



Fecal Calprotectin: A Comprehensive Systematic Review of Its Diagnostic and Monitoring Efficacy in Inflammatory Bowel Disease

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ABSTRACT

Introduction

Inflammatory Bowel Disease (IBD), encompassing Ulcerative Colitis (UC) and Crohn's Disease (CD), is a chronic, relapsing condition demanding continuous, objective surveillance of mucosal inflammation. Due to the burdens associated with invasive endoscopy—the conventional gold standard for assessment—there is a critical need for accurate, non-invasive biomarkers. Fecal Calprotectin (FC), a stable protein released by activated neutrophils, serves as a quantitative surrogate marker that directly correlates with the level and extent of gastrointestinal inflammation. This comprehensive systematic review aggregates high-level meta-analytic evidence to define the precise utility of FC across IBD diagnosis, therapeutic monitoring, and prediction of long-term disease course.

Methods

This systematic review synthesized quantitative findings from

high-quality diagnostic accuracy and prognostic meta-analyses, encompassing data pooled from over fifteen primary studies focusing on adults and children with IBD. The underlying systematic searches utilized extensive database coverage, including PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library. Key performance metrics rigorously extracted included pooled sensitivity, specificity, Area Under the Summary Receiver Operating Characteristic Curve (AUROC), Diagnostic Odds Ratio (DOR), Positive Likelihood Ratio (PLR), and Negative Likelihood Ratio (NLR). The methodological rigor of the aggregated evidence was assessed using the QUADAS-2 framework.

Results

FC demonstrated superior accuracy for differentiating IBD from functional gastrointestinal disorders. At the standard 50 mug/g cut-off, pooled analyses yield high sensitivity (89% to 99%) and a critically high Negative Predictive Value (NPV) of 0.99 for IBD exclusion. In monitoring, FC reliably correlates with endoscopic activity, with optimal performance in UC (AUROC 0.97) but diminished utility in isolated small bowel CD (SB-CD), where the AUROC drops to 0.72 at the 100 mug/g cut-off. For prognostic assessment, the optimal pooled cut-off of 152 mug/g for predicting clinical relapse in adult UC patients in remission yields a robust DOR of 10.54. Furthermore, distinct concentration ranges define Mucosal Healing (MH) targets: 60-75 mug/g for UC (AUC 0.88) versus a higher 180-250 mug/g range for CD (AUC 0.79).

Discussion

FC is confirmed as an essential biomarker, yet its optimal

implementation requires careful consideration of its limitations, including significant quantitative variability (up to 5-fold differences) across commercial assays, which hinders the universal application of precise meta-analytic thresholds. The physiological barrier in detecting proximal small bowel inflammation necessitates integrating FC results with cross-sectional imaging and exploring complementary serum biomarkers. The greatest clinical value of FC lies in its use for continuous, longitudinal surveillance to proactively guide therapeutic intensification and reduce the need for unnecessary endoscopic procedures.

Conclusion and Recommendations

Fecal Calprotectin is established as an indispensable, non-invasive biomarker for IBD triage and continuous surveillance. Its clinical efficacy is maximized through the meticulous application of phenotype- and location-specific cut-offs tailored to the specific clinical query (diagnosis, MH, or relapse prediction). Standardizing commercial FC assays remains the most crucial outstanding challenge to ensure the consistent, reliable, and interchangeable application of these evidence-based thresholds across global healthcare settings.

Keywords : Fecal Calprotectin, Inflammatory Bowel Disease, Diagnostic Accuracy, Mucosal Healing, Disease Monitoring

INTRODUCTION

Background on Inflammatory Bowel Disease and Monitoring Imperatives

Inflammatory Bowel Disease (IBD), which includes Ulcerative Colitis (UC) and Crohn's Disease (CD), is defined by chronic, destructive inflammation of the gastrointestinal tract, necessitating rigorous, objective measures of disease activity (Li et al., 2019). The current standard of care dictates that therapeutic success is best measured by achieving Mucosal Healing (MH), a state strongly predictive of sustained remission and minimized long-term complications, such as strictures and hospitalization (Xiang et al., 2021). Relying solely on invasive endoscopy to confirm MH is costly and burdensome, creating an imperative to adopt highly accurate, non-invasive surrogate tools for surveillance (Li et al., 2019).

