The International Academy of Pathology
Hong Kong Division

HKIAP Scientific Congress 2026

Histologic Disease Activity Scoring in IBD

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Diagnosing IBD

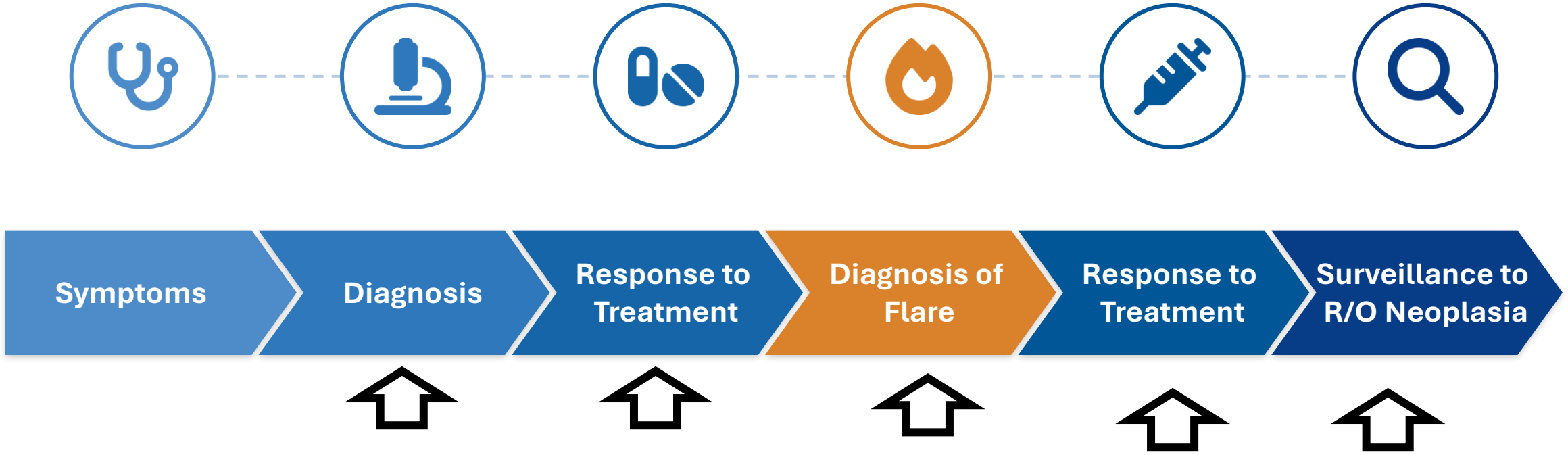
Inflammatory bowel disease is diagnosed using a constellation of clinical, endoscopic (sometimes radiologic) and histologic criteria.

- Diagnostic triad of chronic active colitis pattern:

1. Active (neutrophilic inflammation)
2. Crypt architectural distortion
3. Expanded lamina propria with basal plasmacytosis

- Structural changes of the crypt architecture and basal plasmacytosis have good predictive diagnostic value for IBD versus non-IBD.

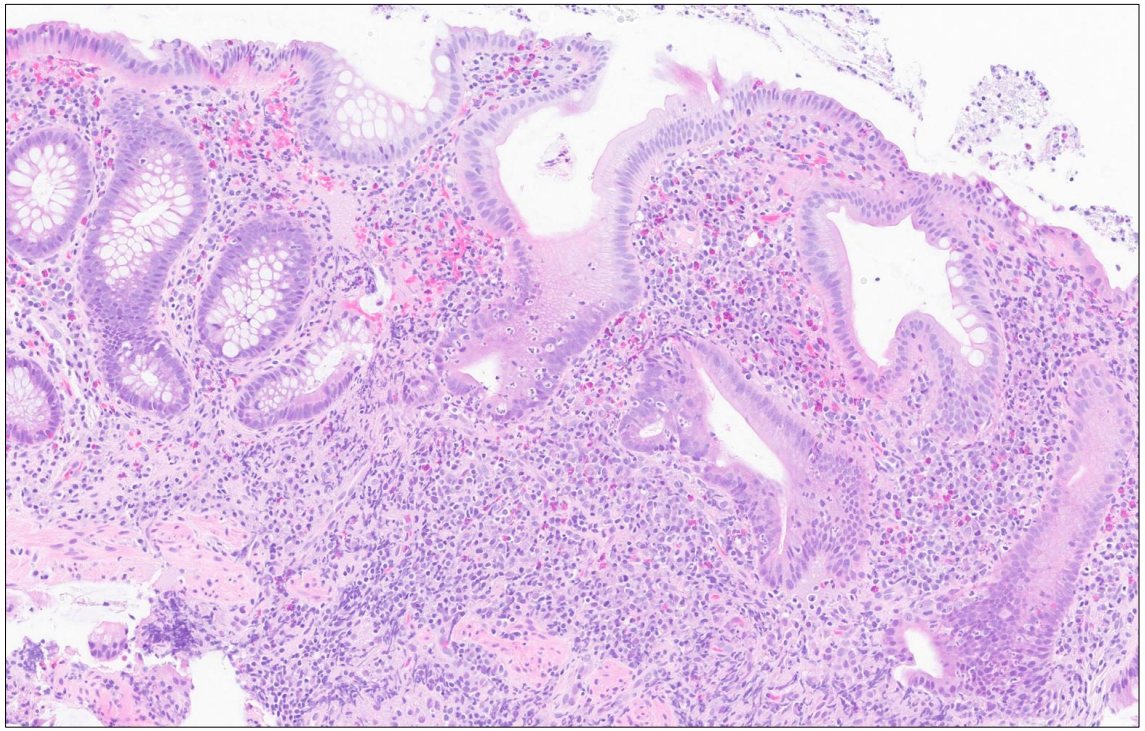
Multiple bx will be obtained over the course of the disease

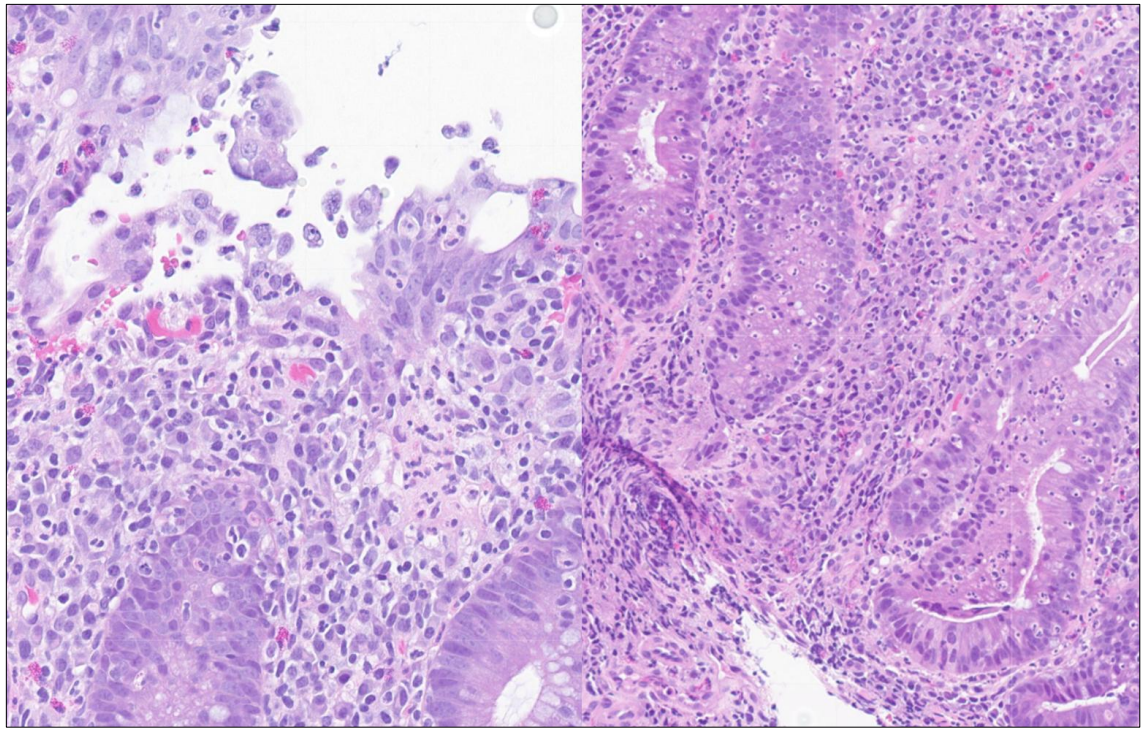


- Biopsies allow to:
  - Reach a diagnosis
  - Assess disease activity (in combination with clinical parameters)
  - Survey the risk of neoplastic progression

Chronic active colitis: histologic features

- Crypt distortion
- Increased lymphocytes and plasma cells (basal plasmacytosis)
- Lamina propria and intraepithelial neutrophils (cryptitis and/or crypt abscesses)
- Lamina propria and intraepithelial neutrophils (cryptitis and/or crypt abscesses)
- Surface injury: surface epithelial attenuation





