Reviewer's report

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

Version: 1 Date: 10 December 2012

Reviewer: Fredrik Norström

Reviewer's report:

General comment

This is a well-written and interesting paper. The authors have performed a study in which they attempt to find factors that explain persistent symptoms and a reduced health-related quality of life despite a strict gluten-free diet. Few studies have previously looked into this topic and the paper contributes with valuable new information. The results from the study can therefore potentially help to identify groups that are in need of more help with their disease after diagnosis. It is also highly interesting that the authors conclude that early diagnosis is one of the crucial parts to improve things for coeliac disease patients. This is in line with many previous studies and highlights the importance of finding ways of detecting the disease earlier.

Major Compulsory Revisions

Method section:

1. The selection of controls must be better described. Now it is unclear how, and where, they were chosen so that they could be comparable with the coeliac disease subjects. The reader needs to be informed about the criteria for being selected as a control. If the only criterion was the currently mentioned (about no first-degree relatives with coeliac disease), it needs to be specified that no actions were taken regarding similarities between the populations in terms of e.g. home district, age and sex. Depending on what is added to the method section it is also likely that the limitations of the comparability between the coeliac disease and the control population need to be mentioned in the discussion 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.

3. The factors that are tested for a relation with both increased gastrointestinal
symptoms and a reduced health-related quality of life are not defined in the
method section. Some of the factors included in Table 2 and Table 3 might be
easily understood, but some of them are harder to judge on. The reader should
be informed about definitions in method section, and at least the less obvious
ones should be clarified also in Table 2 and Table 3.

For instance, I am unsure about how duration of symptoms is measured from the
article. It seems obvious that it was collected from the interview, and I also think
that it is measured from first experienced symptoms to diagnosis. It is also
unclear if you have asked about any symptom or if you have listed a few
symptoms. There is as well as a lack of definition to what group those with
exactly 10 years duration of symptom belong (it is possible with exactly 10 years
of symptom, isn’t it?). The definition of this factor might be the most unclear, but
there are also other variables where the definition is not clear.

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.

Discussion:

5. Page 9, paragraph 2. You mention that coeliac patients showed reduced
health-related quality of life while on a gluten-free diet. There is no such evidence
in the paper. You only present mean PGWB total score for study group and
controls. I suggest that you add such comparison for both GSRS and PGWS in
the result section and also specify the test for such comparison in method
section. I assume that such a test will give you evidence for your statement.

Tables:

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.

Minor Essential Revisions

Abstract:

1. “Patients with extraintestinal presentation at diagnosis had fewer current
symptoms”. Specify who you are comparing to.
Background:

2. You have written “even well-treated coeliac patients have often failed to attain well-being similar to that of the population in general”. Besides Hallert [1998] and Usai [2007], that you refer to, I can only identify Häuser [2006] that have shown this for quality of life, while Casellas [2008], Gray [2010], Kolsteren [2001], Nachman [2009], Norström [2011], Tontini [2011], van Koppen [2010], and Zarkadas [2006], have all shown similar quality of life between coeliac disease patients and the general population. For other issues related to well-being have comparisons rarely been done with persons without coeliac disease diagnosis. My interpretation is therefore that this sentence needs to be rewritten.

3. The main aim of the paper is to find predictors for poorer health-related quality of life in those with coeliac disease. You have referred to Kurppa [2011]. It would add value to the paper if you mentioned the most notable of these factors already in the background section, and then with most focus on the ones you chose to look at yourself.

Method section:

4. On first occasion that you use SD write the word in full form. I am unsure if the standard deviation at individual level or the standard deviation for the mean (commonly called standard error of the mean) is used for comparisons. If the standard error of the mean is used is SD not a proper short form as it is generally referred to the standard deviation at individual level. Could be worth giving both the standard deviation and the threshold value in result section to avoid any doubts on the definition of it.

Result section:

5. Second row at page 7, “food intolerance and gastrointestinal or any” should be “food intolerance, other gastrointestinal disease, and any”, or a similar phrasing.

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.

Discussion:

7. At top of page 10 you write “well-defined study cohort”. As also mentioned later in same paragraph you admit a limitation in your selection, which potentially could cause a selection bias. This contradicts the phrasing “well-defined”. Are you referring to members of your cohort having a well-defined coeliac disease diagnosis? If that is the case you should rewrite the sentence or else you reasonably should remove the word “well-defined”.

Tables:

8. Specify in table 2 and table 3 that you have used bivariate logistic regression.
References:
9. Add dots to surnames also for other authors than Mäki, e.g. Ström and Grännö.

Discretionary Revisions
1. Some of the references in the background section are a bit out of date. I think that the authors should consider updating with more recent and relevant references.

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?

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.

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.