Author's response to reviews

Title: Gastrointestinal symptoms before and during menses in healthy women.

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Author’s response to reviews:

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BMC Women’s Health

Dear Editor:

Re: MS: 1272433734908218
Research article
Gastrointestinal symptoms before and during menses in healthy women

Thank you for forwarding the specifics of the third reviewer’s requested minor edits. As you know, we previously replied to the other reviewers’ feedback in our response dated August 5, 2013. We have added our current changes to the revised manuscript that was submitted at that time, so the manuscript submitted now reflects the changes made in response to all 3 reviewers.

Reviewer 3 requested the following:
1. METHODS: please add a flow chart on subject recruitment.
Authors’ response:
Done; Figure 1 has been added following the tables, and is referenced on page 7 in the first paragraph of the results.

2. DISCUSSION: add a paragraph for “clinical implications of the findings of the study”
Authors’ response:
Done; we have added a paragraph on page 11 just prior to the limitations paragraph, which aims to complement the other information regarding general implications already discussed in this section.

Below I have copied the response to reviewers that we provided in our August
5th, 2013 correspondence, so that the responses to all the reviewer points are included in one document for your convenient review.

I trust that this information addresses the requested clarifications. Please let me know if any further information is needed. As our report is some of the only data available from healthy women about their experience of GI and emotional symptoms in these phases of the menstrual cycle, we appreciated the opportunity to improve the manuscript in order to facilitate dissemination of the information. We look forward to hearing from you.

Sincerely,

Lesley Graff PhD
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Reviewer 1:
1) A notable limitation of this paper is the use of a recall period over three menstrual cycles and the lack of any measure of severity. Prior research using daily diaries with symptom severity ratings have provided more useful data e.g., mild abdominal pain is not often clinically significant, but percent of time with moderate to severe symptoms often is.

Author’s response:
We agree a retrospective study design is not ideal, however it is often useful as a preliminary step to determine if there is potential ‘signal’ in order to proceed with a more in-depth prospective study, which was our intent here. As far as we are aware, there are very few daily diary studies in this area that have looked at this combination of symptoms, they tend to have small sample sizes, and/or only consider one cycle. Given the very preliminary understanding of the potential concurrence of GI symptoms, menstruation and mood symptoms, we were interested in assessing if women had noted any repeating patterns, which would require considering multiple recent cycles. Given the preliminary findings, the next step would be to track these symptoms prospectively with more detailed information on symptoms (including severity) and validated measures where available. In the discussion section, we had acknowledged the limitations related to retrospective design and lack of symptom severity measurement, and have briefly added to that by also stating that the validity of the survey was not established (pg 12).

2) I can appreciate the focus on the pre-menses and menses phase, but it is hard to know what that means outside the context of the whole menstrual cycle or at least the other menstrual phases. The use of a design with minimal burden does not equal useful data.
Authors’ response:

Prior clinical experience suggested that some women had observed gastrointestinal symptoms just before or during menstruation (i.e., not during ovulation or post-menstrual), and of course mood changes just before menstruation have also been established in the clinical literature, so this is why we focused on these points in the menstrual cycle. Additionally, many women are not readily able to reliably identify the timing of other phases in their cycle (e.g.,) ovulation, so for this retrospective study we focused participants on menstruation and provided a specific definition for the premenstrual phase as well (i.e., 5 days prior to onset of menses).

3) The term emotional or psychological symptoms might be better choice of terms to describe the symptoms of depression, anxiety and ‘other emotional symptoms’ than as mood symptoms.

Authors’ response:

We have adjusted the terminology to emotional symptoms from mood symptoms throughout the manuscript.

Reviewer 2:

Major Compulsory Revisions:
Introduction:
- The last paragraph of the Introduction section (page 4) is too confusing. For example, the sentence of the second line says: “this healthy sample of women served as a control group in that study”. It would be helpful if authors rewrite this paragraph.

Authors’ response:

This paragraph has been revised (see pg 5) and hopefully the content is now more clearly expressed.

Material and Methods:
- Please explain about the sociodemographic characteristics of the sample.

Authors response:

Only age and sex were collected as sociodemographic information. All participants were female; the age descriptors are already presented in the first paragraph of the Results section. The standard deviation has been added to this description and the mean/sd have been deleted from Table 1 as per the comment below regarding the table 1 title. We have also added a brief descriptive sentence to the Methods section, participant subsection: “Individuals from a range of socioeconomic backgrounds attend these clinics given universal access for health care”.

- Those women with any GI diagnoses were excluded, but what about women
with PMS or psychiatric disorders? My concern is that the objective of the research was to study healthy women. If authors did not control this variable, they should comment about it in the limitations of the study.

Authors’ response:
This was an oversight in our report. Active psychiatric disease, including depression, anxiety including panic disorder, schizophrenia and PTSD, was also an exclusion criteria and this has now been clarified in the Abstract and Methods.

- I understand that there are no questionnaires to measure GI symptoms in the premenstrual or menstrual phases, but there are questionnaires that measure emotional symptoms such as depression, anxiety and others. Therefore, it should be clarified why the authors did not use one of these questionnaires.

Authors’ response:
Our focus for the current study was to identify the presence of a range of symptoms, emphasizing GI symptoms and including any self-identified depression or anxiety. It was felt to be most parsimonious to use the same response format for each of the symptoms queried for ease of response and comparison. Existing depression and anxiety measures often have a specified time frame, include items on multiple symptoms that may have been confusing or less relevant in this context (e.g., appetite, energy), and many of those measures were validated with the goal of identifying a clinical disorder which was not the intent here. We did not want to give more weight or attention to one type of symptom over another by asking multiple detailed questions about depression symptoms for example, and only single item questions about GI symptoms. However, we have acknowledged in the discussion that our measure was not validated, and that future work may benefit from including validated measures of the variables of interest including depression and anxiety (see response to reviewer 1, point 1 above and page 12 in manuscript).

- Please add the reliability of the questionnaire that was developed, as well as the details about how it was designed. Was it tested before the current study?

Authors’ response:
There is some information in the Methods section already regarding how the content of the questionnaire was identified. The measure was piloted, and brief information about the survey piloting is now included in the Method section (see pg 6).

- The statistical analyses section is too confusing. Please clarify it.

Authors’ response:
In order to improve clarity, we have created a section entitled “Outcomes” describing the main outcomes of interest, and have amended the statistics section to focus on the nature of the statistical testing performed. Essentially, Fisher’s exact test was used for all 2x2 comparisons of proportions for tables 2, 3
and 4 (i.e., abdominal pain yes/no and depressive symptoms yes/no; abdominal pain yes/no and menstrual cycle premenstrual/during menses) as proportions not means were being compared in all cases. The results reported in the tables were streamlined to just indicate the proportion where the GI symptom was present (e.g., abdominal pain-yes/depressive symptoms-yes; abdominal pain-yes depressive symptoms-no; abdominal pain-yes menstrual phase-premenstrual; abdominal pain yes/menstrual phase-during menses).

Results:
- It is not clear which were the statistical tests used to compare the data described on page 7 (first, the authors compared premenstrual vs. menstrual phases. Then, they compared women with vs. without emotional symptoms. So, two different statistical tests should be used).
Authors’ response:
As explained in the preceding point, all comparisons were for proportions not means, and as such Fisher’s exact testing was used to assess any differences in proportions between groups. There were two different types of groupings we used to consider relationships: a comparison of proportions of women reporting various symptoms during premenstrual vs menstrual phases, and a comparison of proportions of women reporting various GI symptoms comparing those with concurrent emotional symptoms versus those without, looking separately at premenstrual and then during menses phases. Fisher’s exact test is understood to be the best approach to analysis for those types of proportional comparisons, regardless of the type of grouping.

Minor Essential Revisions:
Results:
- The titles of both Tables are wrong.
The title of the Table 1 says “Characteristics Related to Menstrual History”, and the table contains the current age of participants.
The title of the Table 2 says “Proportion experiencing GI and mood symptoms”; it should say “Proportion of PARTICIPANTS who...” or “Proportion of WOMEN who...”
Authors’ response:
We have removed the age of participants from Table 1; we have added ‘of women’ to the title of table 2

-There are some repeated results in the text and in the Table 2 (for example, the proportion of women who reported depressive symptoms).
Authors’ response:
The information in the text was intended to highlight and emphasize some of the findings for the reader, with information on all the variables assessed available in
table 2.

- The p value is not enough; please add the values of the tests and the degree of freedom.

Authors’ response:

We have clarified in the prior section (stats/analysis/results reviewer query) and in our manuscript text that the statistical analysis used for all the comparisons of proportions in the tables was Fisher’s exact test. Given that there were not differing types of analyses for the tables, we felt it was most parsimonious to just report the p values. The degree of freedom for any exact test comparing two groups is one, thus it can be safely assumed for these comparisons and as such we felt it would be repetitive to include. However, we have revised the tables to remove all instances of p “>0.2” and provided instead the precise p-value.

Reviewer 3

Minor essential revisions

Authors’ response:

In the reviewer report provided to us, there was no direction from the reviewer regarding which minor essential revisions were to be addressed, and as such did not seem to be anything specific to respond to here. If there is anything specific the reviewer would like us to address over and above what the other reviewers have identified, we will be happy to respond. Given the long period this manuscript was under in submission (> 6 months), we wanted to respond and resubmit in a timely manner. THIS HAS NOW BEEN ADDRESSED; SEE BEGINNING OF LETTER