Author’s response to reviews

Title: Mediation and moderation analyses: exploring the complex pathways between hope and quality of life among patients with schizophrenia

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Author’s response to reviews:

Dear Editor,

Re: “The relationship between hope and quality of life is mediated by depression and resilience and moderated by sex in patients with schizophrenia”

Many thanks for reviewing our manuscript and for inviting a revision. We are very grateful for the reviewers’ thorough reading of our manuscript and for the large number of very favourable comments. We have revised the manuscript, taking into consideration all of the reviewers’ comments (see our responses to the reviewers appended below). In our point-by-point responses to the reviewers’ comments, we stated the page numbers of the manuscript where changes have been made. All references quoted in our replies to the reviewers are listed at the end of this letter.

We greatly appreciate the opportunity to make these revisions. If our replies are not clear or if there are any further misunderstandings, please feel free to contact us.

We hope the revised version of the typescript is now suitable for publication in BMC Psychiatry.

Looking forward to hearing from you.

Best wishes,

Yu-Qiu Zhou, Professor
Technical Comments:

1. Please include the 'Declarations' heading.

2. Please rename 'Purpose' and 'Introduction' to 'Background'.

Authors’ response

We have made changes to the corresponding section as required

Editor Comments:

Please confirm whether informed consent, written or verbal, was obtained from all participants and clearly state this in your manuscript. If verbal, please state the reason and whether the ethics committee approved this procedure. If the need for consent was waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this, including the name of the IRB or a reference to the relevant legislation.

Authors’ response

Written informed consent was obtained from all the participants, and we have made corresponding statements in the “Declarations” section. In the outpatient clinic, after the patient completes the enrollment assessment, we will first briefly introduce the study to the patient. When the formal investigation is conducted, the written informed consent of the questionnaire on the front page of the survey manual requires the participant to sign.

Reviewer #1

The procedure for diagnosing the patients is not clear. It is of relevance for the validity of who did the diagnosing, how it was assessed and so on. Furthermore, ICD-10 includes several diagnostic subtypes of schizophrenia, and a specification of the current sample is recommendable.

Authors’ response

We thank Reviewer #1 for pointing out this issue. The procedure for diagnosing the patients was as follows: all the diagnoses were obtained from electronic patient records and were verified by doctor GuoHua Li, a chief physician at Chifeng Anding Hospital. We have added this information to the manuscript (page 5, line 105-114).

We strongly agree with you that the diagnostic subtypes of schizophrenia are meaningful; however, we did not realize this issue during participant recruitment. Although we attempted to
include them, we may not be able to add these data now because of many restrictions. Thus, we have included this issue in the Limitation section of the manuscript (page 13, line 281-283).

There is a general lack of detail in the description of the methodology used. This includes lack of information on how the participants were recruited. There is not sufficient information on attrition or on the recruitment procedure of participants.

Authors’ response

We thank Reviewer #1 for pointing out this issue. The recruitment procedure of participants in our study was as follows: All of the participants were outpatients of Chifeng Anding Hospital. Patient diagnoses were from their medical records and were verified by a clinical doctor (LGH); other criteria for inclusion were determined by the clinician and the investigator. Patients who met the inclusion criteria were situated in a quiet and comfortable room for the data collection after the investigator obtained written informed consent from each patient. Patients who did not meet the clinical insight and stability criteria at the time of review were recorded and followed up regularly; data collection was performed on any patients who met the criteria before the end of the survey. We have added this information in the Methods section (page 5, line 105-114).

It is not systematically stated who gathered the data on the psychometric tools, for example in the case of the Calgray Depression Scale for Schizophrenia (CDSS) it is assessed during a structured interview, but information on exactly who executed these interviews is not stated.

Author’s response

We thank the reviewer for this excellent comment and suggestion. We have added this information to the “Procedure” section in the manuscript (page 5, line 105-114). All of the data were gathered by the first author of the manuscript, who has good clinical investigation experience.

