ANSWERING REVIEWERS

January 11, 2015

Dear Editor,

On behalf of my co-authors, I would like to thank you for your willingness to reconsider our work for publication in "*World Journal of Gastroenterology*" provided that yours and the reviewers' comments and suggestions are satisfactorily answered. The reviewers' comments have helped to clarify certain parts of our paper and we would like to resubmit our revised manuscript. We are grateful for the enthusiasm shown for this work and for the appreciation of the importance of this research topic. Our revisions are highlightened in the text with track changes. The details of our revisions and our response to your comments and each comment of the reviewers are following.

Please find enclosed the edited manuscript in Word format (file name: 15551-review).

Title: Associations of Sense of Coherence with psychological distress and quality of life in Inflammatory Bowel Disease

Authors: Thiago H. Freitas, Elias Andreoulakis, Gilberto S. Alves, Hesley L. L. Miranda, Lúcia L. B. C. Braga, Thomas Hyphantis, André F. Carvalho

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15551

The manuscript has been improved according to the Editor's and the reviewers' suggestions:

1 Format: Format has been updated according to the Editor's suggestions. We would like, however, to mention that since our manuscript has reached Grade A according to the second reviewer and the first reviewer asked for minor linguistic revisions suggesting also a number of language corrections which we incorporated in the revised text after an additional linguistic revision, we believe that the language of our manuscript has reached the journal's requirements without the need for employing a professional editing service, and a signed personal guarantee for the language presentation of our manuscript has been submitted.

2 Revision has been made according to the suggestions of the reviewers as follows:

Reviewer 1:

(1) *The concept of 'Sense of coherence' ' (SOC) is a sociological index and the reader would benefit from some additional definition, particularly in this paper on psychological perceptions of IBD and quality of life/wellness issues.*

We agree with the reviewer and additional definitions and clarifications regarding the concept of sense of coherence have been added in the introduction section (page 7, line 14 to page 8, line 12).

(2) *The application of SOC as a 'salutogenic index' is not uniformly supported by all studies, and some studies have recommended caution in the application of SOC to different populations (US veterans vs. Swedish patients), SOC did not always positively predict health outcomes (Coe et al., 1998, Atroshi et al., 2002).*

We agree with the reviewer and new text mentioning these limitations has been added in the limitations of the study section (page 21, lines 8-10)

(3) *In addition to the cited 2012 Bengtsson et al., study, the authors should also address a recent report by Opheim which has similar findings (Opheim et al., 'Sense of coherence in patients with inflammatory bowel disease'. Opheim R, Fagermoen MS, Jelsness-Jørgensen LP, Bernklev T, Moum B. Gastroenterol Res Pract. 2014;2014:989038.) The differences between the current study and the Opheim et al. study should be discussed.*

We had previously addressed the study of Opheim et al mentioned by the reviewer (previous ref. No. 25). Based on the reviewer's comment, however, a better description of this study was added in the introduction section (page 8, lines 26-10). In addition, the differences between our study and the Opheim et al study have been discussed in the discussion section (page 19, lines 2-7), according to the reviewer's suggestion.

(4) *Similarly, a supporting reference "Siassi M et al.. Personality rather than clinical variables determines quality of life after major colorectal surgery. Diseases of the Colon & Rectum. 2009;52(4):662–668' should be addressed as it supports findings in the current study.*

We would like to thank the reviewer for drawing our attention to this important reference. The new reference has been cited based on the reviewer's suggestion, and an additional comment was made regarding the role of personality in determining quality of life in IBD (discussion section, page 19, line 30 to page 20, line 5).

(5) *Conversely, Oxelmark et al., (2007) using both SOC and HRQOL metrics found no statistically significant differences in IBDQ or SOC compared to 'normals' (Oxelmark et al., Group-based intervention program in inflammatory bowel disease patients: effects on quality of life. Inflamm Bowel Dis. 2007 Feb;13(2):182-90.) Why might these previous studies have made similar observations?*

We agree with the reviewer that previous findings regarding SOC in IBD and whether people with IBD present similar to the general population levels of SOC are important. However, our aim was to study the contribution of SOC in psychological distress and HRQoL in IBD; therefore, we didn't include a healthy control group, as our aim was not to test whether IBD patients' SOC differs from that of healthy people. We believe thus that a discussion on the SOC differences between IBD patients and healthy people, although of great interest, is not supported by our data and it is beyond of the scope of the present study.

(6) *It was reported that this study had a very "healthy" study group with a relapse rate of only 1 / 46, thus 98% stayed in remission over 1 year. Does successful clinical management thus also have an important effect on SOC /HRQOL? (Reviewed in "Psychological interventions for treatment of inflammatory bowel disease*

(Review) The Cochrane Collaboration. Copyright © 2011." It seems that an important consideration is how effectively these patients are being treated for their disease. The number of patients who had 'moderate' relapses seemed high (41.8%) had 3-5 relapses in 2 years, but were in 'remission' at the time of the study.

We believe that the previously mentioned in Table 1 "mean relapse rate" was rather confusing. The previously reported value of 1.86 ± 0.75 was referring to a mean of "low/moderate/high" relapse rate, which meant that the sample was close to "2", meaning "moderate relapse rate". However, it seems that this reporting was highly confusing and has been omitted.

