number of co-morbid conditions had increased the likelihood of amputation and thus ulcer severity (Markowitz et al., 2006). Another study found that the presence of co-morbid conditions increases the risk of DFU reoccurrence (Khalifa, 2018).

While the number of co-morbid conditions does not affect the ulcer severity in this study, the nature of the co-morbidities does affect ulcer healing. For example, the presence of insufficient renal function and hypertension accelerate ulcer development and prolong healing time, making it an important parameter to evaluate.

It would be very prudent to explicitly state the study design in the methods, this would also guide you in the conclusions there of

AUTHOR: Study design added under "Ethical considerations and setting" – Page 3, paragraph 3, lines 3-4" "The study design chosen was an observational cross-sectional study with retrospective analysis"

You spoke about review of treatment plans of DFUs but you did not talk about the antibiotics used in the management, you dwelt on the diagnosis but not the treatment itself. How are the DFUs being treated, with what antibiotics, are they oral or topical or injectables

AUTHOR: Addressed under the heading "Pharmacological management and treatment practices of DFUs" – Page 8, paragraph 3, lines 5-7 and lines 10-13

"South African guidelines suggest oral antimicrobial therapy of amoxicillin/clavulanic acid, flucloxacillin and clindamycin in the case of penicillin allergy.

Of these, 47.9% complied to those set out in the South African guidelines. Only 14.6% were partially compliant, 33.3% were not compliant and the remaining 4.2% of the protocols could not be assessed for compliance due to a lack of record keeping or unrelated foot conditions (onychomycosis) being treated."

The goals do not seem to agree with the title, you were reviewing treatment plans, but your major objectives were to look at the risk factors

AUTHOR: Title has been amended to align more closely to the study objectives

"This study determined that the South African treatment guidelines and DFU classification system were in need of updating in order to align to international standards." Do you have internal and external validity to come up with a conclusion of this magnitude.

AUTHOR: This study determined that in the majority South African Treatment Guidelines do not align to international standards; nor are current guidelines explicitly and appropriately followed. Despite this, this study does lack a large and representative sample of DFU cases in South Africa and therefore would result in this statement being too ambitious. Therefore, this sentence has been amended under "Significance of main findings" – Page 2, paragraph 1, line 1:

"This study determined that the South African treatment guidelines and DFU classification system do not align to international standards".

The aim does not seem to speak to the title

AUTHOR: Title has been amended to align more closely to the study objectives

What does to attain 50% attrition rate mean

AUTHOR: This statement was removed as no participants dropped out of the study following study enrolment.

Furthermore, the use of preventative measure (s) among DFU patients was poor and that polypharmacy

AUTHOR: Corrected

Ethics (Ethical clearance) was obtained from the Human Research Ethics Committee

AUTHOR: Corrected

as the goal of this research is to understand foot ulceration as a consequence of diabetes Was this the goal of this research?

AUTHOR: Reworded under "Patient selection and classification" – Page 4, paragraph 2, lines 5-6:

"...the goal of this research is to understand the influence of patient specific factors on DFU development and subsequent treatment plans."

A short, structured questionnaire was used in order to determine the use of preventative aids that had not been prescribed. How do you determine the use of something that has not been prescribed?

AUTHOR: Clarification provided under "Patient record review and administration of a structured questionnaire" – Page 4, paragraph 4, lines 9-10:

"A short, structured questionnaire was used in order to determine the use of preventative aids that had been prescribed; or not been prescribed but were independently initiated by participants"

Next, a section on concurrent conditions and chronic medication use was included in order to establish the effect of these factors on ulcer severity. Causation is difficult to determine from a cross sectional study

AUTHOR: While it is acknowledged that cross-sectional studies have limitations in establishing causation due to their snapshot nature, the inclusion of a section on concurrent conditions and chronic medication use was included to explore potential associations and effects. By examining these factors, the study aimed to provide valuable insights into the relationship between concurrent conditions, medication use, and ulcer severity, mitigating some of the challenges associated with establishing causation in cross-sectional designs.

