PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Social inequalities in aggravating factors of somatic symptom persistence (SOMA.SOC): study protocol for a mixed method observational study focussing on irritable bowel syndrome and fatigue
AUTHORS	von dem Knesebeck, Olaf; Barbek, Rieke; Makowski, Anna

VERSION 1 – REVIEW

REVIEWER	Saunders, Chloe Aarhus Universitet
REVIEW RETURNED	07-Mar-2023

GENERAL COMMENTS	This protocol proposes a large scale data collection effort, however the aims of this effort, and whether the study design will be able to address these aims, are not completely clear. I have three major points that can be addressed to help clarify the authors intentions. Major comments: 1. Based on the authors definition of the 'aggravating factors' they have isolated to study (illness beliefs, illness perception, treatment experiences, illness behavior, and health anxiety), hypothesis 1 and 2 (p7), read as the same. Correcting this may be as simple as a need to rephrase the second hypothesis to make it clearer that this relates (as I assume the authors intend) to public stigma towards health complaints expressed by different demographic groups. If this is the intended meaning of hypothesis 2, it is still unclear how results from this study will be integrated to test this hypothesis. To expand on this point: Detail is given in table 3 that the following measures will be captured in the telephone survey (relevant to hypothesis 2 as I assume it is intended to be meant) Illness Perception Questionnaire (brief version, IPQ-B)50 Illness belief E.g. "Do you think that the person in the vignette has a real disorder?" Emotional reactions towards those affected by IBS or fatigue Stereotypes ascribed to persons with IBS or fatigue Emotional reactions towards those affected by IBS or fatigue Modified version of the IBS Stigma Scale51 The authors also state that they intend to explore perceived stigma in the qualitative interviews (p10).

The protocol would benefit from some clarity in terms of the proposed analysis and integration of these results, i.e. on what grounds/terms is hypothesis 2 accepted or rejected? Or is it exploratory only. This relates to a need to describe and justify the study design overall (see point 3), which currently reads as two seperate studies without clear hypotheses or proposed methods of integration.

2. Although I see that data collection has already started, I would like the authors to address concerns that the current study design may paint only a partial picture, and indeed could obscure some important modifiable social determinants of PPS.

To expand on this point: Of the 5 potential ‘aggravating factors’ under focus: illness beliefs, illness perception, treatment experiences, illness behavior, and health anxiety, 4/5 are individualizing (i.e. locate responsibility within the individual). Although cultural and health literacy differences in symptom perception and interpretation are likely to play a role, it may be worth also thinking about other social determinants of health which also may have roles in PPS, like differential traumatic experiences (including ACEs and adult traumatic experiences which are common in refugee groups), or differential built environments (role of urbanization in symptoms). Social factors like these are theorized to have a direct causal impact on the body’s physiological systems, and may result in higher rates of persistent symptoms through mechanisms that are only partially mediated by psychological/cognitive factors. It would be at least worthwhile to consider, in a study concerned with social inequalities, to what degree the impact of social inequalities are mediated psychologically (the focus of this study) and how much are mediated through direct impact on physiology. Even without changing the data collected, authors could utilize causal inference models, attributing an ‘unknown’ factor (i.e. treating the examined 5 aggravating factors as mediating factors in a causal belief structure).

This could be one (statistical) approach to determining to what degree variance in PPS outcomes between SES/migration status, is mediated by the individualizing aggravating factors (+stigma) that have been proposed as the focus of study by the authors, and what proportion of the variance is not mediated by these factors. This would constitute a more comprehensive and helpful analysis of the social determinants of PPS. If the authors chose to continue with their current statistical approach, some exploration of this theme within the discussion could also mitigate concerns that modifiable social determinants of health that require socio-political action are unintentionally made invisible by this study design and selective focus.

3. Although this study is described as a mixed methods study, there is no clear methodology for how the data from the two study designs will be integrated.

