

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Is body mass index associated with symptom severity and health-related quality of life in irritable bowel syndrome? A cross-sectional study
AUTHORS	Dong, Yuanjun; Berens, Sabrina; Eich, Wolfgang; Schaefer, Rainer; Tesarz, Jonas

VERSION 1 – REVIEW

REVIEWER	Luca Neri Fresenius Medical Care, Italy
REVIEW RETURNED	13-Sep-2017

GENERAL COMMENTS	<p>Dr Yuanjun and colleagues explored the interplay between IBS severity and BMI with HRQOL. The research question is relevant because better phenotypical representations might enhance health-care practices. Nevertheless, I have concerns toward several methodological choices and the interpretation of results.</p> <ol style="list-style-type: none">1. The appropriate method to answer the research question is testing for BMI*IBS_severity interaction. Instead, the authors conducted a bunch on unrelated analyses that do not pertain to the research question. For example, sub-type analyses can be interesting, but they do not "speak" to the main aim of the study as declared.2. Despite adequate sample size, there is no adjustment for confounding. The authors collected information on potentially relevant confounders but they did not make any use of that.3. The choice of SF-36 as the only QOL tool is questionable. It is a generic tool which may partly miss the relationship between disease severity and HRQOL4. The discussion is somewhat speculative. The argumentative style is confused at times and the whole point of some sections is not clear. Which is the thesis? how the data support it? how it would fit with state of the art knowledge?5. Additionally, BMI is a very rough representation of many potentially important underlying concepts: fatty mass, dietary habit, other life-style factors such as physical exercise. All such concept might be important moderators of disease severity-> HRQOL relationship. This should be added in the limitation.
-------------------------	--

REVIEWER	Shanti Eswaran, MD University of Michigan, USA
REVIEW RETURNED	29-Oct-2017

GENERAL COMMENTS	The manuscript is well written and further describes the characteristics of IBS populations according to nutritional status as measured by BMI.
-------------------------	---

	<p>While this is welcome knowledge, the question remains is if this type of research is a priority for the journal given that these findings are not necessarily new, but do further characterize this population according to IBS subtype, etc.</p> <p>Re abstract- conclusion- does this really demonstrate that nutritional balance is disturbed in IBS patients? It does demonstrate the IBS subtype does not seem to associate with BMI, and that a higher BMI may have reduced QOL, but how does IBS play into this?</p> <p>The authors submit a well written manuscript describing the nutritional status as measured by BMI of 325 Western European IBS patients via a cross sectional study. They found that the prevalence of a higher BMI was slightly lower than that of the general German population, and that a lower physical QOL associated with a higher BMI. Is it known if the same is true in patients without IBS? The study would have been enriched with a healthy comparator (non-IBS) cohort.</p> <p>Specific comments: Introduction: Line 22-27. is there a reference that IBS subtypes have different eating habits?</p> <p>Discussion: Is it known if a higher BMI associates with a lower physical health in patients without IBS as measured by the SF36? if so, it would be helpful to mention this.</p> <p>page 12, line 7. "..general adult population in germany is higher" -- higher than what? higher than that found in the IBS cohort?</p> <p>page 13, line 2. I believe the authors mean "IBS " rather than IBD</p> <p>page 13, line 41. the last sentence in this paragraph is redundant.</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Luca Neri

Institution and Country: Fresenius Medical Care, Italy

1. The appropriate method to answer the research question is testing for BMI*IBS_severity interaction. Instead, the authors conducted a bunch on unrelated analyses that do not pertain to the research question. For example, sub-type analyses can be interesting, but they do not "speak" to the main aim of the study as declared.

Thank you so much for your interest and professional advice. In order to make the focus of the manuscript more precise, we delete the whole section of the relationship between IBS subtypes and pain. What's more, we include some additional hierarchical multiple regression analyses to help understand the impact of potential confounders. Therefore, all the related parts are rewritten including the analyses as well as the discussion.

