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Editors-in-Chief

World Journal of Gastrointestinal Oncology

Dear Editors:

I would like to resubmit our manuscript, now titled “**Trends of colorectal cancer incidence according to an increase in the number of colonoscopy cases in Korea**” for publication in the *World Journal of Gastrointestinal Oncology*.

My coauthors and I would like to thank you for taking the time to consider our article for publication. We appreciate the detailed suggestions provided by reviewer. We have responded to each comment point-by-point and have incorporated all of suggested modifications in the revised manuscript. Changes in the revised manuscript are highlighted with yellow color.

The manuscript has certainly benefited from the insightful comments that we received.

We do hope that it is now acceptable for publication in the *World Journal of Gastrointestinal Oncology*. Our point-by-point responses to the reviewer's comments can be found below this letter.

Sincerely,

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Reviewer's comments

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: Accept. This paper evaluating the trend in incidence of CRC and preinvasive CRC according to the number of colonoscopies performed in Korea, suggesting that diagnosis of preinvasive CRC has increased with an increase in the number of colonoscopies performed, it was also found that colonoscopy-related complications over age 76 could be reduced if early lesions at risk of developing colorectal cancer were diagnosed and treated under age 75. The manuscript is of good quality and has a guiding effect on colonoscopy screening.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is an interesting article, but I have comments mentioned below:

1- Please add a degree of freedom for each p-value.

Response: Thank you for the detailed point. We performed Cochran-Armitage trend tests to detect each trend in binomial proportions across ordered age groups. Since the test focuses exclusively on the presence of a trend, it utilizes a degree of freedom of 1 in the chi-squared test. We added a degree of freedom for each trend test in Supplementary Table 2.

2- Can your results apply to developing countries?

Response: The number of young colorectal cancer patients has been increasing in developing countries recently, projected to continue over the next decade. However, in low-and middle-income countries, CRC is often presented at a more advanced stage even in younger patients due to lack of awareness and screening programs (*Challenges in the management of colorectal cancer in low- and middle-income countries. Cancer Treat Res Commun. 2023;35:100705*). Therefore, our results can apply to developing countries.

3- Despite advances in screening programs, artificial intelligence, awareness, and endoscopic resection of superficial GI tumors, why the incidence of colorectal cancer is in

creasing?

Response: As you commented, the incidence of not only CRC but also early-onset CRC (diagnosed in patients <50 years of age) has been steadily increasing worldwide without an obvious cause. It may usually be associated with the development of screening methods and treatment techniques, and with life-style factors such as obesity, smoking, physical inactivity, and the frequency of red meat intake.

4- Which age and stage of colorectal cancer is prevalent in your study and why?

Response: We followed the patients using insurance claim data and confirmed the results on the incidence of CRC and preinvasive CRC with disease codes (ICD-10 codes). Therefore, it was difficult to use information on the stage of CRC in each patient. We discussed this limitation in the Discussion section.

It was found that the incidence of CRC was high among aged 50-75 years in this study. This is because screening of CRC is mainly performed on people aged 50-75 years.

5- Is there a role of diet and lifestyle in the increasing incidence of CRC?

Response: Several studies reported that dietary intake of a person, nutritional status and physical activity have shown to be associated with pathogenesis of CRC and suggested to be associated with poor outcomes (*Colorectal cancer and nutrition. Nutrients. 2019 Jan 14;11(1):164*). Although the specific causes underlying the increasing incidence of CRC and preinvasive CRC remain elusive, there is a role of diet and lifestyle in increasing incidence of CRC and preinvasive CRC.