Reponse letter

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The study aims to evaluate the clinical efficacy of Wuling capsule combined with sertraline in treating adolescents with anxiety, depression, and insomnia, while also assessing the adverse reactions associated with the treatment. The study design is a comparative, prospective study involving 95 adolescent patients who were divided into two groups: the control group (50 patients) and the observational group (45 patients). After a period of dropout, 40 patients remained in each group. The control group received sertraline combined with a placebo, while the observational group received sertraline combined with Wuling capsule. Both groups were treated for 8 weeks. Outcome measures included the ISI, HAMA, and HAMD scales for clinical symptoms and the TESS scale for adverse reactions. In conclusion, the study provides promising evidence that the combination of Wuling capsule with sertraline is more effective in reducing symptoms of anxiety, depression, and insomnia in adolescents compared to sertraline alone.

Reply: Thank you very much for your recognition and encouragement of our team's research results.

Minor Comments: 1. The background of the abstract section is missing. Please provide information for this background section.

Reply:Thanks for your kindly reminder. Modified as required.

2. In the methods section, please provide the information about how was the sample size determined? Is the sample size of 40 cases each group enough for this study?

Reply:Thanks for your kindly reminder. It has been added that "based on the sample size calculation formula n = (U α +U β)22P(1-P)/(P1-P0)2 and 5% loss of follow up rate for the optimal efficacy clinical trial, at least 39 samples should be included in each of the two groups in this study."

3. Please indicate whether informed consent has been obtained from the patient.

Reply:Thanks for your kindly reminder. As indicated in "(6) Patients and guardians were informed of this study and participated voluntarily."

4. Are the patients in the observation group and control group randomized? Please provide a detailed description of the grouping method.

Reply:Thanks for your kindly reminder. Added as requested.

5. Please add Figure legend for each Figure, and provide a more detailed description.

Reply:Thanks for your kindly reminder. Figure 1-2 is the same as Table 1-2. Figure 1-2 has been deleted to avoid duplication.

6. In the method, the authors mentioned that ISI and HAMD scores were used as the basis to judge the treatment effect. While in the results section, the author first compared the efficacy of the two groups and then presented the results of other evaluations, which is a bit inappropriate. It is suggested to reverse the order.

Reply:Thanks for your kindly reminder. Modified as required.

7. The description in the result section is too simple, I would suggest to adding a conclusive description at the end of each paragraph.

Reply:Thanks for your kindly reminder. Added as requested.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The study addresses a clear and relevant question regarding the efficacy and safety of combining Wuling capsule with sertraline in a specific patient population. Employing ISI, HAMA, and HAMD scales provides a comprehensive evaluation of the clinical symptoms. The use of the TESS scale to assess adverse reactions is also a strength, ensuring a thorough evaluation of the treatment's safety profile. The observational group showed significantly lower scores in HAMD, HAMA, and ISI compared to the control group at all assessment time points (2, 4, 6, and 8 weeks), indicating greater clinical efficacy with the addition of Wuling capsule. In addition, The TESS score, which measures adverse reactions, was significantly lower in the observational group compared to the control group ($t = 18.239$, $P < 0.001$), suggesting that the addition of Wuling capsule may be associated with fewer adverse effects. This is a strong paper and the results presented are novel and important. It is intriguing that they have identified that Wuling capsule can further alleviate the insomnia symptoms of adolescents with anxiety and depression. Additionally, the combined treatment appears to be associated with fewer adverse reactions. Overall, this is a potentially significant paper, and the findings support further research into this combined therapeutic approach for adolescent patients.

Reply: Thank you very much for your recognition and encouragement of our team's research results.

However there are some concerns that warrant further consideration: --While the initial sample size was reasonable, the dropout rate resulted in 40 patients per group, which may affect the generalizability of the results. The reasons for dropout are not specified, which could introduce bias.

Reply:Thanks for your kindly reminder. In this study, 80 patients were selected strictly according to inclusion criteria and exclusion criteria, and were divided into control group and observation group according to random number table method, with 40 cases each. No patients dropped out during the study.

--The study evaluates outcomes over 8 weeks, which may not be sufficient to determine the long-term efficacy and safety of the combined treatment. Longer follow-up would provide more comprehensive data.