Minor comments:

	1. In the sentence below (p3, abstract), It is unclear which of the list of factors will be depicted in the vignette, and which factors are being 'explored' through the telephone survey. With a vignette design depicting patients varying in sex, condition (IBS/fatigue), occupational status (low/high), and migration (yes/no), public knowledge and beliefs (e.g. health literacy), attitudes (stigma), and personal experiences with the condition (e.g. somatic symptom burden) will be explored. 2. This sentence: (p5) does not make sense to me. If the idea is to summarize in the current knowledge, the sentence should not contain both however and but. However, respective empirical studies mostly use sum scales comprising a number of symptoms but magnitude and mechanisms of inequalities may differ depending on symptom under study.

REVIEWER	Liao, Shih-Cheng National Taiwan University
REVIEW RETURNED	15-Mar-2023

GENERAL COMMENTS	1. This rigorously designed research plan combines quantitative and qualitative approaches, aiming to explore the impact of social inequalities on persistent somatic symptoms. The highly original study is expected to provide new scientific evidence for the sociocultural aspects of persistent somatic symptoms. 2. In the background, the authors provide a comprehensive literature review. However, the measurement tools corresponding to health inequity or social inequalities, these two social factors, need a more detailed description in the research methods section. 3. To verify health inequity due to social and economic status and migration, other factors linking migration experiences and somatic complaints should be considered. For example, in addition to the changes in socioeconomic status caused by migration, how emotional distress and somatic complaints are expressed in the culture in which the immigrant originally grew up is also a factor to be considered. It may even be a confounding factor that needs to be controlled. For example, in the past, when studying why the prevalence of depression was lower among Eastern populations, there was a theory of culturally determined response bias. (Compton et al. Am J Psychiatry 1991;148:1697-704.) 4. The study aims to explore the patterns of persistent somatic symptoms, focusing on irritable bowel syndrome (IBS) and fatigue. Generally speaking, in addition to IBS, chronic fatigue syndrome, and fibromyalgia (both of which have fatigue characteristics), pain-related problems and functional somatic complaints similar to those related to the urinary tract can also be considered. (Henningsen et al. Lancet 2007;369:946-55.) 5. The quantitative part of this study is to conduct a nationally representative telephone survey, which is a feasible research method but may require some methodological clarification. For example, the statistical power of the planned survey is described in the article. Still, it needs to consider the prevalence of the somatic complaints being investigated for complete power

	estimation, such as the prevalence of somatic symptom disorder defined by DSM-5, which is about 5% to 7%. In addition, to sample a sufficient number of immigrants in a nationally representative sample for hypothesis testing, a stratified multistage sampling design may need special treatment for oversampling.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

This protocol proposes a large scale data collection effort, however the aims of this effort, and whether the study design will be able to address these aims, are not completely clear. I have three major points that can be addressed to help clarify the authors intentions.

Thank you for the valuable comments and suggestions that helped to improve the study protocol!

Major comments:

1. Based on the authors definition of the 'aggravating factors' they have isolated to study (illness beliefs, illness perception, treatment experiences, illness behavior, and health anxiety), hypothesis 1 and 2 (p7), read as the same. Correcting this may be as simple as a need to rephrase the second hypothesis to make it clearer that this relates (as I assume the authors intend) to public stigma towards health complaints expressed by different demographic groups. If this is the intended meaning of hypothesis 2, it is still unclear how results from this study will be integrated to test this hypothesis. To expand on this point: Detail is given in table 3 that the following measures will be captured in the telephone survey (relevant to hypothesis 2 as I assume it is intended to be meant):

Illness Perception Questionnaire (brief version, IPQ-B)50

Illness belief E.g. "Do you think that the person in the vignette has a real disorder?"

Emotional reactions towards those affected by IBS or fatigue

Stereotypes ascribed to persons with IBS or fatigue

Emotional reactions towards those affected by IBS or fatigue

Modified version of the IBS Stigma Scale51

The authors also state that they intend to explore perceived stigma in the qualitative interviews (p10).

The protocol would benefit from some clarity in terms of the proposed analysis and integration of these results, i.e. on what grounds/terms is hypothesis 2 accepted or rejected? Or is it exploratory only.