The two patients who participated in the pilot study are of an acceptable sample size as the 121 established sample size for the study is (was) limited

AUTHOR: Corrected

The results from this study demonstrated a higher prevalence of DFU among male participants (60%) in comparison to female participants (40%). What is the gender distribution of the area which is serviced by the hospitals that were included in the study?

AUTHOR: While the study does indeed show a higher prevalence of DFU among male participants (60%) compared to female participants (40%), it's important to recognise that this gender distribution within the study sample may not directly reflect the gender distribution of the entire population serviced by the hospital included in the study. Several factors can contribute to this difference, such as variations in healthcare-seeking behavior, and risk factors. This has been supported within the Discussion section of this manuscript: Page 9, paragraph 2, lines 7-14.

The largest proportion of ulcers were classified as grade one and grade two in severity and these patents (patients) presented with an average number

AUTHOR: Corrected

Thereafter, the use of hydrochlorothiazide (a diuretic used in the treatment of hypertension) and paracetamol (an analgesic and antipyretic) was most frequently noted (33.3%). (you cant define this as most frequent since the drugs in the preceding sentence had a frequency of 40%, can you?

AUTHOR: Reworded under "Medication use and the incidence of polypharmacy" – Page 7, paragraph 1, line 6.

"Thereafter, the use of hydrochlorothiazide (a diuretic used in the treatment of hypertension) and paracetamol (an analgesic and antipyretic) was the next most frequently noted (33.3%). "

In this study, 48.9% of patients did not make use of any preventive measures. The frequency and type of preventative measures used by patients in the... can you please be consistent is it preventive or preventative

AUTHOR: Corrected to preventative

By evaluating the past treatment plan of patients in this cohort, gaps and missed opportunities in past

treatment practices can be identified. This allows for the improvement of future DFU treatment plans. Is this not supposed to be past tense

AUTHOR: Corrected

The findings in this study are consistent with previous studies where 58.3-69.9% of patients presented with hypertension. How is 84% similar to 58.3 – 69.9%?

AUTHOR: Reworded under “Discussion” – Page 10, paragraph 2, line 14.

“The findings in this study are greater than previous studies where 58.3-69.9% of patients presented with hypertension”

Reviewer B: Round 1

Date completed: 15 August 2023

Recommendation: Revisions required

Conflict of interest: None

Does the manuscript fall within the scope of SAJS?

Yes/No

Is the manuscript written in a style suitable for a non-specialist and is it of wider interest than to specialists alone?

Yes/No

Does the manuscript contain sufficient novel and significant information to justify publication?

Yes/No

Do the Title and Abstract clearly and accurately reflect the content of the manuscript?

Yes/No

Is the research problem significant and concisely stated?

Yes/No

Are the methods described comprehensively?

Yes/No

Is the statistical treatment appropriate?

Yes/No/Not applicable/Not qualified to judge

Do you believe somebody with more methodological expertise (in the area of this study) than yourself needs to review this?

Yes/No

If yes, can you suggest the type of expertise needed

Not applicable

Are the interpretations and conclusions justified by the research results?

Yes/Partly/No

Please rate the manuscript on overall contribution to the field

Excellent/**Good**/Average/Below average/Poor

Please rate the manuscript on language, grammar and tone

Excellent/**Good**/Average/Below average/Poor

Is the manuscript succinct and free of repetition and redundancies?

Yes/No

Are the results and discussion confined to relevance to the objective(s)?

Yes/No

The number of tables in the manuscript is

Too few/**Adequate**/Too many/Not applicable

The number of figures in the manuscript is

Too few/**Adequate**/Too many/Not applicable

Is the supplementary material relevant and separated appropriately from the main document?

