PEER REVIEW HISTORY

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ARTICLE DETAILS

| TITLE (PROVISIONAL) | Quality of life among adult patients living with diabetes in Rwanda: a cross-sectional study in outpatient clinics |
|---------------------|---------------------------------------------------------------------------------------------------------------|
| AUTHORS             | Lygidakis, Charilaos; Uwizihiwe, Jean Paul; Bia, Michela; Uwinkindi, Francois; Kallestrup, Per; VÖGELE, Claus |

VERSION 1 – REVIEW

| REVIEWER                        | Papazafiropoulou, Athanasia Geniko Nosokomeio Nikaias Peiraia - Agios Panteleimon |
|---------------------------------|----------------------------------------------------------------------------------|
| REVIEW RETURNED                 | 19-Oct-2020                                                                      |
| GENERAL COMMENTS                | According to my knowledge, it is a novel paper in its field opening new horizons for further evidence. In addition, the object as well as the results are appropriately discussed in the context of previous literature explaining the importance of the manuscript in its field. Authors succeed to present their data in a clear way adding information to the existing literature. Therefore, I have no corrections or further work to propose for the improvement of the manuscript and therefore it can be published unaltered. |

| REVIEWER                        | Corrina Moucheraud University of California Los Angeles |
|---------------------------------|----------------------------------------------------------|
| REVIEW RETURNED                 | 05-Nov-2020                                              |
| GENERAL COMMENTS                | This is a well-written and interesting paper on an important topic. I recommend that the authors strengthen several areas, before I feel it is ready for publication. Major concerns: (1) The methods section should be expanded to include details about how the study design was reflected in the analysis approach (e.g., was there any multi-level structure to the model specification? any clustering of standard errors? any adjustment for multiple outcomes?) (2) Also, the construction of models presented in table 4 is not clear to me. How were the covariates selected (why do they differ from what is shown in tables 1-3)? What motivates the interaction terms? This should all be clearly explained in Methods -- and, the selection & inclusion/operationalization of variables should be based on a conceptual framework. (3) There are important limitations that were not addressed, in my opinion -- for example, by recruiting participants at health facilities, this study is only measuring QOL among people sufficiently healthy (& care-engaged) to be present for inclusion. Also, these are people seeking care at hospitals so may differ from people seeking care at lower-level health facilities. And, this study |


excluded people with certain health concerns -- like hearing impairment and mental health conditions -- which may be associated with QOL & clinical outcomes.

I also have a few minor comments:
- There are so many people reporting time since diagnosis <5 years; I therefore suggest dividing this into smaller groups (especially since it would be interesting to know specifically about newly-diagnosed individuals)
- Most people had at least 1 comorbidity. These should be discussed further -- which were most common, and I was particularly surprised see this included in only certain models in table 4 as it seems like it could be an important factor associated with QOL.
- The use of HbA1c/glycemic control data is not used very robustly -- for example why is it not included throughout table 4; how is it control correlated with other outcomes (from tables 2 & 3); and why include HbA1c as a continuous measure in table 1 & 3 -- rather than a binary controlled Y/N variable? Perhaps this will be explored in a future paper -- but at minimum the final point about using continuous HbA1c vs categorical controlled Y/N should be addressed here.

**VERSION 1 – AUTHOR RESPONSE**

Response to comments of Reviewer 2

(1) The methods section should be expanded to include details about how the study design was reflected in the analysis approach (e.g., was there any multi-level structure to the model specification? any clustering of standard errors? any adjustment for multiple outcomes?)

We employed neither a multi-level structure in our analyses nor clustering of standard errors as the variables examined in this cross-sectional study were not linked to the unit of the randomisation (the small administrative areas in the catchment areas of hospitals). For multiple comparisons, we applied the Bonferroni correction adjusting the level of significance according to the number of comparisons.

(2) Also, the construction of models presented in table 4 is not clear to me. How were the covariates selected (why do they differ from what is shown in tables 1-3)? What motivates the interaction terms? This should all be clearly explained in Methods -- and, the selection & inclusion/operationalization of variables should be based on a conceptual framework.

The construction of models was guided by exploration of a variety of socio-demographic and clinical variables (shown in tables 1 to 3). The variables for which the dimensions of D-39 differed or were correlated significantly, as well as those conceptually similar, were included in the multiple regressions. Interactions were assessed for those variables in which a combination effect was hypothesised (e.g., type of treatment and glycaemic control). For each of the D-39 dimensions, a series of models was produced, and the most appropriate ones were selected after assessing residuals and model fit.
(3) There are important limitations that were not addressed, in my opinion -- for example, by recruiting participants at health facilities, this study is only measuring QOL among people sufficiently healthy (& care-engaged) to be present for inclusion. Also, these are people seeking care at hospitals so may differ from people seeking care at lower-level health facilities. And, this study excluded people with certain health concerns -- like hearing impairment and mental health conditions -- which may be associated with QOL & clinical outcomes.