Fecal Calprotectin as the Non-Invasive Benchmark

Fecal Calprotectin (FC) has secured its position as the preeminent non-invasive biomarker for monitoring intestinal inflammation in IBD (Kennedy et al., 2014). This protein, derived primarily from activated neutrophil granulocytes, is released into the gut lumen in concentrations directly proportional to the degree of mucosal inflammation (Li et al., 2019). FC consistently outperforms traditional systemic markers, such as C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR), which often lack specificity, are affected by systemic factors, and demonstrate a particularly weak correlation with mucosal inflammation in UC patients (; Rokkas et al., 2018).

Research Hypothesis, Gap, and Novelty

The central hypothesis of this systematic review is that FC exhibits high, statistically significant diagnostic and prognostic accuracy, although its performance is critically dependent on appropriate phenotyping and the utilization of context-specific cut-offs (Li et al., 2019; Xiang et al., 2021). Significant clinical gaps persist regarding the precise application of thresholds for different

clinical endpoints and the management of assay variability (Labaere et al, 2014). This review addresses these gaps by synthesizing the rigorous quantitative evidence (DOR, PLR, NLR, AUROC) associated with ten critical clinical outcomes, providing a detailed, evidence-based roadmap for optimizing FC use within a highly personalized and efficient care model (Kennedy et al., 2014).

METHODS

Data Sources, Search Strategy, and Selection Criteria

The evidence base for this systematic review was constructed by synthesizing quantitative results from established, high-quality systematic reviews and meta-analyses, strictly adhering to the PRISMA guidelines for robust reporting (Li et al., 2019). The foundational searches utilized extensive database coverage, including comprehensive querying of PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library. Search terms consistently included controlled vocabulary and free text terms such as "Fecal Calprotectin," "Inflammatory Bowel Disease," "Diagnostic accuracy," "Mucosal Healing," and "Relapse" to ensure a deep and focused retrieval of relevant literature (Labaere et al, 2014).

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Inflammatory Bowel Disease	Crohn Disease	Ulcerative Colitis	IBD Patients
Intervention (I) / Exposure (E)	Fecal Calprotectin	FC	Biomarker	Non-invasive marker
Comparison (C)	Endoscopy	Colonoscopy	Gold Standard	Reference Standard

Outcome (O)	Diagnostic Accuracy	Monitoring	Mucosal Healing	Relapse Prediction
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The Boolean MeSH keywords inputted on databases for this research are: (*"Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients"*) AND (*"Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker"*) AND (*"Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard"*) AND (*"Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction"*)

Study Eligibility, Reference Standards, and Data Extraction

Primary studies aggregated within the meta-analyses typically enrolled patients with suspected IBD (compared against cohorts with functional GI disease) or patients with established IBD followed longitudinally for monitoring (Kennedy et al., 2014; Alibrahim et al., 2015). The gold standards utilized for validation were rigorous, involving endoscopic and histological confirmation for diagnosis, validated endoscopic indices (e.g., Mayo Endoscopy Subscore, CDEIS) for assessing activity, and documented clinical relapse over a specified follow-up period, usually 12 months (Xiang et al., 2021; Li et al., 2019). Data extraction was meticulous, focusing on pooling critical quantitative indices of diagnostic and prognostic accuracy, including sensitivity, specificity, DOR, PLR, NLR, and AUROC (Li et al., 2019; Xiang et al., 2021).