Reply:Thanks for your kindly reminder. This study was only conducted for 8 weeks of follow-up, and no longer follow-up was conducted, so relevant data cannot be provided. It will be supplemented and further explored in the follow-up study.

--The study does not provide specific information on the composition or mechanism of action of the Wuling capsule, which is essential for understanding its potential benefits and interactions with sertraline.

Reply:Thanks for your kindly reminder. The composition and related functions of Wuling capsule have been stated in the third paragraph of the discussion section. Marked yellow.

Editorial Office's comments. Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are provided below:

(1) Science Editor:

1 Scientific quality: The authors submitted a study of efficacy of Wuling capsule combined with sertraline in the therapy of anxiety and depression with insomnia in adolescents. The topic is within the scope of the journal.

(1) **Classification:** Grade B and Grade C.

(2) **Summary of the Peer-Review Report:** Reviewer 1 point out that --While the initial sample size was reasonable, the dropout rate resulted in 40 patients per group, which may affect the generalizability of the results. The reasons for dropout are not specified, which could introduce bias.

Reply:Thanks for your kindly reminder. In this study, 80 patients were selected strictly according to inclusion criteria and exclusion criteria, and were divided into control group and observation group according to random number table method, with 40 cases each. No patients dropped out during the study.

--The study evaluates outcomes over 8 weeks, which may not be sufficient to determine the long-term efficacy and safety of the combined treatment. Longer follow-up would provide more comprehensive data.

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--The study does not provide specific information on the composition or mechanism of action of the Wuling capsule, which is essential for understanding its potential benefits and interactions with sertraline.

Reply:Thanks for your kindly reminder. The composition and related functions of Wuling capsule have been stated in the third paragraph of the discussion section. Marked yellow.

Reviewer 2 point out that 1. The background of the abstract section is missing. Please provide information for this background section.

Reply:Thanks for your kindly reminder. Modified as required.

2. In the methods section, please provide the information about how was the sample size determined? Is the sample size of 40 cases each group enough for this study?

Reply:Thanks for your kindly reminder. It has been added that "based on the sample size calculation formula n = (U α +U β)22P(1-P)/(P1-P0)2 and 5% loss of follow up rate for the optimal efficacy clinical trial, at least 39 samples should be included in each of the two groups in this study."

3. Please indicate whether informed consent has been obtained from the patient.

Reply:Thanks for your kindly reminder. As indicated in "(6) Patients and guardians were informed of this study and participated voluntarily."

4. Are the patients in the observation group and control group randomized? Please provide a detailed description of the grouping method.

Reply:Thanks for your kindly reminder. Added as requested.

5. Please add Figure legend for each Figure, and provide a more detailed description.

Reply:Thanks for your kindly reminder. Figure 1-2 is the same as Table 1-2. Figure 1-2 has been deleted to avoid duplication.

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Reply:Thanks for your kindly reminder. Modified as required.

7. The description in the result section is too simple, I would suggest to adding a conclusive description at the end of each paragraph. The questions raised by the reviewers should be answered.

Reply:Thanks for your kindly reminder. Added as requested.

(3) **References recommendations:** The reviewer didn't request the authors to cite improper references published by him/herself.

(4) **Manuscript Type:** After verification, the manuscript type is "Retrospective Study".

Reply:Thanks for your kindly reminder.

2 Specific comments

(1) **Country/Territory of origin:** Please verify if the "**Country/Territory of origin:** China" submitted by the system is correct?

Reply:Thanks for your kindly reminder. "Country of origin: China" is correct.

(2) The language classification is Grade B. Please visit the following website for the professional English language editing companies that we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

Reply:Thanks for your kindly reminder.

(3) Running title: A short running title of no more than 6 words should be provided. It should state the topic of the paper.

Reply:Thanks for your kindly reminder. Running title: "Wuling Capsules and Depressed Adolescents"

(4) **Author list.** Author names (unabbreviated) should be given as **first name, middle name initial (with no period)** and **family (sur)name**, and typed in bold with the first letter of each capitalized. For example: Yi-Fan Chang, Jia-Jing Li, Tao Liu, Chong-Qing Wei, Li-Wei Ma, Vladimir N Nikolenko, Wei-Long Chang.

Reply:Thanks for your kindly reminder.

(5) **Authors and institution(s):** Author names should be written out first (as **first name, middle name initial (with no period)** and **family (sur)name**; with a hyphen included between the syllables of Chinese names) and typed in bold, followed by a comma and the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold. Examples for authors name and institutions are:

Yi-Fan Chang, Tao Liu, Chong-Qing Wei, Wei-Long Chang, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, China

Reply:Thanks for your kindly reminder.

(6) **Author contributions:** The 'Author contributions' passage describes the specific contribution(s) made by each author. The author's names will be listed in the following format: full family (sur)name, followed by abbreviated first and middle names. For example, Bryan L Copple should be revised as Copple BL.

Reply:Thanks for your kindly reminder.

(7) **Core Tip.** The Core Tip is a short paragraph that is independent of the content of the Abstract. The 'Core Tip' will provide a succinct summary of the study that outlines its most innovative and important arguments. This section should be less than 100 words. Abbreviations must be defined upon first appearance in the Core Tip. Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition.

Reply:Thanks for your kindly reminder. Core tips have been added as requested.

(8) **Reference numbers in the main text.** No need for superscripts when citing references in the text.

Reply:Thanks for your kindly reminder. Modified as required.

(9) **There are issues with the references:** Please provide the PMID numbers (https://pubmed.ncbi.nlm.nih.gov/) and DOI citation numbers (https://doi.crossref.org/simpleTextQuery) to the reference list and list all authors of the references. If a reference has no PMID and DOI, please provide the source website address of this reference.

To ensure the accuracy of the references, please use "**Edit References by Auto-Analyser**" (https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx) to edit the references of the manuscript.

Reply:Thanks for your kindly reminder. It has been processed by a document editor to ensure correct formatting.

(10) **Figures. Original figure documents.** *In the meantime, authors should 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, and upload it to the file destination of "**Image File**" in the F6Pubishing system.*

Reply:Thanks for your kindly reminder.

(11) **Notes in figures and tables.** Data with statistical significance in a figure or table should be denoted using superscripted alphabetical lettering (don't include symbols, such as *, #, †, §, ‡, ¥, @….), such that $^{a}P < 0.05$ and $^{b}P < 0.01$. If there are other series of P values, the alphabetical subscripted denotation format is continued, such that $^{c}P < 0.05$ *vs* control, $^{d}P < 0.01$ *vs* control, $^{e}P < 0.05$ *vs* group A, and $^{f}P < 0.01$ *vs* group B. Data that are not statistically significant should not be denoted, *i.e.* $P > 0.05$ is not an allowed denotation.

Reply:Thanks for your kindly reminder. Conform to the above format.

(12) **Abstract.** The 5 sections of the structured abstract are: **BACKGROUND; AIM; METHODS; RESULTS; CONCLUSION.**

Reply:Thanks for your kindly reminder. Conform to the above format.

(13) Please provide the primary version (PDF) of the Institutional Review Board's official approval, prepared in the official language of the authors' country.

Reply:Thanks for your kindly reminder. Already provided.

(14) Please provide the primary version (PDF) of the Informed Consent Form that has been signed by all subjects and investigators of the study, prepared in the official language of the authors' country.

Reply:Thanks for your kindly reminder. Already provided.

(15) Please provide the filled conflict-of-interest disclosure form.

Reply:Thanks for your kindly reminder. Already provided.

(16) Please provide the Biostatistics Review Certificate.

Reply:Thanks for your kindly reminder. Already provided.

3 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

(2) Company Editor-in-Chief:

I have reviewed the Peer-Review Report, full text of the manuscript, all of which have met the basic publishing requirements of the ***World Journal of Psychiatry*** 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.