2. Despite adequate sample size, there is no adjustment for confounding. The authors collected information on potentially relevant confounders but they did not make any use of that.

Thank you for your reminder. As what is mentioned above, hierarchical multiple regression analysis is added to understand the impact of potential confounders.

3. The choice of SF-36 as the only QOL tool is questionable. It is a generic tool which may partly miss the relationship between disease severity and HRQOL

Thank you for this comment. We fully agree that the SF-36 is a “generic” tool and thus, may partly miss specific aspects of the relationship between disease severity and HRQOL. However, the SF-36 is widely used and is well validated for assessing generic health outcomes. Validation of the German version was performed by Morfeld et al. We found that, many similar studies have chosen SF-36 scale as well. This proves that, this scale is appropriate for this type of research. The benefit of generic tool is that it makes easier for researchers to compare different studies horizontally. But we also agree with you that it would of course have been desirable to include more indicators, particularly those belonging to disease specific assessments of HRQOL, and we now point out this limitation on page 15.

4. The discussion is somewhat speculative. The argumentative style is confused at times and the whole point of some sections is not clear. Which is the thesis? how the data support it? how it would fit with state of the art knowledge?

Thank you for this comment. We have rewritten the discussion to structure the text more clearly now and to make the line of argumentation more precise. We also added several new references.

5. Additionally, BMI is a very rough representation of many potentially important underlying concepts: fatty mass, dietary habit, other life-style factors such as physical exercise. All such concept might be important moderators of disease severity-> HRQOL relationship. This should be added in the limitation.

As you pointed out, the reason we choose BMI is precisely because we think BMI is a comprehensive reflection of many influencing factors. But we highly agree with you that BMI cannot show everything. Therefore, we'd like to add this point into the limitations of the study as follows: “BMI can not fully reflect the impact of the factors of fatty mass, dietary habit, other lifestyle factors such as physical exercise on IBS and more research is needed.”

Reviewer: 2

Reviewer Name: Shanti Eswaran, MD

Institution and Country: University of Michigan, USA

1. Re abstract- conclusion- does this really demonstrate that nutritional balance is disturbed in IBS patients? It does demonstrate the IBS subtype does not seem to associate with BMI, and that a higher BMI may have reduced QOL, but how does IBS play into this?

Thank you so much for your interest and professional advice. Our research found that IBS patients with overweight or obesity may have reduced physical quality of life compared with the IBS patients in normal BMI level. And also, our data show that being overweight is a phenomenon in patients with IBS regardless of IBS subtype. That means, the distribution of weight was similar between the different IBS groups. What is worth noting is that the overweight and obesity rate in the general adult population in Germany is higher than that found in our IBS cohort.

Therefore, we'd like to change the previous conclusion into the following one: “Being overweight is a phenomenon in patients with IBS regardless of IBS subtype. Our findings emphasize that IBS patients with overweight or obesity may have reduced physical quality of life compared with the IBS patients in normal BMI level.”

At the same time, we will change the last sentence of this article into the following one: “The strengths of this study are firstly the use of a large patient cohort with a validated diagnosis of IBS based on the Rome III criteria. The findings from this study suggest that clinical doctors should pay special attention to abnormal weight in patients with IBS because this may be an indicator of a poorer quality of life with regard to physical health. Being overweight is a phenomenon in patients with IBS regardless of IBS subtype. This emphasizes that overweight and obesity are relevant factors in IBS, which may have a more selective influence on quality of life with regard to physical health.”

2. The authors submit a well written manuscript describing the nutritional status as measured by BMI of 325 Western European IBS patients via a cross sectional study. They found that the prevalence of a higher BMI was slightly lower than that of the general German population, and that a lower physical QOL associated with a higher BMI. Is it known if the same is true in patients without IBS? The study would have been enriched with a healthy comparator (non-IBS) cohort.

Thank you for this appreciative comment.