It is indeed possible that some patients with severe conditions may not have been included in our sample and we have adapted the manuscript accordingly.

Nonetheless, it should be noted that the Rwandan health system promotes community care and decentralisation. On the one hand, there is a newly established programme of community health workers ('Home-based Care Practitioners' (HBCPs)), which aims at screening and following-up patients with non-communicable diseases in the communities. HBCPs facilitate linking patients with the healthcare services for non-communicable diseases, including nurse-practitioner-led outpatient clinics. We, therefore, believe that many patients with diabetes and especially those who need medication are already linked to healthcare services.

On the other hand, there is good integration of hospitals and lower-level health facilities (i.e., health centres, which are staffed by nurses). For example, some patients with already diagnosed diabetes, such as those of our sample, receive their medication from health centres every month, while they visit hospitals every six to twelve months for laboratory tests and follow-up by the outpatient clinics for non-communicable diseases. It should also be noted that for the pre-enrolment screening, we invited the nurses of the health centres to refer patients to the outpatient clinics, where they would be checked for eligibility.

Finally, our study excluded subjects with severe mental health conditions and severe hearing and visual impairments. These are patients who require particular attention and care, and often show lower quality of life. To our knowledge, there are no data in the literature on how the D-39 questionnaire performs on such cohorts, and what type of adjustments (e.g., in its way of administration) would be required. Hence, we did not take them into account in its adaptation into Kinyarwanda.

There are so many people reporting time since diagnosis <5 years; I therefore suggest dividing this into smaller groups (especially since it would be interesting to know specifically about newly-diagnosed individuals)

We have further divided the group of patients with a diagnosis of up to 5 years into two groups: patients with a diagnosis up to 2 years and patients between 3 and 5 years. When assessing mean differences across groups, we only identified a marginally significant difference in the “anxiety and worry” dimension ($H(2)=5.977, p=0.050$). However, after adjusting the level of significance to avoid type I error in the post-hoc contrasts, we found no significant differences when comparing the mean difference of the groups with different illness durations (i.e., up to 2 years vs. 3 to 5 years and 6 or more years).

Most people had at least 1 comorbidity. These should be discussed further -- which were most common, and I was particularly surprised see this included in only certain models in table 4 as it seems like it could be an important factor associated with QOL.

We have added the six most frequent comorbidities to Table 1. As mentioned in the discussion section, the majority of the patients presented with hypertension (47.3%), followed by HIV infection.
(7.8%). As with the complications, we expect that there is a certain degree of underreporting due to patient records' not being kept up-to-date. However, as there are governmental programmes promoting management of patients with hypertension and HIV, we expect a more accurate registration of patients with diagnosis of hypertension or HIV infections and we assume that their prevalence is closer to reality — as these conditions were also the easiest to verify triangulating clinical and drug use data. This is supported by the paper of Amendezo et al., which shows a similar prevalence for the two diseases. We have added a sentence to acknowledge possible underreporting. We also added mean differences test on hypertension and HIV infection to Table 3. Finally, although we have used the six most frequent comorbidities as predictors in the regressions, only hypertension modified some of the models.

The use of HbA1c/glycemic control data is not used very robustly -- for example why is it not included throughout table 4; how is it control correlated with other outcomes (from tables 2 & 3); and why include HbA1c as a continuous measure in table 1 & 3 -- rather than a binary controlled Y/N variable? Perhaps this will be explored in a future paper -- but at minimum the final point about using continuous HbA1c vs categorical controlled Y/N should be addressed here.

In the multiple regressions, the most adequate models were selected and presented guided by the model-fit scores. HbA1c was not always included because it did not always contribute to improving the models.

Glycaemic control was not included in table 1 to avoid replication, as it is reported in the results. We had chosen to report only the correlation of the continuous variable for brevity as the cut-offs did not yield differences. However, as suggested by the reviewer, this may be an important piece of information and we have adjusted the third table accordingly.

**VERSION 2 – REVIEW**

| REVIEWER           | Corrina Moucheraud       |
|--------------------|--------------------------|
|                    | University of California Los Angeles, USA |
| REVIEW RETURNED    | 29-Dec-2020              |
| GENERAL COMMENTS   | Thank you for the opportunity to re-review this manuscript. I feel the authors have adequately responded to my comments. |