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Diagnostic accuracy of fecal biomarkers for mucosal and histological healing in ulcerative colitis: a network meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 July 2025 and was last updated on 5 July 2025.

INTRODUCTION

Review question / Objective To compare the diagnostic accuracy (sensitivity, specificity) of fecal calprotectin, FIT, and lactoferrin for predicting mucosal and histological healing in UC remission.

Condition being studied Ulcerative colitis requires frequent monitoring of deep healing, but colonoscopy is invasive. Fecal biomarkers reflect distinct pathways (FC: inflammation; FIT: bleeding; LF: neutrophil activity), yet no NMA compares their accuracy for histological healing.

METHODS

Search strategy ("ulcerative colitis" OR UC) AND ("mucosal healing" OR "histologic remission")
AND ("fecal calprotectin" OR FC OR "fecal immunochemical test" OR FIT OR "lactoferrin" OR LF)
AND ("diagnostic accuracy" OR "sensitivity and specificity" OR "ROC curve").

Participant or population Ulcerative colitis patients in remission.

Intervention FC vs. FIT vs. LF or combination.

Comparator Endoscopic-histological assessment (Mayo=0 for MH; Geboes<2.0 for HREM)mai.

Study designs to be included A diagnostic network meta-analysis.

Eligibility criteria Inclusion Criteria:

Population: Adults (≥18 years) with ulcerative colitis in clinical remission (Mayo clinical score ≤2), confirmed by colonoscopy within 4 weeks. Excluded if coexisting colorectal cancer or intestinal infection.

Interventions: Fecal calprotectin (FC, thresholds 50–250 μg/g), fecal immunochemical test (FIT, ≥10 μg/g feces), or lactoferrin (LF, ≥7.25 μg/g). Detection methods: ELISA or point-of-care tests (POCT).
Comparator: Endoscopic-histological gold standard:
Mucosal healing (MH): Mayo endoscopic subscore=0
Histologic remission (HREM): Geboes index300 μg/g) or non-validated gold standards.

Information sources PubMed, EMBASE, Cochrane Library, Web of Science, CNKI.

Main outcome(s)
1. Sensitivity and specificity of fecal calprotectin (FC), fecal immunochemical test (FIT), and lactoferrin (LF) for:
- Mucosal healing (Mayo endoscopic subscore=0)
- Histological remission (Geboes index<2.0 or Nancy index grade 0–1)
2. Diagnostic odds ratio (DOR) comparing FC, FIT, and LF
3. Area under ROC curve (AUC) for each biomarker.

Additional outcome(s) 1. Positive and negative predictive values (PPV/NPV) at preset thresholds (FC: 50/100/250 μg/g)
2. Optimal cut-off values determined by Youden index
3. Inconsistency analysis via node-splitting for direct/indirect evidence.

Data management Independent dual extraction of 2×2 contingency tables (TP/FP/FN/TN), recording thresholds (like: FC: 50–250 μg/g) and detection methods (ELISA/POCT).

Quality assessment / Risk of bias analysis QUADAS-2 tool to assess spectrum bias (patient selection) and index test bias (blinding of gold standard results).

Strategy of data synthesis Model: Bivariate HSROC model for pooling sensitivity (Sen)/specificity (Spe); Bayesian NMA framework (WinBUGS).
Heterogeneity: Cochran's Q test + I^2 statistic (I^2 > 50% triggers subgroup analysis).
Inconsistency: Node-splitting method to verify direct/indirect evidence consistency.

Subgroup analysis Stratified by FC thresholds (50/100/250 μg/g), disease extent (left-sided/pancolitis), and drug type (e.g., biologics vs. conventional therapy).

Sensitivity analysis Excluding high-risk-of-bias studies (QUADAS-2 score ≤ 4); validating robustness using different effect models (fixed/random effects).

Language restriction None.

Country(ies) involved China.

Keywords ulcerative colitis, fecal calprotectin, fecal immunochemical test, lactoferrin.

Contributions of each author
Author 1 - Jing Li - Author 1 drafted the manuscript, collected data from researches.
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