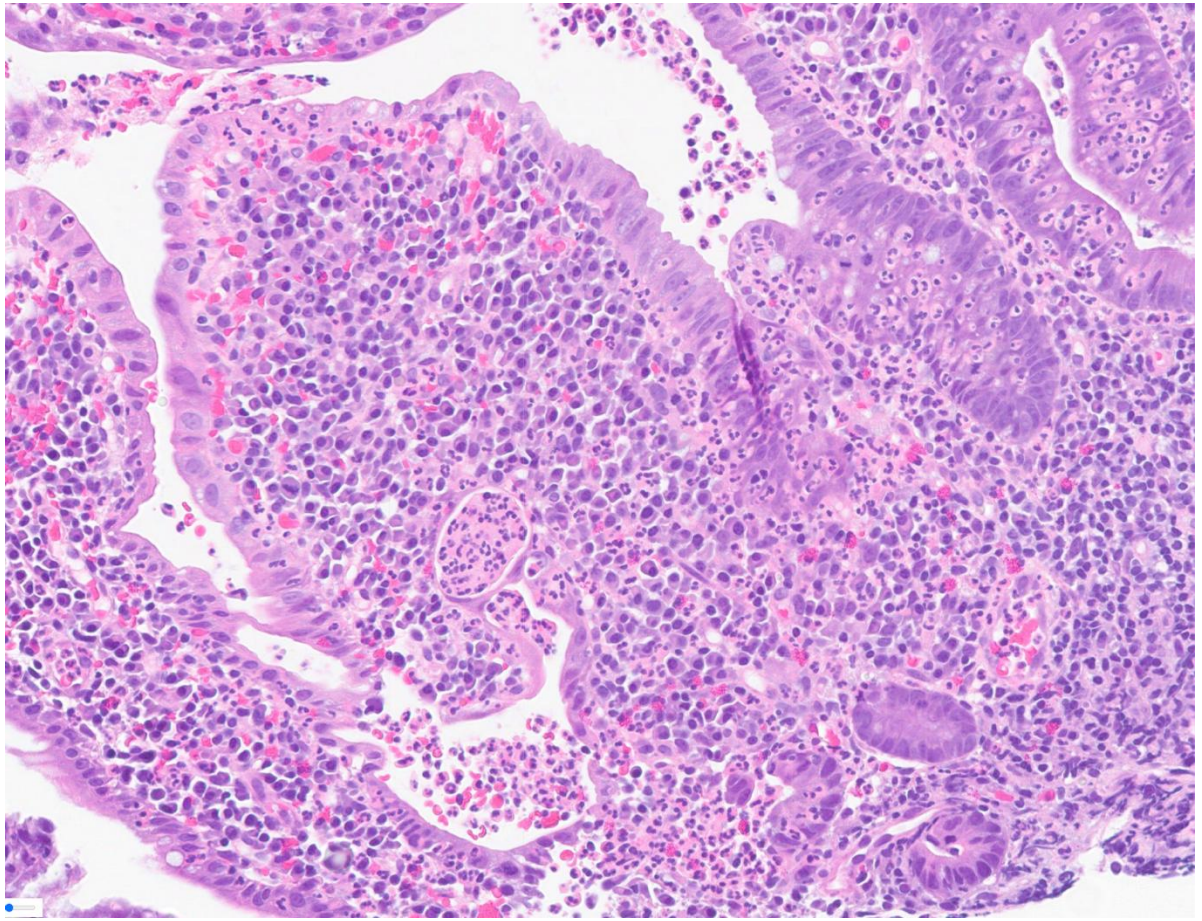
What Makes a Biopsy “Active”?

ACTIVE

Any mucosal neutrophils

Cryptitis, crypt abscesses, surface/lamina propria neutrophils, erosion or ulcer

Histologic remission = complete absence of neutrophils

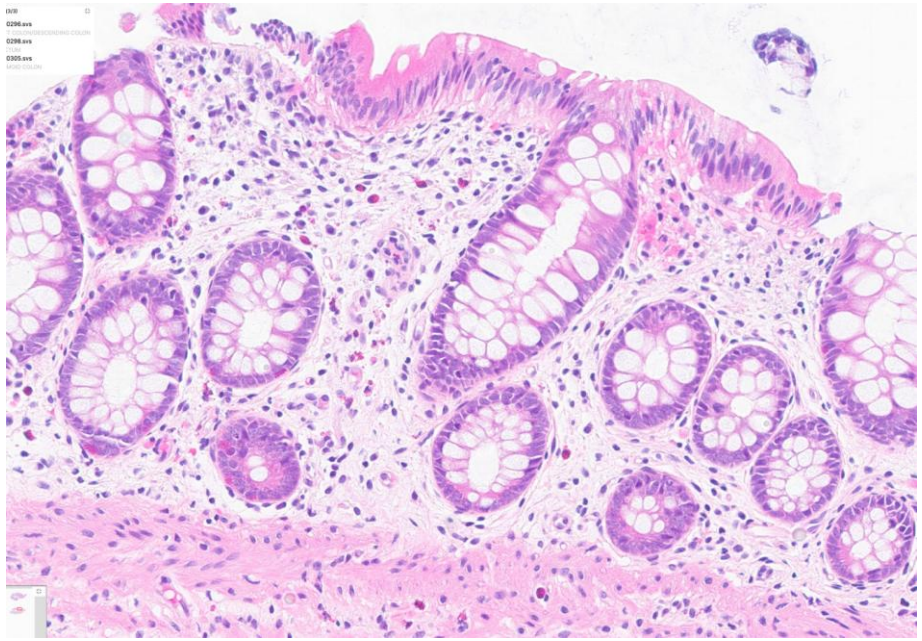


What Makes a Biopsy “Inactive”?

INACTIVE (chronic inactive colitis)

These findings alone do NOT make a biopsy active:

- **Crypt distortion (mild)**
- **Paneth cell metaplasia**
- **↑ Lamina propria mononuclear cells**
- **Basal (lympho)plasmacytosis**
  may predict outcome
- **Eosinophils only**
  even cryptitis / microabscesses
- **Search hard for neutrophils first**



How are the patients managed during follow-up?

1 Clinical

Well being; Reported symptoms

2 Endoscopic

Mayo Endoscopic Subscore

3 Histology

Mucosal neutrophils are an emerging therapeutic parameter

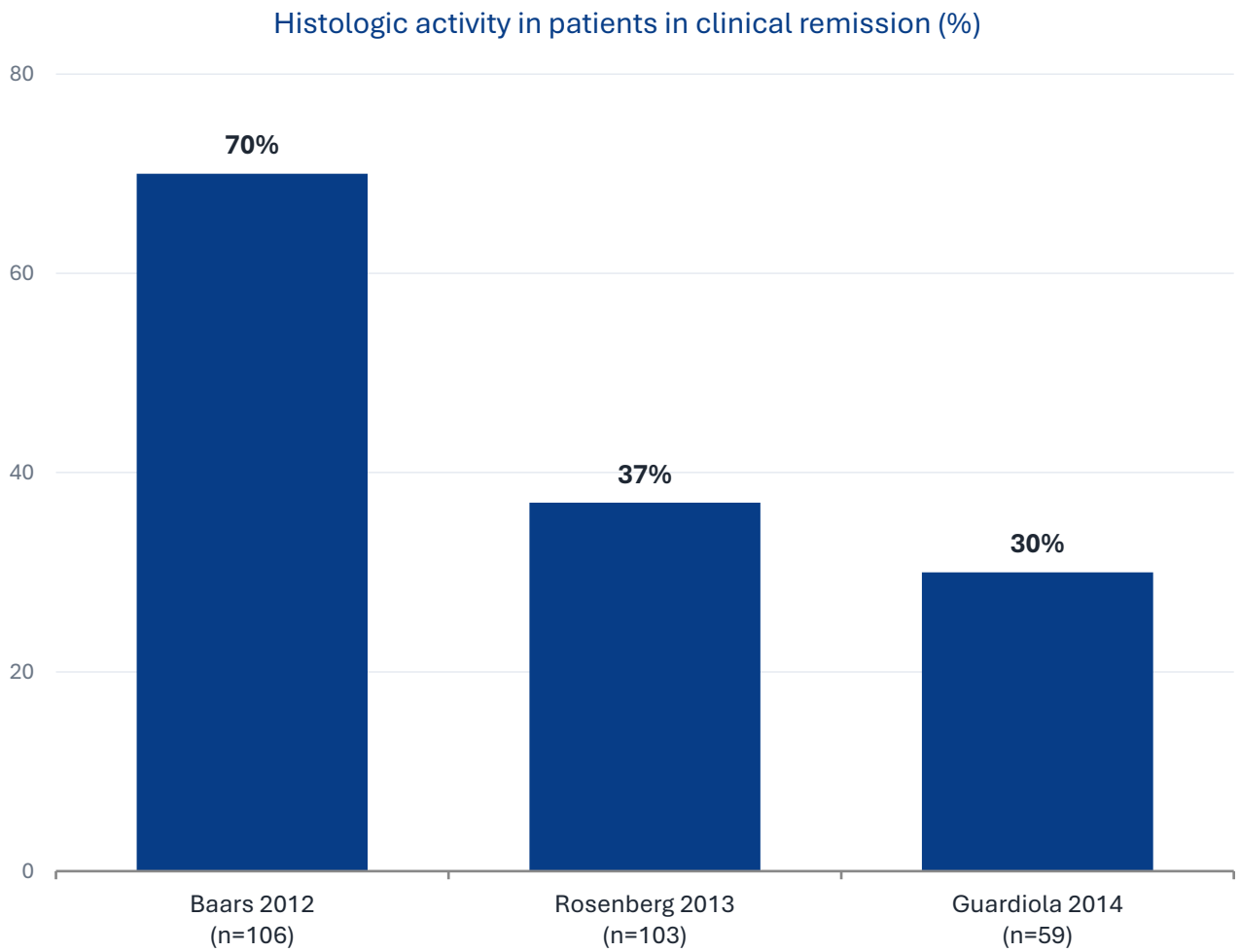
- Everyday management of IBD depends predominantly on general well being of patients/symptoms.
- However, histologic activity can be important in:
  - Choice of drug treatment.
  - Monitoring drug therapy,