Thank you for this comment. Following your suggestion, we rephrased the second hypothesis (p.6). Moreover, we added information on how the two hypotheses will be examined: "In terms of the first hypothesis, associations between social characteristics of the respondents and aggravating factors (e.g. illness and treatment experiences, illness behaviour, health anxiety) will be analysed, while for the second hypothesis, differences in perceptions, attitudes, and beliefs according to migration and occupational status of the person in the vignette will be examined.” (p.7) Further information on the data analyses that will be conducted to test hypothesis 2 is provided on p. 10. We also added information to clarify that the power calculation is explicitly related to hypothesis 2 (p.7).

2. Although I see that data collection has already started, I would like the authors to address concerns that the current study design may paint only a partial picture, and indeed could obscure some important modifiable social determinants of PPS. To expand on this point: Of the 5 potential ‘aggravating factors’ under focus: illness beliefs, illness perception, treatment experiences, illness behavior, and health anxiety, 4/5 are individualizing (i.e. locate responsibility within the individual). Although cultural and health literacy differences in symptom perception and interpretation are likely to play a role, it may be worth also thinking about other social determinants of health which also may have roles in PPS, like differential traumatic experiences (including ACEs and adult traumatic experiences which are common in refugee groups), or differential built environments (role of urbanization in symptoms). Social factors like these are theorized to have a direct causal impact on the body’s physiological systems, and may result in higher rates of persistent symptoms through mechanisms that are only partially mediated by psychological/cognitive factors. It would be at least worthwhile to consider, in a study concerned with social inequalities, to what degree the impact of social inequalities are mediated psychologically (the focus of this study) and how much are mediated through direct impact on physiology. Even without changing the data collected, authors could utilize causal inference models, attributing an ‘unknown’ factor (i.e. treating the examined 5 aggravating factors as mediating factors in a causal belief structure). This could be one (statistical) approach to determining to what degree variance in PPS outcomes between SES/migration status, is mediated by the individualizing aggravating factors (+stigma) that have been proposed as the focus of study by the authors, and what proportion of the variance is not mediated by these factors. This would constitute a more comprehensive and helpful analysis of the social determinants of PPS. If the authors chose to continue with their current statistical approach, some exploration of this theme within the discussion could also mitigate concerns that modifiable social determinants of health that require socio-political action are unintentionally made invisible by this study design and selective focus.

We totally agree with your remark and we are grateful for this idea that will advance our planned data analyses. Following your suggestion, we added the following sentence: “Furthermore, structural equation model approaches will be utilized to explore to what extent social inequalities in PSS are mediated by the aggravating factors under study and to what extent variance is mediated by other (unconsidered) factors.” (p.10)

3. Although this study is described as a mixed methods study, there is no clear methodology for how the data from the two study designs will be integrated.

We agree that this was missing in the protocol. Therefore, we added the following paragraph: “Integration of data of the two study parts will be feasible as there are overlaps in design (variation of social characteristics) and content of the survey/interview (please see assessment and study outcomes). To this end, results of the quantitative part will be triangulated with corresponding statements from the qualitative interviews.” (p. 10) Moreover, we added a reference (57) to provide an example on how this was done in a previous study in which we also used vignettes.

Minor comments:

1. In the sentence below (p3, abstract), It is unclear which of the list of factors will be depicted in the vignette, and which factors are being ‘explored’ through the telephone survey.

“With a vignette design depicting patients varying in sex, condition (IBS/fatigue), occupational status (low/high), and migration (yes/no), public knowledge and beliefs (e.g. health literacy), attitudes (stigma), and personal experiences with the condition (e.g. somatic symptom burden) will be explored.”

We rephrased the sentence and hope that it is clearer now (p.2).

2. This sentence: (p5) does not make sense to me. If the idea is to summarize in the current knowledge, the sentence should not contain both however and but.

“However, respective empirical studies mostly use sum scales comprising a number of symptoms but magnitude and mechanisms of inequalities may differ depending on symptom under study.”

We also rephrased this sentence (p.4).

Reviewer: 2

Comments to the Author:

1. This rigorously designed research plan combines quantitative and qualitative approaches, aiming to explore the impact of social inequalities on persistent somatic symptoms. The highly original study is expected to provide new scientific evidence for the sociocultural aspects of persistent somatic symptoms.

