



PEER-REVIEW REPORT

Name of journal: *World Journal of Virology*

Manuscript NO: 76525

Title: Validity of the Patient Health Questionnaires (PHQ-2 and PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05688164

Position: Peer Reviewer

Academic degree: BSc, MD, PhD

Professional title: Research Fellow

Reviewer's Country/Territory: Hungary

Author's Country/Territory: Pakistan

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

21 March 2022 Review report on the manuscript titled “Validity of the Patient Health Questionnaire (PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan” by Junaid K & Daood M, submitted to World Journal of Psychiatry Manuscript ID: 76525 Dear Authors, Depression is a common finding in patients with HIV, but little attention is paid to the detection of depression in primary care. In the present study entitled “Validity of the Patient Health Questionnaire (PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan”, Junaid and Daood investigated the accuracy and validation of Patient Health Questionnaires (PHQ) for screening depression in HIV patients. For this purpose, the authors screened depression by PHQ-9, patients who scored greater than nine were evaluated by PHQ-2, and the data was statistically analyzed. The results showed that PHQ-9 presents a good validity to detect depression. Finally, the authors concluded that PHQ-9 is an easily applicable test to screen depressive symptoms among HIV-affected patients in primary care. The main strength of this manuscript is that the authors attempt to present the validity of PHQ-9 in detecting depression in patients with HIV, which is of particular interest to care mental illnesses among the population. In general, the idea of this study is really valuable and the author’s fascinating observations on this timely topic may be of interest to the readers of World Journal of Psychiatry. However, some comments as well as some crucial evidence that should be included to support the author’s argumentation, and that need to be addressed to improve the quality of the article, its adequacy, and its readability prior to the publication in the present form. My overall judgment is to publish this article after the authors has carefully considered my suggestions below,



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reshaping parts of the introduction, methods, and conclusion sections by adding more evidence. In general, I recommend the author to use more evidence to back their claims, especially in the introduction of the article, which I believe is currently insufficient. Thus, I advise the authors to attempt to deepen the subject of their manuscript, as the bibliography is too concise: nonetheless less than 60-70 articles for an original paper are insufficient. Currently authors cite only 45 papers, and they are dramatically few. Therefore, I suggest the authors to focus their efforts on researching relevant literature: I believe that adding more studies will help to provide better and more accurate background to this paper. In this review report, I will try to help the authors by suggesting relevant literature that suit their manuscript. Comments: 1. Abstract: a. I suggest clearly presenting the terms such as HIV, HIV infection, and AIDS, as defined. HIV patients can be patients with seropositive, who have not necessarily developed AIDS. b. The background and the aim should be expanded to support the methods and the rationale to use PHQ-9 and PHQ-2 in a consecutive manner. 2. Introduction: I suggest the authors to reorganize the Introduction section, which seems inhomogeneous and dispersive. I think that more information about depressive disorder would provide suitable background here. Thus, I suggest the authors to make an effort to provide a brief overview of the pertinent published literature that offer a perspective on definition, causes and symptoms of depression, because as it stands, this information is not highlighted in the text. Authors should briefly describe the pathogenesis, comorbidity, biomarkers, and diagnosis of depression, antidepressant treatment in general including the mechanism of actions, iatrogenesis, and particular challenge and importance in detecting depression in HIV-positive patients. (<https://doi.org/10.3390/bs11080110>; <https://doi.org/10.3390/biomedicines9070734>; <https://doi.org/10.3390/biomedicines9010082>; doi: 10.1038/s41598-020-73918-z; doi: 10.1016/j.neubiorev.2020.08.010; <https://doi.org/10.3390/biomedicines9040340>;



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<https://doi.org/10.3390/biomedicines8110509>;

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7692261/>;

<https://doi.org/10.3390/biomedicines9040403>;

<https://doi.org/10.3390/ijerph19063333>). In this regard, I believe that it may be useful to have a general overview of psychiatric mood disorders (i.e., depression, anxiety, and PTSD) and, specifically, of the related symptoms, diagnosis and cutting-edge treatments. For this reason, I would suggest some crucial evidence that will methodologically fit with the present manuscript, as new evidence for the implementation of new methods to treat such disorders (i.e., by the means of Non-invasive brain stimulation techniques (NIBS)) in the treatment in mental disorder in humans: for example, a recent review (<https://doi.org/10.1016/j.neubiorev.2021.04.036>) described the potential and effectiveness of non-invasive brain simulation (NIBS) to interfere and modulate the abnormal activity of neural circuits (i.e., amygdala-mPFC-hippocampus) involved in the acquisition and consolidation of fear memories, which are altered in many mood psychiatric disorders (i.e., anxiety disorder, specific phobias, post-traumatic stress disorder or depression). Interestingly, another recent manuscript (<https://doi.org/10.1016/j.jad.2021.02.076>) illustrated the therapeutic potential of NIBS as a valid alternative in the treatment of untypically persistent memories that characterized those patients that do not respond to psychotherapy and/or drug treatments. I may also recommend additional studies that have focused on this issue (<https://doi.org/10.3390/biomedicines10010076>;