The emerging role of histologic disease activity assessment in ulcerative colitis

Rish K. Pai, MD, PhD,[1] Vipul Jairath, MD, PhD,[2,3,4] Niels Vande Casteele, PharmD, PhD,[2,5] Florian Rieder, MD,[6] Claire E. Parker, MLIA, MA,[2] Gregory Y. Lauwers, MD[7]

Scottsdale, Arizona, USA; London, Ontario, Canada; San Diego, La Jolla, California; Cleveland, Ohio; Tampa Bay, Florida, USA

Clinical remission often hides microscopic activity



Even when the mucosa looks healed

14–40% with MES 0 have histologic activity

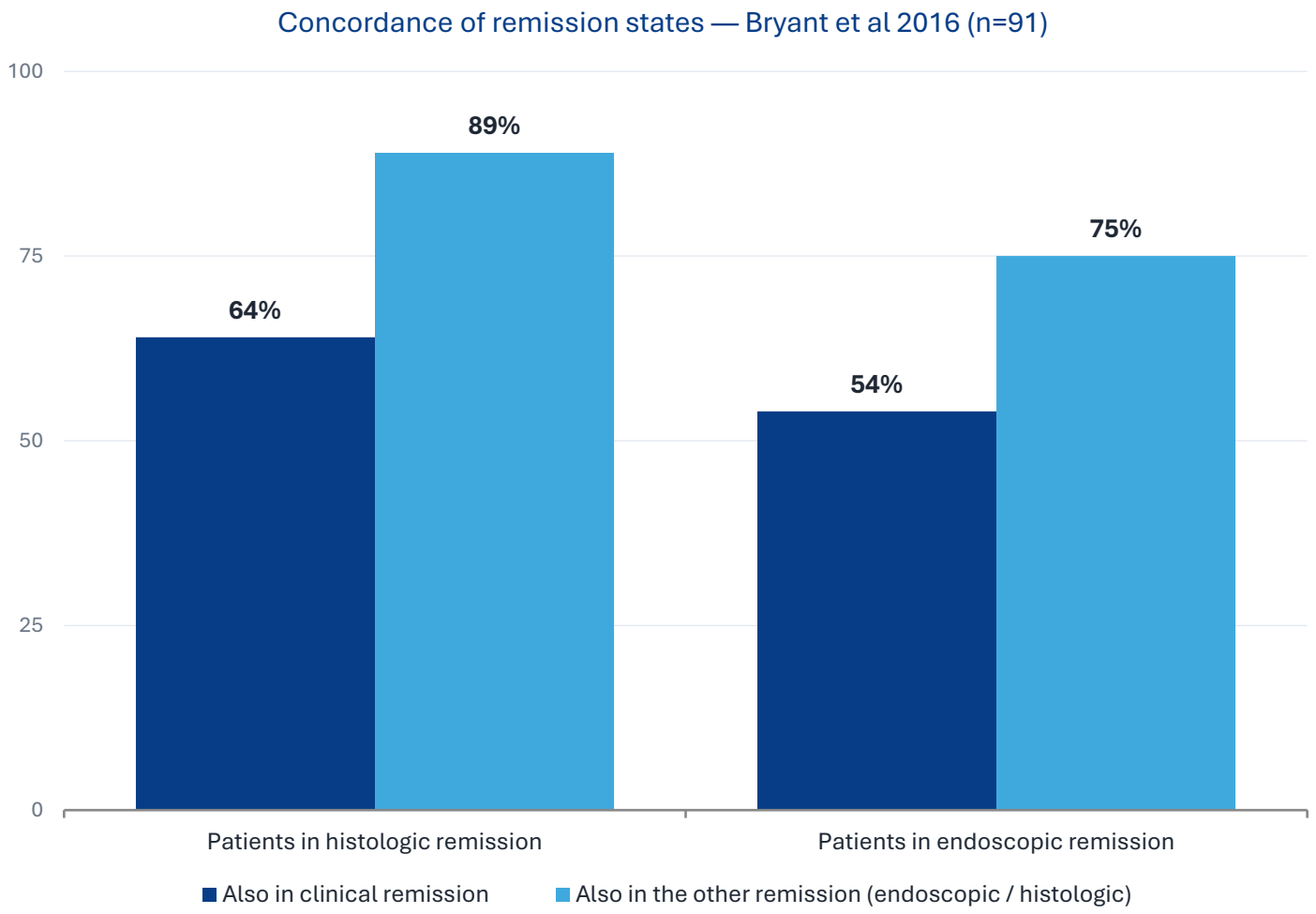
≤50% with MES 1 have active inflammation

14% with MES 1 show erosions/ulcers on biopsy

~10% with MES 2 have no histologic activity

Gastrointest Endosc 2018;88:887-98

Histology tracks clinical remission more closely than endoscopy



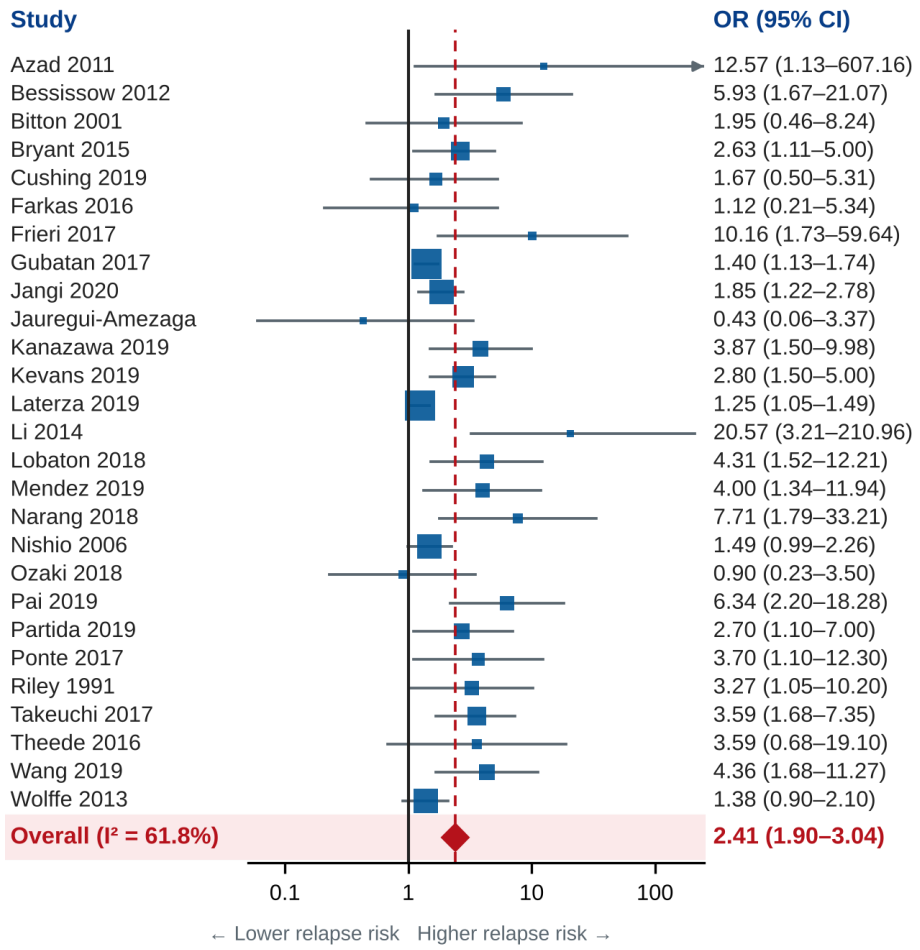
Reading the bars

- Histologic remission captured more clinically quiescent patients (64% vs 54%).
- Nearly all histologic remitters (89%) were also endoscopically healed — not the reverse (75%).
- **Histology is the more sensitive measure of disease activity.**

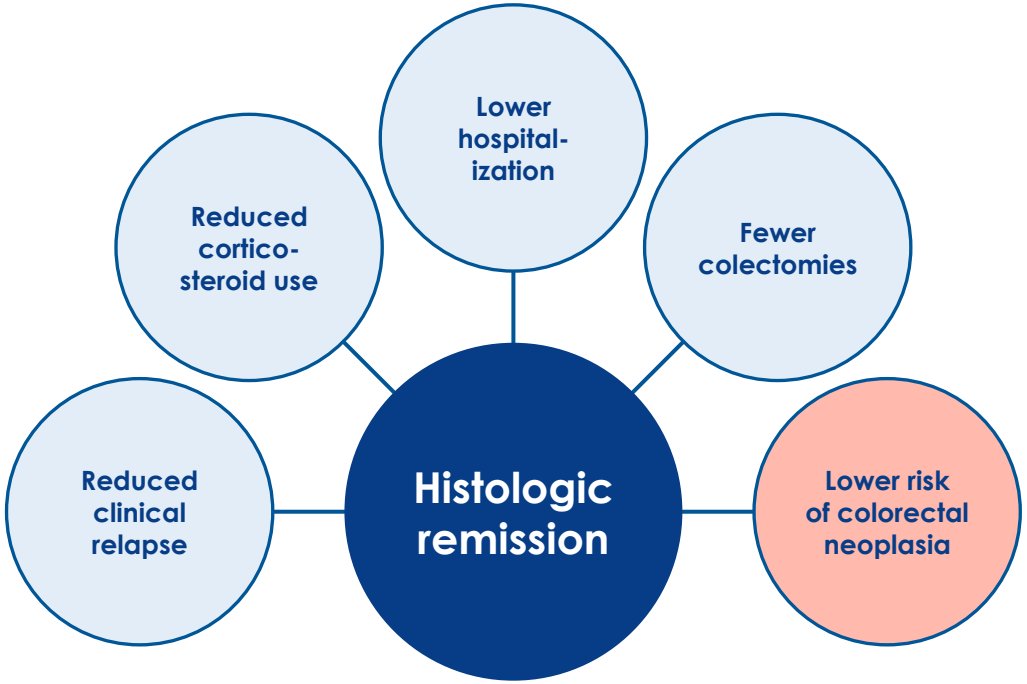
Gastrointest Endosc 2018;88:887-98

Persistent histologic activity despite endoscopic remission is associated with a ~2.4-fold higher odds of clinical relapse

