The University of Oklahoma
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Wasaburo Koizumi, MD, PhD, Hsin-Chen Lee, PhD, Dimitrios Roukos, MD, PhD
Editors-in-Chief, World Journal of Gastrointestinal Oncology

Dear Drs. Koizumi, Lee and Roukos.

Below please find point-by point responses to the reviewer's comments. Our responses are in *italic* and in yellow within the text of the revised manuscript. We believe that all concerns have been addressed.

Comments to the Author:

Reviewer #1: I have no further comments on this well written manuscript.

We appreciate the reviewer's comment.

Reviewer #2: This is a very important clinical question; the aims of the study are clearly of high relevance. Comments; 1. The only major comment is the relatively small cohort size, therefore interpretation of the results should be realistic, and the study as such should be interpreted as a pilot 2. Moreover it is somewhat controversial that patients after declining to consent for colonoscopy were not offered any alternative methods, some of these although could be explained by financial reasons, but in the discussion authors should clearly list this as a limitation and give insight on how the program could be improved by offering alternative methods in referral where the subject declines endoscopy.

We understand the reviewer's concerns. The issue of small cohort size is addressed in the conclusion as follows: CRC-S referrals significantly increased with patient initiated prompting of physicians for such screening. Larger investigations, using this method, directed towards increasing acceptance of CRC-S are warranted. We have included the following statement in the discussion regarding alternative screening methods after declining endoscopy: A limitation to the present study is not using other screening methods available if colonoscopy is declined. As colonoscopy was considered the test of choice and other methods, if positive, result in colonoscopy referral, use of alternative screening tools appeared redundant to the investigators. However, some individuals may prefer colonoscopy only following a positive results from another screening tool and this should be considered in larger scale investigations.

Reviewer #3: This is a well constructed study, of high clinical significance. It seems that it is sufficiently powered to detect pre-specified 25% difference in referral frequency, but in my opinion this sample size is not sufficiently enough to portray independent predictors resulting in declining referral between insured and underinsured patients. Inclusion criteria for CRC-S

are not provided. Some of the results are given for first time in the discussion e.g.: First, college education were more prevalence in patients with medical insurance coverage (43% vs. 11%)….. The most important issue is the lack of a logistic regression model that would unmask independent predictors for referral reject between insured and underinsured patients.

We appreciate the reviewer comments and have included the following statement in the methods for CRC-s inclusion criteria: Those patients meeting criteria for screening but never having been screened previously were considered eligible for the study. The reviewer is incorrect regarding results initially presented in the discussion. Please refer to second paragraph of results as well as table 1 and figures 2-4 for details. Univariate and logistic regression were performed and are found in table 2. In addition, the following text was added to the results: In univariate analysis, factors related CRC-S referrals were having insurance (60% vs. 46%, p=0.045), male gender (38% vs. 54%, p=0.027), knowledge of CRC recommendations (46% vs. 26%, p=0.0085) and patients initiated promoting of PCP (intervention) (58% vs. 18%, p<0.0001). On multivariate logistic regression analysis, male gender (OR=0.49, 95% CI 0.26-0.93, P=0.03) and patient initiated promoting the PCP (OR=6.3, 95% CI 2.9-13.2, p<0.0001) were identified as independent predictors (table 2).

Reviewer #4: The manuscript is interesting conceptually. The intervention is educating patients to educate their primary care provider about screening colonoscopy. This makes sense and forms the basis to increase public awareness of effective screening for cancer. If a patient initiates the discussion about cancer screening, it seems intuitive that the provider will act upon the prompt. On the other hand, it appears that providers are less efficient about recommending screening for colorectal cancer if not prompted by their patients.

We appreciate the reviewer's comment.

Reviewer #5: Interesting concept of the study. In is interesting to know the level of residences of two groups, gender, and age. Can you perform additional analysis according to this paramenters?

We appreciate the reviewer's comment. Please see the response to reviewer 3 for details.

Reviewer #6: Major 1. It is very important issue that only 60% of eligible patients are screened for CRC-S in the US. However, it is also easily expected that prompting of physicians promotes screening referrals. Although the authors selected two types of clinic, results were almost same except financial affordability. 2. It seems to be effective to giving pamphlet, but its contents are important. The authors should describe about pamphlet in detail. 3. Unfortunately, it is though that there is little significance of this study because acceptance rates from referrals did not increase.

We appreciate the reviewer's comment. The pamphlet was adapted from published ACG guidelines listing all available screening methods but preferring colonoscopy as the method of choice. A statement indicating the contents of the pamphlet has been included in the methods as follows: The pamphlet discussed colon cancer incidence, frequency, deaths, prevention, need for screening, risk factors, symptoms, available screening methods with colonoscopy preferred based on ACG guidelines. It is also attached for review.

Thank you again for publishing our work in the World Journal of Gastrointestinal Oncology.

Respectfully yours,

Kenneth J. Vega, MD
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