

## **Point by Point response to Reviewers:**

**Reviewer 00504581**

### **COMMENTS TO AUTHORS**

the editorial is very good , but the reader is waiting for more concrete advices to introduce and apply in their clinical practice At the conclusion, it would be more clear to find a more nitid author's statement about to quit PPI treatment in patients with normal risk of upper gastrointestinal bleeding and some clinical relevant event of LGB experienced before . I would hope some statement about adding probiotics in these patientes with PPI , and which kind of them

**Reply:** We thank the comments made by the reviewer. In conclusions we have added a statement concerning the recommendation not to prescribe PPI treatment in patients with normal risk of upper gastrointestinal bleeding who experienced previous lower gastrointestinal bleeding event. In these patients it is clear that if PPI treatment is not indicated it should be avoided because it may increase risk of lower gastrointestinal bleeding. In any case, we consider that more data are needed to make a strong recommendation. We have also added a statement about the administration of probiotic and which strains should be a good candidate to test in these patients.

**Reviewer 00503883**

### **COMMENTS TO AUTHORS**

Awesome review article. Only minor spelling adjustments are needed.

**Reply:** Thank you for the comments about our manuscript. As you suggest we have submitted the manuscript to an external editing service.

**Reviewer 00159592**

**COMMENTS TO AUTHORS**

1. Comprehensive review of PPI and lower GI bleed 2. A lot of spelling and grammar errors 3. Some sentences do not make sense for example last sentence in page 7 - "Due to the intrinsic nature of observational studies, the finding was explained as probably due to a confounding by indication effect". The authors may want to rewrite to make it clearer what they are trying to get at

**Reply:** Thank you for the comments about our manuscript. We have submitted the manuscript to San Francisco Edit. An external editing service that has provided useful work to us in the past. We have rewritten the sentence that you highlighted in the comments in order to make it clearer. We agree with this comment and explain that the correlation between proton pump inhibitors (PPI) treatment and lower gastrointestinal bleeding (LGB) in observational studies could be explained by a "confounding by indication" bias. PPI use could be a marker of a group of patients that have an increased risk of LGB because of their clinical characteristics rather than the PPI use itself.

**Reviewer 03476034**

**COMMENTS TO AUTHORS**

This is a well and expertly written editorial on an extremely interesting subject. This reviewer has no comments other than that the editorial would benefit from proofreading by an English native speaker.

**Reply:** Thank you for the comments about our manuscript. As you suggest, the manuscript have been revised and proofreaded by an English editing service.