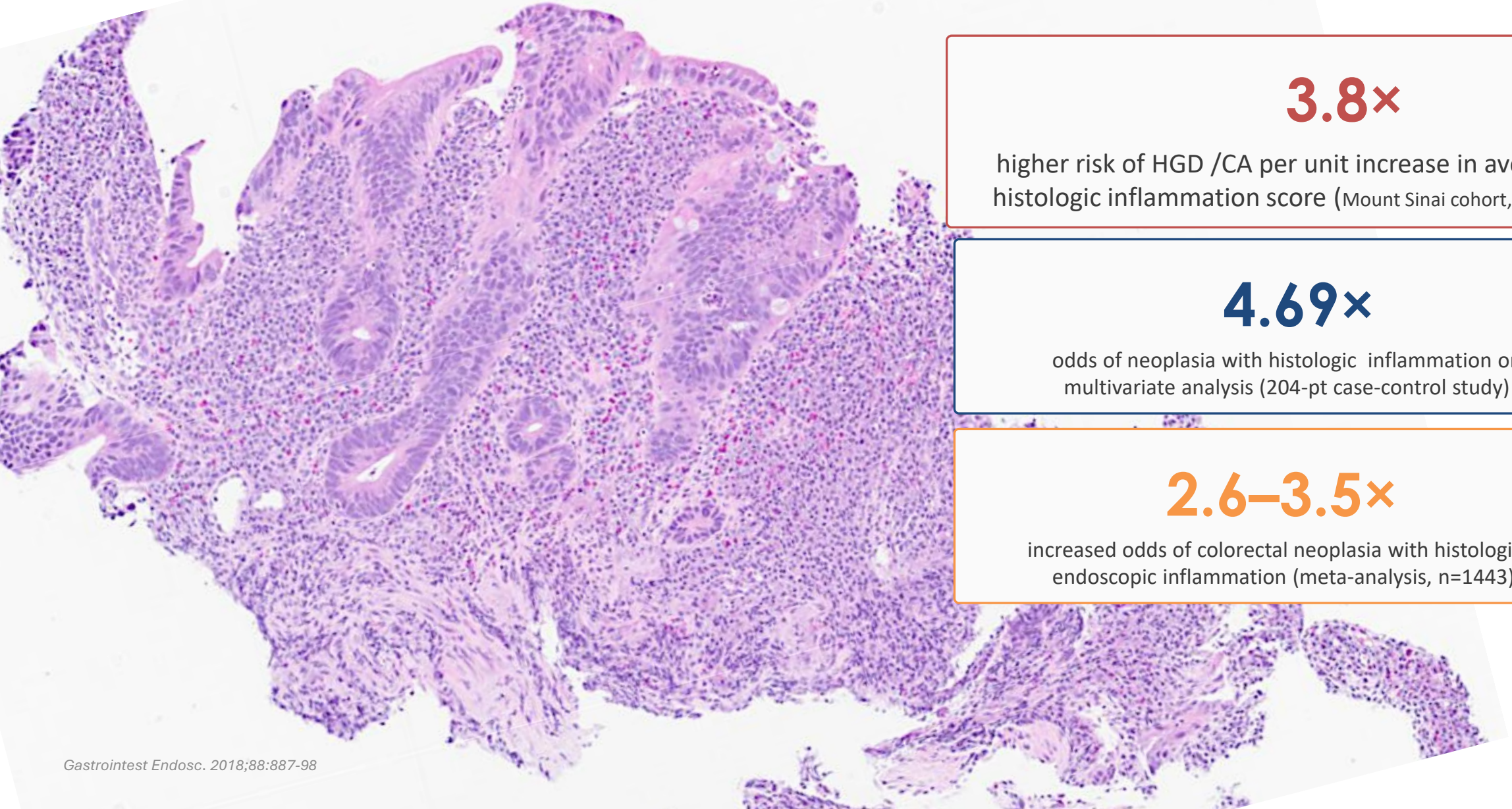
Pooled OR 2.41 (95% CI 1.90–3.04); 27 studies; I^2 = 61.8%



Outcomes associated with histologic remission



Risk of CA in IBD…(general)



3.8×

higher risk of HGD /CA per unit increase in average histologic inflammation score (Mount Sinai cohort, n=418)

4.69×

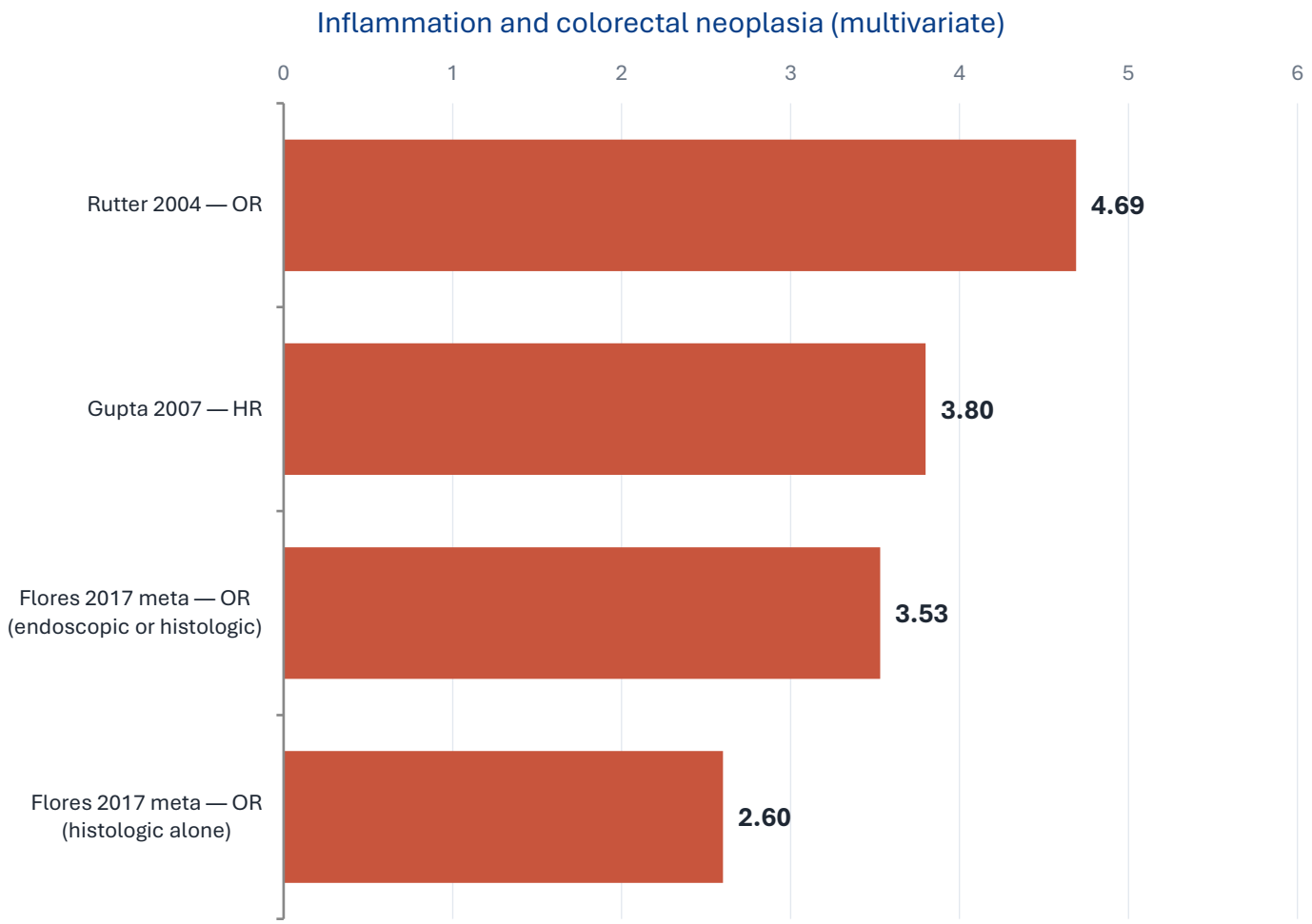
odds of neoplasia with histologic inflammation on multivariate analysis (204-pt case-control study)

2.6–3.5×

increased odds of colorectal neoplasia with histologic ± endoscopic inflammation (meta-analysis, n=1443)

Gastrointest Endosc. 2018;88:887-98

Persistent inflammation drives neoplastic risk



Rutter

204 IBD pts, case-control; only histology survived multivariate analysis

Mount Sinai (Gupta)

418 UC pts, median 6.7 y; 15 HGD/cancer

St Mark's (Choi)

987 pts, median 13 y; 97 neoplasia. Cumulative histologic burden HR 1.08 per unit

Flores meta-analysis

1,443 patients

Pai et al. Gastrointest Endosc 2018;88:887-98

Different scoring systems have been designed:

- Variably combining chronic & acute changes, epithelial as well as inflammatory features.

