Author's response to reviews

Title: Suboptimal blood pressure control in chronic kidney disease stage 3: baseline data from a cohort study in primary care

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Author's response to reviews:

Dear Dr Payne,

Ref: MS: 7264111299318339

Research article: Suboptimal blood pressure control in chronic kidney disease stage 3: baseline data from a cohort study in primary care Simon DS Fraser, Paul J Roderick, Natasha J McIntyre, Scott Harris, Christopher W McIntyre, Richard J Fluck and Maarten W Taal BMC Family Practice (Section: Clinical presentation, diagnosis, and management )

Thank you very much for sending the reviewer’s comments on our paper. We are grateful for the extremely thorough review provided by Dr Tomlinson, and have tried to address all of the comments made. To this end, we have conducted some further analyses and amended the paper accordingly, and include further comments below.

We are grateful for your continued consideration of this paper for publication in BMC Family Practice

Kind regards

Dr Simon Fraser
On behalf of the authors

The key issues raised were:

1) That some of the study participants did not, in fact, have CKD because their eGFR at study entry was # 60ml/min/1.73m2
2) That the blood pressure targets used in the study were not the appropriate ones to use, and that the analyses of blood pressure could more usefully have considered systolic and diastolic BP separately).

3) That the study population is non-representative

4) That the association identified between CVD and increased likelihood of reaching BP targets may be due to reverse causality.

The reviewer recommended that we should:

a) Repeat the analysis including only people with baseline eGFR<60 or treat the people with eGFR # 60 as a separate group and discuss this limitation clearly.

b) Add a new table with SBP and DBP and SD stratified by age and eGFR. In addition provide a full descriptive analysis of the proportion of people with ISH, SDH, IDH and normotension in each age group for all patients.

c) Drop the logistic regression of the KDOQI target since it is not relevant.

d) Re-categorise people into those who do not meet the SBP target and those who do not meet the DBP target and rerun the (NICE) logistic regression for each group. Although this will reduce the power, by creating more homogeneous groups it may strengthen the findings.

e) Rewrite the manuscript with greater regard to the actual characteristics of the population studied and the limitations of the study.

Our responses to these key issues and recommendations are as follows:

Issue 1) and recommendation a)

That some of the study participants did not, in fact, have CKD

This is an important point to raise, and we fully understand the reason for the concern. However, we respectfully disagree that this should mean that people with eGFR # 60 should not be included in these analyses. All the participants met the formal definition for CKD prior to inclusion (including chronicity of low eGFR) and, importantly, were therefore on CKD registers in their respective GP practices. On that basis the BP targets for CKD did apply to them at the time of the baseline visit, regardless of what their baseline GFR turned out to be when conducted in the study setting. However, in the light of the concern, we have repeated the analyses in people with baseline eGFR <60 as recommended above and present this in the paper as a sensitivity analysis. The only difference in this analysis was that the association between KDOQI BP control and male gender on multivariable analysis (table 3) was not observed in the group with eGFR <60. All other associations remained the same (both uni- and multivariate). We have added some comments on this in the statistical analysis section, in the results, and a paragraph in the limitations section to acknowledge this issue.

Issue 2) and recommendations b), c), and d)

The appropriate use of BP targets
Thank you for raising this issue, and for the detailed and helpful comments provided. We acknowledge that there has been uncertainty about the correct BP targets. However, because of the international audience for BMC Family Practice, we feel that it is important to retain the KDOQI target analysis because they were the relevant guidelines at the time of data collection and practitioners in some countries may well have been continuing to work to those standards. We therefore would suggest that we do not drop the KDOQI target analyses as suggested in recommendation c) above, but instead we have now conducted further full analyses using the KDIGO targets to provide a more up to date analysis, and these results have been added, and the paper has been amended accordingly. This includes amendments to tables 2 and 3 and Figure 1. We did not analyse by QOF targets because of the international audience of this journal, and we still believe this is the correct approach. We have removed the statement about the NICE and KDOQI targets being ‘more evidence based’.

We agree with the comments about separating systolic and diastolic hypertension in more detail. This was a very useful point to raise and we are grateful to the reviewer for all of the detailed information provided. We do feel that there is still value in comparing BP control against the standards that, by definition, combine systolic and diastolic into one target, but we have conducted several additional analyses in the light of the suggestions made. We have provided additional tables 4 and 5 as suggested in recommendation b). These describe the distribution of systolic and diastolic blood pressure by age and eGFR in the whole study population, and the proportion in each age group with ISH, SDH, IDH and normotension.

We re-categorised people into those not achieving systolic and diastolic NICE BP targets separately and repeated the logistic regression as suggested in recommendation d). Interestingly, this demonstrated differences in age groups’ achievement of the NICE target, with older people less likely to achieve the systolic target and more likely to achieve the diastolic target on both univariate and multivariate logistic regression. In the light of these new findings, we have included a new section in the results commenting on systolic and diastolic hypertension separately. We are grateful for this recommendation.

We have also added the Vamos reference and a statement about the uncertainty of the correct management of isolated systolic hypertension. Thank you for this suggestion.

Issue 3) and recommendation e)

Non-representativeness of the population

Although we recognise that the study population is not representative of the general population, and is very limited with respect to ethnic minorities, we believe that it is representative of people with CKD 3 in Derbyshire, and probably of the majority of CKD 3 populations in the UK. However, in view of this comment, we have strengthened our recognition of this limitation in the paper. The sentence about the lack of socioeconomic gradient being reassuring has also been removed.
We have therefore not fully 'rewritten' the manuscript, but have made important edits to try and address the issues raised.

Issue 4) The association between CVD and greater achievement of BP targets

Thank you for this comment – we recognised this possibility, and had attempted to acknowledge this though the sensitivity analysis in people without CVD. It is worth noting that our data showed that very few people had heart failure (61 people (<4%) of the total study population). We have altered the wording in the limitation section to try and provide a clearer explanation.