December 22, 2012

The Editor
World Journal of Gastroenterology

Re: Nora B Zschau, Jane M Andrews, Richard H Holloway, Mark N Schoeman, Kylie Lange, William C E Tam, and Gerald J Holtmann Gastroesophageal reflux disease after diagnostic endoscopy in the clinical setting, **ESPS Manuscript NO:** 1212

Dear Editor,

Thank you for considering our manuscript for publication in the *World Journal of Gastroenterology*.

We greatly appreciate the reviewers' comments and suggestions. We have incorporated the suggested changes and clarifications into the revised manuscript and sincerely believe that this has considerably strengthened our manuscript.

Please find below a point by point-response to the reviewers' comments and the revised manuscript in Word format.

Sincerely yours,

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ESPS Manuscript NO: 1212

The authors appreciate the comments and suggestions provided by the reviewer and we would like to respond as follows:

(1) "This study revealed greater tobacco use in patients with non-erosive or grades A and C esophagitis, not grade B and D esophagitis. ."

This observation is based upon the post-hoc data analysis. Thus it needs to be independently confirmed until firm conclusions can be drawn with regard to this point. However, we have addressed this is the revised discussion.

(2) Regarding: "Patients with a BMI>30 kg/m2 had greater improvement in SSS at both two and six months, and advantaged social status and unemployment were both associated with a greater improvement in symptom severity over time. Why? Please discuss in the text."

While this finding is based upon a post-hoc analysis and also requires independent prospective validation, it is reasonable to assume that a BMI > 30 increases reflux of acidic content into the esophagus. Thus inhibiting acid secretion would reduce esophageal acid exposure and improve symptoms. We have explained this in the revised discussion.

3. References and typesetting were corrected

Reviewer 2:

The Author appreciate the valuable comments of reviewer 2 and we would like respond as follows

Selection criteria and number of patients recruited:
The selection criteria are outlined in the methods section of the manuscript. Essentially all patients with GERD as the primary reason for the endoscopy were suitable for inclusion. Thus more than 1001 patients qualified.
However, consistent with most clinical trials a considerable proportion of patients declined to participate or could not participate for various reasons. However, characteristics of patients included into the study were not different from patients not included. Thus our finding and conclusions appear to be relevant for the whole populations. We have discussed this in the revised version of the manuscript.

PPI refractory patients:
As outlined in the Methods section, patients' referred for the endoscopic assessment of GERD were included. Since PPI are now in the clinical setting widely used it is reasonable to assume that a considerable proportion of patients were PPI-non responders. This indeed could explain the persisting symptoms during the follow-up. However, the fact that in GERD patients with symptoms severe enough to warrant endoscopy there is a only modest improvement of symptoms is remarkable and contradicts the very effective control of symptoms found in most clinical trials.

Clinical experience of the endoscopists and the instruments used.

All endoscopists were board certified with more extensive experience in diagnostic and therapeutic endoscopy. State of the art (Olympus) equipment was used. This has been revised in the methods section.

6- months follow-up

The reviewer stated 'In a real-life situation no patient will to choose to be observed for 6 months without some intervention e.g. exclude the intake of ulcerogenic medications'. We completely agree with the reviewer. Indeed, all patients were treated as deemed appropriate by the responsible consultant or referring physician. Thus this study captured the 'normal' course of disease in the clinical setting and it might be interesting to note that in spite of highly potent drugs a considerable proportion of patient continued to have symptoms.