In the section of limitations, the author's state how the cross-sectional study design limits interpretation of casualty. However they do not sufficiently consider the impact on the interpretations, other than the results are assigned less strength. The conclusions made needs to be based on the present cross-sectional design, and design limitations. It is not sufficient to merely state the limitations without actually considering the interpretations in the light of these.

Authors’ response

We completely agree with the reviewer’s suggestion. Results based on a cross-sectional study design need to be interpreted with caution. We have already modified the interpretation of the conclusions to make it more rigorous (page 14, line 295-296).

The presentation of the assessment tools is inconsistent. For instance, in the reporting of the scales range.

Authors’ response
We thank the reviewer for pointing out this issue. We have checked the manuscript and found that there was an inconsistent presentation of the hope assessment scale between the Methods section (“SHS-9”), Table 1 (“SHS”), and Abbreviations (“SHS”). We have modified the presentation in the manuscript (Table 1 and Abbreviations).

The language of this paper is at times unclear, and proof reading by a native speaker is recommendable.

Authors’ response

We thank the reviewer for their suggestion. We have submitted our manuscript to American Journal Experts (AJE) for language editing.

Overall, the choice of included literature is appropriate. However, especially in the introduction/background section there are a number of statements backed up by one reference. For instance on page 1 in line 8 to 11.

Authors’ response

We are very thankful to the reviewer for pointing out this issue. We have checked the manuscript and found that there was a mistake: references 4 and 5 were about the influencing factors of QOL, and reference 6 was about “Hope” in schizophrenia. We have corrected the corresponding statements in the manuscript. (page 1 line 6-11)

In page 1 in line 16 to 17 the paper states that "limited studies have focused on the underlying mechanisms among these psychological variables in patients with schizophrenia". However the scope and actual findings are not clear.

Authors’ response

We thank the reviewer for their suggestion. What we actually wanted to express is that limited studies have been performed to explore the potential relationship between hope and quality of life. Our statement was somewhat misleading; therefore, we have changed it to read “limited studies have focused on the potential underlying mechanisms between hope and QOL in patients with schizophrenia” to make it clear (page 1, lines 15-16).

Reviewer #2

Title: I suggest changing the title to be a bit simpler. It is easy to get lost during reading.

Authors’ response
We thank the reviewer for their suggestion. We have changed the title to “The mediating role of depression and resilience in hope and quality of life in patients with schizophrenia: Exploring moderation by sex”. We think that this title may convey our intention more clearly.

Introduction:

a) It was not just the patient movement that showed that people with mental disorders can lead a good life. Apart from other factors, a number of studies pointed that out as well.

b) "Over the last decades, with advances in pharmacological treatment of acute psychiatric symptoms of schizophrenia, as a patient-based measurement, quality of life (QOL) has become an important way to assess the treatment and care in patients with schizophrenia." - How these relate to one another? QoL is an important concept in schizophrenia because of various reasons - it’s often unfavorable prognosis, the risk of chronicity, or the significant disability that schizophrenia usually brings. Also, the QoL research mostly relates to the WHO definition of health. This is why you should either broaden the connection between schizophrenia treatment and QoL or at least explain more the one presented connection.

c) The part about hope is very clear and concise.

d) Depression has many causes and triggers. It is not balanced to mention just antipsychotics and the here hypothesized core of schizophrenia.

e) The part about resilience needs to be approached more in-depth. How does resilience help patients? Why is it important for them? I suggest putting things into perspective.

f) Schizophrenia is not a disease. It is a disorder or (arguably) an illness.

g) Hypotheses - It should be explained why depression and resilience are mediators and not independent variables. A person can be depressed first and through their (secondary) hopelessness experience lower QoL. The same goes for resilience. What is the basis for these causal assumptions? This one-sided approach is a major limitation of the study.