We highly agree with you. However, we don't have the data of the healthy comparator cohort until now. But we think, this is an important point for future studies.

3. Introduction: Line 22-27. is there a reference that IBS subtypes have different eating habits?

We thankfully notice that the background for this statement was not described sufficiently. We'd like to add several references as follows:

[4] Eswaran S, Chey WD, Jackson K, et al. A Diet Low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols Improves Quality of Life and Reduces Activity Impairment in Patients With Irritable Bowel Syndrome and Diarrhea. *Clinical Gastroenterology and Hepatology* 2017; 15:1817-1819.

[5] Spencer M, Chey WD, Eswaran S. Dietary renaissance in IBS: has food replaced medications as a primary treatment strategy?. *Current treatment options in gastroenterology* 2014; 12: 424-440.

[6] Kubo M, Fujiwara Y, Shiba M, et al. Differences between risk factors among irritable bowel syndrome subtypes in Japanese adults. *Neurogastroenterology & Motility* 2011;23: 249-254.

4. Discussion: Is it known if a higher BMI associates with a lower physical health in patients without IBS as measured by the SF36? if so, it would be helpful to mention this.

We respect and thank you for your comments, and we will conduct further research in this area for non-IBS patients.

5. page 12, line 7. "...general adult population in Germany is higher" --higher than what? higher than that found in the IBS cohort?

We thankfully notice that our phrasing was misleading. We mean of "higher than that found in the IBS cohort". We changed this sentence into the following one: "What is worth noting is that the overweight and obesity rate in the general adult population in Germany is higher than that found in our IBS cohort."

6. page 13, line 2. I believe the authors mean "IBS" rather than IBD.

This is a typing error; we have changed this accordingly.

7. page 13, line 41. the last sentence in this paragraph is redundant.

Thank you for pointing this out; we have changed this paragraph accordingly.

VERSION 2 – REVIEW

REVIEWER	Luca Neri Fresenius Medical Care Italia
REVIEW RETURNED	17-Dec-2017

GENERAL COMMENTS	<p>Thank you for the opportunity to review the revision of this manuscript.</p> <p>Although large improvements in the presentation of the results and in the flow of argumentation, I am still quite confused on the study research question(s) and their effective operationalization into an appropriate analytic strategy.</p> <p>In the abstract, the authors state that "The aim of this study was to explore the association between body mass index (BMI), symptom severity and health-related quality of life (QoL) in different subtypes of patients with irritable bowel syndrome (IBS)."</p> <p>This is quite generic of a statement, but some more specific assertion has been made in the introduction: "Therefore, the aim of this study is to determine the effect of BMI on IBS symptom severity and quality of life for each subtype of IBS based on the Rome III criteria."</p> <p>Finally, the authors begin the discussion section with the following,</p>
-------------------------	--

	<p>"The aim of this study was to determine the effect of BMI on the relationship between symptom severity and quality of life for IBS based on the Rome III criteria."</p> <p>Forgetting the complexities of ascertaining both such research questions with a cross-sectional design (e.g. reverse causality being the most obvious potential bias), these two last statements naturally lead to different analytic approaches. In the first case:</p> <ol style="list-style-type: none"> 1. A test of the association between BMI (independent variable) and Symptom Severity (dependent variable). 2. A test of the association between BMI (independent variable) and SF-36 (dependent variable). 3. A test of interaction between BMI (independent variable) and IBS subtype (moderator) on each one of the self-reported outcomes (severity, QOL). <p>In the second case:</p> <ol style="list-style-type: none"> 1. A test of the association between Symptom Severity (independent variable) and SF-36 (dependent variable). 2. A test of interaction between Symptom Severity (independent variable) and BMI (moderator) on QOL. <p>In any case, the analysis as performed by the authors did not address neither research questions as stated in the introduction or the discussion section.</p> <p>A second main concern in evaluating the paper is the use of multiple regression. It is not clear to me why potential confounders are entered individually (and then removed) into the regression equation. The large sample size allow including all important variables into the model and assess their independent contribution to QOL. In the same model, the appropriate interaction tests can be performed (depending on the research question, please be clear in this choice) while adjusting for confounding. This would be efficient, concise, and would minimized confounding bias given the set of available information.</p> <p>Minor Concern: please revise the manuscript for misspelling, awkward sentences, repetition, grammatical errors.</p>
--	--

