

Manuscript: Burden of illness with Crohn's perianal fistulas: multi-national observational study to assess quality of life and treatment preferences

Rejected by WJG: August 16, 2023.

Recommended for publication in *WJG Surgery*, pending response to reviewer comments.

Reviewer comments:

Reviewer/ comment #	Comments/questions	Response
Reviewer #1		
General comment	Scientific Quality: Grade C (Good) Language Quality: Grade A (Priority publishing) Conclusion: Accept (General priority) Specific Comments to Authors: It is evident that perianal complications in Crohn's disease (CPF) significantly impact the quality of life for patients, which is important not only from the perspective of treating physicians but also from the patients' standpoint. CPF is known to be more common among Asian patients. The conclusion in this paper that CPF has a greater influence on the patient's burden of illness is not a novel one. However, understanding what aspects patients prioritize when making treatment choices provides valuable insights from the perspective of treating physicians.	See responses below on specific comments.
1	Above all, a critical concern of this study lies in how well patients comprehended the survey questions and provided accurate responses	The Materials and Methods section (page 9) already states: 'The questionnaire was pretested by conducting patient interviews (n = 7, 60 min each) across key countries to assess whether the comprehension of the questions was as intended and to identify potential sources of response error.' No major changes were made to the questionnaire based on these pre-test cognitive interviews, however minor wording updates were made based on the feedback received from respondents to ensure appropriate comprehension. This detail has been added to the

		manuscript (Results, page 13): ‘The questionnaire was generally well understood by respondents in the pre-test cognitive interviews and no major changes were required; however, in response to respondent feedback, minor modifications were made to the sentence structure and wording for further clarification.’
2	Another limitation is that, compared to the clinical study of Sahnun (Treatment Preferences in Crohn’s Disease Perianal Fistula: Patient Perspectives. Official journal of the American College of Gastroenterology ACG 2022; 117), this research offers less utility in real-world decision-making within clinical practice. For instance, crucial information regarding a patient's past or current medication history is lacking. In the context of choosing surgery as a treatment option, not only the disease activity level of the patient's condition but also their treatment history holds immense significance. Information such as whether immunomodulators or biologics were used becomes necessary.	In Table 2 we report on current and previous CD-related medication experience. Further details on medications received were not collected as this was out of scope for this project; the purpose of this research was to understand patients’ perspective rather than understanding the decisions made in clinical practise or to inform clinical guidelines. Understanding patients’ experience in terms of disease burden and treatment preferences is valuable and may support clinical decision making in a real-world practice setting, in combination with patient treatment history. No changes to manuscript.
3	Overall, this paper, organized and executed under the auspices of a pharmaceutical company, is systematic and well-planned. However, it feels deficient in terms of the information it provides to practicing physicians compared to existing literature.	N/A
4		
Reviewer #2		
General	Scientific Quality: Grade C (Good) Language Quality: Grade B (Minor language polishing) Conclusion: Accept (General priority) Specific Comments to Authors: This is an observational study to quantify symptom burden and impacts, and treatment experience, satisfaction, and preferences associated with Crohn’s perianal fistulas (CPF) across multiple countries. The manuscript is well written. I have some comments list below.	N/A
1	Seton placement was not included in PF-related procedures. However, seton placement is the most common procedure in CPF patients. Many patients are very cared about the long duration of seton placement, which greatly affect patients’ quality of life.	Seton placement was in fact included in the PF-related surgeries. In the Methods it states that both cohorts 2 and 3 (with and without PF-related surgery) included seton placement. We have modified the text (Methods, page 9) to further clarify this (changes in bold):

		<p>‘Cohort 1 included patients with CD who had never experienced perianal fistulas (non-PF CD), cohort 2 included patients with CPF who had no PF-related surgery in the past 12 months but may have received pharmacotherapy and/or seton placement, and cohort 3 included patients with CPF who had PF-related surgery (in the past 12 mo (with or without pharmacotherapy and/or seton placement)). For the purposes of this study, only reparative/interventional PF-related procedures were considered as surgery (seton placement was not included in this description since almost all patients with CPF will undergo seton placement); hence patients in cohort 2 (without PF-related surgery) as well as patients in cohort 3 may have received seton placement.’</p>
2	The grade of CPF is not reported in the manuscript. However, the grade of CPF is correlated with burden and satisfaction of patients. 3	<p>The grade of CPF was not collected as part of this study as it was not considered meaningful to ask this clinical question in a patient questionnaire due to the risk of inaccurate responses. Patients were asked about the severity of their CD as classified by their physician (Table 3, page 33). No changes made to manuscript.</p>
3	The tile "Burden of illness with Crohn's perianal fistulas" may be modified, usually Burden of illness includes financial and psychological burden.	<p>All Authors: if you are open to changing the manuscript title in response to this comment, we propose the following:</p> <p>‘Multi-national observational study to assess quality of life and treatment preferences in patients with Crohn’s perianal fistulas’</p> <p>Also, the running title needs to be reduced to no more than 6 words for WJG Surgery and burden of illness removed (abbreviations are permitted). We propose the following:</p> <p>‘QoL and treatment preferences in CPF’</p>
Editorial Office's comments		
Science Editor	The manuscript has been peer-reviewed, and it's ready for the first decision. Language Quality: Grade B (Minor language polishing) Scientific Quality: Grade C (Good)	N/A
Editor-in-Chief	I recommend the manuscript to be published in the World Journal of Gastrointestinal Surgery.	Additional reference from 2023 found through RCA and added to discission (page 19), new text in bold:

	<p>Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.</p>	<p>'Furthermore, patients with CPF were shown to have a significant impact on their overall HRQoL. This finding is in line with a study by Spinelli et al. (2023), where patients with CPF reported a greater impact on overall quality of life, well-being, relationships, social life and work life than those with Crohn's disease without CPF.^[48] In the current study, there was no significant difference in reported HRQoL between patients who had PF-related surgery and those who had not. Patients with CPF reported a greater impact of CD/CPF disease attributes on HRQoL, irrespective of PF-related surgery, than patients with non-PF CD.'</p>
General	No abbreviations permitted in figure titles or table titles.	For all figure and table titles: patient-reported outcome tool names have been written out in full, as well as 'Crohn's disease' and 'perianal fistula'.
General	Add new 'Article highlights' section.	Added to page 21-22.