Yes/No/Not applicable

Please rate the manuscript on overall quality
Excellent/ Good /Average/Below average/Poor
Is appropriate and adequate reference made to other work in the field?
Yes/ No
Is it stated that ethical approval was granted by an institutional ethics committee for studies involving human subjects and non-human vertebrates?
Yes/ No /Not applicable
If accepted, would you recommend that the article receives priority publication?
Yes/ No
Are you willing to review a revision of this manuscript?
Yes/ No
Select a recommendation:
Accept / Revisions required / Resubmit for review / Decline
With regard to our policy on ' Publishing peer review reports ', do you give us permission to publish your anonymised peer review report alongside the authors' response, as a supplementary file to the published article? Publication is voluntary and only with permission from both yourself and the author.
Yes/ No
Comments to the Author:
Thank you for this manuscript. My comments are mainly minor (and also help with an international audience).
These include:
<u>A) Introduction</u>
a) Please explain that South Africa has a dual health care system - private and public. However - chosen to investigate the public system as this includes the vast majority of patients in SA (approx. 80% or so) and the Government is moving towards UHC
b) In addition - good to state that CV diseases now the leading cause of death within SA - with increasing concerns regarding the growing prevalence of T2DM and associated complications in Africa. SA (in Godman B et al. Review of Ongoing Activities and Challenges to Improve the Care of Patients With Type 2 Diabetes Across Africa and the Implications for the Future. Front Pharmacol. 2020;11:108) - and critical to treat patients well else develop complications including DFU with its implications for morbidity, mortality and costs (discussed in e.g. Chan JCN et al. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. Lancet. 2021;396:2019-82). The concerns with the rise in NCDs in SA especially CVD has resulted in ongoing strategic plans by the MoH in SA to improve the care of these patients especially in public system (https://www.sancda.org.za/wp-content/uploads/2022/05/NCD-NSP-draft-layout-28-04-22.pdf) - hence this study
c) What is typically the breakdown of patients with T1 vs T2DM in SA - my impression is that the vast majority have T2DM. In addition, what are ongoing activities, if any, in typical PHCs to monitor/ improve the care of patients with especially T2DM (including those with hypertension). My impression based on your findings is limited - but again good to include any details (if published) to lay the foundation for this paper in the Introduction, e.g. Rampamba EM et al. Knowledge of hypertension and its management among hypertensive patients on chronic medicines at primary health care public sector facilities in South Africa; findings and implications. Expert Rev Cardiovasc Ther. 2017;15:639-47; Rampamba EM et al. Evaluation of antihypertensive adherence and its determinants at primary healthcare facilities in rural South Africa. J Comp Eff Res. 2018;7:661-72, Rampamba EM et al. Empowering Hypertensive Patients in South Africa to Improve Their Disease Management: A Pharmacist-Led Intervention. J Res Pharm Pract. 2019;8:208-13 and Moosa A et al. Knowledge regarding medicines management of type 2 diabetes amongst patients attending a Community Health Centre in South Africa. Journal of Pharmaceutical Health Services Research. 2019;10:13-28 to name just a few
d) How representative is KZN for the rest of SA as good to see this paper being used to stimulate such discussions throughout SA with ongoing strategic plans to improve the care of patients with NCDs in SA?

B) Methodology

- a) Define dyslipidaemia in these patients
- b) Overall happy with the questionnaire development based on the literature and a pilot to enhance its development
- c) How are ADRs measured/ captured?
- d) I understand the issues with polypharmacy. However for patients with T2DM not being well controlled would expect them to be prescribed e.g. one to 2 oral antidiabetic medicines with/ without insulin, 1 - 2+ antihypertensives, a statin (e.g. 40mg simvastatin or atorvastatin), low-dose aspirin (e.g. 75mg), etc., and possibly a PPI

C) Results

- a) How many patients were recruited - good to have this figure early in the results and what % did this represent among those approached?
- b) What were the typical antihypertensives prescribed (I would expect to see these including ACEIs or ARBs in view of their protective effects on the kidney)?
- c) What about the extent of statins prescribed and their dose as this can be an issue among African countries, e.g. Mwita JC et al. Statin prescription among patients with type 2 diabetes in Botswana: findings and implications. BMC Endocr Disord. 2020;20:36?