Thank you for the valuable comments and suggestions that helped to improve the study protocol!

2. In the background, the authors provide a comprehensive literature review. However, the measurement tools corresponding to health inequity or social inequalities, these two social factors, need a more detailed description in the research methods section.

We agree that this description was missing. Therefore we added respective information to the section “Assessment and study outcomes” (p.9) and added a reference (51) in which further details on the social inequality indicators are provided.

3. To verify health inequity due to social and economic status and migration, other factors linking migration experiences and somatic complaints should be considered. For example, in addition to the changes in socioeconomic status caused by migration, how emotional distress and somatic complaints are expressed in the culture in which the immigrant originally grew up is also a factor to be considered. It may even be a confounding factor that needs to be controlled. For example, in the past, when studying why the prevalence of depression was lower among Eastern populations, there was a theory of culturally determined response bias. (Compton et al. Am J Psychiatry 1991;148:1697-704.)

We totally agree that these are important factors for persistent somatic symptoms. In fact, this was one reason for integrating the qualitative part into the study and to include patients with and without migration background. Therefore, we expect these migration-related and cultural factors to be mentioned in the qualitative interviews with the patients. We are grateful for your comment and will consider these factors in the analyses of the qualitative data.

4. The study aims to explore the patterns of persistent somatic symptoms, focusing on irritable bowel syndrome (IBS) and fatigue. Generally speaking, in addition to IBS, chronic fatigue syndrome, and fibromyalgia (both of which have fatigue characteristics), pain-related problems and functional somatic complaints similar to those related to the urinary tract can also be considered. (Henningsen et al. Lancet 2007;369:946-55.)

We are sorry, this study is primarily focussed on aggravating factors of IBS and fatigue. However, as we will also measure the Somatic Symptom Scale (SSS-8) in the population survey (please see Table 3 in the manuscript), we will be able to analyse social inequalities in other somatic symptoms.

5. The quantitative part of this study is to conduct a nationally representative telephone survey, which is a feasible research method but may require some methodological clarification. For example, the statistical power of the planned survey is described in the article. Still, it needs to consider the prevalence of the somatic complaints being investigated for complete power estimation, such as the prevalence of somatic symptom disorder defined by DSM-5, which is about 5% to 7%. In addition, to sample a sufficient number of immigrants in a nationally representative sample for hypothesis testing, a stratified multistage sampling design may need special treatment for oversampling.

Our sample size calculation was related to the following two hypotheses: 1) SES and migration are associated with factors contributing to the symptom persistence (aggravating factors) of IBS and fatigue. 2) There are differences in public perceptions of and public beliefs about IBS and fatigue according to the SES and migration status of the afflicted person expressing the symptoms. Thus, power calculation was based on the vignette design (for details please see p.7). It is not the aim of this study to analyse (the prevalence of) somatic symptom disorder. We are sorry for this misunderstanding and hope that we were able to clarify this issue.

In terms of the number of respondents with migration background, we agree that this information was missing in the protocol and added the following statement: “In Germany, about 25% of the general population have a migration background. Accordingly, in our sample (N=2,400), we expect about 600 respondents to have a migration background.” (p.9) We consider this a sufficient sub-sample size to conduct analyses on differences in aggravating factors according to migration status.

We again would like to thank the editor and the reviewers for their comments and hope that we sufficiently addressed all concerns raised.

VERSION 2 – REVIEW

REVIEWER	Saunders, Chloe Aarhus Universitet
REVIEW RETURNED	04-Apr-2023

GENERAL COMMENTS

Dear Authors,

I am afraid I still have some concerns about how well thought through aspects of your proposed methodology is. As this is an important and socially relevant topic, with an expensive and time consuming data collection process, I suggest that more thought and reflexivity should be given to the exact way that conclusions will be drawn, with reference to the mixed methodology literature. The manuscript will also benefit greatly from restructuring and a careful review of the language/grammar to make it clearer for readers to follow what is being proposed.