REVIEWER	Shatni Eswaran University of Michigan, USA
REVIEW RETURNED	06-Dec-2017

GENERAL COMMENTS	<p>The authors have attempted to address the reviewers' concerns, but the question remains- is this type of research a priority for the journal? Several design flaws in the study, as the authors point out, cannot be changed. The manuscript could benefit from several read-throughs to catch grammar and editing errors and to formalize the language. Finally, many of the references are incorrect and need to be checked (some are mentioned below).</p> <p>-----</p> <p>We thankfully notice that the background for this statement was not described sufficiently. We'd like to add several references as follows:</p> <p>[4] Eswaran S, Chey WD, Jackson K, et al. A Diet Low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols Improves Quality of Life and Reduces Activity Impairment in Patients With Irritable Bowel Syndrome and Diarrhea. <i>Clinical Gastroenterology and Hepatology</i> 2017; 15:1817-1819.</p> <p>[5] Spencer M, Chey WD, Eswaran S. Dietary renaissance in IBS: has food replaced medications as a primary treatment strategy?. <i>Current treatment options in gastroenterology</i> 2014; 12: 424-440.</p>
-------------------------	---

	<p>[6] Kubo M, Fujiwara Y, Shiba M, et al. Differences between risk factors among irritable bowel syndrome subtypes in Japanese adults. <i>Neurogastroenterology & Motility</i> 2011;23: 249-254.</p> <p>These references do not support that statement – the first study is in IBS-D patients only, then 2nd study is a review, and the third does not support the statement that ibs subtypes are associated with different eating habits. Please clarify or delete this statement.</p> <p>Page 5: And also the other way round: Underweight (BMI < 18.5 kg/m²) or obese body condition (BMI > 30 kg/m²) are both associated with multiple abdominal symptoms leading to reduced QoL [13, 14]. This could be changed to “in addition, underweight (BMI < 18.5 kg/m²) or obese body condition (BMI > 30 kg/m²) are both associated with multiple abdominal symptoms leading to reduced QoL [13, 14].”</p> <p>“Although extensive research has been carried out on the prevalence of obesity in the general population and in connection with numerous diseases, data on the prevalence and clinical relevance of nutritional status in patients with IBS are sparse.” This sentence is redundant with previous sentence in this paragraph.</p> <p>Reference 16 does not support that statement. That study references how to effectively measure patient reported outcomes in IBS</p> <p>“By the hierarchical multiple regression analysis, we found that in each hierarchy (gender, age, family status, education status, IBS subtypes and BMI), the significantly negative correlations between symptom severity and physical health were found.” This sentence needs to be rewritten.</p>
--	---

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Institution and Country: Fresenius Medical Care, Italy

1. The aim of the study is inconsistent, which leads to the main line of data analysis is not clear. In the abstract, the authors state that "The aim of this study was to explore the association between body mass index (BMI), symptom severity and health-related quality of life (QoL) in different subtypes of patients with irritable bowel syndrome (IBS)." This is quite generic of a statement. In the introduction, the authors state that "Therefore, the aim of this study is to determine the effect of BMI on IBS symptom severity and quality of life for each subtype of IBS based on the Rome III criteria." In the discussion section, the authors state that "The aim of this study was to determine the effect of BMI on the relationship between symptom severity and quality of life for IBS based on the Rome III criteria." These two last statements naturally lead to different analytic approaches.

