WJG PCDAI Review

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The study by Grant et al aimed to analyzes how particular items, objectives and subjective items that compounds the PCDAI, can predict and modify Crohn's disease activity over time. The paper provides interesting data, but there are also some questions to be answered, as follows:

-The introduction is so complete, but very complete introduction, but could explain a description of the items included in the PCDAI to facilitate the comprehension of the work for those unfamiliar with this index.

***Thank you for your comment, we have added more text to the introduction paragraph to describe the items included on the PCDAI. This paragraph now reads as follows:***

*"The PCDAI was developed by a group of clinicians and focuses on: a) subjective reporting of the degree of abdominal pain, stool pattern, and general well-being; b) extra-intestinal manifestations, such as fever, arthritis, rash, and uveitis; c) physical examination findings including abdominal pain, perirectal disease, and extraintestinal manifestations, weight and height; and d) laboratory data, including hematocrit, erythrocyte sedimentation rate (ESR), and serum albumin[1]"*

***Additionally, information around scoring of the PCDAI was added to the measures section as follows:***

*"Severity for each item is assigned a score of 0 (normal), 5 (mild abnormality), or 10 (severe abnormality) except for hematocrit and ESR which are scored as 0, 2.5, or 5. A minimum total index score is zero, and a maximum score is 100."*

- Page 6, line 9: please, define what is " IMPACT ". - Page 9, line 15: please, define what is " HCT".

***We have added a line of text to describe the IMPACT questionnaire, as follows:***

*"...IMPACT, a 35-item health related quality of life self-report measure for paediatric IBD patients[33]...."*

***We have also removed the use of the "HCT" acronym as it was only used sporadically and instead replaced this with the full term 'hematocrit' for clarity.***

-The methodology and Biostatistics analysis are complex but well explained with comprehensive tables and figures.

***Thank you.***

-The first paragraph of the discussion is very general, it should be more concrete about the study so I would start directly with the second paragraph describing the study and the general results.

***We have removed the first paragraph of the discussion given that it was not felt to add to the summary of results.***

-The limitations of the study are well argued and the final conclusion by using both objective and subjective items to assess pediatric Crohn's disease activity is accurate and applicable in clinical practice.

***Thank you, we are content that that this messaging in clinical practice was clear.***

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The study by Grant A et al. examines the single weight of each PCDAI score item on disease activity, dividing them in subjective and objective items and showing also a combined score of only significant items. The quality of collected data is definitely high and the body of the paper is nicely constructed with a regular flow. Despite the thorough analysis, I think the paper might improve following these suggestions/comments below:

- It should be discussed why composite values provide the same R2 of the full PCDAI both at Q1 and Q4 (table 2), as two of the not significant items of the PCDAI have been left out in the composite score. Likewise, I would have expected the authors to carry out the same correlation as in table 3 between PCDAI and composite value (as well as a specific ROC curve for the composite score), and not only for isolated subjective or objective parameters only.

***This is a thoughtful comment. Firstly, as you allude to, the $R^2$ value for the full and composite score at both Q1 and Q4 is the same as the composite simply consists of all the individual PCDAI items that were significantly related to the change in score over these time points. It is showing that the composite is doing just as well as the full score at explaining disease activity. With this point, it would also be reasonable to repeat the composite analysis in table 3 as you suggest. However, the goal of this manuscript was not to recommend yet another PCDAI composite score (as many have done before, with the wPCDAI currently recommended for this reason) but rather to look at whether even smaller subgroups of items would suffice (subjective/objective) to validly identify patients' disease activity. We expect that the composite would act similarly to the full scale, as demonstrated in the regression analysis – which again, is what other authors have demonstrated with other composite versions of the PCDAI. We feel this would detract from the main message we are trying to convey in this manuscript, which is to focus on these smaller subgroups as indicate and thus have elected not to include additional composite analyses in this paper. However, given the importance of this feedback, we have incorporated a few additional sentences into the discussion to describe this point, as follows:***

*"Although the composite of items showed similar performance to the full PCDAI, the goal of this work was not to recommend or endorse a composite PCDAI measure as this work has already been completed[5, 10], and our findings produced similar results as previously described. Rather, the focus of the current work around these smaller subgroups of items reflects the limited ability of either subjective or objective components alone, as measured on the PCDAI, to fully characterize disease activity."*

- An interesting appendix to this analysis would be to "create" a new simplified composite score with the data that are available in this study. I wonder whether the authors have tried to combine

fewer markers together and see if there were some satisfying results as well as the "full composite" score on the right column of table 2.

