Author's response to reviews

Title: Healthcare decision-making in end stage renal disease-patient preferences and clinical correlates

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Author's response to reviews: see over
RESPONSE TO REVIEWER COMMENTS

30th July, 2015

Dr. Anuradha Jayanti
Renal Research Division
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Oxford Road, Manchester
M13 9WL

SUBJECT: MS: 1418978635163923

Dear Editor,

I am submitting the following revised manuscript for consideration in BMC: Nephrology ‘Healthcare decision-making in end stage renal disease- patient preferences and clinical correlates’ I have included the following information below.

1. Response to reviewer comments.

I have revised the paper keeping in mind the reviewer comments. Each one of the points has been addressed and is available in the next page titled ‘responses to reviewer comments’.

2. Statement of author contributions

My co-authors have all contributed to this manuscript and approve of this submission.

3. Statement of prior publication

Neither this manuscript nor substantial parts of it are under consideration for publication.

4. Statement of disclosures of conflict of interest

I have communicated with all of my co-authors and obtained their full disclosures. A disclosure statement is also included within my manuscript before the reference section. My co-authors and I declare no conflicts of interest.

Sincerely,

Anuradha Jayanti
**REVIEWER 1**

<table>
<thead>
<tr>
<th>REVIEWER COMMENT</th>
<th>RESPONSE</th>
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<tbody>
<tr>
<td><strong>Minor Essential Revision</strong></td>
<td></td>
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<tr>
<td>1 There is one minor essential revision and that is on page 5 line 112 and 117. I believe the reference number should be 22 and not 25</td>
<td>This error is acknowledged and has been rectified.</td>
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<tr>
<td><strong>Discretionary Revisions</strong></td>
<td></td>
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<tr>
<td>2 I would suggest the authors consider a sentence linking their background to the study objectives. For example, why out of all the factors they discussed affect decision-making did they research autonomy?</td>
<td>This has been added to the paper (Lines 80-82).</td>
</tr>
<tr>
<td>3 Are there any limitations to using a backward step-wise selection data-driven vs. theory-driven analysis?</td>
<td>A backward step-wise selection model was used but only after consideration of whether variables were clinically meaningful. Firstly, a number of variables – age, education and group – were considered important to adjust for whether or not they were statistically significant. All other considered variables were included in a single variable analysis to determine whether there was any association at the 15% significance level. These variables and the three clinically important variables were included in a multivariable model and the step-wise selection was used until only those variables that were significant at the 5% level remained, along with the clinically important variables.</td>
</tr>
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<td>4 The clinical vignettes did not seem very well described in the paper and thus Figure 3 is not clear</td>
<td>The clinical vignettes have been elaborated on in the paper and a figure legend provided</td>
</tr>
<tr>
<td>5 Figure 4 is difficult to read in black and white</td>
<td>We appreciate it. Different symbols have now been used to highlight the differences in groups. The size of the symbol also determines the number of entries with the same score.</td>
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<td>6 There is qualitative research that you may consider including which supports your claims of complexity, highly personal decisions (not a 'one size fits all') and gender differences in modality decisions with women being more active in the decision-making process (Harwood, L and Clark, A.M. 2014)</td>
<td>Thank you and this has been added to the references (Number 29).</td>
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<td>REVIEWER COMMENT</td>
<td>RESPONSE</td>
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<tr>
<td><strong>Major Compulsory Revisions</strong></td>
<td><strong>The statistical methods section has been updated to make the method used clearer (Pages 6 and 7). Specifically, the backward step-wise selection included the three clinically important variables – age, education and group – and the variables that were significant at the 15% significance level in the single variable analyses. The selection process was run until only those variables that were significant at the 5% significance level remained, along with the three clinically important variables, which remained in the model regardless of statistical significance.</strong></td>
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<tr>
<td><strong>1</strong> To build their multivariate model, the authors selected covariates based on univariate analyses, only including those with a p-value &lt;0.15 (pg.6, lines 161-2). Looking at Table 3, I was expecting 14 covariates to be included in the model presented in Table 4. However, this model only contains 7 factors, suggesting that additional criteria were used for variable selection. The authors should make these criteria explicit.</td>
<td><strong>This is a very important issue and we thank you for raising it. Despite not being included in this paper, it is an area of interest that has been discussed extensively during the writing of this paper. The current paper is a conventional ‘associations’ paper and as such adjusts for possible confounders by including them in the multivariable linear regressions. In this sense, there is consideration given to the issue of confounding. Full causal models will be considered in the future; the dataset has a large number of variables for consideration, each of which needs to be carefully thought about as to whether they may be a potential moderator, mediator or instrumental variable. Our feeling is that such a piece of work would merit its own paper. However, we feel that this paper is still an essential contribution to this field as the initial associations work gives vital information on the causal pathways to further investigate. Dealing with the specific raised potential mediators of group and API-IS, it appears from an initial analysis that group is a mediator of</strong></td>
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<tr>
<td><strong>2</strong> An additional concern regarding the multivariate models is the lack of detail on if and how the authors addressed potential confounding.......I strongly recommend the authors to revisit their multivariate models, and to develop a separate model for each factor to explicitly address the potentially confounding effects.</td>
<td><strong>This is a very important issue and we thank you for raising it. Despite not being included in this paper, it is an area of interest that has been discussed extensively during the writing of this paper. The current paper is a conventional ‘associations’ paper and as such adjusts for possible confounders by including them in the multivariable linear regressions. In this sense, there is consideration given to the issue of confounding. Full causal models will be considered in the future; the dataset has a large number of variables for consideration, each of which needs to be carefully thought about as to whether they may be a potential moderator, mediator or instrumental variable. Our feeling is that such a piece of work would merit its own paper. However, we feel that this paper is still an essential contribution to this field as the initial associations work gives vital information on the causal pathways to further investigate. Dealing with the specific raised potential mediators of group and API-IS, it appears from an initial analysis that group is a mediator of</strong></td>
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</table>
the relationship and API-IS is borderline significant as a mediator. All three variables are included in the final API-DM model (despite education not being significant, it was considered clinically important), so it seems clear that while not all possible relationships have been established, the main associations are present. Interestingly, education is not significant even in the single variable analysis so it does appear it is working through other variables and this is an area of future interest.