D) Discussion

- a) What about next steps for PHCs in SA given the MoH priority for NCDs in SA? There is currently limited discussion (lines 392 - 395) - this needs upgrading in view of the concerns you identified. Your results signify that there are concerns with the extent of preventative measures among patients with e.g. T2DM among PHCs in SA - e.g. making sure comply with lifestyle changes as well as prescribed medicines. In addition, practice good foot hygiene, etc. This is particularly important post COVID-19 pandemic with associated lock down measures

Author response to Reviewer B: Round 1

Please explain that South Africa has a dual health care system - private and public. However - chosen to investigate the public system as this includes the vast majority of patients in SA (approx. 80% or so) and the Government is moving towards UHC

AUTHOR: Included in introduction – Page 2, paragraph 3, lines 1-6.

“South Africa is trying to move towards universal health coverage, however, at the time of this study, healthcare provision in South Africa consisted of an unequal two-tiered system. Firstly, the public sector which is state-funded and services the majority of the population and secondly, the private sector which is funded mostly by individual contributions to medical aid schemes or health insurance (ref). This study focused on patients within the public healthcare system.”

In addition - good to state that CV diseases now the leading cause of death within SA - with increasing concerns regarding the growing prevalence of T2DM and associated complications in Africa. SA (in Godman B et al. Review of Ongoing Activities and Challenges to Improve the Care of Patients With Type 2 Diabetes Across Africa and the Implications for the Future. Front Pharmacol. 2020;11:108) - and critical to treat patients well else develop complications including DFU with its implications for morbidity, mortality and costs (discussed in e.g. Chan JCN et al. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. Lancet. 2021;396:2019-82). The concerns with the rise in NCDs in SA especially CVD has resulted in ongoing strategic plans by the MoH in SA to improve the care of these patients especially in public system (<https://www.sancda.org.za/wp-content/uploads/2022/05/NCD-NSP-draft-layout-28-04-22.pdf>) - hence this study

AUTHOR: Knowledge and practice regarding DFUs, as well as the ability to identify individuals at risk of developing a DFU, is vital in reducing complications and subsequent lower limb amputation. Thus, an understanding of the treatment of DFUs in the South African public healthcare sector by all healthcare professionals is necessary in order to improve patient outcomes through improved treatment guidelines. The aim of this study was to categorise factors that predispose individuals for developing a DFU and to

identify the potential shortcomings in existing treatment plans. In addition, the use of preventative measures and past treatment practices in the management of diabetic foot ulcers was examined.

What is typically the breakdown of patients with T1 vs T2DM in SA - my impression is that the vast majority have T2DM. In addition, what are ongoing activities, if any, in typical PHCs to monitor/ improve the care of patients with especially T2DM (including those with hypertension). My impression based on your findings is limited - but again good to include any details (if published) to lay the foundation for this paper in the Introduction, e.g. Rampamba EM et al. Knowledge of hypertension and its management among hypertensive patients on chronic medicines at primary health care public sector facilities in South Africa; findings and implications. *Expert Rev Cardiovasc Ther.* 2017;15:639-47; Rampamba EM et al. Evaluation of antihypertensive adherence and its determinants at primary healthcare facilities in rural South Africa. *J Comp Eff Res.* 2018;7:661-72, Rampamba EM et al. Empowering Hypertensive Patients in South Africa to Improve Their Disease Management: A Pharmacist-Led Intervention. *J Res Pharm Pract.* 2019;8:208-13 and Moosa A et al. Knowledge regarding medicines management of type 2 diabetes amongst patients attending a Community Health Centre in South Africa. *Journal of Pharmaceutical Health Services Research.* 2019;10:13-28 to name just a few

AUTHOR: More information regarding follow-up appointments provided in the body of the discussion – Page 10, paragraph 2, lines 5-8.

“Patients in this study were expected to present on a monthly basis in order to monitor the progression of their DFU as well as track the management of diabetes and related comorbidities.”

How representative is KZN for the rest of SA as good to see this paper being used to stimulate such discussions throughout SA with ongoing strategic plans to improve the care of patients with NCDs in SA?

AUTHOR: KZN is not entirely representative of the rest of South Africa, however, these landmark studies were the catalyst for ours in Gauteng. We hope this research will allow for further investigation into the other major regions of South Africa so that more valuable conclusions and correlations can be drawn for patient benefit.

