

4<sup>th</sup> March 2019

Dear Editor,

We thank the reviewers for their expert comments and critical appraisal of our manuscript. We are most grateful for the opportunity to respond to the reviewers' comments and submit a revised manuscript, incorporating relevant changes. Please find below a detailed response to each of the reviewers' points.

**Reviewer code 03580207:**

We should like to thank the reviewer for taking the time to review our manuscript and for the complimentary comment made.

**Reviewer code 03479673:**

1. We have amended our manuscript so that abbreviations such as ACPGBI are written in full on their first encounter.
2. As requested, we have included a short section highlighting the differences between 'one-', 'two-', and 'three-stage' pouch surgery, and now present data regarding the use of proximal diversion. This can be found in section 'Indications', subsection 'Ulcerative Colitis'.
3. We thank the reviewer for this suggestion of including a discussion on the important issue of Quality of Life following IPAA. We have now dedicated an entire section on this topic, titled 'Quality of Life Following IPAA Surgery'.
4. We thank the reviewer for raising this question, but stress that data on these novel techniques are still awaited. We have added two more references in Paragraph 7 of section 'History of the Ileal Pouch' which refer to feasibility studies of these novel techniques, but stress the need for more robust data regarding efficacy.

**Reviewer code 03254778:**

1. This narrative review was intended to be a timely 'celebration' of the 40<sup>th</sup> anniversary of the ileal pouch. Its purpose is to review the History, Indications, and Complications of a surgery that has evolved over decades. We as an authorship felt the best format to

present this would be narrative. Indeed, it would be difficult to meta-analyse all aspects that this manuscript covers in the one paper.

That said, the reviewer does raise the salient point that a meta-analysis, particularly of pouch complications, is timely. The last meta-analysis of pouch complications is from 2005 (Hueting et al., *Dig Surg*, 2005). To this end, we are in the process of completing an up-to-date meta-analysis on this sub-topic, and hope to be able to submit this separately for peer-review before years' end.

2. As this is a narrative review, we did not adhere to any strict guidelines such as PRISMA. On reviewing our existing 'Methods' section (subsection 'Literature Search'), we realize a point of confusion could be due to the use of the word 'systematic' in the first sentence. We have removed this word from the manuscript to avoid any confusion.
3. We acknowledge that our 'Introduction' section is short. However, this manuscript aims to cover three significant subjects relating to the pouch, *viz.* its history, indications, and complications. To prevent this manuscript from becoming overly lengthy, we elected to keep the 'Introduction' section relatively short so that the reader delves quickly into the main substance of the manuscript. We hope the reviewer understands this and grants us indulgence on this matter.
4. We respectfully point out again that ours is a narrative, not a systematic review. We are not aware of narrative reviews, which are intentionally formatted to be 'flowing' and easy-to-read, that include flow diagrams of study selection, Kappa statistics, or details of proprietary software.
5. We thank the reviewer for pointing out this oversight. Only articles published in English were included; this detail has been amended in the Abstract. The only exception, as mentioned in the 'Methods' section (sub-section 'Inclusion and Exclusion Criteria') were occasional original articles detailing historical procedures which were published in a language other than English; due to their historical importance, these were included for review.

(NB. Regarding points 2-5, we note that the 'Methods' section has been removed by the Editorial team, in keeping with Journal requirements as a Review article).

6. We are unsure as to what the reviewer is referring to here. We agree that an IPAA is indicated for those who have undergone colectomy for UC/FAP (not for the primary

pathology itself), but would argue that RPC (i.e. proctocolectomy with IPAA) is performed for the pathology as it includes the step of colectomy, which specifically treats the primary pathology.

7. We thank the reviewer for this suggestion, and have amended the text accordingly.
8. We thank the reviewer for this insightful comment. Indeed, colectomy rates have decreased over the past decade, largely owing to the impact of effective medical rescue therapy (including biologics). We have updated this section of the manuscript accordingly, and included more contemporary references for this.
9. We respectfully point out again that we have intended for this paper to be narrative in format. We do not feel that addition of tables highlighting populations, study quality, rates of complications etc. (which would be mainplace in systematic reviews and metaanalyses), adds to the flow of our manuscript.
10. The main difference in patterns of complications between UC and FAP patients is the virtual absence of pouchitis as a complication following FAP. This was demonstrated in a study by Barton et al. 2001 (Am J Surg, 2001), which identified that with the exception of pouchitis, there was no difference in perioperative outcome, morbidity, or functional status between UC and FAP patients. We have included this reference in sub-subsection 'Pouchitis'.
11. A reference has been provided for this statement.
12. This reference has been provided in paragraph 2 of 'Indications': Hueting et al., Dig Surg, 2005. We as an authorship do not usually provide references in our Conclusions section, as this section only summarises what has already been provided in the main body of the text, and does not present new information.
13. We thank the reviewer for pointing out this oversight, and have amended the figure accordingly.

Many thanks once again for the helpful comments that have been raised during the review of our manuscript, and we hope that you consider our responses to these points satisfactory. On the basis of the above changes, we should be extremely grateful if you would re-consider the manuscript for publication.

Yours sincerely,

Prof. Peter M Sagar  
Professor of Colorectal Surgery  
John Goligher Colorectal Unit  
St James's University Hospital, Leeds, UK