Author’s response to reviews

Title: Alternative or complementary attitudes toward alternative and complementary medicines

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Author’s response to reviews:

Dear edits, dear reviewers,

We would like first to thank the two reviewers of our paper for their constructive and thoughtful comments and for the time they have invested in order to help us improve the quality of our manuscript.

Trine Stub, Ph.D. (Reviewer 1):

This study aims to examine distinct patterns of attitudes towards ICHA in people virtually facing chronic illnesses. This was investigated in a web-based study of 1,807 participants.

This is a well-written manuscript. The background is good. The results are presented in a trustworthy manner and the statistical analysis are solid.
Reply: We thank Reviewer 1 for this positive and encouraging comment.

I have however, some methodological concerns regarding the design and will in the following addresses some of these concerns:
Method:
1. This is a web based study and in order to participate you must be familiar and have access to the internet. This implies that people with no internet access did not get the opportunity to participate. It is also reason to believe that the participants is positive to research in general and to the topic of this study in particular. This self-selection is a threat to the validity of the study because the reason for self-referral may be associated with the outcome of the study. In that respect selection bias may have occurred. Please address these methodological issues in the limitation section in the discussion.

Reply 1-1: We agree with this remark that we already addressed in the methods section on p.4. We have now nuanced some sentences of this section:

“(…) Moreover, all eligible members of the pool were invited to the study at hand. Thus, the risk of self-selection bias on the level of this individual study was notably reduced as this study is based on a census rather than a sample of the participant pool.”

We have also added the following comment on the limitation section on p.13:
“As for all web-based research, our sample was confined to people having access to the internet and included participants who were open to this kind of research. But since most people have internet access, potential biases might be higher in a clinical population in view of the large treatment gap in that most people with psychological disorders choose to remain untreated.”

2. I find it problematic that healthy people shall pretend that they are seriously ill, and answer questions based on limited information presented to them. I do not think people can fully understand/imagining the burden of having these diseases. Schizophrenia, MS and major depression may affect cognitive ability and reasoning, making it difficult to know how these groups of patients would have answered the questions. A mix method design, including individual interviews with some of these patients would have improved the validity of this study. Please elaborate on this in the discussion.

Reply 1-2: We agree with this point that we already mentioned in the limitation section. We have thus further emphasized this point in the limitation section on p.13:

“Therapeutic preference might in fact differ between virtual and real-life situations as it might have been difficult for participants to fully understand/imagining the burden of having these diseases. A mixed method design including both web based questionnaires and interviews with patients having these illnesses may have added to the validity of our study. (…) Our results must therefore be interpreted with some caution.”

3. Please include a reference for the Helsinki Declaration

Reply 1-3: Thanks. The reference has been added on p.4

Result:
4. The response rate is low (16%), which is a challenge to the validity of the findings. The non-responders may differ in significant ways from those who responded, and is also a threat to the generalizability of the findings. Please address this in limitations/discussion.

Reply 1-4: We agree that the response rate was low and this was acknowledged in the original paper on p.7 by stressing this rate was “similar to previous web-based studies conducted with the same panel [15].” In fact, participants in this panel are regularly contacted to participate in web-based studies so that participants are not always available and choose against participation. The following comment has been added on p.13:
“(…) While participation was comparable (16%) to previous web-based studies conducted with the
same panel [24], it does not allow generalizability of our findings. For these reasons, our results must be interpreted with some caution.”

Conclusion:
5. Please rewrite the conclusion and include that the result must be interpreted with caution do to the virtual nature of this study.
Reply 1-5: We have altered the conclusion by including the following remark on p.14:
“Bearing in mind the limitations due to the virtual nature of this study, our results highlight the need to take attitudes toward ICHA into account for a better understanding of patients’ preferences to use ICHA.”