Methodological Quality Assessment (QUADAS-2 Framework)

The methodological quality of the underlying primary studies was critically assessed using the QUADAS-2 criteria, revealing recurring systematic risks of bias and applicability concerns (Asiri et al, 2023). While overall study quality was generally reported as high for approximately 65% of studies, significant weaknesses often appeared in the Patient Selection domain (Kennedy et al., 2014; Asiri et al, 2023; Alibrahim et al., 2015). This persistent bias stemmed from the disproportionate enrollment of patients from specialized tertiary care centers rather than

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heterogeneous primary care populations, introducing spectrum bias that can potentially inflate reported diagnostic accuracy when generalized to lower-prevalence settings (Kennedy et al., 2014; Xiang et al., 2016). Furthermore, the absence of clear reporting on the blinding of the index test results constituted another frequent source of potential bias in some studies (Li et al., 2019).

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients") AND ("Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker") AND ("Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard") AND ("Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction")	16
Semantic Scholar	("Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients") AND ("Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker") AND ("Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard") AND ("Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction")	251
Springer	("Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients") AND ("Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker") AND ("Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard") AND ("Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction")	3,473
Google Scholar	("Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients") AND ("Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker") AND ("Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard") AND ("Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction")	18,700
Wiley Online Library	("Inflammatory Bowel Disease" OR "Crohn Disease" OR "Ulcerative Colitis" OR "IBD Patients") AND ("Fecal Calprotectin" OR "FC" OR "Biomarker" OR "Non-invasive marker") AND ("Endoscopy" OR "Colonoscopy" OR "Gold Standard" OR "Reference Standard") AND ("Diagnostic Accuracy" OR "Monitoring" OR "Mucosal Healing" OR "Relapse Prediction")	4,239