Authors’ response

We thank the reviewer for their suggestion.

a) The statement in our manuscript was insufficient; we have modified it according to the reviewer’s suggestion (page 1, line 2-3) and have added the related references (reference list 2 and 3).

b) What we actually wanted to express is that the previous treatment goals of schizophrenia were mainly to control positive symptoms and to reduce suicide and self-injury. With the control of positive symptoms by antipsychotic drugs, we are now paying more attention
to the rehabilitation of patients' social functions and the improvement of individual quality of life.

Our statement may not have been clear and may have caused some misunderstanding.

Just as the reviewer said, schizophrenia is a chronic mental illness, and quality of life is an important clinical outcome evaluation index because of its close relationship with functional outcomes and disability. We have changed our statement in the manuscript to read “QOL is a critical clinical outcome, closely related to patient function and disability, and is often a direct evaluation indicator of personal recovery outcomes among patients with schizophrenia.” (page 1, line 3-5)

c) We thank the reviewer for their positive comment.

d) We have changed the corresponding statement according to your suggestion to make it clearer: “Depression, can be caused by multiple factors, such as antipsychotics or their side effects and potentially the core symptom of schizophrenia, is very common after the recovery of clinical insight, with a post-schizophrenic depression rate of 27%”. (page 1, line 17-19)

e) As we reviewed, there are two views about resilience in patients with schizophrenia: some people view “resilience” as a positive personality characteristic that can enhance individual adaption, and others view “resilience” as the capacity of a dynamic system to withstand or recover from significant challenges that threaten its stability, viability, or development, which may help the individual cope with and gain insight into their illness.

Regarding the importance of “resilience” for schizophrenia, resilience is believed to contribute many clinical functions, such as real-life functioning, quality of life, disability and others. Thus, resilience, as a dynamic structure to maintain the balance of the individual's state, should always be treated as an important target for intervention or the core of intervention programs, which are critical to the recovery of patients. We have added related information to the manuscript (page 2, line 33-40).

References:

(1) Quality of life in stabilized patients with schizophrenia is mainly associated with resilience and self-esteem. DOI: 10.1111/acps.12628

(2) The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. DOI: 10.1002/wps.20167

f) We have changed the corresponding wording in the manuscript (page 3, line 50 ).
g) We completely agree with the reviewer’s comment. As we mentioned in the Limitations section, the cross-section study design was a significant limitation for exploring the causal relationship.

The model was built based on the literature review: Hope has been an active factor in helping people survive and improve their well-being and mental health since it was first identified conceptually. In patients with schizophrenia, hope is a central component of recovery processes, frequently perceived as their starting point or catalyst and affecting a patient’s adaptation to their chronic disease and their participation in effective treatment [1,2]. Studies have shown that having a feeling of hope is of great importance in terms of participating in treatment, which has significant impacts on increasing compliance with medication, subjective well-being, and patient’s self-confidence [3,4]. According to Snyder’s theory, the basic level of hope remains relatively stable over time, which makes it resemble a personality trait [5,6]. Thus, we chose the variable of “hope” as the independent variable.

Studies have shown that hope is a significant predictor of depression and resilience, and an intervention focused on improving the level of hope will also improve the illness process and clinical outcome, such as depression and resilience [4, 7]. It was upon this basis that we constructed our model.

References:


(6) Stability and mutual prospective relationships of stereotyped beliefs about mental illness, hope and depressive symptoms among people with schizophrenia spectrum disorders. https://doi.org/10.1016/j.psychres.2018.08.010
Sample: The sample size is remarkably large for this kind of study. It is great that you thought of potential cognitive deficits in your inclusion criteria. Furthermore, why did you prefer this definition of clinical (in)stability? 50% increase in the last 3 months is a lot. It is not a usual definition of stability. Here are some examples of clinical stability that one can come across:


Authors’ response

We completely agree that there are several criteria for clinical stability in different studies, such as the absence of an acute psychotic relapse or no psychiatric hospitalization, as emphasized by the reviewer. Each criterion was based on a different perspective.