<https://doi.org/10.3390/biomedicines9050517>). I believe that adding this information will help providing a more coherent and defined background. 3. Study design: I suggest fully expanding the study design including the sequence of tests and the number of patients. 4. Results: In my opinion, this section is well organized, but it illustrates findings in an excessively broad way, without really providing full statistical details, to



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ensure in-depth understanding and replicability of the findings. 5. I think the Conclusions paragraph, despite being well organized, is too thin and does not clearly describe what the authors think is the take home message. I believe that this section would benefit from some thoughtful as well as in-depth considerations by the authors, because as it stands, it is very descriptive but not enough theoretical as a discussion should be. Authors should make an effort, trying to explain the theoretical implication as well as the translational application of their research. 6. Figures and Tables: please provide an explanatory title and caption for each figure and table within the text. Overall, the manuscript contains two figures, four tables and 45 references. In my opinion, the number of references it is too low for an original research article, and this issue may prevent the possibility of publishing it in this form. However, the manuscript carries important value presenting the validity of PHQ-9 to detect depression among patients with HIV infection. I hope that, after these careful revisions, the manuscript can meet the Journal's high standards for publication. I am available for a new round of revision of this article. I declare no conflict of interest regarding this manuscript. Best regards,
Reviewer



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05175737

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Spain

Author's Country/Territory: Pakistan

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Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

Thanks for the opportunity of reviewing the paper entitled "Validity of the Patient Health Questionnaire (PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan". The study study aimed to assess some psychometric properties of Patient Health Questionnaires (PHQ-9 and PHQ-2) on a sample of 158 HIV patients. First of all, I would like to acknowledge the effort done by the authors of the manuscript. However there are several crucial methodological issues than impede my support on this paper. Under my opinion, the main limitation I observe in the study is the criteria used as gold standard for diagnosing depression. As authors stated "the PHQ-2 was used as the reference method to diagnose the major depressive disorder". I completely disagree with using this measure (that is included in PHQ-9) as a criteria for calculating ROC curves. Furthermore, I could not be able to understand how ROC curves were calculated for PHQ-2 if the gold standard was the instrument itself. Probably the way it is written is confusing, but I regret to say I could not reach this important methodological issue. The information on the sample size used in each analysis is also unclear to me. While in the participants section 158 patients are mentioned, later in the method section reference is made to 10% of the sample to complete the analysis with the PHQ-2. If this 10% corresponds to 15-16 patients being used for computing ROC analyses, I consider the sample size to be clearly insufficient. Another major issue is related to the hypothesis. I recommend authors to define them, stating which is the expected result, supported by previous research. In addition, considering that the objective of the study is more psychometric in nature (to provide reliability, validity and sensitivity values), it would be desirable that the authors include evidence of the internal structure of the instrument



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and its relationship with other variables to support this adaptation of the instrument. After considering these important methodological concerns, I cannot consider results or discussion.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Virology*

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05688164

Position: Peer Reviewer

Academic degree: BSc, MD, PhD

Professional title: Research Fellow

Reviewer's Country/Territory: Hungary

Author's Country/Territory: Pakistan

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [**Y**] No

SPECIFIC COMMENTS TO AUTHORS

1 June 2022 The 2nd review report on the manuscript titled “Validity of the Patient Health Questionnaire (PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan” by Junaid K & Daood M, submitted to World Journal of Virology Manuscript ID: 76525 Dear Authors, In this observational study by Junaid and colleagues, authors assessed the psychometric properties of PHQ-2 and PHQ-9 for depression diagnosis and estimated the sensitivity and specificity of the PHQ-2 for depression screening in HIV-infected patients. I only have one last suggestion to further improve the theoretical background of the present paper and its argumentation: in this regard, I would recommend focusing on neural substrates of major depressive disorder, specifically on frontal lobe dysfunction, which may cause impairments in patients’ cognitive functions including memory, executive functions, learning or behavioral control (<https://doi.org/10.1016/j.tins.2022.04.003>; <https://doi.org/10.17219/acem/146756>; <https://doi.org/10.3390/ijms21249338>; <https://doi.org/10.1007/s00702-022-02513-5>). Overall, this is a timely and needed manuscript, and I look forward to seeing further research on this issue by these authors in the future. Thank you, Reviewer