***Again, thank you for this comment. We feel that we have sufficiently described the rationale for this above. We hope that the language we have added to this point in the manuscript is sufficient.***

- In the discussion section, please focus a bit more on the combined biomarkers and composite scores, as there is a high potential to suggest a reliable composite score with this paper. Have a look at DOI: 10.1159/000511641 for reference and further discussion.

***Thank you for this suggestion – to keep the manuscript concise we did not previously elaborate on this research. However, as suggested, we have added additional information to the discussion to further describe this work, as follows:***

*"Additionally, work to identify biomarkers that accurately identify disease activity in pediatric CD is ongoing[34], but currently suggest that fecal calprotectin and C-reactive protein are reliable markers with utility in management of a patient's condition.[35] These indices also demonstrate limited correlation with C-reactive protein, and a poor correlation with fecal calprotectin.[15, 16]"*

***We have added additional language to this point in the discussion. Thank you.***

- Other minor comments: Figure 1: please remove the four decimals on the y axis

***The decimal points have been removed.***

-Table 1: age it is best defined as median (IQR) rather than mean + SD

***Since age was normally distributed, we had originally represented this as mean ±SD, however, we have replaced this with the median and IQR as per your recommendation.***

Reviewer #3:
**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** I would like to thank the authors for this extensive and thorough work. I recommend publishing without any further adjustments.

***Thank you for your review and feedback.***

## 4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

## 5 EDITORIAL OFFICE'S COMMENTS

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

**(1)** ***Science editor:***

1 Scientific quality: The manuscript describes a clinical and translational research of the assessing disease activity in pediatric Crohn's disease using the pediatric Crohn's disease activity index. The topic is within the scope of the WJG.

(1) Classification: Grade A, Grade B and Grade B;

(2) Summary of the Peer-Review Report: The study examines the single weight of each PCDAI score item on disease activity, dividing them in subjective and objective items and showing also a combined score of only significant items. The quality of collected data is definitely high and interesting, and the body of the paper is nicely constructed with a regular flow. However, the questions raised by the reviewers should be answered; and

(3) Format: There are 3 tables and 2 figures.

(4) References: A total of 27 references are cited, including 1 reference published in the last 3 years;

(5) Self-cited references: There are 9 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and

***Although we acknowledge that the number of self-cited references is high – Hyams, Griffiths, and Otley are experts in this field, were involved in validation of the PCDAI and/or subsequent publications evaluating scoring and use of this measure, and were involved in studies using the PCDAI in the context of international clinical trials as site lead investigators and thus were involved in publication of related manuscripts involving this measure. Given that the focus of this manuscript is on evaluation of a specific tool, and originally solicited given their respective positions and role in development and validation of the PCDAI over time, there are not substitute publications available to reduce the self-citation rate. These references are the only available that refer directly to the use of the PCDAI and the work involved in evaluating the clinical utility of this tool over time. In order to reduce the self-citation rate to less than 10% we would need over 90 references in total. Given that this is not practical, or feasible, we have added relevant citations throughout the article, reducing the self-citation rate from 34 to 23%.***

(6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Classification: Grade B, Grade B and Grade A.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Clinical Trial Registration Statement.

The authors need to provide the Institutional Review Board Approval Form and Written informed consent.

***Institutional Review Board Approval Forms and copies of informed consent have now been provided.***

No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG.

5 Issues raised:

(1) The title is too long, and it should be no more than 18 words;

***We have reduced the title word count to 18 words.***

(2) The authors did not provide original pictures. 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;

***The original picture for Figure 1 has been modified and placed into a PowerPoint document. The original figures for Figure 2 (ROC curves) are provided as part of SPSS output and are not editable. If this is an issue, we investigate other programs needed to create and produce editable figures.***

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and

***The reference section has been updated to include PMID and DOI numbers, and reformatted according to WJG style.***

(4) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

***An Article Highlights section has been added.***

(6) Recommendation: Conditional acceptance.

**(2)** ***Editorial office director:***

**(3)** ***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 Gastroenterology, 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. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

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***An Article Highlights section has been added.***

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