- Clinical trials (proven utility)
- Measures of activity (semiquantitative, standardized)
- Thresholds for treatment, surgery or surveillance decisions
- Uniform, clear reports that compare across institutions
- Do not replace standard diagnostic terminology but can be used in routine sign-out (not mandatory).

Gut 2000;47:404–409

A reproducible grading scale for histological assessment of inflammation in ulcerative colitis

K Geboes, R Riddell, A Öst, B Jensfelt, T Persson, R Löfberg

Grade	Feature	.0	.1	.2	.3	.4
0	Structural (architectural) change	None	Mild	Mild–moderate diffuse/multifocal	Severe diffuse/multifocal	—
1	Chronic inflammatory infiltrate	No increase	Mild, unequivocal ↑	Moderate ↑	Marked ↑	—
2A	Lamina propria eosinophils	No increase	Mild, unequivocal ↑	Moderate ↑	Marked ↑	—
2B	Lamina propria neutrophils	None	Mild, unequivocal ↑	Moderate ↑	Marked ↑	—
3	Neutrophils in epithelium	None	<5% crypts	<50% crypts	>50% crypts	—
4	Crypt destruction	None	Probable: local neutrophil excess	Probable: marked attenuation	Unequivocal	—
5	Erosion or ulceration	None	Recovering epithelium + inflammation	Probable erosion (focal stripping)	Unequivocal erosion	Ulcer / granulation tissue

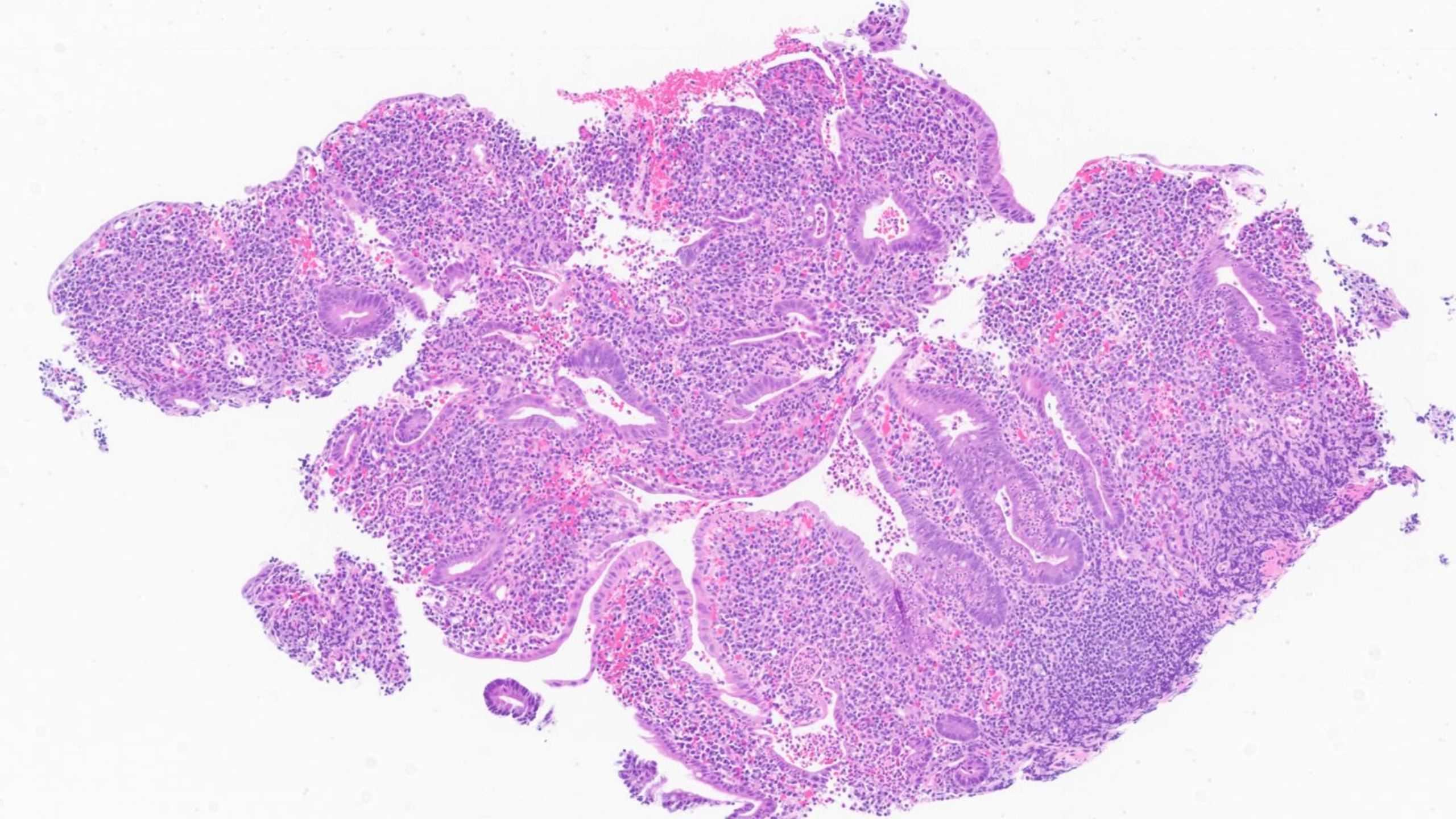
Score the worst area of the biopsy, not the average. Grades are hypothesized to be progressive (higher = more active disease). Grades 3–5 = "activity" (epithelial damage with neutrophils).

Where pathologists disagree

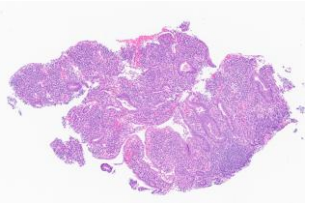
Grade	Complete agreement	1-grade difference	2-grade difference	Observer errors
0 Architecture	23%	51%	27%	10%
1 Chronic infiltrate	48%	49%	3%	2%
2A LP eosinophils	35%	46%	19%	8%
2B LP neutrophils	48%	36%	16%	6%
3 Epithelial neutrophils	66%	31%	3%	1%
4 Crypt destruction	66%	17%	17%	3% (4+5)

Problem area	Finding
Architecture (grade 0)	Key criteria unreadable in tangential cuts
Erosion (grade 5)	Complete agreement 44%; 22% of erosions missed by one reader
"Probable erosion" vs stripping	Caused the 2-grade gap in 5/12 such cases
Overall error rate	3.06–4.67% of observations

- **Using the 5 features based Geboes index:κ 0.59–0.70** inter-observer agreement



Geboes Score



Grade 0
Structural (architectural change)

- ○ **0.0** No abnormality
- ○ **0.1** Mild abnormality
- ○ **0.2** Mild or moderate diffuse or multifocal abnormalities
- ● **0.3** Severe diffuse or multifocal abnormalities

Grade 1
Chronic inflammatory infiltrate

- ○ **1.0** No increase
- ○ **1.1** Mild but unequivocal increase
- ○ **1.2** Moderate increase
- ● **1.3** Marked increase

Grade 2A
Lamina propria eosinophils

- ○ **2A.0** No increase
- ○ **2A.1** Mild but unequivocal increase
- ○ **2A.2** Moderate increase
- ● **2A.3** Marked increase

Grade 2B
Lamina propria neutrophils

- ○ **2B.0** None
- ○ **2B.1** Mild but unequivocal increase
- ○ **2B.2** Moderate increase
- ● **2B.3** Marked increase

Grade 3
Neutrophils in epithelium

- ○ **3.0** None
- ○ **3.1** <5% crypts involved
- ○ **3.2** 5–50% crypts involved
- ● **3.3** >50% crypts involved

Grade 4
Crypt destruction

- ○ **4.0** None
- ○ **4.1** Probable – local excess of neutrophils in part of crypt
- ○ **4.2** Probable – marked attenuation
- ● **4.3** Unequivocal crypt destruction

Grade 5
Erosion or ulceration

- ○ **5.0** No erosion, ulceration, or granulation tissue
- ○ **5.1** Recovering epithelium + adjacent inflammation
- ○ **5.2** Probable erosion – focally stripped
- ○ **5.3** Unequivocal erosion
- ● **5.4** Ulcer or granulation tissue

Scoring

Report the highest grade with a non-zero subgrade (e.g., 3.1); each grade is scored independently.

Grades 0–2B: architecture and lamina propria infiltrates.

Grades 3–5: neutrophil-driven activity — epithelial neutrophils ≥3.1 indicate active disease.

ORIGINAL ARTICLE

Development and validation of the Nancy histological index for UC

- **Goal:** a simple, reproducible, responsive index

Gut 2017;66:43–49.

