

Responses to the Reviewers

Please find below point-by-point responses to each of the reviewers' and the editor's comments.

REVIEWER 1

- 1) The major limitation of the study was the unusual design of the so called "prospective case-control study". If the authors aim to assess the differences of two type of intervention on the outcomes, they just conduct the randomized study in all participants with 1:1 ratio and define the outcome assessment accordingly. Using age, sex and gender-matched to avoid potential confounders before two interventions are not enough, that means this study is prone to have selection biases to evenly distribute the potential factors affecting the knowledge of HCV, such as educational or socioeconomic status, history of HCV infection, vintage of drug uses etc...

RESPONSE: We thank the reviewer for his/her comments and the opportunity to respond. Our participant sample consists of substance users who were recruited from two separate substance use treatment programs. As we and others have identified, the substance use treatment program can be considered a "community" or a social system that includes a "peer pipeline", an informal communication system among clients in the treatment program that disseminates information. Unfortunately, although we agree with the reviewer reference potential bias, the informal communication system creates extreme difficulty in conducting a randomized study in substance use treatment programs particularly for studies with limited budgets. To clarify these points, we took the following steps:

- 1) We incorporated the baseline score as a covariate in our models to obtain unbiased parameter estimation (see [1]).
- 2) Our inability to conduct a randomized trial in this population is explained in the Discussion (Page 14, paragraph 2 counting from the top of the page).

- 3) We listed study limitations in our Discussion section, please see page 16, paragraph 2 counting from the top of the page.
- 2) It was still not clear about the sample size estimation in both groups. The authors stated a 60% differences in outcomes estimation. However, I was confused about the 60% differences (continuous variable or categorical variable improvement?). Did it mean score improvement differences or reach a specific cut-off improvement?

RESPONSE: We thank the reviewer for giving us the opportunity to provide further clarification on the sample size calculation.

Since the design is a case-control 1:1 design and the participants are matched pairs, we use formulas that are appropriate for calculating sample sizes for paired groups [2]. Formula (7.1) on page 70 of the book [2] shows that 60% corresponds to $\pi_{\text{discordant}}$, i.e. $\pi_{\text{discordant}} = 60\%$, which is interpreted as indicating “patients in a matched pair will respond similarly to the different interventions in 40% of the matched pairs”. That is, 60% of the matched pairs will have a discordant response. This translates into an effect size of 0.3 (of the difference in the improvement between the scores) with the level of significance set to 0.05 and power of 80%.

- 2a) Furthermore, it was not clear about the time point comparison for the outcomes (pre- vs. immediate post- or vs. 1-month post). Please clarify it.

RESPONSE: We thank the reviewer for the opportunity to discuss these points. In Methods (page 9, under “Recruitment” starting 4 lines from the bottom of the page), we have added the terms “post-test assessment” and “1-month post-test assessment” to clarify the timepoints when each of these assessments were obtained. We also would like to add that the linear mixed model that we use in our analysis incorporates time as one of the covariates.

- 3) If two groups of participants are well balanced, there is no need to use model adjustment, showing the parameter changes to confirm the authors’ assumption would be fine. To sum up, randomized controlled study would be the suitable design for such study.

RESPONSE: We again thank the reviewer for the opportunity to clarify this point. As mentioned in Reviewer #1, response 1, and in the discussion (Page 14, paragraph 2 from the top of the page; Page 16, paragraph 1 from the top of the page), a randomized design would have been infeasible in the situation of limited resources, as it was this case. In fact, a randomized design possibility to use in this case is the stepped wedge design, and it is well known that it is difficult to implement this design.

REVIEWER 2

- 1) It has been previously reported that alcohol intake may contribute to the worse prognosis of HCV-patients and this should be recalled as previously described and reported (Natural course of chronic HCV and HBV infection and role of alcohol in the general population: the Dionysos Study. *Am J Gastroenterol.* 2008 Sep;103(9):2248-53). 1Another clinically relevant topic to recall is the impact of a proper HCV management to avoid hepatocellular carcinoma occurrence and recurrence as previously demonstrated in a recent meta-analysis (A meta-analysis of single HCV-untreated arm of studies evaluating outcomes after curative treatments of HCV-related hepatocellular carcinoma. *Liver Int.* 2017 Aug;37(8):1157-1166).

RESPONSE: We thank the reviewer for identifying these important points and encouraging us to include these important references. We have added a paragraph to the discussion (pages 15 bottom of the page to Page 16 top of the page with paragraph starting “Increasing PWOUD pursuit of...”) that discusses these points and references the identified important articles.

REVIEWER 3

1. The authors should indicate P values in each Figure and Table. 2.

RESPONSE: We thank that reviewer for pointing out this issue and allowing us the opportunity to clarify the comprehension of the manuscript. In the revised version, we have added P values to Figure 2 as requested. Figure 1 aims to illustrate graphically the distribution of improvement in scores calculated as

the pre-intervention subtracted from the post-intervention scores for both interventions. The pink colored graph refers to the “brochure” while the blue colored graph refers to the “video”. Since this is an exploratory tool to visually depict the distribution of the aforementioned differences, no p-values are attached to Figure 1.

In the revised version of the manuscript, we have included a revised version of Figure 2 that contains p-values illustrating the change in scores comparing the immediate post-intervention to the pre-intervention values and the one month follow up to the immediate post-intervention values. We have also deleted omitted Figure 2B and Table 2 from the original submission since these were largely duplicative of information already contained in Figure 2.

2. In the future, it is important to evaluate whether the differences in educational modalities will lead to behavior changes, such as frequency to screen HCV infection, visit clinics, and receive DAA treatment. The authors should add the related comments.

RESPONSE: We thank the reviewer for this comment as motivation to change behavior is the next step to assess the value of different educational modalities. We have added the following sentence to the Discussion (page 15, last sentence of paragraph 2 from the top of the page) to capture this point.

“Future investigation should evaluate whether different educational modalities will lead to PWOUD pursuit of HCV management.”

SCIENCE EDITOR

In present study, the effect of HCV education by storytelling narratives with video was compared with that by printed format one among PWOUD. Consequently, video assist storytelling narratives showed a great educational impact. This study was interesting and valuable. Authors should address and discuss some limitations pointed by reviewers.

RESPONSE: We thank the Science Editor’s comments on the manuscript’s value. In the revised version of the manuscript, we have attempted to address each of the comments raised by the reviewers.

COMPANY EDITOR-IN-CHIEF:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

RESPONSE: We thank the Editor for the provisional acceptance of the manuscript. As requested, we have attempted to revise the manuscript according to the comments provided by the reviewers and the editor as well as according to the journal's criteria.

Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

RESPONSE: In the revised version, we have prepared the figures using uniform presentation.

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

RESPONSE: In the revised version, we have prepared the figures using Adobe Acrobat with the ability to modify line drawings. Unfortunately, PowerPoint does not support the images depicted.

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RESPONSE: As all figures included in the revised version are originally produced by the authors, we have placed the copyright information in the bottom right-hand side of the image as requested.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

RESPONSE: In the revised version, we have reformatted the tables as requested.

Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

RESPONSE: As requested, we have uploaded the approval documents for the three awards that sponsored this work.

References

1. Senn, S., *Change from baseline and analysis of covariance revisited*. Stat Med, 2006. **25**(24): p. 4334-44.
2. Machin, D., et al., *Sample size tables for Clinical Studies*. Third edition ed. 2008, Chichester, West Sussex, UK: Wiley-Blackwell.