

ANSWERING REVIEWERS

Feb 21, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format
(File name: Flex-Sig MA FINAL R1 02-21-14 cleancopy.doc)

Title: Reduced incidence and mortality from colorectal cancer with flexible sigmoidoscopy screening: A systematic review and meta-analysis

Jennifer Shroff, Nirav Thosani, Sachin Batra, Harminder Singh, Sushovan Guha

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9150

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer
3. References and typesetting were corrected according to World Journal of Gastroenterology's format.

Reviewer #1

Minor Comments:

1a. Results section: I suggest changing the layout of the figure 1 using a traditional flow diagram with rectangular box.

We have changed Figure 1 to a traditional flow diagram.

1a. In addition, the authors report that the literature research produced 1323 articles but the figure 1 shows initially 1783 articles. Why? Furthermore, if we add up the studies in the last box the result obtained is 71 and not 75 as declared in the text. Why?

We thank the Reviewer for pointing out discrepancies in the numbers. The numbers noted in Table 1 is accurate and we have changed (tracked) the numbers accordingly in the manuscript now. We have initially screened 1738 articles (page 8; line 7) and finally reviewed in depth 75 articles. Of 75 articles, we discarded 71 articles as they didn't fit our selection criteria. We have clarified this in our Figure 1.

1b. I wonder why the patients in the control group and in the screened group derived from the table

1 are different from the number declared in the text (249,707 vs 266,000 for the control group and 165,653 vs 173,000 for the screened group).

We again corrected the discrepancies and tracked the changes in manuscript (page 3; line 12 and page 8; line 18). The numbers in Table 1 are accurate (control group: n= 249,707 and screened group: n= 165,659).

2a. Tables: The authors should revise Table 1 adding a comma after the patients per group in the study of Segnan et al. 2011.

We have corrected it accordingly (Table 1).

2b. Table 2 is cited in the text but is not attached in the manuscript. 3. Please check all the references; they are not complying with the journal style.

We checked and modified the references as per WJG instructions.

Point by Point response to Reviewer #2

Reviewer #2 commented that **“This meta-analysis study is well-written and provides good information about the effect of screening with flexible sigmoidoscopy on incidence and mortality of colorectal cancer”**.

Reviewer #2

Minor Comments:

1. First, the authors should entail some information regarding the extent of disagreement between two authors when including the studies for analysis and describe the steps of how consensus was reached among three authors.

We have now included 4 lines in the manuscript (tracked) to describe the process (page 6; lines 19-22). Essentially, only difference among the 3 reviewers was inclusion of Telemark Polyp Study 1, which finally decided to omit after discussion as it didn't fit our selection criteria (non-randomized trial).

2a. Second, the authors should use a traditional flowchart for figure 1.

We have changed Figure 1 to a traditional flow diagram.

2b. Also, the authors indicated that 1323 articles were originally identified via literature search; however, the figure 1 showed initially 1783 articles. Moreover, in the box the authors should clearly indicate that 71 studies were excluded before they delineated the numbers of excluded articles due to various reasons.

We thank the Reviewer for pointing out discrepancies in the numbers. The numbers noted in

Table 1 is accurate and we have changed (tracked) the numbers accordingly in the manuscript now. We have initially screened 1738 articles (page 8; line 7) and finally reviewed in depth 75 articles. Of 75 articles, we discarded 71 articles as they didn't fit our selection criteria. We have clarified this in our Figure 1.

3. Third, in the discussion section the authors indicated "similar CRC incidence reduction in men and women," but there seems no such finding in the result section.

The results are noted in Supplementary Figures 1A and 1B and highlighted in manuscript (page 12; lines 18-22).

4. Fourth, all of the RR results for incidence and mortality were below 1, which means the exposed group is less likely to expose to the disease than the unexposed group. I am curious if the FS screening has potential sensitivity issue?

We don't fully understand the Reviewer's question/comment. We assume the Reviewer meant "exposed group is less likely to develop the outcomes of the disease". The outcome of mortality from proximal CRC showed RR only slightly below 1 (RR = 0.95) with CI crossing 1 by large margins (0.77-1.17). The included studies were randomized studies and hence we do not believe the results are due to selection bias i.e. those undergoing FS were not less likely to have CRC or develop CRC after enrollment - the characteristics of the study subjects randomized to FS were similar to those randomized to the control group. We also believe the diagnostic modality for CRC diagnosis was independent of the performance of FS.

5. Fifth, the numbers of participants in the text were not the same in the Table. Please check all tables carefully.

We again corrected the discrepancies and tracked the changes in manuscript (page 3; line 12 and page 8; line 18). The numbers in Table 1 are accurate (control group: n= 249,707 and screened group: n= 165,659).

6. Lastly, please check whether all the references comply with the journal guideline.

We checked and modified the references as per WJG instructions.

Reviewer #3

Minor Comment:

1. I only want to remark **the lack of references for some affirmations:**

Page 14, line 16: Colonoscopy has become the preferred first test for CRC screening in the US.

We have now included references 29 and 30 (page 14; line 16).

Page 19, Last sentence: proven benefits of FS, lower rates of complications with FS than with colonoscopy and feasibility in clinical practice (demonstrated by use over many years in a very large Health Care Maintenance organization Kaiser Permanente).

We have now included reference 40 (page 19; line 3).

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in blue ink that reads "Sushovan Guha".

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