

October 14, 2013

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Dear Editor,

Please find enclosed the edited manuscript in pdf format (file name: WJG-5679 PROBIOTICS AND H. PYLORI-revised).

Title: Probiotics for the treatment of *Helicobacter pylori* infection in children

Authors: Lucia Pacifico, John Frederick Osborn, Enea Bonci, Sara Romaggioli, Rossella Baldini, Claudio Chiesa

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5679

The manuscript has been improved according to the suggestions of reviewers:

Reviewer # 02536311

1. As suggested by Reviewer, we have added references for the association of *H. pylori* with family size, clustering, low socioeconomic status and education (new references # 2-5) and renumbered all references to coincide with these inclusions;
2. Reviewer is concerned about the sentence that "spontaneous eradication is rare in children". As suggested, we have discussed some studies including those from Mexico addressing this issue: "It is commonly thought that once the *H. pylori* infection is acquired, it evolves toward persistent chronic infection^[6] and that spontaneous clearance is relatively rare. However, in a study of children in which prevalence by age was reported in intervals of 1 year, no increase in prevalence by age was observed. This suggests that transient *H. pylori* infection is not uncommon in children. In 6- to 24-month old children in Mexico, and Texas, researchers found 80% spontaneous reversion of the infection. In a very recent study involving 718 schoolchildren in Mexico City, Duque et al. found that the majority of them maintained their initial status of *H. pylori* infection throughout the follow-up, while 11.7% showed changes in their infection status. Variables related to health status and infection transmission, such as iron status and number of siblings, were shown to be important for the incidence of *H. pylori* and the spontaneous clearance of infection;
3. We included a forest plot (Figure 1) of the seven trials which compared an antibiotic with the same antibiotic plus probiotic. Even though the heterogeneity test was not significant (presumably due to the relatively small sample sizes), given that different antibiotic combinations doses and duration of treatment and different probiotics were used, we do not consider it appropriate to perform a formal meta analysis even though we have included the overall estimate of the odds ratio in the forest plot.

Reviewer # 00074172

1. As suggested by the Reviewer, we have changed the sentence "clarithromycin plus amoxicillin or metronidazole" to read "amoxicillin plus clarithromycin or metronidazole";
2. Also this Reviewer is concerned about the sentence that "spontaneous eradication is rare in children". Thus we have discussed further this issue (please see our response to item # 2 of Reviewer # 02536311);
3. We have modified the sentence "Of the 132 *H. pylori*-positive children withdrew in the beginning because they did not like the cheese" to read "Of the 132 *H. pylori*-positive children, 28 withdrew in the beginning because they did not like the cheese.

Reviewer # 00068184

As suggested by the Reviewer, we have shortened the manuscript, in particular the manuscript's sections "Utilization of probiotics in association with antibiotics in the treatment of *H. pylori*" and "Utilization of probiotics alone", in order to avoid repeated information in text and table.

Reviewer # 00058744

No revision required by this Reviewer

Reviewer # 00503623

No revision required by this Reviewer

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,
Lucia Pacifico, MD



Department of Pediatrics,
Sapienza University of Rome, Viale Regina Elena, 324
00161-Rome, Italy.

E-mail: lucia.pacifico@uniroma1.it

Telephone: +39-06-49979215 Fax: +39-06-49979216