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Response letter to reviewers: ref ESPS Ms NO: 26428

Below please find our response to the reviewers' comments on manuscript No. 26428: "*Favorable lifestyle before diagnosis associated with lower risk of screen-detected advanced colorectal neoplasia*". Our reply is written in italics and the added text to the manuscript (if any) under the reply in normal text format.

Dear Reviewers and editor

Thank you for the very useful comments on the manuscript: Favorable lifestyle before diagnosis associated with lower risk of screen-detected advanced colorectal neoplasia.

Reviewer 00069067 comments

This is an important study investigating whether detection of ACN was associated with the number of modifiable healthy lifestyle factors in CRC screening participants. CRC, which makes a tremendous difference in the quality of human life, is one of the most common cancer types in both women and men. The association between the number of healthy lifestyle factors and the risk of CAN is a valuable study to investigate. It is a well-written manuscript containing interesting results which is useful for most scholars and merits publication

Response: *We have made no changes.*

Reviewer 03317308 comments

Manuscript with title Favorable lifestyle before diagnosis associated with lower risk of screen-detected advanced colorectal neoplasia is observational study about modifiable risk factors of CRC. The study is a sub-study of Bowel Cancer Screening in Norway. The structure of manuscript is complete and language reaches the standard of publishing. Also the content is clear and comprehensive. I have only a few comments:

Comment: Waist circumference could be a better predictor of ACN than BMI.

Response: *We agree that waist circumference would be a better predictor of ACN than BMI. The reason why we have not used waist circumference is that we could not ask this information in the self-response questionnaire, only height and weight.*

Comment: Family history and family risk were not included – but as stated in discussion, only modifiable risk factors were included to this study

Response: *We agree that the study and statistical analysis would benefit from adjusting for family history and family risk of colorectal cancer. However, these are not asked in the BSCN pilot project, so we unfortunately do not have this information available, as written on pg. 11:*

Pg. 11 “The limitations include that we had no information on potential confounders such as energy intake, use of non-steroidal anti-inflammatory drugs and hormone therapy in women, or family history of CRC.”

Comment: FIT and FS as screening modalities might have caused false negative results and misclassification of part of the patients, but this fact is clearly stated in discussion I recommend manuscript for publication.

Response: *We agree that the screening modalities chosen may have caused some missclassification of false negative results. As the reviewer also state, we point this out in the discussion on pg. 12:*

Pg 12 (top): “We acknowledge that FIT and FS as screening modalities might have caused some false negative screening results (misclassification) because one round of FIT has limited sensitivity to discover ACN, and FS only involves the distal segments of the colon^[50, 51]. Any misclassification might have attenuated the association between the lifestyle factors and the risk of ACN.”

Reviewer 00039365 comments

This is another investigation to find out the association between advanced colorectal neoplasia and a lifestyle score. Many studies have already discussed this problem and that kind of investigation. The results are in agreement with results from other published studies, although some differences were seen in the factors that were considered for the lifestyle scores in this investigation.

Comment: The most critical point of that study is the fact that FIT and FS as screening modalities caused some false negative screening results. It is well known that FIT has limited sensitivity to discover ACN, and FS only involves the distal segments of the colon. Any misclassification might attenuate the association between the lifestyle factors and the risk of ACN.

Response: *We agree that the screening modalities chosen might have caused some missclassification of false negative results as stated in our discussion pg. 12:*

Pg 12 (top): “We acknowledge that FIT and FS as screening modalities might have caused some false negative screening results (misclassification) because one round of FIT has limited sensitivity to discover ACN, and FS only involves the distal segments of the colon^[50, 51]. Any misclassification might have attenuated the association between the lifestyle factors and the risk of ACN.”

Comment: The authors should discuss, why these modalities for screening were selected for the investigation.

Response: *Thank you. We acknowledge the relevance of discussing the choice of CRC screening modalities when investigating false negative or positive screening results. However, in the present study, a lifestyle sub-study within the main Bowel Cancer screening in Norway (BCSN) we chose to focus our discussion on the association between lifestyle factors and the probability of ACN diagnosis at screening, and less on the modality choice. FIT and FS were selected as screening modalities for the main BCSN project by The Norwegian Ministry of Health and Care Services.*

But I think this article is of great interest for the readers of the journal and should be published with the above mentioned modifications. The results and findings in the study are well described, but the study shows no superior or surprising results at all, because most of the studies showed similar results. On the other hand the results and findings in the study are adequate described, the methodology is sound, the data support the conclusion and the article is well written with good use of English.