August 28, 2014

Dear Prof. Qi,

Please find enclosed the edited manuscript in Word format (file name: 11800 edited final.docx).

Title: Latent structure of irritable bowel syndrome symptom severity

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been thoroughly revised according to the suggestions of the reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer:

> **Reviewer 00000194 No. 1**: "This is an important topic but I must admit, as a clinical investigator with an interest in IBS, that I found it very hard to follow as will most of the readership of this journal. 1. Terms like "the whole heterogeneous construct", "the three factor analytically derived subscales", "scale unidimensionality", "taxometric", "factor analysis with orthogonal rotation", "a clear loading pattern" and the entire results section will be completely obscure to this readership and must be explained. "
>
> **Response:** We thought that the best place for a short description of the terms mentioned by Reviewer 194 would be under the "Terminology" heading in the "Comments" section at the end of the manuscript:
> "While a *homogenous construct* is typically assessed by a number of items which are very similar to one other (e.g., asking for (1) tiredness, (2) feeling sleepy, and (3) tendency to sleep long) a *heterogeneous construct* is normally assessed by items which differ in terms of wording and/or content (e.g., asking for distress regarding (1) nausea, (2) pain, and (3) diarrhea). The sub scales of a symptom questionnaire are supposed to show high correlations to one another within one subscale and low correlations between distinct subscales. One statistical method to derive such subscales from a questionnaire is factor analysis. Each subscale which is derived in this way is supposed to be *unidimensional*. In case of a so-called orthogonal rotation, the subscales of a questionnaire are not allowed to show any correlation to one another (i.e., r = .00). In factor analysis, a clear *factor loading pattern* means that each item almost entirely belongs to one of the subscales which makes interpretation of the results easier. The main idea behind *Structural Equation Modeling* is to test an a-priori theory regarding the interrelation of questionnaire items (i.e., the "structure"). In case the postulated structure is valid in the particular sample, the fit indices (i.e., here CFI and RMSEA) tend to show good values. These fit indices can also be used to compare

competing models (e.g., one-factor and three factor models). The sole purpose of *taxometric analysis* is to test if a construct is rather continuous (i.e., certain individuals differ *quantitatively* but not *qualitatively* on a given construct, e.g., gastrointestinal symptoms ranging from mild symptoms up to a definitive IBS) or discrete (e.g., whether *qualitatively* distinct subgroups exist, e.g., either suffering from a disease as Morbus Crohn or not)."

Reviewer 00000194 No. 2: "Is this really a symptom severity scale or a symptom frequency scale?"
Response: Thank you for raising this important aspect which is relevant for many questionnaires in this domain. In response to this issue, we added the following passage to the discussion:
"Throughout the whole article we spoke of IBS symptom severity. However, one might argue that the B-IBS questionnaire is rather a measure of symptom frequency instead of severity. Indeed, the items of the B-IBS questionnaire require frequency ratings (*all of the time* to *none of the time*). On the other hand, all of its items require the rating of both, bodily symptoms (e.g. "diarrhea") and distress related ratings. (e.g., Item 10: How often have you "suffered from a feeling of urgency" [14]). Here, without doubt, the term "suffering" is directly related to the severity of the symptoms. We propose that future studies could put more emphasis on the distinction between the sole presence of a symptom and the degree of suffering or distress caused by the symptom. This distinction could also be an interesting feature for future questionnaires in this domain."

Reviewer 00000194 No. 3:
"On page 5 four additional scales are mentioned but only 3 seem to be listed."
Response: Thank you very much for this hint. We have corrected this mistake.

RE 00044980 No. 1: Authors should mention approval of IRB and the informed consent.
Response: (1) Unfortunately, as the study was an internet questionnaire study no written informed consent was requested from the participants. Because the study does not include patients, no IRB approval was required from our institution.

RE 00044980 No. 2: Authors should mention three measures such as fatigue severity scale, pain sensitivity questionnaire and somatoform dissociation questionnaire in details.
Response: In the revised version of the manuscript, we provided the following information regarding the three questionnaires.

"The fatigue severity scale [27] assesses the subjective experience of "physical and mental tiredness, and apathy" ([28], p. 1601). It consists of 9-items which are answered on a 7-point Likert scale (1 to 7) and is regarded as one of the most commonly used measures of fatigue severity[28]."

"Moreover, the participants completed the pain sensitivity questionnaire which asks the respondents to imagine how painful several situations would be on a ten point scale[29]. The PSQ consists of 17 items which describe situations that are more of less painful (e.g., burning ones tongue on a very hot drink). Participants are supposed to rate the painfulness of the situations on a 11-point Likert scale (*not at all painful* to *most*

severe pain imaginable) [29]."

"As a third measure, we included the somatoform dissociation questionnaire (SDQ) [30] which was designed to assess somatoform dissociative symptoms that are characterized by "physical manifestations of a dissociation of the personality" ([31], p. 338). The SDQ consists of 20 items that ask for physical symptoms and body experiences and have to be rated using a 5-point scale (*not at all* to *extremely*). This scale includes three questions (having trouble/pain while urinating, I feel pain in my genitals) which might lead to some relationship of the whole scale with the pain factor of the Birmingham IBS scale. Still, most of its 20 questions are unlikely to produce larger correlations with any measure of gastrointestinal symptoms such as Item 15 with "It is as if my body, or a part of it, has disappeared" ([32], p. 32)."

RE 00045410 No 1:
Would young individuals (mean age 25 years and 77% females) be representative of the true adult population?
Response: This is an important aspect. Therefore we now mention this point explicitly as a limitation of the study:
"Another limitation of this and other internet based studies is that the sample in not representative for the (German) population [50-51]."

RE 00045410 No 2: How was the sample size calculated?
Response: Unfortunately, we did not make a-priori power calculations to determine the optimal sample size for our study. In line with Loehlin (2004), who is cited in the manuscript (No. 35), we assume that the absolute minimum for an SEM is N = 100, better N = 200. Thus, although our model is quite complex we should be on the safe side with *N* = 875. Moreover, typical side-effects of low sample sizes such as overall bad fit indices (for any model) and convergence difficulties did not occur.

RE 00045410 No 3: The 3 disease specific questionnaires and their scoring could be added in appendices.
Response: We agree that the inclusion of the questionnaires in the appendix would be nice. Unfortunately, all questionnaires which were applied in the study are copyrighted by the respective Journals. In order to avoid any possible copyright issues which could occur with the Birmingham IBS scale that we applied in this study (which was originally published in the BMC gastroenterology Journal) we also removed the scale from the Appendix and refer to the BMC Journal website were the scale is available free of charge: "The original version of the scale can be downloaded from the BMC Gastroenterology Website (www.biomedcentral.com/content/supplementary/1471-230X-8-30-S1.pdf). The translation of the scale is available from the authors of this article upon request."

3 References and typesetting were corrected

4. Figures
As you request, we have attached the original Power Point and Excel files that we used to create Figure 1 and Figure 2.

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

Sincerely yours,

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