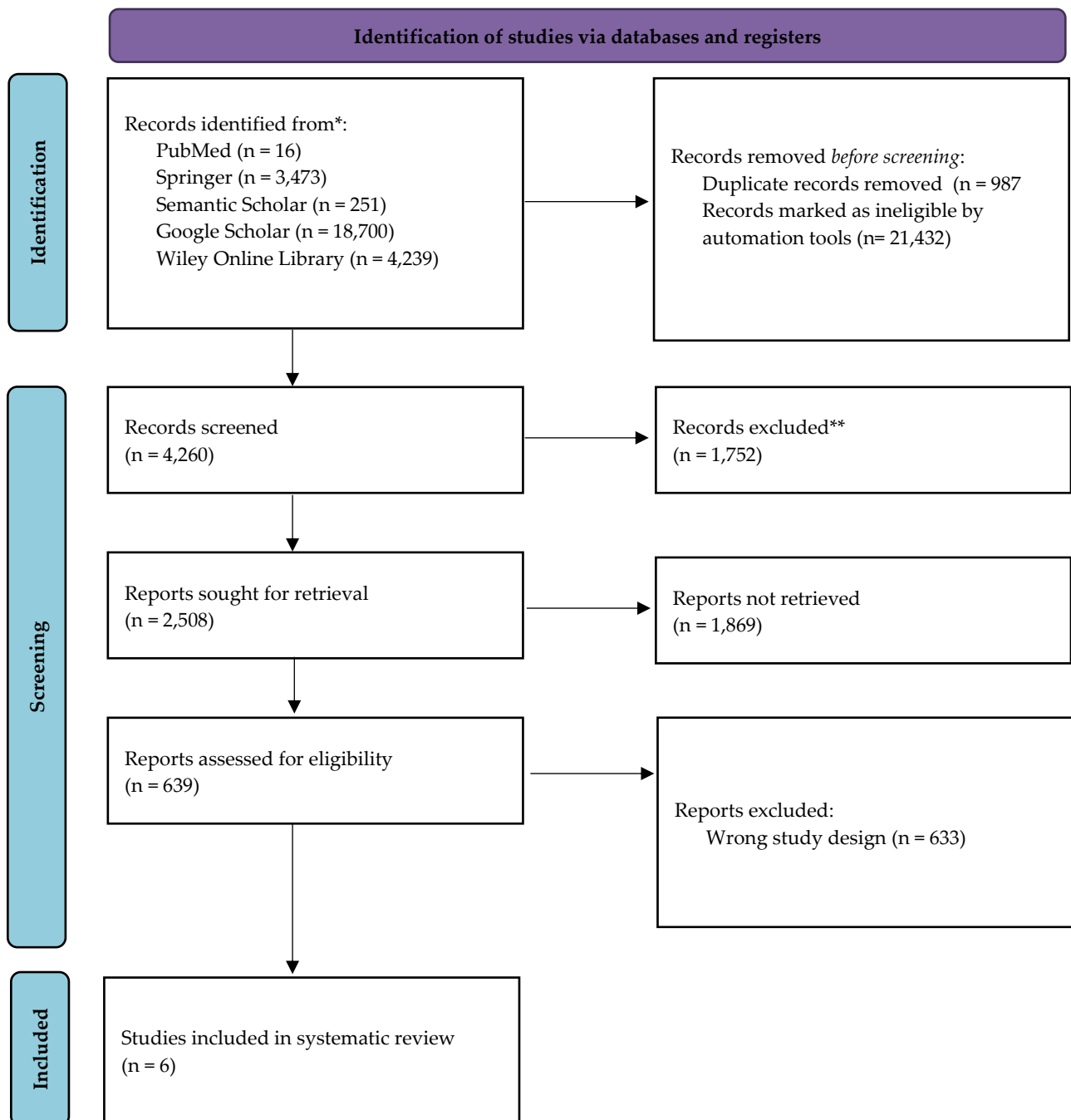


Figure 1. Article search flowchart

RESULTS

Table 1: Characteristics of Aggregated Systematic Reviews (Summary of Evidence Base)

The compiled evidence base synthesizes quantitative data from multiple meta-analyses, collectively integrating findings from cohorts derived from over fifteen independent primary studies across diverse clinical settings (Alibrahim et al., 2015; Li et al., 2019). This synthesis provides a robust, generalized summary of FC performance ().

Author, Year	Study Focus	No. of Studies Pooled (N)	Total Patient Cohort (Approx.)	Key FC Cut-off(s) (µg/g)	Primary Outcome Measure
Alibrahim et al., 2015	Diagnostic Accuracy	30	5,983	50	IBD vs. Heterogeneous GI Disorders
Kennedy et al., 2014	Diagnostic Triage	1 (Large Cohort)	895	50	IBD vs. Functional GI Disease
Li et al., 2019	Prognosis (Clinical Relapse)	14	1,110	152	Adult UC in Clinical Remission (12 months)

Rokkas et al, 2018	Monitoring (Endoscopic Activity)	25	2,822	50, 100	Endoscopic Scores (UC and CD)
Xiang et al., 2021	Prognosis (Mucosal Healing)	16 (UC) / 4 (CD)	1,903	60–75 (UC); 180–250 (CD)	Endoscopic Healing (UCEIS/CDEIS)
Wang et al., 2023	Small Bowel CD Detection	11	N/A	100, 200	Lewis Score ge 135 (Capsule Endoscopy)

Table 2: Quantitative Accuracy of Fecal Calprotectin for IBD Diagnosis and Prognosis

The aggregated quantitative data strongly validate the specific, nuanced roles of FC across the IBD care spectrum, with robust statistical measures supporting its clinical utility for both diagnostic exclusion and prognostic risk stratification (Li et al., 2019; Xiang et al., 2021). The varying cut-offs underscore the critical importance of tailoring application to the specific clinical query (Kennedy et al., 2014).