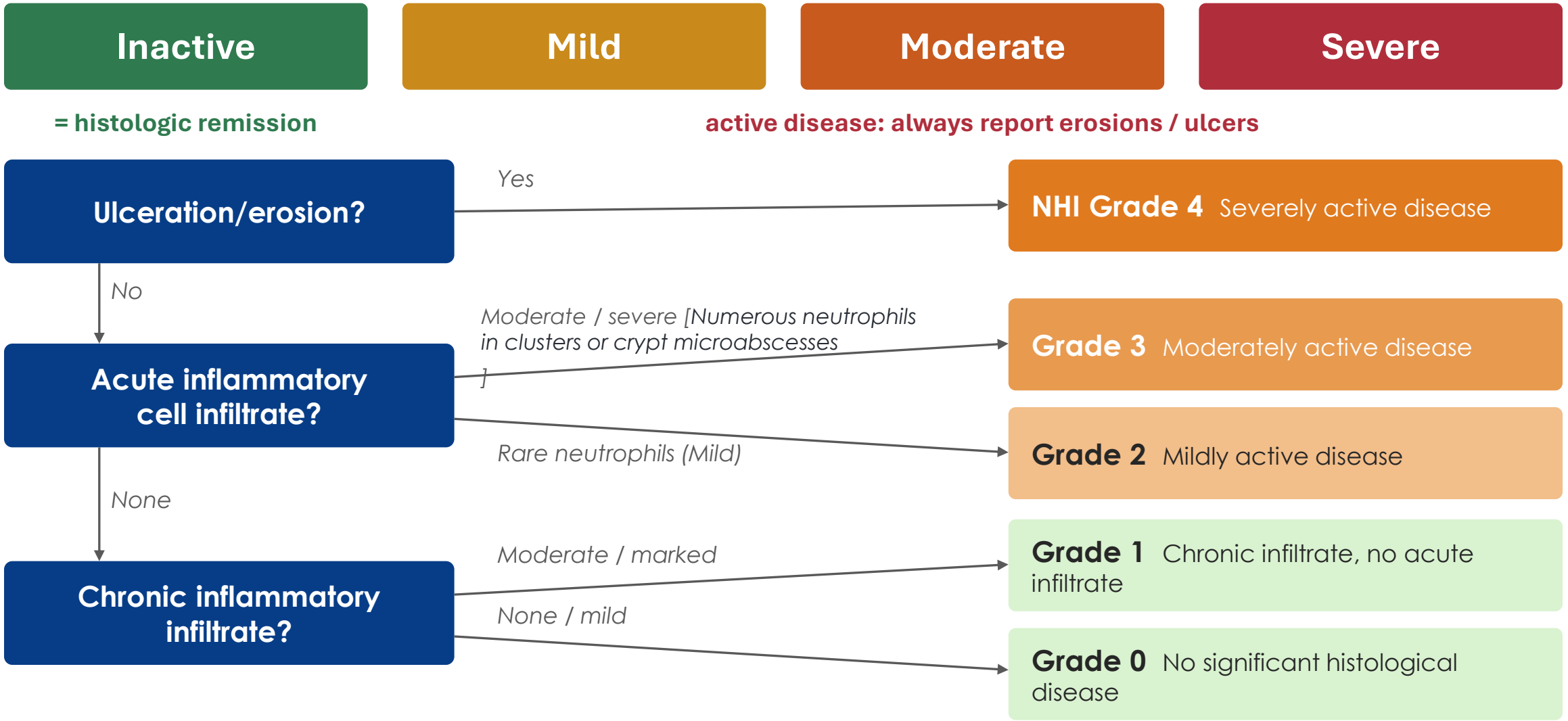
Eight candidate items tested; three retained in the Nancy index

Candidate item
Acute inflammatory cell infiltrate
Neutrophils in lamina propria
Chronic inflammatory infiltrate (lymphocytes + plasma cells)
Serrated architectural abnormalities
Mucin depletion
Ulceration (epithelial injury ± fibrin, neutrophils, granulation)
Neutrophils in epithelium
Basal plasmacytosis

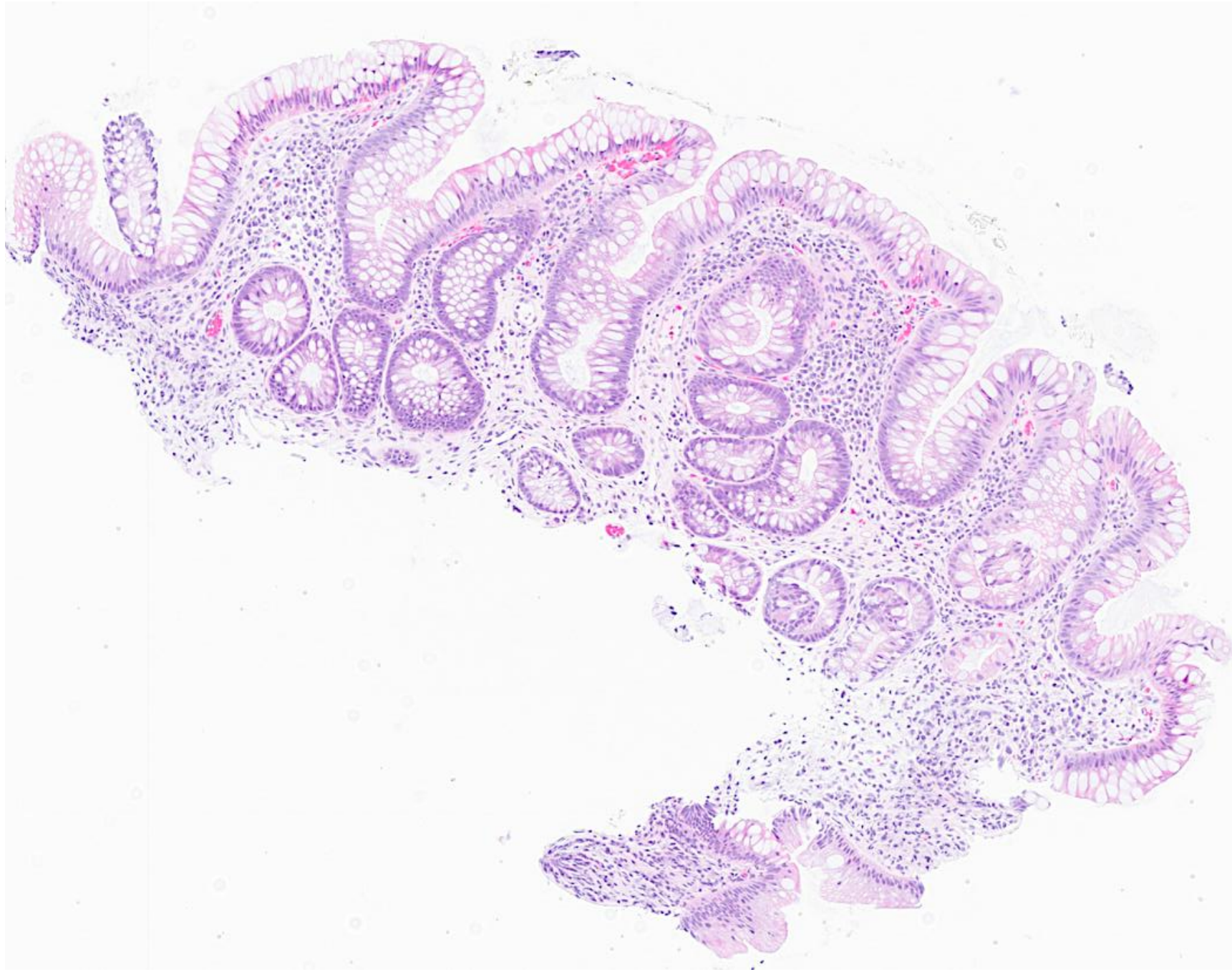
- **Retained in the final index (bootstrap selection ≥70%).** All 8 items predicted GVE, but the other 5 were redundant once these 3 were known.

GVE, global visual evaluation of histologic disease activity. Gut 2017;66:43–49.