James Green (Reviewer 2):
This paper addresses a fascinating research question, looking at treatment preferences between ICHA and conventional approaches in chronic conditions; and then becomes even better, comparing illnesses with clear biological basis with more difficult to pin down.
Reply: We thank Reviewer 1 for this positive comment.

Despite my excitement about the question, I have some real doubts about the legitimacy/validity of having people imagine that they have chronic illness. This is particularly problematic where participants were told of symptoms but that they would not normally be aware of if they had that illness (particularly for Schizophrenia, but also to a less extent recurrent depression). This is featured as a limitation, but I think it has be more heavily underlined.
Reply 2-1: We agree with this point that was also raised by Reviewer 1 (see reply 1-2).
We already mentioned this point in the limitation section but we further emphasize it in the limitation section on p.13:

“Therapeutic preference might in fact differ between hypothetical and real-life situations as it might have been difficult for participants to fully understand/imagining the burden of having these diseases. Therefore, a mixed method design including both online questionnaires and offline interviews with patients having these illnesses may have added to the validity of our study. (…) For all these reasons, our results must be interpreted with some caution.”

Relatedly, I think it would be better to describe these as hypothetical over 'virtual' (as I think virtual too much implies some sort of computer-based simulation). I still think that there is some useful information contained in this, but perhaps in future research it might be better to have participants consider that they were looking at treatments for a family member in their care, where they would actually be aware of the externally presented symptoms.
Reply 2-2: We thank Reviewer 2 for this thoughtful suggestion and replaced virtual by hypothetical along the text.

I also have some strong reservations about the analysis of the results. The coding of treatment preference is not clearly described in section 3.2. Perhaps a worked example would make it clearer, as I can't work out how the ranking of 6 treatments maps precisely onto the four patterns of choice.
Reply 2-3: We thank Reviewer 2 for noticing this lack of precision in our coding. We have now added examples of coding in the supplementary material S1 and reported this on p.7:

“For each clinical vignette, treatment choices were categorized into four patterns of choice (see concrete examples in Supplementary material S1):”
Related to that, I wonder if it would be better to use belief in effectiveness of each treatment as a (quasi) continuous outcome. Ranking is not without its problems, as it does not allow people to have tied preferences, or to show the size of difference between preferences, in a way that a 4-point scale could allow a participant to rank 5 treatments as fully agree, and one treatment as disagree.

Reply 2-4: We thank Reviewer 2 for pointing out this issue. In fact, the analysis of this variable was difficult as each individual had to score the belief in effectiveness for each of the 6 treatment options as well as for mental and for somatic illnesses separately (so that 12 scores were available for each individual). We decided to pool some variables in order to limit the number of predicting variables as mentioned in 3.3.1 on p.9.

We have controlled our analyses by including only the score of belief in effectiveness of pill and of complementary treatment (without mixing the first with long-acting injections and the second with spiritual treatment). Results remained unchanged.

In a more technical fashion, I was just unable to follow the results, despite having a small amount of experience running Bayesian multilevel models. What software package, what sampling did you use for your Bayesian model? (JAGS?). You refer to both multilevel models and multinomial logistic regression models. Were these the same model, with a multinomial outcome in a multilevel model? Was there a covariance structure? You chose a normal distribution over the Student t distribution for your priors. Some of this information is perhaps beyond only the most interested reader, but I think should be recorded somewhere, even if it is just in supplementary materials.

Reply 2-5: We thank Reviewer 2 for making us aware of this missing information. Information about the software and R package have been added on p.7:

“Statistical analyses were performed using Bayesian methods (JAGS [25] for R software [26]).”

In all analyses we used multilevel models “using choice pattern as Level 1 and subject as Level 2.” as stated on p7.

As the dependent variable (treatment preference) consisted in 4 categories, we had to define one category as the reference category (weak complementary in our case) and to create 3 binary dummy variables. All were entered in one regression analysis which is called a multinomial logistic regression analysis.