Answers: Thanks for your kind advice. We agree that the different wordings are misleading and lack consistency. This is partly due to the additional analyses suggested by the reviewers. The primary

aim of this study is to describe the body mass index distribution in patients with irritable bowel syndrome based on the Rome III criteria, and to evaluate the association of BMI with symptom severity and quality of life. We now rewrote the respective sentences to improve the internal consistency and clarity of the manuscript!

2. A second main concern in evaluating the paper is the use of multiple regression. It is not clear to me why potential confounders are entered individually (and then removed) into the regression equation. The large sample size allow including all important variables into the model and assess their independent contribution to QOL. In the same model, the appropriate interaction tests can be performed (depending on the research question, please be clear in this choice) while adjusting for confounding. This would be efficient, concise, and would minimized confounding bias given the set of available information.

Answers: Thank you for this comment! To enter the potential confounders individually is a common strategy of Hierarchical multiple regression analysis [r1]. However, our mistake lies exactly in the mentioned point. The large sample size allows including all important variables into the model and assess their independent contribution to QOL. This would be efficient, concise, and would minimized confounding bias given the set of available information. In the revised manuscript, the hierarchical multiple regression was used to examine the relationship between the dependent variable (QOL) and the independent variables (symptom severity & BMI). In model 1, we included all confounders. In model 2, we added the symptom severity. BMI was added in model 3. For details, please see the revised manuscript.

Reference:

[r1] Tucker L A, Erickson A, LeCheminant J D, et al. Dairy consumption and insulin resistance: the role of body fat, physical activity, and energy intake. Journal of diabetes research 2015.

3. Minor Concern: please revise the manuscript for misspelling, awkward sentences, repetition, grammatical errors.

Answers: This manuscript was well edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English-speaking editors at American Journal Experts.

Reviewer: 2

Institution and Country: University of Michigan, USA

1. Several design flaws in the study, as the authors point out, cannot be changed. The manuscript could benefit from several read-throughs to catch grammar and editing errors and to formalize the language.

Answers: Thank you so much for your interest and professional advice. It could not be denied that, limitations are inevitable in any studies including cross-sectional studies. We should not simply negate the academic value of an article because of its limitations. It is a fact that, BMI was based on the self-

reported height and weight of patients, there is no reason that patients made those numbers up and bear no responsibility for their own health. There is no doubt that, the patients' self-report deserves our trust. At the same time, in the Nutrinet-Santé study, researchers reported that deviations in self-reported BMIs from questionnaires can be ignored because their results confirmed the validity and agreement of self-reported data with measured data. SF-36 is one of the commonly used scales of international clinical study containing relatively comprehensive QOL evaluation of subjects with good reliability and validity. BMI reflects the comprehensive performance including several factors such as genetics and diet. The clinical research often reports the relationship between BMI and certain diseases. Admittedly, it is equally important to study the inheritance. We will in the future study work with experts in genetics to deeper explore the associations. This manuscript was well edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English-speaking editors at American Journal Experts.

2. [4] Eswaran S, Chey WD, Jackson K, et al. A Diet Low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols Improves Quality of Life and Reduces Activity Impairment in Patients With Irritable Bowel Syndrome and Diarrhea. *Clinical Gastroenterology and Hepatology* 2017; 15:1817-1819. [5] Spencer M, Chey WD, Eswaran S. Dietary renaissance in IBS: has food replaced medications as a primary treatment strategy?. *Current treatment options in gastroenterology* 2014; 12: 424-440. [6] Kubo M, Fujiwara Y, Shiba M, et al. Differences between risk factors among irritable bowel syndrome subtypes in Japanese adults. *Neurogastroenterology & Motility* 2011;23: 249-254. These references do not support that statement – the first study is in IBS-D patients only, then 2nd study is a review, and the third does not support the statement that ibs subtypes are associated with different eating habits. Please clarify or delete this statement. We apologize for the imprecise statement that, we have replaced the overall situation with the IBS-D study. It is beyond to me that the review article cannot be quoted here.

