Author’s response to reviews

Title: Quality of life after the initiation of dialysis or maximal conservative management in elderly patients: A longitudinal analysis of the Geriatric assessment in OLder patients starting Dialysis (GOLD) Study

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Author’s response to reviews:

Rebuttal letter (2)

Dear Editor,

We want to thank you for the opportunity of resubmitting our manuscript to BMC Nephrology after major revisions. We appreciate the time the reviewers took to comment on our manuscript. We discussed all items together and revised the manuscript. We addressed these comments below one by one. We think the comment of the reviewers contributed to the improvement of the manuscript.

We hope that the revised version of the manuscript is suitable for publication in your journal.

With kind regards, also on behalf of my co-authors,

Ismay van Loon

Editor
1) The inclusion of patients who were KTx candidates raises validity concerns regarding the health status of the patients in the two arms and whether adjustment could truly account for the differences. At least a sensitivity analysis excluding pts who had a hx of KTx, eventually received a KTx, or were listed is necessary.

We have performed a sensitivity analysis excluding all patients on the waiting list or who received a kidney transplant during follow-up (n=26).

(Only 1 patient had a previous history of kidney transplantation and had residual rest function, we’ve decided not to exclude this patient).

2) Please add a flow diagram showing how many pts were approached, consented, died at 6mo, 12mo, had missing hrqol values at the various observation points (baseline, 6mo).

Done as proposed (see supplementary material appendix 3).

3) For the results, agree with reviewer's comments re: reporting an improvement when the change in values is not statistically significant.

This was corrected.

5) For all tables, when % are given, cell counts (i.e., N) are needed.

Done as requested.

4) Please either offset the VAS results or discuss them before any multivariable analysis of change in eq-5d scores (as noted below, I have concerns re: the multivariable analysis).

&

6) I find the multivariable analysis composite outcome of death/qol decline problematic and would recommend removing it. The informative missingness of hrqol measures at specific time points due to death is a challenging problem in qol research and the investigators' approach cleverly handles this. However, it's not clear to me that these outcomes can be rationally combined. Patients who opt for CM and remain consistent in their choice, are saying that death is preferred to the qol they feel they will experience on dialysis (i.e., death is not a decline in qol compared to dialysis... presumably many of these pts, if they were to start dialysis, would report a substantial decrement in qol with dialysis).
We now present the EQ 5D and VAS scores and subsequently the multivariable analysis of the baseline domains. We have decided to remove the multivariable analysis of the composite outcome.

This brings up a larger issue that the authors should acknowledge in the limitations section and flush out in the discussion: the use of health utilities. These values are judgements from the general population on hqol from an external vantage point. Hence, they do not capture the perception of qol from the patient's perspective and this is central when discussing CM. I would recommend that the authors discuss how this may influence some of the improvements observed in hqol in dialysis pts when compared to their CM counterparts... this may account for some of the differences in this study vs. prior studies.

This was addressed in the discussion:

“Finally, QoL measurements have been developed based on perceived quality of health in the general population. Although the EQ-5D has been widely used among CKD patients25, other values may apply in the conservative care population. When discussing conservative care it is important to find out which values and aspects of physical, cognitive and psychosocial domains matter most to the patient. The EQ-5D does not only capture objective aspects of quality of life, but also includes a subjective or self-rated part, the visual analogue score. In our cohort, the between group difference of overall self-rated quality of life at follow-up was 0.7 points. This number is considered the minimum clinically important difference (MCID) in cancer,18 although others found 0.8 points was a better cut-off value in COPD.17 No MCID for ESKD exists. As the within group differences were small and the between group difference was borderline relevant, we considered the change not clinically relevant overall. But one could argue that conservative patients have also some lower self-rated QoL over time, when interpreting the results more strictly.”

Reviewer 1.

1) Patients who are transplant candidates and/or received a transplant should not be included in this analysis. The authors indicate that the aim of this study is to provide information on differences in trajectories in quality of life between patients treated with dialysis and those who opt for conservative care. They also indicate that this decision is most challenging for older patients with significant comorbidity in whom the benefits of dialysis are least certain. Therefore, it would seem that the population of interest would not be transplant candidates but consist of those for whom the option of dialysis would be as destination (and not bridging) therapy.

See before

2) The presentation of results is uneven, and some conclusions are not supported by the results.
2a) The authors indicate that they repeated the primary analyses after stratifying by eGFR < vs. > 10, however they only present data for the subgroup of patients with eGFR <10.

We have added to the results section:

“In the dialysis patients, two-thirds showed a stable or improved EQ-5D score while this occurred in half of the conservative patients (p<0.001, Table 3). The same results were found for older patients (≥80 years) and for patients with a low GFR. However, for patients with a high GFR the differences between the dialysis group and the conservative group were less pronounced and no significant difference could be found. (Table 3)”

2b) The authors describe that "EQ-D5 Index improved in the dialysis group" during follow-up but the p-value=0.1. They also restate this interpretation of results in the Conclusion.

Corrected as suggested.

2c) In the results, the authors state that "EQ-D5 Index declined significantly in the conservative group" and "overall self-rated quality of life conservative patients decreased" during follow-up, however in the Conclusion, the authors do not state these and instead describe "half of the conservative patients remain in a stable or better quality of life".

Both findings are correct. Presenting both findings helps to interpret how change of QoL was distributed over all patients.

3) As stated above, the purpose of this study was to compare trajectories of quality of life between patients treated with dialysis and those opting for conservative care, however they perform an additional analysis (presented in Table 4) combining the two treatment groups that seems intended to examine factors associated with decline in quality of life. These analyses not only seem out of place in this manuscript but the design of the current study cannot support answering this specific research question.

We have decided to remove the multivariable analysis of the composite outcome (Table 4).

4) How did the authors define "terminal non-renal condition", which was one of their exclusion criteria.

This was based on the estimation of terminal condition of the treating physician and all these patients died before inclusion (patient flow chart, appendix 3).
Reviewer 2.

Methods:

1. The first sentence under the "Follow-up" subheading seems to be incomplete. There is also a misspelling and form should likely be "from" (e.g., After six months, data on... and complications were collected form each center).

Corrected as suggested.

2. The reasoning for sub-group analyses should be explicitly defined in the manuscript. There does not need to be a lot of text to describe this. Your point about quality of life changes with the EQ-D5 and among older individuals in the general population should suffice.

We have added to the methods section:

“In addition, a subgroup analysis was performed for patients aged <80 years and ≥80 years old, as QoL becomes even more relevant in this group as dialysis does not seem to prolong life in this population.19”

Results:

1. Under "Other complications", please use "IQR" in place of "range" to describe median characteristics.

We think range is better here as the IQR would be less informative:

“Among hospitalized patients, median number of admissions was 1 [IQR 1-1] for dialysis patients and 1 [IQR 1-1] for conservative patients (p=0.27)”

We are willing to change it as the editor thinks this would be better.