Reviewer's report

Title: An Italian prospective multicenter survey on patients suspected of having non-celiac gluten sensitivity

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Reviewer: Knut E A Lundin

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The paper by dr. Volta and colleagues describes a prospective effort to evaluate the frequency of non-celiac gluten sensitivity (NCGS) in a multi-center national setting. It is impotant that such efforts are undertaken, because adoption of a restricted diet has gained considerable proportions in the Western population. In the study, a total of 12255 patients were assessed. They found a possible NCGS diagnosis in 3.19% of their patients, compared to a celiac disease diagnosis in 2.77% of their patients. Although interesting, there are some comments to be made:

1. It is unclear if the total number of patients (12255) represent the total number of patients seen in the time period by the participating centres. Were these patients from the endoscopy lists or from consultation lists - or maybe both?
2. It is unclear if the study was done by dedicated clinicians taking part of the study or if this is a summary of all the activity by a number of clinicians. Obviously, this could influence the results.
3. Data on the questionnaire used is missing. Thus, it is difficult to evaluate the data validity.
4. A definition of the criteria for giving the patients a NCGS diagnosis is missing. It is not stated if the centres were monitored from the study organizers as part of the study.
5. It is stated that many NCGS patients were considered to have irritable bowel syndrome, but it is not stated that this diagnosis was made after Rome criteria. I further miss data on gastrointestinal symptom severity (e.g. by GSRS).
6. The frequency of CD patients could be biased because of positive serology taken by the general practionaires. This could explain much of the high frequency of CD diagnosis in the children. Did they collect data on prior serology?
7. The data on other immune disorders and biochemical alterations in the NCGS group is interesting and should be highlighted.
8. The text is rather long and would improve from being shortened. However, the discussion is good and the authors make a number of good observations.
9. It is stated that a short-coming of the paper is that a blinded challenge was not done in all patients. Was it done at all? Any data?
10. They advise the readers to do a 6-week challenge to rule out coeliac disease in NCGS patients. This is a long challenge and more recent guidelines and
papers suggest that a shorter challenge can be performed. The role of HLA typing in this setting should be mentioned. It was reported that coeliac disease is infrequent among NCGS patients (Brottveit et al 2011). Similar data exist from Italy (Biagi et al). This could be mentioned.

11. The figures would improve from better lay-out.

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

None