Reviewer's report

Title: Predictors of persistent symptoms and reduced quality of life in treated coeliac disease patients: a large cross-sectional study

Version: 2 Date: 9 March 2013

Reviewer: Fredrik Norström

Reviewer's report:

General comment
The authors have well taken care of my previous issues. Below is my response to the issues that I still think can/should be improved. I have kept the headers (major, minor and discretionary revisions) of the parts from my previous request of revisions to make it easier to comment on the responses from authors. I consider all my new requests (including the one for other reviewers request) as minor or discretionary revisions.

Reviewer #1
Major compulsory revisions
Method section:
2. The criterion # 1 SD is used to define both increased gastrointestinal symptoms and a reduced health-related quality of life. It is not well motivated why this criterion is used. You refer to studies by Häuser, Zeltzer and Wilt. The papers by Häuser and Zeltzer (no knowledge about Wilt as it was not easily accessible on internet) have not explicitly stated why they chose this criterion. Even if it was well motivated by them, there is still a lack of information as why this criterion is feasible for GSRS and PGWB, as they have used different measurements in their studies (also the case for Wilt). I have not used GSRS or PGWB myself. For that reason I have no recommendation on methods for analyses of these measurements. Your analysis method might be a good alternative. Thus, I do not dismiss the criterion used in the paper, but it needs to be better formulated why it has been used. If you lack good references you should try to motivate, and defend, the choice of criterion in the discussion section.

Response: The aim was to identify subjects with persistent symptoms clearly disturbing their daily life. Hence, we decided to use this fairly objective cut-off value used also in previous studies. It is true that evidence supporting the method is somewhat limited but, as shown in previous response, it turned out to be quite accurate. This issue has now been further discussed as suggested (see page 11, paragraph 1, lines 9-13) and two new references have been provided (references 43 and 44).

Reviewer: My interpretation of the sentence “Nonetheless, it seemed that the proportion of control subjects with increased symptoms was similar to that
previously seen in the general population [43, 44]" is that the references have shown that GSRS and/or PGWB have shown similar results for control subjects as in your paper. Neither of these measures was used in these references. My other possible interpretation is that you want to show that the proportion of control subjects with problems is similar in references as in your study. If so, there is a lack of information about the rate of control subjects with problems in your study and that information needs to be added if so. My concern in previous review round has been taken care of without this statement. You can therefore decide to either remove the sentence or rewrite it.

Result section

4. The mean totals and ranges are specified for cases and controls, but not the SD. Add the value of SD so that the threshold values for high GSRS and low PGWB are available in the paper. Currently it is not even possible to guess the thresholds. I also want it to be specified in the methods section if SD is derived based on cases and/or controls. Currently it is only said that it is 1 SD higher than the control mean. My interpretation is that SD is derived based on controls.

Response: The requested threshold values have now been provided (see Methods, page 5, paragraph 3, lines 9-11 and page 5, paragraph 4, line 6 to page 6, paragraph 1, lines 1-2).

Reviewer: After some thinking I figured out that 2.55 is the threshold for the total GSRS score as it corresponds to the control mean (1.9) + 1 SD (0.66). I suggest that the text is rewritten so that this is easier to understand for the reader. The problem is the same for the description of the threshold value for PGWB.

Discussion:

6. No information about case criterion, i.e. # 1 SD higher or lower, in Table 2 and Table 3. These tables are based on comparing cases and non-cases and this information is too important to not include.

Response: This information has now been provided (see Tables 2 and 3, footnotes).

Reviewer: The suggested improvement is well done. I have another concern regarding these tables that I failed to notice in previous revision round. There is no information in any of the tables about how many that is in each row, i.e. how many has had symptoms for 10 years or less and so on. This is relevant information for the reader. It would also be valuable if the percentage of e.g. participants with psychiatric disease was mentioned in these tables.

Minor Essential Revisions

Background:

6. Row 8-9 at page 7. You show that both the group <10 years and >10 years with symptoms have worse health-related quality of life than those without symptoms. You have written “long duration of symptoms”, which needs to be corrected as both short and long duration give evidence of a worse health-related quality of life according to Table 3.


Response: This issue has now been clarified (see Results page 8, paragraph 1, lines 3-5).

Reviewer: OK. However, grammar needs to be improved. Which instead of with at line 3?

Discretionary Revisions

2. You replace missing with mean value of the item for PGWB and GSRS. How do you motivate this? Maybe it might be an alternative to replace with median values instead?

Response: Both values have been used in the literature, but it is true that in this case use of median would be more logical. However, in our study only a few answers were missing, and this change had no impact on the results whatsoever.

Reviewer: I think that you well motivate the choice of mean values. Thank you for the clarification.

3. At start of the discussion section you refer to more symptoms being shown by Cranney et al. They have not defined symptoms in a similar way as your paper as far as I can interpret it. Is your statement valid? It is also hard to compare with Midhagen et al as they seem to lack a definition on how they define symptoms in their paper. They do report a higher proportion though with same measurement as yours.

Response: This problem has now been further discussed as suggested (see Discussion, page 8, paragraph 2, lines 2-5).

Reviewer: Updated text is good enough for me. However, I suggest that you rewrite the sentences to get a better flow in the text.

Reviewer #2

3) Result section (page 7, line 9): It would be useful for the reader to define the nature of gastrointestinal co-morbidities responsible for persisting symptoms in treated coeliac disease. As stated in the discussion, irritable bowel syndrome is probably a frequent cause, but what about gastro-esophageal reflux disease, which, based on literature data, has been found in 66% of coeliac patients (Barratt SM, Eur J Gastroenterol Hepatol 2011)? The Authors should specify the nature of gastrointestinal co-morbidities and their relative occurrence in determining the persistence of symptoms in treated coeliac disease.

Response: More detailed information for the gastrointestinal disorders has now been provided (see Results, page 7, paragraph 2, lines 6-8).

Reviewer: You have stated “2% diverticulos (2%)” at row 7. 2% has accidently been mentioned twice in this statement. I suggest that “(2%)” is removed from the statement.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests