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# ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 32793

**Title:** Modified Helicobacter Test Using a New Test Meal and a 13C-Urea Breath Test in Helicobacter Pylori Positive and Negative Dyspepsia Patients on Proton Pump Inhibitors

**Reviewer's code:** 03009765

## COMMENTS TO AUTHORS

In this paper the Authors evaluated the efficacy of modified Helicobacter test using a new test meal in Helicobacter pylori positive and negative dyspepsia patients on proton pump inhibitors. The Authors conclude that the new test meal based 13C-UBT is highly accurate in patients on PPIs and can be used in those unable to stop their PPI treatment. Major and minor criticisms can be done: Major criticism: 1) The patient sample treated in this study is small Minor criticism: 1) The Discussion is longer and of not easy lecture

**Answers:**

Due to very stict exclusion criteria ( listed below ) it was not easy to find proper patients for the study. The main problem was to find patients who did not take PPI in the 4 weaks prior to enrolment in the study. Our statistitian dr. Jörg Schnitker calculated sample size based on previous experience with the modified UBT for *H. pylori* infection.[14] This experience showed a sensitivity of at least 90 % after 29 days of PPI medication. Although rare cases of false positive breath tests may occur in *H. pylori* negative patients, if other urea active bacteria than *H. pylori* such as Proteus mirabilis or Staphylococcus aureus colonize gastric lumen in patients with extensive atrophy or intestinal metaplasia.[15] However, specificity of 90 % was still assumed. With a sample size of 43, a two-sided 95 % confidence interval for a single proportion using the large sample normal approximation would extend 9 percentage-points from the observed proportion for an expected proportion of 90 % (width of the 95 % confidence interval of 18 %). With a sample size of n = 43 *H. pylori* positive patients and n = 43 actual *H. pylori* negative patients, sufficient precision for assessing sensitivity

and specificity was expected. The actual sample sizes chosen to be used in the study were slightly larger (*H. pylori* positive: 63 in ITT population, 53 in the PP population; *H. pylori* negative: 51 in ITT population, 49 in PP population).

**Exclusion criteria:**

- Previous Hp eradication therapy.
- Intake of PPI, H2 receptor antagonists, NSAIDs, antibiotics, antisecretory drugs, bismuth compounds, or sucralfate in the 4 weeks prior to enrolment.
- Manifest coagulopathy or any other disorder according to which endoscopy and/or biopsies are contraindicated.
- Participation in a clinical trial with another not approved drug within 30 days before entering the study and/or previous participation in this study.
- Pregnancy

We add exclusion criteria to the manuscript.

The discussion section is not an easy lecture, we agree.

But it has to be written in that way to be able to explain rather complicated nature of H pylori urease activity. H pylori urease is essential for H pylori survival in the stomach and has also a great implication on UBT results at different stomach pH levels and at different H pylori colonisation density. We tried to explain with the data from relevant literature why the new test meal can overcome some limitations of conventional UBT with low dose citric acid meal at the condition of low H pylori colonisation density in patients on PPI therapy.