Define dyslipidaemia in these patients

AUTHOR: Provided in the discussion - Page 10, paragraph 2, lines 17-19.

“(Total cholesterol: >5.2 mmol/L; LDL cholesterol: >2.6 mmol/L; HDL cholesterol: >1.6 mmol/L or triglycerides: >1.7 mmol/L)”

“A total of 210 potential drug-drug interactions were observed in the patient cohort”

This finding was based on potential interactions that could occur when combining two or more drugs – patient specific data concerning the manifestation of these interactions was out of the scope of this study.

I understand the issues with polypharmacy. However, for patients with T2DM not being well controlled would expect them to be prescribed e.g., one to 2 oral antidiabetic medicines with/ without insulin, 1 - 2+ antihypertensives, a statin (e.g. 40mg simvastatin or atorvastatin), low-dose aspirin (e.g. 75mg), etc., and possibly a PPI

AUTHOR: While it is true that some patients with poorly controlled T2DM may require multiple medications to effectively manage their condition and reduce the risk of complications, it's crucial to balance the benefits of polypharmacy with potential risks and individualised patient needs. It's important to consider the potential for simplifying regimens when possible and to regularly review a patient's medication list to ensure that the benefits outweigh the risks and that the treatment is tailored to their individual needs. This study provided insight into how often polypharmacy occurs and highlighted the incidence of risk and lack of monitoring in these patients.

How many patients were recruited - good to have this figure early in the results and what % did this represent among those approached?

AUTHOR: These were highlighted in the following sentence (Page 3, paragraph 2, lines 1-3): “A total of 45 patients with 50 DFUs were recruited for this study meeting the expected sample size for this cohort”.

What were the typical antihypertensives prescribed (I would expect to see these including ACEIs or ARBs in view of their protective effects on the kidney)?

AUTHOR: The most typical antihypertensives prescribed were both ACEIs (enalapril) and Calcium Channel Blockers (amlodipine).

These were highlighted in the following sentence (Page 7, paragraph 1, lines 1-5): “Of the medications that are not anti-diabetic in nature, the most frequently used include simvastatin (for hyperlipidaemia treatment), enalapril and amlodipine (both used in the treatment of hypertension), with 40% of patients found to be using these medications.”

What about the extent of statins prescribed and their dose as this can be an issue among African countries, e.g. Mwita JC et al. Statin prescription among patients with type 2 diabetes in Botswana: findings and implications. *BMC Endocr Disord.* 2020;20:36?

AUTHOR: The researchers could not define the average dosage of all medications prescribed due to negligent and poor record keeping of patient files and prescriptions. However, the medication, simvastatin was the most frequently prescribed non-diabetic medicine with 40% of patients making use of this treatment.

This has been stated in the following sentence (Page 7, paragraph 1, lines 1-5): “Of the medications that are not anti-diabetic in nature, the most frequently used include simvastatin (for hyperlipidaemia treatment), enalapril and amlodipine (both used in the treatment of hypertension), with 40% of patients found to be using these medications.”

What about next steps for PHCs in SA given the MoH priority for NCDs in SA? There is currently limited discussion (lines 392 - 395) - these needs upgrading in view of the concerns you identified. Your results signify that there are concerns with the extent of preventative measures among patients with e.g. T2DM among PHCs in SA - e.g. making sure comply with lifestyle changes as well as prescribed medicines. In addition, practice good foot hygiene, etc. This is particularly important post COVID-19 pandemic with associated lock down measures

AUTHOR: These comments were addressed in the concluding paragraph that was added on page 13.

This reads as follows, “Therefore, in conclusion, addressing the concerns relating to diabetes and DFU management identified in this study are crucial. Large scale studies should be conducted to review the entire South African context for the magnitude of DFU incidence and management concerns including the adherence to treatment plans and the influence of DFU progression. These studies could help to address the development and implementation of more comprehensive patient education programs to ensure that individuals with DFUs are well-informed about the importance of complying with lifestyle changes and prescribed medications. In addition, these studies would aid in establishing robust monitoring and follow-up systems which are required when tracking patient progress in adhering to treatment plans and reducing DFU burden.”

