Author’s response to reviews

Title: Project HELP: A study protocol to pilot test a shared-decision making tool about treatment options for patients with Hepatitis C and Chronic Kidney Disease

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Reviewer 1

Comment: This is a very well written and very interesting article. I have a few suggestions as detailed below: L132 reads "time on dialysis, and ta" and I think it should say "a" rather than "ta"
L143 could "labeling in end organ disease" be further explained? As I'm not a specialist in this field the meaning of this comment was unclear.

Response: Thank you for your comments. We have corrected the error on L132. We apologize about the wording made in L143; we edited this statement to make it clearer as requested.

Comment: It sounds like the tool has been developed iteratively using a range of experts and the literature base and this process would benefit from further description - has this development
work been presented or published elsewhere? If so a reference would be useful. If not, it may be useful to describe this process in more detail...It also sounds like a larger programme of work is being undertaken (eg the qualitative interviews) and this paper would benefit from more clarity regarding the overall project - maybe a figure to show how this piece of work fits into the larger project??

Response: We created a diagram to clarify the overall project goals and have specified that Aim 2’s protocol is being described in this paper. We have also added more details to describe the tool development process.

Comment: Outcome measures: An excellent range of outcome measures are described - do the authors have any insight into the effect sizes likely to be produced? Obviously this will be useful to inform a power calculation in later testing, but it would also be useful to consider what effect sizes other tools/interventions have produced with these outcome measures; as well as, what is a clinically important difference to both the patient and the professional as well as the benefits compared to the cost of administering the tool...

Response: As this is a pilot study, we do not know the effect sizes likely to be produced. However, based on past work in other contexts, we anticipate effect sizes to be small to medium and have estimated effect sizes of approximately 0.3-0.4 in our sample size calculations. After the study, we will conduct post-hoc power calculations to plan for larger studies. We will also conduct interviews with users to learn more about clinically meaningful changes in outcomes. We have added this information to the protocol paper.

Reviewer 2

Comment: Politi et al. present a comprehensive overview of the design and methods of their study, aimed at producing an effective decision aid for patients with CKD and HCV. The authors provide a extensive background of the development of HCV therapies and its relevance to CKD patients. They effectively highlight the important decisions which face clinicians and patients in selecting the most appropriate treatment options. Furthermore, the authors justify the need for improving patient involvement in the treatment process and highlight how a decision aid may be effective at providing the means for this.
This study will help to develop a tool which could help educate and empower HCV + CKD patients, potentially having a significant impact on the wellbeing of these patients. However, I believe in its current form the manuscript does raise some minor questions and comments, which are listed below:

Introduction
* Line 119 has a full stop in the middle of the sentence instead of a comma.
* Lines 127-130, are there any references to support these points which the authors can include?
* There is a spelling mistake at the end of line 132 'ta'.

Response: Thank you for your comments on the paper. We have corrected the errors on Lines 119 and 132. We also cited references to support the points in Lines 127-130.

Comment: Methods
* The authors state on line 199 that patients will be stratified into CKD stage. Will each strata have a target for recruitment or will this just be a covariate in analysis? If a covariate then perhaps this is best stated in the data analysis plan.

Response: We will include this as a covariate in the analysis and have added this to the data analysis plan. We have removed reference to stratifying by CKD stage and instead mention that we will explore differences by CKD stage by including CKD stage as a covariate in our analyses.

Comment: Data analysis plan
* On line 241 the authors state that up to five independent covariates will be included in a multivariable regression but then only list three covariates. Could you please list which other covariates you plan to include in your model, or amend the wording.
Response: We have added CKD stage and prior history of HCV treatment as additional covariates we will consider for our analyses.

Comment: I would also question whether the sample size is large enough to guarantee an unbiased estimate of regression coefficients whilst controlling for this number of covariates; is there a reference which could be included to suggest this analysis would be valid?

Response: We have added this to the limitations section. Given that this is a pilot study, we will not know for sure whether our sample size is large enough to detect differences, but we selected our study design (pre-post within subjects study design) and targeted sample size based on past studies demonstrating a small to medium effect size for most outcomes. We have added this to the limitations section of the manuscript. Future studies will explore these outcomes using a larger sample and a randomized between subjects design, with actual effect sizes from this study used to guide sample size calculations.

Comment: Discussion

In the discussion the authors mention about qualitative interviews. Can they clarify if this is part of this study or planned future work? If part of future plans, perhaps including a separate subsection for these would help to improve clarity to readers.

Response: We have added a diagram to demonstrate our planned future work and clarify this in the discussion.

Comment: General

Is this study registered on a public database (i.e. ISRCTN or clinicaltrials.gov); if so it may be useful to include the registration number.
Response: We did not register this study as it is not a randomized trial, but will register any future randomized trials.