

We thank the reviewers for their thoughtful review of our manuscript, please find specific responses below:

Reviewer 02906602 Comments:

I read with interest this interesting overview article of Halland et al on the recent developments considering Barrett's oesophagus. This article seems to cover the most relevant topics considering this pathology, from risk factors and prevention, to diagnosis, treatment and survival. It is well structured and presented, using up-to-date references. The authors however use (too) many abbreviations, of which some are not explained in full in the text (or not the first time mentioned) and tables. Too many abbreviations hamper readability, especially if they are not all commonly known/used. I just wondered if the authors considered covering the genetic risk factors (heritability) a bit more detail. Now, the authors mention some biomarkers, but not really if there are known genetic hotspots, e.g. found by GWAS? The other thing I missed was a discussion about the potential negative association with *Helicobacter pylori* infection, in association with reflux.

Authors Response:

- *The manuscript has been reviewed so that all abbreviations are now first printed out fully. Multiple changes made to manuscript IN TRACK. We have also reduced some use of abbreviations to improve readability.*
- *We have now added some lines on genetic factors, recent GWAS studies and the role of *Helicobacter pylori*.*

Reviewer 02155135 Comments:

The Authors aimed to review recent updates in the field of Barrett's esophagus: pathogenesis, risk factors, diagnosis, management and current solutions related to screening and surveillance. As the Authors pointed out, the management of the individual patient with BE remains challenging and the optimal approach to EAC prevention on a population level remains uncertain. This paper is therefore of potential importance to a general readership.

Comments This is not a systematic review, however, it is a well-written and comprehensive review. There are few comments to address: Diagnostic Challenges CLE is an abbreviation not previously defined. Updates in Screening New Tools: there are no comments on the latest guidelines on screening of the BGS. I believe that a clearer distinction in diagnostic accuracy and costs should be done between trans-nasal endoscopy and office-based transnasal endoscopy. there is a confusion in the correspondence between the text and references 44 and 45. there is no mention of other molecular biomarkers, for example the use of p53 immunohistochemistry, as adjunct to conventional histopathology in keeping

with the 2013 BSG guidelines recommendations. Advances in endoscopic detection of dysplasia as Authors stated : Newer developments in endoscopic techniques, such as image magnification, chromoendoscopy (dye or filtering techniques which highlight dysplasia) and use of autofluorescence imaging have been evaluated, but have failed to become standard of care either due to lack of efficacy or practicality 64-68. I suggest adding a sentence to strengthen that nowadays HD-WLE with random biopsy analysis detects most cases of neoplasia (Boerwinkel et al Gastroenterology 2014;146:622–629).

Author Response:

- The issue of abbreviations has already been corrected
- We do comment on the latest BGS guidelines, mainly in the Table which compares the recommendations. I have now added further information from these guidelines on the use of p53 immunohistochemistry.
- The confusion on reference 44 and 45 has been corrected
- We agree with the comment on HD-WLE and detection of neoplasia, and the a sentence which reflects the above has been added.

Reviewed by 01799430

This is a good review article about Barrett's esophagus. This article includes updated information on pathogenesis, diagnosis and therapy of Barrett's esophagus. (minor comments) 1. If needed, please insert pathologic pictures showing typical findings of BE or sub-squamous BE. 2. The use of abbreviations is complex. Please revise them. 3. The tables seems somewhat complex. Please revise them, including the use of abbreviations. 4. Reference style is not adequate.

Author Response:

- *We have added a figure on sub-squamous BE*
- *The use of abbreviations has been reviewed and updated.*
- *Tables: we agree the layout of the tables are currently not ideal, but will review this once typesetting has occurred to see whether visual changes are needed at that time. We are currently ok with the contents as is.*
- *The reference style has been updated*

Reviewed by 01220166

I read the paper with interests, entitled “Recent developments in pathogenesis, diagnosis and therapy of Barrett’s esophagus” by Halland M et al. My comments are as follow. 1. The authors described new concepts in diagnosis and management of Barrett’s esophagus, including educational information because it includes understanding differences between current societal guidelines. It is interesting paper consists of important information consists of appropriate figure and tables. 2. The authors should prepare the References according to the style of this journal.

Author Response:

- We thank the reviewer for the comments, and have updated the reference style according to journal guidelines

Reviewed by 02495270

Minor points: - Figure 1 is poor. I would suggest to show more representative endoscopic pictures (with the concurrent histological analysis as well). - Please, check references' style/numbering. - Some important references on this topic are missing (e.g. <http://www.ncbi.nlm.nih.gov/pubmed/25162890>). Please, add these references to your text and modify your assertions accordingly.

Author Response:

- We agree. I have now supplied a more representative endoscopic picture and concurrent histopathology.
- The references has been checked and changed according with Journal style and requirements.

Reviewed by 03039049

This manuscript is a well-done review about Barrett's Esophagus. Its importance is justified by high prevalence of this change in endoscopies and need ongoing surveillance. The manuscript's authors conducted a comprehensive review of this subject. The topics used for text division made this article clear and easy reading. Although this is not a systematic review, the explanation about methodology used in this review strengthens this article. Title: The title of this article is correct and proper. Abstract: The abstract is clear and provide clear delineation of the text. Introduction Although the introduction is appropriate, it would be useful to add information about prevalence of Barrett's esophagus among patients who undergo upper endoscopy. Diagnostic Challenges This topic was very well written, and shows diagnostic difficulty of Barrett's esophagus. New insights into Barrett's pathogenesis The most appropriate title for this topic would be New insights into Barrett's pathogenesis and risk factors. New Tools: This topic was very well written and comprehensive. Updates in Surveillance and Risk of Progression The authors were able to present evidences on this subject clearly and correctly. Advances in endoscopic detection of dysplasia In the phrase "In a study which compared inspection times of less than 1 minute versus longer per 1 centimeter of BE, more patients with endoscopically suspicious lesions (54.2 % vs 13.3%) and HGD/EAC (40.2% vs 6.7%, $p=0.06$) were detected with longer inspection time" the authors forgot to mention the p value of detection of patients with endoscopically suspicious lesions. In the phrase "Among the 192 patients studied, the use of eCLE with targeted biopsies increased the diagnostic yield for both dysplasia and neoplasia" would be useful to cite the numbers of this result, which are expressive. Updates on Outcomes of Endotherapy for BE and Managing Recurrence How durable is endotherapy? This topic was very

well written Updates on chemoprevention In the phrase "Although there is some convincing evidence of a potential role of NSAIDs in preventing neoplastic prevention the overall benefit to harm ratio remains unfavorable" should be rewritten. Authors should cite data which make use of NSAIDs not recommended and should mention in more detail negative result for the use of metformin. Conclusions The authors cite the folate as a potential drug for chemoprevention of Barrett's esophagus, but this was not mentioned in the above article. References References are up-to-date. Although they are in excess number, it is acceptable in a review article.

Author Response:

- We thank the reviewer for extensive and helpful comments:
 - We have now added a sentence about the prevalence of Barrett's esophagus found on upper endoscopy, in the section on diagnosis.
 - We agree with the reviewer and have changes the title of the section on new insights into Barrett's pathogenesis to include Risk factors
 - The p-value has been added to the statement about endoscopic inspection time
 - We have added numbers to the sentence about eCLE as requested by the reviewer
 - We have edited the section on NSAID chemoprevention, we were able to use a recent World Journal reference which clarified this section
 - The data for metformin is cited in reference 91
 - The comment about folate has been removed.