Major points

1. I am still missing a convincing data integration methodology. I believe this would benefit from more thinking about, and perhaps a discussion with a colleague familiar with mixed methodology research.

To expand on this: the authors mention that results from the qualitative interviews will be 'triangulated' with quotes from the interviews along with reference '57'. I am still lacking the detail in this methodology, if they intend to use the methodology outlined in reference 57, please state this clearly, and outline again the method briefly for the readers benefit. What they propose at the moment, reads that they will cherry pick quotes that support their quantitative findings. This is not a scientific method, nor a particularly effective use of the large data collection effort proposed, and needs more thinking about. Please note, that when carrying out mixed methodology research you should maintain the standard of reflexivity of qualitative research, and there should be some statements about this.

Some helpful references to read on this topic might be:

Farmer, T., Robinson, K., Elliott, S.J., Eyles, J., 2006. Developing and Implementing a Triangulation Protocol for Qualitative Health Research. Qual. Health Res. 16, 377–394. https://doi.org/10.1177/1049732305285708
OR O'Cathain, A., Murphy, E., Nicholl, J., 2010. Three techniques for integrating data in mixed methods studies. BMJ 341. https://doi.org/10.1136/bmj.c4587

2. There is no justification for why these particular 'aggravating' factors are chosen. The thing that holds them all together is that they are individualizing psycho-social factors that may be relevant targets of psychological intervention.
The authors do present, in figure 1, an illustration of their overall model of symptom persistence. This is greatly helpful in that it shows how the factors examined here, fit into the larger picture. However this is not referred to in the text. It would be nice for example to highlight that focus is on socio-demographic predisposing factors and psycho-social maintaining factors, with direct reference to the figure. The authors can also then state that

they are not collecting data on psychosocial predisposing factors, triggering factors, or biomedical maintaining factors. It would be greatly helpful if the authors refer to this figure and position their work clearly within it. It makes it much clearer to the reader what the focus, as well as the limitations, of the work will be.

3. The methods section is very confusing, fragmented and poorly organised. Please note, this is a protocol, and should therefore be a step by step guide on how to carry out the research project. Please outline your method like this, so that it is clear in a practical manner what exactly you are planning to do.

Please restructure the whole methods section. I suggest the following headings (in bold) can be used (Optional of course). When you restructure make sure there is no redundancy, and that everything makes sense in the section it is in:

Study Design and Rationale This is where you should outline the methods. Please lay a very clear map for the reader as your study design is complicated involving 2 hypotheses that sit next to each other and 2 forms of data collection. This section should include the method by which you will use to integrate the different data types. The justification for choosing the methods can be included here (in brief).
Participants
-Population survey
-(Power calculation)
-Patient longitudinal interviews
Data collection
-Population Survey
(Vignette design, Structured interview guide/measures)
-Patient longitudinal interviews
(Semi-structured interview guide)

Data analysis and integration
-Quantitative analysis
-Qualitative analysis
-Mixed methods integration

Ethics and reflexivity

Minor Points

4. I am missing clarity in formulation of the relationships being explored. In part this is due to confusing use of language. For example:
Social inequalities in aggravating factors of PSS
This phrasing (p5 and similar) is not clear. The reason for this is that inequalities seems to relate to two objects in the sentence. Are the inequalities social inequalities, or are the inequalities in the aggravating factors? It is necessary to be clearer about the relationships that is being explored. For example the above sentence could be more clearly articulated as:
How are social inequalities associated with psycho-social factors that are known to be important in maintaining PPS.

5. The introduction would benefit from being cut in words, and structured as a simple narrative review. The authors should map the terrain for the reader but should only very carefully include

their own opinions at this stage. (It is a protocol, you don’t have results yet.)

