

## **Answer to reviewers**

Dear Editor

We thank all of the reviewers for their careful read and thoughtful comments on our previous draft. We have carefully taken their suggestions into consideration in preparing our revision, which resulted in a paper that is clearer and more meaningful. The way we responded to our reviewers' comments are shown below.

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** Comments: Very good comments in that "letter to the editor" No comments from my side, just minor revision regarding spelling mistakes "these regimen" should be replaced by "these regimens", needs English editing

Response: We thank reviewer 1# for his/her comments. English were edited by an experienced native speaker of English who is experienced in medical translation

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This is a thoughtful commentary on the previously published article that raises several interesting points. The authors suggest several additional factors that might contribute to the so-called post-colonoscopy syndrome (e.g. visceral distension, microbiome, etc.) but might want to also include references for each of these factors linking them to visceral pain for the reader's benefit. In addition, there is a substantial literature linking repetitive deformation of the gut mucosa to signaling in the mucosa itself with presumably consequent changes in the gut. It might be worth citing this literature and raising the possibility here that the over-distension of the colon that occurs with colonoscopy might itself induce changes in the gut mucosa. See for instance *Metabolism* 2002 Dec;51(12):1525-7. doi:

10.1053/meta.2002.36303. and Cell Signaling. 2009 Aug;21(8):1237-44. doi: 10.1016/j.cellsig.2009.02.011.

Response: We thank the 2<sup>nd</sup> reviewer for his/her thoughtful comments. Among the factors that we induced for the future assessment of the pathophysiology of post colonoscopy syndrome, the 2<sup>nd</sup> reviewer induced an additional factor that can also contribute to the development of this entity. We agree and we incorporated this factor in our letter.

Reviewer #3:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The authors indicated some points of improvement in the article by Di Leo et al. Each indication was appropriate and beneficial for both authors and readers. I expect further discussion about agents for bowel cleaning for colonoscopy in this journal.

Response: We thank the 3<sup>d</sup> reviewer for his/her thoughtful comments. We definitely agree and we added more information about the bowel preparation agents in our letter to the editor.

Sincerely yours,

On behalf of the authors

Konstantinos Argyriou