Answers: Considering the structure of the part of introduction, we decide to agree that, this part should be deleted. However, we'd like to revise the sentence as follows: The symptoms of IBS are associated with different eating habits [4]. In a randomized controlled trial, a diet low in FODMAPs can improve the IBS-D patients' QOL, anxiety, and activity impairment [5]. It has been frequently reported that IBS leads to impaired QoL [7-9]. So far, however, very little attention has been paid to the role of BMI and IBS subtypes on the relationship of symptom severity and QoL in IBS patients.

[4] Hayes P, Corish C, O'mahony E, Quigley EMM. A dietary survey of patients with irritable bowel syndrome. *Journal of human nutrition and dietetics* 2014; 27(s2): 36-47

[5] Eswaran S, Chey WD, Jackson K, et al. A Diet Low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols Improves Quality of Life and Reduces Activity Impairment in Patients with Irritable Bowel Syndrome and Diarrhea. *Clinical Gastroenterology and Hepatology* 2017; 15:1817-1819.

3. Page 5: And also the other way round: Underweight (BMI < 18.5 kg/m²) or obese body condition (BMI > 30 kg/m²) are both associated with multiple abdominal symptoms leading to reduced QoL [13, 14].

Answers: This could be changed to "in addition, underweight (BMI < 18.5 kg/m²) or obese body condition (BMI > 30 kg/m²) are both associated with multiple abdominal symptoms leading to reduced QoL [13, 14]."

We did as the suggestion.

4. "Although extensive research has been carried out on the prevalence of obesity in the general population and in connection with numerous diseases, data on the prevalence and clinical relevance of nutritional status in patients with IBS are sparse." This sentence is redundant with previous sentence in this paragraph.

Answers: Thank you for pointing out this repetitive statement due to our uncaredful proofing. This should be strictly prevented. The sentence is deleted.

5. Reference 16 does not support that statement. That study references how to effectively measure patient reported outcomes in IBS.

Answers: We have re-written the relevant paragraph for the sake of logic.

6. "By the hierarchical multiple regression analysis, we found that in each hierarchy (gender, age, family status, education status, IBS subtypes and BMI), the significantly negative correlations between symptom severity and physical health were found." This sentence needs to be rewritten.

Answers: We thankfully notice that this sentence sounds confusing and rewrote the sentence as follows: Through the hierarchical multiple regression, we tested the relationship between dependent variable (QOL) and independent variables (symptom severity & BMI). We excluded the impact of the confounders (gender, age, family status, education status & IBS subtypes). The correlation between symptom severity and QOL was significantly negative no matter which BMI level was. Our findings show that BMI was significant predictor of physical health of QOL. Patients with higher BMI were more frequently in poor physical health.

VERSION 3 – REVIEW

REVIEWER	Luca Neri Fresenius Medical Care - Italy
REVIEW RETURNED	12-Mar-2018

GENERAL COMMENTS	<p>1. There still are several awkward/wrong sentences. Just few examples:</p> <p>a. "We adjusted all the confounders" -> Better would be: "we adjusted FOR SEVERAL confounders"</p> <p>b. "Taking physical health into consideration, BMI and symptom severity significantly predicted the physical health of QOL" -> Better would be avoiding terms implicitly referring to causal or temporal pattern. The term PREDICT here is not correct because this is a cross-sectional study and there is no validation of the prediction in a test sample. The term ASSOCIATION is better in this context.</p> <p>c. "Being overweight is a phenomenon". This sentence reads awkward. Do you mean a COMMON/RELEVANT phenomenon?</p> <p>d. COMPARE WITH older patients (age > 50), the younger patients (age 18 - 49) reported significantly lower BMI level (t = -3.20, p < 0.01), worse symptom severity (t = 2.039, p < 0.05) and worse mental health (t = -2.528, p < 0.05).-> Do you mean COMPARED</p>
-------------------------	---