For example compare this sentence:
However, hardly any of the studies included in these reviews specifically address PSS. Thus, overall, there are some studies indicating social inequalities in aggravating factors. However, research is fragmented and mostly not related to PSS.
P6

with
Among these aggravating factors are illness beliefs, illness perception, treatment experiences, illness behaviour, and health anxiety. It can be expected that these factors also play an important role for explaining inequalities in PSS p5

These two sentences appear to say very different things. We do not yet know whether these factors play a role, let alone an important role in explaining inequalities in PPS. We do not even know at this stage whether there are inequalities in PPS! It will not make me trust your research to think that you have already decided what you think your results will be. Keep more the tone of the top sentence. This is an accurate reflection of the state of knowledge.
The bottom sentence could be changed to (for example)
Among known psychological maintaining factors in PPS are health anxiety, treatment experiences, and illness beliefs, perception and behaviour. We expect that these factors may partially mediate any differences that might be seen in rates of PPS between those with differential socio-economic or migration status.

6. There are very many long sentences, some of which are grammatically incorrect, which impairs the readability. For example the following sentence:

With a vignette design depicting patients varying in sex, condition (IBS/fatigue), occupational status (low/high), and migration (yes/no), we will assess public knowledge and beliefs (e.g. health literacy), attitudes (stigma), and personal experiences with the condition (e.g. somatic symptom burden) in the survey.
This sentence needs to be 2 sentences. The first sentence about what you will assess with the vignette and the second sentence about how you will assess personal experiences with symptoms.
7. I would suggest changing ‘aggravating’ to a word that is more commonly used in the literature, such as maintaining. (Authors choice)

8. ‘To acknowledge their participation and compensate for expenses, each patient will
receive 15€ for each completed interview, the physicians will receive 50€ per patient included in the study.’

I do find this blatant inequality in the financial compensation somewhat ironic given the topic of the work. As an ethical and reflective researcher, I personally would consider the possibility of at least equalizing payments to 25 Euros each, or reflect on why this is not possible under the ethics and reflexivity part of the methods. (Authors choice)

REVIEWER	Liao, Shih-Cheng National Taiwan University
REVIEW RETURNED	06-Apr-2023

GENERAL COMMENTS	I am satisfied with the revisions and have no further concerns.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1:

Major points

1. I am still missing a convincing data integration methodology. I believe this would benefit from more thinking about, and perhaps a discussion with a colleague familiar with mixed methodology research. To expand on this: the authors mention that results from the qualitative interviews will be 'triangulated' with quotes from the interviews along with reference '57'. I am still lacking the detail in this methodology, if they intend to use the methodology outlined in reference 57, please state this clearly, and outline again the method briefly for the readers benefit. What they propose at the moment, reads that they will cherry pick quotes that support their quantitative findings. This is not a scientific method, nor a particularly effective use of the large data collection effort proposed, and needs more thinking about. Please note, that when carrying out mixed methodology research you should maintain the standard of reflexivity of qualitative research, and there should be some statements about this.

We revised the paragraph on the mixed methods integration (p. 11) and added a respective reference (new number 57, thank you for recommending this reference!).

It now reads:

"Mixed methods integration

Although data from both study parts are collected and analysed separately, they are seen as two complementing perspectives on social aspects that contribute to the symptom persistence of IBS and fatigue. In using these different approaches, we expect a better and more comprehensive understanding of inequalities in aggravating factors of PSS and how they are associated with patients' and the public's characteristics. Integration of findings of the two study parts will be feasible as there are overlaps in design (variation of social characteristics) and content of the survey/interview (please see assessment and study outcomes). The process of integrating findings from the two methods will take place at the interpretation stage when both data sets have been analysed separately. Accordingly, findings from the two components of the study will be listed in a "convergence coding matrix". [57] That means, it will be considered where results from the two study parts agree, offer complementary information on the same issue, or seem to contradict each other."

2. There is no justification for why these particular 'aggravating' factors are chosen. The thing that holds them all together is that they are individualizing psycho-social factors that may be relevant targets of psychological intervention. The authors do present, in figure 1, an illustration of their overall model of symptom persistence. This is greatly helpful in that it shows how the factors examined here, fit into the larger picture. However this is not referred to in the text. It would be nice for example to *highlight that focus is on socio-demographic predisposing factors and psycho-social maintaining factors, with direct reference to the figure. The authors can also then state that they are not collecting data on psychosocial predisposing factors, triggering factors, or biomedical maintaining factors. It would be greatly helpful if the authors refer to this figure and position their work clearly within it. It makes it much clearer to the reader what the focus, as well as the limitations, of the work will be.*

We now explicitly refer to figure 1 in the text and highlight that our focus is on sociodemographic predisposing factors and psychosocial maintaining factors (p.6).