The Nancy index: a three-steps algorithm



Gut 2017;66:43–49



NHI grade: assigned by the most severe feature

Ulceration

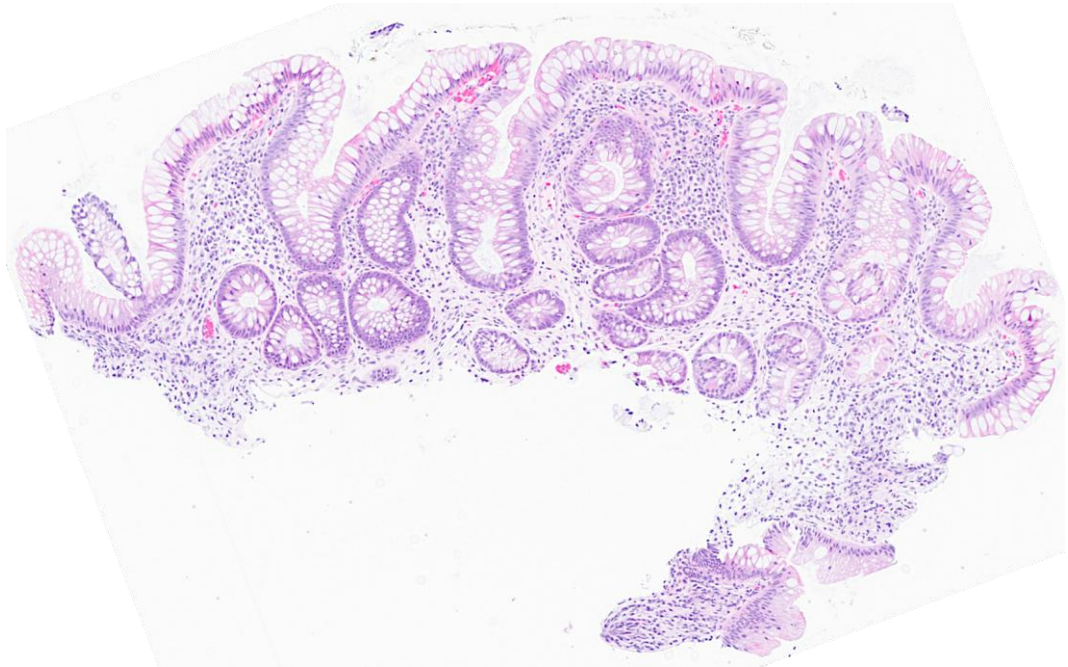
- ● **None**
- ○ Yes

Acute inflammatory cells infiltrate

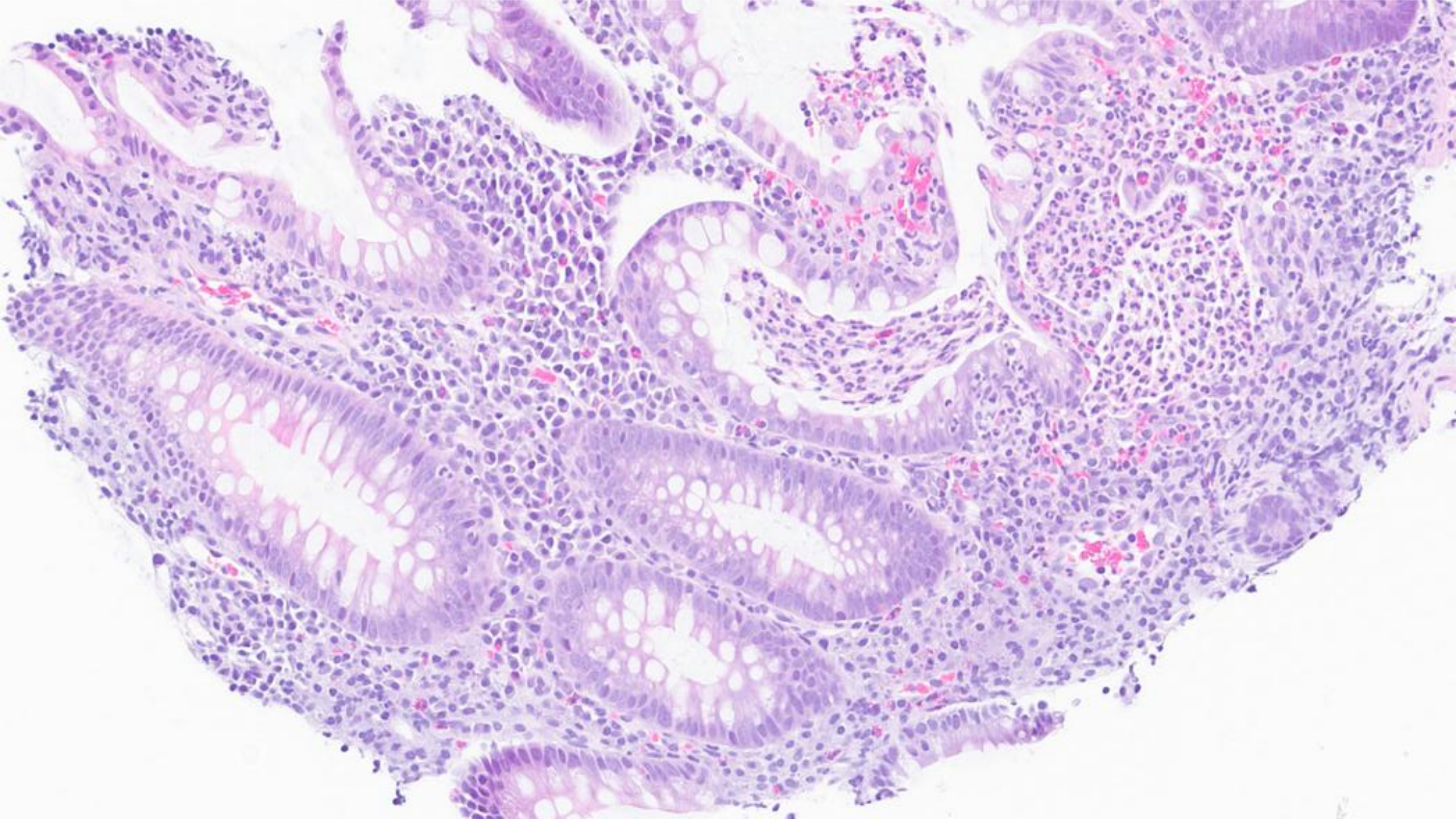
- ● **None**
- ○ Mild
- ○ Moderate or severe