We included this criterion mainly because of two considerations: (1) this criterion was easy to evaluate, and we can see a patient's drug use in the past few months directly from their electronic medical record; (2) Based on our review, the studies about quality of life in patients with schizophrenia mostly chose these criteria, which is beneficial to the comparison between the results of the study. (DOI:10.1111/ppc.12278; DOI:10.1016/j.psychres.2018.09.062).

Compared with the clinical stability standards recommended by the reviewer, the criteria adopted in our study do not seem to be comprehensive enough, but we believe that the criteria still largely capture the essential problem of clinical stability. As the reviewer said, this criterion is not a usual definition of stability. Nevertheless, we also believe that more comprehensive and uniform criteria about clinical stability should be adopted in future research to increase the comparability between studies.

Tools: I appreciate using measures created for the studied population and the calculated alphas.

To my statistical knowledge, the analyses were appropriately planned. I also value the provided explanation of mediation and moderation.

Results are concisely described.

Authors’ response

We thank the reviewer for the positive comments about our work.
a) "In female patients with a high level of hope, the intervention for improving QOL should focus on repairing resilience and relieving depression; however, in male patients and female patients with a low level of hope, enhancing the hope of patients should be considered before another intervention is conducted." - Unfortunately, this cannot be said. First, depressed individuals generally tend to not be hopeful. When a person is depressed, it is depression, that is being treated, not hope. Hope usually catches up as depression recedes. Second, individuals completed a scale measuring severity of depressive symptoms. It is not clear how many of them were really depressed. There may not be much to relieve them from, then. Third, it is a question how much one can repair resilience in hopeful individuals (these two phenomena correlate with each other) and how much it can be simply reinforced.

b) The explanations between men and women should be re-thought a bit. If most men supposedly have more social needs and women are more fearful, it does not make much sense writing that Chinese women tend to have poor social support systems. So, the women tend to be socially deprived, but it is the men who have bigger social needs? This does not make much sense. Also, if women are more fearful why should they rely more on hope than men who supposedly have more social needs? Hope (in Snyder’s theory that is cited in the text) focuses on having goals in life and finding ways and motivation to reach them. Why then should be hope more important for the need of safety and less for the social needs? The results are currently not well interpreted.

c) Limitations should include the one-sided causality that was evaluated (see my comment above).

This is especially significant in this case where the chosen causality was not sufficiently argued in the introduction.

Authors’ response

We thank the reviewer for their critical comments and suggestions.

a) The data may have been over-interpreted to some degree. We deleted the sentence from the corresponding section of the manuscript. Essentially, what we want to express is that an improved understanding of factors that hinder quality of life is vital for treatments to translate into more positive outcomes. Findings from the present study provide a valuable contribution in this direction; in particular, the observed complex associations among investigated predictors, mediators and moderators strongly suggest that integrated and personalized programs should be provided as standard treatment to people with schizophrenia.

b) We thank the reviewer for their thorough reading and valuable suggestion about the Discussion section. We rethought the interpretation about the moderating role of sex on hope and QOL, and, just as the reviewer pointed out, some points were adequately rationalized. We have modified the corresponding parts of the Discussion based on three perspectives: (1) the different effects of hope on QOL may be based on the differences in
personality traits and cognition between male and female schizophrenia patients; (2) a similar relationship between sex and hope was also found in the general population; and (3) our findings support the idea that integrated and personalized intervention should be designed for patients with schizophrenia (page 12, line 248-259).

c) We constructed a one-sided causality model between variables based on the theory and a literature review. This model places some limitations on the interpretation of our results. We have added corresponding text to this effect in the Limitations section. In future research, we will also consider time-varying variables to further explore the causal pathways between these variables. (page 13, line 284-285)

English needs polishing.

Authors’ response

We thank the reviewer for their suggestion. We have submitted our manuscript to American Journal Experts (AJE) for language editing.