

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 65338

Title: Minimum sample size estimates for trials in inflammatory bowel disease: A systematic review of a support resource

Reviewer's code: 00049331

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United Kingdom

Manuscript submission date: 2021-03-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-18 14:56

Reviewer performed review: 2021-04-21 23:15

Review time: 3 Days and 8 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

SPECIFIC COMMENTS TO AUTHORS

In this study, the Authors aimed to review minimum sample size estimation for trials in Inflammatory Bowel Disease. The Authors demonstrated that there is no clear basis or accepted standard for current practice for minimal clinically important difference (MCID) estimation when producing a power calculation for a primary randomised controlled trials within IBD. The Authors showed that a third of intervention studies in Inflammatory Bowel Disease within the last 25 years are underpowered. This review gives us valuable information for the future studies.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 65338

Title: Minimum sample size estimates for trials in inflammatory bowel disease: A systematic review of a support resource

Reviewer's code: 04088775

Position: Editorial Board

Academic degree: BMed, FRACP, PhD

Professional title: Doctor, Staff Physician

Reviewer's Country/Territory: Australia

Author's Country/Territory: United Kingdom

Manuscript submission date: 2021-03-04

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-05-07 20:50

Reviewer performed review: 2021-05-08 02:25

Review time: 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors have performed a novel systematic review to evaluate the minimum sample size that should be used to achieve adequate sample size based on randomised controlled trials in IBD. They found that approximately one third of interventional studies since 1996 were underpowered. The manuscript provides important food for thought in a potentially overlooked area of trial design by clinicians that is actually very important in IBD trials. Some details in the inclusion of trials needs to be clarified as low molecular weight heparin and cannabis were included in the study while ustekinumab and vedolizumab were considered exploratory interventions which does not reflect clinical practice. I have the following suggestions: Page 7, line 150-53 eligibility of trials – the medications mentioned as exploratory therapies have received FDA/NHS/ approval for use in inflammatory bowel disease by necessary authorities in many developed nations. Can this statement be clarified or perhaps more clearly specify which therapies are considered established and only include those. The fact that LMWH and cannabis were included would not fit what is considered standard IBD therapy. The search strategy of the sustematic review primarily focuses on a Cochrane search which is not truely a systematic review - why weren't Medline, Scopus or Web of Science searched? An alternative would be to remove the term systematic review from the manuscript. PRISMA guidelines require the search terms on at least one search engine to be provided and the results of searches should be provided for full transparency. Please provide these. Has this systematic review been registered on PROSPERO or through another review registry? The systematic review identified 105 papers and the manuscript has only 6 papers referenced, none of which are interventional trials in inflammatory bowel disease. This does not provide transparency in which trials were used in the study. Are the authors able to provide a list of included studies and

references? Minor comments: Page 6, line 115 consider changing 'than' to 'then' Page 10, line 221 when referring to in clinical practice can this be further defined. Only randomized controlled trials were included so does this refer to investigator initiated trials?

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 65338

Title: Minimum sample size estimates for trials in inflammatory bowel disease: A systematic review of a support resource

Reviewer's code: 05123103

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Postdoctoral Fellow

Reviewer's Country/Territory: Belgium

Author's Country/Territory: United Kingdom

Manuscript submission date: 2021-03-04

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-05-04 06:17

Reviewer performed review: 2021-05-12 06:33

Review time: 8 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

The manuscript suggested by Morris Gordon et al focused on a very important methodologic aspect of RCT: the minimum sample size estimate. The authors performed a systematic review of available RCTs in IBDs. On 105 trials, a third of intervention studies in IBD within the last 25 years are underpowered. Also, the authors present a sample size estimate resource for future researchers. This is a very interesting paper. To be more useful, the paper should be more practice with a clear framework to help reader for calculating appropriate sample size estimate for future studies. The title reflects the main subject of the manuscript The abstract correctly summarizes and reflects the work described in the manuscript The Key words reflect the focus of the manuscript The Background adequately describes the overview on the topic and correctly present the significance of the study The methods part is not very well distributed. A lot of details are given about the eligibility criteria for selection of papers included in systematic review but less details are given about calculation details for sample size estimation which is quite a pity because this is the purpose of the paper et the most interesting part. Also, authors (line 186, page 8) told about inconsistencies. These inconsistencies could be listed in a supplementary table for reader information. Again, details to obtain the recalculate sample size should be introduced in the methodology part. This would represent a practice framework for readers In the result part, le paragraph line 208 to 212 is not informative and not useful for the topic. To calculate a mean proportion of clinical remission by pooling is not useful at all as there is a huge heterogeneity in study populations and tested drugs. The discussion is well constructed. In line 262 to 264, the authors write that the work present a resource for sample size estimation not just for future study authors, but for study peer reviewers but at this stage, the resource seems not practical enough to be a useful resource. Does the



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manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? About illustrations and tables, it would be easier to read Table 2 if the table 2 is split in Table 2A UC and Table 2B CD No other comments on Biostatistics, Units. References, Quality of manuscript organization and presentation. Research methods and reporting and Ethics statements

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 65338

Title: Minimum sample size estimates for trials in inflammatory bowel disease: A systematic review of a support resource

Reviewer's code: 04088775

Position: Editorial Board

Academic degree: BMed, FRACP, PhD

Professional title: Doctor, Staff Physician

Reviewer's Country/Territory: Australia

Author's Country/Territory: United Kingdom

Manuscript submission date: 2021-03-04

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-07-19 08:18

Reviewer performed review: 2021-07-19 08:29

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors have addressed all the points raised.