3. The methods section is very confusing, fragmented and poorly organised. Please note, this is a protocol, and should therefore be a step by step guide on how to carry out the research project. Please outline your method like this, so that it is clear in a practical manner what exactly you are planning to do. Please restructure the whole methods section. When you restructure make sure there is no redundancy, and that everything makes sense in the section it is in.

We restructured the methods section and added subheadings (pp. 7-11).

Minor Points

4. I am missing clarity in formulation of the relationships being explored. In part this is due to confusing use of language. For example: Social inequalities in aggravating factors of PSS. This phrasing (p5 and similar) is not clear. The reason for this is that inequalities seems to relate to two objects in the sentence. Are the inequalities social inequalities, or are the inequalities in the aggravating factors? It is necessary to be clearer about the relationships that is being explored. For example the above sentence could be more clearly articulated as: How are social inequalities associated with psycho-social factors that are known to be important in maintaining PPS.

We revised the manuscript accordingly (p.5).

5. The introduction would benefit from being cut in words, and structured as a simple narrative review. The authors should map the terrain for the reader but should only very carefully include their own opinions at this stage. (It is a protocol, you don't have results yet.) For example compare this sentence: However, hardly any of the studies included in these reviews specifically address PSS. Thus, overall, there are some studies indicating social inequalities in aggravating factors. However, research is fragmented and mostly not related to PSS. (P6)

with

Among these aggravating factors are illness beliefs, illness perception, treatment experiences, illness behaviour, and health anxiety. It can be expected that these factors also play an important role for explaining inequalities in PSS (p5).

These two sentences appear to say very different things. We do not yet know whether these factors play a role, let alone an important role in explaining inequalities in PPS. We do not even know at this *stage whether there are inequalities in PPS! It will not make me trust your research to think that you have already decided what you think your results will be. Keep more the tone of the top sentence. This is an accurate reflection of the state of knowledge. The bottom sentence could be changed to (for example) Among known psychological maintaining factors in PPS are health anxiety, treatment experiences, and illness beliefs, perception and behaviour. We expect that these factors may partially mediate any differences that might be seen in rates of PPS between those with differential socio-economic or migration status.*

We revised the respective paragraph in the Introduction (p.5f.).

6. There are very many long sentences, some of which are grammatically incorrect, which impairs the readability. For example the following sentence: With a vignette design depicting patients varying in sex, condition (IBS/fatigue), occupational status (low/high), and migration (yes/no), we will assess public knowledge and beliefs (e.g. health literacy), attitudes (stigma), and personal experiences with the condition (e.g. somatic symptom burden) in the survey. This sentence needs to be 2 sentences. The first sentence about what you will assess with the vignette and the second sentence about how you will assess personal experiences with symptoms.

We revised the respective sentence in the Abstract and checked the manuscript for long sentences.

7. I would suggest changing ‘aggravating’ to a word that is more commonly used in the literature, such as maintaining. (Authors choice)

We would like to stick to the term “aggravating”, also because it is part of the project title which cannot be changed anymore. However, we now also mention “maintaining” as an alternative (pp 5,6).

8. ‘To acknowledge their participation and compensate for expenses, each patient will receive 15€ for each completed interview, the physicians will receive 50€ per patient included in the study.’ I do find this blatant inequality in the financial compensation somewhat ironic given the topic of the work. As an ethical and reflective researcher, I personally would consider the possibility of at least equalizing payments to 25 Euros each, or reflect on why this is not possible under the ethics and reflexivity part of the methods. (Authors choice)

We now more precisely point out that the patients will receive 15€ for each completed interview (i.e. 45€ for the three interviews) (p.9). Moreover, we point out that the approval of the Ethics Committee included financial compensations for patients and physicians (p. 11).

We again would like to thank the reviewer for the comments and hope that we sufficiently addressed all concerns raised.