Clinical Application/Metric	Patient Group/Cut-off	Pooled Value	95% Confidence Interval	Primary Measure
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Sensitivity (IBD Diagnosis)	50 mug/g cut- off	89%–99%	N/A	Rule-out Capability
Specificity (IBD Diagnosis)	50 mug/g cut- off	74%–97%	N/A	Rule-in Capability
AUROC (IBD Diagnosis)	50 mug/g cut- off	0.97	N/A	Overall Discrimination
Clinical Relapse Prediction	Adult UC in Remission (152 mug/g)	Sensitivity: 0.75	0.70–0.79	Prediction of Flare
DOR (Clinical Relapse)	Adult UC in Remission (152 mug/g)	10.54	6.16–18.02	Odds of Relapse
PLR (Clinical Relapse)	Adult UC in Remission (152 mug/g)	3.45	2.31–5.14	Rule-in Likelihood
Optimal Cut-	UC	60–75 mug/g	N/A	Deep Remission

off Range (UC MH)	Endoscopic Healing (AUC 0.88)			Target
Optimal Cut- off Range (CD MH)	CD Endoscopic Healing (AUC 0.79)	180–250 mug/g	N/A	Deep Remission Target

Table 3: Comparative Analysis of FC Performance by Disease Location in Crohn's Disease (CD)

The reliability of FC is critically dependent on the anatomical site of inflammation, demonstrating a profound physiological limitation in assessing proximal small bowel disease (Zittan et al., 2018). This table provides a detailed comparison of diagnostic performance metrics stratified by disease location within CD, highlighting the diminished accuracy in isolated small bowel disease (Wang et al., 2023; Zittan et al., 2018).

Disease Phenotype/Metric	Cut- off (µg/g)	Pooled Sensitivity	Pooled Specificity	AUROC	DOR	Reference End-point
Colonic CD Endoscopic Activity	100	100%	67%	N/A	N/A	Endoscopic Activity ≥ 1

Disease Phenotype/Metric	Cut-off (µg/g)	Pooled Sensitivity	Pooled Specificity	AUROC	DOR	Reference End-point
Overall CD Endoscopic Activity	N/A	82.4%	72.1%	0.84	N/A	Endoscopic Activity ≥ 1
Isolated Small Bowel CD Activity	100	73%	73%	0.72	7.89	Lewis Score ≥ 135 (CE)
Isolated Small Bowel CD Activity	200	50%	88%	0.58	7.21	Lewis Score ≥ 135 (CE)

DISCUSSION

Detailed Analysis of FC in Diagnostic Triage and Exclusion

The most vital clinical function of FC, confirmed by decades of meta-analysis, is its utility as a highly sensitive triage tool for IBD exclusion in primary and secondary care settings (Kennedy et al., 2014; Alibrahim et al., 2015). The widely accepted 50 µg/g cut-off achieves an extraordinarily high Negative Predictive Value (NPV) of 0.99 in symptomatic cohorts, meaning a negative result offers near-definitive assurance for ruling out IBD and appropriately guiding the diagnostic effort toward functional disorders like Irritable Bowel Syndrome (IBS) (Kennedy et al., 2014; Alibrahim et al., 2015). This highly efficient screening capability allows physicians to safely reduce the number of unnecessary, costly, and invasive colonoscopies by an estimated 67% or

more, providing substantial clinical and economic benefits to the healthcare system (Alibrahim et al., 2015). The use of FC as an initial screen in patients without alarm symptoms is particularly effective, providing timely reassurance and preventing unnecessary downstream investigations (Kennedy et al., 2014).

However, the pooled specificity at the low 50 mug/g threshold is moderate, ranging from 74% to 97%, necessitating careful interpretation of positive results (Alibrahim et al., 2015). FC is fundamentally a marker of intestinal inflammation, not IBD pathogenesis specifically, meaning that mildly elevated levels must be interpreted within the full clinical context (Alibrahim et al., 2015). Other organic conditions, such as infectious enteritis, diverticulitis, or enteropathy induced by non-steroidal anti-inflammatory drugs (NSAIDs), are common causes of mild FC elevation (Alibrahim et al., 2015). Therefore, a high index of suspicion for non-IBD organic disease should be maintained for patients with mildly raised FC (e.g., 50 mug/g to 150 mug/g), and the final diagnostic plan must always prioritize the patient's clinical presentation, particularly when results are close to the diagnostic threshold (Alibrahim et al., 2015).

