

Cochrane vs Non-Cochrane Review in IBD: A Systematic Review

Relevant links:

Protocol outline - <https://systematicreviewjournal.biomedcentral.com/articles/10.1186/2046-4053-4-1/tables/3>

Gut template - <https://typeset.io/formats/bmj-publishing-group/gut/f532a3179bb9492d856917e00bc5abc0>

Prospero headings - <https://www.crd.york.ac.uk/prospero/documents/PROSPERO%20registration%20form.pdf>

Cochrane vs Non-Cochrane review, Cardiology version - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4686011/>

Prospero Registration Outline

April 22, 2020

1. Review Title
 - a. A matched analysis of meta-analyses in inflammatory bowel disease (IBD): Cochrane versus non-Cochrane systematic reviews.
2. Original language
 - a. English
3. Anticipated or actual start date
 - a. 1st May 2020
4. Anticipated completion date
 - a. 1st September 2020
5. Stage of review at time of this submission
 - a. No for all
6. Named contact
 - a. Professor Morris Gordon
 - b. Consultant Paediatrician with a specialist interest in Gastroenterology
 - c. Strategic clinical lead for quality
 - d. Head of transitions and careers, School of Medicine MBBS
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10. Organisational affiliation of the review
 - a. University of Central Lancashire

11. Review team members and their organisational affiliations
 - a. Morris Gordon - consultant paediatrician with specialist interest in gastroenterology
 - b. Svetlana Lakunina - medical student at the University of Central Lancashire
 - c. Fatemeh Hedayat - medical student at the University of Central Lancashire
 - d. Adriaan Visser - medical student at the University of Central Lancashire
 - e. Hugo Labat - medical student at the University of Central Lancashire
 - f. Anthony Akobeng - professor at Qatar, Sidra Medical Centre
 - g. Ciaran Grafton Clarke - Academic Foundation Year 2 Doctor. School of Life Sciences, University of Leicester, Leicester, UK

12. Funding sources/sponsors
 - a. N/A

13. Conflicts of Interest
 - a. N/A

14. Collaborators
 - a. None

15. Review Question
 - a. In meta-analyses with the same set of interventions and outcomes, what are the differences in terms of methodological and statistical quality, and effect size?

16. Searches
 - a. Databases: PUBMED, MEDLINE, Cochrane Library
 - b. Search dates: 1996 to present
 - c. Restrictions: English language only, no unpublished studies, no abstracts only, excluding before 1999 (as this is the year where PRISMA statement was introduced) and including from 1999 to the date of completion, human studies only
 - d. Re-run searches prior to final analysis

17. URL to search strategy
 - a. (IBD OR Inflammatory bowel disease OR Crohn* OR ulcerative*) AND (Systematic review OR meta-analysis)

18. Condition or domain being studied
 - a. IBD, specifically Crohn's disease or Ulcerative colitis (as defined by the reporting study)

19. Participants/population

- a. Patients of any age diagnosed with either Crohn's Disease or Ulcerative Colitis

20. Interventions exposure

- a. Any treatment (whether pharmacological, non-pharmacological or surgical) for either the induction of remission, or the maintenance of remission, in patients with inflammatory bowel disease.

21. Comparator(s)/Control

- a. Outcome measure(s) from the paired Cochrane systematic review
- b. Outcome measure(s) from the paired non-cochrane systematic review

22. Types of study to be included

- a. Meta-analyses of IBD literature will be included if they comprise of:
 - i. RCTs (non-cochrane reviews included if they only have RCTs in the index review)
 - ii. Reported a dichotomous outcome
 - iii. Reported a common treatment-outcome relationship
- b. Once a list of cochrane reviews has been completed, a matching process will be completed to try and pair each review based on:
 - i. Condition and disease state;
 - ii. Intervention;
 - iii. Clinical outcome measured; and
 - iv. Publication within 5 years of each other.

Because the number of Cochrane reviews is likely to be much less than non-Cochrane reviews, we will start with the Cochrane review, and then seek potential non-Cochrane matches. If there are multiple non-Cochrane reviews, we will use a random number generator to select which paper to include. This will avoid increased weighting from Cochrane reviews with the same cochrane review included in multiple pairs.

Exclusion criteria

Network meta-analysis

Reviews of non-interventional items

Reviews of symptoms control, quality of life, but not induction or maintenance

Reviews not of Crohns or UC, including pouchitis.