3 In the Methods section on Statistical analysis (pg. 6, lines 154-65), the authors report the use of cut-off values that are all arbitrary. These include the values used for dichotomisation of the outcome variable for the information seeking analysis, including variables from the univariate analyses in the multivariate analyses, and cut-off values for creating subgroups based on API decision-making scores. The authors should perform sensitivity analyses to enable assessment of the effect of these arbitrary decisions on the reported results.

This comment gave rise to a discussion about the information seeking variable, which was dichotomised at 75%. Due to the very large number of patients with high information scores, initially it was considered a way of distinguishing very high information seekers from moderately high information seekers. On greater reflection, API-IS has been considered as a continuous variable, both as an outcome and as an independent variable in the API-DM analysis. Sensitivity analyses showed there was little difference when 80% was used as the cut-off. The continuous API-IS variable is associated with the same four variables it was associated when it was binary but marital status is now an additional significant variable. The API-DM final model was the same when API-IS was included as a continuous variable (Supporting analyses provided).

The BDI score and the other four variables in the API-IS model are statistically significant variables whether BDI is grouped or included as a continuous variable. The idea of the grouped BDI variable was that it related approximately to severity of depression.

The subgroup analysis for decision making only appears to change slightly with different cut-offs. When the three groups are split at 25% and 75%, the variables in Table 4 are still significant except marital status and TMT B. When the three groups are split at 35% and
|   | The authors perform a multivariate regression analysis to identify factors that are associated with decision-making preferences as measured by API DM scores. One would expect the factors with the strongest associations to be the ones related to participants being classified as 'delegators' or 'autonomists'. Therefore, I don’t understand why the authors performed an additional univariate analysis with API DM scores as categorical outcome variable to 'understand factors associated with these scores in the highest and lowest tertiles' (pg 6, lines 164-5). It is also unclear why the covariates included in the multivariate model differ from the factors reported in Table 5. Both points warrant further clarification. | Although the multivariable analysis and the subgroup analysis are clearly related, there is a specific clinical interest in finding out if the ‘delegators’ and ‘autonomists’ differ in their characteristics. It appears that they do, with some variables that appeared when considering API-DM as a continuous variable and including ‘all’ patients are no longer significant. Other variables are significantly different between the subgroups but are not related to API-DM when not grouping the patients. That, for example, employment was not significant when including all patients and considering API-DM as a continuous variable, but it is significantly different between the ‘delegators’ and autonomists’ is not necessarily unexpected and the reason for doing the analysis - it is something that separates the two groups. This means that the highest and lowest scorers differed in their employment but when considered as a continuous score and with ‘middle’ scorers included, the relationship between employment and API-DM no longer remains. The variables that differ between the two analyses are now addressed in an additional paragraph. |
|---|---|
|   | The authors should clarify how they accounted for potential centre-level clustering of the data in their analyses. | Given that individual patient level data on information-seeking and decision-making was ascertained in the context of fairly uniform practice in the UK with respect to predialysis education teams and information resources, any centre-level differences in practice are too small to adequately explain reasons for the outcomes in question. |
|   | To better understand to what extent the study population was a selected sample, the authors should provide information on the eligibility criteria for the BASIC-HHD study....potential influence of selection bias on the study’s conclusions should be in the discussion | The only statistically significant difference between those who were missing both the API decision making and API information seeking scores and those who were not missing both is in ethnicity. Non-white patients were more likely not to complete both API scores than... |
Minor Essential Revisions

7 Even though the impact of starting dialysis on decision making preferences was one of the three study objectives, none of the reported results in the abstract refer to it. The authors should consider dedicating a sentence to this part of the findings.