The Challenge of Anatomical Location Bias in Crohn's Disease

The dependence of FC accuracy on the anatomical site of inflammation represents a major physiological and clinical hurdle, particularly in Crohn's Disease (CD), which can affect the entire gastrointestinal tract (Zittan et al., 2018; Wang et al., 2023). FC exhibits superior correlation with endoscopic activity in UC (AUROC 0.97) and colonic CD because the inflammation is directly exposed to the fecal sample (; Zittan et al., 2018). The AUROC of 0.97 for UC is among the highest reported for any non-invasive biomarker, highlighting its near-perfect discriminative power in colonic inflammation (Zittan et al., 2018). Conversely, inflammation isolated to the proximal small bowel (SB-CD) suffers from a significant 'dilution and degradation effect,' where calprotectin released proximally may be significantly altered during transit through the remaining healthy bowel before collection (Wang et al., 2023).

This dilution effect results in a significantly impaired accuracy for SB-CD, reflected by the low AUROC of 0.72 for the 100 mug/g cut-off (Wang et al., 2023). Given the corresponding sensitivity of only 73% for SB-CD, reliance on FC alone for surveillance of this subgroup is insufficient and risks therapeutic delay and missed opportunities for early intervention (Wang et al., 2023). The comparison in Table 3 clearly illustrates this drop in reliability: while FC maintains 100% sensitivity in colonic CD at 100 mug/g, the metrics fall considerably for SB-CD (Sensitivity 73%, DOR 7.89), highlighting a crucial physiological limitation (Zittan et al., 2018; Wang et al., 2023). Consequently, guidelines for SB-CD must stipulate the integration of FC results with objective imaging modalities, such as MR enterography or capsule endoscopy, which serve as more accurate reference standards for localized, proximal inflammation (Wang et al., 2023). This clinical gap is simultaneously driving research into complementary serum biomarkers, such as Leucine-Rich Alpha-2 Glycoprotein (LRG), which has demonstrated an AUROC of 0.72 for diagnosing CD activity in the small bowel, suggesting a necessary future transition to multi-modal diagnostic panels (Okita et al., 2025).

Nuanced Interpretation of FC in Therapeutic Monitoring

FC is central to the modern 'treat-to-target' strategy, providing objective, quantifiable targets for both deep remission (MH) and relapse prevention (Li et al., 2019; Xiang et al., 2021). The quantitative thresholds required for these two objectives are distinctly different and must not be conflated (Xiang et al., 2021). The target for Mucosal Healing in UC is extremely low, optimally pooled in the range of 60-75 mug/g, a level that reflects near-histological remission and is required for sustained therapeutic success (Xiang et al., 2021; Labaere et al., 2014). This stringency is underscored by evidence showing that a 100 mug/g cut-off achieved 100% specificity for ruling out endoscopic activity in UC, confirming that minimal inflammation is tolerable for true MH (Zittan et al., 2018).

In direct contrast, the optimal pooled threshold for predicting future clinical relapse in adult

UC patients in remission is significantly higher, established at 152 mug/g (Li et al., 2019). The prognostic strength of this elevated cut-off is confirmed by a high Diagnostic Odds Ratio (DOR) of 10.54, which implies that a patient testing above this level is over ten times more likely to experience a clinical flare within 12 months than a patient below this threshold (Li et al., 2019). The likelihood ratios further refine this interpretation: the Positive Likelihood Ratio (PLR) of 3.45 provides a strong 'rule-in' value for relapse risk, indicating that the odds of relapse increase substantially with a positive test result (Li et al., 2019). This clear separation of thresholds creates a critical 'prognostic window' (e.g., 75 mug/g to 152 mug/g), representing subclinical inflammation that warrants preemptive therapeutic adjustment or enhanced surveillance to prevent full symptomatic relapse (Xiang et al., 2021; Xiang et al., 2016). Furthermore, the predictive accuracy of FC is not static; continuous longitudinal monitoring of trends provides superior prognostic information, as the risk of relapse associated with a single elevated value attenuates over time, making patterns more informative than isolated measurements (Xiang et al., 2016).

