Author’s response to reviews

Title: Validation of Serrated Polyps (SPs) in Swedish Pathology Registers

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Author’s response to reviews:

Copied from the attached Response letter:

Dear Dr. Pande,

We would like to thank the editors and the journal for the offer to revise our paper.

Below you will find our detailed response to the comments of the peer reviewers. These comments have greatly improved our paper.

In addition to the below changes, we have corrected some grammatical errors and added PPV for year of diagnosis to the abstract. Finally, to increase readability, we have spelled out ”SA” that now reads ”serrated adenoma” throughout the paper. These changes have not affected the content of the manuscript.

We are looking forward to hearing from you.

Yours sincerely,

Soran Rabin Bozorg and Jonas F. Ludvigsson, on behalf of the authors
Responses to points raised by peer reviewers and editor:

Peer reviewer 1: Hideyuki Konishi, M.D., Ph.D.

Authors: We thank the peer reviewer for this comment. We agree with the peer reviewer that lack of re-examination of actual biopsies as well as diversity of pathologists may have contributed to our outcomes. As mentioned by the peer reviewer, we have already acknowledged the limitation posed by the lack of re-examination of biopsies in the discussion. In our revised manuscript, we have added some clarifications on how the diversity of pathologists may contribute to the outcome of the study. In particular, we have acknowledged that the diversity in reporting by pathologists may have decreased the accuracy in polyp classification.

Changes made: We have revised the following lines in the discussion (section Strengths and limitations, page 11, starting from line 394): “Earlier studies have shown inter-observer variability for classification of SPs among pathologists (42, 43), and we cannot rule out some misclassification, especially for the subgroup classification. This could potentially affect the validity of SSA/P since some of the SSA/Ps may have been misdiagnosed as HPs, and vice versa (43). The diversity of pathologists in this study, where some may not specialize in SPs, may have decreased the accuracy in polyp classification.”

Peer reviewer 2: Jessica Yu

Authors: We thank the peer reviewers for this comment. As suggested, we have added some additional descriptions of the ESPRESSO study, including size and linkages to other clinical datasets. We have also made an effort to clarify how individuals with multiple polyps have been analyzed.

Changes made: We have added the following lines to the method (section Study population, page 4, starting from line 116): “The ESPRESSO study consists of gastrointestinal histopathology reports from 2.2 million unique individuals with a total of 6.1 million separate data entries. Some 53.9% of individuals had been biopsied more than once.”…” Overall we had data on 1,618,953 colon biopsies and 771,511 rectal biopsies (8). Through the unique personal identity number (9) assigned to all Swedish residents, histopathology data were linked to the Swedish national health registers (Patient Register (10), Cause of Death Register (11), Cancer Register (12), Medical Birth Register (13), Prescribed Drug Register (14), The LISA database with socioeconomic data (15), as well as the Total Population Register (16)). Details about ESPRESSO and registry linkage have been described previously (8).”
We have also added the following line to the method (section Case definition, page 4, line 144): “Individuals with an SP diagnosis could have one or multiple SPs.”

Editor: Mala Pande

Authors: We thank the editor for this comment. See answer to peer reviewer 1.

Changes made: See answer to peer reviewer 1.