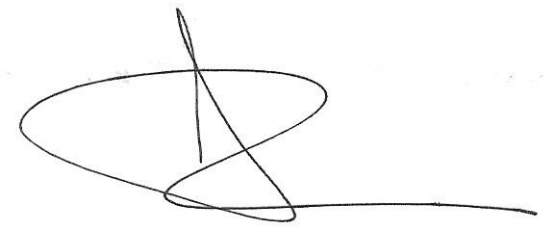
Ourense, 27th June 2021

Dear Editor

We appreciate the opportunity to provide a revised version of the manuscript entitled “Faecal immunochemical test, FIT outside colorectal cancer screening?” (World Journal of Gastroenterology Manuscript NO: 66572).

The revised manuscript has been modified to reflect the very helpful comments provided by the reviewers. Our responses are outlined in this cover letter (blue) and incorporated in the revised manuscript (red). On the other hand, we have made further changes to include recently published evidence of the utmost relevance: Pin et al. Gut 2021, Chandrapalan et al. Alim Pharmacol Ther 2021.



Best wishes,

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In this report, the authors discuss the feasibility of FIT for screening CRC and monitoring after adenoma resection, demonstrating the value of FIT in primary healthcare and surveillance after adenoma resection. I think this part has important significance. However, there are still many problems to be solved urgently:

1. FIT is still affected by hemoglobin degradation and intermittent bleeding, as well as poor compliance of FIT. Please indicate the possible impact of these deficiencies on primary healthcare screening.

The first point I would like to address is that the topic of the article is NOT colorectal cancer screening. We are discussing to relevant topics. The first one is the evaluation of symptomatic patients, in no case colorectal cancer screening as long as these patients are not asymptomatic. The second one is surveillance after adenoma resection. With respect to evaluation of symptomatic patients, compliance has little effect as long as we are using FIT as a mere diagnostic test. With respect to the limitations regarding hemoglobin degradation and intermittent bleeding we have not extended on this topic as long as there is a large amount of bibliography on CRC screening. However, we have provided information regarding hemoglobin concentration and number of determinations (*3.Does one sample with a cut-off point of 10 μg Hb/g of faeces fit everybody?)*

2. FIT screening is used in patients with lower abdominal symptoms in the cited literature[9, 10], please specify whether abdominal symptoms include upper abdominal symptoms in the report. If included, please specify the significance of FIT in patients with upper abdominal symptoms.

We have included a paragraph in the section 2.Accuracy of faecal immunochemical tests to detect significant colonic lesions and gastrointestinal cancer in the patient with abdominal symptoms.

3. This report only compares the advantages and disadvantages with previous screening methods, without comparing new screening methods, such as multi-target fecal DNA (mt-sDNA) test (Cologuard) and plasma SEPT9 DNA methylation test (EpiproColon).

We are aware of the evidence regarding Cologuard, EpiproColon and Colofast in CRC screening. We have not made any reference to this tests because there is no evidence of these tests on the evaluation of symptomatic patients. However we have included a section entitled “Combination of FIT with other non-invasive biomarkers in patients with abdominal symptoms” where we include the available evidence on the combination of other non-invasive tests with FIT.

4. There are some unnecessary abbreviations, such as AA-Advanced adenoma.

I have eliminated the abbreviation and have checked for any other unnecessary one.

5. The paper needs further proofreading. The text contains some language errors (such as singular and plural problems, lack of subject or predicate, etc.), which are sometimes difficult to understand. I suggest further polishing the language of the paper after modifying the content of the paper.

Although it was reviewed by a native speaker, we have performed an additional proofreading and we have polished the language of the paper.