This has been added to the results section of the abstract.

8 The sentence in the abstract stating that 'By understanding factors............to individual patient's preferences' (pg.2, lines 41-3) is not warranted by the results, and should be removed or reformulated into a weaker statement.

This has been modified.

9 References 2-5 in the Introduction are all at least 25 years old. Please replace them with more recent studies to support the statement on the effect of increased patient involvement in decision making.

More up-to-date references have been provided.

10 The study by Flynn et al. also investigated patients' preferences for receiving information and for being involved in treatment decisions, and came to very similar conclusions as Jayanti et al. I would expect the authors to refer to the work by Flynn and how the present study relates to it.

A reference to this work has been made in the discussion segment of the article.

11 Please state in the Methods on (1) which analyses have been adjusted for multiple

(1) The statistical analyses section has been updated to include the adjustments made for
testing and how (pg. 6, line 157), (2) the analysis used to calculate the Cronbach’s alpha values (pg. 6, line 163), and (3) the cut-off value used to dichotomise API IS scores as outcome variable.

multiple testing.
(2) Cronbach’s alpha is a measure that is calculated using most statistical software such as SPSS and Stata. It is based on a formula using the average variance, the covariances between the items and the number of items. We feel that it does not require further explanation.
(3) We have now considered the API-IS as a continuous variable.

In the Results (pg. 7, lines 176-177) the authors state that the ‘group comparisons are important to adjust later analyses for potential confounders’. However, it is unclear how the findings in Table 1 have informed further analyses. This needs clarifying.

The differences between the groups were illustrated in Table 1. Due to clinical importance and due to the fact there were differences between the groups, it was automatically included as a variable in both the API-DM and API-IS analyses. The group variable being included should therefore represent the confounding between the groups i.e. difference between the groups will be due to the differences in the characteristics of the group.

As an overall comment, I would recommend the authors to revisit their tables and figures, and present only those that are essential to answering their research questions. Those that are not should either be removed or be included in a supplement. For example: (1) Why present the results in Table 1 per study group? (See also previous point); (2) Why report item-level results for all participants in Table 2? If the authors consider this information essential, they should include the item descriptions; (3) Why does Table 3 only contain results from the univariate analyses for decision making, and not for information seeking?; (4) Figure 2 could be replaced by one sentence in the results stating that IS and DM scores were significantly different for all study groups.

(1) Table 1 represents the differences between the groups in a variety of variables, necessitating its inclusion as a variable (as a group) in the analyses later in the paper.
(2) Table 2 has been removed.
(3) DM analysis is the most important aspect of the study. API-IS is the secondary result of the study so is fairly important and we have included it as a supplement.
(4) Is probably true but it has only been retained as it captures all relevant information in one figure.

The footnotes in Table 5 are missing. Also, the ways the results are presented in the p-value column are confusing.

The footnotes have been added and the digits in the p-value column have been deleted and replaced with the classes being studied under specific subgroups.

Figure 3 is difficult to interpret without an

The vignettes have been expanded to specify
<table>
<thead>
<tr>
<th></th>
<th>explanation of the scores on the x-axis in the figure caption.</th>
<th>the details in the figure.</th>
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<tbody>
<tr>
<td>16</td>
<td>It is unclear what the dots in Figure 4 represent. For example, the Delegators group consists of 57 participants, but there are only 31 Delegator dots displayed in the figure. This should be clarified.</td>
<td>The figure has been updated to display the number of patients each dot represents.</td>
</tr>
</tbody>
</table>

**Discretionary Revisions**

<table>
<thead>
<tr>
<th></th>
<th>The Introduction is rather long and could benefit from more focus. The authors could consider shortening it by 25-30%, while making sure that readers are guided more straightforwardly towards the study objectives.</th>
<th>This has been attempted and introduction now has key information on the background to the study.</th>
</tr>
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<tbody>
<tr>
<td>17</td>
<td>The statement in the Introduction on pg 4, lines 81-82 (&quot;The dominating concerns ... context of ESRD&quot;) requires a supporting reference.</td>
<td>In editing the introduction this statement has been deleted.</td>
</tr>
<tr>
<td>18</td>
<td>Figure 4 is difficult to understand when using a hard-copy printed in black-and-white. It would help if different groups would be represented with different symbols</td>
<td>Figure 4 has been updated to make it easier to read if printed in black and white.</td>
</tr>
<tr>
<td>19</td>
<td>I suggest the 'Study limitations' section in the Discussion (pg. 13, lines 357-65) to be placed before the Conclusion section.</td>
<td>This has been done.</td>
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</table>