23. Context

- a. Only cochrane and non-cochrane reviews that include RCTs will be included

24. Main outcome(s)

- a. Descriptive outcomes (author, year, intervention, outcome), macro differences between cochrane and non-cochrane reviews (differences in year, sample sizes, number of included studies, number of overlap studies).
- b. Adherence to best practice principles in the systematic review - recording of alignment to cochrane or similar methods, employment of GRADE, using a recognised risk of bias tool (cochrane, higgins criteria) and reporting inline with PRISMA and finally availability of a protocol for review by readers.
- c. If the GRADE approach is used to rate included papers (which are only RCTs in this instance) in the systematic reviews.
- d. Summary effect sizes for matched primary outcomes, including confidence intervals
- e. Differences in citation of published review in both cochrane and non-cochrane reviews.
- f. Comparing the final review conclusions using description and dichotomous as to whether a change in practice is suggested or not
- g. Comparing qualitative judgements of conclusions drawn in the matched pairs.
- h. Comparing the data presented in abstracts to the data presented in the results section.
- i. Number of bibliographical databases used in the cochrane and non-cochrane systematic review.
- j. Inclusion of abstracts only from RCTs used in systematic reviews
- k. If the authors of the systematic reviews contacted the authors of the RCTs to clarify any concerns or clarifications.

25. Additional outcomes

- a. N/A

26. Data extraction (selection and coding)

- a. Study Selection:
 - i. A total of six authors will work collaboratively on the process.
 1. Four authors will extract the titles of all Cochrane systematic reviews that meet the inclusion criteria.
 2. These authors will then identify a list of titles which are potentially relevant, requiring a full-text review.
 3. Each author will independently review the full-text review allocated to them against the inclusion criteria.
 - ii. The four authors will obtain a list of non-cochrane systematic reviews that meet the inclusion criteria.
 - iii. Pairs of authors will start the pairing process (where possible) between Cochrane and non-cochrane reviews.
- b. Data extraction
 - i. An excel file will be created for data extraction
 - ii. Author's name and date, source, main outcomes, sample size, number of citations... what else?
 - iii. 4 authors will extract data, any disagreements will be discussed in between each other and with other 2 authors.
 - iv. If possible, the authors will be contacted for any missing data

27. Risk of bias (quality) assessment

- a. Studies will be compared regarding their risk of bias assessment, including whether they make an assessment
- b. Where available, comparisons will be made between key areas, including Randomisation, allocation, etc. Where differences exist, the dichotomous recording of a difference will be made and recording of which review made the higher risk judgement
- c. Where any single item is high risk in one review and not the other, the specific justification for the pair of judgements will be extracted and compared.

28. Strategy for data synthesis

The Wilcoxon two-sample test will be used to determine if there was a significant difference in the total number of studies and sample sizes between Cochrane and non-Cochrane reviews.

To compare the summary measures of effects within each matched pair, we displayed Cochrane and non-Cochrane summary estimates and corresponding 95% confidence intervals using Forest plots generated via a macro on Microsoft Excel.

We identified pairs with discrepant results, and sorted them based on the nature of the discrepancy using the following categories:

1. Changes of the width of 95% confidence intervals that shifts a statistical interpretation of the meta-analytic result, e.g., one review concludes a statistically significant result and the other non-significant result.
2. The magnitude of the aggregate effect sizes differed by at least 2-fold (but were in the same direction).
3. The direction of the effect size was reversed.

While somewhat controversial, bibliometric measures such as citation rates are widely used as a proxy for the impact of that paper in the scientific literature.

To probe the relationship between citation frequencies and discrepant results we used Google Scholar's search engine, within each category of discordancy and grouped by Cochrane and non-Cochrane to identify the number of times a given review was cited by other studies in the literature subsequently, and displayed these graphically as box/whisker plots.

Descriptive synthesis will be completed when risk of bias disagreements between reviews exist and the authors will investigate to determine which judgement seems the most correct, for example if extra information was presented in one review and not the other. If this cannot be determined, this will be recorded.

Comparison in GRADE rankings for the appropriate primary outcome will also be made and once again, disagreements noted and investigated to determine the primary cause for the discrepancy in judgement.

29. Analysis of subgroups or subsets

a. N/A

30. Type and Method of review

a. Systematic review: Meta-analysis

31. Language

a. English

32. Country

a. United Kingdom

33. Other registration details

a. N/A

34. Reference and/or URL for published protocol

a. Will be published

35. Dissemination plans

a. To submit the publication to a leading journal in the field

36. Keywords

a. Systematic Review, Cochrane Systematic review

b. IBD: Treatment, outcomes

c. Clinical trials

37. Details of any existing review of the same topic by the same authors.

a. N/A

38. Current review status.

a. Not Started

39. Any additional information.

a. N/A

40. Details of final report / publications.

a. N/A

