

See “Does fecal calprotectin equally and accurately measure disease activity in small bowel and large bowel Crohn’s disease? - a systematic review” on page 160-170.

Supplementary Material 1

Search strategies:

A. MEDLINE - Search strategy

1. exp Leukocyte L1 Antigen Complex/
2. (calprotectin* or calgranulin*).mp.
3. (S100A8* or S100A9*).mp.
4. "Leukocyte L1 Antigen Complex".mp.
5. (leu#ocyt* adj3 "L1" adj3 antigen* adj3 complex*).mp.
6. 1 or 2 or 3 or 4 or 5
7. exp Biological Markers/
8. (((bio* or lab* or progn* or predict* or fecal* or faecal* or feces* or faeces*) adj2 marker*) or biomarker* or (biologic* adj marker*) or marker* or surrogat*).mp.
9. 7 or 8
10. exp Crohn Disease/
11. crohn*.mp.
12. exp Inflammatory Bowel Diseases/
13. (ibd* or (inflam* adj3 bowel*)).mp.
14. exp Colitis, Ulcerative/
15. (ulcer* adj3 colitis*).mp.
16. 10 or 11 or 12 or 13 or 14 or 15
17. (fecal* or faecal* or feces* or faeces* or excret* or stool*).mp.
18. 6 and 16
19. 9 and 16 and 17
20. 18 or 19

B. Embase - Search strategy

1. exp calgranulin/
2. (calprotectin* or calgranulin*).mp.
3. "Leukocyte L1 Antigen Complex".mp.
4. (leu#ocyt* adj3 "L1" adj3 antigen* adj3 complex*).mp.
5. (S100A8* or S100A9*).mp.
6. 1 or 2 or 3 or 4 or 5
7. exp biological marker/
8. (((bio* or lab* or progn* or predict* or fecal* or faecal* or feces* or faeces*) adj2 marker*) or biomarker* or (biologic* adj marker*) or surrogat*).mp.
9. 7 or 8
10. exp Crohn disease/
11. exp ulcerative colitis/
12. exp inflammatory bowel disease/
13. crohn*.mp.
14. (ibd* or (inflam* adj3 bowel*)).mp.
15. (ulcer* adj3 colitis*).mp.
16. 10 or 11 or 12 or 13 or 14 or 15

17. (faecal* or fecal* or feces* or faeces* or stool* or excre*).mp.
18. 6 and 16
19. 9 and 16 and 17
20. 18 or 19

C. Cochrane Library (Central) - Search strategy

1. "Inflammatory bowel disease" or "ulcerative colitis" or "Crohn's disease"
2. "disease activity"
3. "calprotectin"
4. (1 OR 2) AND 3

D. Web of Science - Search strategy

1. "Inflammatory bowel disease" or "ulcerative colitis" or "Crohn's disease"
2. "calprotectin" or "calgranulin"
3. 1 AND 2

Supplementary Material 2

The following criteria were assessed in QUADAS-2:

1. Was a consecutive or random sample of subjects enrolled?
2. Was a case-control design avoided?
3. Did the study avoid inappropriate exclusions?
4. Could the selection of subjects have introduced bias?
5. Is there concern that the included subjects do not match the review question?
6. Were the index test results interpreted without knowledge of the results of the reference standard?
7. If a threshold was used, was it pre-specified?
8. Could the conduct or interpretation of the index test have introduced bias?
9. Is there concern that the index test, its conduct, or interpretation differ from the review question?
10. Is the reference standard likely to correctly classify the target condition?
11. Were the reference standard results interpreted without knowledge of the results of the index test?
12. Could the reference standard, its conduct, or its interpretation have introduced bias?
13. Is there concern that the target condition as defined by the reference standard does not match the review question?
14. Was there an appropriate interval between index test(s) and reference standard?
15. Did all subjects receive a reference standard?
16. Did subjects receive the same reference standard?
17. Were all subjects included in the analysis?
18. Could the subject flow have introduced bias?

We modified the application of the QUADAS-2 as previously shown.¹ With regard to question 5, "low concern" was scored if the subjects clearly had established CD and "high concern" if the study sample had subjects presenting for the first time with CD. Question 6 was not scored as fecal calprotectin is an objective test based on laboratory result which is not affected by blinding the index test interpreter to the reference standard. The applicability of the index test (question 9) was not a concern for this review despite the variations in the way the index test was performed and interpreted. For question 10, "yes" was scored for all the studies since endoscopy is considered the gold standard for diagnosis of CD while MRI or CT are considered useful in assessment for CD in the small bowel in the most recent European guidelines.^{2,3} Since the gold standards used for assessment of CD were endoscopy, MRI or CT; question 13 (applicability of reference standard) was considered not of concern.

The responses for the signalling questions were "yes," "no" or "unclear" and the risk of bias was marked as "low," "high" or "unclear." If all the signalling questions for a particular domain were "yes," this would indicate a "low" risk of bias while presence of any "no" would raise the concern for bias. When the information was insufficient, "unclear" has been marked.

REFERENCES

1. Mosli MH, Zou G, Garg SK, et al. C-reactive protein, fecal calprotectin, and stool lactoferrin for detection of endoscopic activity in symptomatic inflammatory bowel disease patients: a systematic review and meta-analysis. *Am J Gastroenterol* 2015;110:802-819.
2. Annese V, Daperno M, Rutter MD, et al. European evidence based consensus for endoscopy in inflammatory bowel disease. *J Crohns Colitis* 2013;7:982-1018.
3. Panes J, Bouhnik Y, Reinisch W, et al. Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. *J Crohns Colitis* 2013;7:556-585.