Revised (Invited) Manuscript Submission Letter

From,

Ms. Michelle Viscaino, Mr. Javier Torres Bustos, Dr. Pablo Muñoz, Dra. Cecilia Auat Cheein, Dr. Fernando Auat Cheein.

To, Prof. Subrata Ghosh

Editor in Chief of the World Journal of Gastroenterology

Dear Sir,

Following your invitation to contribute with your prestigious Journal, we would like to present our revised manuscript entitled **Artificial intelligence on early detection of colorectal cancer: a comprehensive review on its advantages and misconceptions,** for your review and appraisal for publication. The invitation was made last October 22nd, and the invitation ID was 05395415 (free of fees). The invitation letter is included in file 65087supplementary material.

We would like to thank you for this opportunity. In the current manuscript form, we included all the Reviewer's suggestions as well as Editor's comments. Briefly,

- We discussed the importance of imaging quality in detecting flat polyps and included recent applications of artificial intelligence that involve contrast imaging/Chromoscopy.
- As required by the Reviewer, we clarified the text about the contribution of artificial intelligence in polyp classification.
- We updated the format following the guidelines and requirements of your Journal.

All changes are in **blue** text in the revised manuscript. We state that the manuscript is an original work. We also declare that the manuscript has not been published previously or submitted concurrently elsewhere. Below are the details of the corresponding author.

Thanking you,

Fernando Auat Cheein.

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Reviewer #1

Scientific Quality: Grade A (Excellent) Language Quality: Grade A (Priority publishing) Conclusion: Minor revision Specific Comments: Artificial intelligence on early detection of colorectal cancer: a comprehensive review on its advantages and misconceptions Viscaino et al., This is a very detailed and well written review on this interesting and important topic. I have 2 comments for the authors.

We would like to thank the Reviewer for the time spent on the review and we appreciate his feedback.

 Table 3 mentions white light and NBI - but otherwise there is no mention of developments in contrast imaging/ Chromoscopy - could they authors comment on quality of imaging and how this might help with detection of flat polyps - alongside AI developments

We sincerely thank the Reviewer for such a comment. We included a paragraph describing the chromoscopy and how it is a technique that helps the physician in detecting small-size or flat polyps. The discussion also includes both dye-based chromoendoscopy and virtual chromoendoscopy, as well as their advantages and disadvantages from an artificial intelligence perspective. The added paragraph is placed in section "Enhancing colonoscopy outcomes via Artificial Intelligence". We also included some necessary references. All changes, including added references, are highlighted in blue.

2. "The latter is particularly important because it allows the clinician to differentiate between a benign, pre-malignant and malignant polyp to decide whether it requires removal or not." At the moment - though you can have suspicions about polyps - you can only confirm if they are malignant once they are removed and pathology performed. It would be a goal to be able to do this and have AI to help with this diagnosis in real time - but if the authors could just clarify we are not at this point yet - this is the aspiration.

We thank the Reviewer for such comment. As recommended by the Reviewer, we changed the text (in Section "Enhancing colonoscopy outcomes via Artificial Intelligence ") to clarify that it is an aspiration that artificial intelligence can assist the physician in real-time in the differentiation of benign, pre-malignant, and malignant polyps, as follows:

"The latter is particularly important because it would allow the clinician to make a better decision as to whether or not to remove the polyp depending on it seems a benign, pre-malignant, or malignant polyp. Currently, to confirm if a polyp is malignant, the suspected polyp must be removed and then perform a pathology test. However, an expected advance in the future is that artificial intelligence can assist the clinician in differentiating polyps."

Science editor:

1. Scientific quality: The manuscript describes a Minireviews of the Artificial intelligence on early detection of colorectal cancer. The topic is within the scope of the WJG. (1) Classification: Grade A; (2) Summary of the Peer-Review Report: This is a very detailed and well written review on this interesting and important topic. Authors should mention about developments in contrast imaging/ Chromoscopy. The questions raised by the reviewers should be answered; (3) Format: There are 4 tables and 2 figures; (4) References: A total of 78 references are cited, including 17 references published in the last 3 years (2019 2020 2021); (5) Self-cited references: There are 1 self-cited reference.

Thank you very much for your comments. We have modified our manuscript according to the peer-review report.

2. Language evaluation: Classification: Grade A. 3 Academic norms and rules: No academic misconduct was found in the Bing search.

Thank you very much for your comments.

3. Supplementary comments: The study was supported by Chilean National Agency for Research and Development. The topic has not previously been published in the WJG.

Thank you very much for your comments.

4. The "Author Contributions" section is missing. Please provide the author contributions.

We included "Author Contributions" section in the final version of the manuscript.

5. The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

The article is an invited manuscript (we attach the invitation letter as 65087-Supplementary Material), with an initial ID 05395415 (free of fees). Chilean National Agency for Research and Development (ANID) supported the study through the grant for doctoral students. We upload the grant as 65087-Funding Agency Copy. However, we kindly ask not be published with the manuscript as it contains sensitive personal information. 6. The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (5) Please obtain permission for the use of picture(s).

We prepare separate documents to upload both tables and pictures to the system in the required format (65087-Table File and 65087-Image File respectively). The pictures are ours and have not been published elsewhere.

We sincerely thank the Reviewers and Editor. Their comments have further improved our work.