Amager and Hvidovre Hospital, November 18th 2022

Dear Editors of World Journal of Gastrointestinal Surgery.

I hereby submit the revised manuscript "Hereditary Polyposis Syndromes remain a challenging entity of disease – old dilemmas and new insights", with submission number 80701.

This editorial goes through the history of genetic and surgical management of hereditary polyposis and highlights the newest recommendations, as well as current dilemmas.

All named authors agree to the submission of the paper to World Journal of Gastrointestinal Surgery and all authors fulfil the criteria for authorship.

The final version of the manuscript has been approved by all authors.

This is an invited manuscript, and it has been stated in previous correspondence, that publication fees will be exempted.

We hope you will find the manuscript interesting for you and your readers.

Best regards,

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Corresponding/first author

Letter to reviewers:

Reviewer 1:

First of all, thank you for your comments and valid suggestions to improve the quality of the manuscript.
Detail answers can be found below.

Item 1:
GI polyps and polyposis syndromes GI most likely refers to 'gastrointestinal', it should be indicated for greater clarity

Reply: GI has been replaced with gastrointestinal, to avoid confusion.

Item 2:
Genetic devolution - 'Familial Adenomatous Polyposis (FAP)': in this case it can only be indicated with 'FAP', having already explained the acronym previously.

Reply: Familial adenomatous polyposis has been replaced with FAP.

Item 3:
Figure 1 does not shows the genes reported in the text.

Reply: Figure 1 has been edited to include the genes mentioned in the text.

Item 4:
Expand the phenotype This section should be deepened. They report the genotype-phenotype correlation, characteristic of these syndromes. In this regard, the authors could benefit from reading the following articles, the contents of which could be useful for improving the manuscript: 1. PMID: 29954149 DOI: 10.3390/genes9070322 2. PMID: 27326320 DOI: 10.4251/wjgo.v8.i6.509

Reply: Thank you for this comment. We have elaborated in the "phenotype" section including considerations on genotype-phenotype, underlying mechanisms etc. We have integrated the two papers that were suggested.

Item 5:

Surgical management of hereditary polyposis Peutz-Jeghers syndrome (PJS), juvenile polyposis syndromes (JPS): in this case they can only be indicated with 'PJS and JPS', having already explained the acronyms previously.

Reply: Peutz-Jeghers syndrome and juvenile polyposis has been replaced with PJS and JPS

Item 6:

Lower GI endoscopy and surgery This paragraph is reported in a confused way. The authors must treat each syndrome separately, as done in others paragraphs, indicating overview on endoscopic and surgery for each syndrome. In addition they should also refer to chromoendoscopy, and the use of cap-assisted endoscopy that have shown promise for enhanced lesion detection rates

Reply: The section 'Lower GI endoscopy and surgery', has been rewritten for clarity and comments on chromoendoscopy has been included. In the section 'Upper GI endoscopy and surgery' a comment on cap-assisted endoscopy has been included.

Item 7:

Figure 2 - It should be indicate as table 1

Reply: Thank you, this has been changed in legends and throughout the text.

Item 8:

Figure 3 - Figure 3 is not indicated in the text. - In figure 3d reference is made to Cowden's sndrome, not mentioned in the text

Reply: Thank you, figure 2 is now indicated at relevant places in the text, and Cowden syndrome mentioned.

Item 9:

Some relevant documents are missing, among which: PMID: 31705372 DOI: 10.1007/s11938-019-00251-4

Reply: We have included the suggested paper, thank you.

Reviewer 2:

Whether Figure 1 is not fully displayed due to some problems, it looks a bit simple.

Reply: Thank you for your positive comments, and recommendations for improvement. We have revised figure 1.