A covariance structure was included.
A normal distribution was in fact used for the priors in the logit function of each logistic regression. For more clarity we indicate the JAGS script used in the supplementary material S2 and indicate the script's reference in the body text of the manuscript on p.8.

I am further unclear on the results for specifically naming the condition (Conditions B1-B4).

Reply 2-6: We thank Reviewer 2 for pointing this lack of clarity in our manuscript. We have reworded two sentences in the results section on p.9

“In addition, results showed that participants switched from the strong to the weak complementary option when the illness was named in the vignettes compared to the vignettes reporting the only symptoms.”

and p.10

“In combinations B1 to B4, participants still switched from the strong to the weak complementary option if the illness was named…”
Introduction lightly referenced. Both references to medical pluralism dramatically increasing are ~20 years old. There is plenty of more recent evidence of medical pluralism, and it is also very common throughout Low and Middle Income Countries. Switching between ICHA and conventional very common in many contexts; that is the preference is not stable over time. While I think the referencing of your own work was appropriate, it stands out in the context of the relative lack of other references.

Reply 2-7: We thank Reviewer 2 for pointing this. We have now added the following citations in order to improve the quality of our referencing:


More minor comments
1. Table 3 requires explanatory notes if left unchanged (and has too many decimal places, given that even with n = 2000, the margin of error/CI is still +/- 2.3%)

Reply 2-8: The following explanatory note has been added to Table 3 and decimal were reduced to one decimal on both Tables 2 and 3:

“Note: N indicate the number of participants who selected the distinct presented options/combinations of treatment. This number refers to all clinical vignettes (column All illnesses), to mental illnesses only (column Mental illnesses) or to somatic illnesses only (column Somatic illnesses).

The lower part of the table indicates the total number of participants that selected combinations of treatment including one of the existing options (either strictly conventional, weak complementary, strong complementary and alternative) at least once.”

2. Although panel members might be generally representative, they are still heavily self selected. A little more critical discussion

Reply 2-9: We agree with this limitation that we already addressed in the methods section on p.4. We
have now nuanced some sentences of this section (new text is underscored)
“(…) Moreover, all eligible members of the pool were invited to the study at hand. Thus, the risk of self-selection bias on the level of this individual study was notably reduced as this study is based on a census rather than a sample of the participant pool.”
We have also added the following comment on the limitation section on p.13:
“As for all web-based research, our sample was confined to people having access to the internet and included participants who were open to this kind of research. But since most people have internet access, potential biases might be higher in a clinical population in view of the large treatment gap in that most people with psychological disorders choose to remain untreated.”
See also reply 1-4 for other limitations related to this point.

3. No mention of translation/language in which the questionnaire was administered.
Reply 2-10: On p.4 we indicated that “Participants were recruited via WiSoPanel [20, 21], a participant pool with German-speaking members”. We added now the following sentence on p.4: “All instructions and questionnaires were in German.”

4. Section 3.1 "four conditions" should be "eight"? 4 x 225 = 900 participants only
Reply 2-11: Thanks a lot for pointing this out. The required correction has been performed.

5. Section 3.3.2 "significantly more rare" sounds like frequentist rather than Bayesian talk.
Reply 2-12: We fully agree and apologize for this mistake. We reworded “were rarer”.

6. Table 4. Rather than reporting Pr(OR>1) which requires quite a bit of work to interpret, would it be better to bold the OR column?
Reply 2-13: In contradiction to the p value in frequentist statistic, Pr(OR>1) indicates the true probability that an observed difference is above chance level. Even if our results mentioned only those associated with a Pr(OR>1) above an arbitrary level of 5%, a probability of 70% can still be relevant to appreciate the effects of our predictors. For this reason, we think that this information is reliable for the reader and should remain available.

We would like again to thank the two reviewers for their constructive comments and the edits for orchestrating the review process. We hope that both the clarity and the quality of our paper has improved thanks to their constructive comments.

Yours,

Fabrice Berna (on behalf of all authors)