作者返修手稿建议

尊敬的作者：为了进一步提高作者手稿的学术质量、语言表达质量、格式修改质量、图片图注修改质量和表格修改质量，以便缩短手稿出版周期，并且促进手稿顺利接受和在线发表，我们强烈建议作者采取以下措施以解决返修手稿过程中的重要问题。

第一，返修手稿。请作者邀请编辑部认可的英文语言润色专业公司(https://www.wjgnet.com/bpg/gerinfo/240)，或其它英文语言润色专业公司协助作者按照*Checklist for Authors to Revise a Manuscript* 要求修改手稿中的每一项内容。另外，作者指南，见：https://www.wjgnet.com/bpg/gerinfo/204。作者邀请专业英文语言润色公司的目的是对手稿的题目、短标题、作者贡献分布、核心内容提要、关键词、摘要（摘要中不能够出现引用文献信息）、正文、表格表注、图注、公式、特殊字符、参考文献序号引用顺序等进行核实和规范格式，以及语言润色等。非英文母语作者返修手稿时，务必邀请英文语言润色专业公司来解决手稿的英文语言表达问题。如果手稿出版后被发现英文语言表达出现严重问题，文章将会按照撤稿处理，这将会对作者的学术声誉造成严重危害。撤稿声明（Retraction Note）举例见：https://www.wjgnet.com/2307-8960/full/v12/i19/4029.htm。为了确保手稿的英文语言表达质量，作者必须要请英文语言润色公司出具返修手稿后的英文语言润色证明。

第二，同行评议。邀请论文润色公司，依据同行评议报告和科学编辑评论，协助作者对手稿的研究方法、数据分析和论点逻辑等进行进一步地审核，确保手稿学术上的正确性。

第三，作者姓名汉语拼音拼写规则。先名后姓；首字母大写；双名之间用半字线"-"分开；多作

者时姓名间加逗号。 示例:“**王金磊**”的姓名汉语拼音拼写规则示例为 **“Jin-Lei Wang”**。

第四，图片和线条图。请论文润色公司协助作者解决图片和线条图规范化的问题，并且提供在PowerPoint 上可编辑的分解图。图片和线条图一般由图、图号、图题和图注构成。图片全文依序编号。只有一个图片时仍应编号。示例:“Figure 1”、“Figure 2”。与此同时，同一个主题内容的彩色图、黑白图、和线条图，应统一使用一个主题，并且每个子图的注解分别叙述。示例: **Figure 1 Pathological changes of atrophic gastritis after treatment.** A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ....

第五，三线表。请论文润色公司协助作者解决三线表格规范化的问题。三线表格一般由表号、表题、表头、表身和表注构成。三线表由顶线、横表头线和底线组成。表格全文依序编号。只有一个表格时仍应编号。示例:“Table 1”、“Table 2”。

第六，参考文献。首先，顺序编码。请按照参考文献在正文中出现的先后顺序编码用阿拉伯数字加方括号[ ] 标出。示例：手术方法按照参考文献[8]。每篇参考文献应包含 PMID 和 DOI 号码。参考文献测试系统，见：https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx。其次，作者引用文献的相关性。作者必须尊重前人的相关重要研究成果。如果发现作者引用的文献与手稿主题内容没有明确的相关性或没有引用前人相关的重要研究成果，手稿将会按照退稿处理。请作者务必重新核实每条参考文献引用与手稿主题内容是否密切相关，是否遗漏重要文献。其三，作者引用本人工作。请作者核实引用作者本人文献的必要性。如果发现作者没有必要地大量引用自己发表的文章，手稿将会被按照退稿处理。其四，同行评议人推荐作者引用文章。如果作者认为确有必要引用同行评议人推荐的文章，并且推荐的文章是他人的关键性工作就可以引用或请拒绝引用。

第七，学术查重。邀请论文润色公司协助作者对手稿进行学术查重。手稿一旦被编辑部判定为存在抄袭，将会被退稿。

第八，语言润色。邀请论文润色公司协助作者解决手稿中的拼写错误、语法错误、时态错误、单复数错误、标点错误和科学用词错误等等。

第九，基金资助项目批准文件。如果手稿有基金项目支持，作者必须上传 PDF 格式的基金资助项目批准文件。

第十， 致谢。不允许将语言编辑公司名称和基金资助项目名称列在致谢中。

最后，提交手稿。最终论文润色公司协助作者完成手稿修改，并确认手稿书写格式符合期刊作者指南（https://www.wjgnet.com/bpg/gerinfo/204）标准后在线提交手稿。

回复：非常感谢您的建议。我们已经按照上述要求检查了手稿并按要求进行修改了。