Indeed, the number of patients who had 'moderate' relapses (3-5 relapses in 2 years) was rather high (41.8%), but the relevant indices (CDAI/TWT) indicated that they were in 'remission' at the time of the study. This probably indicates that their clinical management around the time of the study was successful, as the reviewer also assumed. Whether, however, a successful clinical management also has an important effect on SOC or HRQOL remains unclear from the results of the present study, as we didn't evaluate the quality of the clinical management and whether there is an association between clinical management and SOC or HRQoL. Nevertheless, we agree with the reviewer, and the limitation of including patients with a rather "stable" disease has been added in the limitations of the study section (page 20, line 26 to page 21, line 3). Also, we added discussion relevant to the importance of a successful clinical management based on the review paper suggested by the reviewer (page 23, lines 3-11).

(7) *The treatment of CDAI/TWT of these patients was grouped cumulatively as 'disease in remission' with 'yes' (i.e. mild disease activity/severity; CDAI score<150 or TWT score≤6, accordingly) vs. 'no' (i.e. moderate or severe disease activity/severity; CDAI score≥150 or TWT score>6, accordingly). Was there an average CDAI / TWT average for each group? It can be appreciated that these are different scoring systems, but how comparable are these groupings on different scales?*

Averages of CDAI and TWT scores have been added in Table 1, according to the reviewer's suggestion. We agree with the reviewer that there are limitations in applying a cumulative index for both diseases. Therefore, the following text has been added in the limitations of the study section (page 21, lines 3-8): "We should also acknowledge that, as the disease activity/severity indices (CDAI/TWT) were categorized cumulatively to obtain a comparable index applicable to both types of IBD, the contribution of current disease state (i.e. in remission or not) to psychological distress and HRQoL should be interpreted with caution, since it was extracted from different scoring systems, although established cut-offs were used".

(8) *It was noticed that the SOCs and HRQoL in CD did not differ from those in UC; did these scores differ from 'normal' controls and is it worth discussing?*

As mentioned earlier, we didn't include a healthy control group, as our aim was not to test whether IBD patients' SOC differs from that of healthy people. Therefore, we believe that a discussion on the SOC differences between IBD patients and healthy people, although of great interest, is not supported by our data. Furthermore, in the absence of normative data for SOC, a discussion on this issue would not be possible, and it would be beyond of the scope of the present study.

(9) Would the authors anticipate that effective coping skills activities would lead to improvement in SOC/HRQOL scoring?

Although a discussion regarding the impact of an effective coping skills on SOC and HRQoL is not supported by our data, previous evidence suggests that strategies aiming at improving SOC had a beneficial effect on patients' HRQoL, and this has been added in the discussion section of the manuscript (page 22, line 18-22).

(10) Do individual SOC scores predict disease activity and maintenance of remission?

Further statistical analyses showed that SOC was not associated with relapse rate or with disease activity/severity at the time of the study in the total sample, and the same applies for CD and UC patient samples. These results have been added in the results section of the manuscript (page 14, lines 20-24), based on the reviewer's concern.

(11) The conclusion that : '…treatment strategies focusing on enhancing SOC might result in lower levels of psychological distress, and in turn enhance HRQoL ....' Can some specific examples of treatment strategies be discussed e.g. psychological treatments to improve coping skills?

Examples of treatment strategies focusing on enhancing SOC had been previously mentioned earlier in the discussion. However, based on the reviewer's concern, we moved and better clarify this issue in the discussion section of the manuscript (page 22, line 18-22).

Minor:

Sense of coherence [has] page 4.

The mistake in the core tip has been corrected; we are sorry for this inconvenience

Disgnostic (diagnostic?) page 7 ; betweenSOC – between SOC; Crohn's spelling is incorrect in some places.

The typos have been corrected, thank you.

… across several dimensions. – please define 'dimensions'

"Dimensions" have been defined, based on the reviewer's suggestion (page 5, line 23)

Reviewer 2:

"This paper focuses on the influence of psychological factors including Sense of Coherence (SOC), psychological distress (PD) and Health Related Quality of Life (HRQoL) in Inflammatory Bowel Disease (IBD). Therefor authors investigated 147 IBD patients with Crohn`s disease (CD) and Ulcerative Colitis (UC). The authors hypothesized that SOC, PD and HRQoL are associated with each other party independently of democratic and disease-related parameters and partly mediated by depressive and anxiety symptoms. Without doubt the topic of the manuscript is interesting and a contemporary issue in the IBD community"

We are grateful to the reviewer for the appreciation of the research topic and for his/her enthusiasm shown for this work.

1. *Abstract; Methods: Spelling of numbers the numbers (sixty-four participants, 83 patients).*

The number of patients reported in the abstract (83) has been spelled-out.

2. *Introduction: Hypothesis 2: In hypothesis 1 disease-related parameters are mentioned, whereas in the second one just disease parameters are written.*

The wording "Disease-related" (parameters) has been replaced the word "disease" in the hypothesis 2, according to the reviewer's suggestion.

3. *In Methods: A scheme/figure would be helpful to retrace how patients are grouped (including low, moderate and high relapse rates).*

A Figure has been added (New Figure 1) according to the reviewer's suggestion.

4. *In Methods; Statistical analysis; second paragraph: Typo Step 2 (capital letter).*

Typos (capital letter Step 2 in two instances) have been corrected in the second paragraph of the statistical analysis section.

---

3 References and typesetting were corrected

There was not any financial interest which could create a potential conflict of interest or the appearance of a conflict of interest with regard to the present submitted work.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.
Sincerely yours,

Thomas Hyphantis
Professor of Psychiatry
Department of Psychiatry
Faculty of Medicine
School of Health Sciences
University of Ioannina,
45110 Ioannina, Greece.
Tel: +30-26510-07322, Fax: +30-26510-07054,
e–mail: tyfantis@cc.uoi.gr; thomashyphantis@outlook.com