Chronic inflammatory infiltrate

- ○ None
- ● **Mild increase**
- ○ Moderate or marked increase



Grade 0
No or mild ↑ chronic infiltrate



NHI grade: assigned by the most severe feature

Ulceration

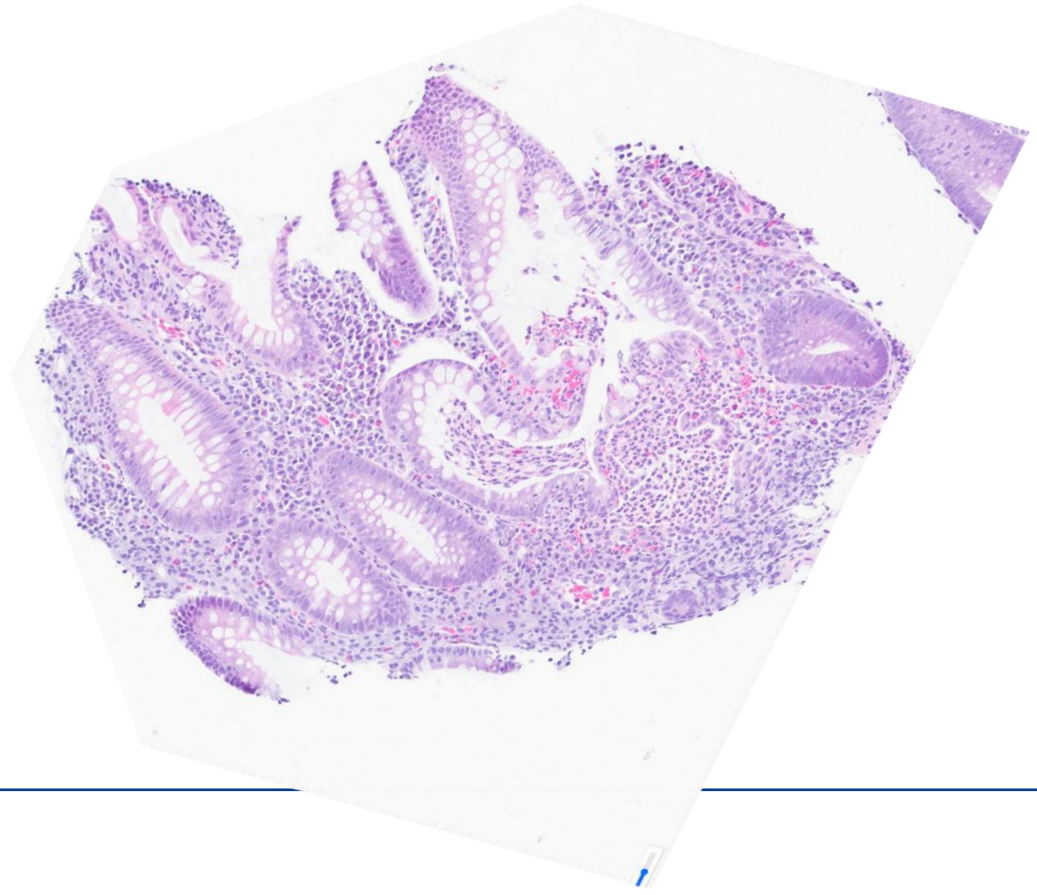
- (●) None
- ( ) Yes

Acute inflammatory cells infiltrate

- ( ) None
- ( ) Mild
- (●) Moderate or severe

Chronic inflammatory infiltrate

- ( ) None
- ( ) Mild increase
- (●) Moderate or marked increase



Grade 3
Moderate/severe acute infiltrate

NHI grade: assigned by the most severe feature

Ulceration

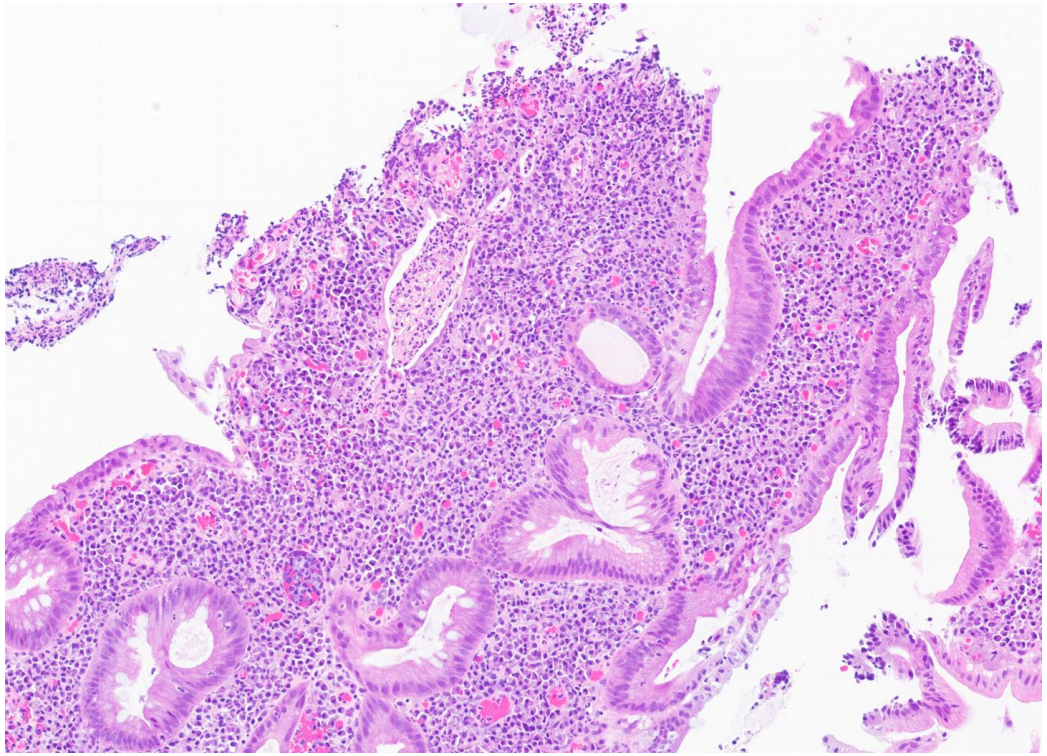
- ○ None
- ● Yes

Acute inflammatory cells infiltrate

- ○ None
- ○ Mild
- ● Moderate or severe

Chronic inflammatory infiltrate

- ○ None
- ○ Mild increase
- ● Moderate or marked increase



Grade 4
Ulceration

What are the histologic targets* and score equivalents

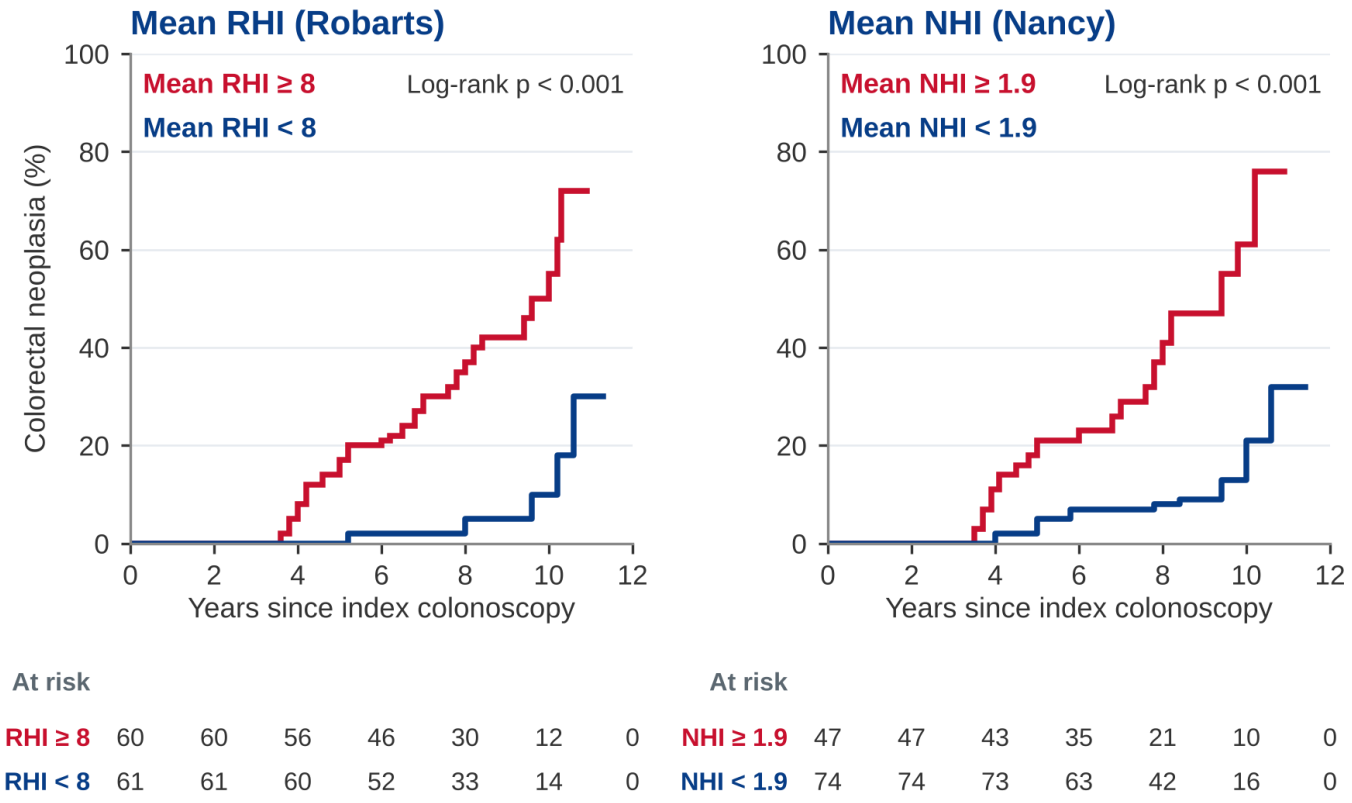
Category	Definition	Geboes	Nancy
Histologic healing	Complete normalization of mucosa	All subscores 0	Cannot determine
Remission (quiescent)	Architectural change ± basal plasmacytosis, no neutrophils	GS < 2B.0	≤1
Remission, no basal plasmacytosis	As above, no basal plasma cells	0.0–0.3, 1.0–1.1, 2A.0–2A.3, 2B.0, 3.0, 4.0, 5.0	Cannot determine
Remission, no BP or ↑ eosinophils	As above + normal LP eosinophils	As above with 2A.0	Cannot determine
Near remission	No basal plasmacytosis, only minimal neutrophils	2B.1 and/or 3.1 allowed	Cannot determine

Minimum target: no neutrophils in lamina propria or epithelium. Clearing basal plasmacytosis is adjunctive; normal eosinophils optional (IOIBD sets all three).
*Clinical trials

Pai et al. Gastrointest Endosc 2018;88:887-98

Histologic activity predicts colorectal neoplasia in UC

Mean histologic activity (RHI and Nancy index) during surveillance and time to colorectal neoplasia



Mean histologic activity over the preceding 5 yrs is a strong predictor of dysplasia development

Histopathologic predictors of colorectal neoplasia

Variable	Period	aHR (95% CI)	p
Mean RHI ≥ 8	**Preceding 5 y**	**7.53 (2.56–12.16)**	<0.001
	Entire surveillance	5.19 (2.21–12.15)	<0.001
Mean NHI ≥ 1.9	**Preceding 5 y**	**5.89 (2.18–15.92)**	<0.001
	Entire surveillance	3.91 (1.69–9.02)	0.001

RHI ≥ 8 translates to more than just rare neutrophils

RHI, Robarts Histopathology Index; NHI, Nancy Histological Index; aHR, adjusted hazard ratio.
Validated indices for histopathologic activity predict development of colorectal neoplasia in ulcerative colitis. J Crohns Colitis 2021;15:1481–1490

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Importance of Histologic Activity in IBD in a nutshell

Histologic activity predicts relapse, steroid use, hospitalization and neoplasia — often better than endoscopy

Microscopic activity persists in many patients in clinical and endoscopic remission

Residual histologic activity should argue against de-escalating therapy

RCTs are needed to show that treating to histologic remission improves outcomes

Gastrointest Endosc 2018;88:887-98

Practical rules for the sign-out

Reporting

1. Grade the worst fragment; as it sets the overall severity
2. Biopsy the ulcer edge, or the most abnormal-looking mucosa
3. Report architectural distortion, basal plasmacytosis and neutrophilic activity
4. Eosinophil quantification not required: poor reproducibility, uncertain meaning
5. Formal scores (GS, NI) optional in practice; helpful for assessing response

Interpretive thresholds

- Any intraepithelial neutrophil is abnormal
- ≥2 lamina propria neutrophils / fragment = abnormal
- Do not count intravascular neutrophils
- Rare branched crypts occur in normal colon; normal rectal crypts may not reach the muscularis mucosae
- Eosinophils are denser in the right colon, with geographic and seasonal variation

- **ECCO 2020:** Histological remission a treatment target in UC, recommending the RHI and NHI for RCTs, and NHI for observational studies and clinical practice.
- **VERDICT:** The first randomized UC trial to prospectively evaluate disease clearance as a specified treatment target. Disease clearance was defined as corticosteroid-free symptomatic, endoscopic and histologic remission (i.e.Geboes score <2B.0).

Pai et al. Gastrointest Endosc 2018;88:887-98

Recommendation for minimal reporting: 5 categories

	Without basal plasmacytosis	With basal plasmacytosis
	1 **Complete normalization** Histologic healing	
Quiescent chronic colitis	**2** **Quiescent, no basal plasmacytosis** Histologic remission	**3** **Quiescent with basal plasmacytosis** Remission; higher relapse risk
Chronic active colitis	**4** **Active, no basal plasmacytosis** Grade the activity	**5** **Active with basal plasmacytosis** Grade the activity — highest risk

Basal plasmacytosis = dense plasma cells separating crypt bases from the muscularis mucosae