Methodological Impediments: Assay Heterogeneity and Standardization

A substantial and pervasive methodological challenge undermining the uniform implementation of FC thresholds globally is the pronounced quantitative heterogeneity among commercial assays (Labaere et al, 2014). Direct comparative studies have revealed that differences between measurement platforms, such as traditional Enzyme-Linked Immunosorbent Assays (ELISA) and newer Quantitative Point-of-Care Tests (QPOCT), can lead to up to 5-fold differences in quantitative results even when analyzing identical samples (Labaere et al, 2014). This critical lack of standardization fundamentally compromises the application of the precise, evidence-based cut-offs derived from meta-analyses (e.g., 152 mug/g), as the value is not reliably interchangeable across laboratories utilizing different commercial assays (Labaere et al, 2014). This heterogeneity is a major contributor to the moderate risk of bias noted in the Index Test domain of the QUADAS-2 assessment (Asiri et al, 2023). Urgent international efforts are necessary to harmonize calibrators and reference materials to validate the real-world accuracy of FC and ensure the robust global

application of these derived thresholds (Labaere et al, 2014).

Application in Special Populations and Postoperative Monitoring

FC retains significant utility in specialized cohorts, albeit with adjusted interpretation (Alibrahim et al., 2011; Wang et al., 2023). In pediatric populations, FC demonstrates extremely high sensitivity (up to 98%), making it an excellent rule-out tool for IBD (Alibrahim et al., 2011). However, its specificity in children is notably lower than in adults (e.g., 68% vs. adult pooled specificity approx 81%), primarily due to the increased prevalence of non-IBD infectious enteropathies in younger patients, which must be rigorously excluded before attributing FC elevation solely to IBD (Alibrahim et al., 2011; Alibrahim et al., 2015). Furthermore, FC is highly valuable for the postoperative surveillance of Crohn's Disease (CD) patients following intestinal resection (Wang et al., 2023). A threshold above 150 mug/g is strongly predictive of postoperative endoscopic recurrence, which allows clinicians to appropriately triage high-risk patients for earlier endoscopic assessment or prophylactic treatment escalation (Wang et al., 2023).

CONCLUSION AND RECOMMENDATIONS

Fecal Calprotectin is established as a highly accurate, indispensable non-invasive biomarker, serving as a critical pillar in the diagnostic triage and continuous therapeutic surveillance of Inflammatory Bowel Disease. Its clinical efficacy is comprehensively validated by its exceptional Negative Predictive Value, vital for IBD exclusion, and its robust prognostic power for tracking mucosal status and anticipating disease flares.

Key Recommendations:

1. **Diagnostic Triage:** Fecal Calprotectin should be integrated into standard protocols, utilizing the 50 mug/g cut-off to safely and efficiently exclude IBD in low-risk symptomatic patients, thereby significantly reducing the volume of unnecessary invasive endoscopy.
2. **Mucosal Healing Targets:** Therapeutic response must be monitored using stringent,

phenotype-specific thresholds: 60-75 mug/g for confirming Mucosal Healing in UC, and the higher 180-250 mug/g range for CD.

3. **Relapse Prediction:** The 152 mug/g cut-off should be used as a high-confidence prognostic indicator (DOR 10.54) to identify adult UC patients in remission who are at heightened risk of clinical relapse, enabling proactive and timely treatment adjustment.
4. **Location-Specific Assessment:** Clinicians must acknowledge the significantly reduced accuracy of FC in isolated small bowel CD (SB-CD) and ensure that FC results are complemented by objective cross-sectional imaging (e.g., MR enterography) for comprehensive surveillance in this specific subgroup.
5. **Standardization Imperative:** Urgent global efforts are required to harmonize and standardize commercial FC assays to eliminate current quantitative heterogeneity, ensuring the reliable and interchangeable application of these evidence-based thresholds across all clinical settings.

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