	<p>TO?</p> <p>e. Married or unmarried cohabitation patients were significantly higher in BMI level than single patients-> this is a convolute sentence. Maybe easier would be: "patients living with a stable partner had higher BMI compared to single participants."</p> <p>Many other can be found throughout the paper. Please, make sure that the manuscript is really edited by a professional medical writer.</p> <p>2. In the Results section, the narration of BMI, severity and QOL correlates is mixed together. This is really confusing. Please make sure that such descriptions are conceptually and graphically separated. It is important that the description of results would follow the logic of the underlying hypotheses. The authors aim at evaluating whether high BMI values and elevated symptom severity are associated with poorer QOL. The theoretical framework presented and the consequent analytic strategy implies that BMI and severity are IVs and QOL is DV. Please, make the narration consistent with this formal and conceptual structure.</p> <p>3. Subsection title: "the predictive role of BMI in physical health and mental health of QOL is misleading. There is no formal validation of predictive ability in the present manuscript. In fact, a statistical association is found and it should be reported as such</p> <p>4. The association of BMI with QOL is likely non-linear. Hence, including BMI as a linear IV may underestimate its association with the DV. Have you inspected the association of BMI categories (underweight, normal, overweight, obese) with DV? Alternatively, have you tried including higher order BMI terms in the regression equation?</p>
--	---

VERSION 3 – AUTHOR RESPONSE

The main responds to the reviewer's comments are as follows:

Q1. There still are several awkward/wrong sentences. Please, make sure that the manuscript is really edited by a professional medical writer.

Answer: Thanks for your kind advice. We did as the suggestion. We now rewrote the respective sentences and also, the manuscript was well re-edited for proper English language, grammar, punctuation, spelling, and overall style by a professional medical writer. For details, please see the revised manuscript.

Q2. In the Results section, the narration of BMI, severity and QOL correlates is mixed together. This is really confusing. Please make sure that such descriptions are conceptually and graphically separated. It is important that the description of results would follow the logic of the underlying hypotheses. The authors aim at evaluating whether high BMI values and elevated symptom severity are associated with poorer QOL. The theoretical framework presented and the consequent analytic strategy implies that BMI and severity are IVs and QOL is DV. Please, make the narration consistent with this formal and conceptual structure.

Answer: We thankfully notice that this sentence sounds confusing and rewrote the sentence as follows: Pearson product-moment correlations indicated that high BMI values and elevated symptom severity were associated with poorer QOL. As shown in Table 2, BMI was negatively correlated with physical health ($r = -0.177, p < 0.01$). Symptom severity was negatively correlated with physical health ($r = -0.394, p < 0.01$) and mental health ($r = -0.268, p < 0.01$). Additionally, age was negatively correlated with symptom severity ($r = -0.129, p < 0.05$) and positively correlated with physical health ($r = 0.167, p < 0.01$).

Q3. Subsection title: "the predictive role of BMI in physical health and mental health of QOL is misleading. There is no formal validation of predictive ability in the present manuscript. In fact, a statistical association is found and it should be reported as such 4. The association of BMI with QOL is likely non-linear. Hence, including BMI as a linear IV may underestimate its association with the DV. Have you inspected the association of BMI categories (underweight, normal, overweight, obese) with DV? Alternatively, have you tried including higher order BMI terms in the regression equation?

Answer: We agree that the term PREDICT here is not correct because this is a cross-sectional study and there is no validation of the prediction in a test sample. Under your suggestion, we tested the association of BMI categories (underweight, normal, overweight, obese) with QOL. The results shown that Model 3 was significant ($\Delta F = 4.605$, $p < 0.01$) and explained 3.7% of the variance in physical health. Obesity ($\beta = -0.177$, $p < 0.01$) was a significant negative factor that influencing physical health. However, BMI didn't account for an additional significant amount of variance in mental health ($\Delta R^2 = 0.007$, $\Delta F = 0.772$, $p > 0.05$). For details, please see the revised manuscript.