

## INTRODUCTION

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory conditions requiring continuous monitoring.

Conventionally, IBD therapy was based on the control of symptoms. However, there is a clear discordance between the presence and severity of symptoms and mucosal status on endoscopic assessment.

Today, endoscopic evaluation using ileocolonoscopy is the gold standard for assessing disease activity. Mucosal healing on endoscopy is associated with lower rates of relapses, hospitalizations, surgery and/or colorectal neoplasia.

However, in many patients, histological assessment may reveal persistent microscopic inflammation despite endoscopic healing. Thus, there is an ongoing debate regarding the role of histological evaluation in clinical decision-making, especially in cases with mild or no endoscopic activity.

## AIMS

We conducted a literature review aiming to summarize the currently available evidence regarding the additional value of histological assessment in the management of UC and CD and its application in everyday clinical practice.

**Table 1.** Summary of cohort studies assessing the impact of histological remission on the risk of relapse in patients with UC in endoscopic remission, published since June 2020 (number of patients = N)

First author	Year	Study design	N*	Inclusion criteria	Histological cut-off	p-value
Shin	2024	prospective	117	MES 0,1	NHI $\geq 3$ NHI $> 2$	0.009 0.193
Seong	2023	retrospective	492	MES 0,1 MES 1	GS $\geq 3.1$	<0.001 0.223
George	2023	retrospective	445	MES 0,1	RHI $> 3$	0.008
Kim	2024	Retrospective	435	MES 0,1	GS $\geq 3.1$	0.03
Narula	2020	retrospective	269	MES 0	activity	0.85
Park	2022	retrospective	142	UCEIS 0,1	RHI $> 3$	0.035
Jangi	2021	retrospective	89	MES 0,1	activity	<0.05
Wang	2023	retrospective	74	MES 0,1	NHI $\geq 2$	0.002
Wei	2024	retrospective	42	MES 0	NHI $> 0$	0.006

**Figure 1.** Practical guide for monitoring IBD patients (Nancy Histopathology Index = NHI, Geboes Score = GS, Roberts Histopathology Index = RHI, Mayo Endoscopic Score = MES, Simple Endoscopic Score for CD = SES-CD, fecal calprotectin = FC, patient-reported outcome = PRO)

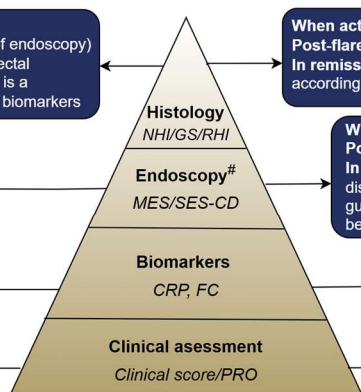
### Ulcerative colitis

**When active**  
**Post-flare:** 2-3 months (at the time of endoscopy)  
**In remission:** according to the colorectal surveillance guideline, or when there is a discrepancy between symptoms and biomarkers

**When active**  
**Post-flare:** within 2-3 months  
**In remission:** according to the colorectal surveillance guideline

**When active**  
**Post-flare:** within 2-3 months  
**In remission:** every 6-12 months

Every visit



### Crohn's disease

**When active**  
**Post-flare:** 3-12 months (at the time of endoscopy)  
**In remission:** not clear, in extensive colonic disease according to the colorectal surveillance guideline

**When active**  
**Post-flare:** within 3-12 months  
**In remission:** not clear, in extensive colonic disease, follow the colorectal surveillance guideline, or when there is a discrepancy between symptoms and biomarkers

**When active**  
**Post-flare:** within 3 months  
**In remission:** every 6-12 months\*

\* mild vs severe disease

# UC: sigmoidoscopy in active disease may be enough but colonoscopy for CRC risk assessment  
CD: typically ileocolonoscopy, other imaging may be needed in small bowel involvement

## CLINICAL OUTCOMES

- A meta-analysis including UC patients in clinical remission found histological healing to be superior to endoscopic and clinical remission in predicting clinical outcomes, with a 52% relative risk reduction in clinical relapse compared to those with histological activity. [Park et al., 2016]
- A meta-analysis examining the association between histological activity and relapse in patients with UC in endoscopic remission from inception to June 2020, reported an increased risk of relapse in the case of histological activity (OR, 2.41; 95% CI, 1.91-3.04) with similar results in patients with a MES of 1 or 0. [Gupta et al., 2020]
- A meta-analysis that included UC patients achieving the composite endpoint of clinical and endoscopic remission found histological remission to result in a 61% risk reduction in clinical relapse in patients with a MES of 0 or 1, and a 63% risk reduction in MES 0. This translates to a 5% estimated annual clinical relapse risk in case of histological remission compared to 13.7% in patients with persistent histological activity. [Yoon et al., 2020]
- Currently data are only available from observational cohort studies. The first RCT providing evidence on the role of histological remission as a treatment target in UC is the ongoing VERDICT trial. It is expected to be a milestone in UC, comparing the outcomes of symptom-only, symptom + endoscopy, and symptom + endoscopy + histology-based objective treatment monitoring. Interim data on biomarker changes were reported at the 2025 ECCO congress, with final results expected in 2026. [Jairath et al., 2025]
- Few retrospective studies are available in CD with conflicting results. A post-hoc analysis of the prospective STORI cohort evaluated the impact of histological remission on predicting clinical relapse in CD. There was no significant difference in relapse rates based on the achievement of histological remission in the total cohort, nor in the subgroup of patients in endoscopic remission. [Reenaers et al 2024]

**Table 2.** Summary of cohort studies assessing the impact of histological remission on the risk of relapse of patients with CD. (number of patients = N, clinical remission = CR, endoscopic remission = ER)

First author	Year	Study design	N	Inclusion criteria	Histological cut-off	p-value
Reenaers	2024	prospective	76 45	CR ER	NHI $> 0$	0.26 0.18
Yoon	2021	retrospective	215	ER	NHI $\geq 2$	0.026
Hu	2021	retrospective	129	ER	activity	0.73
Christensen	2020	retrospective	105	CR	activity	0.008
Brennan	2017	retrospective	62	CR	activity	<0.05

## CONCLUSIONS

### Ulcerative colitis:

- Patients achieving histological healing have improved clinical and long-term outcomes.
- The cost-effectiveness of treating to achieve histological healing must be established.

### An important remaining question is:

- Is achieving histological remission an indicator of an easier to treat patient group or a result of more effective therapy?

### Crohn's disease:

- The concept of treating to achieve histological healing is much less established in CD.
- Further research is needed.