Associate Editors' comments: Round 1

Date sent: 2 November 2023

Comments to the Author:

Kindly restructure your Discussion. Your Discussion contains valuable information, but it could be more concise and still get the right message across. Here is a general guide for the structure of the Discussion: (1) Principal findings of the study (2) Strengths and weaknesses. Why and how are they strengths and weaknesses? (3) Strengths and weaknesses in relation to other studies, interpretation from others' results (i.e., highlight differences between studies in terms of design, setting, etc.) (4) Meanings/implications of the study? Explanations for policy makers and clinicians (5) Conclusion, unanswered questions and future research?

In addition to your self-identified limitations of the study, consider speaking to the following limitations: Generalisability of results in relation to the sample size

Adherence to treatment as a risk factor for the development of DFU.

Thank you for considering these.

Author response to Associate Editors' comments: Round 1

Kindly restructure your Discussion. Your Discussion contains valuable information, but it could be more concise and still get the right message across. Here is a general guide for the structure of the Discussion: (1) Principal findings of the study (2) Strengths and weaknesses. Why and how are they strengths and weaknesses? (3) Strengths and weaknesses in relation to other studies, interpretation from others' results (i.e., highlight differences between studies in terms of design, setting, etc.) (4) Meanings/implications of the study? Explanations for policy makers and clinicians (5) Conclusion, unanswered questions and future research?

AUTHOR: The authors have revised the discussion and made it as concise as possible without losing the salient findings.

In addition to your self-identified limitations of the study, consider speaking to the following limitations:
Generalisability of results in relation to the sample size
Adherence to treatment as a risk factor for the development of DFU.

AUTHOR: These comments were addressed in the concluding paragraph that was added on page 13. This reads as follows, "Therefore, in conclusion, addressing the concerns relating to diabetes and DFU management identified in this study are crucial. Large scale studies should be conducted to review the entire South African context for the magnitude of DFU incidence and management concerns including the adherence to treatment plans and the influence of DFU progression. These studies could help to address the development and implementation of more comprehensive patient education programs to ensure that individuals with DFUs are well-informed about the importance of complying with lifestyle changes and prescribed medications. In addition, these studies would aid in establishing robust monitoring and follow-up systems which are required when tracking patient progress in adhering to treatment plans and reducing DFU burden."

Reviewer A: Round 2

Date completed: 18 January 2024

Recommendation: Accept

Conflict of interest: None

Does the manuscript fall within the scope of SAJS?

Yes/No

Is the manuscript written in a style suitable for a non-specialist and is it of wider interest than to specialists alone?

Yes/No

Does the manuscript contain sufficient novel and significant information to justify publication?

Yes/No

Do the Title and Abstract clearly and accurately reflect the content of the manuscript?

Yes/No

Is the research problem significant and concisely stated?

Yes/No

Are the methods described comprehensively?

Yes/No

Is the statistical treatment appropriate?

Yes/No/**Not applicable**/Not qualified to judge

Do you believe somebody with more methodological expertise (in the area of this study) than yourself needs to review this?

Yes/**No**

If yes, can you suggest the type of expertise needed

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Comments to the Author:
 The authors have addressed my previous comments satisfactorily.

Reviewer B: Round 2

Date completed: 1 December 2023

Recommendation: Accept

Conflict of interest: None

Does the manuscript fall within the scope of SAJS?
Yes/No

Is the manuscript written in a style suitable for a non-specialist and is it of wider interest than to specialists alone?
Yes/No

Does the manuscript contain sufficient novel and significant information to justify publication?
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Do the Title and Abstract clearly and accurately reflect the content of the manuscript?
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Is the research problem significant and concisely stated?
Yes/No
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Is the statistical treatment appropriate?
Yes/No/Not applicable/Not qualified to judge
Do you believe somebody with more methodological expertise (in the area of this study) than yourself needs to review this?
Yes/No
If yes, can you suggest the type of expertise needed
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Are the interpretations and conclusions justified by the research results?
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Yes/No
Did you mentor someone during this peer review?
Yes/No
Comments to the Author:
I have no further comments to make.